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(54) Titre : COMPOSES ET PROCEDES POUR MODULER LA TYROSINE KINASE DE BRUTON
(54) Title: COMPOUNDS AND METHODS FOR MODULATING BRUTON'S TYROSINE KINASE

(57) **Abrégé/Abstract:**

Provided herein, inter alia, are compounds and methods for modulating Bruton's Tyrosine Kinase.

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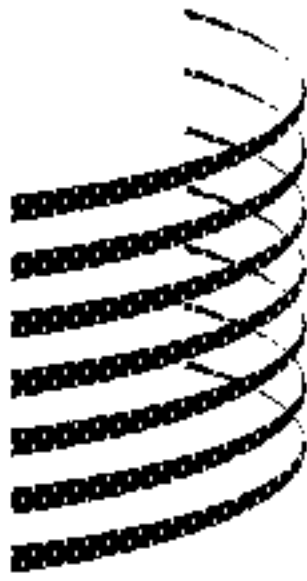
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- (54) Title: COMPOUNDS AND METHODS FOR MODULATING BRUTON'S TYROSINE KINASE

(57) Abstract: Provided herein, *inter alia*, are compounds and methods for modulating Bruton's Tyrosine Kinase.

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

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CONTENANT LES PAGES 1 À 307

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JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 307

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NOTE POUR LE TOME / VOLUME NOTE:

Compounds and Methods for Modulating Bruton's Tyrosine Kinase

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/307,399, filed March 11, 2016, and U.S. Provisional Application No. 62/342,004, filed May 26, 2016, which are incorporated herein by reference in their entirety and for all purposes.

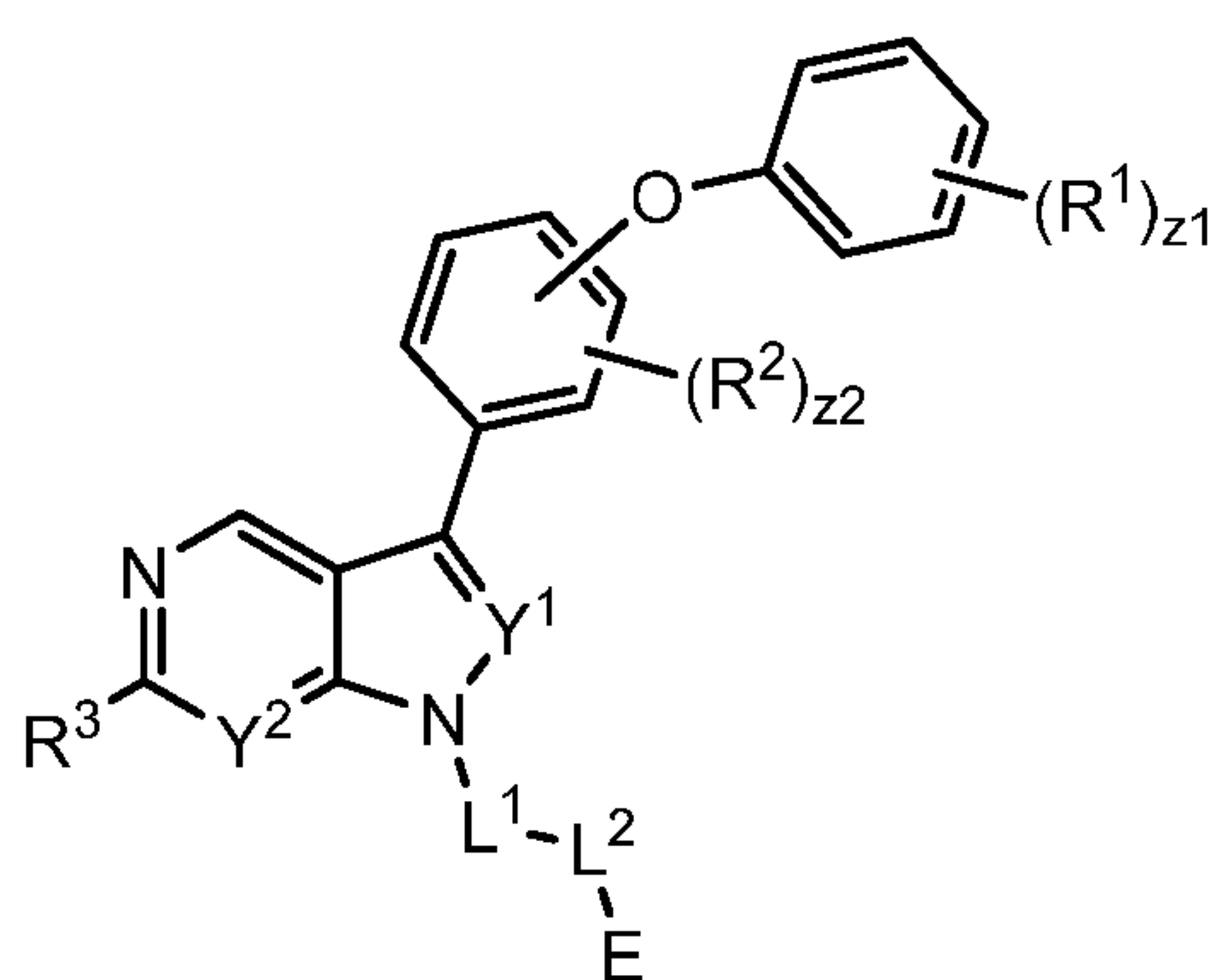
BACKGROUND

[0002] Bruton's Tyrosine Kinase (BTK) plays an important role in B cell development, differentiation, signalling, and maturation. BTK was originally identified as a disease gene for human X-linked agammaglobulinemia, but has further been implicated in inflammation (e.g., inflammatory skin conditions), autoimmune, allergic disease conditions, and cancers (e.g., B-cell cancers such as B-cell lymphoma and lymphoblastic B-cell leukemia). Thus, there is a need in the art for BTK modulators. Disclosed herein, *inter alia*, are solutions to these and other problems in the art.

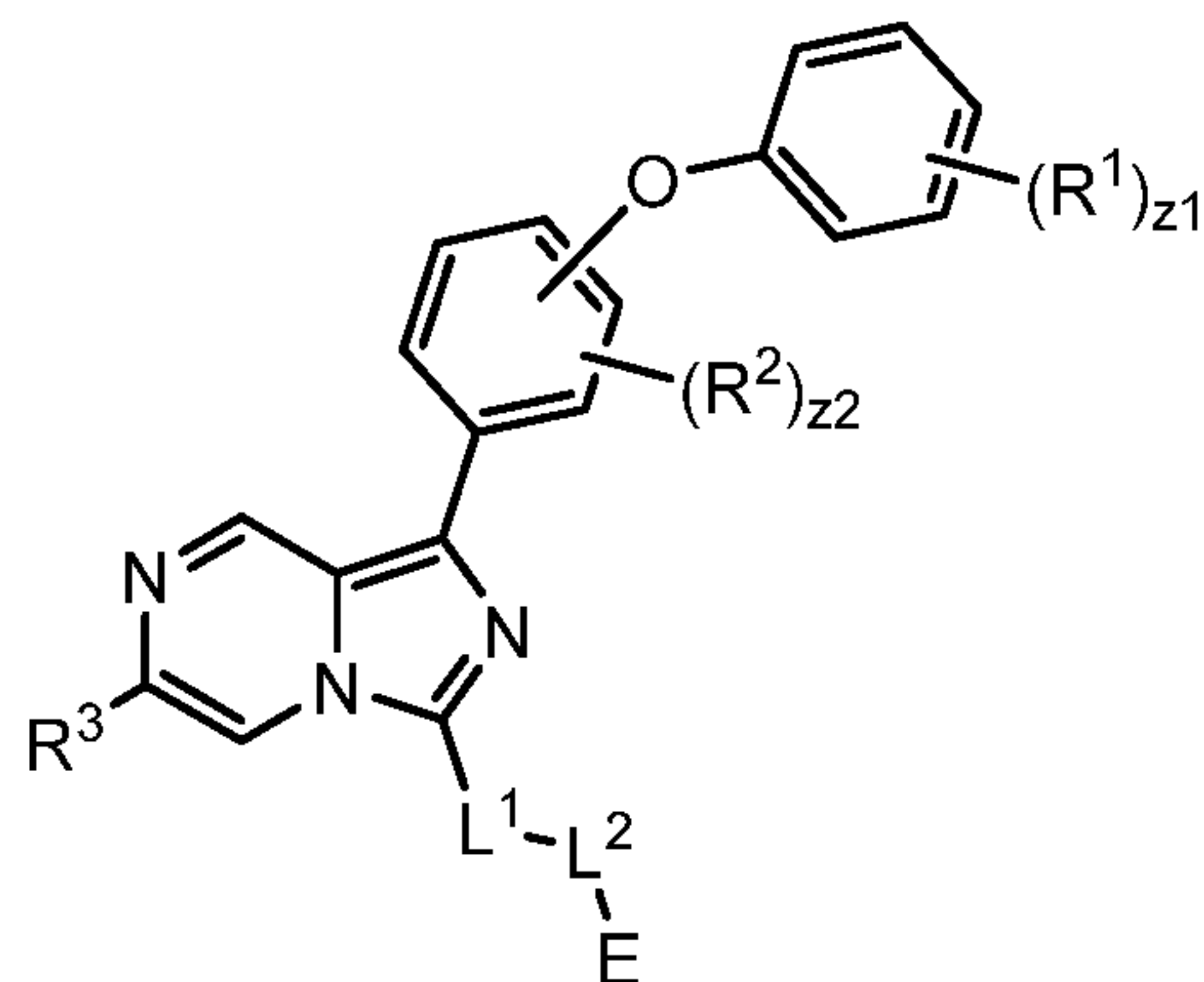
BRIEF SUMMARY OF THE INVENTION

[0003] Herein are provided, *inter alia*, compounds capable of modulating the level of activity of Bruton's Tyrosine Kinase (BTK) and methods of using the same.

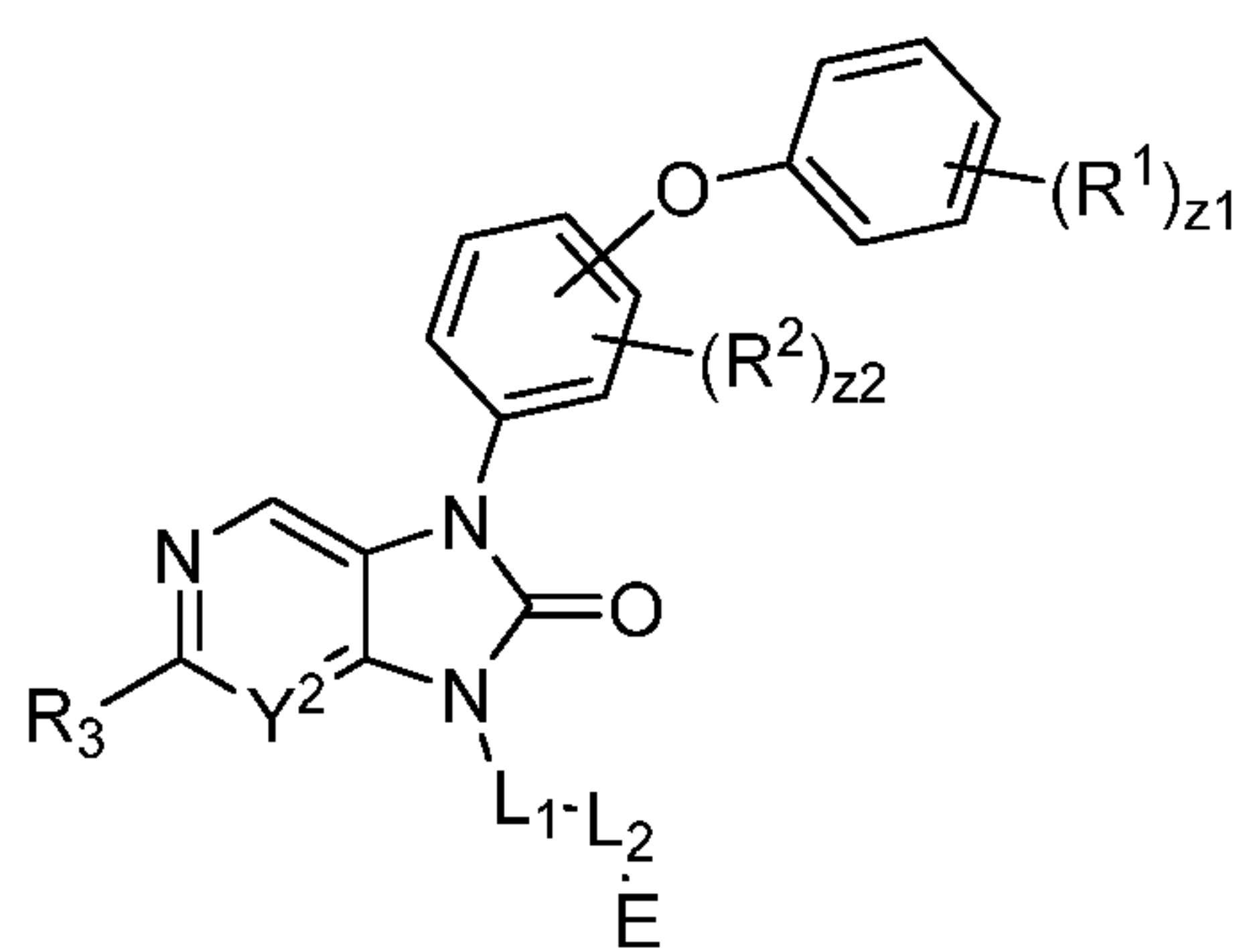
[0004] In an aspect is provided a compound having the formula:



(I), or



(II), or



(III).

[0005] R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, $-CN$, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. Two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbol $z1$ is an integer from 0 to 5. R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, $-CN$, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. Two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbol $z2$ is an integer from 0 to 4. R^3 is hydrogen or $-NH_2$. The symbol Y^1 is N or $C(R^4)$. R^4 is hydrogen, halogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, $-CN$, $-SO_{n4}R^{4D}$, $-SO_{v4}NR^{4A}R^{4B}$, $-NHC(O)NR^{4A}R^{4B}$, $-N(O)_{m4}$, $-NR^{4A}R^{4B}$, $-C(O)R^{4C}$, $-C(O)-OR^{4C}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4D}$, $-NR^{4A}SO_2R^{4D}$, $-NR^{4A}C(O)R^{4C}$, $-NR^{4A}C(O)OR^{4C}$, $-NR^{4A}OR^{4C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbol Y^2 is N or $C(R^5)$. R^5 is hydrogen, halogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, $-CN$, $-SO_{n5}R^{5D}$, $-SO_{v5}NR^{5A}R^{5B}$, $-NHC(O)NR^{5A}R^{5B}$, $-N(O)_{m5}$, $-NR^{5A}R^{5B}$, $-C(O)R^{5C}$, $-C(O)-OR^{5C}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5D}$, $-NR^{5A}SO_2R^{5D}$, $-NR^{5A}C(O)R^{5C}$, $-NR^{5A}C(O)OR^{5C}$, $-NR^{5A}OR^{5C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^6-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^6-$, $-NR^6C(O)-$, $-NR^6C(O)NH-$, $-NHC(O)NR^6-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene,

substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene. R^6 is hydrogen, halogen, $-CX^6_3$, $-CHX^6_2$, $-CH_2X^6$, $-OCX^6_3$, $-OCH_2X^6$, $-OCHX^6_2$, $-CN$, $-SO_{n6}R^{6D}$, $-SO_{v6}NR^{6A}R^{6B}$, $-NHC(O)NR^{6A}R^{6B}$, $-N(O)_{m6}$, $-NR^{6A}R^{6B}$, $-C(O)R^{6C}$, $-C(O)-OR^{6C}$, $-C(O)NR^{6A}R^{6B}$, $-OR^{6D}$, $-NR^{6A}SO_2R^{6D}$, $-NR^{6A}C(O)R^{6C}$, $-NR^{6A}C(O)OR^{6C}$, $-NR^{6A}OR^{6C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

L^2 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^7-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^7-$, $-NR^7C(O)-$, $-NR^7C(O)NH-$, $-NHC(O)NR^7-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene. R^7 is hydrogen, halogen, $-CX^7_3$, $-CHX^7_2$, $-CH_2X^7$, $-OCX^7_3$, $-OCH_2X^7$, $-OCHX^7_2$, $-CN$, $-SO_{n7}R^{7D}$, $-SO_{v7}NR^{7A}R^{7B}$, $-NHC(O)NR^{7A}R^{7B}$, $-N(O)_{m7}$, $-NR^{7A}R^{7B}$, $-C(O)R^{7C}$, $-C(O)-OR^{7C}$, $-C(O)NR^{7A}R^{7B}$, $-OR^{7D}$, $-NR^{7A}SO_2R^{7D}$, $-NR^{7A}C(O)R^{7C}$, $-NR^{7A}C(O)OR^{7C}$, $-NR^{7A}OR^{7C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. E is an electrophilic moiety. Each R^{1A} , R^{1B} , R^{1C} , R^{1D} , R^{2A} , R^{2B} , R^{2C} , R^{2D} , R^{4A} , R^{4B} , R^{4C} , R^{4D} , R^{5A} , R^{5B} , R^{5C} , R^{5D} , R^{6A} , R^{6B} , R^{6C} , R^{6D} , R^{7A} , R^{7B} , R^{7C} , and R^{7D} is independently hydrogen, $-CX_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. Each X , X^1 , X^2 , X^4 , X^5 , X^6 , and X^7 is independently

–F, –Cl, –Br, or –I. The symbols n1, n2, n4, n5, n6, and n7 are independently an integer from 0 to 4. The symbols m1, m2, m4, m5, m6, m7, v1, v2, v4, v5, v6, and v7 are independently an integer from 1 to 2.

[0006] In an aspect is provided a pharmaceutical composition including a compound
5 described herein, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0007] In an aspect is provided a method of treating cancer including administering to a subject in need thereof an effective amount of a compound described herein.

[0008] In an aspect is provided a method of treating an inflammatory disease including
10 administering to a subject in need thereof an effective amount of a compound described herein.

[0009] In an aspect is provided a method of treating a disease associated with Bruton's Tyrosine Kinase activity including administering to a subject in need thereof an effective amount of a compound described herein. In embodiments, the disease is associated with
15 aberrant Bruton's Tyrosine Kinase activity.

[0010] In an aspect is provided a method of inhibiting Bruton's Tyrosine Kinase activity including contacting the Bruton's Tyrosine Kinase with a compound described herein.

[0011] In an aspect is provided a Bruton's tyrosine kinase protein covalently bonded to a compound described herein (e.g., Bruton's Tyrosine Kinase inhibitor, Bruton's Tyrosine
20 Kinase antagonist, compound described herein, or a portion of a compound described herein).

[0012] In an aspect is provided a Bruton's Tyrosine Kinase protein (e.g., human BTK) covalently bonded to a Bruton's Tyrosine Kinase inhibitor (e.g., Bruton's Tyrosine Kinase antagonist, compound described herein, or a portion of a compound described herein).

DETAILED DESCRIPTION

I. Definitions

[0013] The abbreviations used herein have their conventional meaning within the chemical and biological arts. The chemical structures and formulae set forth herein are constructed according to the standard rules of chemical valency known in the chemical arts.

[0014] Where substituent groups are specified by their conventional chemical formulae,
30 written from left to right, they equally encompass the chemically identical substituents that

would result from writing the structure from right to left, e.g., $-\text{CH}_2\text{O}-$ is equivalent to $-\text{OCH}_2-$.

[0015] The term “alkyl,” by itself or as part of another substituent, means, unless otherwise stated, a straight (i.e., unbranched) or branched carbon chain (or carbon), or combination thereof, which may be fully saturated, mono- or polyunsaturated and can include mono-, di- and multivalent radicals, having the number of carbon atoms designated (i.e., $\text{C}_1\text{-C}_{10}$ means one to ten carbons). Alkyl is an uncyclized chain. Examples of saturated hydrocarbon radicals include, but are not limited to, groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, homologs and isomers of, for example, n-pentyl, n-hexyl, n-heptyl, n-octyl, and the like. An unsaturated alkyl group is one having one or more double bonds or triple bonds. Examples of unsaturated alkyl groups include, but are not limited to, vinyl, 2-propenyl, crotyl, 2-isopentenyl, 2-(butadienyl), 2,4-pentadienyl, 3-(1,4-pentadienyl), ethynyl, 1- and 3-propynyl, 3-butylnyl, and the higher homologs and isomers. An alkoxy is an alkyl attached to the remainder of the molecule via an oxygen linker ($-\text{O}-$).

[0016] The term “alkylene,” by itself or as part of another substituent, means, unless otherwise stated, a divalent radical derived from an alkyl, as exemplified, but not limited by, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$. Typically, an alkyl (or alkylene) group will have from 1 to 24 carbon atoms, with those groups having 10 or fewer carbon atoms being preferred herein. A “lower alkyl” or “lower alkylene” is a shorter chain alkyl or alkylene group, generally having eight or fewer carbon atoms. The term “alkenylene,” by itself or as part of another substituent, means, unless otherwise stated, a divalent radical derived from an alkene.

[0017] The term “heteroalkyl,” by itself or in combination with another term, means, unless otherwise stated, a stable straight or branched chain, or combinations thereof, including at least one carbon atom and at least one heteroatom (e.g., O, N, P, Si, or S), and wherein the nitrogen and sulfur atoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized. The heteroatom(s) (e.g., O, N, P, S, B, As, or Si) may be placed at any interior position of the heteroalkyl group or at the position at which the alkyl group is attached to the remainder of the molecule. Heteroalkyl is an uncyclized chain. Examples include, but are not limited to: $-\text{CH}_2\text{-CH}_2\text{-O-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-NH-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-N(CH}_3\text{)-CH}_3$, $-\text{CH}_2\text{-S-CH}_2\text{-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-S(O)-CH}_3$, $-\text{CH}_2\text{-CH}_2\text{-S(O)}_2\text{-CH}_3$, $-\text{CH=CH-O-CH}_3$, $-\text{Si(CH}_3\text{)}_3$, $-\text{CH}_2\text{-CH=N-OCH}_3$, $-\text{CH=CH-N(CH}_3\text{)-CH}_3$, $-\text{O-CH}_3$, $-\text{O-CH}_2\text{-CH}_3$, and $-\text{CN}$. Up to two or three heteroatoms may be consecutive, such as, for example, $-\text{CH}_2\text{-NH-OCH}_3$ and $-\text{CH}_2\text{-O-Si(CH}_3\text{)}_3$. A heteroalkyl moiety may include one heteroatom (e.g., O, N, S, Si, or P).

A heteroalkyl moiety may include two optionally different heteroatoms (e.g., O, N, S, Si, or P). A heteroalkyl moiety may include three optionally different heteroatoms (e.g., O, N, S, Si, or P). A heteroalkyl moiety may include four optionally different heteroatoms (e.g., O, N, S, Si, or P). A heteroalkyl moiety may include five optionally different heteroatoms (e.g., O, N, S, Si, or P). A heteroalkyl moiety may include up to 8 optionally different heteroatoms (e.g., O, N, S, Si, or P).

[0018] Similarly, the term “heteroalkylene,” by itself or as part of another substituent, means, unless otherwise stated, a divalent radical derived from heteroalkyl, as exemplified, but not limited by, $-\text{CH}_2-\text{CH}_2-\text{S}-\text{CH}_2-\text{CH}_2-$ and $-\text{CH}_2-\text{S}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-$. For heteroalkylene groups, heteroatoms can also occupy either or both of the chain termini (e.g., alkyleneoxy, alkylenedioxy, alkyleneamino, alkylenediamino, and the like). Still further, for alkylene and heteroalkylene linking groups, no orientation of the linking group is implied by the direction in which the formula of the linking group is written. For example, the formula $-\text{C}(\text{O})_2\text{R}'$ represents both $-\text{C}(\text{O})_2\text{R}'$ and $-\text{R}'\text{C}(\text{O})_2-$. As described above, heteroalkyl groups, as used herein, include those groups that are attached to the remainder of the molecule through a heteroatom, such as $-\text{C}(\text{O})\text{R}'$, $-\text{C}(\text{O})\text{NR}'$, $-\text{NR}'\text{R}''$, $-\text{OR}'$, $-\text{SR}'$, and/or $-\text{SO}_2\text{R}'$. Where “heteroalkyl” is recited, followed by recitations of specific heteroalkyl groups, such as $-\text{NR}'\text{R}''$ or the like, it will be understood that the terms heteroalkyl and $-\text{NR}'\text{R}''$ are not redundant or mutually exclusive. Rather, the specific heteroalkyl groups are recited to add clarity. Thus, the term “heteroalkyl” should not be interpreted herein as excluding specific heteroalkyl groups, such as $-\text{NR}'\text{R}''$ or the like.

[0019] The terms “cycloalkyl” and “heterocycloalkyl,” by themselves or in combination with other terms, mean, unless otherwise stated, cyclic versions of “alkyl” and “heteroalkyl,” respectively. Cycloalkyl and heterocycloalkyl are not aromatic. Additionally, for heterocycloalkyl, a heteroatom can occupy the position at which the heterocycle is attached to the remainder of the molecule. In embodiments, a cycloalkyl is a spirocyclic cycloalkyl, wherein the spirocyclic rings are cycloalkyl rings. In embodiments, a cycloalkyl is a fused ring cycloalkyl, wherein the fused rings are cycloalkyl rings. In embodiments, a cycloalkyl is a bridged ring cycloalkyl, wherein the bridged rings are cycloalkyl rings. In embodiments, a cycloalkyl is monocyclic. In embodiments, a cycloalkyl is two rings. In embodiments, a cycloalkyl is three rings. In embodiments, a cycloalkyl is four rings. In embodiments, a cycloalkyl is five rings. In embodiments, a cycloalkyl is polycyclic. In embodiments, a heterocycloalkyl is a spirocyclic heterocycloalkyl, wherein the spirocyclic rings are one or more heterocycloalkyl rings and optionally one or more cycloalkyl rings. In embodiments, a

heterocycloalkyl is a fused ring heterocycloalkyl, wherein the fused rings are one or more heterocycloalkyl rings and optionally one or more cycloalkyl rings. In embodiments, a heterocycloalkyl is a bridged ring heterocycloalkyl, wherein the bridged rings are one or more heterocycloalkyl rings and optionally one or more cycloalkyl rings. In embodiments, the rings of a spirocyclic, fused ring, or bridged ring heterocycloalkyl are heterocyclic rings. In embodiments, a heterocycloalkyl is monocyclic. In embodiments, a heterocycloalkyl is two rings. In embodiments, a heterocycloalkyl is three rings. In embodiments, a heterocycloalkyl is four rings. In embodiments, a heterocycloalkyl is five rings. In embodiments, a heterocycloalkyl is polycyclic. Examples of cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 1-cyclohexenyl, 3-cyclohexenyl, cycloheptyl, and the like. Examples of heterocycloalkyl include, but are not limited to, 1-(1,2,5,6-tetrahydropyridyl), 1-piperidiny, 2-piperidiny, 3-piperidiny, 4-morpholinyl, 3-morpholinyl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, 1-piperazinyl, 2-piperazinyl, and the like. A “cycloalkylene” and a “heterocycloalkylene,” alone or as part of another substituent, means a divalent radical derived from a cycloalkyl and heterocycloalkyl, respectively. In embodiments, a cycloalkylene or heterocycloalkylene is polycyclic. In embodiments, a heterocycloalkylene is a spirocyclic heterocycloalkylene, wherein the spirocyclic rings are one or more heterocycloalkyl rings and optionally one or more cycloalkyl rings.

[0020] The terms “halo” or “halogen,” by themselves or as part of another substituent, mean, unless otherwise stated, a fluorine, chlorine, bromine, or iodine atom. Additionally, terms such as “haloalkyl” are meant to include monohaloalkyl and polyhaloalkyl. For example, the term “halo(C₁-C₄)alkyl” includes, but is not limited to, fluoromethyl, difluoromethyl, trifluoromethyl, 2,2,2-trifluoroethyl, 4-chlorobutyl, 3-bromopropyl, and the like.

[0021] The term “acyl” means, unless otherwise stated, -C(O)R where R is a substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

[0022] The term “aryl” means, unless otherwise stated, a polyunsaturated, aromatic, hydrocarbon substituent, which can be a single ring or multiple rings (preferably from 1 to 3 rings) that are fused together (i.e., a fused ring aryl) or linked covalently. A fused ring aryl refers to multiple rings fused together wherein at least one of the fused rings is an aryl ring.

The term “heteroaryl” refers to aryl groups (or rings) that contain at least one heteroatom such as N, O, or S, wherein the nitrogen and sulfur atoms are optionally oxidized, and the nitrogen atom(s) are optionally quaternized. Thus, the term “heteroaryl” includes fused ring heteroaryl groups (i.e., multiple rings fused together wherein at least one of the fused rings is a heteroaromatic ring). A 5,6-fused ring heteroarylene refers to two rings fused together, wherein one ring has 5 members and the other ring has 6 members, and wherein at least one ring is a heteroaryl ring. Likewise, a 6,6-fused ring heteroarylene refers to two rings fused together, wherein one ring has 6 members and the other ring has 6 members, and wherein at least one ring is a heteroaryl ring. And a 6,5-fused ring heteroarylene refers to two rings fused together, wherein one ring has 6 members and the other ring has 5 members, and wherein at least one ring is a heteroaryl ring. A heteroaryl group can be attached to the remainder of the molecule through a carbon or heteroatom. Non-limiting examples of aryl and heteroaryl groups include phenyl, naphthyl, pyrrolyl, pyrazolyl, pyridazinyl, triazinyl, pyrimidinyl, imidazolyl, pyrazinyl, purinyl, oxazolyl, isoxazolyl, thiazolyl, furyl, thienyl, pyridyl, pyrimidyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, benzofuran, isobenzofuranyl, indolyl, isoindolyl, benzothiophenyl, isoquinolyl, quinoxalyl, quinolyl, 1-naphthyl, 2-naphthyl, 4-biphenyl, 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl, 3-pyrazolyl, 2-imidazolyl, 4-imidazolyl, pyrazinyl, 2-oxazolyl, 4-oxazolyl, 2-phenyl-4-oxazolyl, 5-oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidyl, 4-pyrimidyl, 5-benzothiazolyl, purinyl, 2-benzimidazolyl, 5-indolyl, 1-isoquinolyl, 5-isoquinolyl, 2-quinoxalyl, 5-quinoxalyl, 3-quinolyl, and 6-quinolyl. Substituents for each of the above noted aryl and heteroaryl ring systems are selected from the group of acceptable substituents described below. An “arylene” and a “heteroarylene,” alone or as part of another substituent, mean a divalent radical derived from an aryl and heteroaryl, respectively. A heteroaryl group substituent may be -O- bonded to a ring heteroatom nitrogen.

[0023] Spirocyclic rings are two or more rings wherein adjacent rings are attached through a single atom. The individual rings within spirocyclic rings may be identical or different. Individual rings in spirocyclic rings may be substituted or unsubstituted and may have different substituents from other individual rings within a set of spirocyclic rings. Possible substituents for individual rings within spirocyclic rings are the possible substituents for the same ring when not part of spirocyclic rings (e.g. substituents for cycloalkyl or heterocycloalkyl rings). Spirocyclic rings may be substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkyl or

substituted or unsubstituted heterocycloalkylene and individual rings within a spirocyclic ring group may be any of the immediately previous list, including having all rings of one type (e.g. all rings being substituted heterocycloalkylene wherein each ring may be the same or different substituted heterocycloalkylene). When referring to a spirocyclic ring system,

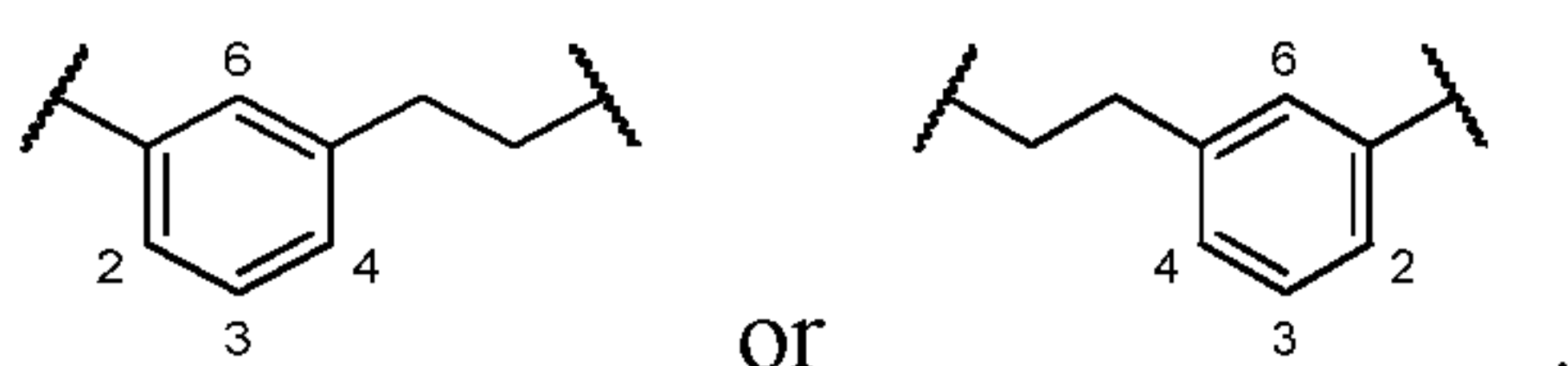
5 heterocyclic spirocyclic rings means a spirocyclic rings wherein at least one ring is a heterocyclic ring and wherein each ring may be a different ring. When referring to a spirocyclic ring system, substituted spirocyclic rings means that at least one ring is substituted and each substituent may optionally be different.

[0024] The symbol “~” denotes the point of attachment of a chemical moiety to the remainder of a molecule or chemical formula.

[0025] The term “oxo,” as used herein, means an oxygen that is double bonded to a carbon atom.

[0026] The term “alkylarylene” as an arylene moiety covalently bonded to an alkylene moiety (also referred to herein as an alkylene linker). In embodiments, the alkylarylene group

15 has the formula:



[0027] An alkylarylene moiety may be substituted (e.g. with a substituent group) on the alkylene moiety or the arylene linker (e.g. at carbons 2, 3, 4, or 6) with halogen, oxo, -N₃, -CF₃, -CCl₃, -CBr₃, -Cl₃, -CN, -CHO, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₂CH₃, -SO₃H, -OSO₃H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, substituted or

20 unsubstituted C₁-C₅ alkyl or substituted or unsubstituted 2 to 5 membered heteroalkyl). In embodiments, the alkylarylene is unsubstituted.

[0028] Each of the above terms (e.g., “alkyl,” “heteroalkyl,” “cycloalkyl,” “heterocycloalkyl,” “aryl,” and “heteroaryl”) includes both substituted and unsubstituted

25 forms of the indicated radical. Preferred substituents for each type of radical are provided below.

[0029] Substituents for the alkyl and heteroalkyl radicals (including those groups often referred to as alkylene, alkenyl, heteroalkylene, heteroalkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, and heterocycloalkenyl) can be one or more of a variety of

30 groups selected from, but not limited to, -OR', =O, =NR', =N-OR', -NR'R'', -SR', -halogen, -SiR'R''R''', -OC(O)R', -C(O)R', -CO₂R', -CONR'R'', -OC(O)NR'R'', -NR''C(O)R', -NR'-

C(O)NR''', -NR''C(O)₂R', -NR-C(NR'R''')=NR''', -NR-C(NR'R'')=NR''', -S(O)R', -S(O)₂R', -S(O)₂NR'R'', -NRSO₂R', -NR'NR''R''', -ONR'R'', -NR'C(O)NR''NR''''R''', -CN, -NO₂, -NR'SO₂R'', -NR'C(O)R'', -NR'C(O)-OR'', -NR'OR'', in a number ranging from zero to (2m'+1), where m' is the total number of carbon atoms in such radical. R, R', R'', R''', and R'''' each preferably independently refer to hydrogen, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl (e.g., aryl substituted with 1-3 halogens), substituted or unsubstituted heteroaryl, substituted or unsubstituted alkyl, alkoxy, or thioalkoxy groups, or arylalkyl groups. When a compound described herein includes more than one R group, for example, each of the R groups is independently selected as are each R', R'', R''', and R'''' group when more than one of these groups is present. When R' and R'' are attached to the same nitrogen atom, they can be combined with the nitrogen atom to form a 4-, 5-, 6-, or 7-membered ring. For example, -NR'R'' includes, but is not limited to, 1-pyrrolidinyl and 4-morpholinyl. From the above discussion of substituents, one of skill in the art will understand that the term "alkyl" is meant to include groups including carbon atoms bound to groups other than hydrogen groups, such as haloalkyl (e.g., -CF₃ and -CH₂CF₃) and acyl (e.g., -C(O)CH₃, -C(O)CF₃, -C(O)CH₂OCH₃, and the like).

[0030] Similar to the substituents described for the alkyl radical, substituents for the aryl and heteroaryl groups are varied and are selected from, for example: -OR', -NR'R'', -SR', -halogen, -SiR'R''R''', -OC(O)R', -C(O)R', -CO₂R', -CONR'R'', -OC(O)NR'R'', -NR''C(O)R', -NR'-C(O)NR''R''', -NR''C(O)₂R', -NR-C(NR'R''')=NR''', -NR-C(NR'R'')=NR''', -S(O)R', -S(O)₂R', -S(O)₂NR'R'', -NRSO₂R', -NR'NR''R''', -ONR'R'', -NR'C(O)NR''NR''''R''', -CN, -NO₂, -R', -N₃, -CH(Ph)₂, fluoro(C₁-C₄)alkoxy, and fluoro(C₁-C₄)alkyl, -NR'SO₂R'', -NR'C(O)R'', -NR'C(O)-OR'', -NR'OR'', in a number ranging from zero to the total number of open valences on the aromatic ring system; and where R', R'', R''', and R'''' are preferably independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl. When a compound described herein includes more than one R group, for example, each of the R groups is independently selected as are each R', R'', R''', and R'''' groups when more than one of these groups is present.

[0031] Substituents for rings (e.g. cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cycloalkylene, heterocycloalkylene, arylene, or heteroarylene) may be depicted as substituents on the ring rather than on a specific atom of a ring (commonly referred to as a

floating substituent). In such a case, the substituent may be attached to any of the ring atoms (obeying the rules of chemical valency) and in the case of fused rings or spirocyclic rings, a substituent depicted as associated with one member of the fused rings or spirocyclic rings (a floating substituent on a single ring), may be a substituent on any of the fused rings or

5 spirocyclic rings (a floating substituent on multiple rings). When a substituent is attached to a ring, but not a specific atom (a floating substituent), and a subscript for the substituent is an integer greater than one, the multiple substituents may be on the same atom, same ring, different atoms, different fused rings, different spirocyclic rings, and each substituent may optionally be different. Where a point of attachment of a ring to the remainder of a molecule

10 is not limited to a single atom (a floating substituent), the attachment point may be any atom of the ring and in the case of a fused ring or spirocyclic ring, any atom of any of the fused rings or spirocyclic rings while obeying the rules of chemical valency. Where a ring, fused rings, or spirocyclic rings contain one or more ring heteroatoms and the ring, fused rings, or spirocyclic rings are shown with one more floating substituents (including, but not limited to,

15 points of attachment to the remainder of the molecule), the floating substituents may be bonded to the heteroatoms. Where the ring heteroatoms are shown bound to one or more hydrogens (e.g. a ring nitrogen with two bonds to ring atoms and a third bond to a hydrogen) in the structure or formula with the floating substituent, when the heteroatom is bonded to the floating substituent, the substituent will be understood to replace the hydrogen, while obeying

20 the rules of chemical valency.

[0032] Two or more substituents may optionally be joined to form aryl, heteroaryl, cycloalkyl, or heterocycloalkyl groups. Such so-called ring-forming substituents are typically, though not necessarily, found attached to a cyclic base structure. In one embodiment, the ring-forming substituents are attached to adjacent members of the base structure. For

25 example, two ring-forming substituents attached to adjacent members of a cyclic base structure create a fused ring structure. In another embodiment, the ring-forming substituents are attached to a single member of the base structure. For example, two ring-forming substituents attached to a single member of a cyclic base structure create a spirocyclic structure. In yet another embodiment, the ring-forming substituents are attached to non-

30 adjacent members of the base structure.

[0033] Two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally form a ring of the formula $-T-C(O)-(CRR')_q-U-$, wherein T and U are independently $-NR-$, $-O-$, $-CRR'-$, or a single bond, and q is an integer of from 0 to 3. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may

optionally be replaced with a substituent of the formula $-A-(CH_2)_r-B-$, wherein A and B are independently $-CRR'-$, $-O-$, $-NR-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-S(O)_2NR'-$, or a single bond, and r is an integer of from 1 to 4. One of the single bonds of the new ring so formed may optionally be replaced with a double bond. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the formula $-(CRR')_s-X'-(C''R''R''')_d-$, where s and d are independently integers of from 0 to 3, and X' is $-O-$, $-NR'-$, $-S-$, $-S(O)-$, $-S(O)_2-$, or $-S(O)_2NR'-$. The substituents R, R', R'', and R''' are preferably independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

[0034] As used herein, the terms “heteroatom” or “ring heteroatom” are meant to include oxygen (O), nitrogen (N), sulfur (S), phosphorus (P), and silicon (Si).

[0035] A “substituent group,” as used herein, means a group selected from the following moieties:

(A) oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(=O)NHNH_2$, $-NHC(=O)NH_2$, $-NHSO_2H$, $-NHC(=O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, unsubstituted heteroaryl, and

(B) alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, substituted with at least one substituent selected from:

(i) oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(=O)NHNH_2$, $-NHC(=O)NH_2$, $-NHSO_2H$, $-NHC(=O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, unsubstituted heteroaryl, and

(ii) alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, substituted with at least one substituent selected from:

(a) oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(=O)NHNH_2$, $-NHC(=O)NH_2$, $-NHSO_2H$, $-NHC(=O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl,

unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, unsubstituted heteroaryl, and

(b) alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, substituted with at least one substituent selected from: oxo,

- 5 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC=(O)NHNH₂, -NHC=(O)NH₂, -NHSO₂H, -NHC=(O)H, -NHC(O)-OH, -NHOH, -OCF₃, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, unsubstituted heteroaryl.
- 10 **[0036]** A “size-limited substituent” or “size-limited substituent group,” as used herein, means a group selected from all of the substituents described above for a “substituent group,” wherein each substituted or unsubstituted alkyl is a substituted or unsubstituted C₁-C₂₀ alkyl, each substituted or unsubstituted heteroalkyl is a substituted or unsubstituted 2 to 20 membered heteroalkyl, each substituted or unsubstituted cycloalkyl is a substituted or
- 15 unsubstituted C₃-C₈ cycloalkyl, each substituted or unsubstituted heterocycloalkyl is a substituted or unsubstituted 3 to 8 membered heterocycloalkyl, each substituted or unsubstituted aryl is a substituted or unsubstituted C₆-C₁₀ aryl, and each substituted or unsubstituted heteroaryl is a substituted or unsubstituted 5 to 10 membered heteroaryl.

- [0037]** A “lower substituent” or “lower substituent group,” as used herein, means a group
- 20 selected from all of the substituents described above for a “substituent group,” wherein each substituted or unsubstituted alkyl is a substituted or unsubstituted C₁-C₈ alkyl, each substituted or unsubstituted heteroalkyl is a substituted or unsubstituted 2 to 8 membered heteroalkyl, each substituted or unsubstituted cycloalkyl is a substituted or unsubstituted C₃-C₇ cycloalkyl, each substituted or unsubstituted heterocycloalkyl is a substituted or
- 25 unsubstituted 3 to 7 membered heterocycloalkyl, each substituted or unsubstituted aryl is a substituted or unsubstituted C₆-C₁₀ aryl, and each substituted or unsubstituted heteroaryl is a substituted or unsubstituted 5 to 9 membered heteroaryl.

- [0038]** In some embodiments, each substituted group described in the compounds herein is substituted with at least one substituent group. More specifically, in some embodiments,
- 30 each substituted alkyl, substituted heteroalkyl, substituted cycloalkyl, substituted heterocycloalkyl, substituted aryl, substituted heteroaryl, substituted alkylene, substituted heteroalkylene, substituted cycloalkylene, substituted heterocycloalkylene, substituted arylene, and/or substituted heteroarylene described in the compounds herein are substituted

with at least one substituent group. In other embodiments, at least one or all of these groups are substituted with at least one size-limited substituent group. In other embodiments, at least one or all of these groups are substituted with at least one lower substituent group.

[0039] In other embodiments of the compounds herein, each substituted or unsubstituted alkyl may be a substituted or unsubstituted C₁-C₂₀ alkyl, each substituted or unsubstituted heteroalkyl is a substituted or unsubstituted 2 to 20 membered heteroalkyl, each substituted or unsubstituted cycloalkyl is a substituted or unsubstituted C₃-C₈ cycloalkyl, each substituted or unsubstituted heterocycloalkyl is a substituted or unsubstituted 3 to 8 membered heterocycloalkyl, each substituted or unsubstituted aryl is a substituted or unsubstituted C₆-C₁₀ aryl, and/or each substituted or unsubstituted heteroaryl is a substituted or unsubstituted 5 to 10 membered heteroaryl. In some embodiments of the compounds herein, each substituted or unsubstituted alkylene is a substituted or unsubstituted C₁-C₂₀ alkylene, each substituted or unsubstituted heteroalkylene is a substituted or unsubstituted 2 to 20 membered heteroalkylene, each substituted or unsubstituted cycloalkylene is a substituted or unsubstituted C₃-C₈ cycloalkylene, each substituted or unsubstituted heterocycloalkylene is a substituted or unsubstituted 3 to 8 membered heterocycloalkylene, each substituted or unsubstituted arylene is a substituted or unsubstituted C₆-C₁₀ arylene, and/or each substituted or unsubstituted heteroarylene is a substituted or unsubstituted 5 to 10 membered heteroarylene.

[0040] In some embodiments, each substituted or unsubstituted alkyl is a substituted or unsubstituted C₁-C₈ alkyl, each substituted or unsubstituted heteroalkyl is a substituted or unsubstituted 2 to 8 membered heteroalkyl, each substituted or unsubstituted cycloalkyl is a substituted or unsubstituted C₃-C₇ cycloalkyl, each substituted or unsubstituted heterocycloalkyl is a substituted or unsubstituted 3 to 7 membered heterocycloalkyl, each substituted or unsubstituted aryl is a substituted or unsubstituted C₆-C₁₀ aryl, and/or each substituted or unsubstituted heteroaryl is a substituted or unsubstituted 5 to 9 membered heteroaryl. In some embodiments, each substituted or unsubstituted alkylene is a substituted or unsubstituted C₁-C₈ alkylene, each substituted or unsubstituted heteroalkylene is a substituted or unsubstituted 2 to 8 membered heteroalkylene, each substituted or unsubstituted cycloalkylene is a substituted or unsubstituted C₃-C₇ cycloalkylene, each substituted or unsubstituted heterocycloalkylene is a substituted or unsubstituted 3 to 7 membered heterocycloalkylene, each substituted or unsubstituted arylene is a substituted or unsubstituted C₆-C₁₀ arylene, and/or each substituted or unsubstituted heteroarylene is a

substituted or unsubstituted 5 to 9 membered heteroarylene. In some embodiments, the compound is a chemical species set forth in the Examples section, figures, or tables below.

[0041] Certain compounds of the present invention possess asymmetric carbon atoms (optical or chiral centers) or double bonds; the enantiomers, racemates, diastereomers, tautomers, geometric isomers, stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (R)- or (S)- or, as (D)- or (L)- for amino acids, and individual isomers are encompassed within the scope of the present invention. The compounds of the present invention do not include those that are known in art to be too unstable to synthesize and/or isolate. The present invention is meant to include compounds in racemic and optically pure forms. Optically active (R)- and (S)-, or (D)- and (L)-isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. When the compounds described herein contain olefinic bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both E and Z geometric isomers.

[0042] As used herein, the term “isomers” refers to compounds having the same number and kind of atoms, and hence the same molecular weight, but differing in respect to the structural arrangement or configuration of the atoms.

[0043] The term “tautomer,” as used herein, refers to one of two or more structural isomers which exist in equilibrium and which are readily converted from one isomeric form to another.

[0044] It will be apparent to one skilled in the art that certain compounds of this invention may exist in tautomeric forms, all such tautomeric forms of the compounds being within the scope of the invention.

[0045] Unless otherwise stated, structures depicted herein are also meant to include all stereochemical forms of the structure; i.e., the R and S configurations for each asymmetric center. Therefore, single stereochemical isomers as well as enantiomeric and diastereomeric mixtures of the present compounds are within the scope of the invention.

[0046] Unless otherwise stated, structures depicted herein are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by ^{13}C - or ^{14}C -enriched carbon are within the scope of this invention.

[0047] Unless otherwise stated, structures depicted herein are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by ^{13}C - or ^{14}C -enriched carbon are within the scope of this invention.

[0048] The compounds of the present invention may also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the compounds may be radiolabeled with radioactive isotopes, such as for example tritium (^3H), iodine-125 (^{125}I), or carbon-14 (^{14}C). All isotopic variations of the compounds of the present invention, whether radioactive or not, are encompassed within the scope of the present invention.

[0049] It should be noted that throughout the application that alternatives are written in Markush groups, for example, each amino acid position that contains more than one possible amino acid. It is specifically contemplated that each member of the Markush group should be considered separately, thereby comprising another embodiment, and the Markush group is not to be read as a single unit.

[0050] "Analog," or "analogue" is used in accordance with its plain ordinary meaning within Chemistry and Biology and refers to a chemical compound that is structurally similar to another compound (i.e., a so-called "reference" compound) but differs in composition, e.g., in the replacement of one atom by an atom of a different element, or in the presence of a particular functional group, or the replacement of one functional group by another functional group, or the absolute stereochemistry of one or more chiral centers of the reference compound. Accordingly, an analog is a compound that is similar or comparable in function and appearance but not in structure or origin to a reference compound.

[0051] The terms "a" or "an," as used in herein means one or more. In addition, the phrase "substituted with a[n]," as used herein, means the specified group may be substituted with one or more of any or all of the named substituents. For example, where a group, such as an alkyl or heteroaryl group, is "substituted with an unsubstituted $\text{C}_1\text{-C}_{20}$ alkyl, or unsubstituted 2 to 20 membered heteroalkyl," the group may contain one or more unsubstituted $\text{C}_1\text{-C}_{20}$ alkyls, and/or one or more unsubstituted 2 to 20 membered heteroalkyls.

[0052] Moreover, where a moiety is substituted with an R substituent, the group may be referred to as "R-substituted." Where a moiety is R-substituted, the moiety is substituted with at least one R substituent and each R substituent is optionally different. Where a particular R

group is present in the description of a chemical genus (such as Formula (I)), a Roman alphabetic symbol may be used to distinguish each appearance of that particular R group. For example, where multiple R^{13} substituents are present, each R^{13} substituent may be distinguished as R^{13A} , R^{13B} , R^{13C} , R^{13D} , etc., wherein each of R^{13A} , R^{13B} , R^{13C} , R^{13D} , etc. is defined within the scope of the definition of R^{13} and optionally differently.

[0053] A “covalent cysteine modifier moiety” as used herein refers to a substituent that is capable of reacting with the sulfhydryl functional group of a cysteine amino acid (e.g. cysteine 481 of the Bruton’s Tyrosine Kinase protein (e.g., human BTK)) to form a covalent bond. Thus, the covalent cysteine modifier moiety is typically electrophilic.

[0054] A “detectable moiety” as used herein refers to a moiety that can be covalently or noncovalently attached to a compound or biomolecule that can be detected for instance, using techniques known in the art. In embodiments, the detectable moiety is covalently attached. The detectable moiety may provide for imaging of the attached compound or biomolecule. The detectable moiety may indicate the contacting between two compounds. Exemplary detectable moieties are fluorophores, antibodies, reactive dyes, radio-labeled moieties, magnetic contrast agents, and quantum dots. Exemplary fluorophores include fluorescein, rhodamine, GFP, coumarin, FITC, Alexa fluor, Cy3, Cy5, BODIPY, and cyanine dyes. Exemplary radionuclides include Fluorine-18, Gallium-68, and Copper-64. Exemplary magnetic contrast agents include gadolinium, iron oxide and iron platinum, and manganese.

[0055] Description of compounds of the present invention are limited by principles of chemical bonding known to those skilled in the art. Accordingly, where a group may be substituted by one or more of a number of substituents, such substitutions are selected so as to comply with principles of chemical bonding and to give compounds which are not inherently unstable and/or would be known to one of ordinary skill in the art as likely to be unstable under ambient conditions, such as aqueous, neutral, and several known physiological conditions. For example, a heterocycloalkyl or heteroaryl is attached to the remainder of the molecule via a ring heteroatom in compliance with principles of chemical bonding known to those skilled in the art thereby avoiding inherently unstable compounds.

[0056] The term “pharmaceutically acceptable salts” is meant to include salts of the active compounds that are prepared with relatively nontoxic acids or bases, depending on the particular substituents found on the compounds described herein. When compounds of the present invention contain relatively acidic functionalities, base addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired

base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amino, or magnesium salt, or a similar salt. When compounds of the present invention contain relatively basic functionalities, acid addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired acid, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable acid addition salts include those derived from inorganic acids like hydrochloric, hydrobromic, nitric, carbonic, monohydrogencarbonic, phosphoric, monohydrogenphosphoric, dihydrogenphosphoric, sulfuric, monohydrogensulfuric, hydriodic, or phosphorous acids and the like, as well as the salts derived from relatively nontoxic organic acids like acetic, propionic, isobutyric, maleic, malonic, benzoic, succinic, suberic, fumaric, lactic, mandelic, phthalic, benzenesulfonic, p-tolylsulfonic, citric, tartaric, oxalic, methanesulfonic, and the like. Also included are salts of amino acids such as arginate and the like, and salts of organic acids like glucuronic or galacturonic acids and the like (*see*, for example, Berge *et al.*, "Pharmaceutical Salts", *Journal of Pharmaceutical Science*, **1977**, 66, 1-19). Certain specific compounds of the present invention contain both basic and acidic functionalities that allow the compounds to be converted into either base or acid addition salts.

[0057] Thus, the compounds of the present invention may exist as salts, such as with pharmaceutically acceptable acids. The present invention includes such salts. Non-limiting examples of such salts include hydrochlorides, hydrobromides, phosphates, sulfates, methanesulfonates, nitrates, maleates, acetates, citrates, fumarates, proprionates, tartrates (e.g., (+)-tartrates, (-)-tartrates, or mixtures thereof including racemic mixtures), succinates, benzoates, and salts with amino acids such as glutamic acid, and quaternary ammonium salts (e.g. methyl iodide, ethyl iodide, and the like). These salts may be prepared by methods known to those skilled in the art.

[0058] The neutral forms of the compounds are preferably regenerated by contacting the salt with a base or acid and isolating the parent compound in the conventional manner. The parent form of the compound may differ from the various salt forms in certain physical properties, such as solubility in polar solvents.

[0059] In addition to salt forms, the present invention provides compounds, which are in a prodrug form. Prodrugs of the compounds described herein are those compounds that readily undergo chemical changes under physiological conditions to provide the compounds of the present invention. Prodrugs of the compounds described herein may be converted *in vivo*

after administration. Additionally, prodrugs can be converted to the compounds of the present invention by chemical or biochemical methods in an *ex vivo* environment, such as, for example, when contacted with a suitable enzyme or chemical reagent.

[0060] Certain compounds of the present invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are encompassed within the scope of the present invention. Certain compounds of the present invention may exist in multiple crystalline or amorphous forms. In general, all physical forms are equivalent for the uses contemplated by the present invention and are intended to be within the scope of the present invention.

[0061] “Pharmaceutically acceptable excipient” and “pharmaceutically acceptable carrier” refer to a substance that aids the administration of an active agent to and absorption by a subject and can be included in the compositions of the present invention without causing a significant adverse toxicological effect on the patient. Non-limiting examples of pharmaceutically acceptable excipients include water, NaCl, normal saline solutions, lactated Ringer’s, normal sucrose, normal glucose, binders, fillers, disintegrants, lubricants, coatings, sweeteners, flavors, salt solutions (such as Ringer’s solution), alcohols, oils, gelatins, carbohydrates such as lactose, amylose or starch, fatty acid esters, hydroxymethylcellulose, polyvinyl pyrrolidone, and colors, and the like. Such preparations can be sterilized and, if desired, mixed with auxiliary agents such as lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure, buffers, coloring, and/or aromatic substances and the like that do not deleteriously react with the compounds of the invention. One of skill in the art will recognize that other pharmaceutical excipients are useful in the present invention.

[0062] The term “preparation” is intended to include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component with or without other carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid dosage forms suitable for oral administration.

[0063] An “Bruton’s Tyrosine Kinase inhibitor” or “BTK compound” or “BTK inhibitor” refers to a compound (e.g. compounds described herein) that reduces the activity of Bruton’s Tyrosine Kinase when compared to a control, such as absence of the compound or a compound with known inactivity.

[0064] The terms “polypeptide,” “peptide” and “protein” are used interchangeably herein to refer to a polymer of amino acid residues, wherein the polymer may optionally be conjugated to a moiety that does not consist of amino acids. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer.

[0065] A polypeptide, or a cell is “recombinant” when it is artificial or engineered, or derived from or contains an artificial or engineered protein or nucleic acid (*e.g.* non-natural or not wild type). For example, a polynucleotide that is inserted into a vector or any other heterologous location, *e.g.*, in a genome of a recombinant organism, such that it is not associated with nucleotide sequences that normally flank the polynucleotide as it is found in nature is a recombinant polynucleotide. A protein expressed *in vitro* or *in vivo* from a recombinant polynucleotide is an example of a recombinant polypeptide. Likewise, a polynucleotide sequence that does not appear in nature, for example a variant of a naturally occurring gene, is recombinant.

[0066] An amino acid residue in a protein “corresponds” to a given residue when it occupies the same essential structural position within the protein as the given residue. For example, a selected residue in a selected protein corresponds to Cys481 of human Bruton’s Tyrosine Kinase when the selected residue occupies the same essential spatial or other structural relationship as Cys481 in human Bruton’s Tyrosine Kinase. In some embodiments, where a selected protein is aligned for maximum homology with the human Bruton’s Tyrosine Kinase protein, the position in the aligned selected protein aligning with Cys481 is said to correspond to Cys481. Instead of a primary sequence alignment, a three dimensional structural alignment can also be used, *e.g.*, where the structure of the selected protein is aligned for maximum correspondence with the human Bruton’s Tyrosine Kinase protein and the overall structures compared. In this case, an amino acid that occupies the same essential position as Cys481 in the structural model is said to correspond to the Cys481 residue.

[0067] “Contacting” is used in accordance with its plain ordinary meaning and refers to the process of allowing at least two distinct species (*e.g.* chemical compounds including biomolecules or cells) to become sufficiently proximal to react, interact or physically touch. It should be appreciated; however, the resulting reaction product can be produced directly from a reaction between the added reagents or from an intermediate from one or more of the added reagents that can be produced in the reaction mixture.

[0068] The term “contacting” may include allowing two species to react, interact, or physically touch, wherein the two species may be a compound as described herein and a protein or enzyme. In some embodiments contacting includes allowing a compound described herein to interact with a protein or enzyme that is involved in a signaling pathway.

5 **[0069]** As defined herein, the term “activation”, “activate”, “activating” and the like in reference to a protein refers to conversion of a protein into a biologically active derivative from an initial inactive or deactivated state. The terms reference activation, or activating, sensitizing, or up-regulating signal transduction or enzymatic activity or the amount of a protein decreased in a disease.

10 **[0070]** As defined herein, the term “inhibition”, “inhibit”, “inhibiting” and the like in reference to a protein-inhibitor interaction means negatively affecting (e.g. decreasing) the activity or function of the protein relative to the activity or function of the protein in the absence of the inhibitor. In embodiments inhibition means negatively affecting (e.g. decreasing) the concentration or levels of the protein relative to the concentration or level of the protein in the absence of the inhibitor. In embodiments inhibition refers to reduction of a disease or symptoms of disease. In embodiments, inhibition refers to a reduction in the activity of a particular protein target. Thus, inhibition includes, at least in part, partially or totally blocking stimulation, decreasing, preventing, or delaying activation, or inactivating, desensitizing, or down-regulating signal transduction or enzymatic activity or the amount of a protein. In embodiments, inhibition refers to a reduction of activity of a target protein resulting from a direct interaction (e.g. an inhibitor binds to the target protein). In embodiments, inhibition refers to a reduction of activity of a target protein from an indirect interaction (e.g. an inhibitor binds to a protein that activates the target protein, thereby preventing target protein activation). A “Bruton’s Tyrosine Kinase inhibitor” and “BTK inhibitor” is a compound that negatively affects (e.g. decreases) the activity or function of Bruton’s Tyrosine Kinase relative to the activity or function of Bruton’s Tyrosine Kinase in the absence of the inhibitor (e.g., wherein the BTK inhibitor binds BTK).

[0071] The terms “Bruton’s Tyrosine Kinase” and “BTK” refer to a protein (including homologs, isoforms, and functional fragments thereof) with Bruton’s Tyrosine Kinase activity. The term includes any recombinant or naturally-occurring form of Bruton’s Tyrosine Kinase or variants thereof that maintain Bruton’s Tyrosine Kinase activity (e.g. within at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% activity compared to wildtype Bruton’s Tyrosine Kinase). In embodiments, the Bruton’s Tyrosine Kinase protein encoded

by the BTK gene has the amino acid sequence set forth in or corresponding to Entrez 695, UniProt Q06187, or RefSeq (protein) NP_000052. In embodiments, the Bruton's Tyrosine Kinase BTK gene has the nucleic acid sequence set forth in RefSeq (mRNA) NM_000061. In embodiments, the amino acid sequence or nucleic acid sequence is the sequence known at
 5 the time of filing of the present application. In embodiments, the sequence corresponds to GI:4557377. In embodiments, the sequence corresponds to NP_000052.1. In embodiments, the sequence corresponds to NM_000061.2. In embodiments, the sequence corresponds to GI: 213385292. In embodiments, the Bruton's Tyrosine Kinase is a human Bruton's Tyrosine Kinase, such as a human cancer causing Bruton's Tyrosine Kinase.

10 **[0072]** The term "expression" includes any step involved in the production of the polypeptide including, but not limited to, transcription, post-transcriptional modification, translation, post-translational modification, and secretion. Expression can be detected using conventional techniques for detecting protein (*e.g.*, ELISA, Western blotting, flow cytometry, immunofluorescence, immunohistochemistry, *etc.*).

15 **[0073]** The terms "disease" or "condition" refer to a state of being or health status of a patient or subject capable of being treated with the compounds or methods provided herein. The disease may be a cancer. The disease may be stroke. The disease may be an inflammatory disease. In some further instances, "cancer" refers to human cancers and carcinomas, sarcomas, adenocarcinomas, lymphomas, leukemias, *etc.*, including solid and
 20 lymphoid cancers, kidney, breast, lung, bladder, colon, ovarian, prostate, pancreas, stomach, brain, head and neck, skin, uterine, testicular, glioma, esophagus, and liver cancer, including hepatocarcinoma, lymphoma, including B-acute lymphoblastic lymphoma, non-Hodgkin's lymphomas (*e.g.*, Burkitt's, Small Cell, and Large Cell lymphomas), Hodgkin's lymphoma, leukemia (including AML, ALL, and CML), or multiple myeloma.

25 **[0074]** As used herein, the term "inflammatory disease" refers to a disease or condition characterized by aberrant inflammation (*e.g.* an increased level of inflammation compared to a control such as a healthy person not suffering from a disease). Examples of inflammatory diseases include autoimmune diseases, arthritis, rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, multiple sclerosis, systemic lupus erythematosus (SLE),
 30 myasthenia gravis, juvenile onset diabetes, diabetes mellitus type 1, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, ankylosing spondylitis, psoriasis, Sjogren's syndrome, vasculitis, glomerulonephritis, auto-immune thyroiditis, Behcet's disease, Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, ichthyosis,

Graves ophthalmopathy, inflammatory bowel disease, Addison's disease, Vitiligo, asthma, allergic asthma, acne vulgaris, celiac disease, chronic prostatitis, inflammatory bowel disease, pelvic inflammatory disease, reperfusion injury, ischemia reperfusion injury, stroke, sarcoidosis, transplant rejection, interstitial cystitis, atherosclerosis, scleroderma, and atopic dermatitis.

[0075] As used herein, the term "cancer" refers to all types of cancer, neoplasm or malignant tumors found in mammals (e.g. humans), including leukemia, carcinomas and sarcomas. Exemplary cancers that may be treated with a compound or method provided herein include brain cancer, glioma, glioblastoma, neuroblastoma, prostate cancer, colorectal cancer, pancreatic cancer, cervical cancer, gastric cancer, ovarian cancer, lung cancer, and cancer of the head. Exemplary cancers that may be treated with a compound or method provided herein include cancer of the thyroid, endocrine system, brain, breast, cervix, colon, head & neck, liver, kidney, lung, non-small cell lung, melanoma, mesothelioma, ovary, sarcoma, stomach, uterus, Medulloblastoma, colorectal cancer, pancreatic cancer. Additional examples include, Hodgkin's Disease, Non-Hodgkin's Lymphoma, multiple myeloma, neuroblastoma, glioma, glioblastoma multiforme, ovarian cancer, rhabdomyosarcoma, primary thrombocytosis, primary macroglobulinemia, primary brain tumors, cancer, malignant pancreatic insulanoma, malignant carcinoid, urinary bladder cancer, premalignant skin lesions, testicular cancer, lymphomas, thyroid cancer, neuroblastoma, esophageal cancer, genitourinary tract cancer, malignant hypercalcemia, endometrial cancer, adrenal cortical cancer, neoplasms of the endocrine or exocrine pancreas, medullary thyroid cancer, medullary thyroid carcinoma, melanoma, colorectal cancer, papillary thyroid cancer, hepatocellular carcinoma, or prostate cancer.

[0076] The term "leukemia" refers broadly to progressive, malignant diseases of the blood-forming organs and is generally characterized by a distorted proliferation and development of leukocytes and their precursors in the blood and bone marrow. Leukemia is generally clinically classified on the basis of (1) the duration and character of the disease-acute or chronic; (2) the type of cell involved; myeloid (myelogenous), lymphoid (lymphogenous), or monocytic; and (3) the increase or non-increase in the number abnormal cells in the blood-leukemic or aleukemic (subleukemic). Exemplary leukemias that may be treated with a compound or method provided herein include, for example, acute nonlymphocytic leukemia, chronic lymphocytic leukemia, acute granulocytic leukemia, chronic granulocytic leukemia, acute promyelocytic leukemia, adult T-cell leukemia, aleukemic leukemia, a leukocythemetic leukemia, basophylic leukemia, blast cell leukemia, bovine leukemia, chronic myelocytic

leukemia, leukemia cutis, embryonal leukemia, eosinophilic leukemia, Gross' leukemia, hairy-cell leukemia, hemoblastic leukemia, hemocytoblastic leukemia, histiocytic leukemia, stem cell leukemia, acute monocytic leukemia, leukopenic leukemia, lymphatic leukemia, lymphoblastic leukemia, lymphocytic leukemia, lymphogenous leukemia, lymphoid

5 leukemia, lymphosarcoma cell leukemia, mast cell leukemia, megakaryocytic leukemia, micromyeloblastic leukemia, monocytic leukemia, myeloblastic leukemia, myelocytic leukemia, myeloid granulocytic leukemia, myelomonocytic leukemia, Naegeli leukemia, plasma cell leukemia, multiple myeloma, plasmacytic leukemia, promyelocytic leukemia, Rieder cell leukemia, Schilling's leukemia, stem cell leukemia, subleukemic leukemia, or

10 undifferentiated cell leukemia.

[0077] The term "sarcoma" generally refers to a tumor which is made up of a substance like the embryonic connective tissue and is generally composed of closely packed cells embedded in a fibrillar or homogeneous substance. Sarcomas that may be treated with a compound or method provided herein include a chondrosarcoma, fibrosarcoma, lymphosarcoma,

15 melanosarcoma, myxosarcoma, osteosarcoma, Abemethy's sarcoma, adipose sarcoma, liposarcoma, alveolar soft part sarcoma, ameloblastic sarcoma, botryoid sarcoma, chloroma sarcoma, chorio carcinoma, embryonal sarcoma, Wilms' tumor sarcoma, endometrial sarcoma, stromal sarcoma, Ewing's sarcoma, fascial sarcoma, fibroblastic sarcoma, giant cell sarcoma, granulocytic sarcoma, Hodgkin's sarcoma, idiopathic multiple pigmented

20 hemorrhagic sarcoma, immunoblastic sarcoma of B cells, lymphoma, immunoblastic sarcoma of T-cells, Jensen's sarcoma, Kaposi's sarcoma, Kupffer cell sarcoma, angiosarcoma, leukosarcoma, malignant mesenchymoma sarcoma, parosteal sarcoma, reticulocytic sarcoma, Rous sarcoma, serocystic sarcoma, synovial sarcoma, or telangiectaltic sarcoma.

[0078] The term "melanoma" is taken to mean a tumor arising from the melanocytic system of the skin and other organs. Melanomas that may be treated with a compound or method provided herein include, for example, acral-lentiginous melanoma, amelanotic melanoma, benign juvenile melanoma, Cloudman's melanoma, S91 melanoma, Harding-Passey melanoma, juvenile melanoma, lentigo maligna melanoma, malignant melanoma, nodular melanoma, subungal melanoma, or superficial spreading melanoma.

[0079] The term "carcinoma" refers to a malignant new growth made up of epithelial cells tending to infiltrate the surrounding tissues and give rise to metastases. Exemplary carcinomas that may be treated with a compound or method provided herein include, for example, medullary thyroid carcinoma, familial medullary thyroid carcinoma, acinar

carcinoma, acinous carcinoma, adenocystic carcinoma, adenoid cystic carcinoma, carcinoma
 adenomatosum, carcinoma of adrenal cortex, alveolar carcinoma, alveolar cell carcinoma,
 basal cell carcinoma, carcinoma basocellulare, basaloid carcinoma, basosquamous cell
 carcinoma, bronchioalveolar carcinoma, bronchiolar carcinoma, bronchogenic carcinoma,
 5 cerebriiform carcinoma, cholangiocellular carcinoma, chorionic carcinoma, colloid
 carcinoma, comedo carcinoma, corpus carcinoma, cribriform carcinoma, carcinoma en
 cuirasse, carcinoma cutaneum, cylindrical carcinoma, cylindrical cell carcinoma, duct
 carcinoma, carcinoma durum, embryonal carcinoma, encephaloid carcinoma, epiermoid
 carcinoma, carcinoma epitheliale adenoides, exophytic carcinoma, carcinoma ex ulcere,
 10 carcinoma fibrosum, gelatiniformi carcinoma, gelatinous carcinoma, giant cell carcinoma,
 carcinoma gigantocellulare, glandular carcinoma, granulosa cell carcinoma, hair-matrix
 carcinoma, hematoid carcinoma, hepatocellular carcinoma, Hurthle cell carcinoma, hyaline
 carcinoma, hypernephroid carcinoma, infantile embryonal carcinoma, carcinoma in situ,
 intraepidermal carcinoma, intraepithelial carcinoma, Krompecher's carcinoma, Kulchitzky-
 15 cell carcinoma, large-cell carcinoma, lenticular carcinoma, carcinoma lenticulare, lipomatous
 carcinoma, lymphoepithelial carcinoma, carcinoma medullare, medullary carcinoma,
 melanotic carcinoma, carcinoma molle, mucinous carcinoma, carcinoma muciparum,
 carcinoma mucocellulare, mucoepidermoid carcinoma, carcinoma mucosum, mucous
 carcinoma, carcinoma myxomatodes, nasopharyngeal carcinoma, oat cell carcinoma,
 20 carcinoma ossificans, osteoid carcinoma, papillary carcinoma, periportal carcinoma,
 preinvasive carcinoma, prickle cell carcinoma, pultaceous carcinoma, renal cell carcinoma of
 kidney, reserve cell carcinoma, carcinoma sarcomatodes, schneiderian carcinoma, scirrhous
 carcinoma, carcinoma scroti, signet-ring cell carcinoma, carcinoma simplex, small-cell
 carcinoma, solanoid carcinoma, spheroidal cell carcinoma, spindle cell carcinoma, carcinoma
 25 spongiosum, squamous carcinoma, squamous cell carcinoma, string carcinoma, carcinoma
 telangiectaticum, carcinoma telangiectodes, transitional cell carcinoma, carcinoma
 tuberosum, tuberous carcinoma, verrucous carcinoma, or carcinoma villosum.

[0080] The terms “treating”, or “treatment” refers to any indicia of success in the therapy or
 amelioration of an injury, disease, pathology or condition, including any objective or
 30 subjective parameter such as abatement; remission; diminishing of symptoms or making the
 injury, pathology or condition more tolerable to the patient; slowing in the rate of
 degeneration or decline; making the final point of degeneration less debilitating; improving a
 patient’s physical or mental well-being. The treatment or amelioration of symptoms can be
 based on objective or subjective parameters; including the results of a physical examination,

neuropsychiatric exams, and/or a psychiatric evaluation. The term "treating" and conjugations thereof, may include prevention of an injury, pathology, condition, or disease. In embodiments, treating is preventing. In embodiments, treating does not include preventing.

[0081] "Patient" or "subject in need thereof" refers to a living organism suffering from or prone to a disease or condition that can be treated by administration of a pharmaceutical composition as provided herein. Non-limiting examples include humans, other mammals, bovines, rats, mice, dogs, monkeys, goat, sheep, cows, deer, and other non-mammalian animals. In some embodiments, a patient is human.

[0082] A "effective amount" is an amount sufficient for a compound to accomplish a stated purpose relative to the absence of the compound (e.g. achieve the effect for which it is administered, treat a disease, reduce enzyme activity, increase enzyme activity, reduce a signaling pathway, or reduce one or more symptoms of a disease or condition). An example of an "effective amount" is an amount sufficient to contribute to the treatment, prevention, or reduction of a symptom or symptoms of a disease, which could also be referred to as a "therapeutically effective amount." A "reduction" of a symptom or symptoms (and grammatical equivalents of this phrase) means decreasing of the severity or frequency of the symptom(s), or elimination of the symptom(s). A "prophylactically effective amount" of a drug is an amount of a drug that, when administered to a subject, will have the intended prophylactic effect, e.g., preventing or delaying the onset (or reoccurrence) of an injury, disease, pathology or condition, or reducing the likelihood of the onset (or reoccurrence) of an injury, disease, pathology, or condition, or their symptoms. The full prophylactic effect does not necessarily occur by administration of one dose, and may occur only after administration of a series of doses. Thus, a prophylactically effective amount may be administered in one or more administrations. An "activity decreasing amount," as used herein, refers to an amount of antagonist required to decrease the activity of an enzyme relative to the absence of the antagonist. A "function disrupting amount," as used herein, refers to the amount of antagonist required to disrupt the function of an enzyme or protein relative to the absence of the antagonist. The exact amounts will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (*see, e.g.,* Lieberman, *Pharmaceutical Dosage Forms* (vols. 1-3, 1992); Lloyd, *The Art, Science and Technology of Pharmaceutical Compounding* (1999); Pickar, *Dosage Calculations* (1999); and *Remington: The Science and Practice of Pharmacy*, 20th Edition, 2003, Gennaro, Ed., Lippincott, Williams & Wilkins).

[0083] For any compound described herein, the therapeutically effective amount can be initially determined from cell culture assays. Target concentrations will be those concentrations of active compound(s) that are capable of achieving the methods described herein, as measured using the methods described herein or known in the art.

5 **[0084]** As is well known in the art, therapeutically effective amounts for use in humans can also be determined from animal models. For example, a dose for humans can be formulated to achieve a concentration that has been found to be effective in animals. The dosage in humans can be adjusted by monitoring compounds effectiveness and adjusting the dosage upwards or downwards, as described above. Adjusting the dose to achieve maximal efficacy
10 in humans based on the methods described above and other methods is well within the capabilities of the ordinarily skilled artisan.

[0085] Dosages may be varied depending upon the requirements of the patient and the compound being employed. The dose administered to a patient, in the context of the present invention should be sufficient to effect a beneficial therapeutic response in the patient over
15 time. The size of the dose also will be determined by the existence, nature, and extent of any adverse side-effects. Determination of the proper dosage for a particular situation is within the skill of the practitioner. Generally, treatment is initiated with smaller dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under circumstances is reached. Dosage amounts and
20 intervals can be adjusted individually to provide levels of the administered compound effective for the particular clinical indication being treated. This will provide a therapeutic regimen that is commensurate with the severity of the individual's disease state.

[0086] As used herein, the term "administering" means oral administration, administration as a suppository, topical contact, intravenous, intraperitoneal, intramuscular, intralesional,
25 intrathecal, intranasal or subcutaneous administration, or the implantation of a slow-release device, *e.g.*, a mini-osmotic pump, to a subject. Administration is by any route, including parenteral and transmucosal (*e.g.*, buccal, sublingual, palatal, gingival, nasal, vaginal, rectal, or transdermal) compatible with the preparation. Parenteral administration includes, *e.g.*, intravenous, intramuscular, intra-arteriole, intradermal, subcutaneous, intraperitoneal,
30 intraventricular, and intracranial. Other modes of delivery include, but are not limited to, the use of liposomal formulations, intravenous infusion, transdermal patches, *etc.*

[0087] "Co-administer" it is meant that a composition described herein is administered at the same time, just prior to, or just after the administration of one or more additional

therapies. The compounds of the invention can be administered alone or can be coadministered to the patient. Coadministration is meant to include simultaneous or sequential administration of the compounds individually or in combination (more than one compound). Thus, the preparations can also be combined, when desired, with other active substances (e.g. to reduce metabolic degradation). The compositions of the present invention can be delivered transdermally, by a topical route, or formulated as applicator sticks, solutions, suspensions, emulsions, gels, creams, ointments, pastes, jellies, paints, powders, and aerosols.

[0088] A “cell” as used herein, refers to a cell carrying out metabolic or other function sufficient to preserve or replicate its genomic DNA. A cell can be identified by well-known methods in the art including, for example, presence of an intact membrane, staining by a particular dye, ability to produce progeny or, in the case of a gamete, ability to combine with a second gamete to produce a viable offspring. Cells may include prokaryotic and eukaryotic cells. Prokaryotic cells include but are not limited to bacteria. Eukaryotic cells include but are not limited to yeast cells and cells derived from plants and animals, for example mammalian, insect (*e.g.*, *spodoptera*) and human cells. Cells may be useful when they are naturally nonadherent or have been treated not to adhere to surfaces, for example by trypsinization.

[0089] “Control” or “control experiment” is used in accordance with its plain ordinary meaning and refers to an experiment in which the subjects or reagents of the experiment are treated as in a parallel experiment except for omission of a procedure, reagent, or variable of the experiment. In some instances, the control is used as a standard of comparison in evaluating experimental effects. In some embodiments, a control is the measurement of the activity of a protein in the absence of a compound as described herein (including embodiments and examples).

[0090] The term “modulator” refers to a composition that increases or decreases the level of a target molecule or the function of a target molecule or the physical state of the target of the molecule. In some embodiments, an Bruton’s Tyrosine Kinase associated disease modulator is a compound that reduces the severity of one or more symptoms of a disease associated with Bruton’s Tyrosine Kinase (*e.g.* cancer, inflammatory disease). A Bruton’s Tyrosine Kinase modulator is a compound that increases or decreases the activity or function or level of activity or level of function of Bruton’s Tyrosine Kinase.

[0091] The term “modulate” is used in accordance with its plain ordinary meaning and refers to the act of changing or varying one or more properties. “Modulation” refers to the

process of changing or varying one or more properties. For example, as applied to the effects of a modulator on a target protein, to modulate means to change by increasing or decreasing a property or function of the target molecule or the amount of the target molecule.

[0092] The term “associated” or “associated with” in the context of a substance or substance activity or function associated with a disease (e.g. a protein associated disease, a cancer associated with Bruton’s Tyrosine Kinase activity, Bruton’s Tyrosine Kinase associated cancer, Bruton’s Tyrosine Kinase associated disease) means that the disease (e.g. cancer, inflammatory disease) is caused by (in whole or in part), or a symptom of the disease is caused by (in whole or in part) the substance or substance activity or function. For example, a cancer associated with Bruton’s Tyrosine Kinase activity or function may be a cancer that results (entirely or partially) from aberrant Bruton’s Tyrosine Kinase function (e.g. enzyme activity, protein-protein interaction, signaling pathway) or a cancer wherein a particular symptom of the disease is caused (entirely or partially) by aberrant Bruton’s Tyrosine Kinase activity or function. As used herein, what is described as being associated with a disease, if a causative agent, could be a target for treatment of the disease. For example, a cancer associated with Bruton’s Tyrosine Kinase activity or function or a Bruton’s Tyrosine Kinase associated cancer, may be treated with a Bruton’s Tyrosine Kinase modulator or Bruton’s Tyrosine Kinase inhibitor, in the instance where increased Bruton’s Tyrosine Kinase activity or function (e.g. signaling pathway activity) causes the cancer. For example, an inflammatory disease associated with Bruton’s Tyrosine Kinase activity or function or an Bruton’s Tyrosine Kinase associated inflammatory disease, may be treated with an Bruton’s Tyrosine Kinase modulator or Bruton’s Tyrosine Kinase inhibitor, in the instance where increased Bruton’s Tyrosine Kinase activity or function (e.g. signaling pathway activity) causes the disease.

[0093] The term “aberrant” as used herein refers to different from normal. When used to describe enzymatic activity or protein function, aberrant refers to activity or function that is greater or less than a normal control or the average of normal non-diseased control samples. Aberrant activity may refer to an amount of activity that results in a disease, wherein returning the aberrant activity to a normal or non-disease-associated amount (e.g. by administering a compound or using a method as described herein), results in reduction of the disease or one or more disease symptoms.

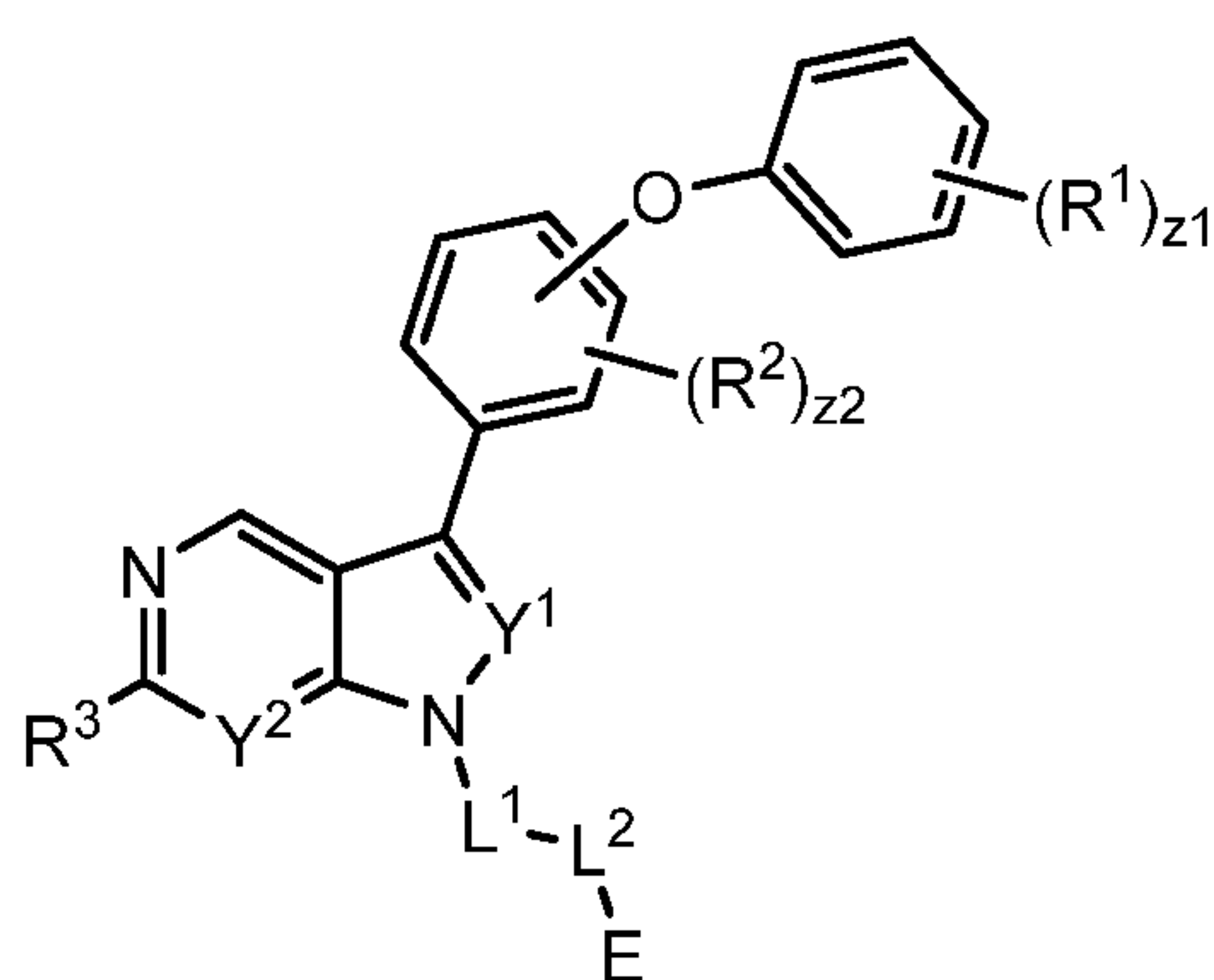
[0094] The term “signaling pathway” as used herein refers to a series of interactions between cellular and optionally extra-cellular components (e.g. proteins, nucleic acids, small

molecules, ions, lipids) that conveys a change in one component to one or more other components, which in turn may convey a change to additional components, which is optionally propagated to other signaling pathway components. For example, binding of a Bruton's Tyrosine Kinase with a compound as described herein may reduce the level of a product of the Bruton's Tyrosine Kinase catalyzed reaction or the level of a downstream derivative of the product or binding may reduce the interactions between the Bruton's Tyrosine Kinase enzyme or an Bruton's Tyrosine Kinase reaction product and downstream effectors or signaling pathway components, resulting in changes in cell growth, proliferation, or survival.

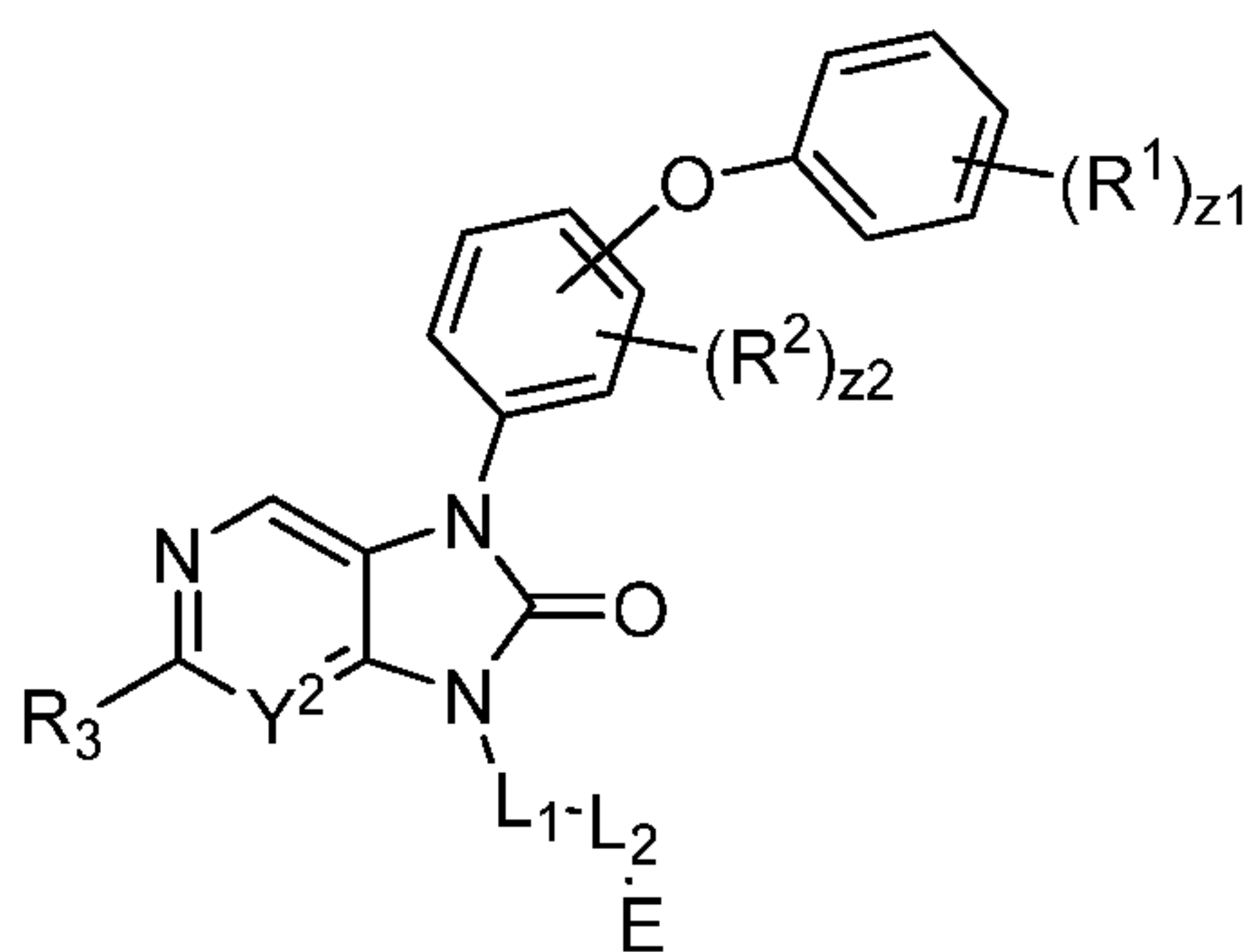
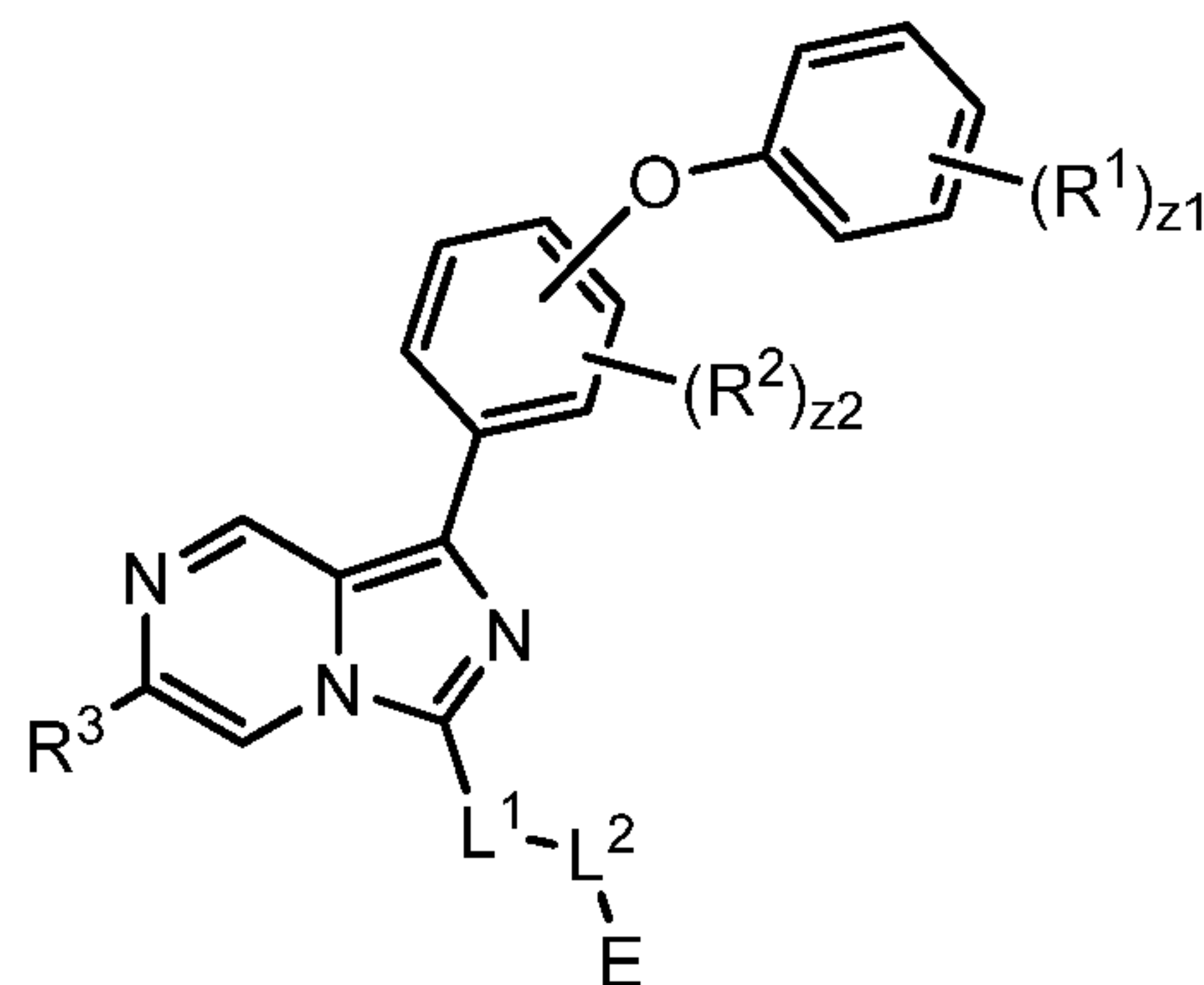
10 [0095] The term "electrophilic chemical moiety" is used in accordance with its plain ordinary chemical meaning and refers to a monovalent chemical group that is electrophilic.

II. Compounds

[0096] In an aspect is provided a compound having the formula:



(I) or



15 (II) or

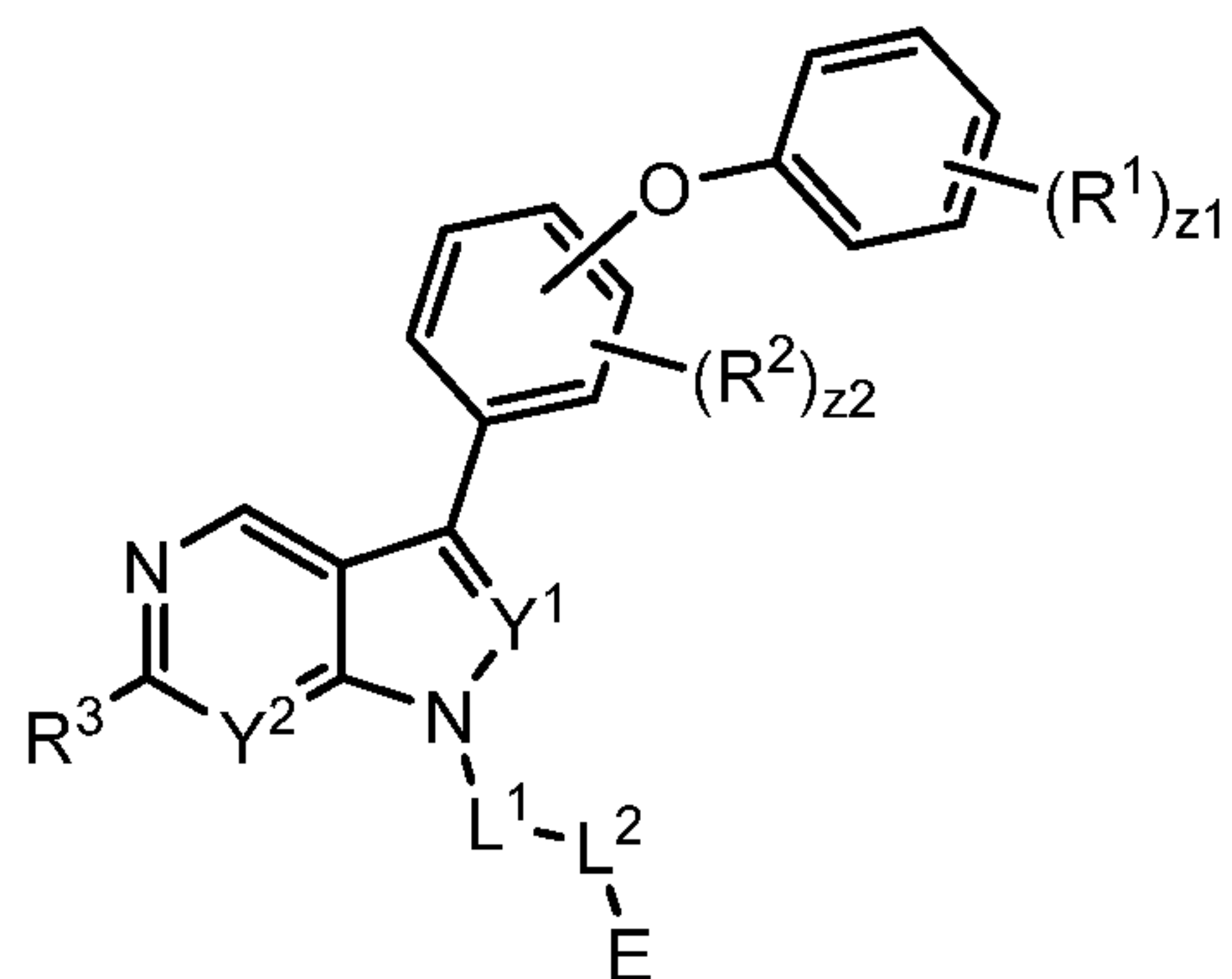
(III).

[0097] R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, $-CN$, $-SO_{nl}R^{1D}$, $-SO_{vl}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{ml}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. Two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl,

substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbol $z1$ is an integer from 0 to 5. R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, $-CN$, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. Two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbol $z2$ is an integer from 0 to 4. R^3 is hydrogen or $-NH_2$. The symbol Y^1 is N or $C(R^4)$. R^4 is hydrogen, halogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, $-CN$, $-SO_{n4}R^{4D}$, $-SO_{v4}NR^{4A}R^{4B}$, $-NHC(O)NR^{4A}R^{4B}$, $-N(O)_{m4}$, $-NR^{4A}R^{4B}$, $-C(O)R^{4C}$, $-C(O)-OR^{4C}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4D}$, $-NR^{4A}SO_2R^{4D}$, $-NR^{4A}C(O)R^{4C}$, $-NR^{4A}C(O)OR^{4C}$, $-NR^{4A}OR^{4C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbol Y^2 is N or $C(R^5)$. R^5 is hydrogen, halogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, $-CN$, $-SO_{n5}R^{5D}$, $-SO_{v5}NR^{5A}R^{5B}$, $-NHC(O)NR^{5A}R^{5B}$, $-N(O)_{m5}$, $-NR^{5A}R^{5B}$, $-C(O)R^{5C}$, $-C(O)-OR^{5C}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5D}$, $-NR^{5A}SO_2R^{5D}$, $-NR^{5A}C(O)R^{5C}$, $-NR^{5A}C(O)OR^{5C}$, $-NR^{5A}OR^{5C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^6-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^6-$, $-NR^6C(O)-$, $-NR^6C(O)NH-$, $-NHC(O)NR^6-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene. R^6 is hydrogen, halogen, $-CX^6_3$, $-CHX^6_2$, $-CH_2X^6$, $-OCX^6_3$, $-OCH_2X^6$, $-OCHX^6_2$, $-CN$, $-SO_{n6}R^{6D}$, $-SO_{v6}NR^{6A}R^{6B}$, $-NHC(O)NR^{6A}R^{6B}$, $-N(O)_{m6}$, $-NR^{6A}R^{6B}$, $-C(O)R^{6C}$, $-C(O)-OR^{6C}$, $-C(O)NR^{6A}R^{6B}$, $-OR^{6D}$, $-NR^{6A}SO_2R^{6D}$, $-NR^{6A}C(O)R^{6C}$, $-NR^{6A}C(O)OR^{6C}$, $-NR^{6A}OR^{6C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. L^2 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^7-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^7-$, $-NR^7C(O)-$, $-NR^7C(O)NH-$, $-NHC(O)NR^7-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or

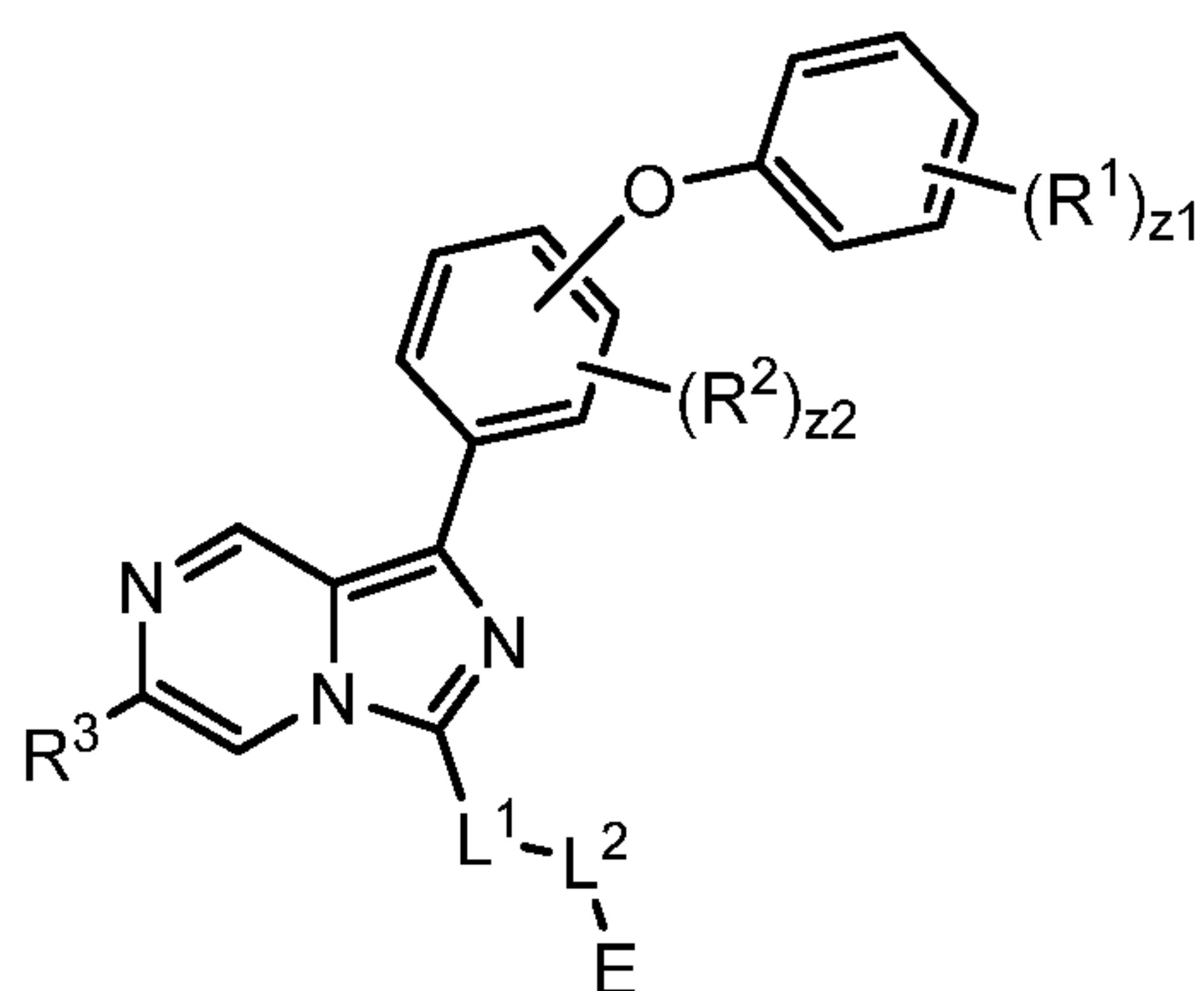
unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or
 unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or
 unsubstituted heteroarylene. R^7 is hydrogen, halogen, $-CX^7_3$, $-CHX^7_2$, $-CH_2X^7$, $-OCX^7_3$, $-$
 OCH_2X^7 , $-OCHX^7_2$, $-CN$, $-SO_{n7}R^{7D}$, $-SO_{v7}NR^{7A}R^{7B}$, $-NHC(O)NR^{7A}R^{7B}$, $-N(O)_{m7}$, $-NR^{7A}R^{7B}$,
 5 $-C(O)R^{7C}$, $-C(O)-OR^{7C}$, $-C(O)NR^{7A}R^{7B}$, $-OR^{7D}$, $-NR^{7A}SO_2R^{7D}$, $-NR^{7A}C(O)R^{7C}$, $-NR^{7A}C(O)O$
 R^{7C} , $-NR^{7A}OR^{7C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl,
 substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl,
 substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. E is an
 electrophilic moiety. Each R^{1A} , R^{1B} , R^{1C} , R^{1D} , R^{2A} , R^{2B} , R^{2C} , R^{2D} , R^{4A} , R^{4B} , R^{4C} , R^{4D} , R^{5A} ,
 10 R^{5B} , R^{5C} , R^{5D} , R^{6A} , R^{6B} , R^{6C} , R^{6D} , R^{7A} , R^{7B} , R^{7C} , and R^{7D} is independently
 hydrogen, $-CX_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl,
 substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or
 unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or
 unsubstituted heteroaryl. R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may
 15 optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or
 unsubstituted heteroaryl. R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may
 optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or
 unsubstituted heteroaryl. R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may
 optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or
 20 unsubstituted heteroaryl. R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may
 optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or
 unsubstituted heteroaryl. R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may
 optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or
 unsubstituted heteroaryl. R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may
 25 optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or
 unsubstituted heteroaryl. Each X, X^1 , X^2 , X^4 , X^5 , X^6 , and X^7 is independently $-F$, $-Cl$, $-Br$, or
 $-I$. The symbols $n1$, $n2$, $n4$, $n5$, $n6$, and $n7$ are independently an integer from 0 to 4. The
 symbols $m1$, $m2$, $m4$, $m5$, $m6$, $m7$, $v1$, $v2$, $v4$, $v5$, $v6$, and $v7$ are independently an integer
 from 1 to 2.

30 **[0098]** In embodiments, the compound has the formula



(I). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , $z1$, $z2$, and E are as described herein.

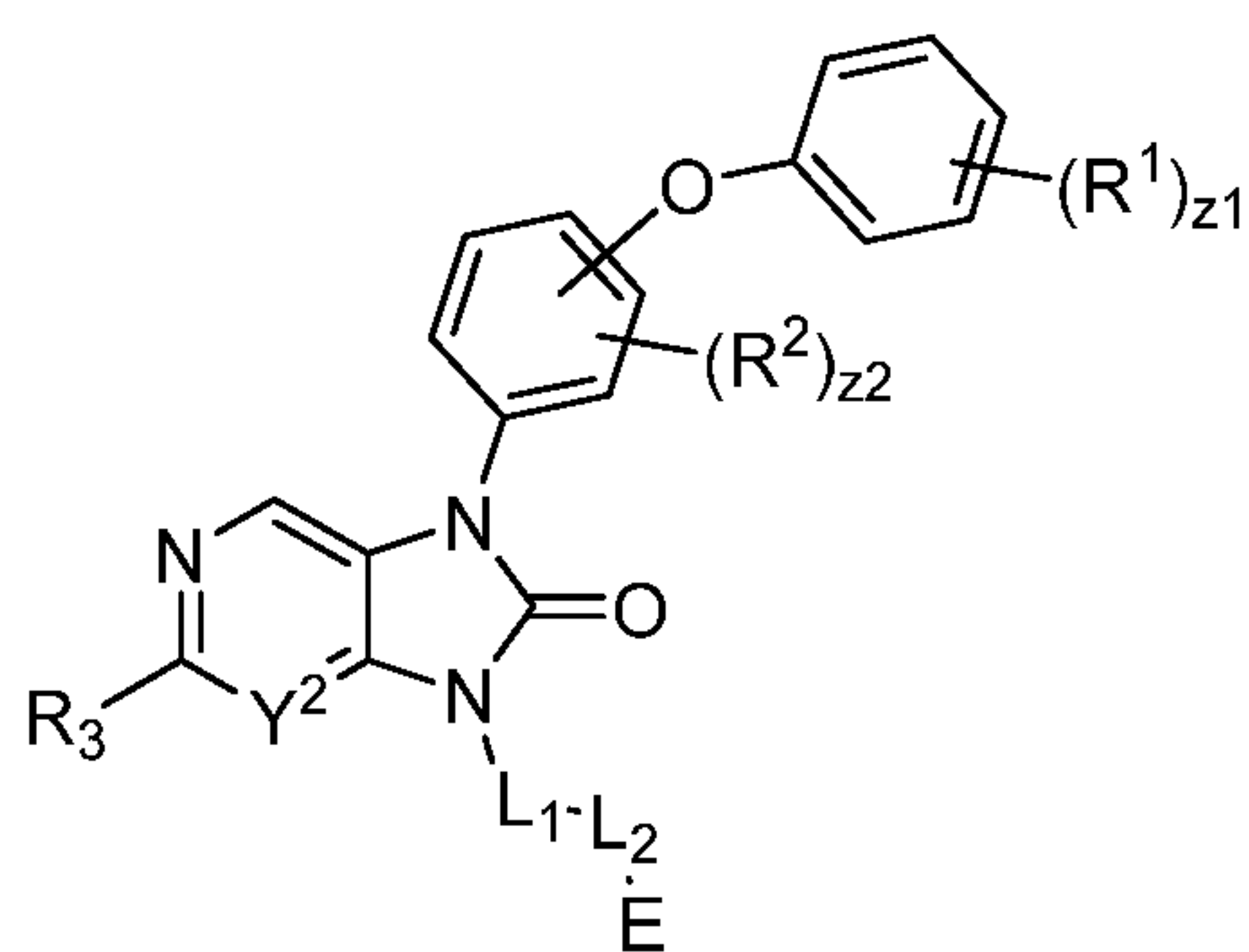
[0099] In embodiments, the compound has the formula



(II). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, $z2$, and E are as described

5 herein.

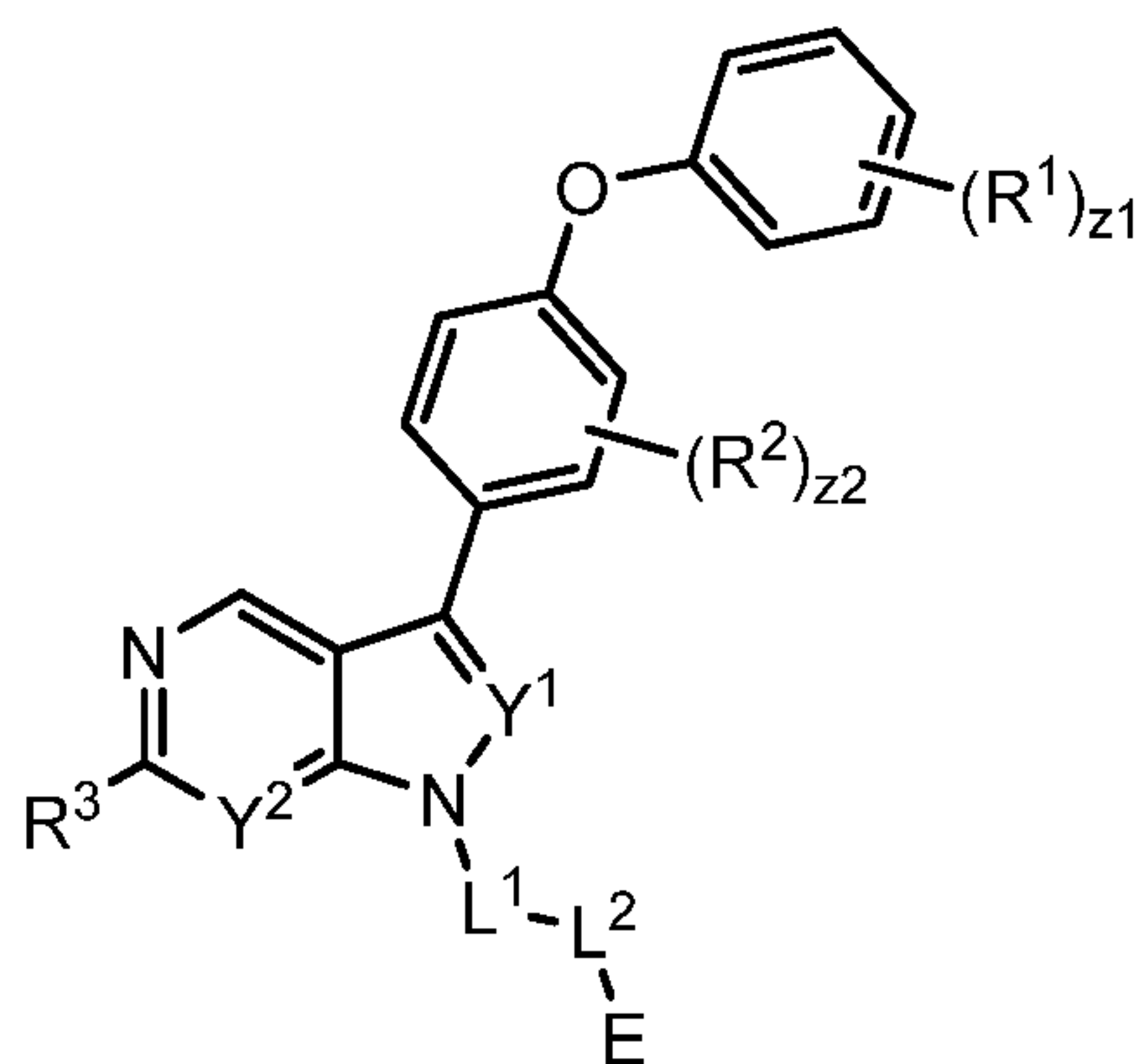
[0100] In embodiments, the compound has the formula



(III). R^1 , R^2 , R^3 , L^1 , L^2 , Y^2 , $z1$, $z2$, and E are as described

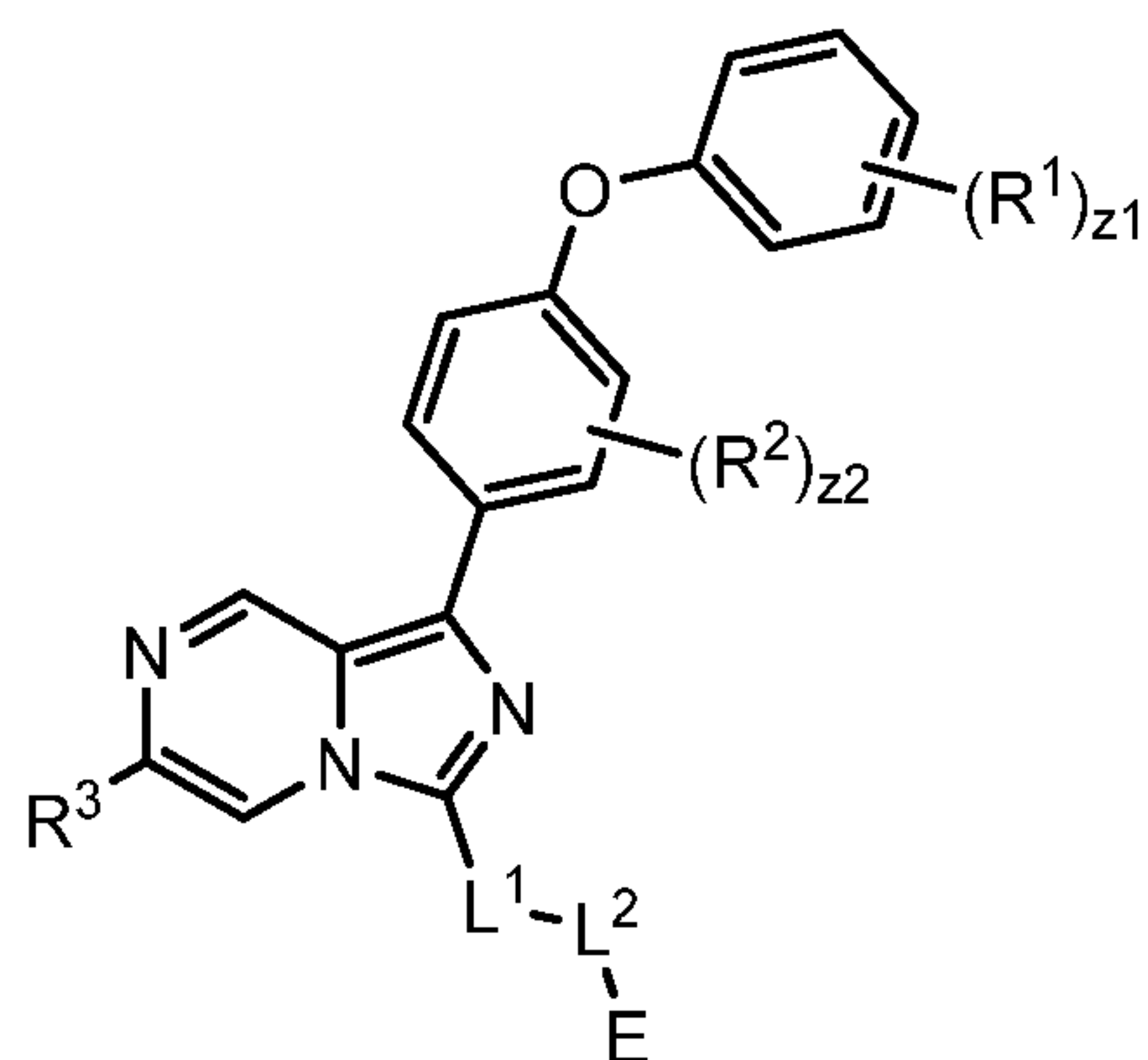
herein.

[0101] In embodiments, the compound has the formula



(IA). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , z_1 , z_2 , and E are as described herein.

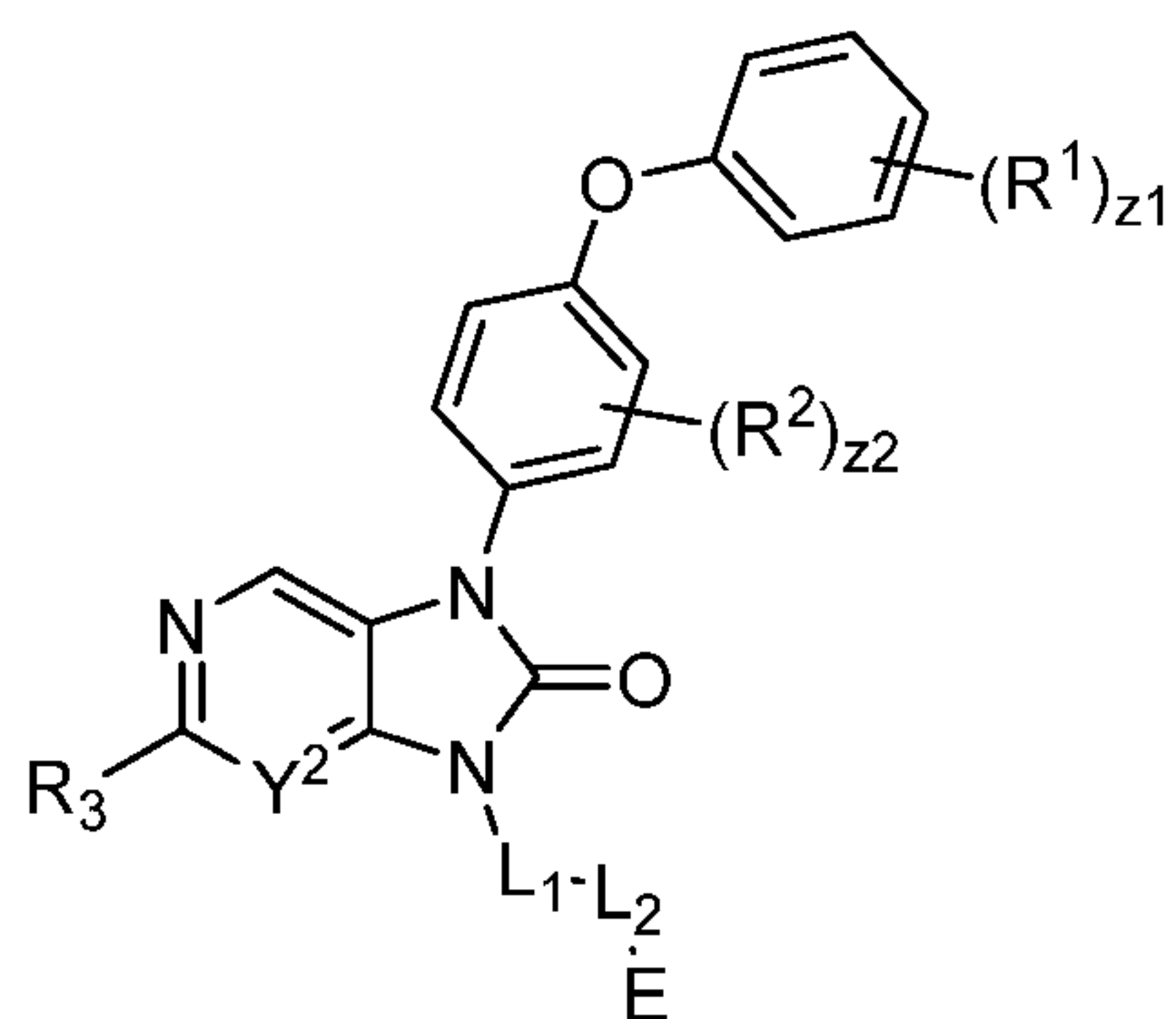
[0102] In embodiments, the compound has the formula



(IIA). R^1 , R^2 , R^3 , L^1 , L^2 , z_1 , z_2 , and E are as described

5 herein.

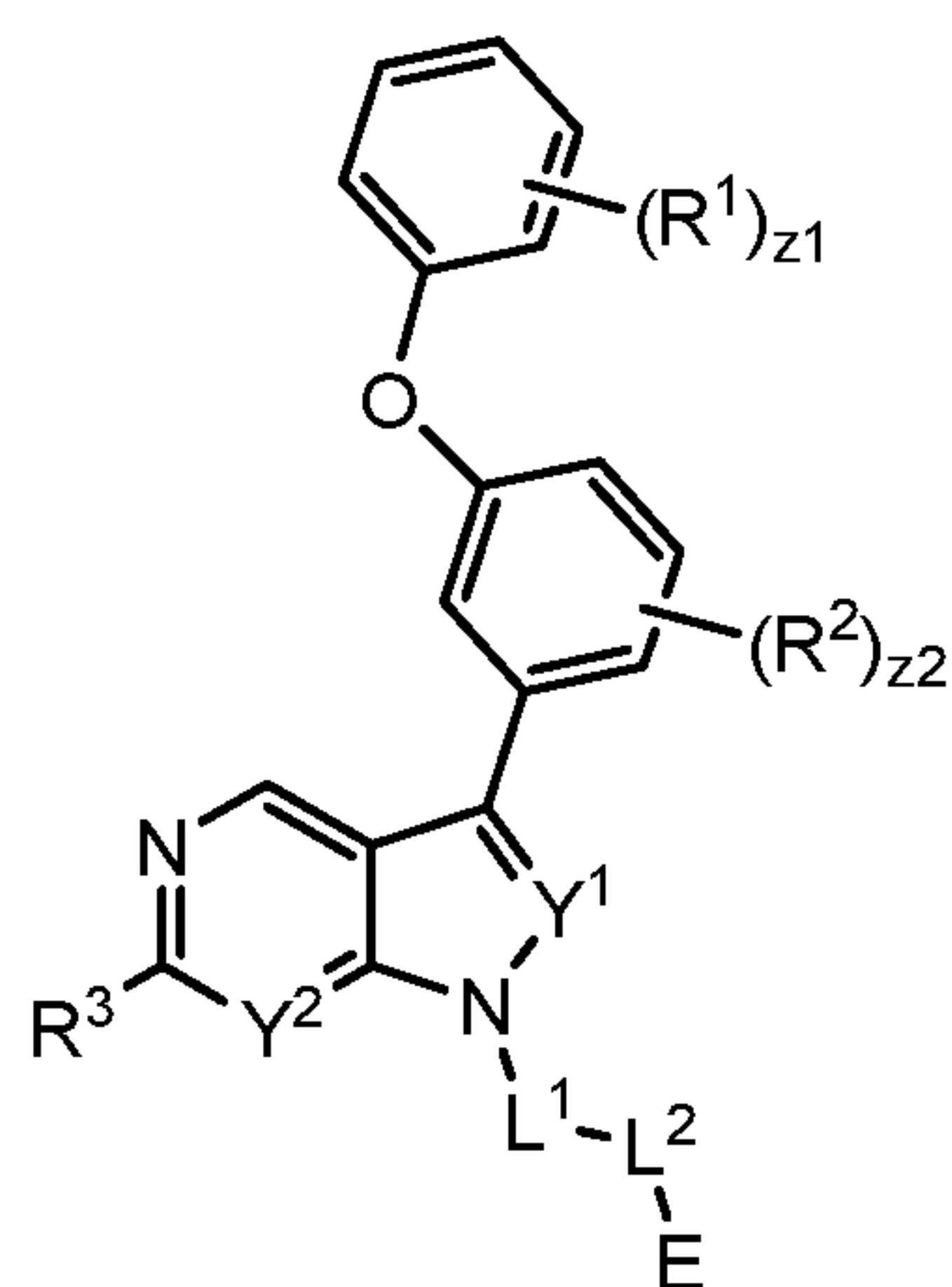
[0103] In embodiments, the compound has the formula



(IIIA). R^1 , R^2 , R^3 , L^1 , L^2 , Y^2 , z_1 , z_2 , and E are as described

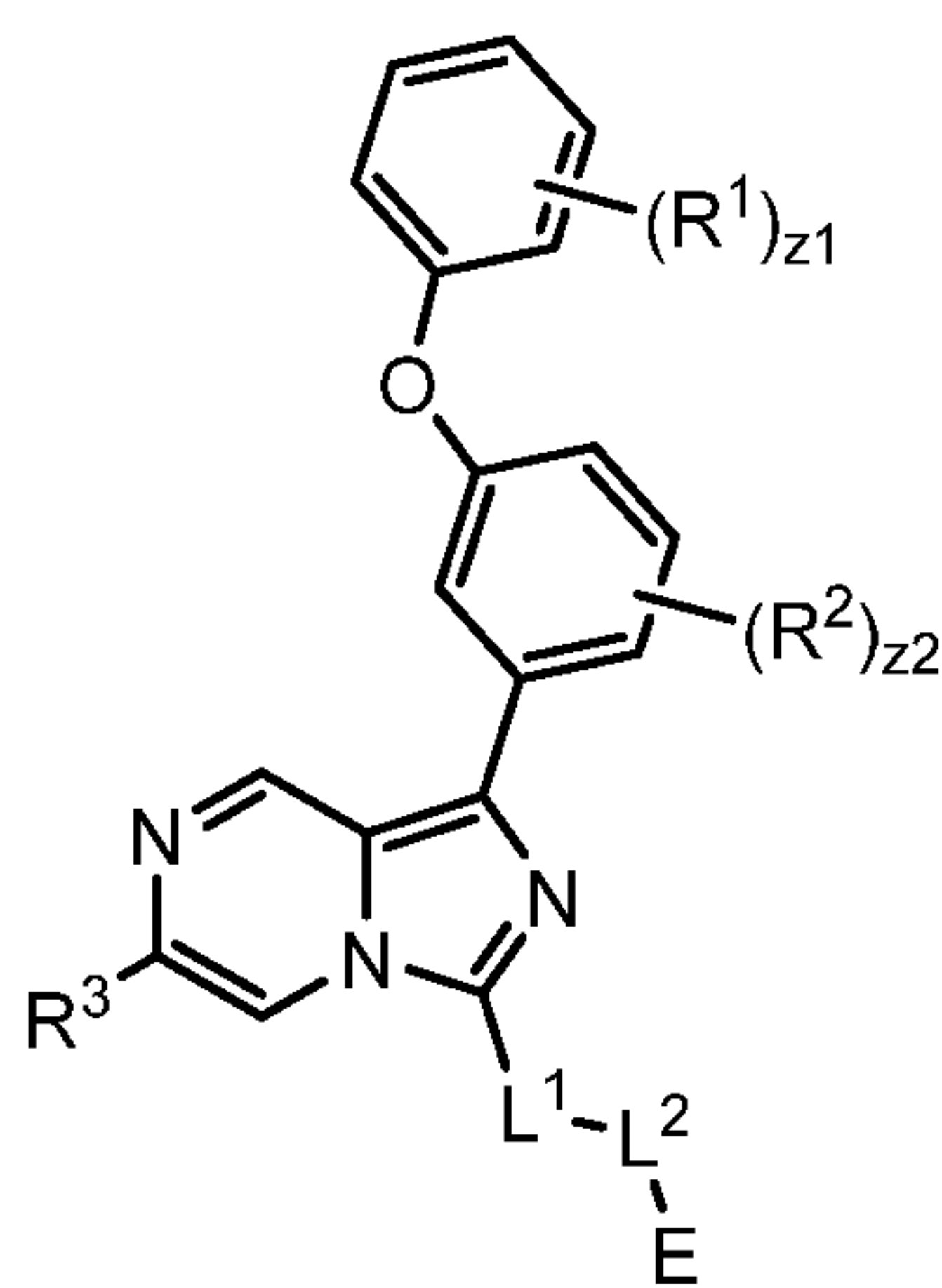
herein.

[0104] In embodiments, the compound has the formula



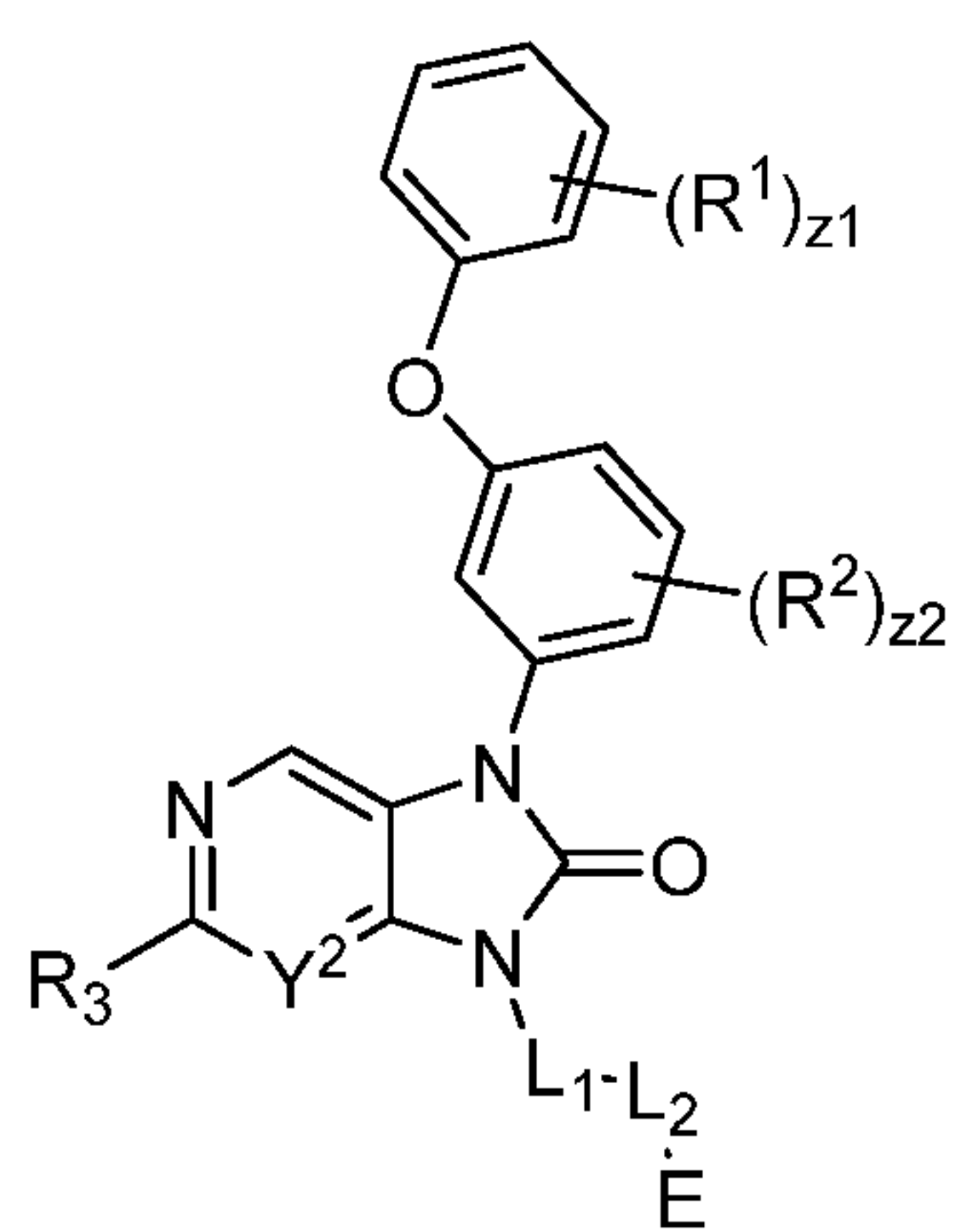
(IB). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , z_1 , z_2 , and E are as described herein.

[0105] In embodiments, the compound has the formula



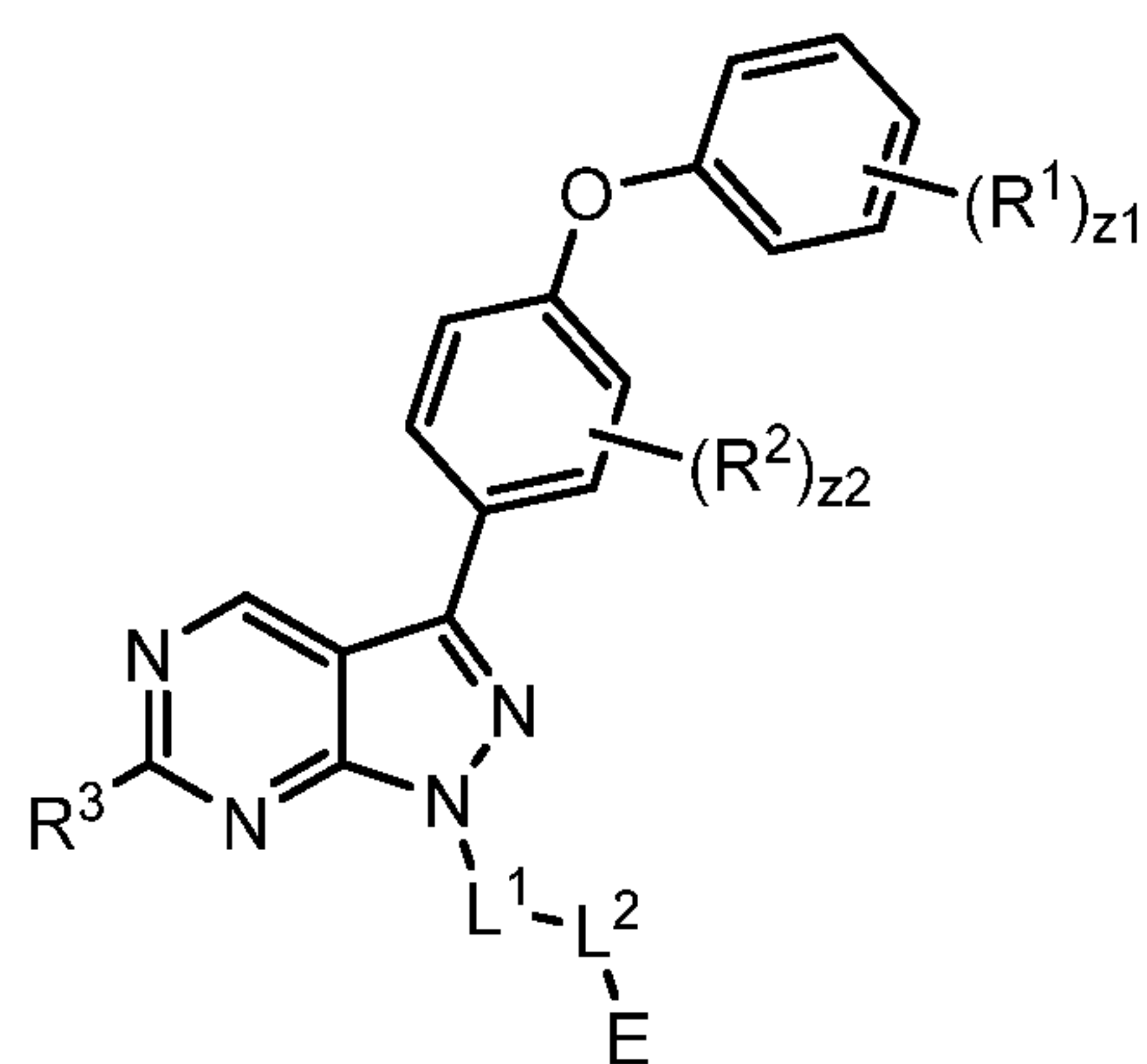
(IIB). R^1 , R^2 , R^3 , L^1 , L^2 , z_1 , z_2 , and E are as described herein.

5 [0106] In embodiments, the compound has the formula



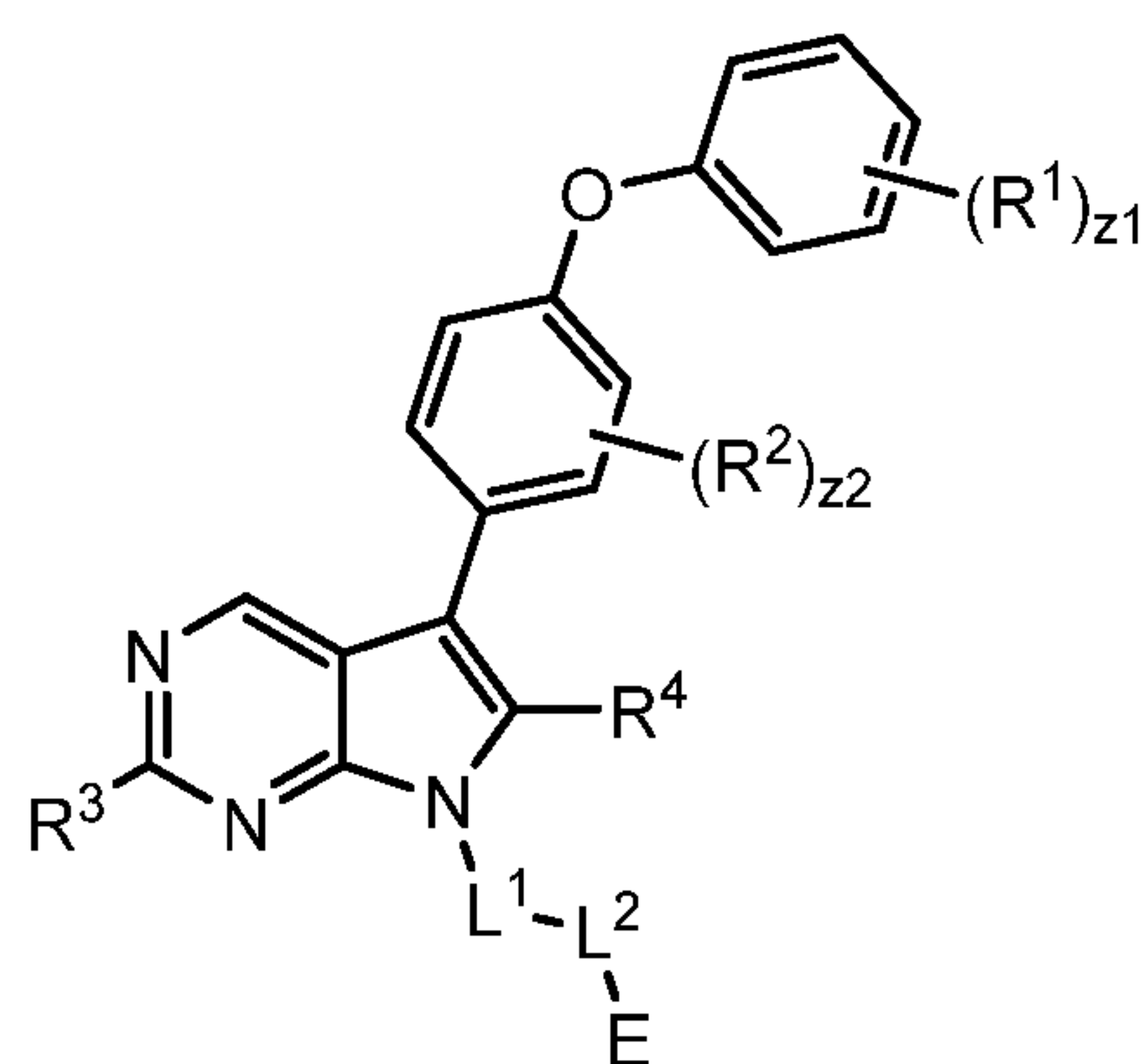
(IIIB). R^1 , R^2 , R^3 , L^1 , L^2 , Y^2 , z_1 , z_2 , and E are as described herein.

[0107] In embodiments, the compound has the formula



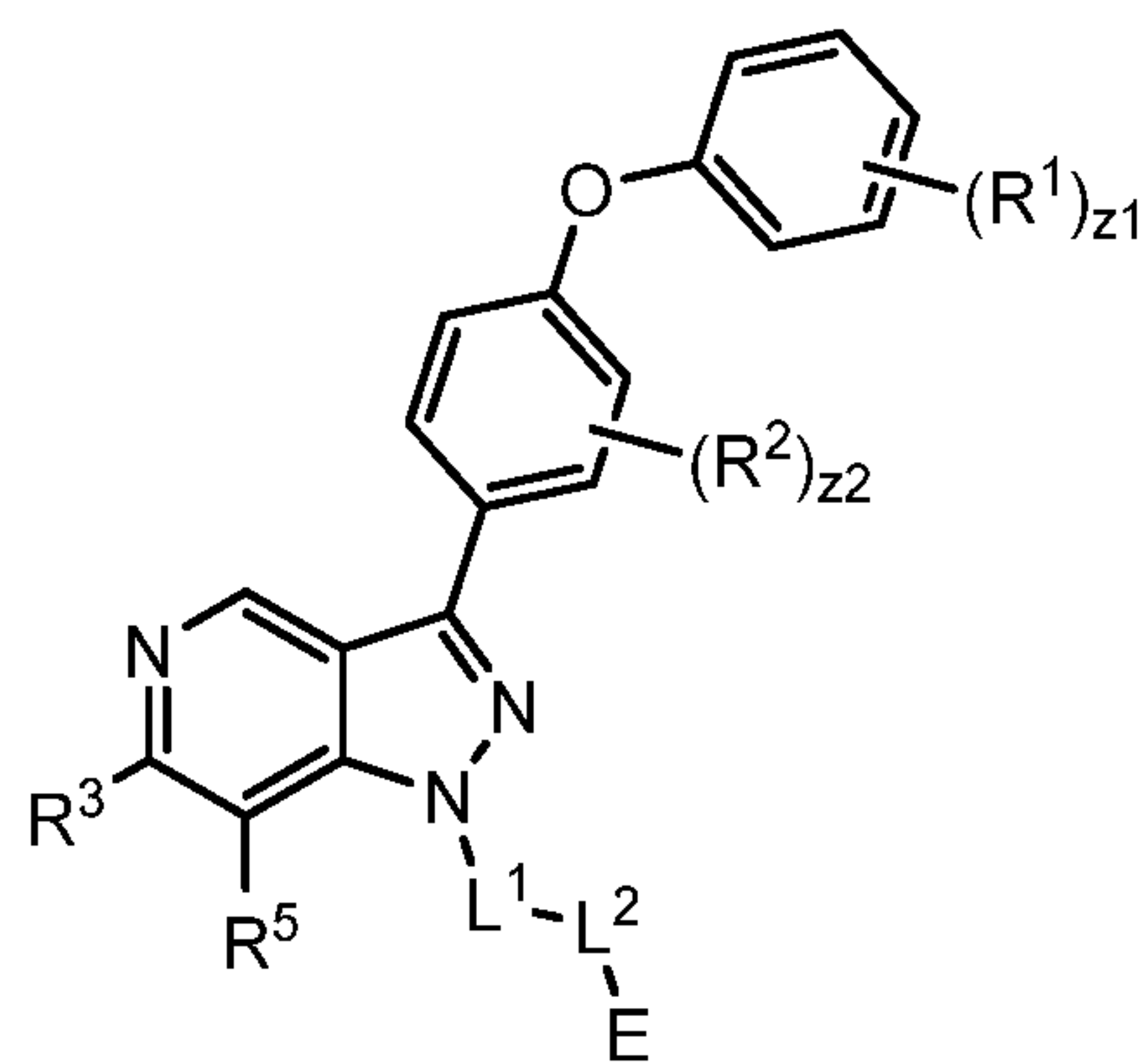
(IC). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, $z2$, and E are as described herein.

[0108] In embodiments, the compound has the formula



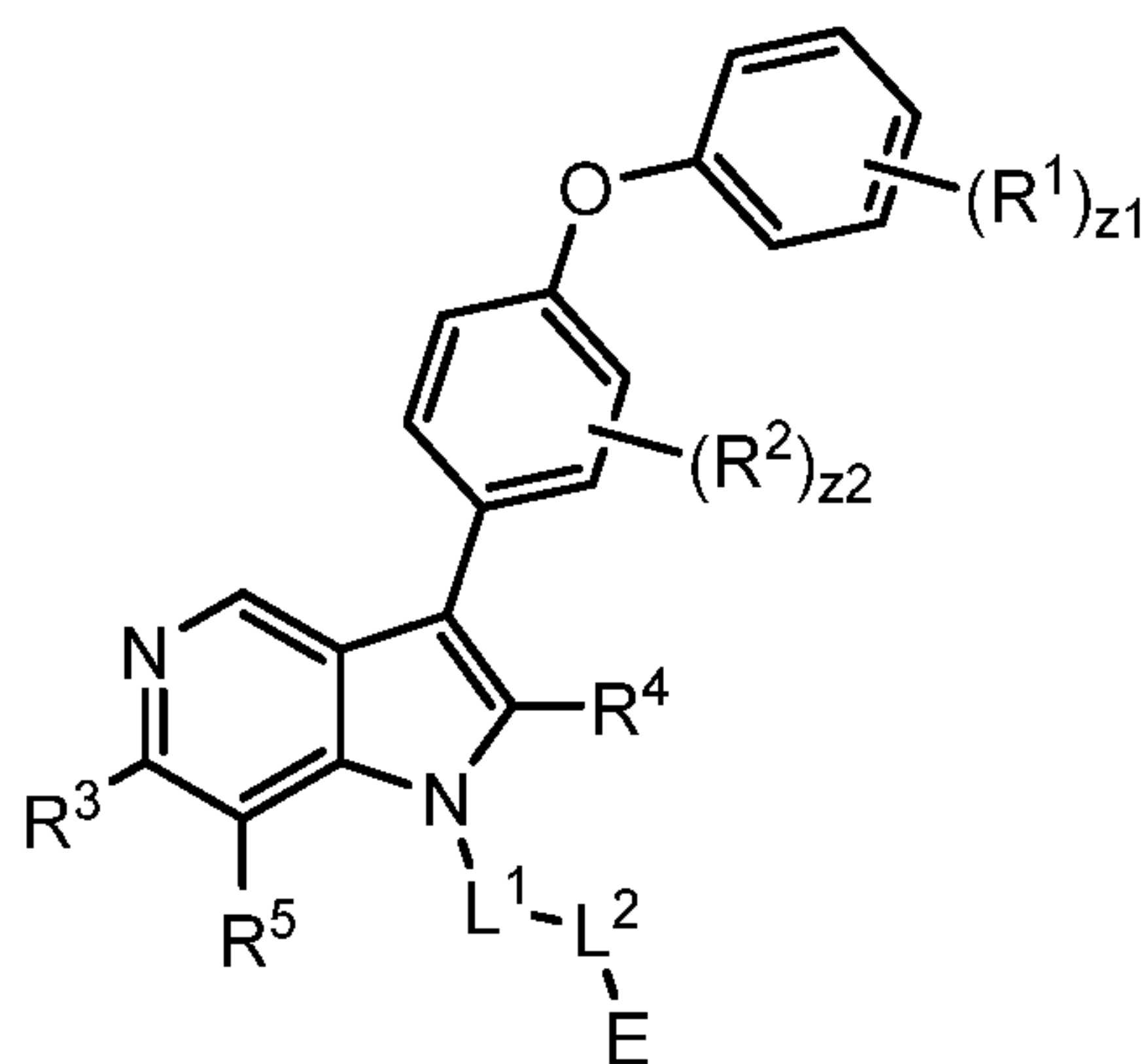
(ID). R^1 , R^2 , R^3 , R^4 , L^1 , L^2 , $z1$, $z2$, and E are as described herein.

[0109] In embodiments, the compound has the formula



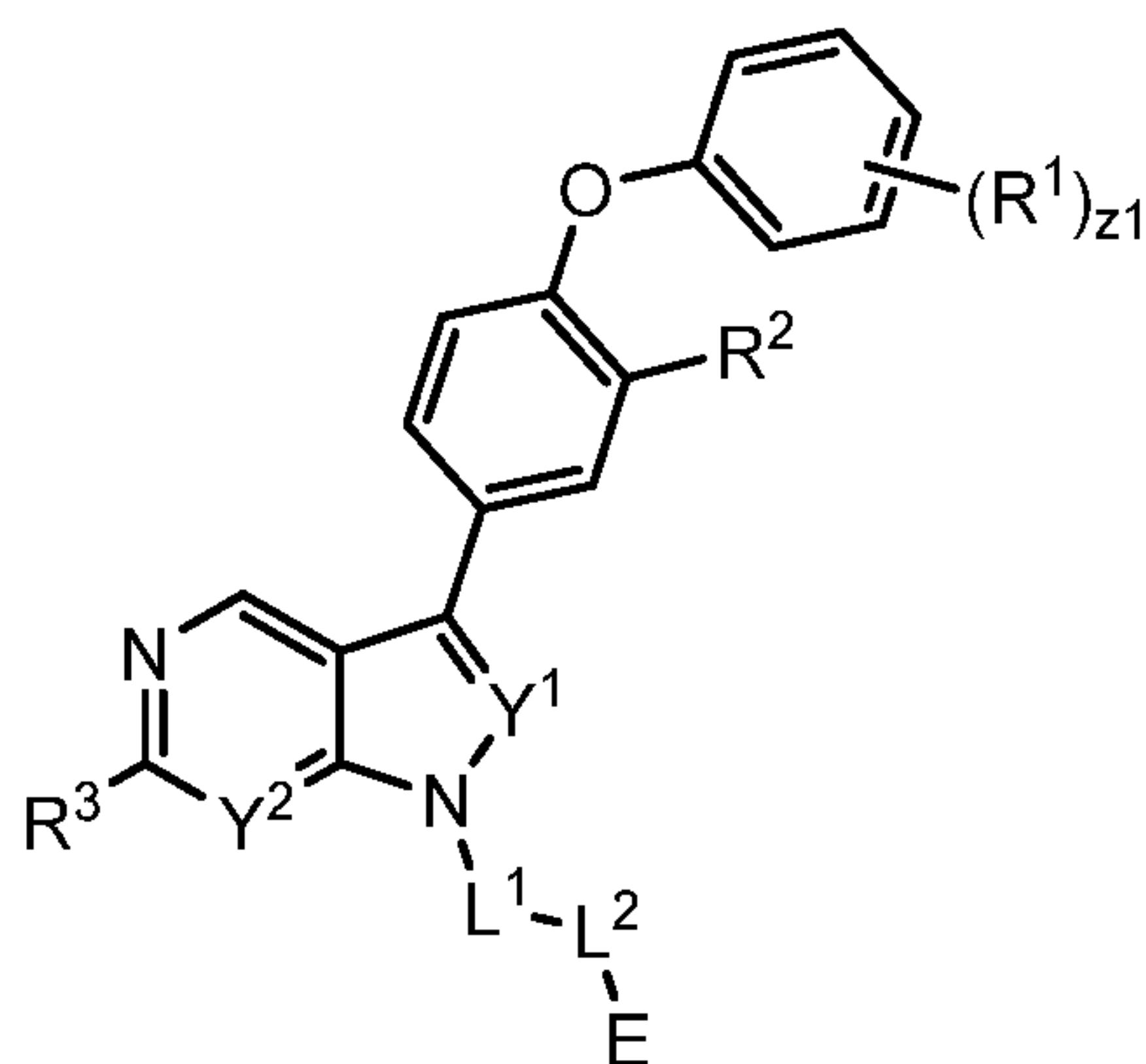
(IE). R^1 , R^2 , R^3 , R^5 , L^1 , L^2 , $z1$, $z2$, and E are as described herein.

[0110] In embodiments, the compound has the formula



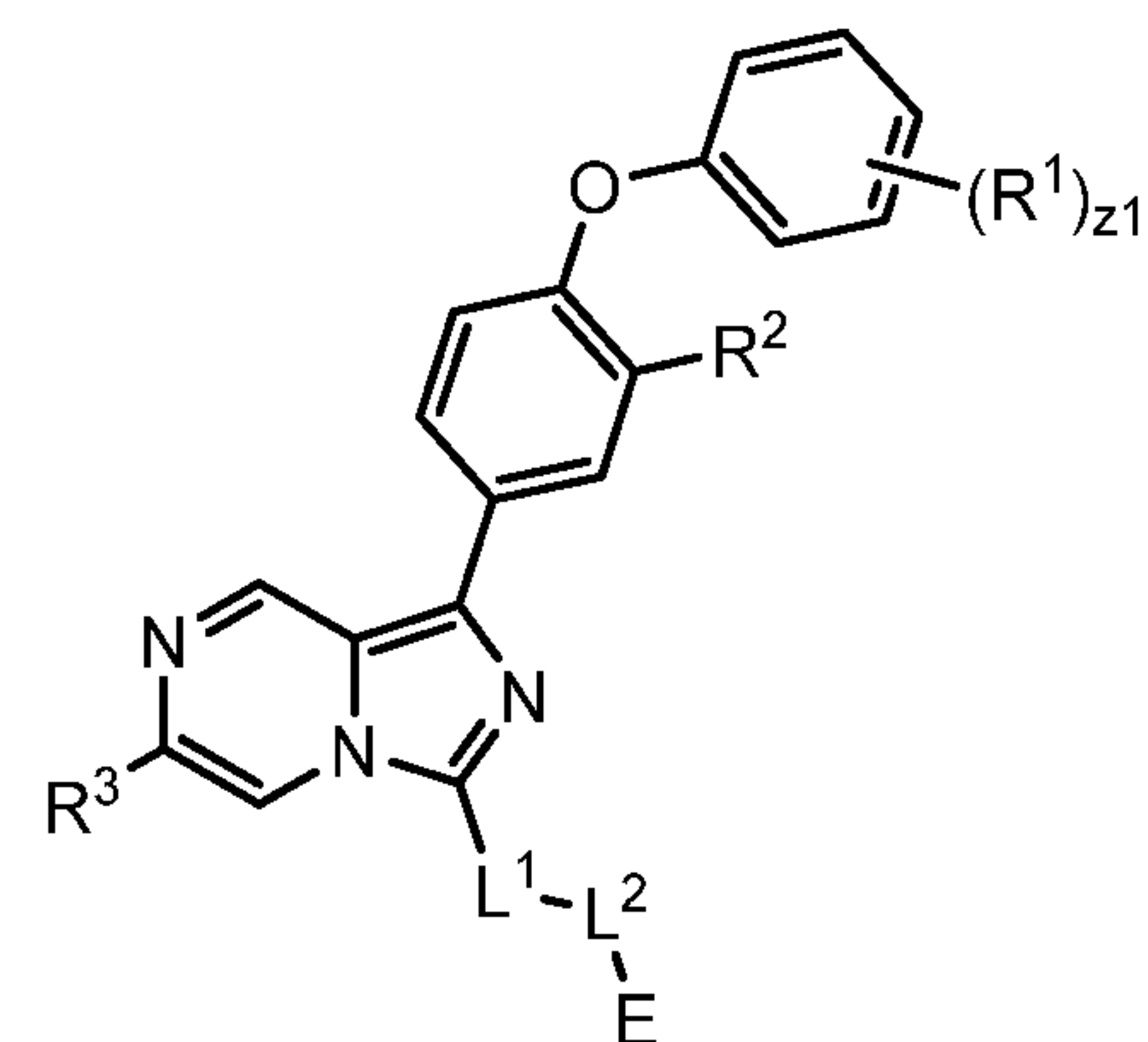
(IF). R^1 , R^2 , R^3 , R^4 , R^5 , L^1 , L^2 , $z1$, $z2$, and E are as described herein.

[0111] In embodiments, the compound has the formula



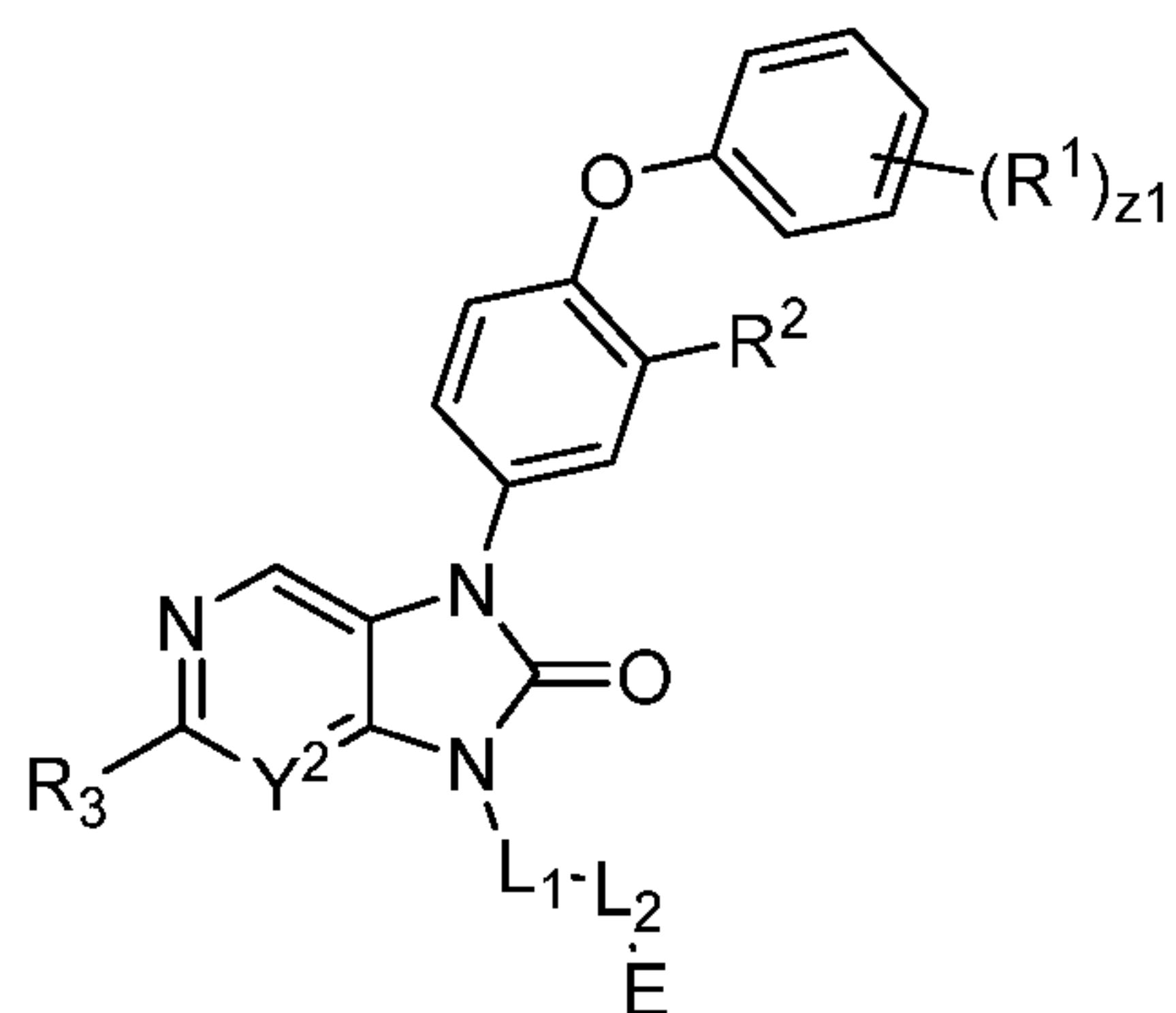
(IAi). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , $z1$, and E are as described
5 herein.

[0112] In embodiments, the compound has the formula



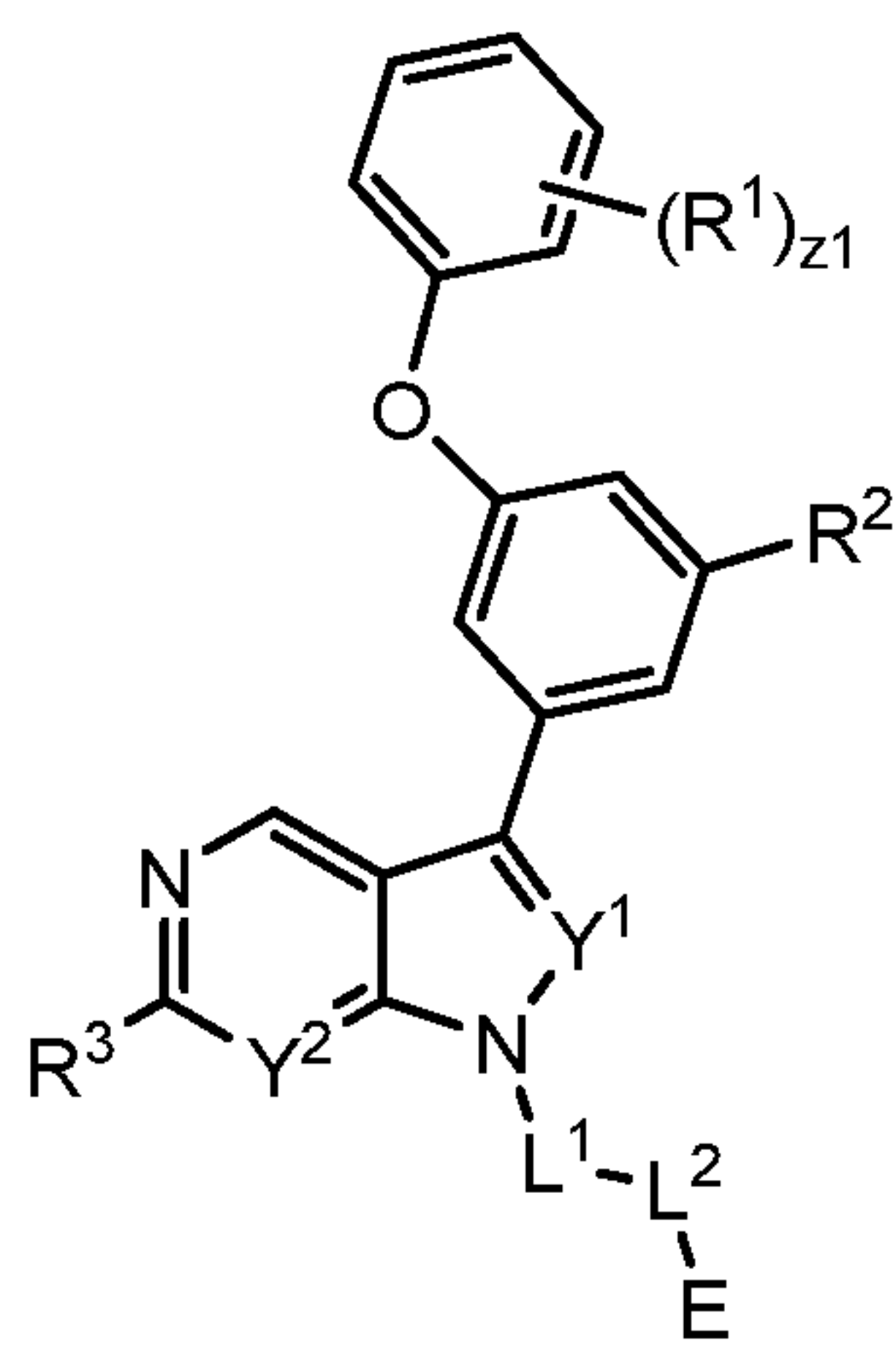
(IIAi). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, and E are as described herein.

[0113] In embodiments, the compound has the formula



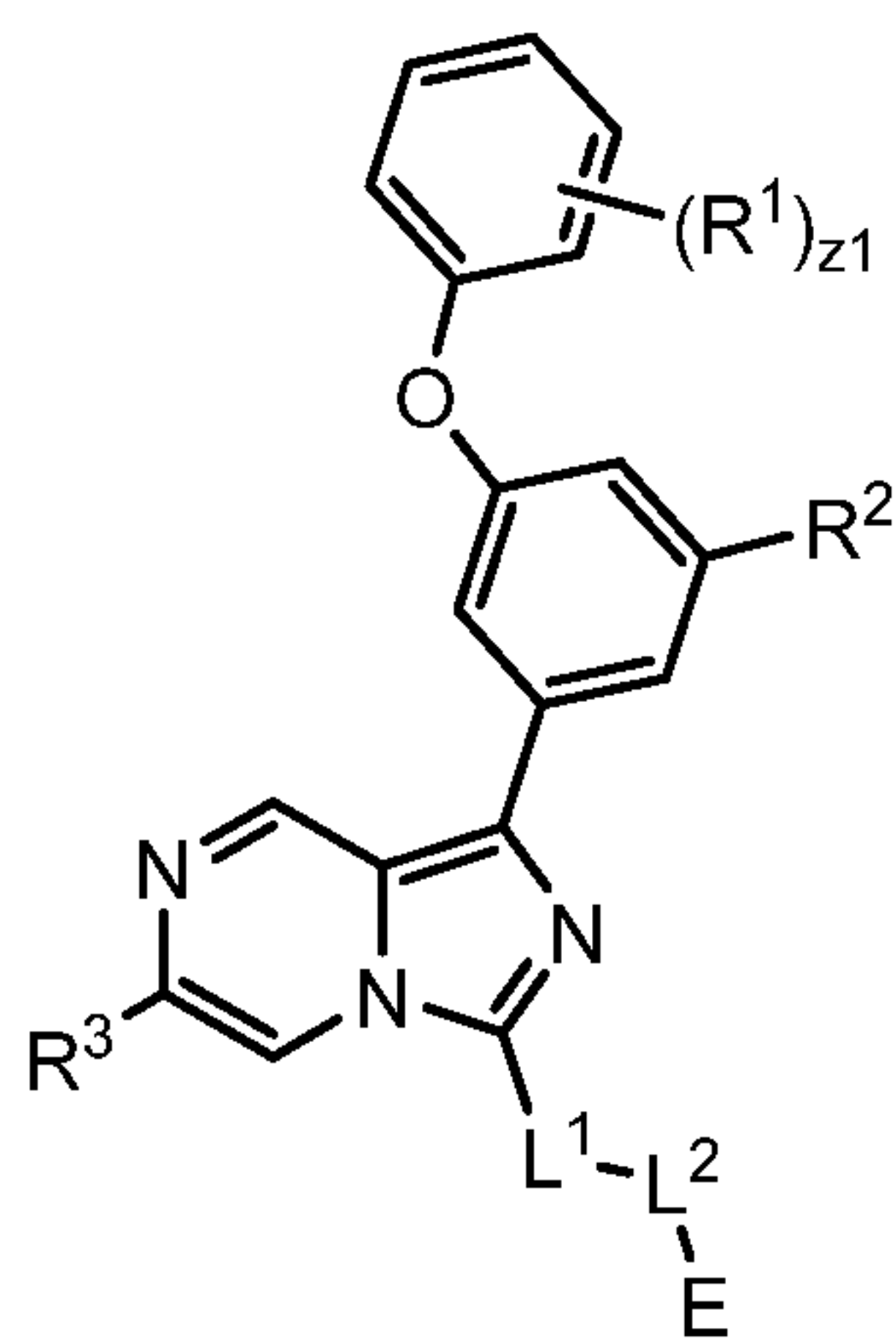
(IIIAi). R^1 , R^2 , R^3 , L^1 , L^2 , Y^2 , $z1$, and E are as described herein.

[0114] In embodiments, the compound has the formula



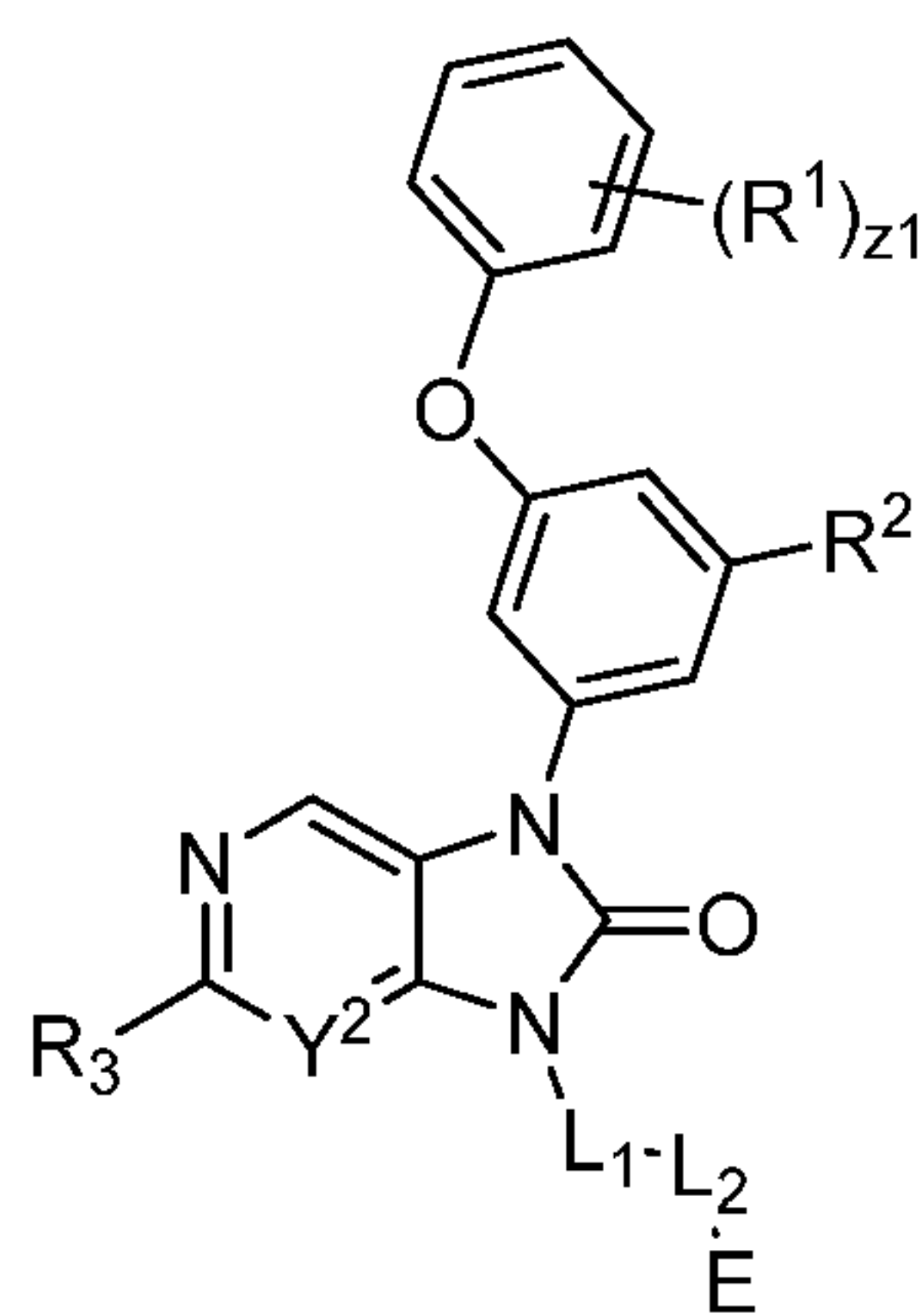
(IBi). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , $z1$, and E are as described herein.

5 [0115] In embodiments, the compound has the formula



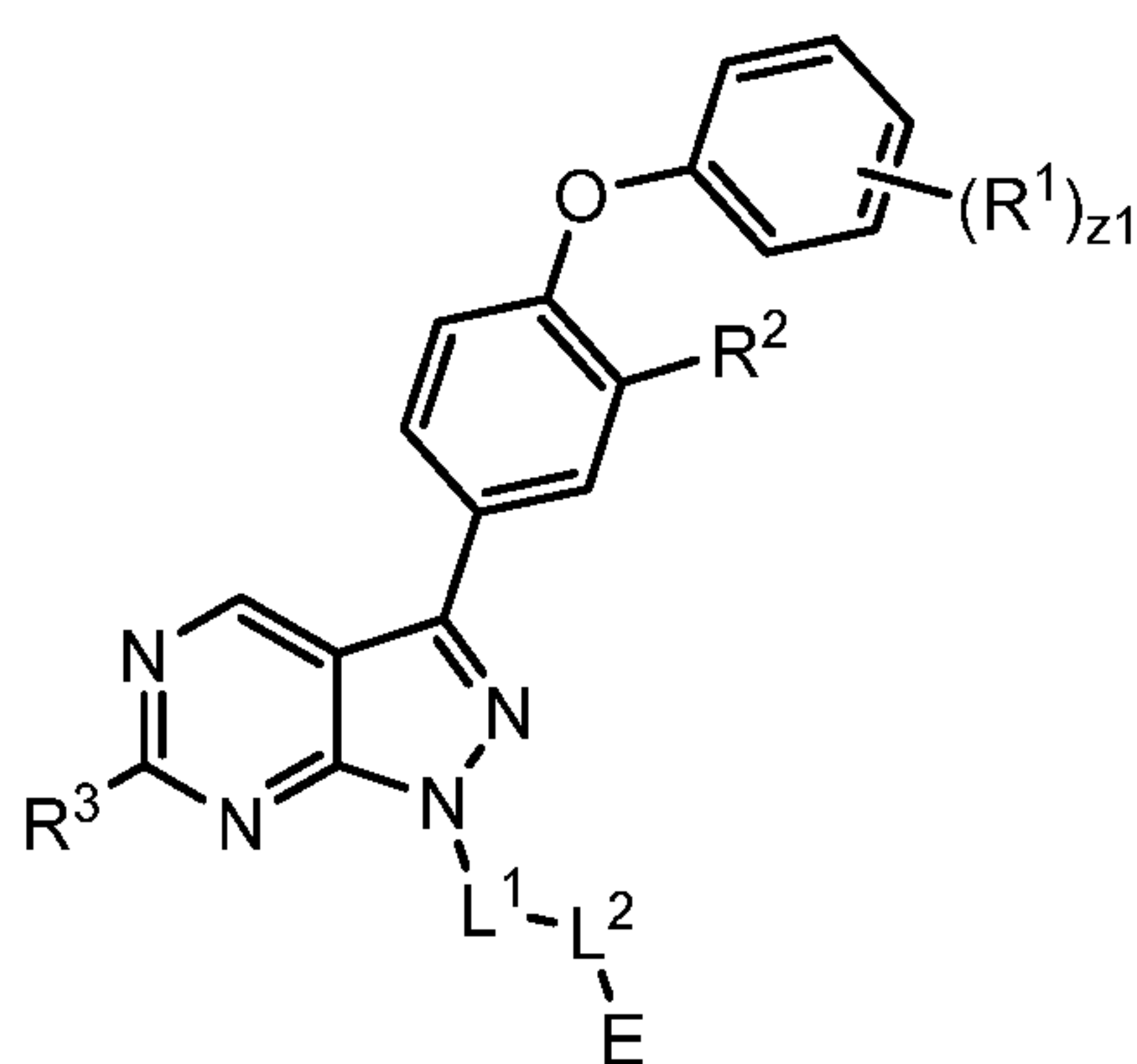
(IIBi). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, and E are as described herein.

[0116] In embodiments, the compound has the formula



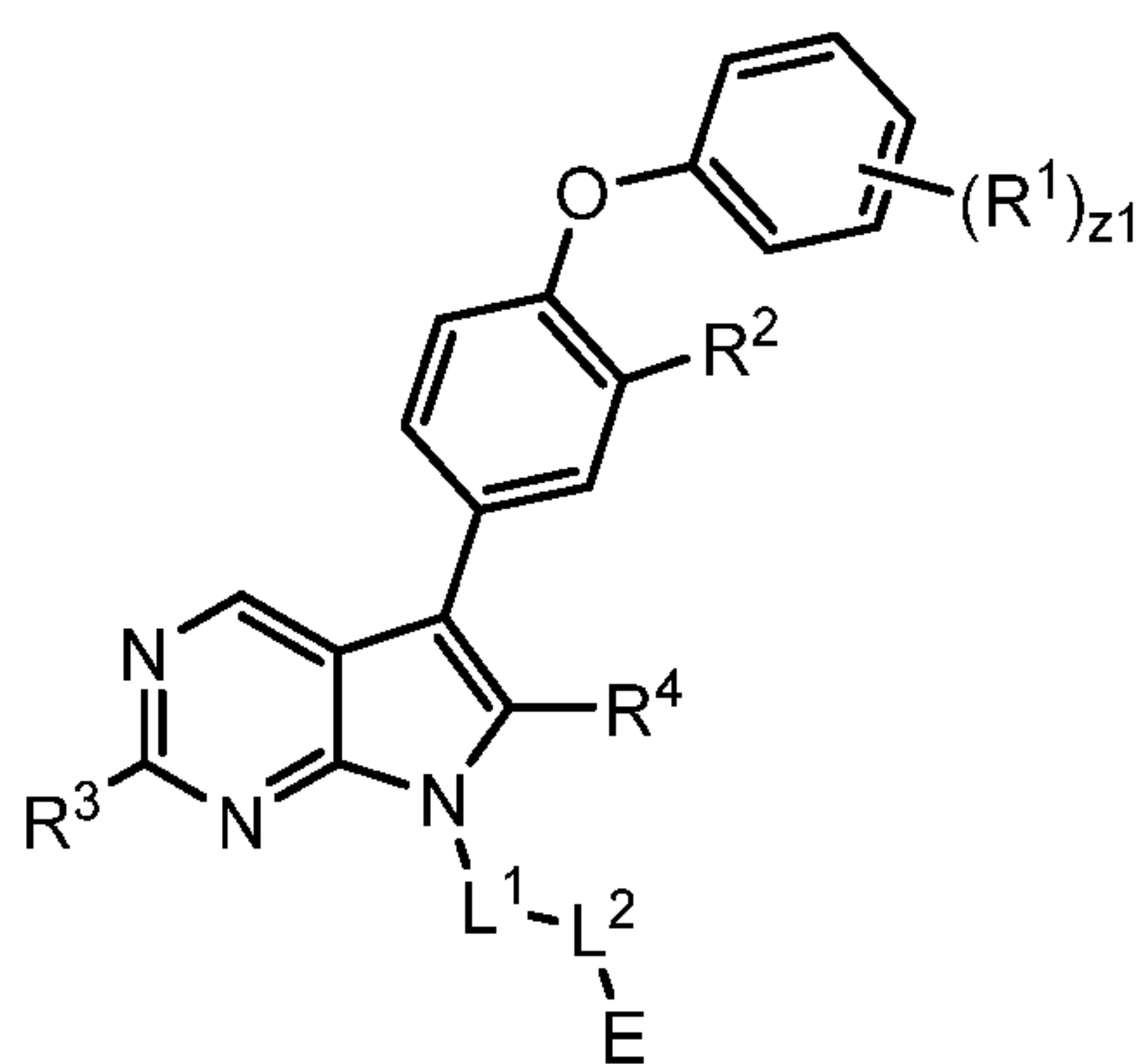
(IIIBi). R^1 , R^2 , R^3 , L^1 , L^2 , Y^2 , $z1$, and E are as described herein.

[0117] In embodiments, the compound has the formula



(ICi). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, and E are as described herein.

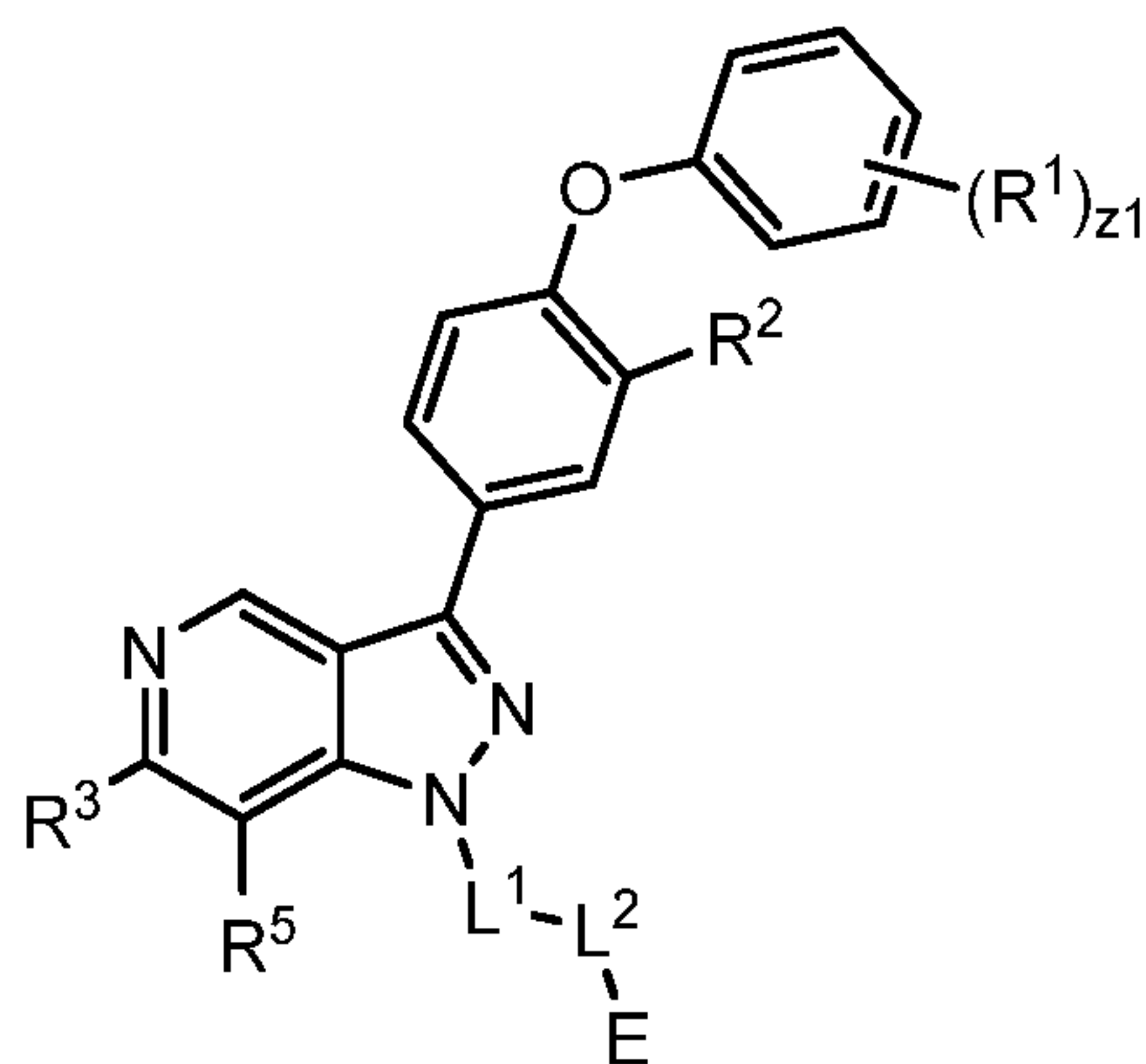
[0118] In embodiments, the compound has the formula



(IDi). R^1 , R^2 , R^3 , R^4 , L^1 , L^2 , $z1$, and E are as described

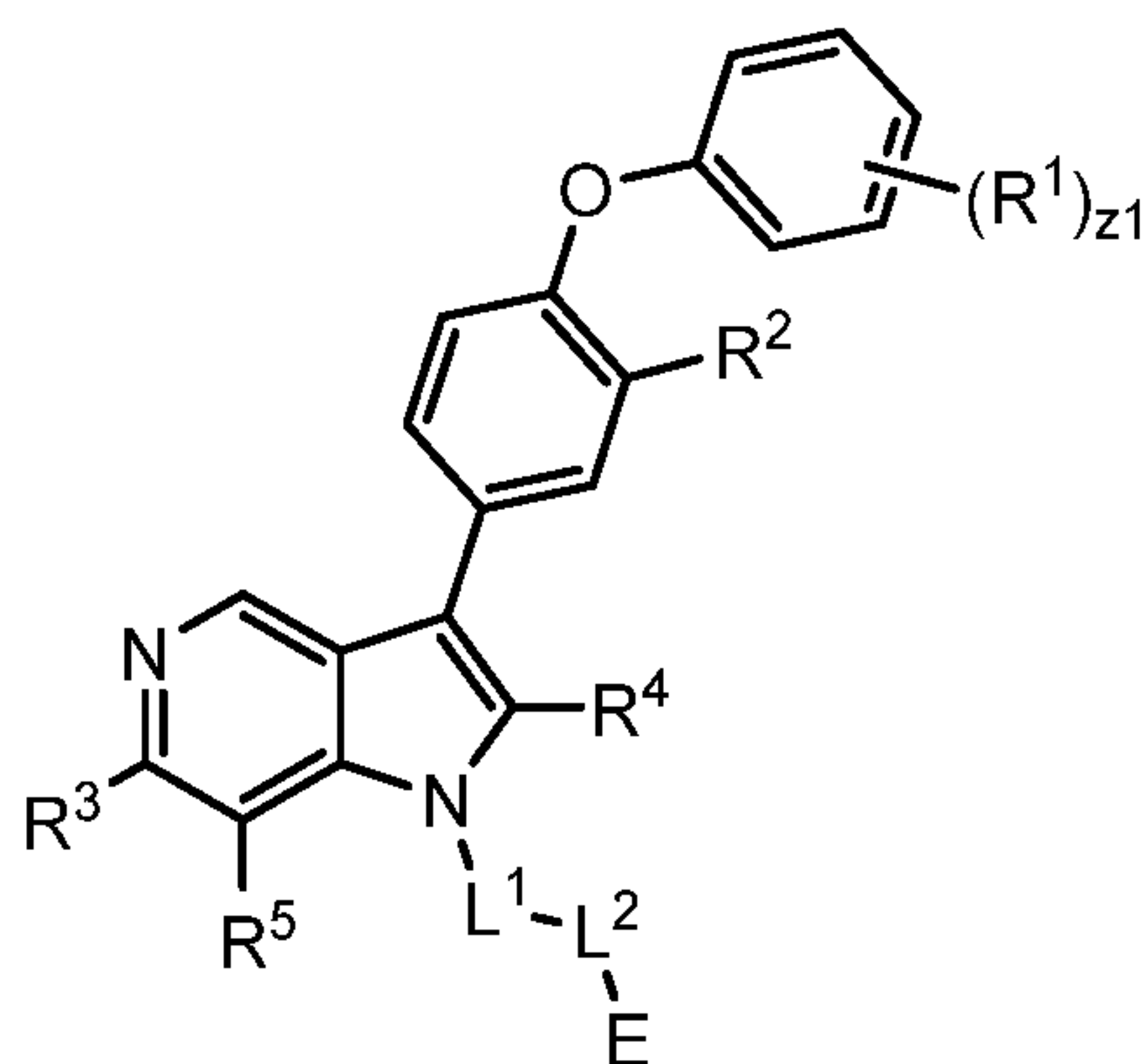
herein.

[0119] In embodiments, the compound has the formula



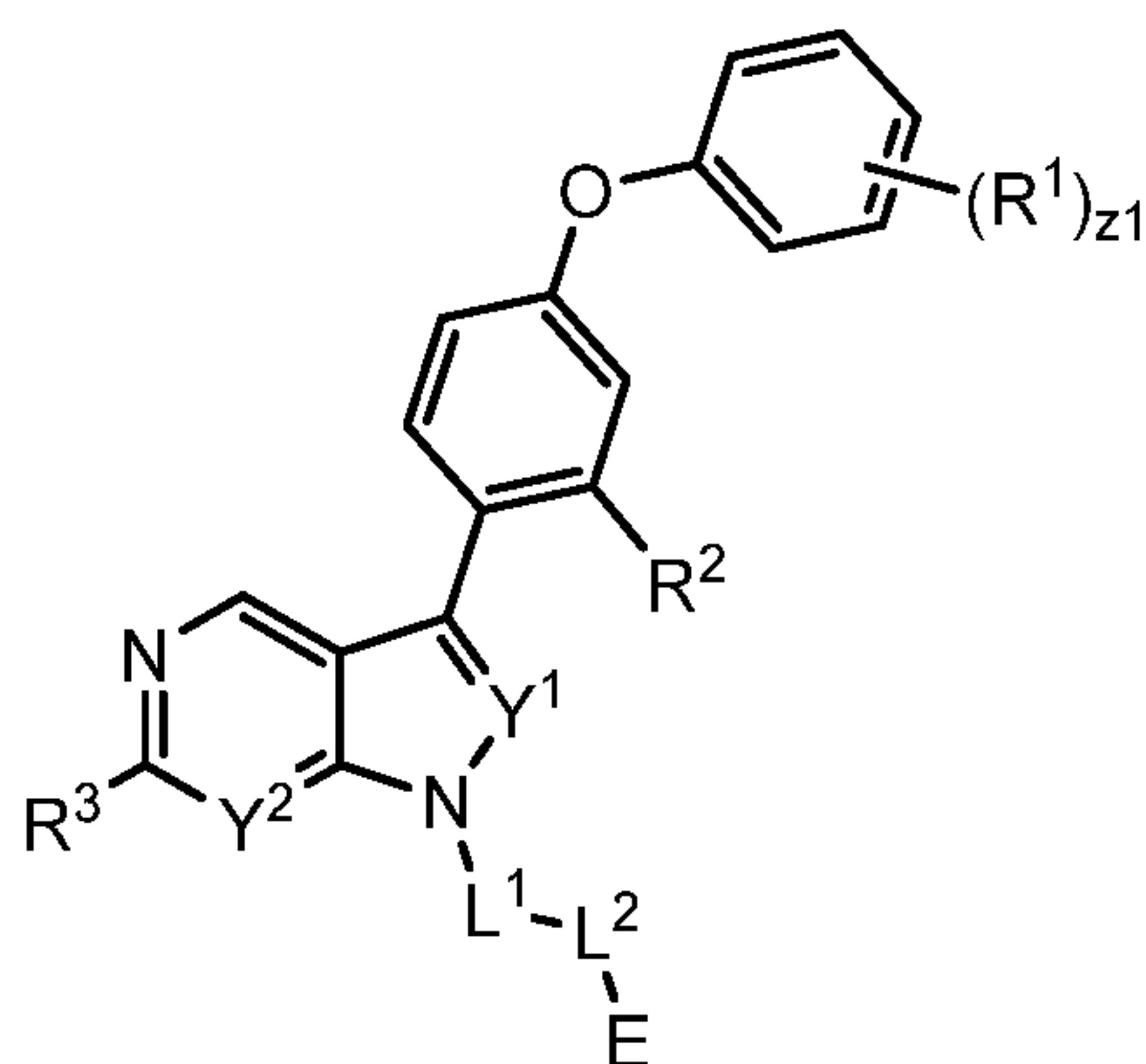
(IEi). R^1 , R^2 , R^3 , R^5 , L^1 , L^2 , $z1$, and E are as described herein.

[0120] In embodiments, the compound has the formula



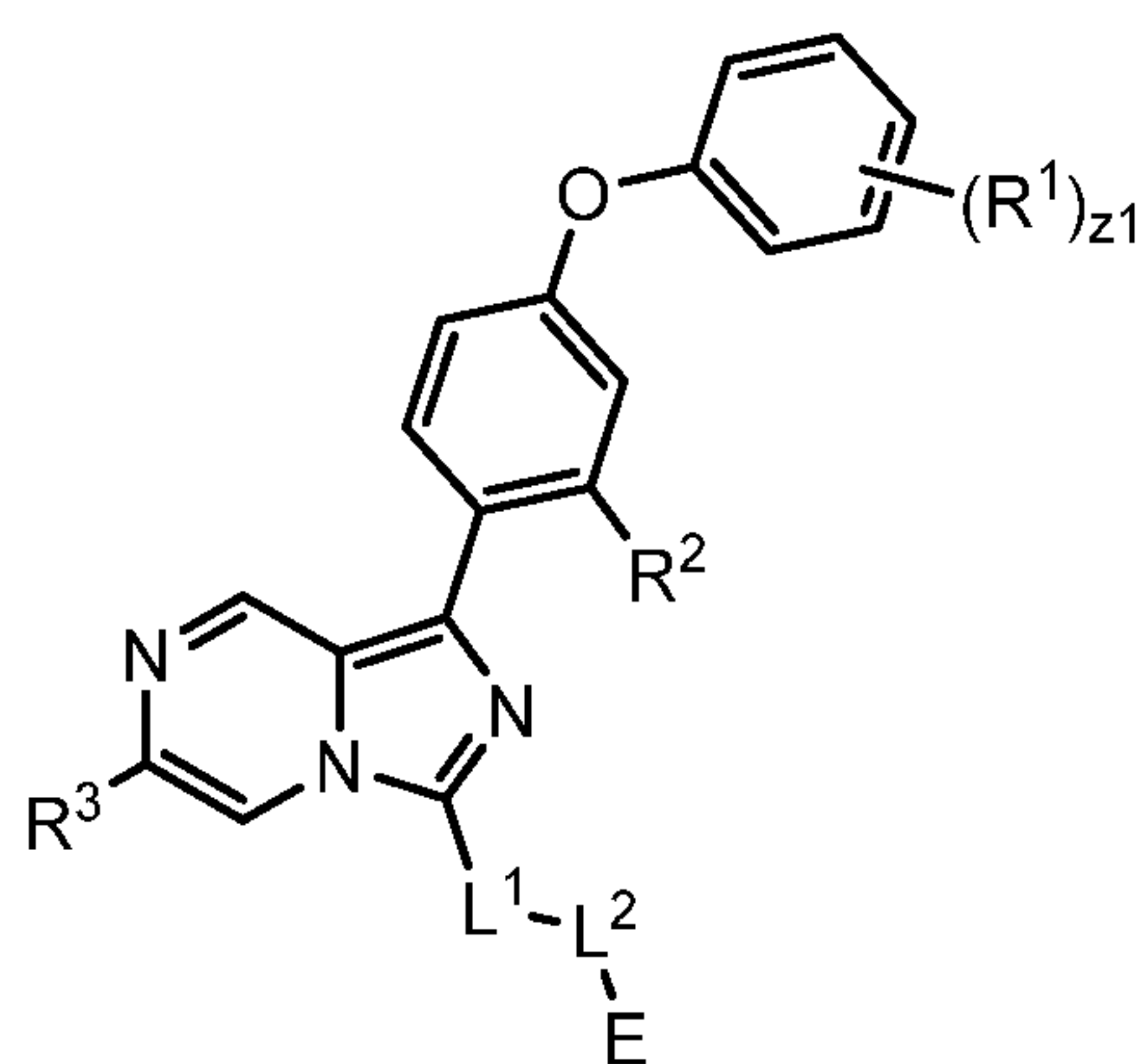
(IFi). R^1 , R^2 , R^3 , R^4 , R^5 , L^1 , L^2 , $z1$, and E are as described
5 herein.

[0121] In embodiments, the compound has the formula



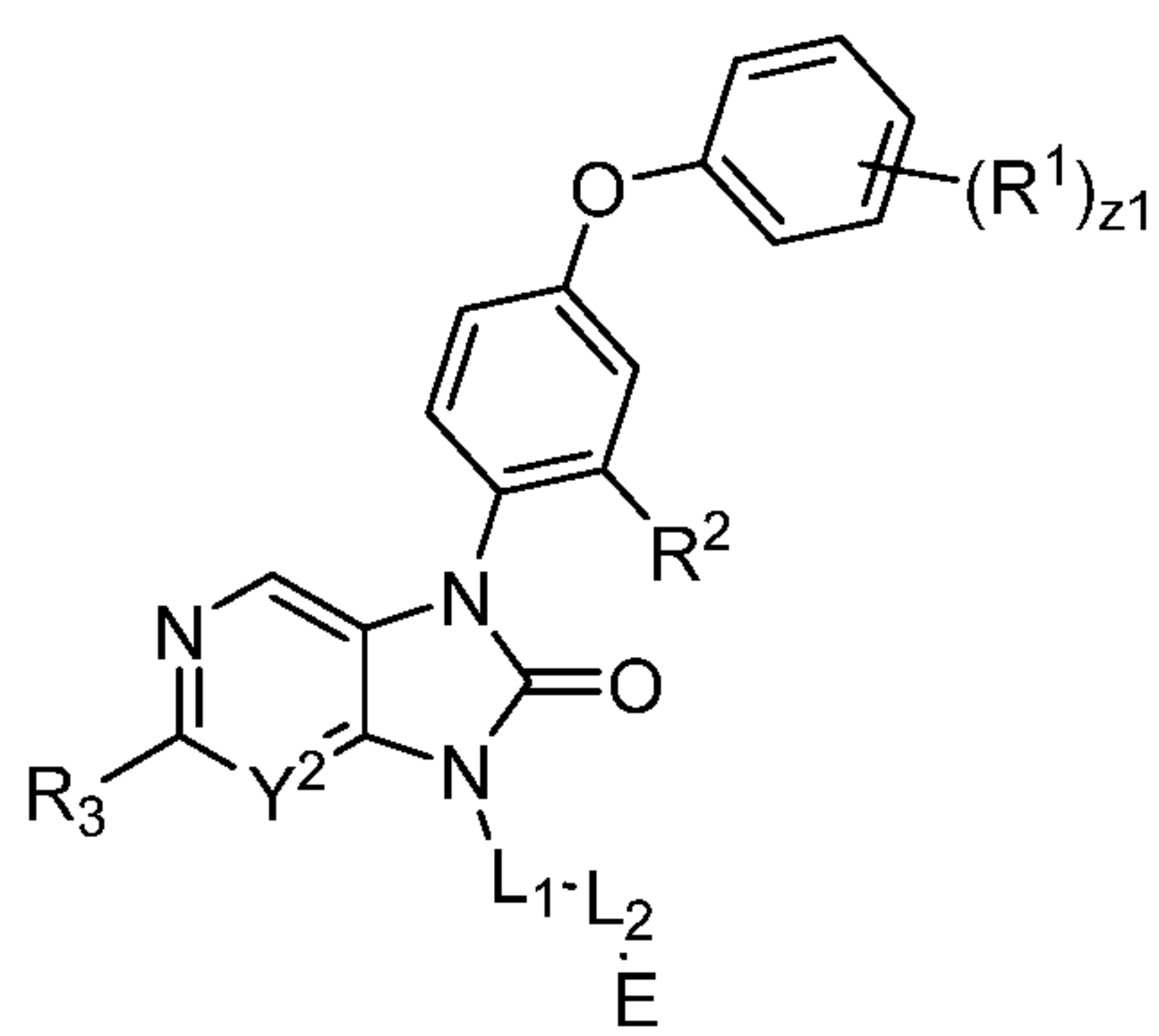
(IAii). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , $z1$, and E are as described herein.

[0122] In embodiments, the compound has the formula



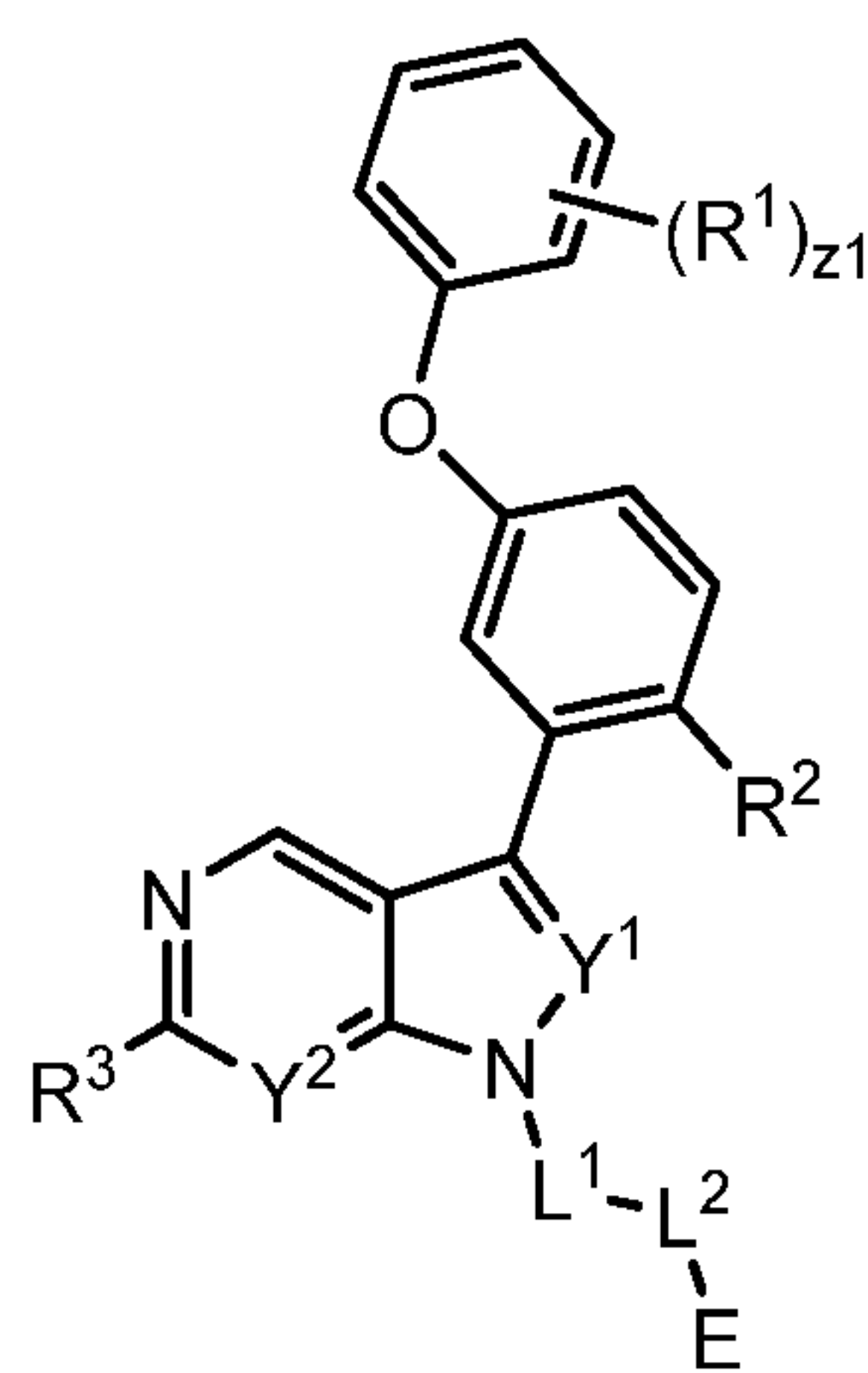
(IIAii). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, and E are as described herein.

[0123] In embodiments, the compound has the formula



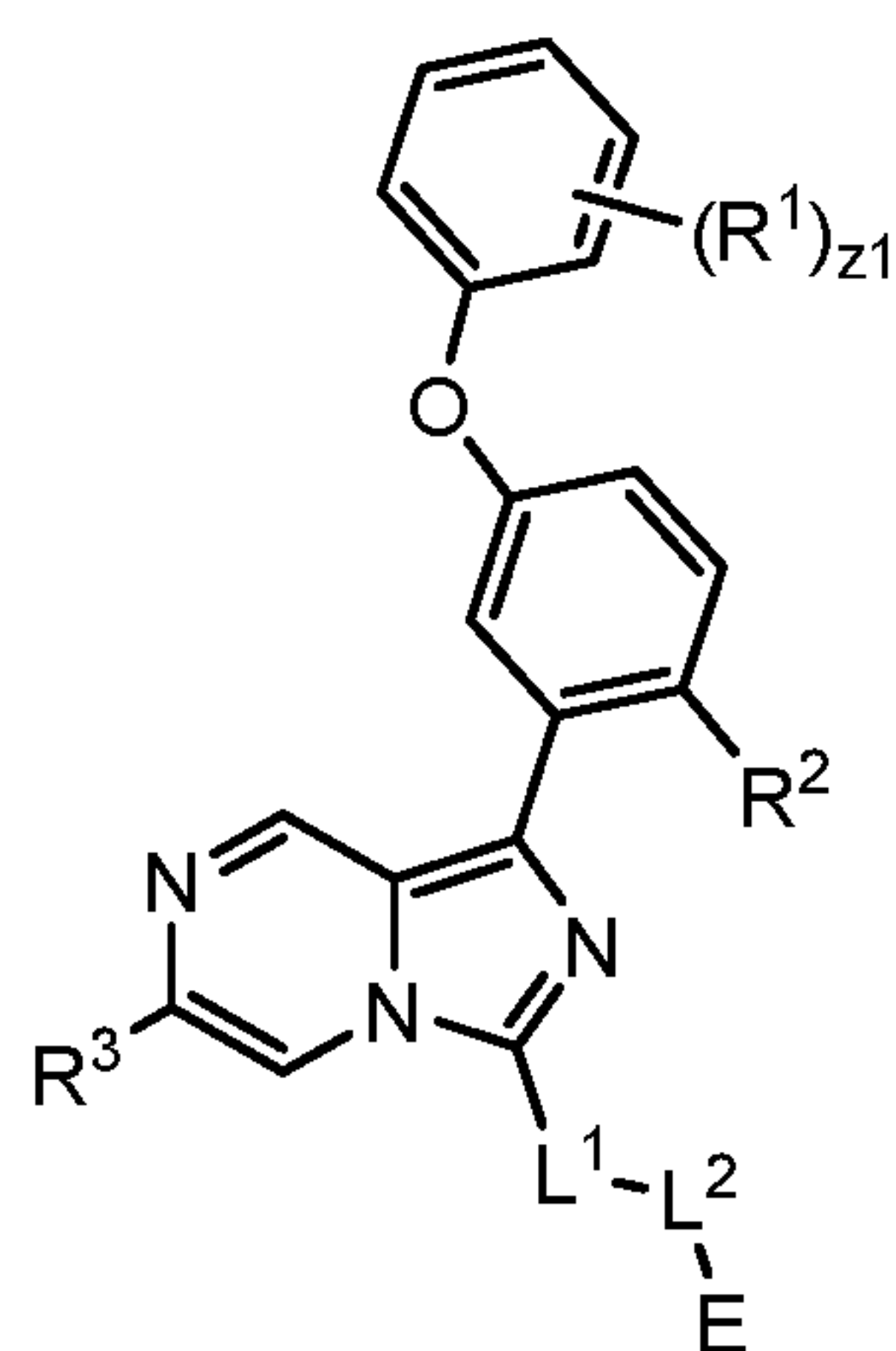
(IIIAii). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , $z1$, and E are as described herein.

[0124] In embodiments, the compound has the formula



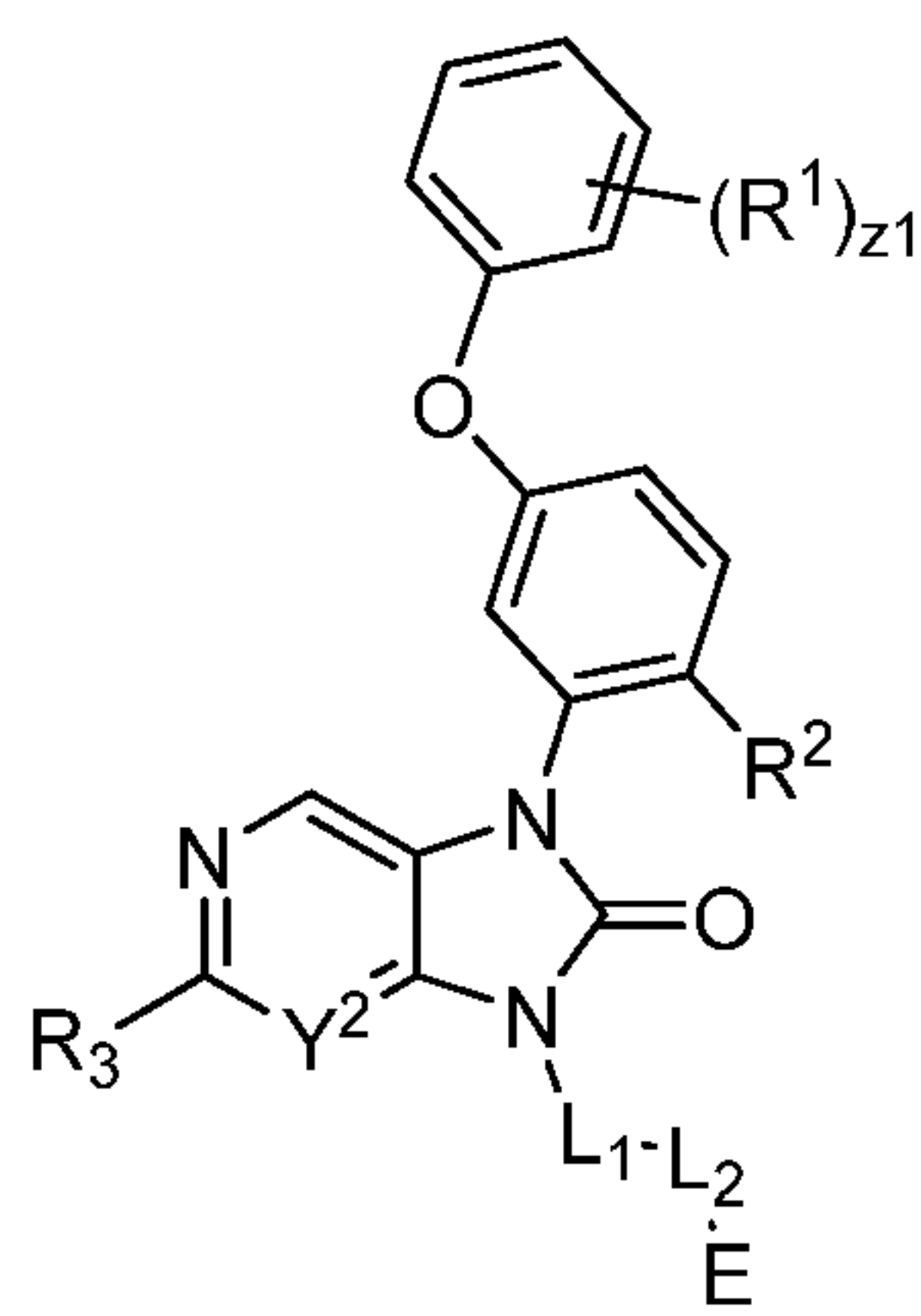
(IBii). R^1 , R^2 , R^3 , L^1 , L^2 , Y^1 , Y^2 , $z1$, and E are as described herein.

[0125] In embodiments, the compound has the formula



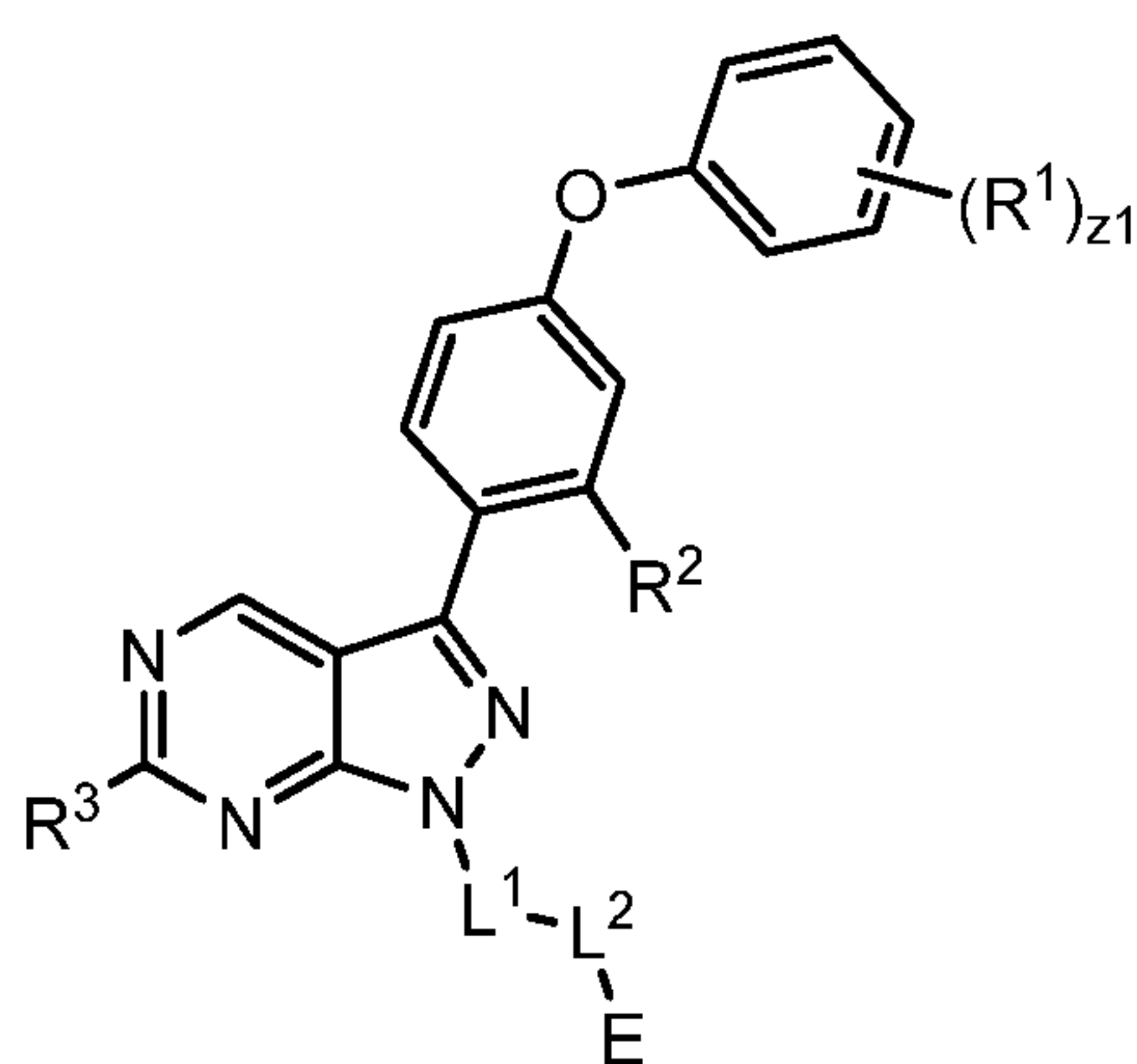
(IIBii). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, and E are as described herein.

[0126] In embodiments, the compound has the formula



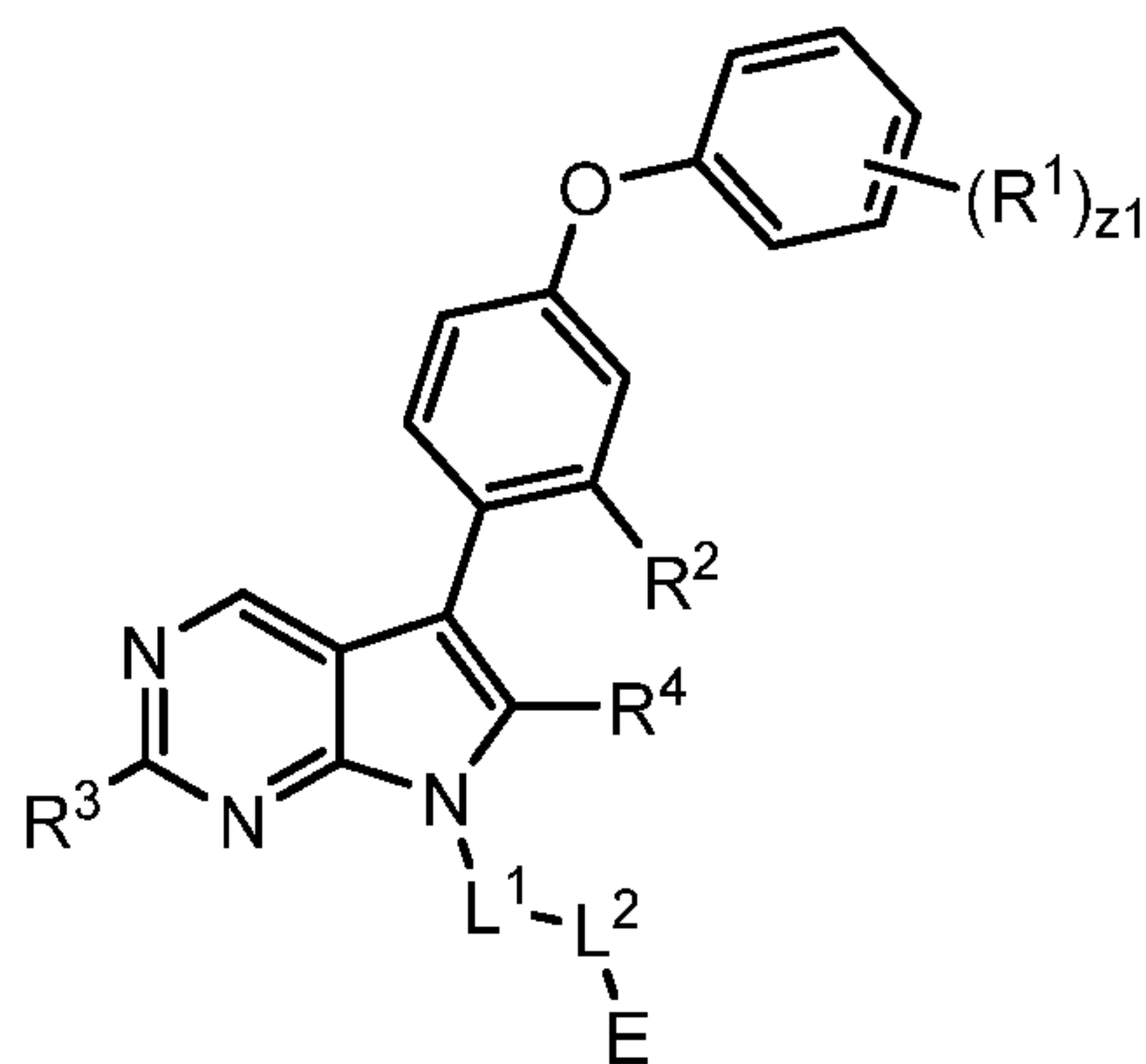
(IIIBii). R^1 , R^2 , R^3 , L^1 , L^2 , Y^2 , $z1$, and E are as described herein.

[0127] In embodiments, the compound has the formula



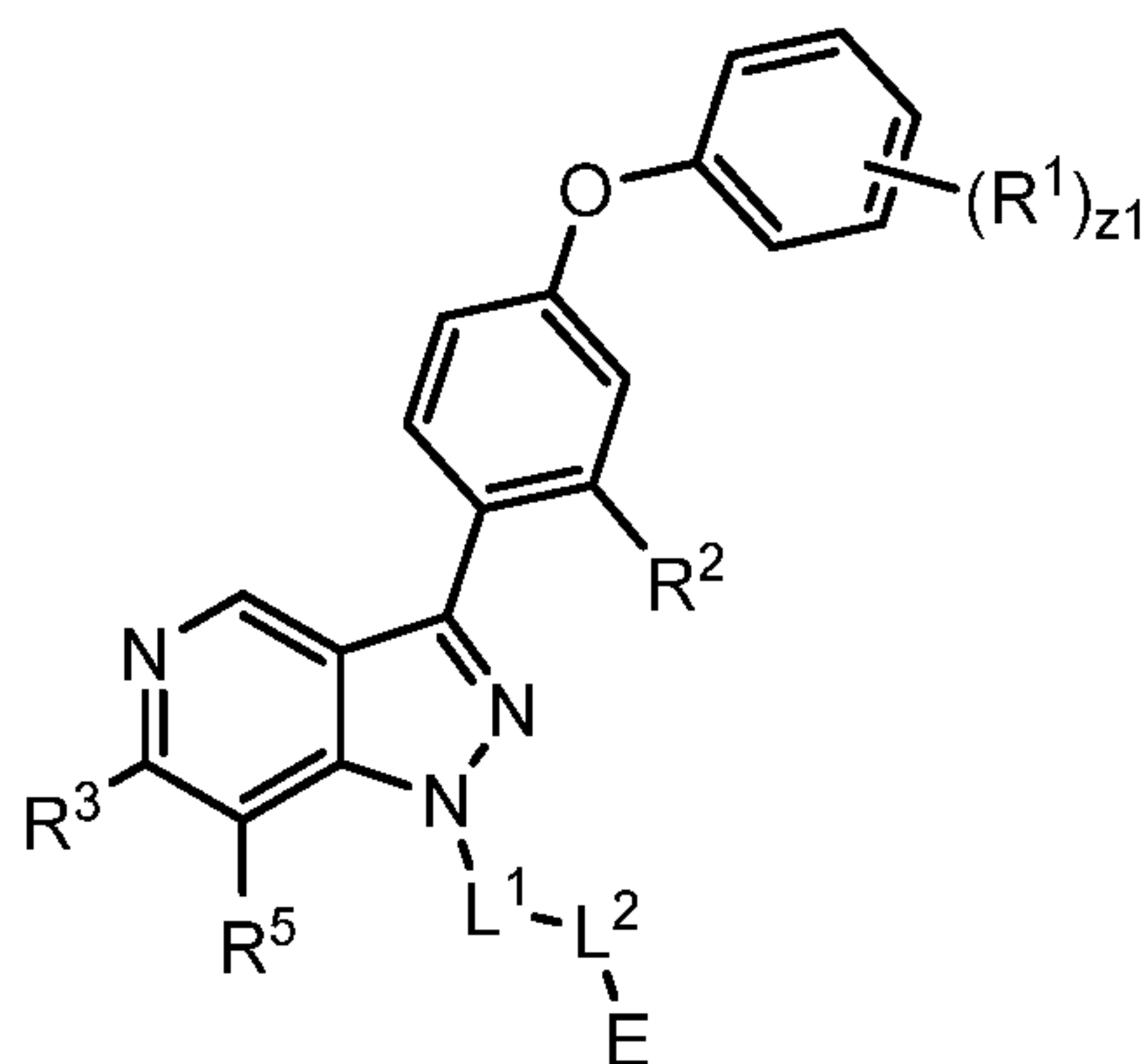
(ICii). R^1 , R^2 , R^3 , L^1 , L^2 , $z1$, and E are as described herein.

[0128] In embodiments, the compound has the formula



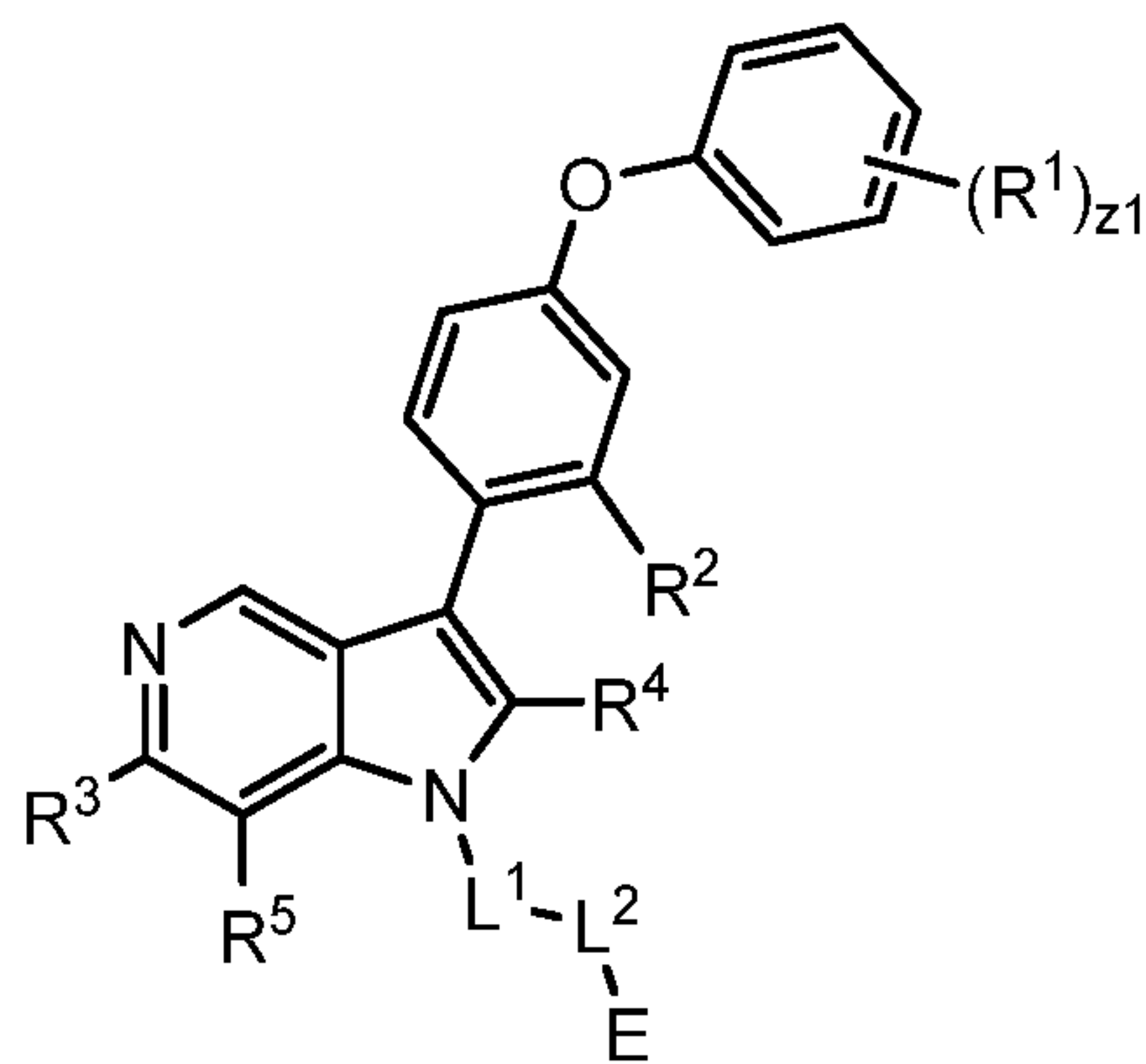
(IDii). R^1 , R^2 , R^3 , R^4 , L^1 , L^2 , $z1$, and E are as described herein.

[0129] In embodiments, the compound has the formula



(IEii). R^1 , R^2 , R^3 , R^5 , L^1 , L^2 , $z1$, and E are as described herein.

[0130] In embodiments, the compound has the formula



(IFii). R^1 , R^2 , R^3 , R^4 , R^5 , L^1 , L^2 , $z1$, and E are as described herein.

[0131] In embodiments, R^1 is independently

halogen, $-CX^1_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-OCX^1_3$, $-OCHX^1_2$, $-CHX^1_2$, $-CH_2X^1$, substituted or unsubstituted C_1 - C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl; two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_8 cycloalkyl, substituted or unsubstituted 3 to 8 membered

heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^1 is independently halogen, $-CX^1_3$, $-CN$, unsubstituted C_1 - C_4 alkyl, or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^1 is independently halogen, $-CX^1_3$, $-CN$, unsubstituted methyl, unsubstituted ethyl, unsubstituted methoxy, or unsubstituted ethoxy. In embodiments, R^1 is independently unsubstituted methyl. In embodiments, R^1 is independently unsubstituted ethyl. In embodiments, R^1 is independently unsubstituted propyl. In embodiments, R^1 is independently unsubstituted n-propyl. In embodiments, R^1 is independently unsubstituted isopropyl. In embodiments, R^1 is independently unsubstituted butyl. In embodiments, R^1 is independently unsubstituted n-butyl. In embodiments, R^1 is independently unsubstituted isobutyl. In embodiments, R^1 is independently unsubstituted tert-butyl. In embodiments, R^1 is independently unsubstituted pentyl. In embodiments, R^1 is independently unsubstituted hexyl. In embodiments, R^1 is independently unsubstituted heptyl. In embodiments, R^1 is independently unsubstituted octyl. In embodiments, R^1 is independently $-F$. In embodiments, R^1 is independently $-Cl$. In embodiments, R^1 is independently $-Br$. In embodiments, R^1 is independently $-I$. In embodiments, R^1 is independently unsubstituted methoxy. In embodiments, R^1 is independently unsubstituted ethoxy. In embodiments, R^1 is independently $-CF_3$. In embodiments, R^1 is independently halogen. In embodiments, R^1 is independently $-CCl_3$.

[0132] In embodiments, R^1 is independently $-CX^1_3$. In embodiments, R^1 is independently $-CHX^1_2$. In embodiments, R^1 is independently $-CH_2X^1$. In embodiments, R^1 is independently $-OCX^1_3$. In embodiments, R^1 is independently $-OCH_2X^1$. In embodiments, R^1 is independently $-OCHX^1_2$. In embodiments, R^1 is independently $-CN$. In embodiments, R^1 is independently $-SO_{n1}R^{1D}$. In embodiments, R^1 is independently $-SO_{v1}NR^{1A}R^{1B}$. In embodiments, R^1 is independently $-NHC(O)NR^{1A}R^{1B}$. In embodiments, R^1 is independently $-N(O)_{m1}$. In embodiments, R^1 is independently $-NR^{1A}R^{1B}$. In embodiments, R^1 is independently $-C(O)R^{1C}$. In embodiments, R^1 is independently $-C(O)-OR^{1C}$. In embodiments, R^1 is independently $-C(O)NR^{1A}R^{1B}$. In embodiments, R^1 is independently $-OR^{1D}$. In embodiments, R^1 is independently $-NR^{1A}SO_2R^{1D}$. In embodiments, R^1 is independently $-NR^{1A}C(O)R^{1C}$. In embodiments, R^1 is independently $-NR^{1A}C(O)OR^{1C}$. In embodiments, R^1 is independently $-NR^{1A}OR^{1C}$. In embodiments, R^1 is independently $-OH$. In embodiments, R^1 is independently $-NH_2$. In embodiments, R^1 is independently $-COOH$. In embodiments, R^1 is independently $-CONH_2$. In embodiments, R^1 is independently $-NO_2$. In embodiments, R^1 is independently $-SH$.

[0133] In embodiments, R^1 is independently substituted or unsubstituted alkyl. In
embodiments, R^1 is independently substituted or unsubstituted heteroalkyl. In embodiments,
 R^1 is independently substituted or unsubstituted cycloalkyl. In embodiments, R^1 is
independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^1 is
5 independently substituted or unsubstituted aryl. In embodiments, R^1 is independently
substituted or unsubstituted heteroaryl. In embodiments, R^1 is independently substituted
alkyl. In embodiments, R^1 is independently substituted heteroalkyl. In embodiments, R^1 is
independently substituted cycloalkyl. In embodiments, R^1 is independently, substituted
heterocycloalkyl. In embodiments, R^1 is independently substituted aryl. In embodiments, R^1
10 is independently substituted heteroaryl. In embodiments, R^1 is independently unsubstituted
alkyl. In embodiments, R^1 is independently unsubstituted heteroalkyl. In embodiments, R^1 is
independently unsubstituted cycloalkyl. In embodiments, R^1 is independently, unsubstituted
heterocycloalkyl. In embodiments, R^1 is independently unsubstituted aryl. In embodiments,
 R^1 is independently unsubstituted heteroaryl. In embodiments, R^1 is independently
15 substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^1 is independently substituted or
unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^1 is independently substituted
or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^1 is independently, substituted or
unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^1 is independently
substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^1 is independently substituted or
20 unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^1 is independently substituted
 C_1 - C_8 alkyl. In embodiments, R^1 is independently substituted 2 to 8 membered heteroalkyl.
In embodiments, R^1 is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^1 is
independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^1 is
independently substituted C_6 - C_{10} aryl. In embodiments, R^1 is independently substituted 5 to
25 10 membered heteroaryl. In embodiments, R^1 is independently unsubstituted C_1 - C_8 alkyl. In
embodiments, R^1 is independently unsubstituted 2 to 8 membered heteroalkyl. In
embodiments, R^1 is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^1 is
independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^1 is
independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^1 is independently unsubstituted
30 5 to 10 membered heteroaryl. In embodiments, R^1 is independently substituted or
unsubstituted C_1 - C_4 alkyl. In embodiments, R^1 is independently substituted or unsubstituted
2 to 4 membered heteroalkyl. In embodiments, R^1 is independently substituted or
unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^1 is independently, substituted or
unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^1 is independently
35 substituted or unsubstituted phenyl. In embodiments, R^1 is independently substituted or

unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^1 is independently substituted C_1 - C_4 alkyl. In embodiments, R^1 is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^1 is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^1 is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^1 is independently substituted phenyl. In embodiments, R^1 is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^1 is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^1 is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^1 is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^1 is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^1 is independently unsubstituted phenyl. In embodiments, R^1 is independently unsubstituted 5 to 6 membered heteroaryl.

[0134] In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted aryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted aryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted aryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted C_3 - C_8 cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally

be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted C_6 - C_{10} aryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted C_3 - C_8 cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted C_6 - C_{10} aryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted phenyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted C_3 - C_6 cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted phenyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted C_3 - C_6 cycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted phenyl. In embodiments, two adjacent R^1 substituents may optionally be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0135] In embodiments, R^{1A} is independently hydrogen. In embodiments, R^{1A} is independently $-CX^{1A}_3$. In embodiments, R^{1A} is independently $-CHX^{1A}_2$. In embodiments, R^{1A} is independently $-CH_2X^{1A}$. In embodiments, R^{1A} is independently $-CN$. In embodiments, R^{1A} is independently $-COOH$. In embodiments, R^{1A} is independently $-CONH_2$. In embodiments, R^{1A} is independently substituted or unsubstituted alkyl. In embodiments, R^{1A} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{1A} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{1A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{1A} is

independently substituted or unsubstituted aryl. In embodiments, R^{1A} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{1A} is independently substituted alkyl. In embodiments, R^{1A} is independently substituted heteroalkyl. In embodiments, R^{1A} is independently substituted cycloalkyl. In embodiments, R^{1A} is independently, substituted

5 heterocycloalkyl. In embodiments, R^{1A} is independently substituted aryl. In embodiments, R^{1A} is independently substituted heteroaryl. In embodiments, R^{1A} is independently unsubstituted alkyl. In embodiments, R^{1A} is independently unsubstituted heteroalkyl. In embodiments, R^{1A} is independently unsubstituted cycloalkyl. In embodiments, R^{1A} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{1A} is independently

10 unsubstituted aryl. In embodiments, R^{1A} is independently unsubstituted heteroaryl. In embodiments, R^{1A} is independently substituted or unsubstituted C₁-C₈ alkyl. In embodiments, R^{1A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1A} is independently substituted or unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{1A} is independently, substituted or unsubstituted 3 to 8 membered

15 heterocycloalkyl. In embodiments, R^{1A} is independently substituted or unsubstituted C₆-C₁₀ aryl. In embodiments, R^{1A} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1A} is independently substituted C₁-C₈ alkyl. In embodiments, R^{1A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{1A} is independently substituted C₃-C₈ cycloalkyl. In embodiments, R^{1A} is independently,

20 substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1A} is independently substituted C₆-C₁₀ aryl. In embodiments, R^{1A} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{1A} is independently unsubstituted C₁-C₈ alkyl. In embodiments, R^{1A} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1A} is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{1A} is

25 independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1A} is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R^{1A} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1A} is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R^{1A} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{1A} is independently substituted or

30 unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{1A} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1A} is independently substituted or unsubstituted phenyl. In embodiments, R^{1A} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1A} is independently substituted C₁-C₄ alkyl. In embodiments, R^{1A} is independently substituted 2 to 4 membered heteroalkyl.

35 In embodiments, R^{1A} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{1A} is

independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1A} is independently substituted phenyl. In embodiments, R^{1A} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{1A} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{1A} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 5 embodiments, R^{1A} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{1A} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1A} is independently unsubstituted phenyl. In embodiments, R^{1A} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1A} is independently unsubstituted methyl. In embodiments, R^{1A} is independently unsubstituted ethyl. In embodiments, R^{1A} is
 10 independently unsubstituted propyl. In embodiments, R^{1A} is independently unsubstituted isopropyl. In embodiments, R^{1A} is independently unsubstituted tert-butyl.

[0136] In embodiments, R^{1B} is independently hydrogen. In embodiments, R^{1B} is independently $-CX^{1B}_3$. In embodiments, R^{1B} is independently $-CHX^{1B}_2$. In embodiments, R^{1B} is independently $-CH_2X^{1B}$. In embodiments, R^{1B} is independently $-CN$. In embodiments,
 15 R^{1B} is independently $-COOH$. In embodiments, R^{1B} is independently $-CONH_2$. In embodiments, R^{1B} is independently substituted or unsubstituted alkyl. In embodiments, R^{1B} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{1B} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{1B} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{1B} is independently
 20 substituted or unsubstituted aryl. In embodiments, R^{1B} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{1B} is independently substituted alkyl. In embodiments, R^{1B} is independently substituted heteroalkyl. In embodiments, R^{1B} is independently substituted cycloalkyl. In embodiments, R^{1B} is independently, substituted heterocycloalkyl. In embodiments, R^{1B} is independently substituted aryl. In embodiments,
 25 R^{1B} is independently substituted heteroaryl. In embodiments, R^{1B} is independently unsubstituted alkyl. In embodiments, R^{1B} is independently unsubstituted heteroalkyl. In embodiments, R^{1B} is independently unsubstituted cycloalkyl. In embodiments, R^{1B} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{1B} is independently unsubstituted aryl. In embodiments, R^{1B} is independently unsubstituted heteroaryl. In
 30 embodiments, R^{1B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{1B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{1B} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1B} is independently substituted or unsubstituted C_6 - C_{10}

aryl. In embodiments, R^{1B} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1B} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{1B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{1B} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{1B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1B} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{1B} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{1B} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{1B} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{1B} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1B} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{1B} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1B} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{1B} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{1B} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{1B} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1B} is independently substituted or unsubstituted phenyl. In embodiments, R^{1B} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1B} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{1B} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{1B} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{1B} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1B} is independently substituted phenyl. In embodiments, R^{1B} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{1B} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{1B} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{1B} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{1B} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1B} is independently unsubstituted phenyl. In embodiments, R^{1B} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1B} is independently unsubstituted methyl. In embodiments, R^{1B} is independently unsubstituted ethyl. In embodiments, R^{1B} is independently unsubstituted propyl. In embodiments, R^{1B} is independently unsubstituted isopropyl. In embodiments, R^{1B} is independently unsubstituted tert-butyl.

[0137] In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted or

unsubstituted heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0138] In embodiments, R^{1C} is independently hydrogen. In embodiments, R^{1C} is independently $-CX^{1C}_3$. In embodiments, R^{1C} is independently $-CHX^{1C}_2$. In embodiments, R^{1C} is independently $-CH_2X^{1C}$. In embodiments, R^{1C} is independently $-CN$. In embodiments, R^{1C} is independently $-COOH$. In embodiments, R^{1C} is independently $-CONH_2$. In embodiments, R^{1C} is independently substituted or unsubstituted alkyl. In embodiments, R^{1C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{1C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{1C} is independently,

substituted or unsubstituted heterocycloalkyl. In embodiments, R^{1C} is independently substituted or unsubstituted aryl. In embodiments, R^{1C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{1C} is independently substituted alkyl. In embodiments, R^{1C} is independently substituted heteroalkyl. In embodiments, R^{1C} is independently substituted cycloalkyl. In embodiments, R^{1C} is independently, substituted heterocycloalkyl. In embodiments, R^{1C} is independently substituted aryl. In embodiments, R^{1C} is independently substituted heteroaryl. In embodiments, R^{1C} is independently unsubstituted alkyl. In embodiments, R^{1C} is independently unsubstituted heteroalkyl. In embodiments, R^{1C} is independently unsubstituted cycloalkyl. In embodiments, R^{1C} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{1C} is independently unsubstituted aryl. In embodiments, R^{1C} is independently unsubstituted heteroaryl. In embodiments, R^{1C} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{1C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1C} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{1C} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1C} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{1C} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1C} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{1C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{1C} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{1C} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1C} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{1C} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{1C} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{1C} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1C} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{1C} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1C} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{1C} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1C} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{1C} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{1C} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{1C} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1C} is independently substituted or unsubstituted phenyl. In embodiments, R^{1C} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1C} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{1C} is independently substituted 2 to 4 membered heteroalkyl.

In embodiments, R^{1C} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{1C} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1C} is independently substituted phenyl. In embodiments, R^{1C} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{1C} is independently unsubstituted C_1 - C_4 alkyl. In
 5 embodiments, R^{1C} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{1C} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{1C} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1C} is
 independently unsubstituted phenyl. In embodiments, R^{1C} is independently unsubstituted 5 to
 6 membered heteroaryl. In embodiments, R^{1C} is independently unsubstituted methyl. In
 10 embodiments, R^{1C} is independently unsubstituted ethyl. In embodiments, R^{1C} is
 independently unsubstituted propyl. In embodiments, R^{1C} is independently unsubstituted
 isopropyl. In embodiments, R^{1C} is independently unsubstituted tert-butyl.

[0139] In embodiments, R^{1D} is independently hydrogen. In embodiments, R^{1D} is
 independently $-CX^{1D}_3$. In embodiments, R^{1D} is independently $-CHX^{1D}_2$. In embodiments,
 15 R^{1D} is independently $-CH_2X^{1D}$. In embodiments, R^{1D} is independently $-CN$. In
 embodiments, R^{1D} is independently $-COOH$. In embodiments, R^{1D} is
 independently $-CONH_2$. In embodiments, R^{1D} is independently substituted or unsubstituted
 alkyl. In embodiments, R^{1D} is independently substituted or unsubstituted heteroalkyl. In
 embodiments, R^{1D} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 20 R^{1D} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{1D} is
 independently substituted or unsubstituted aryl. In embodiments, R^{1D} is independently
 substituted or unsubstituted heteroaryl. In embodiments, R^{1D} is independently substituted
 alkyl. In embodiments, R^{1D} is independently substituted heteroalkyl. In embodiments, R^{1D} is
 independently substituted cycloalkyl. In embodiments, R^{1D} is independently, substituted
 25 heterocycloalkyl. In embodiments, R^{1D} is independently substituted aryl. In embodiments,
 R^{1D} is independently substituted heteroaryl. In embodiments, R^{1D} is independently
 unsubstituted alkyl. In embodiments, R^{1D} is independently unsubstituted heteroalkyl. In
 embodiments, R^{1D} is independently unsubstituted cycloalkyl. In embodiments, R^{1D} is
 independently, unsubstituted heterocycloalkyl. In embodiments, R^{1D} is independently
 30 unsubstituted aryl. In embodiments, R^{1D} is independently unsubstituted heteroaryl. In
 embodiments, R^{1D} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{1D} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
 In embodiments, R^{1D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
 embodiments, R^{1D} is independently, substituted or unsubstituted 3 to 8 membered

heterocycloalkyl. In embodiments, R^{1D} is independently substituted or unsubstituted C_6-C_{10} aryl. In embodiments, R^{1D} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1D} is independently substituted C_1-C_8 alkyl. In embodiments, R^{1D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{1D} is independently substituted C_3-C_8 cycloalkyl. In embodiments, R^{1D} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1D} is independently substituted C_6-C_{10} aryl. In embodiments, R^{1D} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{1D} is independently unsubstituted C_1-C_8 alkyl. In embodiments, R^{1D} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{1D} is independently unsubstituted C_3-C_8 cycloalkyl. In embodiments, R^{1D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{1D} is independently unsubstituted C_6-C_{10} aryl. In embodiments, R^{1D} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{1D} is independently substituted or unsubstituted C_1-C_4 alkyl. In embodiments, R^{1D} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{1D} is independently substituted or unsubstituted C_3-C_6 cycloalkyl. In embodiments, R^{1D} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1D} is independently substituted or unsubstituted phenyl. In embodiments, R^{1D} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1D} is independently substituted C_1-C_4 alkyl. In embodiments, R^{1D} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{1D} is independently substituted C_3-C_6 cycloalkyl. In embodiments, R^{1D} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1D} is independently substituted phenyl. In embodiments, R^{1D} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{1D} is independently unsubstituted C_1-C_4 alkyl. In embodiments, R^{1D} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{1D} is independently unsubstituted C_3-C_6 cycloalkyl. In embodiments, R^{1D} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{1D} is independently unsubstituted phenyl. In embodiments, R^{1D} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{1D} is independently unsubstituted methyl. In embodiments, R^{1D} is independently unsubstituted ethyl. In embodiments, R^{1D} is independently unsubstituted propyl. In embodiments, R^{1D} is independently unsubstituted isopropyl. In embodiments, R^{1D} is independently unsubstituted tert-butyl.

[0140] In embodiments, R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, $-CN$, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}$

R^{1B} , $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, R^{20} -substituted or unsubstituted alkyl, R^{20} -substituted or unsubstituted heteroalkyl, R^{20} -substituted or unsubstituted cycloalkyl, R^{20} -substituted or unsubstituted heterocycloalkyl, R^{20} -substituted or unsubstituted aryl, or R^{20} -substituted or unsubstituted heteroaryl. In embodiments, R^1 is independently halogen, $-CX^1_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^1_3$, $-OCHX^1_2$, R^{20} -substituted or unsubstituted alkyl, R^{20} -substituted or unsubstituted heteroalkyl, R^{20} -substituted or unsubstituted cycloalkyl, R^{20} -substituted or unsubstituted heterocycloalkyl, R^{20} -substituted or unsubstituted aryl, or R^{20} -substituted or unsubstituted heteroaryl. In embodiments, R^1 is independently halogen, $-CX^1_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^1_3$, $-OCHX^1_2$, R^{20} -substituted or unsubstituted C_1 - C_8 alkyl, R^{20} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{20} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{20} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{20} -substituted or unsubstituted phenyl, or R^{20} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^1 is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^1 is independently hydrogen. In embodiments, R^1 is independently methyl. In embodiments, R^1 is independently ethyl. In embodiments, R^1 is CX_3 . In embodiments, R^1 is CHX_2 . In embodiments, R^1 is CH_2X . In embodiments, R^1 is CF_3 . In embodiments, R^1 is CHF_2 . In embodiments, R^1 is CH_2F .

[0141] In embodiments, two adjacent R^1 substituents may optionally be joined to form a R^{20} -substituted or unsubstituted cycloalkyl, R^{20} -substituted or unsubstituted heterocycloalkyl, R^{20} -substituted or unsubstituted aryl, or R^{20} -substituted or unsubstituted heteroaryl. In embodiments, two adjacent R^1 substituents may optionally be joined to form a R^{20} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{20} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{20} -substituted or unsubstituted phenyl, or R^{20} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0142] R^{20} is independently oxo, halogen, $-CX^{20}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20}_3$, $-OCHX^{20}_2$, R^{21} -substituted or unsubstituted alkyl, R^{21} -substituted or unsubstituted heteroalkyl, R^{21} -substituted or unsubstituted cycloalkyl, R^{21} -substituted or unsubstituted heterocycloalkyl, R^{21} -substituted or unsubstituted aryl, or R^{21} -substituted or

unsubstituted heteroaryl. In embodiments, R^{20} is independently oxo, halogen, $-CX^{20}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20}_3$, $-OCHX^{20}_2$, R^{21} -substituted or unsubstituted C_1 - C_8 alkyl, R^{21} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{21} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{21} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{21} -substituted or unsubstituted phenyl, or R^{21} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{20} is $-F$, $-Cl$, $-Br$, or $-I$.

[0143] R^{21} is independently oxo,

halogen, $-CX^{21}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21}_3$, $-OCHX^{21}_2$, R^{22} -substituted or unsubstituted alkyl, R^{22} -substituted or unsubstituted heteroalkyl, R^{22} -substituted or unsubstituted cycloalkyl, R^{22} -substituted or unsubstituted heterocycloalkyl, R^{22} -substituted or unsubstituted aryl, or R^{22} -substituted or unsubstituted heteroaryl. In embodiments, R^{21} is independently oxo, halogen, $-CX^{21}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21}_3$, $-OCHX^{21}_2$, R^{22} -substituted or unsubstituted C_1 - C_8 alkyl, R^{22} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{22} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{22} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{22} -substituted or unsubstituted phenyl, or R^{22} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{21} is $-F$, $-Cl$, $-Br$, or $-I$.

[0144] In embodiments, R^{1A} is independently

hydrogen, $-CX^{1A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{1A}_2$, $-CH_2X^{1A}$, R^{20A} -substituted or unsubstituted alkyl, R^{20A} -substituted or unsubstituted heteroalkyl, R^{20A} -substituted or unsubstituted cycloalkyl, R^{20A} -substituted or unsubstituted heterocycloalkyl, R^{20A} -substituted or unsubstituted aryl, or R^{20A} -substituted or unsubstituted heteroaryl. In embodiments, R^{1A} is independently hydrogen, $-CX^{1A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{1A}_2$, $-CH_2X^{1A}$, R^{20A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{20A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{20A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{20A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{20A} -substituted or unsubstituted phenyl, or R^{20A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{1A} is $-F$, $-Cl$, $-Br$, or $-I$. In

embodiments, R^{1A} is independently hydrogen. In embodiments, R^{1A} is independently methyl. In embodiments, R^{1A} is independently ethyl.

[0145] In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{20A} -substituted or unsubstituted heterocycloalkyl or R^{20A} -

5 substituted or unsubstituted heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{20A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{20A} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0146] R^{20A} is independently oxo,

10 halogen, $-CX^{20A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20A}_3$, $-OCHX^{20A}_2$, R^{21A} -substituted or unsubstituted alkyl, R^{21A} -substituted or unsubstituted heteroalkyl, R^{21A} -substituted or unsubstituted cycloalkyl, R^{21A} -substituted or unsubstituted heterocycloalkyl, R^{21A} -substituted or unsubstituted aryl, or R^{21A} -substituted or

15 unsubstituted heteroaryl. In embodiments, R^{20A} is independently oxo, halogen, $-CX^{20A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20A}_3$, $-OCHX^{20A}_2$, R^{21A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{21A} -substituted or unsubstituted 2 to 8 membered

20 heteroalkyl, R^{21A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{21A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{21A} -substituted or unsubstituted phenyl, or R^{21A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{20A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0147] R^{21A} is independently oxo,

halogen, $-CX^{21A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21A}_3$, $-OCHX^{21A}_2$, R^{22A} -substituted or unsubstituted alkyl, R^{22A} -substituted or unsubstituted heteroalkyl, R^{22A} -substituted or unsubstituted cycloalkyl, R^{22A} -substituted or unsubstituted heterocycloalkyl, R^{22A} -substituted or unsubstituted aryl, or R^{22A} -substituted or unsubstituted heteroaryl. In embodiments, R^{21A} is independently oxo,

25 halogen, $-CX^{21A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21A}_3$, $-OCHX^{21A}_2$, R^{22A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{22A} -substituted or unsubstituted 2 to 8 membered

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heteroalkyl, R^{22A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{22A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{22A} -substituted or unsubstituted phenyl, or R^{22A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{21A} is -F, -Cl, -Br, or -I.

[0148] In embodiments, R^{1B} is independently

- 5 hydrogen, $-CX^{1B}_3$, -CN, -COOH, -CONH₂, $-CHX^{1B}_2$, $-CH_2X^{1B}$, R^{20B} -substituted or unsubstituted alkyl, R^{20B} -substituted or unsubstituted heteroalkyl, R^{20B} -substituted or unsubstituted cycloalkyl, R^{20B} -substituted or unsubstituted heterocycloalkyl, R^{20B} -substituted or unsubstituted aryl, or R^{20B} -substituted or unsubstituted heteroaryl. In embodiments, R^{1B} is independently hydrogen, $-CX^{1B}_3$, -CN, -COOH, -CONH₂, $-CHX^{1B}_2$, $-CH_2X^{1B}$, R^{20B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{20B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{20B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{20B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{20B} -substituted or unsubstituted phenyl, or R^{20B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{1B} is -F, -Cl, -Br, or -I. In embodiments, R^{1B} is independently hydrogen. In embodiments, R^{1B} is independently methyl.
- 10
- 15 In embodiments, R^{1B} is independently ethyl.

[0149] In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{20B} -substituted or unsubstituted heterocycloalkyl or R^{20B} -substituted or unsubstituted heteroaryl. In embodiments, R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{20B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{20B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

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[0150] R^{20B} is independently oxo,

- halogen, $-CX^{20B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{20B}_3$, $-OCHX^{20B}_2$, R^{21B} -substituted or unsubstituted alkyl, R^{21B} -substituted or unsubstituted heteroalkyl, R^{21B} -substituted or unsubstituted cycloalkyl, R^{21B} -substituted or unsubstituted heterocycloalkyl, R^{21B} -substituted or unsubstituted aryl, or R^{21B} -substituted or unsubstituted heteroaryl. In embodiments, R^{20B} is independently oxo,
- 25
- halogen, $-CX^{20B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{20B}_3$, $-OCHX^{20B}_2$, R^{21B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{21B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{21B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{21B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{21B} -
- 30

substituted or unsubstituted phenyl, or R^{21B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{20B} is -F, -Cl, -Br, or -I.

[0151] R^{21B} is independently oxo,

halogen, $-CX^{21B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

5 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{21B}_3$, $-OCHX^{21B}_2$, R^{22B} -substituted or unsubstituted alkyl, R^{22B} -substituted or

unsubstituted heteroalkyl, R^{22B} -substituted or unsubstituted cycloalkyl, R^{22B} -substituted or

unsubstituted heterocycloalkyl, R^{22B} -substituted or unsubstituted aryl, or R^{22B} -substituted or

unsubstituted heteroaryl. In embodiments, R^{21B} is independently oxo,

10 halogen, $-CX^{21B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{21B}_3$, $-OCHX^{21B}_2$, R^{22B} -substituted or unsubstituted C₁-C₈ alkyl, R^{22B} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{22B} -substituted or unsubstituted

C₃-C₈ cycloalkyl, R^{22B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{22B} -

15 substituted or unsubstituted phenyl, or R^{22B} -substituted or unsubstituted 5 to 6 membered

heteroaryl. X^{21B} is -F, -Cl, -Br, or -I.

[0152] In embodiments, R^{1C} is independently

hydrogen, $-CX^{1C}_3$, -CN, -COOH, -CONH₂, $-CHX^{1C}_2$, $-CH_2X^{1C}$, R^{20C} -substituted or

unsubstituted alkyl, R^{20C} -substituted or unsubstituted heteroalkyl, R^{20C} -substituted or

20 unsubstituted cycloalkyl, R^{20C} -substituted or unsubstituted heterocycloalkyl, R^{20C} -substituted

or unsubstituted aryl, or R^{20C} -substituted or unsubstituted heteroaryl. In embodiments, R^{1C} is

independently hydrogen, $-CX^{1C}_3$, -CN, -COOH, -CONH₂, $-CHX^{1C}_2$, $-CH_2X^{1C}$, R^{20C} -

substituted or unsubstituted C₁-C₈ alkyl, R^{20C} -substituted or unsubstituted 2 to 8 membered

heteroalkyl, R^{20C} -substituted or unsubstituted C₃-C₈ cycloalkyl, R^{20C} -substituted or

25 unsubstituted 3 to 6 membered heterocycloalkyl, R^{20C} -substituted or unsubstituted phenyl, or

R^{20C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{1C} is -F, -Cl, -Br, or -I. In

embodiments, R^{1C} is independently hydrogen. In embodiments, R^{1C} is independently methyl.

In embodiments, R^{1C} is independently ethyl.

[0153] R^{20C} is independently oxo,

30 halogen, $-CX^{20C}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{20C}_3$, $-OCHX^{20C}_2$, R^{21C} -substituted or unsubstituted alkyl, R^{21C} -substituted or

unsubstituted heteroalkyl, R^{21C} -substituted or unsubstituted cycloalkyl, R^{21C} -substituted or

unsubstituted heterocycloalkyl, R^{21C} -substituted or unsubstituted aryl, or R^{21C} -substituted or unsubstituted heteroaryl. In embodiments, R^{20C} is independently oxo, halogen, $-CX^{20C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20C}_3$, $-OCHX^{20C}_2$, R^{21C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{21C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{21C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{21C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{21C} -substituted or unsubstituted phenyl, or R^{21C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{20C} is $-F$, $-Cl$, $-Br$, or $-I$.

10 **[0154]** R^{21C} is independently oxo, halogen, $-CX^{21C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21C}_3$, $-OCHX^{21C}_2$, R^{22C} -substituted or unsubstituted alkyl, R^{22C} -substituted or unsubstituted heteroalkyl, R^{22C} -substituted or unsubstituted cycloalkyl, R^{22C} -substituted or unsubstituted heterocycloalkyl, R^{22C} -substituted or unsubstituted aryl, or R^{22C} -substituted or unsubstituted heteroaryl. In embodiments, R^{21C} is independently oxo, halogen, $-CX^{21C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21C}_3$, $-OCHX^{21C}_2$, R^{22C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{22C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{22C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{22C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{22C} -substituted or unsubstituted phenyl, or R^{22C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{21C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0155] In embodiments, R^{1D} is independently hydrogen, $-CX^{1D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{1D}_2$, $-CH_2X^{1D}$, R^{20D} -substituted or unsubstituted alkyl, R^{20D} -substituted or unsubstituted heteroalkyl, R^{20D} -substituted or unsubstituted cycloalkyl, R^{20D} -substituted or unsubstituted heterocycloalkyl, R^{20D} -substituted or unsubstituted aryl, or R^{20D} -substituted or unsubstituted heteroaryl. In embodiments, R^{1D} is independently hydrogen, $-CX^{1D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{1D}_2$, $-CH_2X^{1D}$, R^{20D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{20D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{20D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{20D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{20D} -substituted or unsubstituted phenyl, or R^{20D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{1D} is $-F$, $-Cl$, $-Br$, or $-I$. In

embodiments, R^{1D} is independently hydrogen. In embodiments, R^{1D} is independently methyl. In embodiments, R^{1D} is independently ethyl.

[0156] R^{20D} is independently oxo,

halogen, $-CX^{20D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
5 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20D}_3$, $-OCHX^{20D}_2$, R^{21D} -substituted or unsubstituted alkyl, R^{21D} -substituted or unsubstituted heteroalkyl, R^{21D} -substituted or unsubstituted cycloalkyl, R^{21D} -substituted or unsubstituted heterocycloalkyl, R^{21D} -substituted or unsubstituted aryl, or R^{21D} -substituted or unsubstituted heteroaryl. In

embodiments, R^{20D} is independently oxo,

halogen, $-CX^{20D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
10 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{20D}_3$, $-OCHX^{20D}_2$, R^{21D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{21D} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{21D} -substituted or unsubstituted

15 C_3 - C_8 cycloalkyl, R^{21D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{21D} -substituted or unsubstituted phenyl, or R^{21D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{20D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0157] R^{21D} is independently oxo,

halogen, $-CX^{21D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
20 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

$-NHOH$, $-OCX^{21D}_3$, $-OCHX^{21D}_2$, R^{22D} -substituted or unsubstituted alkyl, R^{22D} -substituted or unsubstituted heteroalkyl, R^{22D} -substituted or unsubstituted cycloalkyl, R^{22D} -substituted or unsubstituted heterocycloalkyl, R^{22D} -substituted or unsubstituted aryl, or R^{22D} -substituted or unsubstituted heteroaryl. In embodiments, R^{21D} is independently oxo,

25 halogen, $-CX^{21D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{21D}_3$, $-OCHX^{21D}_2$, R^{22D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{22D} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{22D} -substituted or unsubstituted

C_3 - C_8 cycloalkyl, R^{22D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{22D} -

30 substituted or unsubstituted phenyl, or R^{22D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{21D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0158] R^{22} , R^{22A} , R^{22B} , R^{22C} , and R^{22D} are independently hydrogen, oxo,

halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$

O₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,
 -NHC(O)NH₂, -NHSO₂H, -NHC(O)H,
 -NHC(O)OH, -NHOH, -OCCl₃, -OCF₃, -OCBr₃, -OCl₃, -OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF
 2, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
 5 heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R²², R^{22A},
 R^{22B}, R^{22C}, and R^{22D} are independently oxo,
 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCF₃, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted
 10 cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In
 embodiments, R²², R^{22A}, R^{22B}, R^{22C}, and R^{22D} are independently oxo,
 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCF₃, -OCHF₂, unsubstituted C₁-C₈ alkyl, unsubstituted 2 to 8 membered
 15 heteroalkyl, unsubstituted C₃-C₈ cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl,
 unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0159] In embodiments, R¹ is independently halogen. In embodiments, R¹ is independently
 hydrogen. In embodiments, z₁ is 2 and R¹ is independently hydrogen or halogen. In
 embodiments, z₁ is 2 and one R¹ is independently hydrogen and one R¹ is halogen.

20 **[0160]** In embodiments, R¹ is independently methyl. In embodiments, R¹ is independently
 C₁-C₄ alkyl. In embodiments, z₁ is 2 and one R¹ is independently halogen and one R¹ is
 unsubstituted C₁-C₄ alkyl. In embodiments, z₁ is 2 and one R¹ is independently halogen and
 one R¹ is unsubstituted C₁-C₃ alkyl. In embodiments, z₁ is 2 and one R¹ is independently
 halogen and one R¹ is unsubstituted C₁-C₂ alkyl. In embodiments, R¹ is independently
 25 halogen or unsubstituted C₁-C₃ alkyl. In embodiments, z₁ is 2 and one R¹ is independently
 halogen and one R¹ is methyl.

[0161] In embodiments, R¹ is independently substituted or unsubstituted methyl. In
 embodiments, R¹ is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments,
 R¹ is independently halogen or substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R¹
 30 is independently halogen or substituted or unsubstituted C₁-C₃ alkyl. In embodiments, R¹ is
 independently halogen or substituted or unsubstituted C₁-C₂ alkyl. In embodiments, R¹ is
 independently halogen or substituted or unsubstituted methyl. In embodiments, R¹ is
 independently substituted methyl. In embodiments, R¹ is independently substituted C₁-C₄

alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is substituted C₁-C₄ alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is substituted C₁-C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is substituted C₁-C₂ alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is substituted methyl. In embodiments, R¹ is independently unsubstituted methyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is unsubstituted C₁-C₄ alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is unsubstituted C₁-C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is unsubstituted C₁-C₂ alkyl. In embodiments, z1 is 2 and one R¹ is independently halogen and one R¹ is unsubstituted methyl.

[0162] In embodiments, z1 is 2 and one R¹ is independently substituted or unsubstituted C₁-C₄ alkyl and one R¹ is substituted or unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted or unsubstituted C₁-C₃ alkyl and one R¹ is substituted or unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted or unsubstituted C₁-C₂ alkyl and one R¹ is substituted or unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted or unsubstituted methyl and one R¹ is substituted or unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted or unsubstituted methyl and one R¹ is substituted or unsubstituted isopropyl.

[0163] In embodiments, z1 is 2 and one R¹ is independently unsubstituted C₁-C₄ alkyl and one R¹ is unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently unsubstituted C₁-C₃ alkyl and one R¹ is unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently unsubstituted C₁-C₂ alkyl and one R¹ is unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently unsubstituted methyl and one R¹ is unsubstituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently unsubstituted methyl and one R¹ is unsubstituted isopropyl.

[0164] In embodiments, z1 is 2 and one R¹ is independently substituted C₁-C₄ alkyl and one R¹ substituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted C₁-C₃ alkyl and one R¹ is substituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted C₁-C₂ alkyl and one R¹ is substituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted methyl and one R¹ is substituted C₃ alkyl. In embodiments, z1 is 2 and one R¹ is independently substituted methyl and one R¹ is substituted isopropyl.

[0165] In embodiments, z_1 is 2 and one R^1 is independently substituted C_1 - C_4 alkyl and one R^1 is unsubstituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently substituted C_1 - C_3 alkyl and one R^1 is unsubstituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently substituted C_1 - C_2 alkyl and one R^1 is unsubstituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently substituted methyl and one R^1 is unsubstituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently substituted methyl and one R^1 is unsubstituted isopropyl.

[0166] In embodiments, z_1 is 2 and one R^1 is independently unsubstituted C_1 - C_4 alkyl and one R^1 is substituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently unsubstituted C_1 - C_3 alkyl and one R^1 is substituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently unsubstituted C_1 - C_2 alkyl and one R^1 is substituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently unsubstituted methyl and one R^1 is substituted C_3 alkyl. In embodiments, z_1 is 2 and one R^1 is independently unsubstituted methyl and one R^1 is substituted isopropyl.

[0167] In embodiments, z_1 is 0. In embodiments, z_1 is 1. In embodiments, z_1 is 2. In embodiments, z_1 is 3. In embodiments, z_1 is 4. In embodiments, z_1 is 5.

[0168] In embodiments, R^2 is independently halogen, $-CX^2_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-OCX^2_3$, $-OCHX^2_2$, $-CHX^2_2$, $-CH_2X^2$, substituted or unsubstituted C_1 - C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_8 cycloalkyl, substituted or unsubstituted 3 to 8 membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^2 is independently halogen, $-CX^2_3$, $-CN$, unsubstituted C_1 - C_4 alkyl, or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^2 is independently halogen, $-CX^2_3$, $-CN$, unsubstituted methyl, unsubstituted ethyl, unsubstituted methoxy, or unsubstituted ethoxy. In embodiments, R^2 is independently unsubstituted methyl. In embodiments, R^2 is independently unsubstituted ethyl. In embodiments, R^2 is independently unsubstituted propyl. In embodiments, R^2 is independently unsubstituted n-propyl. In embodiments, R^2 is independently unsubstituted isopropyl. In embodiments, R^2 is independently unsubstituted butyl. In embodiments, R^2 is independently unsubstituted n-butyl. In embodiments, R^2 is independently unsubstituted isobutyl. In embodiments, R^2 is independently unsubstituted tert-butyl. In embodiments, R^2 is independently unsubstituted pentyl. In embodiments, R^2 is independently unsubstituted

hexyl. In embodiments, R^2 is independently unsubstituted heptyl. In embodiments, R^2 is independently unsubstituted octyl. In embodiments, R^2 is independently -F. In embodiments, R^2 is independently -Cl. In embodiments, R^2 is independently -Br. In embodiments, R^2 is independently -I. In embodiments, R^2 is independently unsubstituted methoxy. In embodiments, R^2 is independently unsubstituted ethoxy. In embodiments, R^2 is independently halogen. In embodiments, R^2 is independently -CF₃. In embodiments, R^2 is independently -CCl₃.

[0169] In embodiments, R^2 is independently halogen, -CX²₃. In embodiments, R^2 is independently -CHX²₂. In embodiments, R^2 is independently -CH₂X². In embodiments, R^2 is independently -OCX²₃. In embodiments, R^2 is independently -OCH₂X². In embodiments, R^2 is independently -OCHX²₂. In embodiments, R^2 is independently -CN. In embodiments, R^2 is independently -SO_{n2}R^{2D}. In embodiments, R^2 is independently -SO_{v2}NR^{2A}R^{2B}. In embodiments, R^2 is independently -NHC(O)NR^{2A}R^{2B}. In embodiments, R^2 is independently -N(O)_{m2}. In embodiments, R^2 is independently -NR^{2A}R^{2B}. In embodiments, R^2 is independently -C(O)R^{2C}. In embodiments, R^2 is independently -C(O)-OR^{2C}. In embodiments, R^2 is independently -C(O)NR^{2A}R^{2B}. In embodiments, R^2 is independently -OR^{2D}. In embodiments, R^2 is independently -NR^{2A}SO₂R^{2D}. In embodiments, R^2 is independently -NR^{2A}C(O)R^{2C}. In embodiments, R^2 is independently -NR^{2A}C(O)OR^{2C}. In embodiments, R^2 is independently -NR^{2A}OR^{2C}. In embodiments, R^2 is independently -OH. In embodiments, R^2 is independently -NH₂. In embodiments, R^2 is independently -COOH. In embodiments, R^2 is independently -CONH₂. In embodiments, R^2 is independently -NO₂. In embodiments, R^2 is independently -SH.

[0170] In embodiments, R^2 is independently substituted or unsubstituted alkyl. In embodiments, R^2 is independently substituted or unsubstituted heteroalkyl. In embodiments, R^2 is independently substituted or unsubstituted cycloalkyl. In embodiments, R^2 is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^2 is independently substituted or unsubstituted aryl. In embodiments, R^2 is independently substituted or unsubstituted heteroaryl. In embodiments, R^2 is independently substituted alkyl. In embodiments, R^2 is independently substituted heteroalkyl. In embodiments, R^2 is independently substituted cycloalkyl. In embodiments, R^2 is independently, substituted heterocycloalkyl. In embodiments, R^2 is independently substituted aryl. In embodiments, R^2 is independently substituted heteroaryl. In embodiments, R^2 is independently unsubstituted alkyl. In embodiments, R^2 is independently unsubstituted heteroalkyl. In embodiments, R^2 is independently unsubstituted cycloalkyl. In embodiments, R^2 is independently, unsubstituted

heterocycloalkyl. In embodiments, R^2 is independently unsubstituted aryl. In embodiments, R^2 is independently unsubstituted heteroaryl. In embodiments, R^2 is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^2 is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^2 is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^2 is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^2 is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^2 is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^2 is independently substituted C_1 - C_8 alkyl. In embodiments, R^2 is independently substituted 2 to 8 membered heteroalkyl.

10 In embodiments, R^2 is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^2 is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^2 is independently substituted C_6 - C_{10} aryl. In embodiments, R^2 is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^2 is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^2 is independently unsubstituted 2 to 8 membered heteroalkyl. In

15 embodiments, R^2 is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^2 is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^2 is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^2 is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^2 is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^2 is independently substituted or unsubstituted

20 2 to 4 membered heteroalkyl. In embodiments, R^2 is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^2 is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^2 is independently substituted or unsubstituted phenyl. In embodiments, R^2 is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^2 is independently substituted

25 C_1 - C_4 alkyl. In embodiments, R^2 is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^2 is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^2 is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^2 is independently substituted phenyl. In embodiments, R^2 is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^2 is independently unsubstituted C_1 - C_4 alkyl. In

30 embodiments, R^2 is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^2 is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^2 is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^2 is independently unsubstituted phenyl. In embodiments, R^2 is independently unsubstituted 5 to 6 membered heteroaryl.

[0171] In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted aryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted aryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted aryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted C_3 - C_8 cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted C_6 - C_{10} aryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted C_3 - C_8 cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted C_6 - C_{10} aryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, two

adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted phenyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted C_3 - C_6 cycloalkyl. In

5 embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted phenyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form a substituted 5 to 6 membered heteroaryl. In

10 embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted C_3 - C_6 cycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted phenyl. In embodiments, two adjacent R^2 substituents may optionally be joined to form an unsubstituted 5 to 6 membered heteroaryl.

15 **[0172]** In embodiments, R^{2A} is independently hydrogen. In embodiments, R^{2A} is independently $-CX^{2A}_3$. In embodiments, R^{2A} is independently $-CHX^{2A}_2$. In embodiments, R^{2A} is independently $-CH_2X^{2A}$. In embodiments, R^{2A} is independently $-CN$. In embodiments, R^{2A} is independently $-COOH$. In embodiments, R^{2A} is independently $-CONH_2$. In embodiments, R^{2A} is independently substituted or unsubstituted

20 alkyl. In embodiments, R^{2A} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{2A} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{2A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{2A} is independently substituted or unsubstituted aryl. In embodiments, R^{2A} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{2A} is independently substituted

25 alkyl. In embodiments, R^{2A} is independently substituted heteroalkyl. In embodiments, R^{2A} is independently substituted cycloalkyl. In embodiments, R^{2A} is independently, substituted heterocycloalkyl. In embodiments, R^{2A} is independently substituted aryl. In embodiments, R^{2A} is independently substituted heteroaryl. In embodiments, R^{2A} is independently unsubstituted alkyl. In embodiments, R^{2A} is independently unsubstituted heteroalkyl. In

30 embodiments, R^{2A} is independently unsubstituted cycloalkyl. In embodiments, R^{2A} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{2A} is independently unsubstituted aryl. In embodiments, R^{2A} is independently unsubstituted heteroaryl. In embodiments, R^{2A} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{2A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.

In embodiments, R^{2A} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
 embodiments, R^{2A} is independently, substituted or unsubstituted 3 to 8 membered
 heterocycloalkyl. In embodiments, R^{2A} is independently substituted or unsubstituted C_6 - C_{10}
 aryl. In embodiments, R^{2A} is independently substituted or unsubstituted 5 to 10 membered
 5 heteroaryl. In embodiments, R^{2A} is independently substituted C_1 - C_8 alkyl. In embodiments,
 R^{2A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{2A} is
 independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{2A} is independently,
 substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2A} is independently
 substituted C_6 - C_{10} aryl. In embodiments, R^{2A} is independently substituted 5 to 10 membered
 10 heteroaryl. In embodiments, R^{2A} is independently unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{2A} is independently unsubstituted 2 to 8 membered heteroalkyl. In
 embodiments, R^{2A} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2A} is
 independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2A} is
 independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2A} is independently unsubstituted
 15 5 to 10 membered heteroaryl. In embodiments, R^{2A} is independently substituted or
 unsubstituted C_1 - C_4 alkyl. In embodiments, R^{2A} is independently substituted or unsubstituted
 2 to 4 membered heteroalkyl. In embodiments, R^{2A} is independently substituted or
 unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{2A} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2A} is independently
 20 substituted or unsubstituted phenyl. In embodiments, R^{2A} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{2A} is independently substituted
 C_1 - C_4 alkyl. In embodiments, R^{2A} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{2A} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{2A} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2A} is
 25 independently substituted phenyl. In embodiments, R^{2A} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{2A} is independently unsubstituted C_1 - C_4 alkyl. In
 embodiments, R^{2A} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{2A} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{2A} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2A} is
 30 independently unsubstituted phenyl. In embodiments, R^{2A} is independently unsubstituted 5
 to 6 membered heteroaryl. In embodiments, R^{2A} is independently unsubstituted methyl. In
 embodiments, R^{2A} is independently unsubstituted ethyl. In embodiments, R^{2A} is
 independently unsubstituted propyl. In embodiments, R^{2A} is independently unsubstituted
 isopropyl. In embodiments, R^{2A} is independently unsubstituted tert-butyl.

[0173] In embodiments, R^{2B} is independently hydrogen. In embodiments, R^{2B} is independently $-CX^{2B}_3$. In embodiments, R^{2B} is independently $-CHX^{2B}_2$. In embodiments, R^{2B} is independently $-CH_2X^{2B}$. In embodiments, R^{2B} is independently $-CN$. In embodiments, R^{2B} is independently $-COOH$. In embodiments, R^{2B} is independently $-CONH_2$. In

5 embodiments, R^{2B} is independently substituted or unsubstituted alkyl. In embodiments, R^{2B} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{2B} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{2B} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{2B} is independently substituted or unsubstituted aryl. In embodiments, R^{2B} is independently substituted or

10 unsubstituted heteroaryl. In embodiments, R^{2B} is independently substituted alkyl. In embodiments, R^{2B} is independently substituted heteroalkyl. In embodiments, R^{2B} is independently substituted cycloalkyl. In embodiments, R^{2B} is independently, substituted heterocycloalkyl. In embodiments, R^{2B} is independently substituted aryl. In embodiments, R^{2B} is independently substituted heteroaryl. In embodiments, R^{2B} is independently

15 unsubstituted alkyl. In embodiments, R^{2B} is independently unsubstituted heteroalkyl. In embodiments, R^{2B} is independently unsubstituted cycloalkyl. In embodiments, R^{2B} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{2B} is independently unsubstituted aryl. In embodiments, R^{2B} is independently unsubstituted heteroaryl. In embodiments, R^{2B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In

20 embodiments, R^{2B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{2B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2B} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2B} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2B} is independently substituted or unsubstituted 5 to 10 membered

25 heteroaryl. In embodiments, R^{2B} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{2B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{2B} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{2B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2B} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{2B} is independently substituted 5 to 10 membered

30 heteroaryl. In embodiments, R^{2B} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{2B} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{2B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2B} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2B} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2B} is independently unsubstituted

35 5 to 10 membered heteroaryl. In embodiments, R^{2B} is independently substituted or

unsubstituted C₁-C₄ alkyl. In embodiments, R^{2B} is independently substituted or unsubstituted
 2 to 4 membered heteroalkyl. In embodiments, R^{2B} is independently substituted or
 unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{2B} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2B} is independently
 5 substituted or unsubstituted phenyl. In embodiments, R^{2B} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{2B} is independently substituted
 C₁-C₄ alkyl. In embodiments, R^{2B} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{2B} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{2B} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2B} is
 10 independently substituted phenyl. In embodiments, R^{2B} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{2B} is independently unsubstituted C₁-C₄ alkyl. In
 embodiments, R^{2B} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{2B} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{2B} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2B} is
 15 independently unsubstituted phenyl. In embodiments, R^{2B} is independently unsubstituted 5 to
 6 membered heteroaryl. In embodiments, R^{2B} is independently unsubstituted methyl. In
 embodiments, R^{2B} is independently unsubstituted ethyl. In embodiments, R^{2B} is
 independently unsubstituted propyl. In embodiments, R^{2B} is independently unsubstituted
 isopropyl. In embodiments, R^{2B} is independently unsubstituted tert-butyl.

20 **[0174]** In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may be
 joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{2A} and R^{2B}
 substituents bonded to the same nitrogen atom may be joined to form a substituted or
 unsubstituted heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same
 nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{2A}
 25 and R^{2B} substituents bonded to the same nitrogen atom may be joined to form a substituted
 heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may
 be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{2A} and R^{2B}
 substituents bonded to the same nitrogen atom may be joined to form an unsubstituted
 heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may
 30 be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In
 embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may be joined to
 form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{2A} and
 R^{2B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8
 membered heterocycloalkyl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same

nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In
embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may be joined to
form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2A} and R^{2B}
substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10
5 membered heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same
nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered
heterocycloalkyl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen
atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In
embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may be joined to
10 form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2A} and R^{2B}
substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6
membered heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same
nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In
embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may be joined to
15 form an unsubstituted 5 to 6 membered heteroaryl.

[0175] In embodiments, R^{2C} is independently hydrogen. In embodiments, R^{2C} is
independently $-CX^{2C}_3$. In embodiments, R^{2C} is independently $-CHX^{2C}_2$. In embodiments,
 R^{2C} is independently $-CH_2X^{2C}$. In embodiments, R^{2C} is independently $-CN$. In embodiments,
 R^{2C} is independently $-COOH$. In embodiments, R^{2C} is independently $-CONH_2$. In
20 embodiments, R^{2C} is independently substituted or unsubstituted alkyl. In embodiments, R^{2C}
is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{2C} is
independently substituted or unsubstituted cycloalkyl. In embodiments, R^{2C} is independently,
substituted or unsubstituted heterocycloalkyl. In embodiments, R^{2C} is independently
substituted or unsubstituted aryl. In embodiments, R^{2C} is independently substituted or
25 unsubstituted heteroaryl. In embodiments, R^{2C} is independently substituted alkyl. In
embodiments, R^{2C} is independently substituted heteroalkyl. In embodiments, R^{2C} is
independently substituted cycloalkyl. In embodiments, R^{2C} is independently, substituted
heterocycloalkyl. In embodiments, R^{2C} is independently substituted aryl. In embodiments,
 R^{2C} is independently substituted heteroaryl. In embodiments, R^{2C} is independently
30 unsubstituted alkyl. In embodiments, R^{2C} is independently unsubstituted heteroalkyl. In
embodiments, R^{2C} is independently unsubstituted cycloalkyl. In embodiments, R^{2C} is
independently, unsubstituted heterocycloalkyl. In embodiments, R^{2C} is independently
unsubstituted aryl. In embodiments, R^{2C} is independently unsubstituted heteroaryl. In
embodiments, R^{2C} is independently substituted or unsubstituted C_1 - C_8 alkyl. In

embodiments, R^{2C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{2C} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2C} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2C} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2C} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{2C} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{2C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{2C} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{2C} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2C} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{2C} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{2C} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{2C} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{2C} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2C} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2C} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2C} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{2C} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{2C} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{2C} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{2C} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2C} is independently substituted or unsubstituted phenyl. In embodiments, R^{2C} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{2C} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{2C} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{2C} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{2C} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2C} is independently substituted phenyl. In embodiments, R^{2C} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{2C} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{2C} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{2C} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{2C} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2C} is independently unsubstituted phenyl. In embodiments, R^{2C} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{2C} is independently unsubstituted methyl. In embodiments, R^{2C} is independently unsubstituted ethyl. In embodiments, R^{2C} is independently unsubstituted propyl. In embodiments, R^{2C} is independently unsubstituted isopropyl. In embodiments, R^{2C} is independently unsubstituted tert-butyl.

[0176] In embodiments, R^{2D} is independently hydrogen. In embodiments, R^{2D} is independently $-CX^{2D}_3$. In embodiments, R^{2D} is independently $-CHX^{2D}_2$. In embodiments, R^{2D} is independently $-CH_2X^{2D}$. In embodiments, R^{2D} is independently $-CN$. In embodiments, R^{2D} is independently $-COOH$. In embodiments, R^{2D} is independently $-CONH_2$. In embodiments, R^{2D} is independently substituted or unsubstituted alkyl. In embodiments, R^{2D} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{2D} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{2D} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{2D} is independently substituted or unsubstituted aryl. In embodiments, R^{2D} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{2D} is independently substituted alkyl. In embodiments, R^{2D} is independently substituted heteroalkyl. In embodiments, R^{2D} is independently substituted cycloalkyl. In embodiments, R^{2D} is independently, substituted heterocycloalkyl. In embodiments, R^{2D} is independently substituted aryl. In embodiments, R^{2D} is independently substituted heteroaryl. In embodiments, R^{2D} is independently unsubstituted alkyl. In embodiments, R^{2D} is independently unsubstituted heteroalkyl. In embodiments, R^{2D} is independently unsubstituted cycloalkyl. In embodiments, R^{2D} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{2D} is independently unsubstituted aryl. In embodiments, R^{2D} is independently unsubstituted heteroaryl. In embodiments, R^{2D} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{2D} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{2D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2D} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2D} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2D} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{2D} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{2D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{2D} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{2D} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2D} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{2D} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{2D} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{2D} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{2D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{2D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{2D} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{2D} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{2D} is independently substituted or

unsubstituted C₁-C₄ alkyl. In embodiments, R^{2D} is independently substituted or unsubstituted
 2 to 4 membered heteroalkyl. In embodiments, R^{2D} is independently substituted or
 unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{2D} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2D} is independently
 5 substituted or unsubstituted phenyl. In embodiments, R^{2D} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{2D} is independently substituted
 C₁-C₄ alkyl. In embodiments, R^{2D} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{2D} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{2D} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2D} is
 10 independently substituted phenyl. In embodiments, R^{2D} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{2D} is independently unsubstituted C₁-C₄ alkyl. In
 embodiments, R^{2D} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{2D} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{2D} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{2D} is
 15 independently unsubstituted phenyl. In embodiments, R^{2D} is independently unsubstituted 5
 to 6 membered heteroaryl. In embodiments, R^{2D} is independently unsubstituted methyl. In
 embodiments, R^{2D} is independently unsubstituted ethyl. In embodiments, R^{2D} is
 independently unsubstituted propyl. In embodiments, R^{2D} is independently unsubstituted
 isopropyl. In embodiments, R^{2D} is independently unsubstituted tert-butyl.

20 **[0177]** In embodiments, R² is independently
 halogen, -CX²₃, -CHX²₂, -CH₂X², -OCX²₃, -OCH₂X², -OCHX²₂, -CN, -SO_{n2}R^{2D}, -SO_{v2}NR^{2A}
 R^{2B}, -NHC(O)NR^{2A}R^{2B}, -N(O)_{m2}, -NR^{2A}R^{2B}, -C(O)R^{2C}, -C(O)OR^{2C}, -C(O)NR^{2A}R^{2B}, -OR^{2D}, -
 NR^{2A}SO₂R^{2D}, -NR^{2A}C(O)R^{2C}, -NR^{2A}C(O)OR^{2C}, -NR^{2A}OR^{2C}, R²³-substituted or unsubstituted
 alkyl, R²³-substituted or unsubstituted heteroalkyl, R²³-substituted or unsubstituted
 25 cycloalkyl, R²³-substituted or unsubstituted heterocycloalkyl, R²³-substituted or unsubstituted
 aryl, or R²³-substituted or unsubstituted heteroaryl. In embodiments, R² is independently
 halogen, -CX²₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCX²₃, -OCHX²₂, R²³-substituted or unsubstituted alkyl, R²³-substituted or
 30 unsubstituted heteroalkyl, R²³-substituted or unsubstituted cycloalkyl, R²³-substituted or
 unsubstituted heterocycloalkyl, R²³-substituted or unsubstituted aryl, or R²³-substituted or
 unsubstituted heteroaryl. In embodiments, R² is independently
 halogen, -CX²₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-\text{OCX}^2_3$, $-\text{OCHX}^2_2$, R^{23} -substituted or unsubstituted C_1 - C_8 alkyl, R^{23} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{23} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{23} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{23} -substituted or unsubstituted phenyl, or R^{23} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^2 is –
 5 F, -Cl, -Br, or -I. In embodiments, R^2 is independently hydrogen. In embodiments, R^2 is independently methyl. In embodiments, R^2 is independently ethyl.

[0178] In embodiments, two adjacent R^2 substituents may optionally be joined to form a R^{23} -substituted or unsubstituted cycloalkyl, R^{23} -substituted or unsubstituted heterocycloalkyl, R^{23} -substituted or unsubstituted aryl, or R^{23} -substituted or unsubstituted heteroaryl. In
 10 embodiments, two adjacent R^2 substituents may optionally be joined to form a R^{23} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{23} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{23} -substituted or unsubstituted phenyl, or R^{23} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0179] R^{23} is independently oxo,
 15 halogen, $-\text{CX}^{23}_3$, -CN, -OH, - NH_2 , -COOH, -CONH $_2$, -NO $_2$, -SH, -SO $_3$ H, -SO $_4$ H, -SO $_2$ NH $_2$, -NHNH $_2$, -ONH $_2$, -NHC(O)NHNH $_2$, -NHC(O)NH $_2$, -NHSO $_2$ H, -NHC(O)H, -NHC(O)OH, -NHOH, $-\text{OCX}^{23}_3$, $-\text{OCHX}^{23}_2$, R^{24} -substituted or unsubstituted alkyl, R^{24} -substituted or unsubstituted heteroalkyl, R^{24} -substituted or unsubstituted cycloalkyl, R^{24} -substituted or unsubstituted heterocycloalkyl, R^{24} -substituted or unsubstituted aryl, or R^{24} -substituted or
 20 unsubstituted heteroaryl. In embodiments, R^{23} is independently oxo,
 halogen, $-\text{CX}^{23}_3$, -CN, -OH, - NH_2 , -COOH, -CONH $_2$, -NO $_2$, -SH, -SO $_3$ H, -SO $_4$ H, -SO $_2$ NH $_2$, -NHNH $_2$, -ONH $_2$, -NHC(O)NHNH $_2$, -NHC(O)NH $_2$, -NHSO $_2$ H, -NHC(O)H, -NHC(O)OH, -NHOH, $-\text{OCX}^{23}_3$, $-\text{OCHX}^{23}_2$, R^{24} -substituted or unsubstituted C_1 - C_8 alkyl, R^{24} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{24} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 25 R^{24} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{24} -substituted or unsubstituted phenyl, or R^{24} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{23} is -F, -Cl, -Br, or -I.

[0180] R^{24} is independently oxo,
 halogen, $-\text{CX}^{24}_3$, -CN, -OH, - NH_2 , -COOH, -CONH $_2$, -NO $_2$, -SH, -SO $_3$ H, -SO $_4$ H, -SO $_2$ NH $_2$,
 30 -NHNH $_2$, -ONH $_2$, -NHC(O)NHNH $_2$, -NHC(O)NH $_2$, -NHSO $_2$ H, -NHC(O)H, -NHC(O)OH, -NHOH, $-\text{OCX}^{24}_3$, $-\text{OCHX}^{24}_2$, R^{25} -substituted or unsubstituted alkyl, R^{25} -substituted or unsubstituted heteroalkyl, R^{25} -substituted or unsubstituted cycloalkyl, R^{25} -substituted or unsubstituted heterocycloalkyl, R^{25} -substituted or unsubstituted aryl, or R^{25} -substituted or

unsubstituted heteroaryl. In embodiments, R^{24} is independently oxo, halogen, $-CX^{24}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{24}_3$, $-OCHX^{24}_2$, R^{25} -substituted or unsubstituted C_1 - C_8 alkyl, R^{25} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{25} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{25} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{25} -substituted or unsubstituted phenyl, or R^{25} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{24} is $-F$, $-Cl$, $-Br$, or $-I$.

[0181] In embodiments, R^{2A} is independently

hydrogen, $-CX^{2A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{2A}_2$, $-CH_2X^{2A}$, R^{23A} -substituted or unsubstituted alkyl, R^{23A} -substituted or unsubstituted heteroalkyl, R^{23A} -substituted or unsubstituted cycloalkyl, R^{23A} -substituted or unsubstituted heterocycloalkyl, R^{23A} -substituted or unsubstituted aryl, or R^{23A} -substituted or unsubstituted heteroaryl. In embodiments, R^{2A} is independently hydrogen, $-CX^{2A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{2A}_2$, $-CH_2X^{2A}$, R^{23A} -

substituted or unsubstituted C_1 - C_8 alkyl, R^{23A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{23A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{23A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{23A} -substituted or unsubstituted phenyl, or R^{23A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{2A} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{2A} is independently hydrogen. In embodiments, R^{2A} is independently methyl.

In embodiments, R^{2A} is independently ethyl.

[0182] In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{23A} -substituted or unsubstituted heterocycloalkyl or R^{23A} -substituted or unsubstituted heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{23A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{23A} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0183] R^{23A} is independently oxo,

halogen, $-CX^{23A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{23A}_3$, $-OCHX^{23A}_2$, R^{24A} -substituted or unsubstituted alkyl, R^{24A} -substituted or unsubstituted heteroalkyl, R^{24A} -substituted or unsubstituted cycloalkyl, R^{24A} -substituted or unsubstituted heterocycloalkyl, R^{24A} -substituted or unsubstituted aryl, or R^{24A} -substituted or unsubstituted heteroaryl. In embodiments, R^{23A} is independently oxo,

halogen, $-CX^{23A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{23A}_3$, $-OCHX^{23A}_2$, R^{24A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{24A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{24A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{24A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{24A} -substituted or unsubstituted phenyl, or R^{24A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{23A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0184] R^{24A} is independently oxo,

halogen, $-CX^{24A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{24A}_3$, $-OCHX^{24A}_2$, R^{25A} -substituted or unsubstituted alkyl, R^{25A} -substituted or unsubstituted heteroalkyl, R^{25A} -substituted or unsubstituted cycloalkyl, R^{25A} -substituted or unsubstituted heterocycloalkyl, R^{25A} -substituted or unsubstituted aryl, or R^{25A} -substituted or unsubstituted heteroaryl. In embodiments, R^{24A} is independently oxo,

halogen, $-CX^{24A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{24A}_3$, $-OCHX^{24A}_2$, R^{25A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{25A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{25A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{25A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{25A} -substituted or unsubstituted phenyl, or R^{25A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{24A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0185] In embodiments, R^{2B} is independently

hydrogen, $-CX^{2B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{2B}_2$, $-CH_2X^{2B}$, R^{23B} -substituted or unsubstituted alkyl, R^{23B} -substituted or unsubstituted heteroalkyl, R^{23B} -substituted or unsubstituted cycloalkyl, R^{23B} -substituted or unsubstituted heterocycloalkyl, R^{23B} -substituted or unsubstituted aryl, or R^{23B} -substituted or unsubstituted heteroaryl. In embodiments, R^{2B} is independently hydrogen, $-CX^{2B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{2B}_2$, $-CH_2X^{2B}$, R^{23B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{23B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{23B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{23B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{23B} -substituted or unsubstituted phenyl, or R^{23B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{2B} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{2B} is independently hydrogen. In embodiments, R^{2B} is independently methyl. In embodiments, R^{2B} is independently ethyl.

[0186] In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{23B} -substituted or unsubstituted heterocycloalkyl or R^{23B} -substituted or unsubstituted heteroaryl. In embodiments, R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{23B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{23B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0187] R^{23B} is independently oxo, halogen, $-CX^{23B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{23B}_3$, $-OCHX^{23B}_2$, R^{24B} -substituted or unsubstituted alkyl, R^{24B} -substituted or unsubstituted heteroalkyl, R^{24B} -substituted or unsubstituted cycloalkyl, R^{24B} -substituted or unsubstituted heterocycloalkyl, R^{24B} -substituted or unsubstituted aryl, or R^{24B} -substituted or unsubstituted heteroaryl. In embodiments, R^{23B} is independently oxo, halogen, $-CX^{23B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{23B}_3$, $-OCHX^{23B}_2$, R^{24B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{24B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{24B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{24B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{24B} -substituted or unsubstituted phenyl, or R^{24B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{23B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0188] R^{24B} is independently oxo, halogen, $-CX^{24B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{24B}_3$, $-OCHX^{24B}_2$, R^{25B} -substituted or unsubstituted alkyl, R^{25B} -substituted or unsubstituted heteroalkyl, R^{25B} -substituted or unsubstituted cycloalkyl, R^{25B} -substituted or unsubstituted heterocycloalkyl, R^{25B} -substituted or unsubstituted aryl, or R^{25B} -substituted or unsubstituted heteroaryl. In embodiments, R^{24B} is independently oxo, halogen, $-CX^{24B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{24B}_3$, $-OCHX^{24B}_2$, R^{25B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{25B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{25B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{25B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{25B} -substituted or unsubstituted phenyl, or R^{25B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{24B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0189] In embodiments, R^{2C} is independently hydrogen, $-CX^{2C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{2C}_2$, $-CH_2X^{2C}$, R^{23C} -substituted or unsubstituted alkyl, R^{23C} -substituted or unsubstituted heteroalkyl, R^{23C} -substituted or unsubstituted cycloalkyl, R^{23C} -substituted or unsubstituted heterocycloalkyl, R^{23C} -substituted or unsubstituted aryl, or R^{23C} -substituted or unsubstituted heteroaryl. In embodiments, R^{2C} is independently hydrogen, $-CX^{2C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{2C}_2$, $-CH_2X^{2C}$, R^{23C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{23C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{23C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{23C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{23C} -substituted or unsubstituted phenyl, or R^{23C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{2C} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{2C} is independently hydrogen. In embodiments, R^{2C} is independently methyl. In embodiments, R^{2C} is independently ethyl.

[0190] R^{23C} is independently oxo, halogen, $-CX^{23C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{23C}_3$, $-OCHX^{23C}_2$, R^{24C} -substituted or unsubstituted alkyl, R^{24C} -substituted or unsubstituted heteroalkyl, R^{24C} -substituted or unsubstituted cycloalkyl, R^{24C} -substituted or unsubstituted heterocycloalkyl, R^{24C} -substituted or unsubstituted aryl, or R^{24C} -substituted or unsubstituted heteroaryl. In embodiments, R^{23C} is independently oxo, halogen, $-CX^{23C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{23C}_3$, $-OCHX^{23C}_2$, R^{24C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{24C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{24C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{24C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{24C} -substituted or unsubstituted phenyl, or R^{24C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{23C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0191] R^{24C} is independently oxo, halogen, $-CX^{24C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{24C}_3$, $-OCHX^{24C}_2$, R^{25C} -substituted or unsubstituted alkyl, R^{25C} -substituted or unsubstituted heteroalkyl, R^{25C} -substituted or unsubstituted cycloalkyl, R^{25C} -substituted or unsubstituted heterocycloalkyl, R^{25C} -substituted or unsubstituted aryl, or R^{25C} -substituted or unsubstituted heteroaryl. In embodiments, R^{24C} is independently oxo, halogen, $-CX^{24C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCX}^{24\text{C}}_3$, $-\text{OCHX}^{24\text{C}}_2$, $\text{R}^{25\text{C}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{25\text{C}}$ -
substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{25\text{C}}$ -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, $\text{R}^{25\text{C}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{25\text{C}}$ -
5 substituted or unsubstituted phenyl, or $\text{R}^{25\text{C}}$ -substituted or unsubstituted 5 to 6 membered
heteroaryl. $\text{X}^{24\text{C}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0192] In embodiments, $\text{R}^{2\text{D}}$ is independently

hydrogen, $-\text{CX}^{2\text{D}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{2\text{D}}_2$, $-\text{CH}_2\text{X}^{2\text{D}}$, $\text{R}^{23\text{D}}$ -substituted or
unsubstituted alkyl, $\text{R}^{23\text{D}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{23\text{D}}$ -substituted or
10 unsubstituted cycloalkyl, $\text{R}^{23\text{D}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{23\text{D}}$ -substituted
or unsubstituted aryl, or $\text{R}^{23\text{D}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{2\text{D}}$ is
independently hydrogen, $-\text{CX}^{2\text{D}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{2\text{D}}_2$, $-\text{CH}_2\text{X}^{2\text{D}}$, $\text{R}^{23\text{D}}$ -
substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{23\text{D}}$ -substituted or unsubstituted 2 to 8 membered
heteroalkyl, $\text{R}^{23\text{D}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{23\text{D}}$ -substituted or
15 unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{23\text{D}}$ -substituted or unsubstituted phenyl, or
 $\text{R}^{23\text{D}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{2\text{D}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$. In
embodiments, $\text{R}^{2\text{D}}$ is independently hydrogen. In embodiments, $\text{R}^{2\text{D}}$ is independently methyl.
In embodiments, $\text{R}^{2\text{D}}$ is independently ethyl.

[0193] $\text{R}^{23\text{D}}$ is independently oxo,

20 halogen, $-\text{CX}^{23\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCX}^{23\text{D}}_3$, $-\text{OCHX}^{23\text{D}}_2$, $\text{R}^{24\text{D}}$ -substituted or unsubstituted alkyl, $\text{R}^{24\text{D}}$ -substituted or
unsubstituted heteroalkyl, $\text{R}^{24\text{D}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{24\text{D}}$ -substituted or
unsubstituted heterocycloalkyl, $\text{R}^{24\text{D}}$ -substituted or unsubstituted aryl, or $\text{R}^{24\text{D}}$ -substituted or
25 unsubstituted heteroaryl. In embodiments, $\text{R}^{23\text{D}}$ is independently oxo,
halogen, $-\text{CX}^{23\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCX}^{23\text{D}}_3$, $-\text{OCHX}^{23\text{D}}_2$, $\text{R}^{24\text{D}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{24\text{D}}$ -
substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{24\text{D}}$ -substituted or unsubstituted
30 C_3 - C_8 cycloalkyl, $\text{R}^{24\text{D}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{24\text{D}}$ -
substituted or unsubstituted phenyl, or $\text{R}^{24\text{D}}$ -substituted or unsubstituted 5 to 6 membered
heteroaryl. $\text{X}^{23\text{D}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0194] R^{24D} is independently oxo,

halogen, $-CX^{24D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{24D}_3$, $-OCHX^{24D}_2$, R^{25D} -substituted or unsubstituted alkyl, R^{25D} -substituted or
5 unsubstituted heteroalkyl, R^{25D} -substituted or unsubstituted cycloalkyl, R^{25D} -substituted or
unsubstituted heterocycloalkyl, R^{25D} -substituted or unsubstituted aryl, or R^{25D} -substituted or
unsubstituted heteroaryl. In embodiments, R^{24D} is independently oxo,
halogen, $-CX^{24D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
10 $-NHOH$, $-OCX^{24D}_3$, $-OCHX^{24D}_2$, R^{25D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{25D} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{25D} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{25D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{25D} -
substituted or unsubstituted phenyl, or R^{25D} -substituted or unsubstituted 5 to 6 membered
heteroaryl. X^{24D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0195] R^{25} , R^{25A} , R^{25B} , R^{25C} , and R^{25D} are independently hydrogen, oxo,

halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$
 O_4H , $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$,
 $-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$
20 $_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{25} , R^{25A} ,
 R^{25B} , R^{25C} , and R^{25D} are independently oxo,
halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
25 $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted
cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In
embodiments, R^{25} , R^{25A} , R^{25B} , R^{25C} , and R^{25D} are independently oxo,
halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
30 $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered
heteroalkyl, unsubstituted C_3 - C_8 cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl,
unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0196] In embodiments, R^2 is independently halogen. In embodiments, R^2 is independently hydrogen. In embodiments, R^2 is independently hydrogen or halogen. In embodiments, R^2 is independently methyl. In embodiments, R^2 is independently C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or C_1 - C_3 alkyl. In embodiments, R^2 is independently halogen or C_1 - C_2 alkyl. In embodiments, R^2 is independently halogen or methyl. In embodiments, R^2 is independently substituted or unsubstituted methyl. In embodiments, R^2 is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or substituted or unsubstituted C_1 - C_3 alkyl. In embodiments, R^2 is independently halogen or substituted or unsubstituted C_1 - C_2 alkyl. In embodiments, R^2 is independently halogen or substituted or unsubstituted methyl. In embodiments, R^2 is independently substituted methyl. In embodiments, R^2 is independently substituted C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or substituted C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or substituted C_1 - C_3 alkyl. In embodiments, R^2 is independently halogen or substituted C_1 - C_2 alkyl. In embodiments, R^2 is independently halogen or substituted methyl. In embodiments, R^2 is independently unsubstituted methyl. In embodiments, R^2 is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or unsubstituted C_1 - C_4 alkyl. In embodiments, R^2 is independently halogen or unsubstituted C_1 - C_3 alkyl. In embodiments, R^2 is independently halogen or unsubstituted C_1 - C_2 alkyl. In embodiments, R^2 is independently halogen or unsubstituted methyl.

[0197] In embodiments, R^2 is independently C_1 - C_4 alkyl. In embodiments, R^2 is independently C_1 - C_3 alkyl. In embodiments, R^2 is independently C_1 - C_2 alkyl. In embodiments, R^2 is independently methyl. In embodiments, R^2 is independently isopropyl. In embodiments, R^2 is independently substituted or unsubstituted methyl or substituted or unsubstituted isopropyl.

[0198] In embodiments, R^2 is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^2 is independently substituted or unsubstituted C_1 - C_3 alkyl. In embodiments, R^2 is independently substituted or unsubstituted C_1 - C_2 alkyl. In embodiments, R^2 is independently substituted or unsubstituted methyl.

[0199] In embodiments, z_2 is 0. In embodiments, z_2 is 1. In embodiments, z_2 is 2. In embodiments, z_2 is 3. In embodiments, z_2 is 4.

[0200] In embodiments, R^3 is hydrogen. In embodiments, R^3 is $-NH_2$.

[0201] In embodiments, the symbol Y^1 is N. In embodiments, the symbol Y^1 is $C(R^4)$.

[0202] In embodiments, R^4 is hydrogen, substituted or unsubstituted C_1 - C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl.

[0203] In embodiments, R^4 is independently hydrogen. In embodiments, R^4 is independently halogen. In embodiments, R^4 is independently $-CX^4_3$. In embodiments, R^4 is independently $-CHX^4_2$. In embodiments, R^4 is independently $-CH_2X^4$. In embodiments, R^4 is independently $-OCX^4_3$. In embodiments, R^4 is independently $-OCH_2X^4$. In embodiments, R^4 is independently $-OCHX^4_2$. In embodiments, R^4 is independently $-CN$. In embodiments, R^4 is independently $-SO_{n4}R^{4D}$. In embodiments, R^4 is independently $-SO_{v4}NR^{4A}R^{4B}$. In
 5 independently $-NHC(O)NR^{4A}R^{4B}$. In embodiments, R^4 is independently $-N(O)_{m4}$. In embodiments, R^4 is independently $-NR^{4A}R^{4B}$. In embodiments, R^4 is independently $-C(O)R^{4C}$. In embodiments, R^4 is independently $-C(O)-OR^{4C}$. In
 10 independently $-C(O)NR^{4A}R^{4B}$. In embodiments, R^4 is independently $-OR^{4D}$. In embodiments, R^4 is independently $-NR^{4A}SO_2R^{4D}$. In embodiments, R^4 is independently $-NR^{4A}C(O)R^{4C}$. In embodiments, R^4 is independently $-NR^{4A}C(O)OR^{4C}$.
 15 In embodiments, R^4 is independently $-NR^{4A}OR^{4C}$. In embodiments, R^4 is independently $-OH$. In embodiments, R^4 is independently $-NH_2$. In embodiments, R^4 is independently $-COOH$. In embodiments, R^4 is independently $-CONH_2$. In embodiments, R^4 is independently $-NO_2$. In embodiments, R^4 is independently $-SH$.

[0204] In embodiments, R^4 is independently substituted or unsubstituted alkyl. In
 20 independently substituted or unsubstituted heteroalkyl. In embodiments, R^4 is independently substituted or unsubstituted cycloalkyl. In embodiments, R^4 is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^4 is independently substituted or unsubstituted aryl. In embodiments, R^4 is independently
 25 substituted or unsubstituted heteroaryl. In embodiments, R^4 is independently substituted alkyl. In embodiments, R^4 is independently substituted heteroalkyl. In embodiments, R^4 is independently substituted cycloalkyl. In embodiments, R^4 is independently, substituted heterocycloalkyl. In embodiments, R^4 is independently substituted aryl. In embodiments, R^4 is independently substituted heteroaryl. In embodiments, R^4 is independently unsubstituted
 30 alkyl. In embodiments, R^4 is independently unsubstituted heteroalkyl. In embodiments, R^4 is independently unsubstituted cycloalkyl. In embodiments, R^4 is independently, unsubstituted heterocycloalkyl. In embodiments, R^4 is independently unsubstituted aryl. In embodiments, R^4 is independently unsubstituted heteroaryl. In embodiments, R^4 is independently

substituted or unsubstituted C₁-C₈ alkyl. In embodiments, R⁴ is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R⁴ is independently substituted or unsubstituted C₃-C₈ cycloalkyl. In embodiments, R⁴ is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁴ is independently substituted or unsubstituted C₆-C₁₀ aryl. In embodiments, R⁴ is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R⁴ is independently substituted C₁-C₈ alkyl. In embodiments, R⁴ is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R⁴ is independently substituted C₃-C₈ cycloalkyl. In embodiments, R⁴ is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁴ is independently substituted C₆-C₁₀ aryl. In embodiments, R⁴ is independently substituted 5 to 10 membered heteroaryl. In embodiments, R⁴ is independently unsubstituted C₁-C₈ alkyl. In embodiments, R⁴ is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R⁴ is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R⁴ is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁴ is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R⁴ is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R⁴ is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R⁴ is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R⁴ is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R⁴ is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁴ is independently substituted or unsubstituted phenyl. In embodiments, R⁴ is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R⁴ is independently substituted C₁-C₄ alkyl. In embodiments, R⁴ is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R⁴ is independently substituted C₃-C₆ cycloalkyl. In embodiments, R⁴ is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁴ is independently substituted phenyl. In embodiments, R⁴ is independently substituted 5 to 6 membered heteroaryl. In embodiments, R⁴ is independently unsubstituted C₁-C₄ alkyl. In embodiments, R⁴ is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R⁴ is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R⁴ is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁴ is independently unsubstituted phenyl. In embodiments, R⁴ is independently unsubstituted 5 to 6 membered heteroaryl.

[0205] In embodiments, R^{4A} is independently hydrogen. In embodiments, R^{4A} is independently -CX^{4A}₃. In embodiments, R^{4A} is independently -CHX^{4A}₂. In embodiments,

R^{4A} is independently $-CH_2X^{4A}$. In embodiments, R^{4A} is independently $-CN$. In
embodiments, R^{4A} is independently $-COOH$. In embodiments, R^{4A} is
independently $-CONH_2$. In embodiments, R^{4A} is independently substituted or unsubstituted
alkyl. In embodiments, R^{4A} is independently substituted or unsubstituted heteroalkyl. In
5 embodiments, R^{4A} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 R^{4A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{4A} is
independently substituted or unsubstituted aryl. In embodiments, R^{4A} is independently
substituted or unsubstituted heteroaryl. In embodiments, R^{4A} is independently substituted
alkyl. In embodiments, R^{4A} is independently substituted heteroalkyl. In embodiments, R^{4A} is
10 independently substituted cycloalkyl. In embodiments, R^{4A} is independently, substituted
heterocycloalkyl. In embodiments, R^{4A} is independently substituted aryl. In embodiments,
 R^{4A} is independently substituted heteroaryl. In embodiments, R^{4A} is independently
unsubstituted alkyl. In embodiments, R^{4A} is independently unsubstituted heteroalkyl. In
embodiments, R^{4A} is independently unsubstituted cycloalkyl. In embodiments, R^{4A} is
15 independently, unsubstituted heterocycloalkyl. In embodiments, R^{4A} is independently
unsubstituted aryl. In embodiments, R^{4A} is independently unsubstituted heteroaryl. In
embodiments, R^{4A} is independently substituted or unsubstituted C_1-C_8 alkyl. In
embodiments, R^{4A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
In embodiments, R^{4A} is independently substituted or unsubstituted C_3-C_8 cycloalkyl. In
20 embodiments, R^{4A} is independently, substituted or unsubstituted 3 to 8 membered
heterocycloalkyl. In embodiments, R^{4A} is independently substituted or unsubstituted C_6-C_{10}
aryl. In embodiments, R^{4A} is independently substituted or unsubstituted 5 to 10 membered
heteroaryl. In embodiments, R^{4A} is independently substituted C_1-C_8 alkyl. In embodiments,
 R^{4A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{4A} is
25 independently substituted C_3-C_8 cycloalkyl. In embodiments, R^{4A} is independently,
substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4A} is independently
substituted C_6-C_{10} aryl. In embodiments, R^{4A} is independently substituted 5 to 10 membered
heteroaryl. In embodiments, R^{4A} is independently unsubstituted C_1-C_8 alkyl. In
embodiments, R^{4A} is independently unsubstituted 2 to 8 membered heteroalkyl. In
30 embodiments, R^{4A} is independently unsubstituted C_3-C_8 cycloalkyl. In embodiments, R^{4A} is
independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4A} is
independently unsubstituted C_6-C_{10} aryl. In embodiments, R^{4A} is independently unsubstituted
5 to 10 membered heteroaryl. In embodiments, R^{4A} is independently substituted or
unsubstituted C_1-C_4 alkyl. In embodiments, R^{4A} is independently substituted or unsubstituted
35 2 to 4 membered heteroalkyl. In embodiments, R^{4A} is independently substituted or

unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{4A} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4A} is independently
 substituted or unsubstituted phenyl. In embodiments, R^{4A} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{4A} is independently substituted
 5 C₁-C₄ alkyl. In embodiments, R^{4A} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{4A} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{4A} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4A} is
 independently substituted phenyl. In embodiments, R^{4A} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{4A} is independently unsubstituted C₁-C₄ alkyl. In
 10 embodiments, R^{4A} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{4A} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{4A} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4A} is
 independently unsubstituted phenyl. In embodiments, R^{4A} is independently unsubstituted 5
 to 6 membered heteroaryl. In embodiments, R^{4A} is independently unsubstituted methyl. In
 15 embodiments, R^{4A} is independently unsubstituted ethyl. In embodiments, R^{4A} is
 independently unsubstituted propyl. In embodiments, R^{4A} is independently unsubstituted
 isopropyl. In embodiments, R^{4A} is independently unsubstituted tert-butyl.

[0206] In embodiments, R^{4B} is independently hydrogen. In embodiments, R^{4B} is
 independently -CX^{4B}₃. In embodiments, R^{4B} is independently -CHX^{4B}₂. In embodiments,
 20 R^{4B} is independently -CH₂X^{4B}. In embodiments, R^{4B} is independently -CN. In embodiments,
 R^{4B} is independently -COOH. In embodiments, R^{4B} is independently -CONH₂. In
 embodiments, R^{4B} is independently substituted or unsubstituted alkyl. In embodiments, R^{4B}
 is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{4B} is
 independently substituted or unsubstituted cycloalkyl. In embodiments, R^{4B} is independently,
 25 substituted or unsubstituted heterocycloalkyl. In embodiments, R^{4B} is independently
 substituted or unsubstituted aryl. In embodiments, R^{4B} is independently substituted or
 unsubstituted heteroaryl. In embodiments, R^{4B} is independently substituted alkyl. In
 embodiments, R^{4B} is independently substituted heteroalkyl. In embodiments, R^{4B} is
 independently substituted cycloalkyl. In embodiments, R^{4B} is independently, substituted
 30 heterocycloalkyl. In embodiments, R^{4B} is independently substituted aryl. In embodiments,
 R^{4B} is independently substituted heteroaryl. In embodiments, R^{4B} is independently
 unsubstituted alkyl. In embodiments, R^{4B} is independently unsubstituted heteroalkyl. In
 embodiments, R^{4B} is independently unsubstituted cycloalkyl. In embodiments, R^{4B} is
 independently, unsubstituted heterocycloalkyl. In embodiments, R^{4B} is independently

unsubstituted aryl. In embodiments, R^{4B} is independently unsubstituted heteroaryl. In
 embodiments, R^{4B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{4B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
 In embodiments, R^{4B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
 5 embodiments, R^{4B} is independently, substituted or unsubstituted 3 to 8 membered
 heterocycloalkyl. In embodiments, R^{4B} is independently substituted or unsubstituted C_6 - C_{10}
 aryl. In embodiments, R^{4B} is independently substituted or unsubstituted 5 to 10 membered
 heteroaryl. In embodiments, R^{4B} is independently substituted C_1 - C_8 alkyl. In embodiments,
 R^{4B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{4B} is
 10 independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{4B} is independently,
 substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4B} is independently
 substituted C_6 - C_{10} aryl. In embodiments, R^{4B} is independently substituted 5 to 10 membered
 heteroaryl. In embodiments, R^{4B} is independently unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{4B} is independently unsubstituted 2 to 8 membered heteroalkyl. In
 15 embodiments, R^{4B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{4B} is
 independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4B} is
 independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{4B} is independently unsubstituted
 5 to 10 membered heteroaryl. In embodiments, R^{4B} is independently substituted or
 unsubstituted C_1 - C_4 alkyl. In embodiments, R^{4B} is independently substituted or unsubstituted
 20 2 to 4 membered heteroalkyl. In embodiments, R^{4B} is independently substituted or
 unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{4B} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4B} is independently
 substituted or unsubstituted phenyl. In embodiments, R^{4B} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{4B} is independently substituted
 25 C_1 - C_4 alkyl. In embodiments, R^{4B} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{4B} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{4B} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4B} is
 independently substituted phenyl. In embodiments, R^{4B} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{4B} is independently unsubstituted C_1 - C_4 alkyl. In
 30 embodiments, R^{4B} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{4B} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{4B} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4B} is
 independently unsubstituted phenyl. In embodiments, R^{4B} is independently unsubstituted 5 to
 6 membered heteroaryl. In embodiments, R^{4B} is independently unsubstituted methyl. In
 35 embodiments, R^{4B} is independently unsubstituted ethyl. In embodiments, R^{4B} is

independently unsubstituted propyl. In embodiments, R^{4B} is independently unsubstituted isopropyl. In embodiments, R^{4B} is independently unsubstituted tert-butyl.

[0207] In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0208] In embodiments, R^{4C} is independently hydrogen. In embodiments, R^{4C} is independently $-CX^{4C}_3$. In embodiments, R^{4C} is independently $-CHX^{4C}_2$. In embodiments,

R^{4C} is independently $-CH_2X^{4C}$. In embodiments, R^{4C} is independently $-CN$. In embodiments, R^{4C} is independently $-COOH$. In embodiments, R^{4C} is independently $-CONH_2$. In embodiments, R^{4C} is independently substituted or unsubstituted alkyl. In embodiments, R^{4C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{4C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{4C} is independently substituted or unsubstituted heterocycloalkyl. In embodiments, R^{4C} is independently substituted or unsubstituted aryl. In embodiments, R^{4C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{4C} is independently substituted alkyl. In embodiments, R^{4C} is independently substituted heteroalkyl. In embodiments, R^{4C} is independently substituted cycloalkyl. In embodiments, R^{4C} is independently substituted heterocycloalkyl. In embodiments, R^{4C} is independently substituted aryl. In embodiments, R^{4C} is independently substituted heteroaryl. In embodiments, R^{4C} is independently unsubstituted alkyl. In embodiments, R^{4C} is independently unsubstituted heteroalkyl. In embodiments, R^{4C} is independently unsubstituted cycloalkyl. In embodiments, R^{4C} is independently unsubstituted heterocycloalkyl. In embodiments, R^{4C} is independently unsubstituted aryl. In embodiments, R^{4C} is independently unsubstituted heteroaryl. In embodiments, R^{4C} is independently substituted or unsubstituted C_1-C_8 alkyl. In embodiments, R^{4C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{4C} is independently substituted or unsubstituted C_3-C_8 cycloalkyl. In embodiments, R^{4C} is independently substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4C} is independently substituted or unsubstituted C_6-C_{10} aryl. In embodiments, R^{4C} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{4C} is independently substituted C_1-C_8 alkyl. In embodiments, R^{4C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{4C} is independently substituted C_3-C_8 cycloalkyl. In embodiments, R^{4C} is independently substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4C} is independently substituted C_6-C_{10} aryl. In embodiments, R^{4C} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{4C} is independently unsubstituted C_1-C_8 alkyl. In embodiments, R^{4C} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{4C} is independently unsubstituted C_3-C_8 cycloalkyl. In embodiments, R^{4C} is independently unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4C} is independently unsubstituted C_6-C_{10} aryl. In embodiments, R^{4C} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{4C} is independently substituted or unsubstituted C_1-C_4 alkyl. In embodiments, R^{4C} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{4C} is independently substituted or

unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{4C} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4C} is independently
 substituted or unsubstituted phenyl. In embodiments, R^{4C} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{4C} is independently substituted
 5 C₁-C₄ alkyl. In embodiments, R^{4C} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{4C} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{4C} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4C} is
 independently substituted phenyl. In embodiments, R^{4C} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{4C} is independently unsubstituted C₁-C₄ alkyl. In
 10 embodiments, R^{4C} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{4C} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{4C} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4C} is
 independently unsubstituted phenyl. In embodiments, R^{4C} is independently unsubstituted 5 to
 6 membered heteroaryl. In embodiments, R^{4C} is independently unsubstituted methyl. In
 15 embodiments, R^{4C} is independently unsubstituted ethyl. In embodiments, R^{4C} is
 independently unsubstituted propyl. In embodiments, R^{4C} is independently unsubstituted
 isopropyl. In embodiments, R^{4C} is independently unsubstituted tert-butyl.

[0209] In embodiments, R^{4D} is independently hydrogen. In embodiments, R^{4D} is
 independently -CX^{4D}₃. In embodiments, R^{4D} is independently -CHX^{4D}₂. In embodiments,
 20 R^{4D} is independently -CH₂X^{4D}. In embodiments, R^{4D} is independently -CN. In
 embodiments, R^{4D} is independently -COOH. In embodiments, R^{4D} is
 independently -CONH₂. In embodiments, R^{4D} is independently substituted or unsubstituted
 alkyl. In embodiments, R^{4D} is independently substituted or unsubstituted heteroalkyl. In
 embodiments, R^{4D} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 25 R^{4D} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{4D} is
 independently substituted or unsubstituted aryl. In embodiments, R^{4D} is independently
 substituted or unsubstituted heteroaryl. In embodiments, R^{4D} is independently substituted
 alkyl. In embodiments, R^{4D} is independently substituted heteroalkyl. In embodiments, R^{4D} is
 independently substituted cycloalkyl. In embodiments, R^{4D} is independently, substituted
 30 heterocycloalkyl. In embodiments, R^{4D} is independently substituted aryl. In embodiments,
 R^{4D} is independently substituted heteroaryl. In embodiments, R^{4D} is independently
 unsubstituted alkyl. In embodiments, R^{4D} is independently unsubstituted heteroalkyl. In
 embodiments, R^{4D} is independently unsubstituted cycloalkyl. In embodiments, R^{4D} is
 independently, unsubstituted heterocycloalkyl. In embodiments, R^{4D} is independently

unsubstituted aryl. In embodiments, R^{4D} is independently unsubstituted heteroaryl. In
 embodiments, R^{4D} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{4D} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
 In embodiments, R^{4D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
 5 embodiments, R^{4D} is independently, substituted or unsubstituted 3 to 8 membered
 heterocycloalkyl. In embodiments, R^{4D} is independently substituted or unsubstituted C_6 - C_{10}
 aryl. In embodiments, R^{4D} is independently substituted or unsubstituted 5 to 10 membered
 heteroaryl. In embodiments, R^{4D} is independently substituted C_1 - C_8 alkyl. In embodiments,
 R^{4D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{4D} is
 10 independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{4D} is independently,
 substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4D} is independently
 substituted C_6 - C_{10} aryl. In embodiments, R^{4D} is independently substituted 5 to 10 membered
 heteroaryl. In embodiments, R^{4D} is independently unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{4D} is independently unsubstituted 2 to 8 membered heteroalkyl. In
 15 embodiments, R^{4D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{4D} is
 independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{4D} is
 independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{4D} is independently unsubstituted
 5 to 10 membered heteroaryl. In embodiments, R^{4D} is independently substituted or
 unsubstituted C_1 - C_4 alkyl. In embodiments, R^{4D} is independently substituted or unsubstituted
 20 2 to 4 membered heteroalkyl. In embodiments, R^{4D} is independently substituted or
 unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{4D} is independently, substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4D} is independently
 substituted or unsubstituted phenyl. In embodiments, R^{4D} is independently substituted or
 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{4D} is independently substituted
 25 C_1 - C_4 alkyl. In embodiments, R^{4D} is independently substituted 2 to 4 membered heteroalkyl.
 In embodiments, R^{4D} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{4D} is
 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4D} is
 independently substituted phenyl. In embodiments, R^{4D} is independently substituted 5 to 6
 membered heteroaryl. In embodiments, R^{4D} is independently unsubstituted C_1 - C_4 alkyl. In
 30 embodiments, R^{4D} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 embodiments, R^{4D} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{4D} is
 independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{4D} is
 independently unsubstituted phenyl. In embodiments, R^{4D} is independently unsubstituted 5
 to 6 membered heteroaryl. In embodiments, R^{4D} is independently unsubstituted methyl. In
 35 embodiments, R^{4D} is independently unsubstituted ethyl. In embodiments, R^{4D} is

independently unsubstituted propyl. In embodiments, R^{4D} is independently unsubstituted isopropyl. In embodiments, R^{4D} is independently unsubstituted tert-butyl.

[0210] In embodiments, R^4 is independently hydrogen,

halogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, $-CN$, $-SO_{n4}R^{4D}$, $-SO_{v4}NR^{4A}$
 R^{4B} , $-NHC(O)NR^{4A}R^{4B}$, $-N(O)_{m4}$, $-NR^{4A}R^{4B}$, $-C(O)R^{4C}$, $-C(O)OR^{4C}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4D}$, $-$
 $NR^{4A}SO_2R^{4D}$, $-NR^{4A}C(O)R^{4C}$, $-NR^{4A}C(O)OR^{4C}$, $-NR^{4A}OR^{4C}$, R^{29} -substituted or unsubstituted
alkyl, R^{29} -substituted or unsubstituted heteroalkyl, R^{29} -substituted or unsubstituted
cycloalkyl, R^{29} -substituted or unsubstituted heterocycloalkyl, R^{29} -substituted or unsubstituted
aryl, or R^{29} -substituted or unsubstituted heteroaryl. In embodiments, R^4 is independently
halogen, $-CX^4_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^4_3$, $-OCHX^4_2$, R^{29} -substituted or unsubstituted alkyl, R^{29} -substituted or
unsubstituted heteroalkyl, R^{29} -substituted or unsubstituted cycloalkyl, R^{29} -substituted or
unsubstituted heterocycloalkyl, R^{29} -substituted or unsubstituted aryl, or R^{29} -substituted or
unsubstituted heteroaryl. In embodiments, R^4 is independently
halogen, $-CX^4_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^4_3$, $-OCHX^4_2$, R^{29} -substituted or unsubstituted C_1 - C_8 alkyl, R^{29} -substituted or
unsubstituted 2 to 8 membered heteroalkyl, R^{29} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 R^{29} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{29} -substituted or
unsubstituted phenyl, or R^{29} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^4 is $-$
 F , $-Cl$, $-Br$, or $-I$. In embodiments, R^4 is independently hydrogen. In embodiments, R^4 is
independently methyl. In embodiments, R^4 is independently ethyl.

[0211] R^{29} is independently oxo,

halogen, $-CX^{29}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{29}_3$, $-OCHX^{29}_2$, R^{30} -substituted or unsubstituted alkyl, R^{30} -substituted or
unsubstituted heteroalkyl, R^{30} -substituted or unsubstituted cycloalkyl, R^{30} -substituted or
unsubstituted heterocycloalkyl, R^{30} -substituted or unsubstituted aryl, or R^{30} -substituted or
unsubstituted heteroaryl. In embodiments, R^{29} is independently oxo,
halogen, $-CX^{29}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{29}_3$, $-OCHX^{29}_2$, R^{30} -substituted or unsubstituted C_1 - C_8 alkyl, R^{30} -substituted or
unsubstituted 2 to 8 membered heteroalkyl, R^{30} -substituted or unsubstituted C_3 - C_8 cycloalkyl,

R^{30} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{30} -substituted or unsubstituted phenyl, or R^{30} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{29} is -F, -Cl, -Br, or -I.

[0212] R^{30} is independently oxo,

- 5 halogen, $-CX^{30}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{30}_3$, $-OCHX^{30}_2$, R^{31} -substituted or unsubstituted alkyl, R^{31} -substituted or unsubstituted heteroalkyl, R^{31} -substituted or unsubstituted cycloalkyl, R^{31} -substituted or unsubstituted heterocycloalkyl, R^{31} -substituted or unsubstituted aryl, or R^{31} -substituted or
- 10 unsubstituted heteroaryl. In embodiments, R^{30} is independently oxo, halogen, $-CX^{30}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{30}_3$, $-OCHX^{30}_2$, R^{31} -substituted or unsubstituted C₁-C₈ alkyl, R^{31} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{31} -substituted or unsubstituted C₃-C₈ cycloalkyl,
- 15 R^{31} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{31} -substituted or unsubstituted phenyl, or R^{31} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{30} is -F, -Cl, -Br, or -I.

[0213] In embodiments, R^{4A} is independently

- hydrogen, $-CX^{4A}_3$, -CN, -COOH, -CONH₂, $-CHX^{4A}_2$, $-CH_2X^{4A}$, R^{29A} -substituted or
- 20 unsubstituted alkyl, R^{29A} -substituted or unsubstituted heteroalkyl, R^{29A} -substituted or unsubstituted cycloalkyl, R^{29A} -substituted or unsubstituted heterocycloalkyl, R^{29A} -substituted or unsubstituted aryl, or R^{29A} -substituted or unsubstituted heteroaryl. In embodiments, R^{4A} is independently hydrogen, $-CX^{4A}_3$, -CN, -COOH, -CONH₂, $-CHX^{4A}_2$, $-CH_2X^{4A}$, R^{29A} -substituted or unsubstituted C₁-C₈ alkyl, R^{29A} -substituted or unsubstituted 2 to 8 membered
- 25 heteroalkyl, R^{29A} -substituted or unsubstituted C₃-C₈ cycloalkyl, R^{29A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{29A} -substituted or unsubstituted phenyl, or R^{29A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{4A} is -F, -Cl, -Br, or -I. In embodiments, R^{4A} is independently hydrogen. In embodiments, R^{4A} is independently methyl. In embodiments, R^{4A} is independently ethyl.

- 30 **[0214]** In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{29A} -substituted or unsubstituted heterocycloalkyl or R^{29A} -substituted or unsubstituted heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{29A} -substituted or unsubstituted

3 to 6 membered heterocycloalkyl or R^{29A} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0215] R^{29A} is independently oxo,

halogen, $-CX^{29A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

5 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

$-NHOH$, $-OCX^{29A}_3$, $-OCHX^{29A}_2$, R^{30A} -substituted or unsubstituted alkyl, R^{30A} -substituted or

unsubstituted heteroalkyl, R^{30A} -substituted or unsubstituted cycloalkyl, R^{30A} -substituted or

unsubstituted heterocycloalkyl, R^{30A} -substituted or unsubstituted aryl, or R^{30A} -substituted or

unsubstituted heteroaryl. In embodiments, R^{29A} is independently oxo,

10 halogen, $-CX^{29A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

$-NHOH$, $-OCX^{29A}_3$, $-OCHX^{29A}_2$, R^{30A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{30A} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{30A} -substituted or unsubstituted

C_3 - C_8 cycloalkyl, R^{30A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{30A} -

15 substituted or unsubstituted phenyl, or R^{30A} -substituted or unsubstituted 5 to 6 membered

heteroaryl. X^{29A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0216] R^{30A} is independently oxo,

halogen, $-CX^{30A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

20 $-NHOH$, $-OCX^{30A}_3$, $-OCHX^{30A}_2$, R^{31A} -substituted or unsubstituted alkyl, R^{31A} -substituted or

unsubstituted heteroalkyl, R^{31A} -substituted or unsubstituted cycloalkyl, R^{31A} -substituted or

unsubstituted heterocycloalkyl, R^{31A} -substituted or unsubstituted aryl, or R^{31A} -substituted or

unsubstituted heteroaryl. In embodiments, R^{30A} is independently oxo,

halogen, $-CX^{30A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

25 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

$-NHOH$, $-OCX^{30A}_3$, $-OCHX^{30A}_2$, R^{31A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{31A} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{31A} -substituted or unsubstituted

C_3 - C_8 cycloalkyl, R^{31A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{31A} -

substituted or unsubstituted phenyl, or R^{31A} -substituted or unsubstituted 5 to 6 membered

30 heteroaryl. X^{30A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0217] In embodiments, R^{4B} is independently

hydrogen, $-CX^{4B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{4B}_2$, $-CH_2X^{4B}$, R^{29B} -substituted or

unsubstituted alkyl, R^{29B} -substituted or unsubstituted heteroalkyl, R^{29B} -substituted or

unsubstituted cycloalkyl, R^{29B} -substituted or unsubstituted heterocycloalkyl, R^{29B} -substituted or unsubstituted aryl, or R^{29B} -substituted or unsubstituted heteroaryl. In embodiments, R^{4B} is independently hydrogen, $-CX^{4B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{4B}_2$, $-CH_2X^{4B}$, R^{29B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{29B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{29B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{29B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{29B} -substituted or unsubstituted phenyl, or R^{29B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{4B} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{4B} is independently hydrogen. In embodiments, R^{4B} is independently methyl. In embodiments, R^{4B} is independently ethyl.

10 **[0218]** In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{29B} -substituted or unsubstituted heterocycloalkyl or R^{29B} -substituted or unsubstituted heteroaryl. In embodiments, R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{29B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{29B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0219] R^{29B} is independently oxo, halogen, $-CX^{29B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{29B}_3$, $-OCHX^{29B}_2$, R^{30B} -substituted or unsubstituted alkyl, R^{30B} -substituted or unsubstituted heteroalkyl, R^{30B} -substituted or unsubstituted cycloalkyl, R^{30B} -substituted or unsubstituted heterocycloalkyl, R^{30B} -substituted or unsubstituted aryl, or R^{30B} -substituted or unsubstituted heteroaryl. In embodiments, R^{29B} is independently oxo, halogen, $-CX^{29B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{29B}_3$, $-OCHX^{29B}_2$, R^{30B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{30B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{30B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{30B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{30B} -substituted or unsubstituted phenyl, or R^{30B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{29B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0220] R^{30B} is independently oxo, halogen, $-CX^{30B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{30\text{B}}_3$, $-\text{OCHX}^{30\text{B}}_2$, $\text{R}^{31\text{B}}$ -substituted or unsubstituted alkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted aryl, or $\text{R}^{31\text{B}}$ -substituted or unsubstituted heteroaryl. In
 5 embodiments, $\text{R}^{30\text{B}}$ is independently oxo, halogen, $-\text{CX}^{30\text{B}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{30\text{B}}_3$, $-\text{OCHX}^{30\text{B}}_2$, $\text{R}^{31\text{B}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted
 10 C_3 - C_8 cycloalkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{31\text{B}}$ -substituted or unsubstituted phenyl, or $\text{R}^{31\text{B}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{30\text{B}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0221] In embodiments, $\text{R}^{4\text{C}}$ is independently hydrogen, $-\text{CX}^{4\text{C}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{4\text{C}}_2$, $-\text{CH}_2\text{X}^{4\text{C}}$, $\text{R}^{29\text{C}}$ -substituted or
 15 unsubstituted alkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted aryl, or $\text{R}^{29\text{C}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{4\text{C}}$ is independently hydrogen, $-\text{CX}^{4\text{C}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{4\text{C}}_2$, $-\text{CH}_2\text{X}^{4\text{C}}$, $\text{R}^{29\text{C}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted 2 to 8 membered
 20 heteroalkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{29\text{C}}$ -substituted or unsubstituted phenyl, or $\text{R}^{29\text{C}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{4\text{C}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$. In embodiments, $\text{R}^{4\text{C}}$ is independently hydrogen. In embodiments, $\text{R}^{4\text{C}}$ is independently methyl. In embodiments, $\text{R}^{4\text{C}}$ is independently ethyl.

25 **[0222]** $\text{R}^{29\text{C}}$ is independently oxo, halogen, $-\text{CX}^{29\text{C}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{29\text{C}}_3$, $-\text{OCHX}^{29\text{C}}_2$, $\text{R}^{30\text{C}}$ -substituted or unsubstituted alkyl, $\text{R}^{30\text{C}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{30\text{C}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{30\text{C}}$ -substituted or
 30 unsubstituted heterocycloalkyl, $\text{R}^{30\text{C}}$ -substituted or unsubstituted aryl, or $\text{R}^{30\text{C}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{29\text{C}}$ is independently oxo, halogen, $-\text{CX}^{29\text{C}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{29\text{C}}_3$, $-\text{OCHX}^{29\text{C}}_2$, $\text{R}^{30\text{C}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{30\text{C}}$ -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{30C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{30C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{30C} -substituted or unsubstituted phenyl, or R^{30C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{29C} is -F, -Cl, -Br, or -I.

- 5 **[0223]** R^{30C} is independently oxo,
halogen, $-CX^{30C}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
-NHOH, $-OCX^{30C}_3$, $-OCHX^{30C}_2$, R^{31C} -substituted or unsubstituted alkyl, R^{31C} -substituted or
unsubstituted heteroalkyl, R^{31C} -substituted or unsubstituted cycloalkyl, R^{31C} -substituted or
10 unsubstituted heterocycloalkyl, R^{31C} -substituted or unsubstituted aryl, or R^{31C} -substituted or
unsubstituted heteroaryl. In embodiments, R^{30C} is independently oxo,
halogen, $-CX^{30C}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
-NHOH, $-OCX^{30C}_3$, $-OCHX^{30C}_2$, R^{31C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{31C} -
15 substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{31C} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{31C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{31C} -
substituted or unsubstituted phenyl, or R^{31C} -substituted or unsubstituted 5 to 6 membered
heteroaryl. X^{30C} is -F, -Cl, -Br, or -I.

- [0224]** In embodiments, R^{4D} is independently
20 hydrogen, $-CX^{4D}_3$, -CN, -COOH, -CONH₂, $-CHX^{4D}_2$, $-CH_2X^{4D}$, R^{29D} -substituted or
unsubstituted alkyl, R^{29D} -substituted or unsubstituted heteroalkyl, R^{29D} -substituted or
unsubstituted cycloalkyl, R^{29D} -substituted or unsubstituted heterocycloalkyl, R^{29D} -substituted
or unsubstituted aryl, or R^{29D} -substituted or unsubstituted heteroaryl. In embodiments, R^{4D} is
independently hydrogen, $-CX^{4D}_3$, -CN, -COOH, -CONH₂, $-CHX^{4D}_2$, $-CH_2X^{4D}$, R^{29D} -
25 substituted or unsubstituted C_1 - C_8 alkyl, R^{29D} -substituted or unsubstituted 2 to 8 membered
heteroalkyl, R^{29D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{29D} -substituted or
unsubstituted 3 to 6 membered heterocycloalkyl, R^{29D} -substituted or unsubstituted phenyl, or
 R^{29D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{4D} is -F, -Cl, -Br, or -I. In
embodiments, R^{4D} is independently hydrogen. In embodiments, R^{4D} is independently methyl.
30 In embodiments, R^{4D} is independently ethyl.

[0225] R^{29D} is independently oxo,
halogen, $-CX^{29D}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-\text{OCX}^{29\text{D}}_3$, $-\text{OCHX}^{29\text{D}}_2$, $\text{R}^{30\text{D}}$ -substituted or unsubstituted alkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted aryl, or $\text{R}^{30\text{D}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{29\text{D}}$ is independently oxo,

- 5 halogen, $-\text{CX}^{29\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{29\text{D}}_3$, $-\text{OCHX}^{29\text{D}}_2$, $\text{R}^{30\text{D}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{30\text{D}}$ -substituted or unsubstituted phenyl, or $\text{R}^{30\text{D}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{29\text{D}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0226] $\text{R}^{30\text{D}}$ is independently oxo,

- halogen, $-\text{CX}^{30\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 15 $-\text{NHOH}$, $-\text{OCX}^{30\text{D}}_3$, $-\text{OCHX}^{30\text{D}}_2$, $\text{R}^{31\text{D}}$ -substituted or unsubstituted alkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted aryl, or $\text{R}^{31\text{D}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{30\text{D}}$ is independently oxo,
 halogen, $-\text{CX}^{30\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
 20 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{30\text{D}}_3$, $-\text{OCHX}^{30\text{D}}_2$, $\text{R}^{31\text{D}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{31\text{D}}$ -substituted or unsubstituted phenyl, or $\text{R}^{31\text{D}}$ -substituted or unsubstituted 5 to 6 membered
 25 heteroaryl. $\text{X}^{30\text{D}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0227] R^{31} , $\text{R}^{31\text{A}}$, $\text{R}^{31\text{B}}$, $\text{R}^{31\text{C}}$, and $\text{R}^{31\text{D}}$ are independently hydrogen, oxo,

- halogen, $-\text{CCl}_3$, $-\text{CBr}_3$, $-\text{CF}_3$, $-\text{Cl}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$,
 $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$,
 30 $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCCl}_3$, $-\text{OCF}_3$, $-\text{OCBr}_3$, $-\text{OCl}_3$, $-\text{OCHCl}_2$, $-\text{OCHBr}_2$, $-\text{OCHI}_2$, $-\text{OCHF}_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{31} , $\text{R}^{31\text{A}}$, $\text{R}^{31\text{B}}$, $\text{R}^{31\text{C}}$, and $\text{R}^{31\text{D}}$ are independently oxo,
 halogen, $-\text{CF}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,

–NHNH₂, –ONH₂, –NHC(O)NHNH₂, –NHC(O)NH₂, –NHSO₂H, –NHC(O)H, –NHC(O)OH, –NHOH, –OCF₃, –OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R³¹, R^{31A}, R^{31B}, R^{31C}, and R^{31D} are independently oxo,

5 halogen, –CF₃, –CN, –OH, –NH₂, –COOH, –CONH₂, –NO₂, –SH, –SO₃H, –SO₄H, –SO₂NH₂, –NHNH₂, –ONH₂, –NHC(O)NHNH₂, –NHC(O)NH₂, –NHSO₂H, –NHC(O)H, –NHC(O)OH, –NHOH, –OCF₃, –OCHF₂, unsubstituted C₁–C₈ alkyl, unsubstituted 2 to 8 membered heteroalkyl, unsubstituted C₃–C₈ cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

10 **[0228]** In embodiments, the symbol Y² is N. In embodiments, the symbol Y² is C(R⁵).

[0229] In embodiments, R⁵ is hydrogen, substituted or unsubstituted C₁–C₈ alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl.

[0230] In embodiments, R⁵ is independently hydrogen. In embodiments, R⁵ is independently halogen. In embodiments, R⁵ is independently –CX⁵₃. In embodiments, R⁵ is independently –CHX⁵₂. In embodiments, R⁵ is independently –CH₂X⁵. In embodiments, R⁵ is independently –OCX⁵₃. In embodiments, R⁵ is independently –OCH₂X⁵. In embodiments, R⁵ is independently –OCHX⁵₂. In embodiments, R⁵ is independently –CN. In embodiments, R⁵ is independently –SO_{n5}R^{5D}. In embodiments, R⁵ is independently –SO_{v5}NR^{5A}R^{5B}. In embodiments, R⁵ is independently –NHC(O)NR^{5A}R^{5B}. In embodiments, R⁵ is independently –N(O)_{m5}. In embodiments, R⁵ is independently –NR^{5A}R^{5B}. In embodiments, R⁵ is independently –C(O)R^{5C}. In embodiments, R⁵ is independently –C(O)–OR^{5C}. In embodiments, R⁵ is independently –C(O)NR^{5A}R^{5B}. In embodiments, R⁵ is independently –OR^{5D}. In embodiments, R⁵ is independently –NR^{5A}SO₂R^{5D}. In embodiments, R⁵ is independently –NR^{5A}C(O)R^{5C}. In embodiments, R⁵ is independently –NR^{5A}C(O)OR^{5C}. In embodiments, R⁵ is independently –NR^{5A}OR^{5C}. In embodiments, R⁵ is independently –OH. In embodiments, R⁵ is independently –NH₂. In embodiments, R⁵ is independently –COOH. In embodiments, R⁵ is independently –CONH₂. In embodiments, R⁵ is independently –NO₂. In embodiments, R⁵ is independently –SH. In embodiments, R⁵ is independently –F.

[0231] In embodiments, R⁵ is independently substituted or unsubstituted alkyl. In embodiments, R⁵ is independently substituted or unsubstituted heteroalkyl. In embodiments, R⁵ is independently substituted or unsubstituted cycloalkyl. In embodiments, R⁵ is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R⁵ is independently substituted or unsubstituted aryl. In embodiments, R⁵ is independently

substituted or unsubstituted heteroaryl. In embodiments, R⁵ is independently substituted alkyl. In embodiments, R⁵ is independently substituted heteroalkyl. In embodiments, R⁵ is independently substituted cycloalkyl. In embodiments, R⁵ is independently, substituted heterocycloalkyl. In embodiments, R⁵ is independently substituted aryl. In embodiments, R⁵ is independently substituted heteroaryl. In embodiments, R⁵ is independently unsubstituted alkyl. In embodiments, R⁵ is independently unsubstituted heteroalkyl. In embodiments, R⁵ is independently unsubstituted cycloalkyl. In embodiments, R⁵ is independently, unsubstituted heterocycloalkyl. In embodiments, R⁵ is independently unsubstituted aryl. In embodiments, R⁵ is independently unsubstituted heteroaryl. In embodiments, R⁵ is independently substituted or unsubstituted C₁-C₈ alkyl. In embodiments, R⁵ is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R⁵ is independently substituted or unsubstituted C₃-C₈ cycloalkyl. In embodiments, R⁵ is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁵ is independently substituted or unsubstituted C₆-C₁₀ aryl. In embodiments, R⁵ is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R⁵ is independently substituted C₁-C₈ alkyl. In embodiments, R⁵ is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R⁵ is independently substituted C₃-C₈ cycloalkyl. In embodiments, R⁵ is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁵ is independently substituted C₆-C₁₀ aryl. In embodiments, R⁵ is independently substituted 5 to 10 membered heteroaryl. In embodiments, R⁵ is independently unsubstituted C₁-C₈ alkyl. In embodiments, R⁵ is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R⁵ is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R⁵ is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁵ is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R⁵ is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R⁵ is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R⁵ is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R⁵ is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R⁵ is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁵ is independently substituted or unsubstituted phenyl. In embodiments, R⁵ is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R⁵ is independently substituted C₁-C₄ alkyl. In embodiments, R⁵ is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R⁵ is independently substituted C₃-C₆ cycloalkyl. In embodiments, R⁵ is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁵ is independently substituted phenyl. In embodiments, R⁵ is independently substituted 5 to 6

membered heteroaryl. In embodiments, R^5 is independently unsubstituted C_1 - C_4 alkyl. In
embodiments, R^5 is independently unsubstituted 2 to 4 membered heteroalkyl. In
embodiments, R^5 is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^5 is
independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^5 is
5 independently unsubstituted phenyl. In embodiments, R^5 is independently unsubstituted 5 to
6 membered heteroaryl.

[0232] In embodiments, R^{5A} is independently hydrogen. In embodiments, R^{5A} is
independently $-CX^{5A}_3$. In embodiments, R^{5A} is independently $-CHX^{5A}_2$. In embodiments,
 R^{5A} is independently $-CH_2X^{5A}$. In embodiments, R^{5A} is independently $-CN$. In
10 embodiments, R^{5A} is independently $-COOH$. In embodiments, R^{5A} is
independently $-CONH_2$. In embodiments, R^{5A} is independently substituted or unsubstituted
alkyl. In embodiments, R^{5A} is independently substituted or unsubstituted heteroalkyl. In
embodiments, R^{5A} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 R^{5A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{5A} is
15 independently substituted or unsubstituted aryl. In embodiments, R^{5A} is independently
substituted or unsubstituted heteroaryl. In embodiments, R^{5A} is independently substituted
alkyl. In embodiments, R^{5A} is independently substituted heteroalkyl. In embodiments, R^{5A} is
independently substituted cycloalkyl. In embodiments, R^{5A} is independently, substituted
heterocycloalkyl. In embodiments, R^{5A} is independently substituted aryl. In embodiments,
20 R^{5A} is independently substituted heteroaryl. In embodiments, R^{5A} is independently
unsubstituted alkyl. In embodiments, R^{5A} is independently unsubstituted heteroalkyl. In
embodiments, R^{5A} is independently unsubstituted cycloalkyl. In embodiments, R^{5A} is
independently, unsubstituted heterocycloalkyl. In embodiments, R^{5A} is independently
unsubstituted aryl. In embodiments, R^{5A} is independently unsubstituted heteroaryl. In
25 embodiments, R^{5A} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
embodiments, R^{5A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
In embodiments, R^{5A} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
embodiments, R^{5A} is independently, substituted or unsubstituted 3 to 8 membered
heterocycloalkyl. In embodiments, R^{5A} is independently substituted or unsubstituted C_6 - C_{10}
30 aryl. In embodiments, R^{5A} is independently substituted or unsubstituted 5 to 10 membered
heteroaryl. In embodiments, R^{5A} is independently substituted C_1 - C_8 alkyl. In embodiments,
 R^{5A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{5A} is
independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{5A} is independently,
substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5A} is independently

substituted C₆-C₁₀ aryl. In embodiments, R^{5A} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{5A} is independently unsubstituted C₁-C₈ alkyl. In embodiments, R^{5A} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{5A} is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{5A} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5A} is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R^{5A} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5A} is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R^{5A} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{5A} is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{5A} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5A} is independently substituted or unsubstituted phenyl. In embodiments, R^{5A} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5A} is independently substituted C₁-C₄ alkyl. In embodiments, R^{5A} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{5A} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{5A} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5A} is independently substituted phenyl. In embodiments, R^{5A} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{5A} is independently unsubstituted C₁-C₄ alkyl. In embodiments, R^{5A} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{5A} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{5A} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5A} is independently unsubstituted phenyl. In embodiments, R^{5A} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5A} is independently unsubstituted methyl. In embodiments, R^{5A} is independently unsubstituted ethyl. In embodiments, R^{5A} is independently unsubstituted propyl. In embodiments, R^{5A} is independently unsubstituted isopropyl. In embodiments, R^{5A} is independently unsubstituted tert-butyl.

[0233] In embodiments, R^{5B} is independently hydrogen. In embodiments, R^{5B} is independently -CX^{5B}₃. In embodiments, R^{5B} is independently -CHX^{5B}₂. In embodiments, R^{5B} is independently -CH₂X^{5B}. In embodiments, R^{5B} is independently -CN. In embodiments, R^{5B} is independently -COOH. In embodiments, R^{5B} is independently -CONH₂. In embodiments, R^{5B} is independently substituted or unsubstituted alkyl. In embodiments, R^{5B} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{5B} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{5B} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{5B} is independently

substituted or unsubstituted aryl. In embodiments, R^{5B} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{5B} is independently substituted alkyl. In embodiments, R^{5B} is independently substituted heteroalkyl. In embodiments, R^{5B} is independently substituted cycloalkyl. In embodiments, R^{5B} is independently, substituted heterocycloalkyl. In embodiments, R^{5B} is independently substituted aryl. In embodiments, R^{5B} is independently substituted heteroaryl. In embodiments, R^{5B} is independently unsubstituted alkyl. In embodiments, R^{5B} is independently unsubstituted heteroalkyl. In embodiments, R^{5B} is independently unsubstituted cycloalkyl. In embodiments, R^{5B} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{5B} is independently unsubstituted aryl. In embodiments, R^{5B} is independently unsubstituted heteroaryl. In embodiments, R^{5B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{5B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{5B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{5B} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5B} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{5B} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5B} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{5B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{5B} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{5B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5B} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{5B} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{5B} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{5B} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{5B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{5B} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5B} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{5B} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5B} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{5B} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{5B} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{5B} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5B} is independently substituted or unsubstituted phenyl. In embodiments, R^{5B} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5B} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{5B} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{5B} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{5B} is

independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5B} is independently substituted phenyl. In embodiments, R^{5B} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{5B} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{5B} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 5 embodiments, R^{5B} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{5B} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5B} is independently unsubstituted phenyl. In embodiments, R^{5B} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5B} is independently unsubstituted methyl. In embodiments, R^{5B} is independently unsubstituted ethyl. In embodiments, R^{5B} is
 10 independently unsubstituted propyl. In embodiments, R^{5B} is independently unsubstituted isopropyl. In embodiments, R^{5B} is independently unsubstituted tert-butyl.

[0234] In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted or
 15 unsubstituted heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{5A} and R^{5B}
 20 substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5A} and
 25 R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5A} and R^{5B}
 30 substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In

embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0235] In embodiments, R^{5C} is independently hydrogen. In embodiments, R^{5C} is independently $-CX^{5C}_3$. In embodiments, R^{5C} is independently $-CHX^{5C}_2$. In embodiments, R^{5C} is independently $-CH_2X^{5C}$. In embodiments, R^{5C} is independently $-CN$. In embodiments, R^{5C} is independently $-COOH$. In embodiments, R^{5C} is independently $-CONH_2$. In embodiments, R^{5C} is independently substituted or unsubstituted alkyl. In embodiments, R^{5C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{5C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{5C} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{5C} is independently substituted or unsubstituted aryl. In embodiments, R^{5C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{5C} is independently substituted alkyl. In embodiments, R^{5C} is independently substituted heteroalkyl. In embodiments, R^{5C} is independently substituted cycloalkyl. In embodiments, R^{5C} is independently, substituted heterocycloalkyl. In embodiments, R^{5C} is independently substituted aryl. In embodiments, R^{5C} is independently substituted heteroaryl. In embodiments, R^{5C} is independently unsubstituted alkyl. In embodiments, R^{5C} is independently unsubstituted heteroalkyl. In embodiments, R^{5C} is independently unsubstituted cycloalkyl. In embodiments, R^{5C} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{5C} is independently unsubstituted aryl. In embodiments, R^{5C} is independently unsubstituted heteroaryl. In embodiments, R^{5C} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{5C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{5C} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{5C} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5C} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{5C} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5C} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{5C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{5C} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{5C} is independently,

substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5C} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{5C} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{5C} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{5C} is independently unsubstituted 2 to 8 membered heteroalkyl. In

5 embodiments, R^{5C} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{5C} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5C} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{5C} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5C} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{5C} is independently substituted or unsubstituted

10 2 to 4 membered heteroalkyl. In embodiments, R^{5C} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{5C} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5C} is independently substituted or unsubstituted phenyl. In embodiments, R^{5C} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5C} is independently substituted

15 C_1 - C_4 alkyl. In embodiments, R^{5C} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{5C} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{5C} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5C} is independently substituted phenyl. In embodiments, R^{5C} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{5C} is independently unsubstituted C_1 - C_4 alkyl. In

20 embodiments, R^{5C} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{5C} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{5C} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5C} is independently unsubstituted phenyl. In embodiments, R^{5C} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5C} is independently unsubstituted methyl. In

25 embodiments, R^{5C} is independently unsubstituted ethyl. In embodiments, R^{5C} is independently unsubstituted propyl. In embodiments, R^{5C} is independently unsubstituted isopropyl. In embodiments, R^{5C} is independently unsubstituted tert-butyl.

[0236] In embodiments, R^{5D} is independently hydrogen. In embodiments, R^{5D} is independently $-CX^{5D}_3$. In embodiments, R^{5D} is independently $-CHX^{5D}_2$. In embodiments,

30 R^{5D} is independently $-CH_2X^{5D}$. In embodiments, R^{5D} is independently $-CN$. In embodiments, R^{5D} is independently $-COOH$. In embodiments, R^{5D} is independently $-CONH_2$. In embodiments, R^{5D} is independently substituted or unsubstituted alkyl. In embodiments, R^{5D} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{5D} is independently substituted or unsubstituted cycloalkyl. In embodiments,

R^{5D} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{5D} is independently substituted or unsubstituted aryl. In embodiments, R^{5D} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{5D} is independently substituted alkyl. In embodiments, R^{5D} is independently substituted heteroalkyl. In embodiments, R^{5D} is independently substituted cycloalkyl. In embodiments, R^{5D} is independently, substituted heterocycloalkyl. In embodiments, R^{5D} is independently substituted aryl. In embodiments, R^{5D} is independently substituted heteroaryl. In embodiments, R^{5D} is independently unsubstituted alkyl. In embodiments, R^{5D} is independently unsubstituted heteroalkyl. In embodiments, R^{5D} is independently unsubstituted cycloalkyl. In embodiments, R^{5D} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{5D} is independently unsubstituted aryl. In embodiments, R^{5D} is independently unsubstituted heteroaryl. In embodiments, R^{5D} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{5D} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{5D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{5D} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5D} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{5D} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5D} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{5D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{5D} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{5D} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5D} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{5D} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{5D} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{5D} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{5D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{5D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{5D} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{5D} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{5D} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{5D} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{5D} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{5D} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5D} is independently substituted or unsubstituted phenyl. In embodiments, R^{5D} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5D} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{5D} is independently substituted 2 to 4 membered heteroalkyl.

In embodiments, R^{5D} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{5D} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5D} is independently substituted phenyl. In embodiments, R^{5D} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{5D} is independently unsubstituted C_1 - C_4 alkyl. In
 5 embodiments, R^{5D} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{5D} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{5D} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{5D} is independently unsubstituted phenyl. In embodiments, R^{5D} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{5D} is independently unsubstituted methyl. In
 10 embodiments, R^{5D} is independently unsubstituted ethyl. In embodiments, R^{5D} is independently unsubstituted propyl. In embodiments, R^{5D} is independently unsubstituted isopropyl. In embodiments, R^{5D} is independently unsubstituted tert-butyl.

[0237] In embodiments, R^5 is independently hydrogen, halogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, $-CN$, $-SO_{n5}R^{5D}$, $-SO_{v5}NR^{5A}$
 15 R^{5B} , $-NHC(O)NR^{5A}R^{5B}$, $-N(O)_{m5}$, $-NR^{5A}R^{5B}$, $-C(O)R^{5C}$, $-C(O)OR^{5C}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5D}$, $-NR^{5A}SO_2R^{5D}$, $-NR^{5A}C(O)R^{5C}$, $-NR^{5A}C(O)OR^{5C}$, $-NR^{5A}OR^{5C}$, R^{32} -substituted or unsubstituted alkyl, R^{32} -substituted or unsubstituted heteroalkyl, R^{32} -substituted or unsubstituted cycloalkyl, R^{32} -substituted or unsubstituted heterocycloalkyl, R^{32} -substituted or unsubstituted aryl, or R^{32} -substituted or unsubstituted heteroaryl. In embodiments, R^5 is independently
 20 halogen, $-CX^5_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^5_3$, $-OCHX^5_2$, R^{32} -substituted or unsubstituted alkyl, R^{32} -substituted or unsubstituted heteroalkyl, R^{32} -substituted or unsubstituted cycloalkyl, R^{32} -substituted or unsubstituted heterocycloalkyl, R^{32} -substituted or unsubstituted aryl, or R^{32} -substituted or
 25 unsubstituted heteroaryl. In embodiments, R^5 is independently halogen, $-CX^5_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^5_3$, $-OCHX^5_2$, R^{32} -substituted or unsubstituted C_1 - C_8 alkyl, R^{32} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{32} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 30 R^{32} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{32} -substituted or unsubstituted phenyl, or R^{32} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^5 is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^5 is independently methyl. In embodiments, R^5 is independently ethyl.

[0238] R^{32} is independently oxo,

halogen, $-CX^{32}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{32}_3$, $-OCHX^{32}_2$, R^{33} -substituted or unsubstituted alkyl, R^{33} -substituted or
5 unsubstituted heteroalkyl, R^{33} -substituted or unsubstituted cycloalkyl, R^{33} -substituted or
unsubstituted heterocycloalkyl, R^{33} -substituted or unsubstituted aryl, or R^{33} -substituted or
unsubstituted heteroaryl. In embodiments, R^{32} is independently oxo,
halogen, $-CX^{32}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
10 $-NHOH$, $-OCX^{32}_3$, $-OCHX^{32}_2$, R^{33} -substituted or unsubstituted C_1 - C_8 alkyl, R^{33} -substituted or
unsubstituted 2 to 8 membered heteroalkyl, R^{33} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 R^{33} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{33} -substituted or
unsubstituted phenyl, or R^{33} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{32} is
 $-F$, $-Cl$, $-Br$, or $-I$.

[0239] R^{33} is independently oxo,

halogen, $-CX^{33}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{33}_3$, $-OCHX^{33}_2$, R^{34} -substituted or unsubstituted alkyl, R^{34} -substituted or
unsubstituted heteroalkyl, R^{34} -substituted or unsubstituted cycloalkyl, R^{34} -substituted or
20 unsubstituted heterocycloalkyl, R^{34} -substituted or unsubstituted aryl, or R^{34} -substituted or
unsubstituted heteroaryl. In embodiments, R^{33} is independently oxo,
halogen, $-CX^{33}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{33}_3$, $-OCHX^{33}_2$, R^{34} -substituted or unsubstituted C_1 - C_8 alkyl, R^{34} -substituted or
25 unsubstituted 2 to 8 membered heteroalkyl, R^{34} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 R^{34} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{34} -substituted or
unsubstituted phenyl, or R^{34} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{33} is
 $-F$, $-Cl$, $-Br$, or $-I$.

[0240] In embodiments, R^{5A} is independently

30 hydrogen, $-CX^{5A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5A}_2$, $-CH_2X^{5A}$, R^{32A} -substituted or
unsubstituted alkyl, R^{32A} -substituted or unsubstituted heteroalkyl, R^{32A} -substituted or
unsubstituted cycloalkyl, R^{32A} -substituted or unsubstituted heterocycloalkyl, R^{32A} -substituted
or unsubstituted aryl, or R^{32A} -substituted or unsubstituted heteroaryl. In embodiments, R^{5A} is
independently hydrogen, $-CX^{5A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5A}_2$, $-CH_2X^{5A}$, R^{32A} -

substituted or unsubstituted C₁-C₈ alkyl, R^{32A}-substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{32A}-substituted or unsubstituted C₃-C₈ cycloalkyl, R^{32A}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{32A}-substituted or unsubstituted phenyl, or R^{32A}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{5A} is -F, -Cl, -Br, or -I. In
 5 embodiments, R^{5A} is independently hydrogen. In embodiments, R^{5A} is independently methyl. In embodiments, R^{5A} is independently ethyl.

[0241] In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{32A}-substituted or unsubstituted heterocycloalkyl or R^{32A}-substituted or unsubstituted heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to
 10 the same nitrogen atom may optionally be joined to form a R^{32A}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{32A}-substituted or unsubstituted 5 to 6 membered heteroaryl.

[0242] R^{32A} is independently oxo,
 halogen, -CX^{32A}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 15 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{32A}₃, -OCHX^{32A}₂, R^{33A}-substituted or unsubstituted alkyl, R^{33A}-substituted or unsubstituted heteroalkyl, R^{33A}-substituted or unsubstituted cycloalkyl, R^{33A}-substituted or unsubstituted heterocycloalkyl, R^{33A}-substituted or unsubstituted aryl, or R^{33A}-substituted or unsubstituted heteroaryl. In embodiments, R^{32A} is independently oxo,
 20 halogen, -CX^{32A}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{32A}₃, -OCHX^{32A}₂, R^{33A}-substituted or unsubstituted C₁-C₈ alkyl, R^{33A}-substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{33A}-substituted or unsubstituted C₃-C₈ cycloalkyl, R^{33A}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{33A}-substituted or unsubstituted phenyl, or R^{33A}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{32A} is -F, -Cl, -Br, or -I.

[0243] R^{33A} is independently oxo,
 halogen, -CX^{33A}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 30 -NHOH, -OCX^{33A}₃, -OCHX^{33A}₂, R^{34A}-substituted or unsubstituted alkyl, R^{34A}-substituted or unsubstituted heteroalkyl, R^{34A}-substituted or unsubstituted cycloalkyl, R^{34A}-substituted or unsubstituted heterocycloalkyl, R^{34A}-substituted or unsubstituted aryl, or R^{34A}-substituted or unsubstituted heteroaryl. In embodiments, R^{33A} is independently oxo,

halogen, $-CX^{33A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33A}_3$, $-OCHX^{33A}_2$, R^{34A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{34A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{34A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{34A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{34A} -substituted or unsubstituted phenyl, or R^{34A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{33A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0244] In embodiments, R^{5B} is independently

hydrogen, $-CX^{5B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5B}_2$, $-CH_2X^{5B}$, R^{32B} -substituted or unsubstituted alkyl, R^{32B} -substituted or unsubstituted heteroalkyl, R^{32B} -substituted or unsubstituted cycloalkyl, R^{32B} -substituted or unsubstituted heterocycloalkyl, R^{32B} -substituted or unsubstituted aryl, or R^{32B} -substituted or unsubstituted heteroaryl. In embodiments, R^{5B} is independently hydrogen, $-CX^{5B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5B}_2$, $-CH_2X^{5B}$, R^{32B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{32B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{32B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{32B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{32B} -substituted or unsubstituted phenyl, or R^{32B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{5B} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{5B} is independently hydrogen. In embodiments, R^{5B} is independently methyl. In embodiments, R^{5B} is independently ethyl.

[0245] In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{32B} -substituted or unsubstituted heterocycloalkyl or R^{32B} -substituted or unsubstituted heteroaryl. In embodiments, R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{32B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{32B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0246] R^{32B} is independently oxo,

halogen, $-CX^{32B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{32B}_3$, $-OCHX^{32B}_2$, R^{33B} -substituted or unsubstituted alkyl, R^{33B} -substituted or unsubstituted heteroalkyl, R^{33B} -substituted or unsubstituted cycloalkyl, R^{33B} -substituted or unsubstituted heterocycloalkyl, R^{33B} -substituted or unsubstituted aryl, or R^{33B} -substituted or unsubstituted heteroaryl. In embodiments, R^{32B} is independently oxo,

halogen, $-CX^{32B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{32B}_3$, $-OCHX^{32B}_2$, R^{33B} -
substituted or unsubstituted C_1 - C_8 alkyl, R^{33B} -substituted or unsubstituted 2 to 8 membered
5 heteroalkyl, R^{33B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{33B} -substituted or
unsubstituted 3 to 6 membered heterocycloalkyl, R^{33B} -substituted or unsubstituted phenyl, or
 R^{33B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{32B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0247] R^{33B} is independently oxo,

halogen, $-CX^{33B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
10 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33B}_3$, $-OCHX^{33B}_2$, R^{34B} -
substituted or unsubstituted alkyl, R^{34B} -substituted or unsubstituted heteroalkyl, R^{34B} -
substituted or unsubstituted cycloalkyl, R^{34B} -substituted or unsubstituted heterocycloalkyl,
 R^{34B} -substituted or unsubstituted aryl, or R^{34B} -substituted or unsubstituted heteroaryl. In

15 embodiments, R^{33B} is independently oxo,

halogen, $-CX^{33B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33B}_3$, $-OCHX^{33B}_2$, R^{34B} -
substituted or unsubstituted C_1 - C_8 alkyl, R^{34B} -substituted or unsubstituted 2 to 8 membered
20 heteroalkyl, R^{34B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{34B} -substituted or
unsubstituted 3 to 6 membered heterocycloalkyl, R^{34B} -substituted or unsubstituted phenyl, or
 R^{34B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{33B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0248] In embodiments, R^{5C} is independently

hydrogen, $-CX^{5C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5C}_2$, $-CH_2X^{5C}$, R^{32C} -substituted or
25 unsubstituted alkyl, R^{32C} -substituted or unsubstituted heteroalkyl, R^{32C} -substituted or
unsubstituted cycloalkyl, R^{32C} -substituted or unsubstituted heterocycloalkyl, R^{32C} -substituted
or unsubstituted aryl, or R^{32C} -substituted or unsubstituted heteroaryl. In embodiments, R^{5C} is
independently hydrogen, $-CX^{5C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5C}_2$, $-CH_2X^{5C}$, R^{32C} -
substituted or unsubstituted C_1 - C_8 alkyl, R^{32C} -substituted or unsubstituted 2 to 8 membered
30 heteroalkyl, R^{32C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{32C} -substituted or
unsubstituted 3 to 6 membered heterocycloalkyl, R^{32C} -substituted or unsubstituted phenyl, or
 R^{32C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{5C} is $-F$, $-Cl$, $-Br$, or $-I$. In

embodiments, R^{5C} is independently hydrogen. In embodiments, R^{5C} is independently methyl. In embodiments, R^{5C} is independently ethyl.

[0249] R^{32C} is independently oxo,

halogen, $-CX^{32C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

5 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{32C}_3$, $-OCHX^{32C}_2$, R^{33C} -

substituted or unsubstituted alkyl, R^{33C} -substituted or unsubstituted heteroalkyl, R^{33C} -

substituted or unsubstituted cycloalkyl, R^{33C} -substituted or unsubstituted heterocycloalkyl,

R^{33C} -substituted or unsubstituted aryl, or R^{33C} -substituted or unsubstituted heteroaryl. In

10 embodiments, R^{32C} is independently oxo,

halogen, $-CX^{32C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{32C}_3$, $-OCHX^{32C}_2$, R^{33C} -

substituted or unsubstituted C_1 - C_8 alkyl, R^{33C} -substituted or unsubstituted 2 to 8 membered

15 heteroalkyl, R^{33C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{33C} -substituted or

unsubstituted 3 to 6 membered heterocycloalkyl, R^{33C} -substituted or unsubstituted phenyl, or

R^{33C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{32C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0250] R^{33C} is independently oxo,

halogen, $-CX^{33C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

20 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33C}_3$, $-OCHX^{33C}_2$, R^{34C} -

substituted or unsubstituted alkyl, R^{34C} -substituted or unsubstituted heteroalkyl, R^{34C} -

substituted or unsubstituted cycloalkyl, R^{34C} -substituted or unsubstituted heterocycloalkyl,

R^{34C} -substituted or unsubstituted aryl, or R^{34C} -substituted or unsubstituted heteroaryl. In

25 embodiments, R^{33C} is independently oxo,

halogen, $-CX^{33C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33C}_3$, $-OCHX^{33C}_2$, R^{34C} -

substituted or unsubstituted C_1 - C_8 alkyl, R^{34C} -substituted or unsubstituted 2 to 8 membered

30 heteroalkyl, R^{34C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{34C} -substituted or

unsubstituted 3 to 6 membered heterocycloalkyl, R^{34C} -substituted or unsubstituted phenyl, or

R^{34C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{33C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0251] In embodiments, R^{5D} is independently hydrogen, $-CX^{5D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5D}_2$, $-CH_2X^{5D}$, R^{32D} -substituted or unsubstituted alkyl, R^{32D} -substituted or unsubstituted heteroalkyl, R^{32D} -substituted or unsubstituted cycloalkyl, R^{32D} -substituted or unsubstituted heterocycloalkyl, R^{32D} -substituted or unsubstituted aryl, or R^{32D} -substituted or unsubstituted heteroaryl. In embodiments, R^{5D} is independently hydrogen, $-CX^{5D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{5D}_2$, $-CH_2X^{5D}$, R^{32D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{32D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{32D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{32D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{32D} -substituted or unsubstituted phenyl, or R^{32D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{5D} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{5D} is independently hydrogen. In embodiments, R^{5D} is independently methyl. In embodiments, R^{5D} is independently ethyl.

[0252] R^{32D} is independently oxo, halogen, $-CX^{32D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{32D}_3$, $-OCHX^{32D}_2$, R^{33D} -substituted or unsubstituted alkyl, R^{33D} -substituted or unsubstituted heteroalkyl, R^{33D} -substituted or unsubstituted cycloalkyl, R^{33D} -substituted or unsubstituted heterocycloalkyl, R^{33D} -substituted or unsubstituted aryl, or R^{33D} -substituted or unsubstituted heteroaryl. In embodiments, R^{32D} is independently oxo, halogen, $-CX^{32D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{32D}_3$, $-OCHX^{32D}_2$, R^{33D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{33D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{33D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{33D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{33D} -substituted or unsubstituted phenyl, or R^{33D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{32D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0253] R^{33D} is independently oxo, halogen, $-CX^{33D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33D}_3$, $-OCHX^{33D}_2$, R^{34D} -substituted or unsubstituted alkyl, R^{34D} -substituted or unsubstituted heteroalkyl, R^{34D} -substituted or unsubstituted cycloalkyl, R^{34D} -substituted or unsubstituted heterocycloalkyl,

R^{34D} -substituted or unsubstituted aryl, or R^{34D} -substituted or unsubstituted heteroaryl. In embodiments, R^{33D} is independently oxo, halogen, $-CX^{33D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

5 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{33D}_3$, $-OCHX^{33D}_2$, R^{34D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{34D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{34D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{34D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{34D} -substituted or unsubstituted phenyl, or R^{34D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{33D} is $-F$, $-Cl$, $-Br$, or $-I$.

10 **[0254]** R^{34} , R^{34A} , R^{34B} , R^{34C} , and R^{34D} are independently hydrogen, oxo, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$
 15 $_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{34} , R^{34A} , R^{34B} , R^{34C} , and R^{34D} are independently oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 20 $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{34} , R^{34A} , R^{34B} , R^{34C} , and R^{34D} are independently oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 25 $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered heteroalkyl, unsubstituted C_3 - C_8 cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0255] In embodiments, L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, substituted or unsubstituted C_1 - C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, substituted or
 30 unsubstituted C_3 - C_8 cycloalkylene, substituted or unsubstituted 3 to 8 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^1 is a bond. In embodiments, L^1 is a substituted or unsubstituted C_1 - C_6 alkylene, substituted or unsubstituted 2 to 6 membered

heteroalkylene, substituted or unsubstituted C₃-C₆ cycloalkylene, substituted or unsubstituted 3 to 6 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L¹ is an unsubstituted C₁-C₆ alkylene, unsubstituted 2 to 6 membered heteroalkylene, or unsubstituted C₃-C₆

5 cycloalkylene. In embodiments, L¹ is an unsubstituted methylene.

[0256] In embodiments, L¹ is a bond. In embodiments, L¹ is -S(O)₂-. In embodiments, L¹ is -S(O)₂-Ph-. In embodiments, L¹ is -NR⁶-. In embodiments, L¹ is -O-. In embodiments, L¹ is -S-. In embodiments, L¹ is -C(O)-. In embodiments, L¹ is -C(O)NR⁶-. In embodiments, L¹ is -NR⁶C(O)-. In embodiments, L¹ is -NR⁶C(O)NH-. In embodiments, L¹ is -NHC(O)NR⁶-. In embodiments, L¹ is -C(O)O-. In embodiments, L¹ is -OC(O)-. In
10 embodiments, L¹ is -NH-. In embodiments, L¹ is -C(O)NH-. In embodiments, L¹ is -NHC(O)-. In embodiments, L¹ is -NHC(O)NH-. In embodiments, L¹ is -CH₂-. In embodiments, L¹ is -OCH₂-. In embodiments, L¹ is -CH₂O-. In embodiments, L¹ is -CH₂CH₂-. In embodiments, L¹ is -SCH₂-. In embodiments, L¹ is -CH₂S-. In embodiments, L¹ is -CHCH-. In embodiments, L¹ is -CC-. In embodiments, L¹ is -NHCH₂-. In
15 embodiments, L¹ is -CH₂NH-.

[0257] In embodiments, L¹ is a substituted or unsubstituted alkylene. In embodiments, L¹ is a substituted or unsubstituted heteroalkylene. In embodiments, L¹ is a substituted or unsubstituted cycloalkylene. In embodiments, L¹ is a substituted or unsubstituted
20 heterocycloalkylene. In embodiments, L¹ is a substituted or unsubstituted arylene. In embodiments, L¹ is a substituted or unsubstituted heteroarylene. In embodiments, L¹ is a substituted alkylene. In embodiments, L¹ is a substituted heteroalkylene. In embodiments, L¹ is a substituted cycloalkylene. In embodiments, L¹ is a substituted heterocycloalkylene. In embodiments, L¹ is a substituted arylene. In embodiments, L¹ is a substituted
25 heteroarylene. In embodiments, L¹ is an unsubstituted alkylene. In embodiments, L¹ is an unsubstituted heteroalkylene. In embodiments, L¹ is an unsubstituted cycloalkylene. In embodiments, L¹ is an unsubstituted heterocycloalkylene. In embodiments, L¹ is an unsubstituted arylene. In embodiments, L¹ is an unsubstituted heteroarylene. In
embodiments, L¹ is a substituted or unsubstituted C₁-C₈ alkylene. In embodiments, L¹ is a
30 substituted or unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L¹ is a substituted or unsubstituted C₃-C₈ cycloalkylene. In embodiments, L¹ is a substituted or unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments, L¹ is a substituted or unsubstituted C₆-C₁₀ arylene. In embodiments, L¹ is a substituted or unsubstituted 5 to 10 membered heteroarylene. In embodiments, L¹ is a substituted C₁-C₈ alkylene. In

embodiments, L^1 is a substituted 2 to 8 membered heteroalkylene. In embodiments, L^1 is a substituted C_3 - C_8 cycloalkylene. In embodiments, L^1 is a substituted 3 to 8 membered heterocycloalkylene. In embodiments, L^1 is a substituted C_6 - C_{10} arylene. In embodiments, L^1 is a substituted 5 to 10 membered heteroarylene. In embodiments, L^1 is an unsubstituted C_1 - C_8 alkylene. In embodiments, L^1 is an unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^1 is an unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^1 is an unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments, L^1 is an unsubstituted C_6 - C_{10} arylene. In embodiments, L^1 is an unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^1 is a substituted or unsubstituted C_1 - C_4 alkylene. In embodiments, L^1 is a substituted or unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^1 is a substituted or unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^1 is a substituted or unsubstituted 3 to 6 membered heterocycloalkylene. In embodiments, L^1 is a substituted or unsubstituted phenylene. In embodiments, L^1 is a substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^1 is a substituted C_1 - C_4 alkylene. In embodiments, L^1 is a substituted 2 to 4 membered heteroalkylene. In embodiments, L^1 is a substituted C_3 - C_6 cycloalkylene. In embodiments, L^1 is a substituted 3 to 6 membered heterocycloalkylene. In embodiments, L^1 is a substituted phenylene. In embodiments, L^1 is a substituted 5 to 6 membered heteroarylene. In embodiments, L^1 is an unsubstituted C_1 - C_4 alkylene. In embodiments, L^1 is an unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^1 is an unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^1 is an unsubstituted 3 to 6 membered heterocycloalkylene. In embodiments, L^1 is an unsubstituted phenylene. In embodiments, L^1 is an unsubstituted 5 to 6 membered heteroarylene.

[0258] In embodiments, L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^6-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^6-$, $-NR^6C(O)-$, $-NR^6C(O)NH-$, $-NHC(O)NR^6-$, $-C(O)O-$, $-OC(O)-$, R^{41} -substituted or unsubstituted alkylene, R^{41} -substituted or unsubstituted heteroalkylene, R^{41} -substituted or unsubstituted cycloalkylene, R^{41} -substituted or unsubstituted heterocycloalkylene, R^{41} -substituted or unsubstituted arylene, or R^{41} -substituted or unsubstituted heteroarylene. In embodiments, L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NH-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHC(O)NH-$, $-C(O)O-$, $-OC(O)-$, R^{41} -substituted or unsubstituted alkylene, R^{41} -substituted or unsubstituted heteroalkylene, R^{41} -substituted or unsubstituted cycloalkylene, R^{41} -substituted or unsubstituted heterocycloalkylene, R^{41} -substituted or unsubstituted arylene, or R^{41} -substituted or unsubstituted heteroarylene. In embodiments, L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NH-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHC(O)NH-$, $-C(O)O-$, $-OC(O)-$, R^{41} -substituted or unsubstituted alkylene, R^{41} -substituted or unsubstituted heteroalkylene, R^{41} -substituted or unsubstituted cycloalkylene, R^{41} -substituted or unsubstituted heterocycloalkylene, R^{41} -substituted or unsubstituted arylene, or R^{41} -substituted or unsubstituted heteroarylene. In embodiments, L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NH-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHC(O)NH-$, $-C(O)O-$, $-OC(O)-$, R^{41} -substituted or unsubstituted alkylene, R^{41} -substituted or unsubstituted heteroalkylene, R^{41} -substituted or unsubstituted cycloalkylene, R^{41} -substituted or unsubstituted heterocycloalkylene, R^{41} -substituted or unsubstituted arylene, or R^{41} -substituted or unsubstituted heteroarylene.

O)O-, -OC(O)-, R^{41} -substituted or unsubstituted C_1 - C_8 alkylene, R^{41} -substituted or unsubstituted 2 to 8 membered heteroalkylene, R^{41} -substituted or unsubstituted C_3 - C_8 cycloalkylene, R^{41} -substituted or unsubstituted 3 to 6 membered heterocycloalkylene, R^{41} -substituted or unsubstituted phenylene, or R^{41} -substituted or unsubstituted 5 to 6 membered heteroarylene.

[0259] R^{41} is independently oxo,

halogen, $-CX^{41}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,

-NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{41}_3$, $-OCHX^{41}_2$, R^{42} -

substituted or unsubstituted alkyl, R^{42} -substituted or unsubstituted heteroalkyl, R^{42} -

substituted or unsubstituted cycloalkyl, R^{42} -substituted or unsubstituted heterocycloalkyl,

R^{42} -substituted or unsubstituted aryl, or R^{42} -substituted or unsubstituted heteroaryl. In

embodiments, R^{41} is independently oxo,

halogen, $-CX^{41}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂,

-NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{41}_3$, $-OCHX^{41}_2$, R^{42} -

substituted or unsubstituted C_1 - C_8 alkyl, R^{42} -substituted or unsubstituted 2 to 8 membered

heteroalkyl, R^{42} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{42} -substituted or

unsubstituted 3 to 6 membered heterocycloalkyl, R^{42} -substituted or unsubstituted phenyl, or

R^{42} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{41} is -F, -Cl, -Br, or -I.

[0260] R^{42} is independently oxo,

halogen, $-CX^{42}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{42}_3$, $-OCHX^{42}_2$, R^{43} -substituted or unsubstituted alkyl, R^{43} -substituted or

unsubstituted heteroalkyl, R^{43} -substituted or unsubstituted cycloalkyl, R^{43} -substituted or

unsubstituted heterocycloalkyl, R^{43} -substituted or unsubstituted aryl, or R^{43} -substituted or

unsubstituted heteroaryl. In embodiments, R^{42} is independently oxo,

halogen, $-CX^{42}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{42}_3$, $-OCHX^{42}_2$, R^{43} -substituted or unsubstituted C_1 - C_8 alkyl, R^{43} -substituted or

unsubstituted 2 to 8 membered heteroalkyl, R^{43} -substituted or unsubstituted C_3 - C_8 cycloalkyl,

R^{43} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{43} -substituted or

unsubstituted phenyl, or R^{43} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{42} is -F, -Cl, -Br, or -I.

[0261] R^{43} is independently hydrogen, oxo,
 halogen, -CCl₃, -CBr₃, -CF₃, -CI₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -S
 5 O₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,
 -NHC(O)NH₂, -NHSO₂H, -NHC(O)H,
 -NHC(O)OH, -NHOH, -OCCl₃, -OCF₃, -OCBr₃, -OCI₃, -OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF
 2, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
 heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{43} is
 10 independently oxo,
 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCF₃, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted
 cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In
 15 embodiments, R^{43} is independently oxo,
 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCF₃, -OCHF₂, unsubstituted C₁-C₈ alkyl, unsubstituted 2 to 8 membered
 heteroalkyl, unsubstituted C₃-C₈ cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl,
 20 unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0262] In embodiments, L^1 is a bond. In embodiments, L^1 is R^{41} -substituted or
 unsubstituted C₁-C₂ alkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted C₁-C₄
 alkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted C₁-C₆ alkylene. In
 embodiments, L^1 is R^{41} -substituted or unsubstituted C₁-C₈ alkylene. In embodiments, L^1 is
 25 R^{41} -substituted or unsubstituted alkylene (e.g., C₁-C₈ alkylene, C₁-C₆ alkylene, C₁-C₄
 alkylene, C₁-C₂ alkylene). In embodiments, L^1 is R^{41} -substituted C₁-C₂ alkylene. In
 embodiments, L^1 is R^{41} -substituted C₁-C₄ alkylene. In embodiments, L^1 is R^{41} -substituted
 C₁-C₆ alkylene. In embodiments, L^1 is R^{41} -substituted C₁-C₈ alkylene. In embodiments, L^1 is
 R^{41} -substituted alkylene (e.g., C₁-C₈ alkylene, C₁-C₆ alkylene, C₁-C₄ alkylene, C₁-C₂
 30 alkylene). In embodiments, L^1 is R^{41} -substituted methylene. In embodiments, L^1 is
 unsubstituted C₁-C₂ alkylene. In embodiments, L^1 is unsubstituted C₁-C₄ alkylene. In
 embodiments, L^1 is unsubstituted C₁-C₆ alkylene. In embodiments, L^1 is unsubstituted C₁-C₈
 alkylene. In embodiments, L^1 is unsubstituted alkylene (e.g., C₁-C₈ alkylene, C₁-C₆ alkylene,
 C₁-C₄ alkylene, C₁-C₂ alkylene). In embodiments, L^1 is R^{41} -substituted or unsubstituted

methylene. In embodiments, L^1 is R^{41} -substituted methylene. In embodiments, L^1 is unsubstituted methylene.

[0263] In embodiments, L^1 is R^{41} -substituted or unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In embodiments, L^1 is R^{41} -substituted 2 to 4 membered heteroalkylene. In embodiments, L^1 is R^{41} -substituted 2 to 6 membered heteroalkylene. In embodiments, L^1 is R^{41} -substituted 2 to 8 membered heteroalkylene. In embodiments, L^1 is R^{41} -substituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In embodiments, L^1 is unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^1 is unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L^1 is unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^1 is unsubstituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene).

[0264] In embodiments, L^1 is R^{41} -substituted or unsubstituted ethylaminylene. In embodiments, L^1 is R^{41} -substituted ethylaminylene. In embodiments, L^1 is unsubstituted ethylaminylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted propylaminylene. In embodiments, L^1 is R^{41} -substituted propyl aminylene. In embodiments, L^1 is unsubstituted propylaminylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted butylaminylene. In embodiments, L^1 is R^{41} -substituted butylaminylene. In embodiments, L^1 is unsubstituted butylaminylene.

[0265] In embodiments, L^1 is R^{41} -substituted or unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted C_4 - C_6 cycloalkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted C_5 - C_6 cycloalkylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted cycloalkylene (e.g., C_3 - C_8 cycloalkylene, C_4 - C_6 cycloalkylene, or C_5 - C_6 cycloalkylene). In embodiments, L^1 is R^{41} -substituted C_3 - C_8 cycloalkylene. In embodiments, L^1 is R^{41} -substituted C_4 - C_6 cycloalkylene. In embodiments, L^1 is R^{41} -substituted C_5 - C_6 cycloalkylene. In embodiments, L^1 is R^{41} -substituted cycloalkylene (e.g., C_3 - C_8 cycloalkylene, C_4 - C_6 cycloalkylene, or C_5 - C_6 cycloalkylene). In embodiments, L^1 is unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^1 is unsubstituted C_4 - C_6 cycloalkylene. In embodiments, L^1 is unsubstituted C_5 - C_6 cycloalkylene. In embodiments, L^1 is

unsubstituted cycloalkylene (e.g., C₃-C₈ cycloalkylene, C₄-C₆ cycloalkylene, or C₅-C₆ cycloalkylene).

[0266] In embodiments, L¹ is R⁴¹-substituted or unsubstituted 4 membered heterocycloalkylene. In embodiments, L¹ is R⁴¹-substituted or unsubstituted 5 membered heterocycloalkylene. In embodiments, L¹ is R⁴¹-substituted or unsubstituted 6 membered heterocycloalkylene. In embodiments, L¹ is R⁴¹-substituted or unsubstituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L¹ is R⁴¹-substituted 4 membered heterocycloalkylene. In embodiments, L¹ is R⁴¹-substituted 5 membered heterocycloalkylene. In embodiments, L¹ is R⁴¹-substituted 6 membered heterocycloalkylene. In embodiments, L¹ is R⁴¹-substituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L¹ is unsubstituted 4 membered heterocycloalkylene. In embodiments, L¹ is unsubstituted 5 membered heterocycloalkylene. In embodiments, L¹ is unsubstituted 6 membered heterocycloalkylene. In embodiments, L¹ is unsubstituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene).

[0267] In embodiments, L¹ is R⁴¹-substituted or unsubstituted arylene (e.g. C₆-C₁₀ arylene or C₆ arylene). In embodiments, L¹ is R⁴¹-substituted or unsubstituted C₆-C₁₀ arylene. In embodiments, L¹ is R⁴¹-substituted or unsubstituted C₆ arylene. In embodiments, L¹ is R⁴¹-substituted arylene (e.g. C₆-C₁₀ arylene or C₆ arylene). In embodiments, L¹ is R⁴¹-substituted C₆-C₁₀ arylene. In embodiments, L¹ is R⁴¹-substituted C₆ arylene. In embodiments, L¹ is unsubstituted C₆-C₁₀ arylene. In embodiments, L¹ is unsubstituted C₆ arylene.

[0268] In embodiments, L¹ is R⁴¹-substituted or unsubstituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L¹ is R⁴¹-substituted or unsubstituted 5 to 10 membered heteroarylene. In embodiments, L¹ is R⁴¹-substituted or unsubstituted 5 to 9 membered heteroarylene. In embodiments, L¹ is R⁴¹-substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L¹ is R⁴¹-substituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L¹ is R⁴¹-substituted 5 to 10 membered heteroarylene. In embodiments, L¹ is R⁴¹-substituted 5 to 9 membered heteroarylene. In embodiments, L¹ is R⁴¹-substituted 5 to 6 membered heteroarylene. In embodiments, L¹ is unsubstituted heteroarylene (e.g. 5 to 10 membered

heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In
embodiments, L^1 is unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^1 is
unsubstituted 5 to 9 membered heteroarylene. In embodiments, L^1 is unsubstituted 5 to 6
membered heteroarylene. In embodiments, L^1 is R^{41} -substituted or unsubstituted
5 indolinyne. In embodiments, L^1 is R^{41} -substituted or unsubstituted indazolyne. In
embodiments, L^1 is R^{41} -substituted or unsubstituted benzimidazolyne. In embodiments, L^1
is R^{41} -substituted or unsubstituted benzoxazolyne. In embodiments, L^1 is R^{41} -substituted or
unsubstituted azaindolyne. In embodiments, L^1 is R^{41} -substituted or unsubstituted
purinyne. In embodiments, L^1 is R^{41} -substituted or unsubstituted indolyne. In
10 embodiments, L^1 is R^{41} -substituted or unsubstituted pyrazinyne. In embodiments, L^1 is R^{41} -
substituted or unsubstituted pyrrolyne. In embodiments, L^1 is R^{41} -substituted or
unsubstituted imidazolyne. In embodiments, L^1 is R^{41} -substituted or unsubstituted
pyrazolyne. In embodiments, L^1 is R^{41} -substituted or unsubstituted triazolyne. In
embodiments, L^1 is R^{41} -substituted or unsubstituted tetrazolyne.

15 **[0269]** In embodiments, L^1 is R^{41} -substituted indolinyne. In embodiments, L^1 is R^{41} -
substituted indazolyne. In embodiments, L^1 is R^{41} -substituted benzimidazolyne. In
embodiments, L^1 is R^{41} -substituted benzoxazolyne. In embodiments, L^1 is R^{41} -substituted
azaindolyne. In embodiments, L^1 is R^{41} -substituted purinyne. In embodiments, L^1 is R^{41} -
substituted indolyne. In embodiments, L^1 is R^{41} -substituted pyrazinyne. In embodiments,
20 L^1 is R^{41} -substituted pyrrolyne. In embodiments, L^1 is R^{41} -substituted imidazolyne. In
embodiments, L^1 is R^{41} -substituted pyrazolyne. In embodiments, L^1 is R^{41} -substituted
triazolyne. In embodiments, L^1 is R^{41} -substituted tetrazolyne.

[0270] In embodiments, L^1 is unsubstituted indolinyne. In embodiments, L^1 is
unsubstituted indazolyne. In embodiments, L^1 is unsubstituted benzimidazolyne. In
25 embodiments, L^1 is unsubstituted benzoxazolyne. In embodiments, L^1 is unsubstituted
azaindolyne. In embodiments, L^1 is unsubstituted purinyne. In embodiments, L^1 is
unsubstituted indolyne. In embodiments, L^1 is unsubstituted pyrazinyne. In
embodiments, L^1 is unsubstituted pyrrolyne. In embodiments, L^1 is unsubstituted
imidazolyne. In embodiments, L^1 is unsubstituted pyrazolyne. In embodiments, L^1 is
30 unsubstituted triazolyne. In embodiments, L^1 is unsubstituted tetrazolyne.

[0271] In embodiments, R^6 is independently hydrogen. In embodiments, R^6 is
independently halogen. In embodiments, R^6 is independently $-CX^6_3$. In embodiments, R^6 is
independently $-CHX^6_2$. In embodiments, R^6 is independently $-CH_2X^6$. In embodiments, R^6 is

independently $-\text{OCX}^6_3$. In embodiments, R^6 is independently $-\text{OCH}_2\text{X}^6$. In embodiments, R^6 is independently $-\text{OCHX}^6_2$. In embodiments, R^6 is independently $-\text{CN}$. In embodiments, R^6 is independently $-\text{SO}_{n6}\text{R}^{6D}$. In embodiments, R^6 is independently $-\text{SO}_{v6}\text{NR}^{6A}\text{R}^{6B}$. In embodiments, R^6 is independently $-\text{NHC}(\text{O})\text{NR}^{6A}\text{R}^{6B}$. In embodiments, R^6 is independently $-\text{N}(\text{O})_{m6}$. In embodiments, R^6 is independently $-\text{NR}^{6A}\text{R}^{6B}$. In embodiments, R^6 is independently $-\text{C}(\text{O})\text{R}^{6C}$. In embodiments, R^6 is independently $-\text{C}(\text{O})-\text{OR}^{6C}$. In embodiments, R^6 is independently $-\text{C}(\text{O})\text{NR}^{6A}\text{R}^{6B}$. In embodiments, R^6 is independently $-\text{OR}^{6D}$. In embodiments, R^6 is independently $-\text{NR}^{6A}\text{SO}_2\text{R}^{6D}$. In embodiments, R^6 is independently $-\text{NR}^{6A}\text{C}(\text{O})\text{R}^{6C}$. In embodiments, R^6 is independently $-\text{NR}^{6A}\text{C}(\text{O})\text{OR}^{6C}$. In embodiments, R^6 is independently $-\text{NR}^{6A}\text{OR}^{6C}$. In embodiments, R^6 is independently $-\text{OH}$. In embodiments, R^6 is independently $-\text{NH}_2$. In embodiments, R^6 is independently $-\text{COOH}$. In embodiments, R^6 is independently $-\text{CONH}_2$. In embodiments, R^6 is independently $-\text{NO}_2$. In embodiments, R^6 is independently $-\text{SH}$.

[0272] In embodiments, R^6 is independently substituted or unsubstituted alkyl. In embodiments, R^6 is independently substituted or unsubstituted heteroalkyl. In embodiments, R^6 is independently substituted or unsubstituted cycloalkyl. In embodiments, R^6 is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^6 is independently substituted or unsubstituted aryl. In embodiments, R^6 is independently substituted or unsubstituted heteroaryl. In embodiments, R^6 is independently substituted alkyl. In embodiments, R^6 is independently substituted heteroalkyl. In embodiments, R^6 is independently substituted cycloalkyl. In embodiments, R^6 is independently, substituted heterocycloalkyl. In embodiments, R^6 is independently substituted aryl. In embodiments, R^6 is independently substituted heteroaryl. In embodiments, R^6 is independently unsubstituted alkyl. In embodiments, R^6 is independently unsubstituted heteroalkyl. In embodiments, R^6 is independently unsubstituted cycloalkyl. In embodiments, R^6 is independently, unsubstituted heterocycloalkyl. In embodiments, R^6 is independently unsubstituted aryl. In embodiments, R^6 is independently unsubstituted heteroaryl. In embodiments, R^6 is independently substituted or unsubstituted $\text{C}_1\text{-C}_8$ alkyl. In embodiments, R^6 is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^6 is independently substituted or unsubstituted $\text{C}_3\text{-C}_8$ cycloalkyl. In embodiments, R^6 is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^6 is independently substituted or unsubstituted $\text{C}_6\text{-C}_{10}$ aryl. In embodiments, R^6 is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^6 is independently substituted $\text{C}_1\text{-C}_8$ alkyl. In embodiments, R^6 is independently substituted 2 to 8 membered heteroalkyl.

In embodiments, R^6 is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^6 is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^6 is independently substituted C_6 - C_{10} aryl. In embodiments, R^6 is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^6 is independently unsubstituted C_1 - C_8 alkyl. In
5 embodiments, R^6 is independently unsubstituted 2 to 8 membered heteroalkyl. In
embodiments, R^6 is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^6 is
independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^6 is
independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^6 is independently unsubstituted
5 to 10 membered heteroaryl. In embodiments, R^6 is independently substituted or
10 unsubstituted C_1 - C_4 alkyl. In embodiments, R^6 is independently substituted or unsubstituted
2 to 4 membered heteroalkyl. In embodiments, R^6 is independently substituted or
unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^6 is independently, substituted or
unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^6 is independently
substituted or unsubstituted phenyl. In embodiments, R^6 is independently substituted or
15 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^6 is independently substituted
 C_1 - C_4 alkyl. In embodiments, R^6 is independently substituted 2 to 4 membered heteroalkyl.
In embodiments, R^6 is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^6 is
independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^6 is
independently substituted phenyl. In embodiments, R^6 is independently substituted 5 to 6
20 membered heteroaryl. In embodiments, R^6 is independently unsubstituted C_1 - C_4 alkyl. In
embodiments, R^6 is independently unsubstituted 2 to 4 membered heteroalkyl. In
embodiments, R^6 is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^6 is
independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^6 is
independently unsubstituted phenyl. In embodiments, R^6 is independently unsubstituted 5 to
25 6 membered heteroaryl.

[0273] In embodiments, R^{6A} is independently hydrogen. In embodiments, R^{6A} is
independently $-CX^{6A}_3$. In embodiments, R^{6A} is independently $-CHX^{6A}_2$. In embodiments,
 R^{6A} is independently $-CH_2X^{6A}$. In embodiments, R^{6A} is independently $-CN$. In
embodiments, R^{6A} is independently $-COOH$. In embodiments, R^{6A} is
30 independently $-CONH_2$. In embodiments, R^{6A} is independently substituted or unsubstituted
alkyl. In embodiments, R^{6A} is independently substituted or unsubstituted heteroalkyl. In
embodiments, R^{6A} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 R^{6A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{6A} is
independently substituted or unsubstituted aryl. In embodiments, R^{6A} is independently

substituted or unsubstituted heteroaryl. In embodiments, R^{6A} is independently substituted alkyl. In embodiments, R^{6A} is independently substituted heteroalkyl. In embodiments, R^{6A} is independently substituted cycloalkyl. In embodiments, R^{6A} is independently, substituted heterocycloalkyl. In embodiments, R^{6A} is independently substituted aryl. In embodiments,

5 R^{6A} is independently substituted heteroaryl. In embodiments, R^{6A} is independently unsubstituted alkyl. In embodiments, R^{6A} is independently unsubstituted heteroalkyl. In embodiments, R^{6A} is independently unsubstituted cycloalkyl. In embodiments, R^{6A} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{6A} is independently unsubstituted aryl. In embodiments, R^{6A} is independently unsubstituted heteroaryl. In

10 embodiments, R^{6A} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{6A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6A} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{6A} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6A} is independently substituted or unsubstituted C_6 - C_{10}

15 aryl. In embodiments, R^{6A} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6A} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{6A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{6A} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{6A} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6A} is independently

20 substituted C_6 - C_{10} aryl. In embodiments, R^{6A} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{6A} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{6A} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6A} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{6A} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6A} is

25 independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{6A} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6A} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6A} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6A} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6A} is independently, substituted or

30 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6A} is independently substituted or unsubstituted phenyl. In embodiments, R^{6A} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6A} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{6A} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{6A} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{6A} is

35 independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6A} is

independently substituted phenyl. In embodiments, R^{6A} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{6A} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6A} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6A} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6A} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6A} is independently unsubstituted phenyl. In embodiments, R^{6A} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6A} is independently unsubstituted methyl. In embodiments, R^{6A} is independently unsubstituted ethyl. In embodiments, R^{6A} is independently unsubstituted propyl. In embodiments, R^{6A} is independently unsubstituted isopropyl. In embodiments, R^{6A} is independently unsubstituted tert-butyl.

[0274] In embodiments, R^{6B} is independently hydrogen. In embodiments, R^{6B} is independently $-CX^{6B}_3$. In embodiments, R^{6B} is independently $-CHX^{6B}_2$. In embodiments, R^{6B} is independently $-CH_2X^{6B}$. In embodiments, R^{6B} is independently $-CN$. In embodiments, R^{6B} is independently $-COOH$. In embodiments, R^{6B} is independently $-CONH_2$. In embodiments, R^{6B} is independently substituted or unsubstituted alkyl. In embodiments, R^{6B} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{6B} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{6B} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{6B} is independently substituted or unsubstituted aryl. In embodiments, R^{6B} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{6B} is independently substituted alkyl. In embodiments, R^{6B} is independently substituted heteroalkyl. In embodiments, R^{6B} is independently substituted cycloalkyl. In embodiments, R^{6B} is independently, substituted heterocycloalkyl. In embodiments, R^{6B} is independently substituted aryl. In embodiments, R^{6B} is independently substituted heteroaryl. In embodiments, R^{6B} is independently unsubstituted alkyl. In embodiments, R^{6B} is independently unsubstituted heteroalkyl. In embodiments, R^{6B} is independently unsubstituted cycloalkyl. In embodiments, R^{6B} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{6B} is independently unsubstituted aryl. In embodiments, R^{6B} is independently unsubstituted heteroaryl. In embodiments, R^{6B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{6B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{6B} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6B} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{6B} is independently substituted or unsubstituted 5 to 10 membered

heteroaryl. In embodiments, R^{6B} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{6B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{6B} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{6B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6B} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{6B} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{6B} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{6B} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{6B} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6B} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{6B} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6B} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6B} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6B} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6B} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6B} is independently substituted or unsubstituted phenyl. In embodiments, R^{6B} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6B} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{6B} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{6B} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{6B} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6B} is independently substituted phenyl. In embodiments, R^{6B} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{6B} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6B} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6B} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6B} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6B} is independently unsubstituted phenyl. In embodiments, R^{6B} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6B} is independently unsubstituted methyl. In embodiments, R^{6B} is independently unsubstituted ethyl. In embodiments, R^{6B} is independently unsubstituted propyl. In embodiments, R^{6B} is independently unsubstituted isopropyl. In embodiments, R^{6B} is independently unsubstituted tert-butyl.

[0275] In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same

nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0276] In embodiments, R^{6C} is independently hydrogen. In embodiments, R^{6C} is independently $-CX^{6C}_3$. In embodiments, R^{6C} is independently $-CHX^{6C}_2$. In embodiments, R^{6C} is independently $-CH_2X^{6C}$. In embodiments, R^{6C} is independently $-CN$. In embodiments, R^{6C} is independently $-COOH$. In embodiments, R^{6C} is independently $-CONH_2$. In embodiments, R^{6C} is independently substituted or unsubstituted alkyl. In embodiments, R^{6C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{6C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{6C} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{6C} is independently

substituted or unsubstituted aryl. In embodiments, R^{6C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{6C} is independently substituted alkyl. In embodiments, R^{6C} is independently substituted heteroalkyl. In embodiments, R^{6C} is independently substituted cycloalkyl. In embodiments, R^{6C} is independently, substituted heterocycloalkyl. In embodiments, R^{6C} is independently substituted aryl. In embodiments, R^{6C} is independently substituted heteroaryl. In embodiments, R^{6C} is independently unsubstituted alkyl. In embodiments, R^{6C} is independently unsubstituted heteroalkyl. In embodiments, R^{6C} is independently unsubstituted cycloalkyl. In embodiments, R^{6C} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{6C} is independently unsubstituted aryl. In embodiments, R^{6C} is independently unsubstituted heteroaryl. In embodiments, R^{6C} is independently substituted or unsubstituted C₁-C₈ alkyl. In embodiments, R^{6C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6C} is independently substituted or unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{6C} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6C} is independently substituted or unsubstituted C₆-C₁₀ aryl. In embodiments, R^{6C} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6C} is independently substituted C₁-C₈ alkyl. In embodiments, R^{6C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{6C} is independently substituted C₃-C₈ cycloalkyl. In embodiments, R^{6C} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6C} is independently substituted C₆-C₁₀ aryl. In embodiments, R^{6C} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{6C} is independently unsubstituted C₁-C₈ alkyl. In embodiments, R^{6C} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6C} is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{6C} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6C} is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R^{6C} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6C} is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R^{6C} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6C} is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{6C} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6C} is independently substituted or unsubstituted phenyl. In embodiments, R^{6C} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6C} is independently substituted C₁-C₄ alkyl. In embodiments, R^{6C} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{6C} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{6C} is

independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6C} is independently substituted phenyl. In embodiments, R^{6C} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{6C} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6C} is independently unsubstituted 2 to 4 membered heteroalkyl. In
 5 embodiments, R^{6C} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6C} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6C} is independently unsubstituted phenyl. In embodiments, R^{6C} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6C} is independently unsubstituted methyl. In
 10 embodiments, R^{6C} is independently unsubstituted ethyl. In embodiments, R^{6C} is independently unsubstituted propyl. In embodiments, R^{6C} is independently unsubstituted isopropyl. In embodiments, R^{6C} is independently unsubstituted tert-butyl.

[0277] In embodiments, R^{6D} is independently hydrogen. In embodiments, R^{6D} is independently $-CX^{6D}_3$. In embodiments, R^{6D} is independently $-CHX^{6D}_2$. In embodiments, R^{6D} is independently $-CH_2X^{6D}$. In embodiments, R^{6D} is independently $-CN$. In
 15 embodiments, R^{6D} is independently $-COOH$. In embodiments, R^{6D} is independently $-CONH_2$. In embodiments, R^{6D} is independently substituted or unsubstituted alkyl. In embodiments, R^{6D} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{6D} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{6D} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{6D} is
 20 independently substituted or unsubstituted aryl. In embodiments, R^{6D} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{6D} is independently substituted alkyl. In embodiments, R^{6D} is independently substituted heteroalkyl. In embodiments, R^{6D} is independently substituted cycloalkyl. In embodiments, R^{6D} is independently, substituted heterocycloalkyl. In embodiments, R^{6D} is independently substituted aryl. In embodiments,
 25 R^{6D} is independently substituted heteroaryl. In embodiments, R^{6D} is independently unsubstituted alkyl. In embodiments, R^{6D} is independently unsubstituted heteroalkyl. In embodiments, R^{6D} is independently unsubstituted cycloalkyl. In embodiments, R^{6D} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{6D} is independently unsubstituted aryl. In embodiments, R^{6D} is independently unsubstituted heteroaryl. In
 30 embodiments, R^{6D} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{6D} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{6D} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6D} is independently substituted or unsubstituted C_6 - C_{10}

aryl. In embodiments, R^{6D} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6D} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{6D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{6D} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{6D} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6D} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{6D} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{6D} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{6D} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{6D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{6D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{6D} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{6D} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{6D} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6D} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6D} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6D} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6D} is independently substituted or unsubstituted phenyl. In embodiments, R^{6D} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6D} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{6D} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{6D} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{6D} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6D} is independently substituted phenyl. In embodiments, R^{6D} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{6D} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{6D} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{6D} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{6D} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{6D} is independently unsubstituted phenyl. In embodiments, R^{6D} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{6D} is independently unsubstituted methyl. In embodiments, R^{6D} is independently unsubstituted ethyl. In embodiments, R^{6D} is independently unsubstituted propyl. In embodiments, R^{6D} is independently unsubstituted isopropyl. In embodiments, R^{6D} is independently unsubstituted tert-butyl.

[0278] In embodiments, R^6 is independently hydrogen, halogen, $-CX^6_3$, $-CHX^6_2$, $-CH_2X^6$, $-OCX^6_3$, $-OCH_2X^6$, $-OCHX^6_2$, $-CN$, $-SO_{n6}R^{6D}$, $-SO_{v6}NR^{6A}$, R^{6B} , $-NHC(O)NR^{6A}R^{6B}$, $-N(O)_{m6}$, $-NR^{6A}R^{6B}$, $-C(O)R^{6C}$, $-C(O)OR^{6C}$, $-C(O)NR^{6A}R^{6B}$, $-OR^{6D}$, -

$\text{NR}^{6\text{A}}\text{SO}_2\text{R}^{6\text{D}}$, $-\text{NR}^{6\text{A}}\text{C}(\text{O})\text{R}^{6\text{C}}$, $-\text{NR}^{6\text{A}}\text{C}(\text{O})\text{OR}^{6\text{C}}$, $-\text{NR}^{6\text{A}}\text{OR}^{6\text{C}}$, R^{35} -substituted or unsubstituted alkyl, R^{35} -substituted or unsubstituted heteroalkyl, R^{35} -substituted or unsubstituted cycloalkyl, R^{35} -substituted or unsubstituted heterocycloalkyl, R^{35} -substituted or unsubstituted aryl, or R^{35} -substituted or unsubstituted heteroaryl. In embodiments, R^6 is independently
 5 halogen, $-\text{CX}^6_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^6_3$, $-\text{OCHX}^6_2$, R^{35} -substituted or unsubstituted alkyl, R^{35} -substituted or unsubstituted heteroalkyl, R^{35} -substituted or unsubstituted cycloalkyl, R^{35} -substituted or unsubstituted heterocycloalkyl, R^{35} -substituted or unsubstituted aryl, or R^{35} -substituted or
 10 unsubstituted heteroaryl. In embodiments, R^6 is independently halogen, $-\text{CX}^6_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^6_3$, $-\text{OCHX}^6_2$, R^{35} -substituted or unsubstituted C_1 - C_8 alkyl, R^{35} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{35} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 15 R^{35} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{35} -substituted or unsubstituted phenyl, or R^{35} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^6 is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$. In embodiments, R^6 is independently hydrogen. In embodiments, R^6 is independently methyl. In embodiments, R^6 is independently ethyl.

[0279] R^{35} is independently oxo,
 20 halogen, $-\text{CX}^{35}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{35}_3$, $-\text{OCHX}^{35}_2$, R^{36} -substituted or unsubstituted alkyl, R^{36} -substituted or unsubstituted heteroalkyl, R^{36} -substituted or unsubstituted cycloalkyl, R^{36} -substituted or unsubstituted heterocycloalkyl, R^{36} -substituted or unsubstituted aryl, or R^{36} -substituted or
 25 unsubstituted heteroaryl. In embodiments, R^{35} is independently oxo, halogen, $-\text{CX}^{35}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{35}_3$, $-\text{OCHX}^{35}_2$, R^{36} -substituted or unsubstituted C_1 - C_8 alkyl, R^{36} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{36} -substituted or unsubstituted C_3 - C_8 cycloalkyl,
 30 R^{36} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{36} -substituted or unsubstituted phenyl, or R^{36} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{35} is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0280] R^{36} is independently oxo,
 halogen, $-\text{CX}^{36}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCX³⁶₃, -OCHX³⁶₂, R³⁷-substituted or unsubstituted alkyl, R³⁷-substituted or
 unsubstituted heteroalkyl, R³⁷-substituted or unsubstituted cycloalkyl, R³⁷-substituted or
 unsubstituted heterocycloalkyl, R³⁷-substituted or unsubstituted aryl, or R³⁷-substituted or
 5 unsubstituted heteroaryl. In embodiments, R³⁶ is independently oxo,
 halogen, -CX³⁶₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCX³⁶₃, -OCHX³⁶₂, R³⁷-substituted or unsubstituted C₁-C₈ alkyl, R³⁷-substituted or
 unsubstituted 2 to 8 membered heteroalkyl, R³⁷-substituted or unsubstituted C₃-C₈ cycloalkyl,
 10 R³⁷-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R³⁷-substituted or
 unsubstituted phenyl, or R³⁷-substituted or unsubstituted 5 to 6 membered heteroaryl. X³⁶ is
 -F, -Cl, -Br, or -I.

[0281] In embodiments, R^{6A} is independently
 hydrogen, -CX^{6A}₃, -CN, -COOH, -CONH₂, -CHX^{6A}₂, -CH₂X^{6A}, R^{35A}-substituted or
 15 unsubstituted alkyl, R^{35A}-substituted or unsubstituted heteroalkyl, R^{35A}-substituted or
 unsubstituted cycloalkyl, R^{35A}-substituted or unsubstituted heterocycloalkyl, R^{35A}-substituted
 or unsubstituted aryl, or R^{35A}-substituted or unsubstituted heteroaryl. In embodiments, R^{6A} is
 independently hydrogen, -CX^{6A}₃, -CN, -COOH, -CONH₂, -CHX^{6A}₂, -CH₂X^{6A}, R^{35A}-
 substituted or unsubstituted C₁-C₈ alkyl, R^{35A}-substituted or unsubstituted 2 to 8 membered
 20 heteroalkyl, R^{35A}-substituted or unsubstituted C₃-C₈ cycloalkyl, R^{35A}-substituted or
 unsubstituted 3 to 6 membered heterocycloalkyl, R^{35A}-substituted or unsubstituted phenyl, or
 R^{35A}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{6A} is -F, -Cl, -Br, or -I. In
 embodiments, R^{6A} is independently hydrogen. In embodiments, R^{6A} is independently methyl.
 In embodiments, R^{6A} is independently ethyl.

25 **[0282]** In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may
 optionally be joined to form a R^{35A}-substituted or unsubstituted heterocycloalkyl or R^{35A}-
 substituted or unsubstituted heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to
 the same nitrogen atom may optionally be joined to form a R^{35A}-substituted or unsubstituted
 3 to 6 membered heterocycloalkyl or R^{35A}-substituted or unsubstituted 5 to 6 membered
 30 heteroaryl.

[0283] R^{35A} is independently oxo,
 halogen, -CX^{35A}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-\text{OCX}^{35\text{A}}_3$, $-\text{OCHX}^{35\text{A}}_2$, $\text{R}^{36\text{A}}$ -substituted or unsubstituted alkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted aryl, or $\text{R}^{36\text{A}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{35\text{A}}$ is independently oxo,

- 5 halogen, $-\text{CX}^{35\text{A}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{35\text{A}}_3$, $-\text{OCHX}^{35\text{A}}_2$, $\text{R}^{36\text{A}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{36\text{A}}$ -substituted or unsubstituted phenyl, or $\text{R}^{36\text{A}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{35\text{A}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0284] $\text{R}^{36\text{A}}$ is independently oxo,

halogen, $-\text{CX}^{36\text{A}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{36\text{A}}_3$, $-\text{OCHX}^{36\text{A}}_2$, $\text{R}^{37\text{A}}$ -substituted or unsubstituted alkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted aryl, or $\text{R}^{37\text{A}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{36\text{A}}$ is independently oxo,

- 15 halogen, $-\text{CX}^{36\text{A}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{36\text{A}}_3$, $-\text{OCHX}^{36\text{A}}_2$, $\text{R}^{37\text{A}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{37\text{A}}$ -substituted or unsubstituted phenyl, or $\text{R}^{37\text{A}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{36\text{A}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0285] In embodiments, $\text{R}^{6\text{B}}$ is independently

hydrogen, $-\text{CX}^{6\text{B}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{6\text{B}}_2$, $-\text{CH}_2\text{X}^{6\text{B}}$, $\text{R}^{35\text{B}}$ -substituted or unsubstituted alkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted aryl, or $\text{R}^{35\text{B}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{6\text{B}}$ is independently hydrogen, $-\text{CX}^{6\text{B}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{6\text{B}}_2$, $-\text{CH}_2\text{X}^{6\text{B}}$, $\text{R}^{35\text{B}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{35\text{B}}$ -substituted or unsubstituted phenyl, or

R^{35B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{6B} is -F, -Cl, -Br, or -I. In embodiments, R^{6B} is independently hydrogen. In embodiments, R^{6B} is independently methyl. In embodiments, R^{6B} is independently ethyl.

[0286] In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{35B} -substituted or unsubstituted heterocycloalkyl or R^{35B} -substituted or unsubstituted heteroaryl. In embodiments, R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{35B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{35B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0287] R^{35B} is independently oxo, halogen, $-CX^{35B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{35B}_3$, $-OCHX^{35B}_2$, R^{36B} -substituted or unsubstituted alkyl, R^{36B} -substituted or unsubstituted heteroalkyl, R^{36B} -substituted or unsubstituted cycloalkyl, R^{36B} -substituted or unsubstituted heterocycloalkyl, R^{36B} -substituted or unsubstituted aryl, or R^{36B} -substituted or unsubstituted heteroaryl. In embodiments, R^{35B} is independently oxo, halogen, $-CX^{35B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{35B}_3$, $-OCHX^{35B}_2$, R^{36B} -substituted or unsubstituted C₁-C₈ alkyl, R^{36B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{36B} -substituted or unsubstituted C₃-C₈ cycloalkyl, R^{36B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{36B} -substituted or unsubstituted phenyl, or R^{36B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{35B} is -F, -Cl, -Br, or -I.

[0288] R^{36B} is independently oxo, halogen, $-CX^{36B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{36B}_3$, $-OCHX^{36B}_2$, R^{37B} -substituted or unsubstituted alkyl, R^{37B} -substituted or unsubstituted heteroalkyl, R^{37B} -substituted or unsubstituted cycloalkyl, R^{37B} -substituted or unsubstituted heterocycloalkyl, R^{37B} -substituted or unsubstituted aryl, or R^{37B} -substituted or unsubstituted heteroaryl. In embodiments, R^{36B} is independently oxo, halogen, $-CX^{36B}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{36B}_3$, $-OCHX^{36B}_2$, R^{37B} -substituted or unsubstituted C₁-C₈ alkyl, R^{37B} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{37B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{37B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{37B} -substituted or unsubstituted phenyl, or R^{37B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{36B} is -F, -Cl, -Br, or -I.

- 5 **[0289]** In embodiments, R^{6C} is independently hydrogen, $-CX^{6C}_3$, -CN, -COOH, -CONH₂, $-CHX^{6C}_2$, $-CH_2X^{6C}$, R^{35C} -substituted or unsubstituted alkyl, R^{35C} -substituted or unsubstituted heteroalkyl, R^{35C} -substituted or unsubstituted cycloalkyl, R^{35C} -substituted or unsubstituted heterocycloalkyl, R^{35C} -substituted or unsubstituted aryl, or R^{35C} -substituted or unsubstituted heteroaryl. In embodiments, R^{6C} is
- 10 independently hydrogen, $-CX^{6C}_3$, -CN, -COOH, -CONH₂, $-CHX^{6C}_2$, $-CH_2X^{6C}$, R^{35C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{35C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{35C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{35C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{35C} -substituted or unsubstituted phenyl, or R^{35C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{6C} is -F, -Cl, -Br, or -I. In
- 15 embodiments, R^{6C} is independently hydrogen. In embodiments, R^{6C} is independently methyl. In embodiments, R^{6C} is independently ethyl.

- [0290]** R^{35C} is independently oxo, halogen, $-CX^{35C}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
- 20 -NHOH, $-OCX^{35C}_3$, $-OCHX^{35C}_2$, R^{36C} -substituted or unsubstituted alkyl, R^{36C} -substituted or unsubstituted heteroalkyl, R^{36C} -substituted or unsubstituted cycloalkyl, R^{36C} -substituted or unsubstituted heterocycloalkyl, R^{36C} -substituted or unsubstituted aryl, or R^{36C} -substituted or unsubstituted heteroaryl. In embodiments, R^{35C} is independently oxo, halogen, $-CX^{35C}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
- 25 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCX^{35C}_3$, $-OCHX^{35C}_2$, R^{36C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{36C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{36C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{36C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{36C} -substituted or unsubstituted phenyl, or R^{36C} -substituted or unsubstituted 5 to 6 membered
- 30 heteroaryl. X^{35C} is -F, -Cl, -Br, or -I.

[0291] R^{36C} is independently oxo, halogen, $-CX^{36C}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-\text{OCX}^{36\text{C}}_3$, $-\text{OCHX}^{36\text{C}}_2$, $\text{R}^{37\text{C}}$ -substituted or unsubstituted alkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted aryl, or $\text{R}^{37\text{C}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{36\text{C}}$ is independently oxo,

- 5 halogen, $-\text{CX}^{36\text{C}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{36\text{C}}_3$, $-\text{OCHX}^{36\text{C}}_2$, $\text{R}^{37\text{C}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{37\text{C}}$ -substituted or unsubstituted phenyl, or $\text{R}^{37\text{C}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{36\text{C}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0292] In embodiments, $\text{R}^{6\text{D}}$ is independently

hydrogen, $-\text{CX}^{6\text{D}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{6\text{D}}_2$, $-\text{CH}_2\text{X}^{6\text{D}}$, $\text{R}^{35\text{D}}$ -substituted or unsubstituted alkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{35\text{D}}$ -substituted or

- 15 unsubstituted cycloalkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted aryl, or $\text{R}^{35\text{D}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{6\text{D}}$ is independently hydrogen, $-\text{CX}^{6\text{D}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{6\text{D}}_2$, $-\text{CH}_2\text{X}^{6\text{D}}$, $\text{R}^{35\text{D}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{35\text{D}}$ -substituted or unsubstituted phenyl, or $\text{R}^{35\text{D}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{6\text{D}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$. In embodiments, $\text{R}^{6\text{D}}$ is independently hydrogen. In embodiments, $\text{R}^{6\text{D}}$ is independently methyl. In embodiments, $\text{R}^{6\text{D}}$ is independently ethyl.

[0293] $\text{R}^{35\text{D}}$ is independently oxo,

- 25 halogen, $-\text{CX}^{35\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{35\text{D}}_3$, $-\text{OCHX}^{35\text{D}}_2$, $\text{R}^{36\text{D}}$ -substituted or unsubstituted alkyl, $\text{R}^{36\text{D}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{36\text{D}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{36\text{D}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{36\text{D}}$ -substituted or unsubstituted aryl, or $\text{R}^{36\text{D}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{35\text{D}}$ is independently oxo,
- 30 halogen, $-\text{CX}^{35\text{D}}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{35\text{D}}_3$, $-\text{OCHX}^{35\text{D}}_2$, $\text{R}^{36\text{D}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{36\text{D}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{36\text{D}}$ -substituted or unsubstituted

C₃-C₈ cycloalkyl, R^{36D}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{36D}-substituted or unsubstituted phenyl, or R^{36D}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{35D} is -F, -Cl, -Br, or -I.

[0294] R^{36D} is independently oxo,

- 5 halogen, -CX^{36D}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{36D}₃, -OCHX^{36D}₂, R^{37D}-substituted or unsubstituted alkyl, R^{37D}-substituted or unsubstituted heteroalkyl, R^{37D}-substituted or unsubstituted cycloalkyl, R^{37D}-substituted or unsubstituted heterocycloalkyl, R^{37D}-substituted or unsubstituted aryl, or R^{37D}-substituted or unsubstituted heteroaryl. In embodiments, R^{36D} is independently oxo,
- 10 halogen, -CX^{36D}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{36D}₃, -OCHX^{36D}₂, R^{37D}-substituted or unsubstituted C₁-C₈ alkyl, R^{37D}-substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{37D}-substituted or unsubstituted
- 15 C₃-C₈ cycloalkyl, R^{37D}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{37D}-substituted or unsubstituted phenyl, or R^{37D}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{36D} is -F, -Cl, -Br, or -I.

[0295] R³⁷, R^{37A}, R^{37B}, R^{37C}, and R^{37D} are independently hydrogen, oxo,

- halogen, -CCl₃, -CBr₃, -CF₃, -Cl₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -S
- 20 O₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCCl₃, -OCF₃, -OCBr₃, -OCl₃, -OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R³⁷, R^{37A}, R^{37B}, R^{37C}, and R^{37D} are independently oxo,
- 25 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCF₃, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In
- 30 embodiments, R³⁷, R^{37A}, R^{37B}, R^{37C}, and R^{37D} are independently oxo,
- halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCF₃, -OCHF₂, unsubstituted C₁-C₈ alkyl, unsubstituted 2 to 8 membered

heteroalkyl, unsubstituted C₃-C₈ cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0296] In embodiments, L¹ is given by the formula L¹⁰⁰-L¹⁰⁸.

[0297] L¹⁰⁰ is a

5 bond, -S(O)₂-, -S(O)₂-Ph-, -NR¹⁰¹-, -O-, -S-, -C(O)-, -C(O)NR¹⁰¹-, -NR¹⁰¹C(O)-, -NR¹⁰¹C(O)NH-, -NHC(O)NR¹⁰¹-, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene. R¹⁰¹ is hydrogen, halogen, -CX¹⁰¹₃, -CHX¹⁰¹₂, -
10 CH₂X¹⁰¹, -OCX¹⁰¹₃, -
OCH₂X¹⁰¹, -OCHX¹⁰¹₂, -CN, -SO_{n101}R^{101D}, -SO_{v101}NR^{101A}R^{101B}, -NHC(O)NR^{101A}R^{101B}, -N(O)_{m101}, -NR^{101A}R^{101B}, -C(O)R^{101C}, -C(O)-OR^{101C}, -C(O)NR^{101A}R^{101B}, -OR^{101D}, -NR^{101A}SO₂R^{101D}, -NR^{101A}C(O)R^{101C}, -NR^{101A}C(O)OR^{101C}, -NR^{101A}OR^{101C}, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted
15 cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbols v101 and m101 are independently an integer from 1 to 2. The symbol n101 is an integer from 0 to 4.

[0298] L¹⁰⁸ is a

bond, -S(O)₂-, -S(O)₂-Ph-, -NR¹⁰⁹-, -O-, -S-, -C(O)-, -C(O)NR¹⁰⁹-, -NR¹⁰⁹C(O)-, -NR¹⁰⁹C(O)NH-, -NHC(O)NR¹⁰⁹-, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene. R¹⁰⁹ is hydrogen, halogen, -CX¹⁰⁹₃, -CHX¹⁰⁹₂, -
20 CH₂X¹⁰⁹, -OCX¹⁰⁹₃, -
OCH₂X¹⁰⁹, -OCHX¹⁰⁹₂, -CN, -SO_{n109}R^{109D}, -SO_{v109}NR^{109A}R^{109B}, -NHC(O)NR^{109A}R^{109B}, -N(O)_{m109}, -NR^{109A}R^{109B}, -C(O)R^{109C}, -C(O)-OR^{109C}, -C(O)NR^{109A}R^{109B}, -OR^{109D}, -NR^{109A}SO₂R^{109D}, -NR^{109A}C(O)R^{109C}, -NR^{109A}C(O)OR^{109C}, -NR^{109A}OR^{109C}, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted
25 cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl. The symbols v109 and m109 are independently an integer from 1 to 2. The symbol n109 is an integer from 0 to 4.
30

[0299] In embodiments, L¹⁰⁰ is a bond, -S(O)₂-, -S(O)₂-Ph-, substituted or unsubstituted C₁-C₈ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, substituted or

unsubstituted C₃-C₈ cycloalkylene, substituted or unsubstituted 3 to 8 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L¹⁰⁰ is a bond. In embodiments, L¹⁰⁰ is a substituted or unsubstituted C₁-C₆ alkylene, substituted or unsubstituted 2 to 6 membered heteroalkylene, substituted or unsubstituted C₃-C₆ cycloalkylene, substituted or unsubstituted 3 to 6 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L¹⁰⁰ is an unsubstituted C₁-C₆ alkylene, unsubstituted 2 to 6 membered heteroalkylene, or unsubstituted C₃-C₆ cycloalkylene. In embodiments, L¹⁰⁰ is an unsubstituted methylene.

10 **[0300]** In embodiments, L¹⁰⁰ is a bond. In embodiments, L¹⁰⁰ is -S(O)₂-. In embodiments, L¹⁰⁰ is -S(O)₂-Ph-. In embodiments, L¹⁰⁰ is -NR¹⁰¹-. In embodiments, L¹⁰⁰ is -O-. In embodiments, L¹⁰⁰ is -S-. In embodiments, L¹⁰⁰ is -C(O)-. In embodiments, L¹⁰⁰ is -C(O)NR¹⁰¹-. In embodiments, L¹⁰⁰ is -NR¹⁰¹C(O)-. In embodiments, L¹⁰⁰ is -NR¹⁰¹C(O)NH-. In embodiments, L¹⁰⁰ is -NHC(O)NR¹⁰¹-. In embodiments, L¹⁰⁰ is -C(O)O-. In embodiments, L¹⁰⁰ is -OC(O)-. In embodiments, L¹⁰⁰ is -NH-. In
15 embodiments, L¹⁰⁰ is -C(O)NH-. In embodiments, L¹⁰⁰ is -NHC(O)-. In embodiments, L¹⁰⁰ is -NHC(O)NH-. In embodiments, L¹⁰⁰ is -CH₂-. In embodiments, L¹⁰⁰ is -OCH₂-. In embodiments, L¹⁰⁰ is -CH₂O-. In embodiments, L¹⁰⁰ is -CH₂CH₂-. In embodiments, L¹⁰⁰ is -SCH₂-. In embodiments, L¹⁰⁰ is -CH₂S-. In embodiments, L¹⁰⁰ is -CHCH-. In
20 embodiments, L¹⁰⁰ is -CC-. In embodiments, L¹⁰⁰ is -NHCH₂-. In embodiments, L¹⁰⁰ is -CH₂NH-.

[0301] In embodiments, L¹⁰⁰ is a substituted or unsubstituted alkylene. In embodiments, L¹⁰⁰ is a substituted or unsubstituted heteroalkylene. In embodiments, L¹⁰⁰ is a substituted or unsubstituted cycloalkylene. In embodiments, L¹⁰⁰ is a substituted or unsubstituted
25 heterocycloalkylene. In embodiments, L¹⁰⁰ is a substituted or unsubstituted arylene. In embodiments, L¹⁰⁰ is a substituted or unsubstituted heteroarylene. In embodiments, L¹⁰⁰ is a substituted alkylene. In embodiments, L¹⁰⁰ is a substituted heteroalkylene. In embodiments, L¹⁰⁰ is a substituted cycloalkylene. In embodiments, L¹⁰⁰ is a substituted heterocycloalkylene. In embodiments, L¹⁰⁰ is a substituted arylene. In embodiments, L¹⁰⁰ is
30 a substituted heteroarylene. In embodiments, L¹⁰⁰ is an unsubstituted alkylene. In embodiments, L¹⁰⁰ is an unsubstituted heteroalkylene. In embodiments, L¹⁰⁰ is an unsubstituted cycloalkylene. In embodiments, L¹⁰⁰ is an unsubstituted heterocycloalkylene. In embodiments, L¹⁰⁰ is an unsubstituted arylene. In embodiments, L¹⁰⁰ is an unsubstituted heteroarylene. In embodiments, L¹⁰⁰ is a substituted or unsubstituted C₁-C₈ alkylene. In

embodiments, L^{100} is a substituted or unsubstituted 2 to 8 membered heteroalkylene. In
embodiments, L^{100} is a substituted or unsubstituted C_3 - C_8 cycloalkylene. In embodiments,
 L^{100} is a substituted or unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments,
 L^{100} is a substituted or unsubstituted C_6 - C_{10} arylene. In embodiments, L^{100} is a substituted or
5 unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{100} is a substituted C_1 - C_8
alkylene. In embodiments, L^{100} is a substituted 2 to 8 membered heteroalkylene. In
embodiments, L^{100} is a substituted C_3 - C_8 cycloalkylene. In embodiments, L^{100} is a substituted
3 to 8 membered heterocycloalkylene. In embodiments, L^{100} is a substituted C_6 - C_{10} arylene.
In embodiments, L^{100} is a substituted 5 to 10 membered heteroarylene. In embodiments, L^{100}
10 is an unsubstituted C_1 - C_8 alkylene. In embodiments, L^{100} is an unsubstituted 2 to 8
membered heteroalkylene. In embodiments, L^{100} is an unsubstituted C_3 - C_8 cycloalkylene. In
embodiments, L^{100} is an unsubstituted 3 to 8 membered heterocycloalkylene. In
embodiments, L^{100} is an unsubstituted C_6 - C_{10} arylene. In embodiments, L^{100} is an
unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{100} is a substituted or
15 unsubstituted C_1 - C_4 alkylene. In embodiments, L^{100} is a substituted or unsubstituted 2 to 4
membered heteroalkylene. In embodiments, L^{100} is a substituted or unsubstituted C_3 - C_6
cycloalkylene. In embodiments, L^{100} is a substituted or unsubstituted 3 to 6 membered
heterocycloalkylene. In embodiments, L^{100} is a substituted or unsubstituted phenylene. In
embodiments, L^{100} is a substituted or unsubstituted 5 to 6 membered heteroarylene. In
20 embodiments, L^{100} is a substituted C_1 - C_4 alkylene. In embodiments, L^{100} is a substituted 2 to
4 membered heteroalkylene. In embodiments, L^{100} is a substituted C_3 - C_6 cycloalkylene. In
embodiments, L^{100} is a substituted 3 to 6 membered heterocycloalkylene. In embodiments,
 L^{100} is a substituted phenylene. In embodiments, L^{100} is a substituted 5 to 6 membered
heteroarylene. In embodiments, L^{100} is an unsubstituted C_1 - C_4 alkylene. In embodiments,
25 L^{100} is an unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^{100} is an
unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^{100} is an unsubstituted 3 to 6
membered heterocycloalkylene. In embodiments, L^{100} is an unsubstituted phenylene. In
embodiments, L^{100} is an unsubstituted 5 to 6 membered heteroarylene.

[0302] In embodiments, L^{100} is a
30 bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^{101}-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^{101}-$, $-NR^{101}C(O)-$, $-NR^{101}C(O)$
 $NH-$, $-NHC(O)NR^{101}-$, $-C(O)O-$, $-OC(O)-$, R^{105} -substituted or unsubstituted alkylene, R^{105} -
substituted or unsubstituted heteroalkylene, R^{105} -substituted or unsubstituted cycloalkylene,
 R^{105} -substituted or unsubstituted heterocycloalkylene, R^{105} -substituted or unsubstituted
arylene, or R^{105} -substituted or unsubstituted heteroarylene. In embodiments, L^{100} is a

bond, -S(O)₂-, -S(O)₂-Ph-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, R¹⁰⁵-substituted or unsubstituted alkylene, R¹⁰⁵-substituted or unsubstituted heteroalkylene, R¹⁰⁵-substituted or unsubstituted cycloalkylene, R¹⁰⁵-substituted or unsubstituted heterocycloalkylene, R¹⁰⁵-substituted or unsubstituted arylene, or R¹⁰⁵-

5 substituted or unsubstituted heteroarylene. In embodiments, L¹⁰⁰ is a bond, -S(O)₂-, -S(O)₂-Ph-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, R¹⁰⁵-substituted or unsubstituted C₁-C₈ alkylene, R¹⁰⁵-substituted or unsubstituted 2 to 8 membered heteroalkylene, R¹⁰⁵-substituted or unsubstituted C₃-C₈ cycloalkylene, R¹⁰⁵-substituted or unsubstituted 3 to 6 membered heterocycloalkylene, R¹⁰⁵-
10 substituted or unsubstituted phenylene, or R¹⁰⁵-substituted or unsubstituted 5 to 6 membered heteroarylene.

[0303] R¹⁰⁵ is independently oxo,

halogen, -CX¹⁰⁵₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,

15 -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX¹⁰⁵₃, -OCHX¹⁰⁵₂, R¹⁰⁶-substituted or unsubstituted alkyl, R¹⁰⁶-substituted or unsubstituted heteroalkyl, R¹⁰⁶-substituted or unsubstituted cycloalkyl, R¹⁰⁶-substituted or unsubstituted heterocycloalkyl, R¹⁰⁶-substituted or unsubstituted aryl, or R¹⁰⁶-substituted or unsubstituted heteroaryl. In embodiments, R¹⁰⁵ is independently oxo,

20 halogen, -CX¹⁰⁵₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,

-NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX¹⁰⁵₃, -OCHX¹⁰⁵₂, R¹⁰⁶-substituted or unsubstituted C₁-C₈ alkyl, R¹⁰⁶-substituted or unsubstituted 2 to 8 membered heteroalkyl, R¹⁰⁶-substituted or unsubstituted C₃-C₈ cycloalkyl, R¹⁰⁶-substituted or

25 unsubstituted 3 to 6 membered heterocycloalkyl, R¹⁰⁶-substituted or unsubstituted phenyl, or R¹⁰⁶-substituted or unsubstituted 5 to 6 membered heteroaryl. X¹⁰⁵ is -F, -Cl, -Br, or -I.

[0304] R¹⁰⁶ is independently oxo,

halogen, -CX¹⁰⁶₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

30 -NHOH, -OCX¹⁰⁶₃, -OCHX¹⁰⁶₂, R¹⁰⁷-substituted or unsubstituted alkyl, R¹⁰⁷-substituted or unsubstituted heteroalkyl, R¹⁰⁷-substituted or unsubstituted cycloalkyl, R¹⁰⁷-substituted or unsubstituted heterocycloalkyl, R¹⁰⁷-substituted or unsubstituted aryl, or R¹⁰⁷-substituted or unsubstituted heteroaryl. In embodiments, R¹⁰⁶ is independently oxo,

halogen, -CX¹⁰⁶₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

$-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCX}^{106}_3$, $-\text{OCHX}^{106}_2$, R^{107} -substituted or unsubstituted C_1 - C_8 alkyl, R^{107} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{107} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{107} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{107} -
5 substituted or unsubstituted phenyl, or R^{107} -substituted or unsubstituted 5 to 6 membered
heteroaryl. X^{106} is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0305] R^{107} is independently hydrogen, oxo,

halogen, $-\text{CCl}_3$, $-\text{CBr}_3$, $-\text{CF}_3$, $-\text{Cl}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{S}$
 O_4H , $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$,

10 $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$,

$-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCCl}_3$, $-\text{OCF}_3$, $-\text{OCBr}_3$, $-\text{OCl}_3$, $-\text{OCHCl}_2$, $-\text{OCHBr}_2$, $-\text{OCHI}_2$, $-\text{OCHF}$
 $_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{107} is
independently oxo,

15 halogen, $-\text{CF}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCF}_3$, $-\text{OCHF}_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted
cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In
embodiments, R^{107} is independently oxo,

20 halogen, $-\text{CF}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCF}_3$, $-\text{OCHF}_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered
heteroalkyl, unsubstituted C_3 - C_8 cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl,
unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

25 **[0306]** In embodiments, L^{100} is a bond. In embodiments, L^{100} is R^{105} -substituted or
unsubstituted C_1 - C_2 alkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted C_1 -
 C_4 alkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted C_1 - C_6 alkylene. In
embodiments, L^{100} is R^{105} -substituted or unsubstituted C_1 - C_8 alkylene. In embodiments, L^{100}
is R^{105} -substituted or unsubstituted alkylene (e.g., C_1 - C_8 alkylene, C_1 - C_6 alkylene, C_1 - C_4
30 alkylene, C_1 - C_2 alkylene). In embodiments, L^{100} is R^{105} -substituted C_1 - C_2 alkylene. In
embodiments, L^{100} is R^{105} -substituted C_1 - C_4 alkylene. In embodiments, L^{100} is R^{105} -
substituted C_1 - C_6 alkylene. In embodiments, L^{100} is R^{105} -substituted C_1 - C_8 alkylene. In
embodiments, L^{100} is R^{105} -substituted alkylene (e.g., C_1 - C_8 alkylene, C_1 - C_6 alkylene, C_1 - C_4
alkylene, C_1 - C_2 alkylene). In embodiments, L^{100} is R^{105} -substituted methylene. In

embodiments, L^{100} is unsubstituted C_1 - C_2 alkylene. In embodiments, L^{100} is unsubstituted C_1 - C_4 alkylene. In embodiments, L^{100} is unsubstituted C_1 - C_6 alkylene. In embodiments, L^{100} is unsubstituted C_1 - C_8 alkylene. In embodiments, L^{100} is unsubstituted alkylene (e.g., C_1 - C_8 alkylene, C_1 - C_6 alkylene, C_1 - C_4 alkylene, C_1 - C_2 alkylene). In embodiments, L^{100} is R^{105} -substituted or unsubstituted methylene. In embodiments, L^{100} is R^{105} -substituted methylene. In embodiments, L^{100} is unsubstituted methylene.

[0307] In embodiments, L^{100} is R^{105} -substituted or unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In embodiments, L^{100} is R^{105} -substituted 2 to 4 membered heteroalkylene. In embodiments, L^{100} is R^{105} -substituted 2 to 6 membered heteroalkylene. In embodiments, L^{100} is R^{105} -substituted 2 to 8 membered heteroalkylene. In embodiments, L^{100} is R^{105} -substituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In embodiments, L^{100} is unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^{100} is unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L^{100} is unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^{100} is unsubstituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene).

[0308] In embodiments, L^{100} is R^{105} -substituted or unsubstituted ethylaminylene. In embodiments, L^{100} is R^{105} -substituted ethylaminylene. In embodiments, L^{100} is unsubstituted ethylaminylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted propylaminylene. In embodiments, L^{100} is R^{105} -substituted propyl aminylene. In embodiments, L^{100} is unsubstituted propylaminylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted butylaminylene. In embodiments, L^{100} is R^{105} -substituted butylaminylene. In embodiments, L^{100} is unsubstituted butylaminylene.

[0309] In embodiments, L^{100} is R^{105} -substituted or unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted C_4 - C_6 cycloalkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted C_5 - C_6 cycloalkylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted cycloalkylene (e.g., C_3 - C_8 cycloalkylene, C_4 - C_6 cycloalkylene, or C_5 - C_6 cycloalkylene). In embodiments, L^{100} is R^{105} -substituted C_3 - C_8 cycloalkylene. In embodiments, L^{100} is R^{105} -substituted C_4 - C_6 cycloalkylene. In embodiments, L^{100} is R^{105} -

substituted C₅-C₆ cycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted cycloalkylene (e.g., C₃-C₈ cycloalkylene, C₄-C₆ cycloalkylene, or C₅-C₆ cycloalkylene). In embodiments, L¹⁰⁰ is unsubstituted C₃-C₈ cycloalkylene. In embodiments, L¹⁰⁰ is unsubstituted C₄-C₆ cycloalkylene. In embodiments, L¹⁰⁰ is unsubstituted C₅-C₆ cycloalkylene. In embodiments, L¹⁰⁰ is unsubstituted cycloalkylene (e.g., C₃-C₈ cycloalkylene, C₄-C₆ cycloalkylene, or C₅-C₆ cycloalkylene).

[0310] In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted 4 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted 5 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted 6 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted 4 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted 5 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted 6 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L¹⁰⁰ is unsubstituted 4 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is unsubstituted 5 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is unsubstituted 6 membered heterocycloalkylene. In embodiments, L¹⁰⁰ is unsubstituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene).

[0311] In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted arylene (e.g. C₆-C₁₀ arylene or C₆ arylene). In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted C₆-C₁₀ arylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted C₆ arylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted arylene (e.g. C₆-C₁₀ arylene or C₆ arylene). In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted C₆-C₁₀ arylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted C₆ arylene. In embodiments, L¹⁰⁰ is unsubstituted C₆-C₁₀ arylene. In embodiments, L¹⁰⁰ is unsubstituted C₆ arylene.

[0312] In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted 5 to 10 membered heteroarylene. In embodiments, L¹⁰⁰ is R¹⁰⁵-substituted or unsubstituted 5 to 9 membered heteroarylene. In

embodiments, L^{100} is R^{105} -substituted or unsubstituted 5 to 6 membered heteroarylene. In
embodiments, L^{100} is R^{105} -substituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5
to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L^{100} is
 R^{105} -substituted 5 to 10 membered heteroarylene. In embodiments, L^{100} is R^{105} -substituted 5
5 to 9 membered heteroarylene. In embodiments, L^{100} is R^{105} -substituted 5 to 6 membered
heteroarylene. In embodiments, L^{100} is unsubstituted heteroarylene (e.g. 5 to 10 membered
heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In
embodiments, L^{100} is unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{100} is
unsubstituted 5 to 9 membered heteroarylene. In embodiments, L^{100} is unsubstituted 5 to 6
10 membered heteroarylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted
indolinylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted indazolylene. In
embodiments, L^{100} is R^{105} -substituted or unsubstituted benzimidazolylene. In embodiments,
 L^{100} is R^{105} -substituted or unsubstituted benzoxazolylene. In embodiments, L^{100} is R^{105} -
substituted or unsubstituted azaindolylene. In embodiments, L^{100} is R^{105} -substituted or
15 unsubstituted purinylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted
indolylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted pyrazinylene. In
embodiments, L^{100} is R^{105} -substituted or unsubstituted pyrrolylene. In embodiments, L^{100} is
 R^{105} -substituted or unsubstituted imidazolylene. In embodiments, L^{100} is R^{105} -substituted or
unsubstituted pyrazolylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted
20 triazolylene. In embodiments, L^{100} is R^{105} -substituted or unsubstituted tetrazolylene.

[0313] In embodiments, L^{100} is R^{105} -substituted indolinylene. In embodiments, L^{100} is R^{105} -
substituted indazolylene. In embodiments, L^{100} is R^{105} -substituted benzimidazolylene. In
embodiments, L^{100} is R^{105} -substituted benzoxazolylene. In embodiments, L^{100} is R^{105} -
substituted azaindolylene. In embodiments, L^{100} is R^{105} -substituted purinylene. In
25 embodiments, L^{100} is R^{105} -substituted indolylene. In embodiments, L^{100} is R^{105} -substituted
pyrazinylene. In embodiments, L^{100} is R^{105} -substituted pyrrolylene. In embodiments, L^{100} is
 R^{105} -substituted imidazolylene. In embodiments, L^{100} is R^{105} -substituted pyrazolylene. In
embodiments, L^{100} is R^{105} -substituted triazolylene. In embodiments, L^{100} is R^{105} -substituted
tetrazolylene.

[0314] In embodiments, L^{100} is unsubstituted indolinylene. In embodiments, L^{100} is
unsubstituted indazolylene. In embodiments, L^{100} is unsubstituted benzimidazolylene. In
embodiments, L^{100} is unsubstituted benzoxazolylene. In embodiments, L^{100} is unsubstituted
azaindolylene. In embodiments, L^{100} is unsubstituted purinylene. In embodiments, L^{100} is
unsubstituted indolylene. In embodiments, L^{100} is unsubstituted pyrazinylene. In

embodiments, L^{100} is unsubstituted pyrrolylene. In embodiments, L^{100} is unsubstituted imidazolylene. In embodiments, L^{100} is unsubstituted pyrazolylene. In embodiments, L^{100} is unsubstituted triazolylene. In embodiments, L^{100} is unsubstituted tetrazolylene.

[0315] In embodiments, R^{101} is independently hydrogen. In embodiments, R^{101} is independently halogen. In embodiments, R^{101} is independently $-CX^{101}_3$. In embodiments, R^{101} is independently $-CHX^{101}_2$. In embodiments, R^{101} is independently $-CH_2X^{101}$. In embodiments, R^{101} is independently $-OCX^{101}_3$. In embodiments, R^{101} is independently $-OCH_2X^{101}$. In embodiments, R^{101} is independently $-OCHX^{101}_2$. In embodiments, R^{101} is independently $-CN$. In embodiments, R^{101} is independently $-SO_{n101}R^{101D}$. In embodiments, R^{101} is independently $-SO_{v101}NR^{101A}R^{101B}$. In embodiments, R^{101} is independently $-NHC(O)NR^{101A}R^{101B}$. In embodiments, R^{101} is independently $-N(O)_{m101}$. In embodiments, R^{101} is independently $-NR^{101A}R^{101B}$. In embodiments, R^{101} is independently $-C(O)R^{101C}$. In embodiments, R^{101} is independently $-C(O)-OR^{101C}$. In embodiments, R^{101} is independently $-C(O)NR^{101A}R^{101B}$. In embodiments, R^{101} is independently $-OR^{101D}$. In embodiments, R^{101} is independently $-NR^{101A}SO_2R^{101D}$. In embodiments, R^{101} is independently $-NR^{101A}C(O)R^{101C}$. In embodiments, R^{101} is independently $-NR^{101A}C(O)OR^{101C}$. In embodiments, R^{101} is independently $-NR^{101A}OR^{101C}$. In embodiments, R^{101} is independently $-OH$. In embodiments, R^{101} is independently $-NH_2$. In embodiments, R^{101} is independently $-COOH$. In embodiments, R^{101} is independently $-CONH_2$. In embodiments, R^{101} is independently $-NO_2$. In embodiments, R^{101} is independently $-SH$.

[0316] In embodiments, R^{101} is independently substituted or unsubstituted alkyl. In embodiments, R^{101} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{101} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{101} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{101} is independently substituted or unsubstituted aryl. In embodiments, R^{101} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{101} is independently substituted alkyl. In embodiments, R^{101} is independently substituted heteroalkyl. In embodiments, R^{101} is independently substituted cycloalkyl. In embodiments, R^{101} is independently, substituted heterocycloalkyl. In embodiments, R^{101} is independently substituted aryl. In embodiments, R^{101} is independently substituted heteroaryl. In embodiments, R^{101} is independently unsubstituted alkyl. In embodiments, R^{101} is independently unsubstituted heteroalkyl. In embodiments, R^{101} is independently unsubstituted cycloalkyl. In embodiments, R^{101} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{101} is independently

unsubstituted aryl. In embodiments, R^{101} is independently unsubstituted heteroaryl. In
embodiments, R^{101} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
embodiments, R^{101} is independently substituted or unsubstituted 2 to 8 membered
heteroalkyl. In embodiments, R^{101} is independently substituted or unsubstituted C_3 - C_8
5 cycloalkyl. In embodiments, R^{101} is independently, substituted or unsubstituted 3 to 8
membered heterocycloalkyl. In embodiments, R^{101} is independently substituted or
unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101} is independently substituted or unsubstituted
5 to 10 membered heteroaryl. In embodiments, R^{101} is independently substituted C_1 - C_8 alkyl.
In embodiments, R^{101} is independently substituted 2 to 8 membered heteroalkyl. In
10 embodiments, R^{101} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{101} is
independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101} is
independently substituted C_6 - C_{10} aryl. In embodiments, R^{101} is independently substituted 5 to
10 membered heteroaryl. In embodiments, R^{101} is independently unsubstituted C_1 - C_8 alkyl.
In embodiments, R^{101} is independently unsubstituted 2 to 8 membered heteroalkyl. In
15 embodiments, R^{101} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101} is
independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101} is
independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101} is independently
unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101} is independently
substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101} is independently substituted
20 or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101} is independently
substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101} is independently,
substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101} is
independently substituted or unsubstituted phenyl. In embodiments, R^{101} is independently
substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101} is
25 independently substituted C_1 - C_4 alkyl. In embodiments, R^{101} is independently substituted 2
to 4 membered heteroalkyl. In embodiments, R^{101} is independently substituted C_3 - C_6
cycloalkyl. In embodiments, R^{101} is independently, substituted 3 to 6 membered
heterocycloalkyl. In embodiments, R^{101} is independently substituted phenyl. In
embodiments, R^{101} is independently substituted 5 to 6 membered heteroaryl. In
30 embodiments, R^{101} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101} is
independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101} is
independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101} is independently
unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101} is independently
unsubstituted phenyl. In embodiments, R^{101} is independently unsubstituted 5 to 6 membered
35 heteroaryl.

[0317] In embodiments, R^{101A} is independently hydrogen. In embodiments, R^{101A} is independently $-CX^{101A}_3$. In embodiments, R^{101A} is independently $-CHX^{101A}_2$. In embodiments, R^{101A} is independently $-CH_2X^{101A}$. In embodiments, R^{101A} is independently $-CN$. In embodiments, R^{101A} is independently $-COOH$. In embodiments, R^{101A} is independently $-CONH_2$. In embodiments, R^{101A} is independently substituted or unsubstituted alkyl. In embodiments, R^{101A} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{101A} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{101A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{101A} is independently substituted or unsubstituted aryl. In embodiments, R^{101A} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{101A} is independently substituted alkyl. In embodiments, R^{101A} is independently substituted heteroalkyl. In embodiments, R^{101A} is independently substituted cycloalkyl. In embodiments, R^{101A} is independently, substituted heterocycloalkyl. In embodiments, R^{101A} is independently substituted aryl. In embodiments, R^{101A} is independently substituted heteroaryl. In embodiments, R^{101A} is independently unsubstituted alkyl. In embodiments, R^{101A} is independently unsubstituted heteroalkyl. In embodiments, R^{101A} is independently unsubstituted cycloalkyl. In embodiments, R^{101A} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{101A} is independently unsubstituted aryl. In embodiments, R^{101A} is independently unsubstituted heteroaryl. In embodiments, R^{101A} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{101A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{101A} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101A} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101A} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101A} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101A} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{101A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{101A} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{101A} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101A} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{101A} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{101A} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{101A} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{101A} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101A} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101A} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101A} is independently

unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101A} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101A} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101A} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101A} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101A} is independently substituted or unsubstituted phenyl. In embodiments, R^{101A} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101A} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{101A} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{101A} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{101A} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101A} is independently substituted phenyl. In embodiments, R^{101A} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{101A} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101A} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101A} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101A} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101A} is independently unsubstituted phenyl. In embodiments, R^{101A} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101A} is independently unsubstituted methyl. In embodiments, R^{101A} is independently unsubstituted ethyl. In embodiments, R^{101A} is independently unsubstituted propyl. In embodiments, R^{101A} is independently unsubstituted isopropyl. In embodiments, R^{101A} is independently unsubstituted tert-butyl.

[0318] In embodiments, R^{101B} is independently hydrogen. In embodiments, R^{101B} is independently $-CX^{101B}_3$. In embodiments, R^{101B} is independently $-CHX^{101B}_2$. In embodiments, R^{101B} is independently $-CH_2X^{101B}$. In embodiments, R^{101B} is independently $-CN$. In embodiments, R^{101B} is independently $-COOH$. In embodiments, R^{101B} is independently $-CONH_2$. In embodiments, R^{101B} is independently substituted or unsubstituted alkyl. In embodiments, R^{101B} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{101B} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{101B} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{101B} is independently substituted or unsubstituted aryl. In embodiments, R^{101B} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{101B} is independently substituted alkyl. In embodiments, R^{101B} is independently substituted heteroalkyl. In embodiments, R^{101B} is independently substituted cycloalkyl. In embodiments, R^{101B} is independently, substituted heterocycloalkyl. In embodiments, R^{101B} is

independently substituted aryl. In embodiments, R^{101B} is independently substituted heteroaryl. In embodiments, R^{101B} is independently unsubstituted alkyl. In embodiments, R^{101B} is independently unsubstituted heteroalkyl. In embodiments, R^{101B} is independently unsubstituted cycloalkyl. In embodiments, R^{101B} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{101B} is independently unsubstituted aryl. In 5
embodiments, R^{101B} is independently unsubstituted heteroaryl. In embodiments, R^{101B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{101B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{101B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101B} 10
is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101B} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101B} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101B} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{101B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{101B} is 15
independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{101B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101B} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{101B} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{101B} is independently unsubstituted C_1 - C_8 alkyl. In 20
embodiments, R^{101B} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{101B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101B} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101B} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101B} is independently 25
unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101B} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101B} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101B} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101B} is independently, 30
substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101B} is independently substituted or unsubstituted phenyl. In embodiments, R^{101B} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101B} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{101B} is independently substituted 2 35
to 4 membered heteroalkyl. In embodiments, R^{101B} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{101B} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101B} is independently substituted phenyl. In embodiments, R^{101B} is independently substituted 5 to 6 membered heteroaryl. In 40
embodiments, R^{101B} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101B} is

independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101B} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101B} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101B} is independently unsubstituted phenyl. In embodiments, R^{101B} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101B} is independently unsubstituted methyl. In embodiments, R^{101B} is independently unsubstituted ethyl. In embodiments, R^{101B} is independently unsubstituted propyl. In embodiments, R^{101B} is independently unsubstituted isopropyl. In embodiments, R^{101B} is independently unsubstituted tert-butyl.

[0319] In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen

atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0320] In embodiments, R^{101C} is independently hydrogen. In embodiments, R^{101C} is independently $-CX^{101C}_3$. In embodiments, R^{101C} is independently $-CHX^{101C}_2$. In embodiments, R^{101C} is independently $-CH_2X^{101C}$. In embodiments, R^{101C} is independently $-CN$. In embodiments, R^{101C} is independently $-COOH$. In embodiments, R^{101C} is independently $-CONH_2$. In embodiments, R^{101C} is independently substituted or unsubstituted alkyl. In embodiments, R^{101C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{101C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{101C} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{101C} is independently substituted or unsubstituted aryl. In embodiments, R^{101C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{101C} is independently substituted alkyl. In embodiments, R^{101C} is independently substituted heteroalkyl. In embodiments, R^{101C} is independently substituted cycloalkyl. In embodiments, R^{101C} is independently, substituted heterocycloalkyl. In embodiments, R^{101C} is independently substituted aryl. In embodiments, R^{101C} is independently substituted heteroaryl. In embodiments, R^{101C} is independently unsubstituted alkyl. In embodiments, R^{101C} is independently unsubstituted heteroalkyl. In embodiments, R^{101C} is independently unsubstituted cycloalkyl. In embodiments, R^{101C} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{101C} is independently unsubstituted aryl. In embodiments, R^{101C} is independently unsubstituted heteroaryl. In embodiments, R^{101C} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{101C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{101C} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101C} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101C} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101C} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101C} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{101C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{101C} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{101C} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101C} is independently

substituted C₆-C₁₀ aryl. In embodiments, R^{101C} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{101C} is independently unsubstituted C₁-C₈ alkyl. In embodiments, R^{101C} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{101C} is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{101C} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101C} is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R^{101C} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101C} is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R^{101C} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101C} is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{101C} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101C} is independently substituted or unsubstituted phenyl. In embodiments, R^{101C} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101C} is independently substituted C₁-C₄ alkyl. In embodiments, R^{101C} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{101C} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{101C} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101C} is independently substituted phenyl. In embodiments, R^{101C} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{101C} is independently unsubstituted C₁-C₄ alkyl. In embodiments, R^{101C} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101C} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{101C} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101C} is independently unsubstituted phenyl. In embodiments, R^{101C} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101C} is independently unsubstituted methyl. In embodiments, R^{101C} is independently unsubstituted ethyl. In embodiments, R^{101C} is independently unsubstituted propyl. In embodiments, R^{101C} is independently unsubstituted isopropyl. In embodiments, R^{101C} is independently unsubstituted tert-butyl.

[0321] In embodiments, R^{101D} is independently hydrogen. In embodiments, R^{101D} is independently -CX^{101D}₃. In embodiments, R^{101D} is independently -CHX^{101D}₂. In embodiments, R^{101D} is independently -CH₂X^{101D}. In embodiments, R^{101D} is independently -CN. In embodiments, R^{101D} is independently -COOH. In embodiments, R^{101D} is independently -CONH₂. In embodiments, R^{101D} is independently substituted or unsubstituted alkyl. In embodiments, R^{101D} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{101D} is independently substituted or unsubstituted cycloalkyl.

In embodiments, R^{101D} is independently, substituted or unsubstituted heterocycloalkyl. In
embodiments, R^{101D} is independently substituted or unsubstituted aryl. In embodiments,
 R^{101D} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{101D} is
independently substituted alkyl. In embodiments, R^{101D} is independently substituted
5 heteroalkyl. In embodiments, R^{101D} is independently substituted cycloalkyl. In
embodiments, R^{101D} is independently, substituted heterocycloalkyl. In embodiments, R^{101D} is
independently substituted aryl. In embodiments, R^{101D} is independently substituted
heteroaryl. In embodiments, R^{101D} is independently unsubstituted alkyl. In embodiments,
 R^{101D} is independently unsubstituted heteroalkyl. In embodiments, R^{101D} is independently
10 unsubstituted cycloalkyl. In embodiments, R^{101D} is independently, unsubstituted
heterocycloalkyl. In embodiments, R^{101D} is independently unsubstituted aryl. In
embodiments, R^{101D} is independently unsubstituted heteroaryl. In embodiments, R^{101D} is
independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{101D} is
independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments,
15 R^{101D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{101D}
is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In
embodiments, R^{101D} is independently substituted or unsubstituted C_6 - C_{10} aryl. In
embodiments, R^{101D} is independently substituted or unsubstituted 5 to 10 membered
heteroaryl. In embodiments, R^{101D} is independently substituted C_1 - C_8 alkyl. In
20 embodiments, R^{101D} is independently substituted 2 to 8 membered heteroalkyl. In
embodiments, R^{101D} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{101D} is
independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{101D} is
independently substituted C_6 - C_{10} aryl. In embodiments, R^{101D} is independently substituted 5
to 10 membered heteroaryl. In embodiments, R^{101D} is independently unsubstituted C_1 - C_8
25 alkyl. In embodiments, R^{101D} is independently unsubstituted 2 to 8 membered heteroalkyl.
In embodiments, R^{101D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments,
 R^{101D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments,
 R^{101D} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{101D} is independently
unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{101D} is independently
30 substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{101D} is independently substituted
or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101D} is independently
substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{101D} is independently,
substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101D} is
independently substituted or unsubstituted phenyl. In embodiments, R^{101D} is independently
35 substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{101D} is

independently substituted C₁-C₄ alkyl. In embodiments, R^{101D} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{101D} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{101D} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101D} is independently substituted phenyl. In

5 embodiments, R^{101D} is independently substituted 5 to 6 membered heteroaryl. In
embodiments, R^{101D} is independently unsubstituted C₁-C₄ alkyl. In embodiments, R^{101D} is
independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{101D} is
independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{101D} is independently
unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{101D} is independently
10 unsubstituted phenyl. In embodiments, R^{101D} is independently unsubstituted 5 to 6 membered
heteroaryl. In embodiments, R^{101D} is independently unsubstituted methyl. In embodiments,
R^{101D} is independently unsubstituted ethyl. In embodiments, R^{101D} is independently
unsubstituted propyl. In embodiments, R^{101D} is independently unsubstituted isopropyl. In
embodiments, R^{101D} is independently unsubstituted tert-butyl.

15 **[0322]** In embodiments, R¹⁰¹ is independently hydrogen,
halogen, -CX¹⁰¹₃, -CHX¹⁰¹₂, -CH₂X¹⁰¹, -OCX¹⁰¹₃, -OCH₂X¹⁰¹, -OCHX¹⁰¹₂, -CN, -SO_{n101}R^{101D},
, -SO_{v101}NR^{101A}R^{101B}, -NHC(O)NR^{101A}R^{101B}, -N(O)_{m101}, -NR^{101A}R^{101B}, -C(O)R^{101C}, -C(O)OR^{101C},
-C(O)NR^{101A}R^{101B}, -OR^{101D}, -NR^{101A}SO₂R^{101D}, -NR^{101A}C(O)R^{101C}, -NR^{101A}C(O)OR^{101C},
-NR^{101A}OR^{101C}, R¹⁰²-substituted or unsubstituted alkyl, R¹⁰²-substituted or unsubstituted
20 heteroalkyl, R¹⁰²-substituted or unsubstituted cycloalkyl, R¹⁰²-substituted or unsubstituted
heterocycloalkyl, R¹⁰²-substituted or unsubstituted aryl, or R¹⁰²-substituted or unsubstituted
heteroaryl. In embodiments, R¹⁰¹ is independently
halogen, -CX¹⁰¹₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
25 -NHOH, -OCX¹⁰¹₃, -OCHX¹⁰¹₂, R¹⁰²-substituted or unsubstituted alkyl, R¹⁰²-substituted or
unsubstituted heteroalkyl, R¹⁰²-substituted or unsubstituted cycloalkyl, R¹⁰²-substituted or
unsubstituted heterocycloalkyl, R¹⁰²-substituted or unsubstituted aryl, or R¹⁰²-substituted or
unsubstituted heteroaryl. In embodiments, R¹⁰¹ is independently
halogen, -CX¹⁰¹₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
30 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
-NHOH, -OCX¹⁰¹₃, -OCHX¹⁰¹₂, R¹⁰²-substituted or unsubstituted C₁-C₈ alkyl, R¹⁰²-
substituted or unsubstituted 2 to 8 membered heteroalkyl, R¹⁰²-substituted or unsubstituted
C₃-C₈ cycloalkyl, R¹⁰²-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R¹⁰²-
substituted or unsubstituted phenyl, or R¹⁰²-substituted or unsubstituted 5 to 6 membered

heteroaryl. X^{101} is -F, -Cl, -Br, or -I. In embodiments, R^{101} is independently hydrogen. In embodiments, R^{101} is independently methyl. In embodiments, R^{101} is independently ethyl.

[0323] In embodiments, R^{101} is independently

halogen, $-CX^{101}_3$, -CN, -OH, -COOH, -CONH₂, $-OCX^{101}_3$, $-OCHX^{101}_2$, R^{102} -substituted or

5 unsubstituted C₁-C₈ alkyl, R^{102} -substituted or unsubstituted 2 to 8 membered heteroalkyl,

R^{102} -substituted or unsubstituted C₃-C₈ cycloalkyl, R^{102} -substituted or unsubstituted 3 to 6

membered heterocycloalkyl, R^{102} -substituted or unsubstituted phenyl, or R^{102} -substituted or

unsubstituted 5 to 6 membered heteroaryl. X^{101} is -F, -Cl, -Br, or -I. In embodiments, R^{101} is

independently hydrogen. In embodiments, R^{101} is independently methyl. In embodiments,

10 R^{101} is independently ethyl.

[0324] R^{102} is independently oxo,

halogen, $-CX^{102}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{102}_3$, $-OCHX^{102}_2$, R^{103} -substituted or unsubstituted alkyl, R^{103} -substituted or

15 unsubstituted heteroalkyl, R^{103} -substituted or unsubstituted cycloalkyl, R^{103} -substituted or

unsubstituted heterocycloalkyl, R^{103} -substituted or unsubstituted aryl, or R^{103} -substituted or

unsubstituted heteroaryl. In embodiments, R^{102} is independently oxo,

halogen, $-CX^{102}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

20 -NHOH, $-OCX^{102}_3$, $-OCHX^{102}_2$, R^{103} -substituted or unsubstituted C₁-C₈ alkyl, R^{103} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{103} -substituted or unsubstituted

C₃-C₈ cycloalkyl, R^{103} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{103} -

substituted or unsubstituted phenyl, or R^{103} -substituted or unsubstituted 5 to 6 membered

heteroaryl. X^{102} is -F, -Cl, -Br, or -I.

25 **[0325]** R^{103} is independently oxo,

halogen, $-CX^{103}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{103}_3$, $-OCHX^{103}_2$, R^{104} -substituted or unsubstituted alkyl, R^{104} -substituted or

unsubstituted heteroalkyl, R^{104} -substituted or unsubstituted cycloalkyl, R^{104} -substituted or

30 unsubstituted heterocycloalkyl, R^{104} -substituted or unsubstituted aryl, or R^{104} -substituted or

unsubstituted heteroaryl. In embodiments, R^{103} is independently oxo,

halogen, $-CX^{103}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-\text{OCX}^{103}_3$, $-\text{OCHX}^{103}_2$, R^{104} -substituted or unsubstituted C_1 - C_8 alkyl, R^{104} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{104} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{104} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{104} -substituted or unsubstituted phenyl, or R^{104} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{103} is -F, -Cl, -Br, or -I.

[0326] In embodiments, $\text{R}^{101\text{A}}$ is independently hydrogen, $-\text{CX}^{101\text{A}}_3$, -CN, -COOH, -CONH₂, $-\text{CHX}^{101\text{A}}_2$, $-\text{CH}_2\text{X}^{101\text{A}}$, $\text{R}^{102\text{A}}$ -substituted or unsubstituted alkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted aryl, or $\text{R}^{102\text{A}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{101\text{A}}$ is independently hydrogen, $-\text{CX}^{101\text{A}}_3$, -CN, -COOH, -CONH₂, $-\text{CHX}^{101\text{A}}_2$, $-\text{CH}_2\text{X}^{101\text{A}}$, $\text{R}^{102\text{A}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{102\text{A}}$ -substituted or unsubstituted phenyl, or $\text{R}^{102\text{A}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{101\text{A}}$ is -F, -Cl, -Br, or -I. In embodiments, $\text{R}^{101\text{A}}$ is independently hydrogen. In embodiments, $\text{R}^{101\text{A}}$ is independently methyl. In embodiments, $\text{R}^{101\text{A}}$ is independently ethyl.

[0327] In embodiments, $\text{R}^{101\text{A}}$ and $\text{R}^{101\text{B}}$ substituents bonded to the same nitrogen atom may optionally be joined to form a $\text{R}^{102\text{A}}$ -substituted or unsubstituted heterocycloalkyl or $\text{R}^{102\text{A}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{101\text{A}}$ and $\text{R}^{101\text{B}}$ substituents bonded to the same nitrogen atom may optionally be joined to form a $\text{R}^{102\text{A}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or $\text{R}^{102\text{A}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0328] $\text{R}^{102\text{A}}$ is independently oxo, halogen, $-\text{CX}^{102\text{A}}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, $-\text{OCX}^{102\text{A}}_3$, $-\text{OCHX}^{102\text{A}}_2$, $\text{R}^{103\text{A}}$ -substituted or unsubstituted alkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted aryl, or $\text{R}^{103\text{A}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{102\text{A}}$ is independently oxo, halogen, $-\text{CX}^{102\text{A}}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-\text{OCX}^{102\text{A}}_3$, $-\text{OCHX}^{102\text{A}}_2$, $\text{R}^{103\text{A}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{103\text{A}}$ -substituted or unsubstituted phenyl, or $\text{R}^{103\text{A}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{102\text{A}}$ is -F, -Cl, -Br, or -I.

[0329] $\text{R}^{103\text{A}}$ is independently oxo, halogen, $-\text{CX}^{103\text{A}}_3$, -CN, -OH, - NH_2 , -COOH, -CONH $_2$, -NO $_2$, -SH, -SO $_3\text{H}$, -SO $_4\text{H}$, -SO $_2\text{NH}_2$, -NHNH $_2$, -ONH $_2$, -NHC(O)NHNH $_2$, -NHC(O)NH $_2$, -NHSO $_2\text{H}$, -NHC(O)H, -NHC(O)OH, -NHOH, $-\text{OCX}^{103\text{A}}_3$, $-\text{OCHX}^{103\text{A}}_2$, $\text{R}^{104\text{A}}$ -substituted or unsubstituted alkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted aryl, or $\text{R}^{104\text{A}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{103\text{A}}$ is independently oxo, halogen, $-\text{CX}^{103\text{A}}_3$, -CN, -OH, - NH_2 , -COOH, -CONH $_2$, -NO $_2$, -SH, -SO $_3\text{H}$, -SO $_4\text{H}$, -SO $_2\text{NH}_2$, -NHNH $_2$, -ONH $_2$, -NHC(O)NHNH $_2$, -NHC(O)NH $_2$, -NHSO $_2\text{H}$, -NHC(O)H, -NHC(O)OH, -NHOH, $-\text{OCX}^{103\text{A}}_3$, $-\text{OCHX}^{103\text{A}}_2$, $\text{R}^{104\text{A}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{104\text{A}}$ -substituted or unsubstituted phenyl, or $\text{R}^{104\text{A}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{103\text{A}}$ is -F, -Cl, -Br, or -I.

[0330] In embodiments, $\text{R}^{101\text{B}}$ is independently hydrogen, $-\text{CX}^{101\text{B}}_3$, -CN, -COOH, -CONH $_2$, $-\text{CHX}^{101\text{B}}_2$, $-\text{CH}_2\text{X}^{101\text{B}}$, $\text{R}^{102\text{B}}$ -substituted or unsubstituted alkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted cycloalkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted aryl, or $\text{R}^{102\text{B}}$ -substituted or unsubstituted heteroaryl. In embodiments, $\text{R}^{101\text{B}}$ is independently hydrogen, $-\text{CX}^{101\text{B}}_3$, -CN, -COOH, -CONH $_2$, $-\text{CHX}^{101\text{B}}_2$, $-\text{CH}_2\text{X}^{101\text{B}}$, $\text{R}^{102\text{B}}$ -substituted or unsubstituted C_1 - C_8 alkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, $\text{R}^{102\text{B}}$ -substituted or unsubstituted phenyl, or $\text{R}^{102\text{B}}$ -substituted or unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{101\text{B}}$ is -F, -Cl, -Br, or -I. In embodiments, $\text{R}^{101\text{B}}$ is independently hydrogen. In embodiments, $\text{R}^{101\text{B}}$ is independently methyl. In embodiments, $\text{R}^{101\text{B}}$ is independently ethyl.

[0331] In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{102B} -substituted or unsubstituted heterocycloalkyl or R^{102B} -substituted or unsubstituted heteroaryl. In embodiments, R^{101A} and R^{101B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{102B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{102B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0332] R^{102B} is independently oxo, halogen, $-CX^{102B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{102B}_3$, $-OCHX^{102B}_2$, R^{103B} -substituted or unsubstituted alkyl, R^{103B} -substituted or unsubstituted heteroalkyl, R^{103B} -substituted or unsubstituted cycloalkyl, R^{103B} -substituted or unsubstituted heterocycloalkyl, R^{103B} -substituted or unsubstituted aryl, or R^{103B} -substituted or unsubstituted heteroaryl. In embodiments, R^{102B} is independently oxo, halogen, $-CX^{102B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{102B}_3$, $-OCHX^{102B}_2$, R^{103B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{103B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{103B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{103B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{103B} -substituted or unsubstituted phenyl, or R^{103B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{102B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0333] R^{103B} is independently oxo, halogen, $-CX^{103B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{103B}_3$, $-OCHX^{103B}_2$, R^{104B} -substituted or unsubstituted alkyl, R^{104B} -substituted or unsubstituted heteroalkyl, R^{104B} -substituted or unsubstituted cycloalkyl, R^{104B} -substituted or unsubstituted heterocycloalkyl, R^{104B} -substituted or unsubstituted aryl, or R^{104B} -substituted or unsubstituted heteroaryl. In embodiments, R^{103B} is independently oxo, halogen, $-CX^{103B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{103B}_3$, $-OCHX^{103B}_2$, R^{104B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{104B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{104B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{104B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{104B} -substituted or unsubstituted phenyl, or R^{104B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{103B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0334] In embodiments, R^{101C} is independently

hydrogen, $-CX^{101C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{101C}_2$, $-CH_2X^{101C}$, R^{102C} -substituted or unsubstituted alkyl, R^{102C} -substituted or unsubstituted heteroalkyl, R^{102C} -substituted or unsubstituted cycloalkyl, R^{102C} -substituted or unsubstituted heterocycloalkyl, R^{102C} -

5 substituted or unsubstituted aryl, or R^{102C} -substituted or unsubstituted heteroaryl. In embodiments, R^{101C} is independently

hydrogen, $-CX^{101C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{101C}_2$, $-CH_2X^{101C}$, R^{102C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{102C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{102C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{102C} -substituted or unsubstituted 3 to 6
10 membered heterocycloalkyl, R^{102C} -substituted or unsubstituted phenyl, or R^{102C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{101C} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{101C} is independently hydrogen. In embodiments, R^{101C} is independently methyl. In embodiments, R^{101C} is independently ethyl.

[0335] R^{102C} is independently oxo,

15 halogen, $-CX^{102C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{102C}_3$, $-OCHX^{102C}_2$, R^{103C} -substituted or unsubstituted alkyl, R^{103C} -substituted or unsubstituted heteroalkyl, R^{103C} -substituted or unsubstituted cycloalkyl, R^{103C} -substituted or unsubstituted heterocycloalkyl, R^{103C} -substituted or unsubstituted aryl, or R^{103C} -substituted
20 or unsubstituted heteroaryl. In embodiments, R^{102C} is independently oxo, halogen, $-CX^{102C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{102C}_3$, $-OCHX^{102C}_2$, R^{103C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{103C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{103C} -substituted or unsubstituted
25 C_3 - C_8 cycloalkyl, R^{103C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{103C} -substituted or unsubstituted phenyl, or R^{103C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{102C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0336] R^{103C} is independently oxo,

halogen, $-CX^{103C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
30 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{103C}_3$, $-OCHX^{103C}_2$, R^{104C} -substituted or unsubstituted alkyl, R^{104C} -substituted or unsubstituted heteroalkyl, R^{104C} -substituted or unsubstituted cycloalkyl, R^{104C} -substituted or unsubstituted heterocycloalkyl, R^{104C} -substituted or unsubstituted aryl, or R^{104C} -substituted or unsubstituted heteroaryl. In embodiments, R^{103C} is independently oxo,

halogen, $-CX^{103C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{103C}_3$, $-OCHX^{103C}_2$, R^{104C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{104C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{104C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{104C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{104C} -substituted or unsubstituted phenyl, or R^{104C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{103C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0337] In embodiments, R^{101D} is independently

hydrogen, $-CX^{101D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{101D}_2$, $-CH_2X^{101D}$, R^{102D} -substituted or unsubstituted alkyl, R^{102D} -substituted or unsubstituted heteroalkyl, R^{102D} -substituted or unsubstituted cycloalkyl, R^{102D} -substituted or unsubstituted heterocycloalkyl, R^{102D} -substituted or unsubstituted aryl, or R^{102D} -substituted or unsubstituted heteroaryl. In

embodiments, R^{101D} is independently

hydrogen, $-CX^{101D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{101D}_2$, $-CH_2X^{101D}$, R^{102D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{102D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{102D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{102D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{102D} -substituted or unsubstituted phenyl, or R^{102D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{101D} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{101D} is independently hydrogen. In embodiments, R^{101D} is independently methyl. In

[0338] R^{102D} is independently oxo,

halogen, $-CX^{102D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{102D}_3$, $-OCHX^{102D}_2$, R^{103D} -substituted or unsubstituted alkyl, R^{103D} -substituted or unsubstituted heteroalkyl, R^{103D} -substituted or unsubstituted cycloalkyl, R^{103D} -substituted or unsubstituted heterocycloalkyl, R^{103D} -substituted or unsubstituted aryl, or R^{103D} -substituted or unsubstituted heteroaryl. In embodiments, R^{102D} is independently oxo,

halogen, $-CX^{102D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{102D}_3$, $-OCHX^{102D}_2$, R^{103D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{103D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{103D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{103D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{103D} -substituted or unsubstituted phenyl, or R^{103D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{102D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0339] R^{103D} is independently oxo,

halogen, $-CX^{103D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{103D}_3$, $-OCHX^{103D}_2$, R^{104D} -substituted or unsubstituted alkyl, R^{104D} -substituted
5 or unsubstituted heteroalkyl, R^{104D} -substituted or unsubstituted cycloalkyl, R^{104D} -substituted
or unsubstituted heterocycloalkyl, R^{104D} -substituted or unsubstituted aryl, or R^{104D} -substituted
or unsubstituted heteroaryl. In embodiments, R^{103D} is independently oxo,
halogen, $-CX^{103D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
10 $-NHOH$, $-OCX^{103D}_3$, $-OCHX^{103D}_2$, R^{104D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{104D} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{104D} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{104D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl,
 R^{104D} -substituted or unsubstituted phenyl, or R^{104D} -substituted or unsubstituted 5 to 6
membered heteroaryl. X^{103D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0340] R^{104} , R^{104A} , R^{104B} , R^{104C} , and R^{104D} are hydrogen, oxo,

halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$
 O_4H , $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$,

$-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$
20 $_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{104} ,
 R^{104A} , R^{104B} , R^{104C} , and R^{104D} are independently oxo,

halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$
 O_4H , $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$,
 $-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$
25 $_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{104} ,

R^{104A} , R^{104B} , R^{104C} , and R^{104D} are independently hydrogen, oxo,

halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$
 O_4H , $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$,

$-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$
30 $_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered heteroalkyl, unsubstituted C_3 - C_8

cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0341] In embodiments, L^{108} is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, substituted or unsubstituted C_3-C_8 cycloalkylene, substituted or unsubstituted 3 to 8 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is a bond. In embodiments, L^{108} is a substituted or unsubstituted C_1-C_6 alkylene, substituted or unsubstituted 2 to 6 membered heteroalkylene, substituted or unsubstituted C_3-C_6 cycloalkylene, substituted or unsubstituted 3 to 6 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is an unsubstituted C_1-C_6 alkylene, unsubstituted 2 to 6 membered heteroalkylene, or unsubstituted C_3-C_6 cycloalkylene. In embodiments, L^{108} is an unsubstituted methylene.

[0342] In embodiments, L^{108} is a bond. In embodiments, L^{108} is $-S(O)_2-$. In embodiments, L^{108} is $-S(O)_2-Ph-$. In embodiments, L^{108} is $-NR^{109}-$. In embodiments, L^{108} is $-O-$. In embodiments, L^{108} is $-S-$. In embodiments, L^{108} is $-C(O)-$. In embodiments, L^{108} is $-C(O)NR^{109}-$. In embodiments, L^{108} is $-NR^{109}C(O)-$. In embodiments, L^{108} is $-NR^{109}C(O)NH-$. In embodiments, L^{108} is $-NHC(O)NR^{109}-$. In embodiments, L^{108} is $-C(O)O-$. In embodiments, L^{108} is $-OC(O)-$. In embodiments, L^{108} is $-NH-$. In embodiments, L^{108} is $-C(O)NH-$. In embodiments, L^{108} is $-NHC(O)-$. In embodiments, L^{108} is $-NHC(O)NH-$. In embodiments, L^{108} is $-CH_2-$. In embodiments, L^{108} is $-OCH_2-$. In embodiments, L^{108} is $-CH_2O-$. In embodiments, L^{108} is $-CH_2CH_2-$. In embodiments, L^{108} is $-SCH_2-$. In embodiments, L^{108} is $-CH_2S-$. In embodiments, L^{108} is $-CHCH-$. In embodiments, L^{108} is $-CC-$. In embodiments, L^{108} is $-NHCH_2-$. In embodiments, L^{108} is $-CH_2NH-$.

[0343] In embodiments, L^{108} is a substituted or unsubstituted alkylene. In embodiments, L^{108} is a substituted or unsubstituted heteroalkylene. In embodiments, L^{108} is a substituted or unsubstituted cycloalkylene. In embodiments, L^{108} is a substituted or unsubstituted heterocycloalkylene. In embodiments, L^{108} is a substituted or unsubstituted arylene. In embodiments, L^{108} is a substituted or unsubstituted heteroarylene. In embodiments, L^{108} is a substituted alkylene. In embodiments, L^{108} is a substituted heteroalkylene. In embodiments, L^{108} is a substituted cycloalkylene. In embodiments, L^{108} is a substituted heterocycloalkylene. In embodiments, L^{108} is a substituted arylene. In embodiments, L^{108} is a substituted heteroarylene. In embodiments, L^{108} is an unsubstituted alkylene. In

embodiments, L^{108} is an unsubstituted heteroalkylene. In embodiments, L^{108} is an unsubstituted cycloalkylene. In embodiments, L^{108} is an unsubstituted heterocycloalkylene. In embodiments, L^{108} is an unsubstituted arylene. In embodiments, L^{108} is an unsubstituted heteroarylene. In embodiments, L^{108} is a substituted or unsubstituted C_1 - C_8 alkylene. In
5 embodiments, L^{108} is a substituted or unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^{108} is a substituted or unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^{108} is a substituted or unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments, L^{108} is a substituted or unsubstituted C_6 - C_{10} arylene. In embodiments, L^{108} is a substituted or unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{108} is a substituted C_1 - C_8
10 alkylene. In embodiments, L^{108} is a substituted 2 to 8 membered heteroalkylene. In embodiments, L^{108} is a substituted C_3 - C_8 cycloalkylene. In embodiments, L^{108} is a substituted 3 to 8 membered heterocycloalkylene. In embodiments, L^{108} is a substituted C_6 - C_{10} arylene. In embodiments, L^{108} is a substituted 5 to 10 membered heteroarylene. In embodiments, L^{108} is an unsubstituted C_1 - C_8 alkylene. In embodiments, L^{108} is an unsubstituted 2 to 8
15 membered heteroalkylene. In embodiments, L^{108} is an unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^{108} is an unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments, L^{108} is an unsubstituted C_6 - C_{10} arylene. In embodiments, L^{108} is an unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{108} is a substituted or unsubstituted C_1 - C_4 alkylene. In embodiments, L^{108} is a substituted or unsubstituted 2 to 4
20 membered heteroalkylene. In embodiments, L^{108} is a substituted or unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^{108} is a substituted or unsubstituted 3 to 6 membered heterocycloalkylene. In embodiments, L^{108} is a substituted or unsubstituted phenylene. In embodiments, L^{108} is a substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is a substituted C_1 - C_4 alkylene. In embodiments, L^{108} is a substituted 2 to
25 4 membered heteroalkylene. In embodiments, L^{108} is a substituted C_3 - C_6 cycloalkylene. In embodiments, L^{108} is a substituted 3 to 6 membered heterocycloalkylene. In embodiments, L^{108} is a substituted phenylene. In embodiments, L^{108} is a substituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is an unsubstituted C_1 - C_4 alkylene. In embodiments, L^{108} is an unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^{108} is an
30 unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^{108} is an unsubstituted 3 to 6 membered heterocycloalkylene. In embodiments, L^{108} is an unsubstituted phenylene. In embodiments, L^{108} is an unsubstituted 5 to 6 membered heteroarylene.

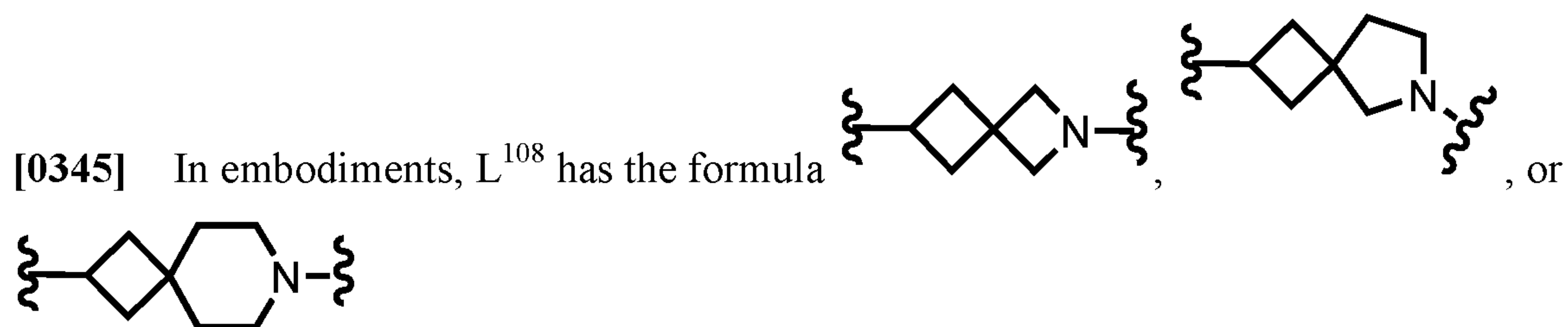
[0344] In embodiments, L^{108} is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^{109}-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^{109}-$, $-NR^{109}C(O)-$, $-NR^{109}C(O)$

NH-, -NHC(O)NR¹⁰⁹-, -C(O)O-, -OC(O)-, R¹¹³-substituted or unsubstituted alkylene, R¹¹³-substituted or unsubstituted heteroalkylene, R¹¹³-substituted or unsubstituted cycloalkylene, R¹¹³-substituted or unsubstituted heterocycloalkylene, R¹¹³-substituted or unsubstituted arylene, or R¹¹³-substituted or unsubstituted heteroarylene. In embodiments, L¹⁰⁸ is a

5 bond, -S(O)₂-, -S(O)₂-Ph-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, R¹¹³-substituted or unsubstituted alkylene, R¹¹³-substituted or unsubstituted heteroalkylene, R¹¹³-substituted or unsubstituted cycloalkylene, R¹¹³-substituted or unsubstituted heterocycloalkylene, R¹¹³-substituted or unsubstituted arylene, or R¹¹³-substituted or unsubstituted heteroarylene. In embodiments, L¹⁰⁸ is a

10 bond, -S(O)₂-, -S(O)₂-Ph-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, R¹¹³-substituted or unsubstituted C₁-C₈ alkylene, R¹¹³-substituted or unsubstituted 2 to 8 membered heteroalkylene, R¹¹³-substituted or unsubstituted C₃-C₈ cycloalkylene, R¹¹³-substituted or unsubstituted 3 to 6 membered heterocycloalkylene, R¹¹³-substituted or unsubstituted phenylene, or R¹¹³-substituted or unsubstituted 5 to 6 membered

15 heteroarylene.



[0346] R¹¹³ is independently oxo, halogen, -CX¹¹³₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX¹¹³₃, -OCHX¹¹³₂, R¹¹⁴-substituted or unsubstituted alkyl, R¹¹⁴-substituted or unsubstituted heteroalkyl, R¹¹⁴-substituted or unsubstituted cycloalkyl, R¹¹⁴-substituted or unsubstituted heterocycloalkyl, R¹¹⁴-substituted or unsubstituted aryl, or R¹¹⁴-substituted or unsubstituted heteroaryl. In

25 embodiments, R¹¹³ is independently oxo, halogen, -CX¹¹³₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX¹¹³₃, -OCHX¹¹³₂, R¹¹⁴-substituted or unsubstituted C₁-C₈ alkyl, R¹¹⁴-substituted or unsubstituted 2 to 8 membered

30 heteroalkyl, R¹¹⁴-substituted or unsubstituted C₃-C₈ cycloalkyl, R¹¹⁴-substituted or

unsubstituted 3 to 6 membered heterocycloalkyl, R^{114} -substituted or unsubstituted phenyl, or R^{114} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{113} is -F, -Cl, -Br, or -I.

[0347] R^{114} is independently oxo,

halogen, $-CX^{114}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

5 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{114}_3$, $-OCHX^{114}_2$, R^{115} -substituted or unsubstituted alkyl, R^{115} -substituted or

unsubstituted heteroalkyl, R^{115} -substituted or unsubstituted cycloalkyl, R^{115} -substituted or

unsubstituted heterocycloalkyl, R^{115} -substituted or unsubstituted aryl, or R^{115} -substituted or

unsubstituted heteroaryl. In embodiments, R^{114} is independently oxo,

10 halogen, $-CX^{114}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, $-OCX^{114}_3$, $-OCHX^{114}_2$, R^{115} -substituted or unsubstituted C₁-C₈ alkyl, R^{115} -

substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{115} -substituted or unsubstituted

C₃-C₈ cycloalkyl, R^{115} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{115} -

15 substituted or unsubstituted phenyl, or R^{115} -substituted or unsubstituted 5 to 6 membered

heteroaryl. X^{114} is -F, -Cl, -Br, or -I.

[0348] R^{115} is independently hydrogen, oxo,

halogen, -CCl₃, -CBr₃, -CF₃, -CI₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -S

O₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,

20 -NHC(O)NH₂, -NHSO₂H, -NHC(O)H,

-NHC(O)OH, -NHOH, -OCCl₃, -OCF₃, -OCBr₃, -OCI₃, -OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF

2, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted

heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{115} is

independently oxo,

25 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, -OCF₃, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted

cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In

embodiments, R^{115} is independently oxo,

30 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,

-NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,

-NHOH, -OCF₃, -OCHF₂, unsubstituted C₁-C₈ alkyl, unsubstituted 2 to 8 membered

heteroalkyl, unsubstituted C₃-C₈ cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0349] In embodiments, L¹⁰⁸ is a bond. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted C₁-C₂ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted C₁-C₄ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted C₁-C₆ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted C₁-C₈ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted alkylene (e.g., C₁-C₈ alkylene, C₁-C₆ alkylene, C₁-C₄ alkylene, C₁-C₂ alkylene). In embodiments, L¹⁰⁸ is R¹¹³-substituted C₁-C₂ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted C₁-C₄ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted C₁-C₆ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted C₁-C₈ alkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted alkylene (e.g., C₁-C₈ alkylene, C₁-C₆ alkylene, C₁-C₄ alkylene, C₁-C₂ alkylene). In embodiments, L¹⁰⁸ is R¹¹³-substituted methylene. In embodiments, L¹⁰⁸ is unsubstituted C₁-C₂ alkylene. In embodiments, L¹⁰⁸ is unsubstituted C₁-C₄ alkylene. In embodiments, L¹⁰⁸ is unsubstituted C₁-C₆ alkylene. In embodiments, L¹⁰⁸ is unsubstituted C₁-C₈ alkylene. In embodiments, L¹⁰⁸ is unsubstituted alkylene (e.g., C₁-C₈ alkylene, C₁-C₆ alkylene, C₁-C₄ alkylene, C₁-C₂ alkylene). In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted methylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted methylene. In embodiments, L¹⁰⁸ is unsubstituted methylene.

[0350] In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted or unsubstituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In embodiments, L¹⁰⁸ is R¹¹³-substituted 2 to 4 membered heteroalkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted 2 to 6 membered heteroalkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted 2 to 8 membered heteroalkylene. In embodiments, L¹⁰⁸ is R¹¹³-substituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In embodiments, L¹⁰⁸ is unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L¹⁰⁸ is unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L¹⁰⁸ is unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L¹⁰⁸ is unsubstituted heteroalkylene (e.g., 2 to 8 membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene).

[0351] In embodiments, L^{108} is R^{113} -substituted or unsubstituted ethylaminylene. In
embodiments, L^{108} is R^{113} -substituted ethylaminylene. In embodiments, L^{108} is unsubstituted
ethylaminylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted propylaminylene.
In embodiments, L^{108} is R^{113} -substituted propyl aminylene. In embodiments, L^{108} is
5 unsubstituted propylaminylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted
butylaminylene. In embodiments, L^{108} is R^{113} -substituted butylaminylene. In embodiments,
 L^{108} is unsubstituted butylaminylene.

[0352] In embodiments, L^{108} is R^{113} -substituted or unsubstituted C_3 - C_8 cycloalkylene. In
embodiments, L^{108} is R^{113} -substituted or unsubstituted C_4 - C_6 cycloalkylene. In embodiments,
10 L^{108} is R^{113} -substituted or unsubstituted C_5 - C_6 cycloalkylene. In embodiments, L^{108} is R^{113} -
substituted or unsubstituted cycloalkylene (e.g., C_3 - C_8 cycloalkylene, C_4 - C_6 cycloalkylene, or
 C_5 - C_6 cycloalkylene). In embodiments, L^{108} is R^{113} -substituted C_3 - C_8 cycloalkylene. In
embodiments, L^{108} is R^{113} -substituted C_4 - C_6 cycloalkylene. In embodiments, L^{108} is R^{113} -
substituted C_5 - C_6 cycloalkylene. In embodiments, L^{108} is R^{113} -substituted cycloalkylene
15 (e.g., C_3 - C_8 cycloalkylene, C_4 - C_6 cycloalkylene, or C_5 - C_6 cycloalkylene). In embodiments,
 L^{108} is unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^{108} is unsubstituted C_4 - C_6
cycloalkylene. In embodiments, L^{108} is unsubstituted C_5 - C_6 cycloalkylene. In embodiments,
 L^{108} is unsubstituted cycloalkylene (e.g., C_3 - C_8 cycloalkylene, C_4 - C_6 cycloalkylene, or C_5 - C_6
cycloalkylene).

[0353] In embodiments, L^{108} is R^{113} -substituted or unsubstituted 4 membered
heterocycloalkylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted 5 membered
heterocycloalkylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted 6 membered
heterocycloalkylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted
heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered
25 heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L^{108} is R^{113} -
substituted 4 membered heterocycloalkylene. In embodiments, L^{108} is R^{113} -substituted 5
membered heterocycloalkylene. In embodiments, L^{108} is R^{113} -substituted 6 membered
heterocycloalkylene. In embodiments, L^{108} is R^{113} -substituted heterocycloalkylene (e.g., 3 to
6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered
30 heterocycloalkylene). In embodiments, L^{108} is unsubstituted 4 membered
heterocycloalkylene. In embodiments, L^{108} is unsubstituted 5 membered
heterocycloalkylene. In embodiments, L^{108} is unsubstituted 6 membered heterocycloalkylene.
In embodiments, L^{108} is unsubstituted heterocycloalkylene (e.g., 3 to 6 membered

heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene).

[0354] In embodiments, L^{108} is R^{113} -substituted or unsubstituted arylene (e.g. C_6 - C_{10} arylene or C_6 arylene). In embodiments, L^{108} is R^{113} -substituted or unsubstituted C_6 - C_{10} arylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted C_6 arylene. In embodiments, L^{108} is R^{113} -substituted arylene (e.g. C_6 - C_{10} arylene or C_6 arylene). In embodiments, L^{108} is R^{113} -substituted C_6 - C_{10} arylene. In embodiments, L^{108} is R^{113} -substituted C_6 arylene. In embodiments, L^{108} is unsubstituted C_6 - C_{10} arylene. In embodiments, L^{108} is unsubstituted C_6 arylene.

[0355] In embodiments, L^{108} is R^{113} -substituted or unsubstituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L^{108} is R^{113} -substituted or unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted 5 to 9 membered heteroarylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is R^{113} -substituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L^{108} is R^{113} -substituted 5 to 10 membered heteroarylene. In embodiments, L^{108} is R^{113} -substituted 5 to 9 membered heteroarylene. In embodiments, L^{108} is R^{113} -substituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is unsubstituted heteroarylene (e.g. 5 to 10 membered heteroarylene, 5 to 9 membered heteroarylene, or 5 to 6 membered heteroarylene). In embodiments, L^{108} is unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^{108} is unsubstituted 5 to 9 membered heteroarylene. In embodiments, L^{108} is unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^{108} is R^{113} -substituted or unsubstituted indolinylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted indazolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted benzimidazolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted benzoxazolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted azaindolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted purinylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted indolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted pyrazinylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted pyrrolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted imidazolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted pyrazolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted triazolylenes. In embodiments, L^{108} is R^{113} -substituted or unsubstituted tetrazolylenes.

[0356] In embodiments, L^{108} is R^{113} -substituted indolinylenes. In embodiments, L^{108} is R^{113} -substituted indazolylenes. In embodiments, L^{108} is R^{113} -substituted benzimidazolylenes. In embodiments, L^{108} is R^{113} -substituted benzoxazolylenes. In embodiments, L^{108} is R^{113} -substituted azaindolylenes. In embodiments, L^{108} is R^{113} -substituted purinylenes. In
 5 embodiments, L^{108} is R^{113} -substituted indolylenes. In embodiments, L^{108} is R^{113} -substituted pyrazinylenes. In embodiments, L^{108} is R^{113} -substituted pyrrolylenes. In embodiments, L^{108} is R^{113} -substituted imidazolylenes. In embodiments, L^{108} is R^{113} -substituted pyrazolylenes. In embodiments, L^{108} is R^{113} -substituted triazolylenes. In embodiments, L^{108} is R^{113} -substituted tetrazolylenes.

10 **[0357]** In embodiments, L^{108} is unsubstituted indolinylenes. In embodiments, L^{108} is unsubstituted indazolylenes. In embodiments, L^{108} is unsubstituted benzimidazolylenes. In embodiments, L^{108} is unsubstituted benzoxazolylenes. In embodiments, L^{108} is unsubstituted azaindolylenes. In embodiments, L^{108} is unsubstituted purinylenes. In embodiments, L^{108} is unsubstituted indolylenes. In embodiments, L^{108} is unsubstituted pyrazinylenes. In
 15 embodiments, L^{108} is unsubstituted pyrrolylenes. In embodiments, L^{108} is unsubstituted imidazolylenes. In embodiments, L^{108} is unsubstituted pyrazolylenes. In embodiments, L^{108} is unsubstituted triazolylenes. In embodiments, L^{108} is unsubstituted tetrazolylenes.

[0358] In embodiments, R^{109} is independently hydrogen. In embodiments, R^{109} is independently halogen. In embodiments, R^{109} is independently $-CX^{109}_3$. In embodiments,
 20 R^{109} is independently $-CHX^{109}_2$. In embodiments, R^{109} is independently $-CH_2X^{109}$. In embodiments, R^{109} is independently $-OCX^{109}_3$. In embodiments, R^{109} is independently $-OCH_2X^{109}$. In embodiments, R^{109} is independently $-OCHX^{109}_2$. In embodiments, R^{109} is independently $-CN$. In embodiments, R^{109} is independently $-SO_{n109}R^{109D}$. In embodiments, R^{109} is independently $-SO_{v109}NR^{109A}R^{109B}$. In embodiments, R^{109} is
 25 independently $-NHC(O)NR^{109A}R^{109B}$. In embodiments, R^{109} is independently $-N(O)_{m109}$. In embodiments, R^{109} is independently $-NR^{109A}R^{109B}$. In embodiments, R^{109} is independently $-C(O)R^{109C}$. In embodiments, R^{109} is independently $-C(O)-OR^{109C}$. In embodiments, R^{109} is independently $-C(O)NR^{109A}R^{109B}$. In embodiments, R^{109} is independently $-OR^{109D}$. In embodiments, R^{109} is independently $-NR^{109A}SO_2R^{109D}$. In
 30 embodiments, R^{109} is independently $-NR^{109A}C(O)R^{109C}$. In embodiments, R^{109} is independently $-NR^{109A}C(O)OR^{109C}$. In embodiments, R^{109} is independently $-NR^{109A}OR^{109C}$. In embodiments, R^{109} is independently $-OH$. In embodiments, R^{109} is independently $-NH_2$. In embodiments, R^{109} is independently $-COOH$. In embodiments, R^{109} is

independently $-\text{CONH}_2$. In embodiments, R^{109} is independently $-\text{NO}_2$. In embodiments, R^{109} is independently $-\text{SH}$.

[0359] In embodiments, R^{109} is independently substituted or unsubstituted alkyl. In
embodiments, R^{109} is independently substituted or unsubstituted heteroalkyl. In
5 embodiments, R^{109} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 R^{109} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{109} is
independently substituted or unsubstituted aryl. In embodiments, R^{109} is independently
substituted or unsubstituted heteroaryl. In embodiments, R^{109} is independently substituted
alkyl. In embodiments, R^{109} is independently substituted heteroalkyl. In embodiments, R^{109}
10 is independently substituted cycloalkyl. In embodiments, R^{109} is independently, substituted
heterocycloalkyl. In embodiments, R^{109} is independently substituted aryl. In embodiments,
 R^{109} is independently substituted heteroaryl. In embodiments, R^{109} is independently
unsubstituted alkyl. In embodiments, R^{109} is independently unsubstituted heteroalkyl. In
embodiments, R^{109} is independently unsubstituted cycloalkyl. In embodiments, R^{109} is
15 independently, unsubstituted heterocycloalkyl. In embodiments, R^{109} is independently
unsubstituted aryl. In embodiments, R^{109} is independently unsubstituted heteroaryl. In
embodiments, R^{109} is independently substituted or unsubstituted $\text{C}_1\text{-C}_8$ alkyl. In
embodiments, R^{109} is independently substituted or unsubstituted 2 to 8 membered
heteroalkyl. In embodiments, R^{109} is independently substituted or unsubstituted $\text{C}_3\text{-C}_8$
20 cycloalkyl. In embodiments, R^{109} is independently, substituted or unsubstituted 3 to 8
membered heterocycloalkyl. In embodiments, R^{109} is independently substituted or
unsubstituted $\text{C}_6\text{-C}_{10}$ aryl. In embodiments, R^{109} is independently substituted or unsubstituted
5 to 10 membered heteroaryl. In embodiments, R^{109} is independently substituted $\text{C}_1\text{-C}_8$ alkyl.
In embodiments, R^{109} is independently substituted 2 to 8 membered heteroalkyl. In
25 embodiments, R^{109} is independently substituted $\text{C}_3\text{-C}_8$ cycloalkyl. In embodiments, R^{109} is
independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109} is
independently substituted $\text{C}_6\text{-C}_{10}$ aryl. In embodiments, R^{109} is independently substituted 5 to
10 membered heteroaryl. In embodiments, R^{109} is independently unsubstituted $\text{C}_1\text{-C}_8$ alkyl.
In embodiments, R^{109} is independently unsubstituted 2 to 8 membered heteroalkyl. In
30 embodiments, R^{109} is independently unsubstituted $\text{C}_3\text{-C}_8$ cycloalkyl. In embodiments, R^{109} is
independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109} is
independently unsubstituted $\text{C}_6\text{-C}_{10}$ aryl. In embodiments, R^{109} is independently
unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109} is independently
substituted or unsubstituted $\text{C}_1\text{-C}_4$ alkyl. In embodiments, R^{109} is independently substituted

or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109} is independently substituted or unsubstituted phenyl. In embodiments, R^{109} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{109} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{109} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{109} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109} is independently substituted phenyl. In embodiments, R^{109} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{109} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109} is independently unsubstituted phenyl. In embodiments, R^{109} is independently unsubstituted 5 to 6 membered heteroaryl.

[0360] In embodiments, R^{109A} is independently hydrogen. In embodiments, R^{109A} is independently $-CX^{109A}_3$. In embodiments, R^{109A} is independently $-CHX^{109A}_2$. In embodiments, R^{109A} is independently $-CH_2X^{109A}$. In embodiments, R^{109A} is independently $-CN$. In embodiments, R^{109A} is independently $-COOH$. In embodiments, R^{109A} is independently $-CONH_2$. In embodiments, R^{109A} is independently substituted or unsubstituted alkyl. In embodiments, R^{109A} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{109A} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{109A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{109A} is independently substituted or unsubstituted aryl. In embodiments, R^{109A} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{109A} is independently substituted alkyl. In embodiments, R^{109A} is independently substituted heteroalkyl. In embodiments, R^{109A} is independently substituted cycloalkyl. In embodiments, R^{109A} is independently, substituted heterocycloalkyl. In embodiments, R^{109A} is independently substituted aryl. In embodiments, R^{109A} is independently substituted heteroaryl. In embodiments, R^{109A} is independently unsubstituted alkyl. In embodiments, R^{109A} is independently unsubstituted heteroalkyl. In embodiments, R^{109A} is independently unsubstituted cycloalkyl. In embodiments, R^{109A} is independently, unsubstituted

heterocycloalkyl. In embodiments, R^{109A} is independently unsubstituted aryl. In
embodiments, R^{109A} is independently unsubstituted heteroaryl. In embodiments, R^{109A} is
independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{109A} is
independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments,
5 R^{109A} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109A}
is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In
embodiments, R^{109A} is independently substituted or unsubstituted C_6 - C_{10} aryl. In
embodiments, R^{109A} is independently substituted or unsubstituted 5 to 10 membered
heteroaryl. In embodiments, R^{109A} is independently substituted C_1 - C_8 alkyl. In
10 embodiments, R^{109A} is independently substituted 2 to 8 membered heteroalkyl. In
embodiments, R^{109A} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{109A} is
independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109A} is
independently substituted C_6 - C_{10} aryl. In embodiments, R^{109A} is independently substituted 5
to 10 membered heteroaryl. In embodiments, R^{109A} is independently unsubstituted C_1 - C_8
15 alkyl. In embodiments, R^{109A} is independently unsubstituted 2 to 8 membered heteroalkyl.
In embodiments, R^{109A} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments,
 R^{109A} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments,
 R^{109A} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{109A} is independently
unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109A} is independently
20 substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109A} is independently substituted
or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109A} is independently
substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109A} is independently,
substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109A} is
independently substituted or unsubstituted phenyl. In embodiments, R^{109A} is independently
25 substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109A} is
independently substituted C_1 - C_4 alkyl. In embodiments, R^{109A} is independently substituted 2
to 4 membered heteroalkyl. In embodiments, R^{109A} is independently substituted C_3 - C_6
cycloalkyl. In embodiments, R^{109A} is independently, substituted 3 to 6 membered
heterocycloalkyl. In embodiments, R^{109A} is independently substituted phenyl. In
30 embodiments, R^{109A} is independently substituted 5 to 6 membered heteroaryl. In
embodiments, R^{109A} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109A} is
independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109A} is
independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109A} is independently
unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109A} is independently
35 unsubstituted phenyl. In embodiments, R^{109A} is independently unsubstituted 5 to 6 membered

heteroaryl. In embodiments, R^{109A} is independently unsubstituted methyl. In embodiments, R^{109A} is independently unsubstituted ethyl. In embodiments, R^{109A} is independently unsubstituted propyl. In embodiments, R^{109A} is independently unsubstituted isopropyl. In embodiments, R^{109A} is independently unsubstituted tert-butyl.

- 5 **[0361]** In embodiments, R^{109B} is independently hydrogen. In embodiments, R^{109B} is independently $-CX^{109B}_3$. In embodiments, R^{109B} is independently $-CHX^{109B}_2$. In embodiments, R^{109B} is independently $-CH_2X^{109B}$. In embodiments, R^{109B} is independently $-CN$. In embodiments, R^{109B} is independently $-COOH$. In embodiments, R^{109B} is independently $-CONH_2$. In embodiments, R^{109B} is independently substituted or
- 10 unsubstituted alkyl. In embodiments, R^{109B} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{109B} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{109B} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{109B} is independently substituted or unsubstituted aryl. In embodiments, R^{109B} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{109B} is
- 15 independently substituted alkyl. In embodiments, R^{109B} is independently substituted heteroalkyl. In embodiments, R^{109B} is independently substituted cycloalkyl. In embodiments, R^{109B} is independently, substituted heterocycloalkyl. In embodiments, R^{109B} is independently substituted aryl. In embodiments, R^{109B} is independently substituted heteroaryl. In embodiments, R^{109B} is independently unsubstituted alkyl. In embodiments,
- 20 R^{109B} is independently unsubstituted heteroalkyl. In embodiments, R^{109B} is independently unsubstituted cycloalkyl. In embodiments, R^{109B} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{109B} is independently unsubstituted aryl. In embodiments, R^{109B} is independently unsubstituted heteroaryl. In embodiments, R^{109B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{109B} is
- 25 independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{109B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109B} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109B} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{109B} is independently substituted or unsubstituted 5 to 10 membered
- 30 heteroaryl. In embodiments, R^{109B} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{109B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{109B} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{109B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109B} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{109B} is independently substituted 5 to 10

membered heteroaryl. In embodiments, R^{109B} is independently unsubstituted C_1 - C_8 alkyl. In
 embodiments, R^{109B} is independently unsubstituted 2 to 8 membered heteroalkyl. In
 embodiments, R^{109B} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109B}
 is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109B} is
 5 independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{109B} is independently
 unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109B} is independently
 substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109B} is independently substituted
 or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109B} is independently
 substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109B} is independently,
 10 substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109B} is
 independently substituted or unsubstituted phenyl. In embodiments, R^{109B} is independently
 substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109B} is
 independently substituted C_1 - C_4 alkyl. In embodiments, R^{109B} is independently substituted 2
 to 4 membered heteroalkyl. In embodiments, R^{109B} is independently substituted C_3 - C_6
 15 cycloalkyl. In embodiments, R^{109B} is independently, substituted 3 to 6 membered
 heterocycloalkyl. In embodiments, R^{109B} is independently substituted phenyl. In
 embodiments, R^{109B} is independently substituted 5 to 6 membered heteroaryl. In
 embodiments, R^{109B} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109B} is
 independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109B} is
 20 independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109B} is independently
 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109B} is independently
 unsubstituted phenyl. In embodiments, R^{109B} is independently unsubstituted 5 to 6 membered
 heteroaryl. In embodiments, R^{109B} is independently unsubstituted methyl. In embodiments,
 R^{109B} is independently unsubstituted ethyl. In embodiments, R^{109B} is independently
 25 unsubstituted propyl. In embodiments, R^{109B} is independently unsubstituted isopropyl. In
 embodiments, R^{109B} is independently unsubstituted tert-butyl.

[0362] In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom
 may be joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments,
 R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a
 30 substituted or unsubstituted heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded
 to the same nitrogen atom may be joined to form a substituted heterocycloalkyl. In
 embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined
 to form a substituted heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the
 same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In

embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0363] In embodiments, R^{109C} is independently hydrogen. In embodiments, R^{109C} is independently $-CX^{109C}_3$. In embodiments, R^{109C} is independently $-CHX^{109C}_2$. In embodiments, R^{109C} is independently $-CH_2X^{109C}$. In embodiments, R^{109C} is independently $-CN$. In embodiments, R^{109C} is independently $-COOH$. In embodiments, R^{109C} is independently $-CONH_2$. In embodiments, R^{109C} is independently substituted or unsubstituted alkyl. In embodiments, R^{109C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{109C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{109C} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{109C} is independently substituted or unsubstituted aryl. In embodiments, R^{109C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{109C} is independently substituted alkyl. In embodiments, R^{109C} is independently substituted

heteroalkyl. In embodiments, R^{109C} is independently substituted cycloalkyl. In
embodiments, R^{109C} is independently, substituted heterocycloalkyl. In embodiments, R^{109C} is
independently substituted aryl. In embodiments, R^{109C} is independently substituted
heteroaryl. In embodiments, R^{109C} is independently unsubstituted alkyl. In embodiments,
5 R^{109C} is independently unsubstituted heteroalkyl. In embodiments, R^{109C} is independently
unsubstituted cycloalkyl. In embodiments, R^{109C} is independently, unsubstituted
heterocycloalkyl. In embodiments, R^{109C} is independently unsubstituted aryl. In
embodiments, R^{109C} is independently unsubstituted heteroaryl. In embodiments, R^{109C} is
independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{109C} is
10 independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments,
 R^{109C} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109C}
is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In
embodiments, R^{109C} is independently substituted or unsubstituted C_6 - C_{10} aryl. In
embodiments, R^{109C} is independently substituted or unsubstituted 5 to 10 membered
15 heteroaryl. In embodiments, R^{109C} is independently substituted C_1 - C_8 alkyl. In embodiments,
 R^{109C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{109C} is
independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{109C} is independently,
substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109C} is independently
substituted C_6 - C_{10} aryl. In embodiments, R^{109C} is independently substituted 5 to 10
20 membered heteroaryl. In embodiments, R^{109C} is independently unsubstituted C_1 - C_8 alkyl. In
embodiments, R^{109C} is independently unsubstituted 2 to 8 membered heteroalkyl. In
embodiments, R^{109C} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109C}
is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109C} is
independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{109C} is independently
25 unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109C} is independently
substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109C} is independently substituted
or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109C} is independently
substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109C} is independently,
substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109C} is
30 independently substituted or unsubstituted phenyl. In embodiments, R^{109C} is independently
substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109C} is
independently substituted C_1 - C_4 alkyl. In embodiments, R^{109C} is independently substituted 2
to 4 membered heteroalkyl. In embodiments, R^{109C} is independently substituted C_3 - C_6
cycloalkyl. In embodiments, R^{109C} is independently, substituted 3 to 6 membered
35 heterocycloalkyl. In embodiments, R^{109C} is independently substituted phenyl. In

embodiments, R^{109C} is independently substituted 5 to 6 membered heteroaryl. In
embodiments, R^{109C} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109C} is
independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109C} is
independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109C} is independently
5 unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109C} is independently
unsubstituted phenyl. In embodiments, R^{109C} is independently unsubstituted 5 to 6 membered
heteroaryl. In embodiments, R^{109C} is independently unsubstituted methyl. In embodiments,
 R^{109C} is independently unsubstituted ethyl. In embodiments, R^{109C} is independently
unsubstituted propyl. In embodiments, R^{109C} is independently unsubstituted isopropyl. In
10 embodiments, R^{109C} is independently unsubstituted tert-butyl.

[0364] In embodiments, R^{109D} is independently hydrogen. In embodiments, R^{109D} is
independently $-CX^{109D}_3$. In embodiments, R^{109D} is independently $-CHX^{109D}_2$. In
embodiments, R^{109D} is independently $-CH_2X^{109D}$. In embodiments, R^{109D} is
independently $-CN$. In embodiments, R^{109D} is independently $-COOH$. In embodiments,
15 R^{109D} is independently $-CONH_2$. In embodiments, R^{109D} is independently substituted or
unsubstituted alkyl. In embodiments, R^{109D} is independently substituted or unsubstituted
heteroalkyl. In embodiments, R^{109D} is independently substituted or unsubstituted cycloalkyl.
In embodiments, R^{109D} is independently, substituted or unsubstituted heterocycloalkyl. In
embodiments, R^{109D} is independently substituted or unsubstituted aryl. In embodiments,
20 R^{109D} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{109D} is
independently substituted alkyl. In embodiments, R^{109D} is independently substituted
heteroalkyl. In embodiments, R^{109D} is independently substituted cycloalkyl. In
embodiments, R^{109D} is independently, substituted heterocycloalkyl. In embodiments, R^{109D} is
independently substituted aryl. In embodiments, R^{109D} is independently substituted
25 heteroaryl. In embodiments, R^{109D} is independently unsubstituted alkyl. In embodiments,
 R^{109D} is independently unsubstituted heteroalkyl. In embodiments, R^{109D} is independently
unsubstituted cycloalkyl. In embodiments, R^{109D} is independently, unsubstituted
heterocycloalkyl. In embodiments, R^{109D} is independently unsubstituted aryl. In
embodiments, R^{109D} is independently unsubstituted heteroaryl. In embodiments, R^{109D} is
30 independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{109D} is
independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments,
 R^{109D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109D}
is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In
embodiments, R^{109D} is independently substituted or unsubstituted C_6 - C_{10} aryl. In

embodiments, R^{109D} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109D} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{109D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{109D} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{109D} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109D} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{109D} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{109D} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{109D} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{109D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{109D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{109D} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{109D} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{109D} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109D} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109D} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109D} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109D} is independently substituted or unsubstituted phenyl. In embodiments, R^{109D} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109D} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{109D} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{109D} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{109D} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109D} is independently substituted phenyl. In embodiments, R^{109D} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{109D} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{109D} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{109D} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{109D} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{109D} is independently unsubstituted phenyl. In embodiments, R^{109D} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{109D} is independently unsubstituted methyl. In embodiments, R^{109D} is independently unsubstituted ethyl. In embodiments, R^{109D} is independently unsubstituted propyl. In embodiments, R^{109D} is independently unsubstituted isopropyl. In embodiments, R^{109D} is independently unsubstituted tert-butyl.

[0365] In embodiments, R^{109} is independently hydrogen, halogen, $-CX^{109}_3$, $-CHX^{109}_2$, $-CH_2X^{109}$, $-OCX^{109}_3$, $-OCH_2X^{109}$, $-OCHX^{109}_2$, $-CN$, $-SO_{n109}R^{109D}$

, $-\text{SO}_{\nu 109}\text{NR}^{109\text{A}}\text{R}^{109\text{B}}$, $-\text{NHC}(\text{O})\text{NR}^{109\text{A}}\text{R}^{109\text{B}}$, $-\text{N}(\text{O})_{\text{m}109}$, $-\text{NR}^{109\text{A}}\text{R}^{109\text{B}}$, $-\text{C}(\text{O})\text{R}^{109\text{C}}$, $-\text{C}(\text{O})\text{OR}^{109\text{C}}$, $-\text{C}(\text{O})\text{NR}^{109\text{A}}\text{R}^{109\text{B}}$, $-\text{OR}^{109\text{D}}$, $-\text{NR}^{109\text{A}}\text{SO}_2\text{R}^{109\text{D}}$, $-\text{NR}^{109\text{A}}\text{C}(\text{O})\text{R}^{109\text{C}}$, $-\text{NR}^{109\text{A}}\text{C}(\text{O})\text{OR}^{109\text{C}}$, $-\text{NR}^{109\text{A}}\text{OR}^{109\text{C}}$, R^{110} -substituted or unsubstituted alkyl, R^{110} -substituted or unsubstituted heteroalkyl, R^{110} -substituted or unsubstituted cycloalkyl, R^{110} -substituted or unsubstituted heterocycloalkyl, R^{110} -substituted or unsubstituted aryl, or R^{110} -substituted or unsubstituted heteroaryl. In embodiments, R^{109} is independently halogen, $-\text{CX}^{109}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{109}_3$, $-\text{OCHX}^{109}_2$, R^{110} -substituted or unsubstituted alkyl, R^{110} -substituted or unsubstituted heteroalkyl, R^{110} -substituted or unsubstituted cycloalkyl, R^{110} -substituted or unsubstituted heterocycloalkyl, R^{110} -substituted or unsubstituted aryl, or R^{110} -substituted or unsubstituted heteroaryl. In embodiments, R^{109} is independently halogen, $-\text{CX}^{109}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{109}_3$, $-\text{OCHX}^{109}_2$, R^{110} -substituted or unsubstituted C_1 - C_8 alkyl, R^{110} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{110} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{110} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{110} -substituted or unsubstituted phenyl, or R^{110} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{109} is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$. In embodiments, R^{109} is independently hydrogen. In embodiments, R^{109} is independently methyl. In embodiments, R^{109} is independently ethyl.

[0366] In embodiments, R^{109} is independently halogen, $-\text{CX}^{109}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{OCX}^{109}_3$, $-\text{OCHX}^{109}_2$, R^{110} -substituted or unsubstituted C_1 - C_8 alkyl, R^{110} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{110} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{110} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{110} -substituted or unsubstituted phenyl, or R^{110} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0367] R^{110} is independently oxo, halogen, $-\text{CX}^{110}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{110}_3$, $-\text{OCHX}^{110}_2$, R^{111} -substituted or unsubstituted alkyl, R^{111} -substituted or unsubstituted heteroalkyl, R^{111} -substituted or unsubstituted cycloalkyl, R^{111} -substituted or unsubstituted heterocycloalkyl, R^{111} -substituted or unsubstituted aryl, or R^{111} -substituted or unsubstituted heteroaryl. In embodiments, R^{110} is independently oxo, halogen, $-\text{CX}^{110}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,

$-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCX}^{110}_3$, $-\text{OCHX}^{110}_2$, R^{111} -substituted or unsubstituted C_1 - C_8 alkyl, R^{111} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{111} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{111} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{111} -
5 substituted or unsubstituted phenyl, or R^{111} -substituted or unsubstituted 5 to 6 membered
heteroaryl. X^{110} is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0368] R^{111} is independently oxo,

halogen, $-\text{CX}^{111}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
10 $-\text{NHOH}$, $-\text{OCX}^{111}_3$, $-\text{OCHX}^{111}_2$, R^{112} -substituted or unsubstituted alkyl, R^{112} -substituted or
unsubstituted heteroalkyl, R^{112} -substituted or unsubstituted cycloalkyl, R^{112} -substituted or
unsubstituted heterocycloalkyl, R^{112} -substituted or unsubstituted aryl, or R^{112} -substituted or
unsubstituted heteroaryl. In embodiments, R^{111} is independently oxo,

halogen, $-\text{CX}^{111}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$,
15 $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$,
 $-\text{NHOH}$, $-\text{OCX}^{111}_3$, $-\text{OCHX}^{111}_2$, R^{112} -substituted or unsubstituted C_1 - C_8 alkyl, R^{112} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{112} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{112} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{112} -
substituted or unsubstituted phenyl, or R^{112} -substituted or unsubstituted 5 to 6 membered
20 heteroaryl. X^{111} is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0369] In embodiments, $\text{R}^{109\text{A}}$ is independently

hydrogen, $-\text{CX}^{109\text{A}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{109\text{A}}_2$, $-\text{CH}_2\text{X}^{109\text{A}}$, $\text{R}^{110\text{A}}$ -substituted or
unsubstituted alkyl, $\text{R}^{110\text{A}}$ -substituted or unsubstituted heteroalkyl, $\text{R}^{110\text{A}}$ -substituted or
unsubstituted cycloalkyl, $\text{R}^{110\text{A}}$ -substituted or unsubstituted heterocycloalkyl, $\text{R}^{110\text{A}}$ -

25 substituted or unsubstituted aryl, or $\text{R}^{110\text{A}}$ -substituted or unsubstituted heteroaryl. In
embodiments, $\text{R}^{109\text{A}}$ is independently

hydrogen, $-\text{CX}^{109\text{A}}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}^{109\text{A}}_2$, $-\text{CH}_2\text{X}^{109\text{A}}$, $\text{R}^{110\text{A}}$ -substituted or
unsubstituted C_1 - C_8 alkyl, $\text{R}^{110\text{A}}$ -substituted or unsubstituted 2 to 8 membered heteroalkyl,
 $\text{R}^{110\text{A}}$ -substituted or unsubstituted C_3 - C_8 cycloalkyl, $\text{R}^{110\text{A}}$ -substituted or unsubstituted 3 to 6
30 membered heterocycloalkyl, $\text{R}^{110\text{A}}$ -substituted or unsubstituted phenyl, or $\text{R}^{110\text{A}}$ -substituted or
unsubstituted 5 to 6 membered heteroaryl. $\text{X}^{109\text{A}}$ is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$. In embodiments,
 $\text{R}^{109\text{A}}$ is independently hydrogen. In embodiments, $\text{R}^{109\text{A}}$ is independently methyl. In
embodiments, $\text{R}^{109\text{A}}$ is independently ethyl.

[0370] In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{110A} -substituted or unsubstituted heterocycloalkyl or R^{110A} -substituted or unsubstituted heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{110A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{110A} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0371] R^{110A} is independently oxo, halogen, $-CX^{110A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{110A}_3$, $-OCHX^{110A}_2$, R^{111A} -substituted or unsubstituted alkyl, R^{111A} -substituted or unsubstituted heteroalkyl, R^{111A} -substituted or unsubstituted cycloalkyl, R^{111A} -substituted or unsubstituted heterocycloalkyl, R^{111A} -substituted or unsubstituted aryl, or R^{111A} -substituted or unsubstituted heteroaryl. In embodiments, R^{110A} is independently oxo, halogen, $-CX^{110A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{110A}_3$, $-OCHX^{110A}_2$, R^{111A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{111A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{111A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{111A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{111A} -substituted or unsubstituted phenyl, or R^{111A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{110A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0372] R^{111A} is independently oxo, halogen, $-CX^{111A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{111A}_3$, $-OCHX^{111A}_2$, R^{112A} -substituted or unsubstituted alkyl, R^{112A} -substituted or unsubstituted heteroalkyl, R^{112A} -substituted or unsubstituted cycloalkyl, R^{112A} -substituted or unsubstituted heterocycloalkyl, R^{112A} -substituted or unsubstituted aryl, or R^{112A} -substituted or unsubstituted heteroaryl. In embodiments, R^{111A} is independently oxo, halogen, $-CX^{111A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{111A}_3$, $-OCHX^{111A}_2$, R^{112A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{112A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{112A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{112A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{112A} -substituted or unsubstituted phenyl, or R^{112A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{111A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0373] In embodiments, R^{109B} is independently

hydrogen, $-CX^{109B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{109B}_2$, $-CH_2X^{109B}$, R^{110B} -substituted or unsubstituted alkyl, R^{110B} -substituted or unsubstituted heteroalkyl, R^{110B} -substituted or unsubstituted cycloalkyl, R^{110B} -substituted or unsubstituted heterocycloalkyl, R^{110B} -

5 substituted or unsubstituted aryl, or R^{110B} -substituted or unsubstituted heteroaryl. In embodiments, R^{109B} is independently

hydrogen, $-CX^{109B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{109B}_2$, $-CH_2X^{109B}$, R^{110B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{110B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{110B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{110B} -substituted or unsubstituted 3 to 6
10 membered heterocycloalkyl, R^{110B} -substituted or unsubstituted phenyl, or R^{110B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{109B} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{109B} is independently hydrogen. In embodiments, R^{109B} is independently methyl. In embodiments, R^{109B} is independently ethyl.

[0374] In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom

15 may optionally be joined to form a R^{110B} -substituted or unsubstituted heterocycloalkyl or R^{110B} -substituted or unsubstituted heteroaryl. In embodiments, R^{109A} and R^{109B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{110B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{110B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

20 [0375] R^{110B} is independently oxo,

halogen, $-CX^{110B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{110B}_3$, $-OCHX^{110B}_2$, R^{111B} -substituted or unsubstituted alkyl, R^{111B} -substituted or unsubstituted heteroalkyl, R^{111B} -substituted or unsubstituted cycloalkyl, R^{111B} -substituted or unsubstituted heterocycloalkyl, R^{111B} -substituted or unsubstituted aryl, or R^{111B} -substituted or unsubstituted heteroaryl. In embodiments, R^{110B} is independently oxo,
25 halogen, $-CX^{110B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{110B}_3$, $-OCHX^{110B}_2$, R^{111B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{111B} -

30 substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{111B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{111B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{111B} -substituted or unsubstituted phenyl, or R^{111B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{110B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0376] R^{111B} is independently oxo,

halogen, $-CX^{111B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{111B}_3$, $-OCHX^{111B}_2$, R^{112B} -substituted or unsubstituted alkyl, R^{112B} -substituted
5 or unsubstituted heteroalkyl, R^{112B} -substituted or unsubstituted cycloalkyl, R^{112B} -substituted
or unsubstituted heterocycloalkyl, R^{112B} -substituted or unsubstituted aryl, or R^{112B} -substituted
or unsubstituted heteroaryl. In embodiments, R^{111B} is independently oxo,
halogen, $-CX^{111B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
10 $-NHOH$, $-OCX^{111B}_3$, $-OCHX^{111B}_2$, R^{112B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{112B} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{112B} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{112B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{112B} -
substituted or unsubstituted phenyl, or R^{112B} -substituted or unsubstituted 5 to 6 membered
heteroaryl. X^{111B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0377] In embodiments, R^{109C} is independently

hydrogen, $-CX^{109C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{109C}_2$, $-CH_2X^{109C}$, R^{110C} -substituted or
unsubstituted alkyl, R^{110C} -substituted or unsubstituted heteroalkyl, R^{110C} -substituted or
unsubstituted cycloalkyl, R^{110C} -substituted or unsubstituted heterocycloalkyl, R^{110C} -
substituted or unsubstituted aryl, or R^{110C} -substituted or unsubstituted heteroaryl. In

embodiments, R^{109C} is independently

hydrogen, $-CX^{109C}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{109C}_2$, $-CH_2X^{109C}$, R^{110C} -substituted or
unsubstituted C_1 - C_8 alkyl, R^{110C} -substituted or unsubstituted 2 to 8 membered heteroalkyl,
 R^{110C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{110C} -substituted or unsubstituted 3 to 6
membered heterocycloalkyl, R^{110C} -substituted or unsubstituted phenyl, or R^{110C} -substituted or
25 unsubstituted 5 to 6 membered heteroaryl. X^{109C} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments,
 R^{109C} is independently hydrogen. In embodiments, R^{109C} is independently methyl. In
embodiments, R^{109C} is independently ethyl.

[0378] R^{110C} is independently oxo,

halogen, $-CX^{110C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
30 $-NHOH$, $-OCX^{110C}_3$, $-OCHX^{110C}_2$, R^{111C} -substituted or unsubstituted alkyl, R^{111C} -substituted
or unsubstituted heteroalkyl, R^{111C} -substituted or unsubstituted cycloalkyl, R^{111C} -substituted
or unsubstituted heterocycloalkyl, R^{111C} -substituted or unsubstituted aryl, or R^{111C} -substituted
or unsubstituted heteroaryl. In embodiments, R^{110C} is independently oxo,

halogen, $-CX^{110C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{110C}_3$, $-OCHX^{110C}_2$, R^{111C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{111C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{111C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{111C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{111C} -substituted or unsubstituted phenyl, or R^{111C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{110C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0379] R^{111C} is independently oxo,

halogen, $-CX^{111C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{111C}_3$, $-OCHX^{111C}_2$, R^{112C} -substituted or unsubstituted alkyl, R^{112C} -substituted or unsubstituted heteroalkyl, R^{112C} -substituted or unsubstituted cycloalkyl, R^{112C} -substituted or unsubstituted heterocycloalkyl, R^{112C} -substituted or unsubstituted aryl, or R^{112C} -substituted or unsubstituted heteroaryl. In embodiments, R^{111C} is independently oxo, halogen, $-CX^{111C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{111C}_3$, $-OCHX^{111C}_2$, R^{112C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{112C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{112C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{112C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{112C} -substituted or unsubstituted phenyl, or R^{112C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{111C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0380] In embodiments, R^{109D} is independently

hydrogen, $-CX^{109D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{109D}_2$, $-CH_2X^{109D}$, R^{110D} -substituted or unsubstituted alkyl, R^{110D} -substituted or unsubstituted heteroalkyl, R^{110D} -substituted or unsubstituted cycloalkyl, R^{110D} -substituted or unsubstituted heterocycloalkyl, R^{110D} -substituted or unsubstituted aryl, or R^{110D} -substituted or unsubstituted heteroaryl. In embodiments, R^{109D} is independently hydrogen, $-CX^{109D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{109D}_2$, $-CH_2X^{109D}$, R^{110D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{110D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{110D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{110D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{110D} -substituted or unsubstituted phenyl, or R^{110D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{109D} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{109D} is independently hydrogen. In embodiments, R^{109D} is independently methyl. In embodiments, R^{109D} is independently ethyl.

[0381] R^{110D} is independently oxo,

halogen, $-CX^{110D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{110D}_3$, $-OCHX^{110D}_2$, R^{111D} -substituted or unsubstituted alkyl, R^{111D} -substituted
5 or unsubstituted heteroalkyl, R^{111D} -substituted or unsubstituted cycloalkyl, R^{111D} -substituted
or unsubstituted heterocycloalkyl, R^{111D} -substituted or unsubstituted aryl, or R^{111D} -substituted
or unsubstituted heteroaryl. In embodiments, R^{110D} is independently oxo,
halogen, $-CX^{110D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
10 $-NHOH$, $-OCX^{110D}_3$, $-OCHX^{110D}_2$, R^{111D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{111D} -
substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{111D} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{111D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl,
 R^{111D} -substituted or unsubstituted phenyl, or R^{111D} -substituted or unsubstituted 5 to 6
membered heteroaryl. X^{110D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0382] R^{111D} is independently oxo,

halogen, $-CX^{111D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{111D}_3$, $-OCHX^{111D}_2$, R^{112D} -substituted or unsubstituted alkyl, R^{112D} -substituted
or unsubstituted heteroalkyl, R^{112D} -substituted or unsubstituted cycloalkyl, R^{112D} -substituted
20 or unsubstituted heterocycloalkyl, R^{112D} -substituted or unsubstituted aryl, or R^{112D} -substituted
or unsubstituted heteroaryl. In embodiments, R^{111D} is independently oxo,
halogen, $-CX^{111D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,
 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,
 $-NHOH$, $-OCX^{111D}_3$, $-OCHX^{111D}_2$, R^{112D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{112D} -
25 substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{112D} -substituted or unsubstituted
 C_3 - C_8 cycloalkyl, R^{112D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl,
 R^{112D} -substituted or unsubstituted phenyl, or R^{112D} -substituted or unsubstituted 5 to 6
membered heteroaryl. X^{111D} is $-F$, $-Cl$, $-Br$, or $-I$.

[0383] R^{112} , R^{112A} , R^{112B} , R^{112C} , and R^{112D} are independently hydrogen, oxo,

30 halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$
 O_4H , $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,
 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$,
 $-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$

2, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{112} , R^{112A} , R^{112B} , R^{112C} , and R^{112D} are independently oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{112} , R^{112A} , R^{112B} , R^{112C} , and R^{112D} are independently oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered heteroalkyl, unsubstituted C_3 - C_8 cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0384] In embodiments, L^2 is $-NR^7-$ or substituted or unsubstituted heterocycloalkylene including a ring nitrogen bonded directly to E. In embodiments, L^2 is $-NR^7-$. In embodiments, L^2 is substituted or unsubstituted heterocycloalkylene. In embodiments, L^2 is substituted or unsubstituted piperidinylenes or substituted or unsubstituted pyrrolindinylenes. In embodiments, L^2 is unsubstituted piperidinylenes or unsubstituted pyrrolindinylenes.

[0385] In embodiments, L^2 is a bond. In embodiments, L^2 is $-S(O)_2-$. In embodiments, L^2 is $-S(O)_2-Ph-$. In embodiments, L^2 is $-NR^7-$. In embodiments, L^2 is $-O-$. In embodiments, L^2 is $-S-$. In embodiments, L^2 is $-C(O)-$. In embodiments, L^2 is $-C(O)NR^7-$. In embodiments, L^2 is $-NR^7C(O)-$. In embodiments, L^2 is $-NR^7C(O)NH-$. In embodiments, L^2 is $-NHC(O)NR^7-$. In embodiments, L^2 is $-C(O)O-$. In embodiments, L^2 is $-OC(O)-$. In embodiments, L^2 is $-NH-$. In embodiments, L^2 is $-C(O)NH-$. In embodiments, L^2 is $-NHC(O)-$. In embodiments, L^2 is $-NHC(O)NH-$. In embodiments, L^2 is $-CH_2-$. In embodiments, L^2 is $-OCH_2-$. In embodiments, L^2 is $-CH_2O-$. In embodiments, L^2 is $-CH_2CH_2-$. In embodiments, L^2 is $-SCH_2-$. In embodiments, L^2 is $-CH_2S-$. In embodiments, L^2 is $-CHCH-$. In embodiments, L^2 is $-CC-$. In embodiments, L^2 is $-NHCH_2-$. In embodiments, L^2 is $-CH_2NH-$.

[0386] In embodiments, L^2 is a substituted or unsubstituted alkylene. In embodiments, L^2 is a substituted or unsubstituted heteroalkylene. In embodiments, L^2 is a substituted or unsubstituted cycloalkylene. In embodiments, L^2 is a substituted or unsubstituted heterocycloalkylene. In embodiments, L^2 is a substituted or unsubstituted arylene. In embodiments, L^2 is a substituted or unsubstituted heteroarylene. In embodiments, L^2 is a

substituted alkylene. In embodiments, L^2 is a substituted heteroalkylene. In embodiments, L^2 is a substituted cycloalkylene. In embodiments, L^2 is a substituted heterocycloalkylene. In embodiments, L^2 is a substituted arylene. In embodiments, L^2 is a substituted heteroarylene. In embodiments, L^2 is an unsubstituted alkylene. In embodiments, L^2 is an unsubstituted heteroalkylene. In embodiments, L^2 is an unsubstituted cycloalkylene. In embodiments, L^2 is an unsubstituted heterocycloalkylene. In embodiments, L^2 is an unsubstituted arylene. In embodiments, L^2 is an unsubstituted heteroarylene. In embodiments, L^2 is a substituted or unsubstituted C_1 - C_8 alkylene. In embodiments, L^2 is a substituted or unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^2 is a substituted or unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^2 is a substituted or unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments, L^2 is a substituted or unsubstituted C_6 - C_{10} arylene. In embodiments, L^2 is a substituted or unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^2 is a substituted C_1 - C_8 alkylene. In embodiments, L^2 is a substituted 2 to 8 membered heteroalkylene. In embodiments, L^2 is a substituted C_3 - C_8 cycloalkylene. In embodiments, L^2 is a substituted 3 to 8 membered heterocycloalkylene. In embodiments, L^2 is a substituted C_6 - C_{10} arylene. In embodiments, L^2 is a substituted 5 to 10 membered heteroarylene. In embodiments, L^2 is an unsubstituted C_1 - C_8 alkylene. In embodiments, L^2 is an unsubstituted 2 to 8 membered heteroalkylene. In embodiments, L^2 is an unsubstituted C_3 - C_8 cycloalkylene. In embodiments, L^2 is an unsubstituted 3 to 8 membered heterocycloalkylene. In embodiments, L^2 is an unsubstituted C_6 - C_{10} arylene. In embodiments, L^2 is an unsubstituted 5 to 10 membered heteroarylene. In embodiments, L^2 is a substituted or unsubstituted C_1 - C_4 alkylene. In embodiments, L^2 is a substituted or unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^2 is a substituted or unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^2 is a substituted or unsubstituted 3 to 6 membered heterocycloalkylene. In embodiments, L^2 is a substituted or unsubstituted phenylene. In embodiments, L^2 is a substituted or unsubstituted 5 to 6 membered heteroarylene. In embodiments, L^2 is a substituted C_1 - C_4 alkylene. In embodiments, L^2 is a substituted 2 to 4 membered heteroalkylene. In embodiments, L^2 is a substituted C_3 - C_6 cycloalkylene. In embodiments, L^2 is a substituted 3 to 6 membered heterocycloalkylene. In embodiments, L^2 is a substituted phenylene. In embodiments, L^2 is a substituted 5 to 6 membered heteroarylene. In embodiments, L^2 is an unsubstituted C_1 - C_4 alkylene. In embodiments, L^2 is an unsubstituted 2 to 4 membered heteroalkylene. In embodiments, L^2 is an unsubstituted C_3 - C_6 cycloalkylene. In embodiments, L^2 is an unsubstituted 3 to 6 membered heterocycloalkylene. In embodiments, L^2 is an unsubstituted phenylene. In embodiments, L^2 is an unsubstituted 5 to 6 membered heteroarylene.

[0387] In embodiments, L^2 is a

bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^7-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^7-$, $-NR^7C(O)-$, $-NR^7C(O)NH-$, $-NHC(O)NR^7-$, $-C(O)O-$, $-OC(O)-$, R^{44} -substituted or unsubstituted alkylene, R^{44} -substituted or unsubstituted heteroalkylene, R^{44} -substituted or unsubstituted cycloalkylene, R^{44} -

5 substituted or unsubstituted heterocycloalkylene, R^{44} -substituted or unsubstituted arylene, or R^{44} -substituted or unsubstituted heteroarylene. In embodiments, L^2 is a

bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NH-$, $-O-$, $-S-$,

$-C(O)-$, $-C(O)NH-$, $-NHC(O)-$, $-NHC(O)NH-$, $-C(O)O-$, $-OC(O)-$, R^{44} -substituted or

unsubstituted alkylene, R^{44} -substituted or unsubstituted heteroalkylene, R^{44} -substituted or

10 unsubstituted cycloalkylene, R^{44} -substituted or unsubstituted heterocycloalkylene, R^{44} -

substituted or unsubstituted arylene, or R^{44} -substituted or unsubstituted heteroarylene. In

embodiments, L^2 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NH-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NH-$,

$-NHC(O)-$, $-NHC(O)NH-$, $-C(O)O-$, $-OC(O)-$, R^{44} -substituted or unsubstituted C_1-C_8

alkylene, R^{44} -substituted or unsubstituted 2 to 8 membered heteroalkylene, R^{44} -substituted or

15 unsubstituted C_3-C_8 cycloalkylene, R^{44} -substituted or unsubstituted 3 to 6 membered

heterocycloalkylene, R^{44} -substituted or unsubstituted phenylene, or R^{44} -substituted or

unsubstituted 5 to 6 membered heteroarylene.

[0388] R^{44} is independently oxo, halogen, $-CX^{44}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$,

$-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

20 $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{44}_3$, $-OCHX^{44}_2$, R^{45} -

substituted or unsubstituted alkyl, R^{45} -substituted or unsubstituted heteroalkyl, R^{45} -

substituted or unsubstituted cycloalkyl, R^{45} -substituted or unsubstituted heterocycloalkyl,

R^{45} -substituted or unsubstituted aryl, or R^{45} -substituted or unsubstituted heteroaryl. In

embodiments, R^{44} is independently oxo,

25 halogen, $-CX^{44}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

$-NHOH$, $-OCX^{44}_3$, $-OCHX^{44}_2$, R^{45} -substituted or unsubstituted C_1-C_8 alkyl, R^{45} -substituted or

unsubstituted 2 to 8 membered heteroalkyl, R^{45} -substituted or unsubstituted C_3-C_8 cycloalkyl,

R^{45} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{45} -substituted or

30 unsubstituted phenyl, or R^{45} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{44} is

$-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{44} is $-CH_3$. In embodiments, R^{44} is $-F$.

[0389] R^{45} is independently oxo,

halogen, $-CX^{45}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

$-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

-NHOH, $-\text{OCX}^{45}_3$, $-\text{OCHX}^{45}_2$, R^{46} -substituted or unsubstituted alkyl, R^{46} -substituted or unsubstituted heteroalkyl, R^{46} -substituted or unsubstituted cycloalkyl, R^{46} -substituted or unsubstituted heterocycloalkyl, R^{46} -substituted or unsubstituted aryl, or R^{46} -substituted or unsubstituted heteroaryl. In embodiments, R^{45} is independently oxo,

- 5 halogen, $-\text{CX}^{45}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCX}^{45}_3$, $-\text{OCHX}^{45}_2$, R^{46} -substituted or unsubstituted C_1 - C_8 alkyl, R^{46} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{46} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{46} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{46} -substituted or unsubstituted phenyl, or R^{46} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{45} is $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$.

[0390] R^{46} is independently hydrogen, oxo,

halogen, $-\text{CCl}_3$, $-\text{CBr}_3$, $-\text{CF}_3$, $-\text{Cl}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$,

- 15 $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCCl}_3$, $-\text{OCF}_3$, $-\text{OCBr}_3$, $-\text{OCl}_3$, $-\text{OCHCl}_2$, $-\text{OCHBr}_2$, $-\text{OCHI}_2$, $-\text{OCHF}_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{46} is independently oxo,

- 20 halogen, $-\text{CF}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCF}_3$, $-\text{OCHF}_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{46} is independently oxo,

- 25 halogen, $-\text{CF}_3$, $-\text{CN}$, $-\text{OH}$, $-\text{NH}_2$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{NO}_2$, $-\text{SH}$, $-\text{SO}_3\text{H}$, $-\text{SO}_4\text{H}$, $-\text{SO}_2\text{NH}_2$, $-\text{NHNH}_2$, $-\text{ONH}_2$, $-\text{NHC}(\text{O})\text{NHNH}_2$, $-\text{NHC}(\text{O})\text{NH}_2$, $-\text{NHSO}_2\text{H}$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{OH}$, $-\text{NHOH}$, $-\text{OCF}_3$, $-\text{OCHF}_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered heteroalkyl, unsubstituted C_3 - C_8 cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

- 30 **[0391]** In embodiments, L^2 is R^{44} -substituted or unsubstituted 4 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted 5 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted 6 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted 7 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted

heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L^2 is R^{44} -substituted 4 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted 5 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted 6 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted 7 membered heterocycloalkylene. In embodiments, L^2 is R^{44} -substituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments, L^2 is unsubstituted 4 membered heterocycloalkylene. In embodiments, L^2 is unsubstituted 5 membered heterocycloalkylene. In embodiments, L^2 is unsubstituted 6 membered heterocycloalkylene. In embodiments, L^2 is unsubstituted 7 membered heterocycloalkylene. In embodiments, L^2 is unsubstituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6 membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene).

[0392] In embodiments, L^2 is R^{44} -substituted or unsubstituted piperidinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted pyrrolidinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted imidazolidinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted pyrazolidinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted piperazinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted piperazinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted azetidinylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted aziridinylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted morpholinylene.

[0393] In embodiments, L^2 is R^{44} -substituted piperidinylene. In embodiments, L^2 is R^{44} -substituted R^{44} -substituted pyrrolidinylene. In embodiments, L^2 is R^{44} -substituted imidazolidinylene. In embodiments, L^2 is R^{44} -substituted pyrazolidinylene. In embodiments, L^2 is R^{44} -substituted piperazinylene. In embodiments, L^2 is R^{44} -substituted azetidinylen. In embodiments, L^2 is R^{44} -substituted aziridinylene. In embodiments, L^2 is R^{44} -substituted morpholinylene.

[0394] In embodiments, L^2 is methyl-substituted piperidinylene. In embodiments, L^2 is methyl-substituted methyl-substituted pyrrolidinylene. In embodiments, L^2 is methyl-substituted imidazolidinylene. In embodiments, L^2 is methyl-substituted pyrazolidinylene. In embodiments, L^2 is methyl-substituted piperazinylene. In embodiments, L^2 is methyl-substituted azetidinylen. In embodiments, L^2 is methyl-substituted aziridinylene. In embodiments, L^2 is methyl-substituted morpholinylene.

[0395] In embodiments, L^2 is unsubstituted 5 membered heterocycloalkylene. In
embodiments, L^2 unsubstituted 6 membered heterocycloalkylene. In embodiments, L^2 is
unsubstituted heterocycloalkylene (e.g., 3 to 6 membered heterocycloalkylene, 4 to 6
membered heterocycloalkylene, or 5 to 6 membered heterocycloalkylene). In embodiments,
5 L^2 is unsubstituted piperidinylen. In embodiments, L^2 is unsubstituted pyrrolidinylen. In
embodiments, L^2 is unsubstituted imidazolidinylen. In embodiments, L^2 is unsubstituted
pyrazolidinylen. In embodiments, L^2 is unsubstituted piperazinylen. In embodiments, L^2 is
unsubstituted azetidinylen. In embodiments, L^2 is unsubstituted aziridinylen. In
embodiments, L^2 is unsubstituted morpholinylen.

10 **[0396]** In embodiments, L^2 is a R^{44} -substituted or unsubstituted 5 to 10 membered
heteroarylen. In embodiments, L^2 is a R^{44} -substituted or unsubstituted 5 to 6 membered
heteroarylen. In embodiments, L^2 is a R^{44} -substituted or unsubstituted pyridinylen,
pyridazinylen, pyrimidinylen, pyrazinylen, or triazinylen.

[0397] In embodiments, L^2 is a R^{44} -substituted 5 to 10 membered heteroarylen. In
15 embodiments, L^2 is a R^{44} -substituted 5 to 6 membered heteroarylen. In embodiments, L^2 is
a R^{44} -substituted pyridinylen, pyridazinylen, pyrimidinylen, pyrazinylen, or triazinylen.
In embodiments, L^2 is unsubstituted 5 to 10 membered heteroarylen. In embodiments, L^2 is
unsubstituted 5 to 6 membered heteroarylen. In embodiments, L^2 is unsubstituted
pyridinylen, pyridazinylen, pyrimidinylen, pyrazinylen, or triazinylen. In embodiments,
20 L^2 is R^{44} -substituted or unsubstituted indolinylen. In embodiments, L^2 is R^{44} -substituted or
unsubstituted indazolylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted
benzimidazolylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted benzoxazolylen.
In embodiments, L^2 is R^{44} -substituted or unsubstituted azaindolylen. In embodiments, L^2 is
 R^{44} -substituted or unsubstituted purinylen. In embodiments, L^2 is R^{44} -substituted or
25 unsubstituted indolylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted
pyrazinylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted pyrrolylen. In
embodiments, L^2 is R^{44} -substituted or unsubstituted imidazolylen. In embodiments, L^2 is
 R^{44} -substituted or unsubstituted pyrazolylen. In embodiments, L^2 is R^{44} -substituted or
unsubstituted triazolylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted
30 tetrazolylen. In embodiments, L^2 is R^{44} -substituted or unsubstituted azepanylen. In
embodiments, L^2 is R^{44} -substituted or unsubstituted azepinylen.

[0398] In embodiments, L^2 is R^{44} -substituted indolinylen. In embodiments, L^2 is R^{44} -
substituted indazolylen. In embodiments, L^2 is R^{44} -substituted benzimidazolylen. In

embodiments, L^2 is R^{44} -substituted benzoxazolylenes. In embodiments, L^2 is R^{44} -substituted azaindolylenes. In embodiments, L^2 is R^{44} -substituted purinylenes. In embodiments, L^2 is R^{44} -substituted indolylenes. In embodiments, L^2 is R^{44} -substituted pyrazinylenes. In embodiments, L^2 is R^{44} -substituted pyrrolylenes. In embodiments, L^2 is R^{44} -substituted imidazolylenes. In
 5 embodiments, L^2 is R^{44} -substituted pyrazolylenes. In embodiments, L^2 is R^{44} -substituted triazolylenes. In embodiments, L^2 is R^{44} -substituted tetrazolylenes. In embodiments, L^2 is R^{44} -substituted azepanylenes. In embodiments, L^2 is R^{44} -substituted azepinylenes.

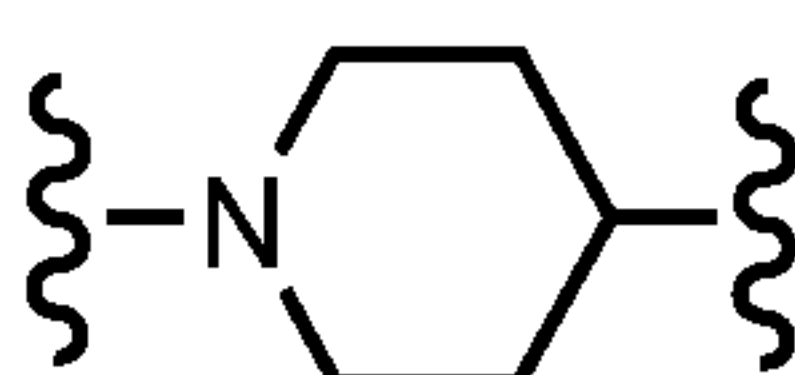
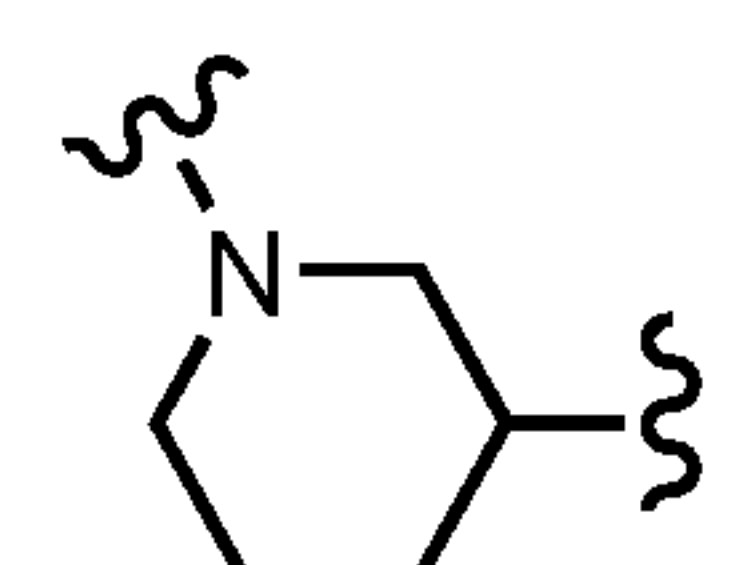
[0399] In embodiments, L^2 is unsubstituted indolinylenes. In embodiments, L^2 is unsubstituted indazolylenes. In embodiments, L^2 is unsubstituted benzimidazolylenes. In
 10 embodiments, L^2 is unsubstituted benzoxazolylenes. In embodiments, L^2 is unsubstituted azaindolylenes. In embodiments, L^2 is unsubstituted purinylenes. In embodiments, L^2 is unsubstituted indolylenes. In embodiments, L^2 is unsubstituted pyrazinylenes. In
 embodiments, L^2 is unsubstituted pyrrolylenes. In embodiments, L^2 is unsubstituted imidazolylenes. In embodiments, L^2 is unsubstituted pyrazolylenes. In embodiments, L^2 is
 15 unsubstituted triazolylenes. In embodiments, L^2 is unsubstituted tetrazolylenes. In
 embodiments, L^2 is unsubstituted azepanylenes. In embodiments, L^2 is unsubstituted azepinylenes.

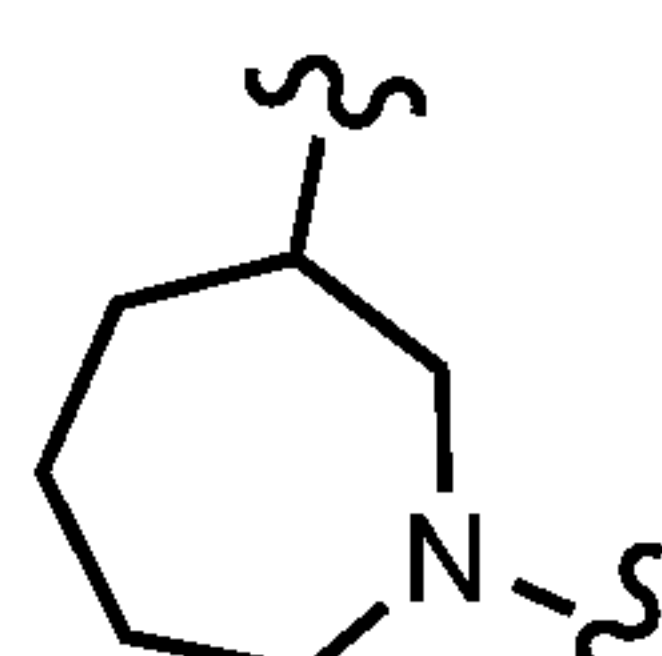
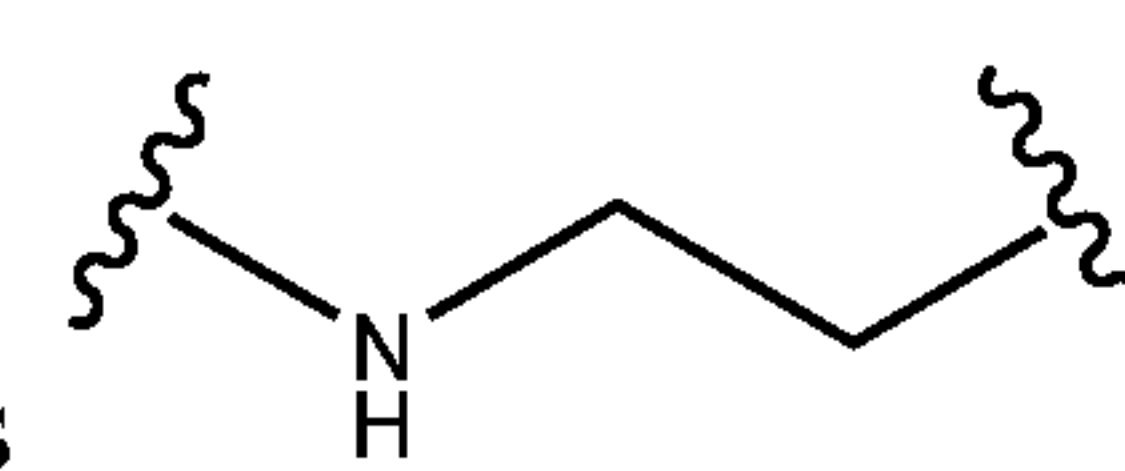
[0400] In embodiments, L^2 is R^{44} -substituted or unsubstituted C_3 - C_8 cycloalkylenes. In
 embodiments, L^2 is R^{44} -substituted or unsubstituted C_4 - C_6 cycloalkylenes. In embodiments,
 20 L^2 is R^{44} -substituted or unsubstituted C_5 - C_6 cycloalkylenes. In embodiments, L^2 is R^{44} -substituted or unsubstituted cycloalkylenes (e.g., C_3 - C_8 cycloalkylenes, C_4 - C_6 cycloalkylenes, or
 C_5 - C_6 cycloalkylenes). In embodiments, L^2 is R^{44} -substituted C_3 - C_8 cycloalkylenes. In
 embodiments, L^2 is R^{44} -substituted C_4 - C_6 cycloalkylenes. In embodiments, L^2 is R^{44} -substituted C_5 - C_6 cycloalkylenes. In embodiments, L^2 is R^{44} -substituted cycloalkylenes (e.g.,
 25 C_3 - C_8 cycloalkylenes, C_4 - C_6 cycloalkylenes, or C_5 - C_6 cycloalkylenes). In embodiments, L^2 is
 unsubstituted C_3 - C_8 cycloalkylenes. In embodiments, L^2 is unsubstituted C_4 - C_6 cycloalkylenes.
 In embodiments, L^2 is unsubstituted C_5 - C_6 cycloalkylenes. In embodiments, L^2 is
 unsubstituted cycloalkylenes (e.g., C_3 - C_8 cycloalkylenes, C_4 - C_6 cycloalkylenes, or C_5 - C_6
 cycloalkylenes).

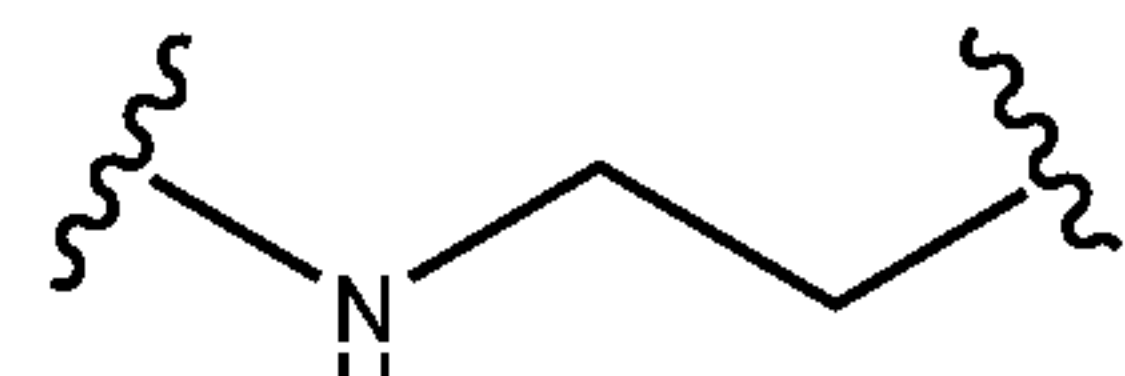
[0401] In embodiments, L^2 is R^{44} -substituted or unsubstituted alkylens (e.g., C_1 - C_8
 30 alkylens, C_1 - C_6 alkylens, C_1 - C_4 alkylens, C_1 - C_2 alkylens). In embodiments, L^2 is R^{44} -substituted or unsubstituted C_1 - C_8 alkylens. In embodiments, L^2 is R^{44} -substituted or
 unsubstituted C_1 - C_6 alkylens. In embodiments, L^2 is R^{44} -substituted or unsubstituted C_1 - C_4

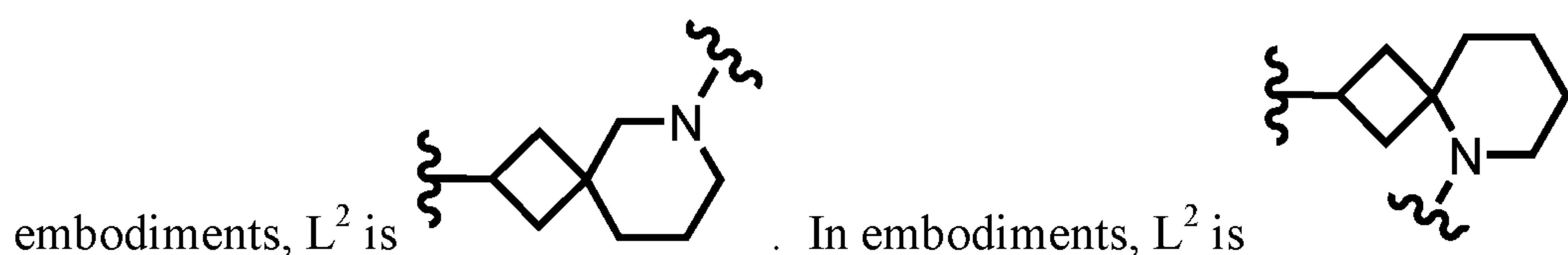
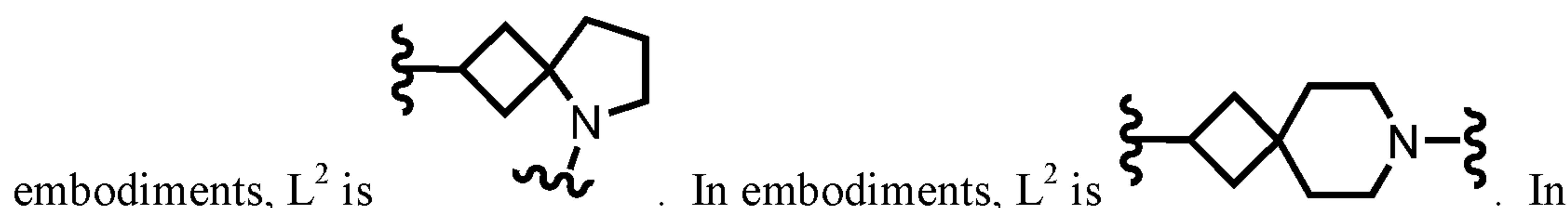
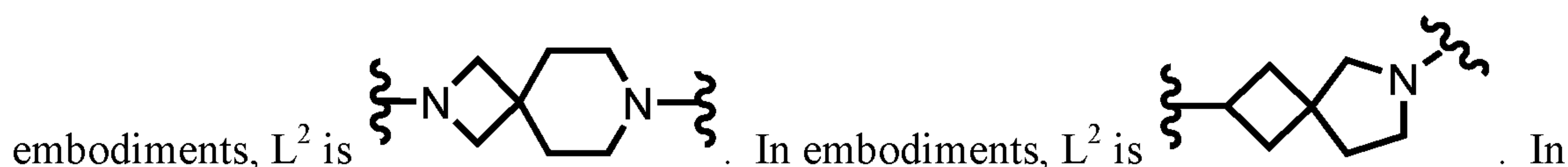
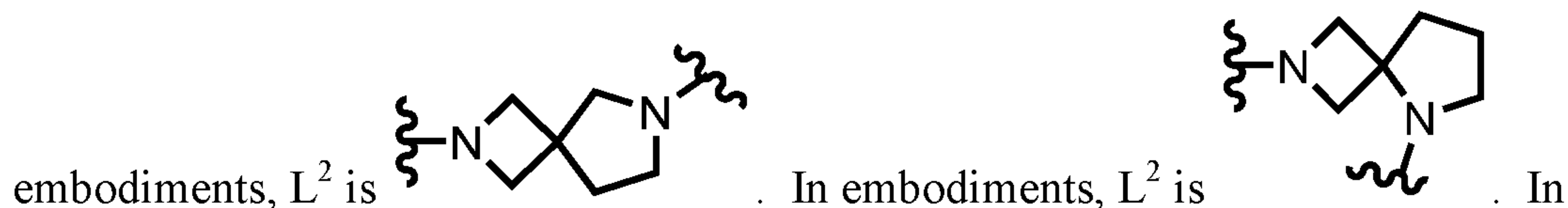
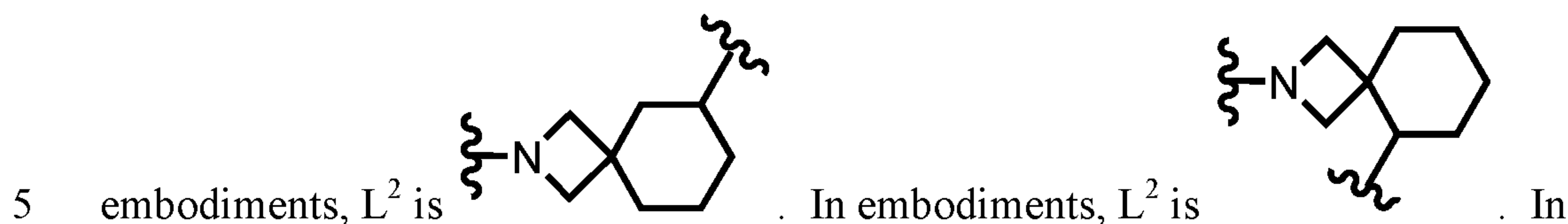
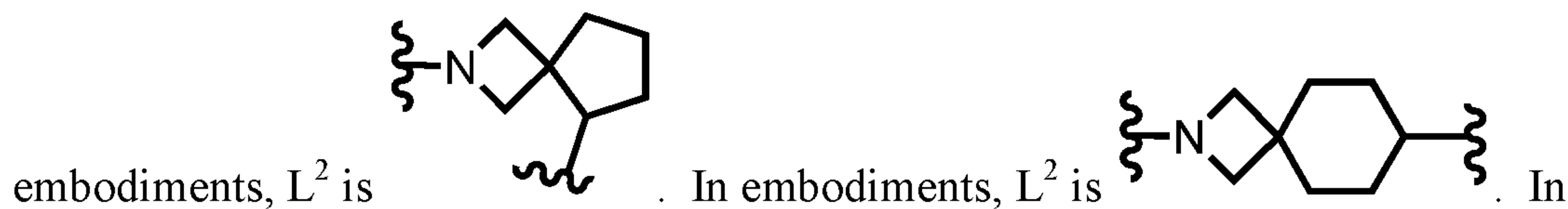
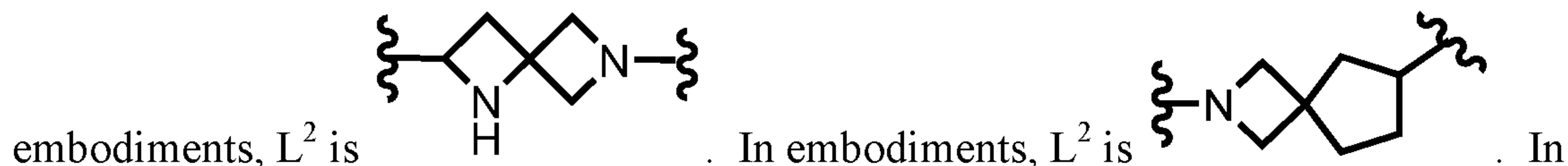
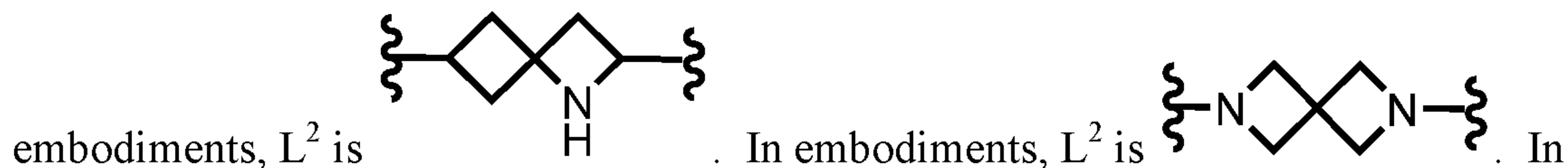
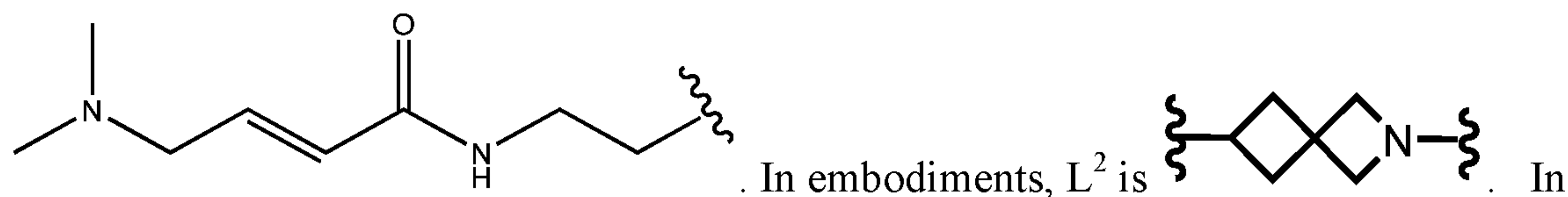
alkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted C_1 - C_2 alkylene. In
embodiments, L^2 is R^{44} -substituted alkylene (e.g., C_1 - C_8 alkylene, C_1 - C_6 alkylene, C_1 - C_4
alkylene, C_1 - C_2 alkylene). In embodiments, L^2 is R^{44} -substituted C_1 - C_8 alkylene. In
embodiments, L^2 is R^{44} -substituted C_1 - C_6 alkylene. In embodiments, L^2 is R^{44} -substituted C_1 -
5 C_4 alkylene. In embodiments, L^2 is R^{44} -substituted C_1 - C_2 alkylene. In embodiments, L^2 is
unsubstituted alkylene (e.g., C_1 - C_8 alkylene, C_1 - C_6 alkylene, C_1 - C_4 alkylene, C_1 - C_2 alkylene).
In embodiments, L^2 is unsubstituted C_1 - C_8 alkylene. In embodiments, L^2 is unsubstituted C_1 -
 C_6 alkylene. In embodiments, L^2 is unsubstituted C_1 - C_4 alkylene. In embodiments, L^2 is
unsubstituted C_1 - C_2 alkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted
10 methylene. In embodiments, L^2 is unsubstituted methylene.

[0402] In embodiments, L^2 is R^{44} -substituted or unsubstituted heteroalkylene (e.g., 2 to 8
membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered
heteroalkylene). In embodiments, L^2 is R^{44} -substituted or unsubstituted 2 to 8 membered
heteroalkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted 2 to 6 membered
15 heteroalkylene. In embodiments, L^2 is R^{44} -substituted or unsubstituted 2 to 4 membered
heteroalkylene. In embodiments, L^2 is R^{44} -substituted heteroalkylene (e.g., 2 to 8 membered
heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered heteroalkylene). In
embodiments, L^2 is R^{44} -substituted 2 to 8 membered heteroalkylene. In embodiments, L^2 is
 R^{44} -substituted 2 to 6 membered heteroalkylene. In embodiments, L^2 is R^{44} -substituted 2 to 4
20 membered heteroalkylene. In embodiments, L^2 is unsubstituted heteroalkylene (e.g., 2 to 8
membered heteroalkylene, 2 to 6 membered heteroalkylene, 2 to 4 membered
heteroalkylene). In embodiments, L^2 is unsubstituted 2 to 8 membered heteroalkylene. In
embodiments, L^2 is unsubstituted 2 to 6 membered heteroalkylene. In embodiments, L^2 is
unsubstituted 2 to 4 membered heteroalkylene.

25 **[0403]** In embodiments, L^2 is . In embodiments, L^2 is . In

embodiments, L^2 is . In embodiments, L^1 is . In

embodiments, L^2 is . In embodiments, L^2 -E is



- 10 **[0404]** In embodiments, R^7 is hydrogen, substituted or unsubstituted C_1 - C_6 alkyl, or substituted or unsubstituted 2 to 6 membered heteroalkyl. In embodiments, R^7 is hydrogen or unsubstituted C_1 - C_3 alkyl. In embodiments, R^7 is hydrogen.

- 15 **[0405]** In embodiments, R^7 is independently hydrogen. In embodiments, R^7 is independently halogen. In embodiments, R^7 is independently $-CX^7_3$. In embodiments, R^7 is independently $-CHX^7_2$. In embodiments, R^7 is independently $-CH_2X^7$. In embodiments, R^7 is independently $-OCX^7_3$. In embodiments, R^7 is independently $-OCH_2X^7$. In embodiments, R^7 is independently $-OCHX^7_2$. In embodiments, R^7 is independently $-CN$. In embodiments, R^7

is independently $-\text{SO}_{n7}\text{R}^{7\text{D}}$. In embodiments, R^7 is independently $-\text{SO}_{v7}\text{NR}^{7\text{A}}\text{R}^{7\text{B}}$. In
embodiments, R^7 is independently $-\text{NHC}(\text{O})\text{NR}^{7\text{A}}\text{R}^{7\text{B}}$. In embodiments, R^7 is
independently $-\text{N}(\text{O})_{m7}$. In embodiments, R^7 is independently $-\text{NR}^{7\text{A}}\text{R}^{7\text{B}}$. In embodiments,
 R^7 is independently $-\text{C}(\text{O})\text{R}^{7\text{C}}$. In embodiments, R^7 is independently $-\text{C}(\text{O})-\text{OR}^{7\text{C}}$. In
5 embodiments, R^7 is independently $-\text{C}(\text{O})\text{NR}^{7\text{A}}\text{R}^{7\text{B}}$. In embodiments, R^7 is
independently $-\text{OR}^{7\text{D}}$. In embodiments, R^7 is independently $-\text{NR}^{7\text{A}}\text{SO}_2\text{R}^{7\text{D}}$. In embodiments,
 R^7 is independently $-\text{NR}^{7\text{A}}\text{C}(\text{O})\text{R}^{7\text{C}}$. In embodiments, R^7 is independently $-\text{NR}^{7\text{A}}\text{C}(\text{O})\text{OR}^{7\text{C}}$.
In embodiments, R^7 is independently $-\text{NR}^{7\text{A}}\text{OR}^{7\text{C}}$. In embodiments, R^7 is independently $-\text{OH}$.
In embodiments, R^7 is independently $-\text{NH}_2$. In embodiments, R^7 is independently $-\text{COOH}$.
10 In embodiments, R^7 is independently $-\text{CONH}_2$. In embodiments, R^7 is independently $-\text{NO}_2$.
In embodiments, R^7 is independently $-\text{SH}$.

[0406] In embodiments, R^7 is independently substituted or unsubstituted alkyl. In
embodiments, R^7 is independently substituted or unsubstituted heteroalkyl. In embodiments,
 R^7 is independently substituted or unsubstituted cycloalkyl. In embodiments, R^7 is
15 independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^7 is
independently substituted or unsubstituted aryl. In embodiments, R^7 is independently
substituted or unsubstituted heteroaryl. In embodiments, R^7 is independently substituted
alkyl. In embodiments, R^7 is independently substituted heteroalkyl. In embodiments, R^7 is
independently substituted cycloalkyl. In embodiments, R^7 is independently, substituted
20 heterocycloalkyl. In embodiments, R^7 is independently substituted aryl. In embodiments, R^7
is independently substituted heteroaryl. In embodiments, R^7 is independently unsubstituted
alkyl. In embodiments, R^7 is independently unsubstituted heteroalkyl. In embodiments, R^7 is
independently unsubstituted cycloalkyl. In embodiments, R^7 is independently, unsubstituted
heterocycloalkyl. In embodiments, R^7 is independently unsubstituted aryl. In embodiments,
25 R^7 is independently unsubstituted heteroaryl. In embodiments, R^7 is independently
substituted or unsubstituted $\text{C}_1\text{-C}_8$ alkyl. In embodiments, R^7 is independently substituted or
unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^7 is independently substituted
or unsubstituted $\text{C}_3\text{-C}_8$ cycloalkyl. In embodiments, R^7 is independently, substituted or
unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^7 is independently
30 substituted or unsubstituted $\text{C}_6\text{-C}_{10}$ aryl. In embodiments, R^7 is independently substituted or
unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^7 is independently substituted
 $\text{C}_1\text{-C}_8$ alkyl. In embodiments, R^7 is independently substituted 2 to 8 membered heteroalkyl.
In embodiments, R^7 is independently substituted $\text{C}_3\text{-C}_8$ cycloalkyl. In embodiments, R^7 is
independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^7 is

independently substituted C₆-C₁₀ aryl. In embodiments, R⁷ is independently substituted 5 to 10 membered heteroaryl. In embodiments, R⁷ is independently unsubstituted C₁-C₈ alkyl. In embodiments, R⁷ is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R⁷ is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R⁷ is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R⁷ is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R⁷ is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R⁷ is independently substituted or unsubstituted C₁-C₄ alkyl. In embodiments, R⁷ is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R⁷ is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R⁷ is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁷ is independently substituted or unsubstituted phenyl. In embodiments, R⁷ is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R⁷ is independently substituted C₁-C₄ alkyl. In embodiments, R⁷ is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R⁷ is independently substituted C₃-C₆ cycloalkyl. In embodiments, R⁷ is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁷ is independently substituted phenyl. In embodiments, R⁷ is independently substituted 5 to 6 membered heteroaryl. In embodiments, R⁷ is independently unsubstituted C₁-C₄ alkyl. In embodiments, R⁷ is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R⁷ is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R⁷ is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R⁷ is independently unsubstituted phenyl. In embodiments, R⁷ is independently unsubstituted 5 to 6 membered heteroaryl.

[0407] In embodiments, R^{7A} is independently hydrogen. In embodiments, R^{7A} is independently -CX^{7A}₃. In embodiments, R^{7A} is independently -CHX^{7A}₂. In embodiments, R^{7A} is independently -CH₂X^{7A}. In embodiments, R^{7A} is independently -CN. In embodiments, R^{7A} is independently -COOH. In embodiments, R^{7A} is independently -CONH₂. In embodiments, R^{7A} is independently substituted or unsubstituted alkyl. In embodiments, R^{7A} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{7A} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{7A} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{7A} is independently substituted or unsubstituted aryl. In embodiments, R^{7A} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{7A} is independently substituted alkyl. In embodiments, R^{7A} is independently substituted heteroalkyl. In embodiments, R^{7A} is

independently substituted cycloalkyl. In embodiments, R^{7A} is independently, substituted heterocycloalkyl. In embodiments, R^{7A} is independently substituted aryl. In embodiments, R^{7A} is independently substituted heteroaryl. In embodiments, R^{7A} is independently unsubstituted alkyl. In embodiments, R^{7A} is independently unsubstituted heteroalkyl. In

5 embodiments, R^{7A} is independently unsubstituted cycloalkyl. In embodiments, R^{7A} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{7A} is independently unsubstituted aryl. In embodiments, R^{7A} is independently unsubstituted heteroaryl. In embodiments, R^{7A} is independently substituted or unsubstituted C_1 - C_8 alkyl. In embodiments, R^{7A} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.

10 In embodiments, R^{7A} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{7A} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7A} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{7A} is independently substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{7A} is independently substituted C_1 - C_8 alkyl. In embodiments,

15 R^{7A} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{7A} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{7A} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7A} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{7A} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{7A} is independently unsubstituted C_1 - C_8 alkyl. In

20 embodiments, R^{7A} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{7A} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{7A} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7A} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{7A} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{7A} is independently substituted or

25 unsubstituted C_1 - C_4 alkyl. In embodiments, R^{7A} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{7A} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{7A} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7A} is independently substituted or unsubstituted phenyl. In embodiments, R^{7A} is independently substituted or

30 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{7A} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{7A} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{7A} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{7A} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7A} is independently substituted phenyl. In embodiments, R^{7A} is independently substituted 5 to 6

35 membered heteroaryl. In embodiments, R^{7A} is independently unsubstituted C_1 - C_4 alkyl. In

embodiments, R^{7A} is independently unsubstituted 2 to 4 membered heteroalkyl. In
embodiments, R^{7A} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{7A} is
independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7A} is
independently unsubstituted phenyl. In embodiments, R^{7A} is independently unsubstituted 5
5 to 6 membered heteroaryl. In embodiments, R^{7A} is independently unsubstituted methyl. In
embodiments, R^{7A} is independently unsubstituted ethyl. In embodiments, R^{7A} is
independently unsubstituted propyl. In embodiments, R^{7A} is independently unsubstituted
isopropyl. In embodiments, R^{7A} is independently unsubstituted tert-butyl.

[0408] In embodiments, R^{7B} is independently hydrogen. In embodiments, R^{7B} is
10 independently $-CX^{7B}_3$. In embodiments, R^{7B} is independently $-CHX^{7B}_2$. In embodiments,
 R^{7B} is independently $-CH_2X^{7B}$. In embodiments, R^{7B} is independently $-CN$. In embodiments,
 R^{7B} is independently $-COOH$. In embodiments, R^{7B} is independently $-CONH_2$. In
embodiments, R^{7B} is independently substituted or unsubstituted alkyl. In embodiments, R^{7B}
is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{7B} is
15 independently substituted or unsubstituted cycloalkyl. In embodiments, R^{7B} is independently,
substituted or unsubstituted heterocycloalkyl. In embodiments, R^{7B} is independently
substituted or unsubstituted aryl. In embodiments, R^{7B} is independently substituted or
unsubstituted heteroaryl. In embodiments, R^{7B} is independently substituted alkyl. In
embodiments, R^{7B} is independently substituted heteroalkyl. In embodiments, R^{7B} is
20 independently substituted cycloalkyl. In embodiments, R^{7B} is independently, substituted
heterocycloalkyl. In embodiments, R^{7B} is independently substituted aryl. In embodiments,
 R^{7B} is independently substituted heteroaryl. In embodiments, R^{7B} is independently
unsubstituted alkyl. In embodiments, R^{7B} is independently unsubstituted heteroalkyl. In
embodiments, R^{7B} is independently unsubstituted cycloalkyl. In embodiments, R^{7B} is
25 independently, unsubstituted heterocycloalkyl. In embodiments, R^{7B} is independently
unsubstituted aryl. In embodiments, R^{7B} is independently unsubstituted heteroaryl. In
embodiments, R^{7B} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
embodiments, R^{7B} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
In embodiments, R^{7B} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
30 embodiments, R^{7B} is independently, substituted or unsubstituted 3 to 8 membered
heterocycloalkyl. In embodiments, R^{7B} is independently substituted or unsubstituted C_6 - C_{10}
aryl. In embodiments, R^{7B} is independently substituted or unsubstituted 5 to 10 membered
heteroaryl. In embodiments, R^{7B} is independently substituted C_1 - C_8 alkyl. In embodiments,
 R^{7B} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{7B} is

independently substituted C₃-C₈ cycloalkyl. In embodiments, R^{7B} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7B} is independently substituted C₆-C₁₀ aryl. In embodiments, R^{7B} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{7B} is independently unsubstituted C₁-C₈ alkyl. In

5 embodiments, R^{7B} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{7B} is independently unsubstituted C₃-C₈ cycloalkyl. In embodiments, R^{7B} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7B} is independently unsubstituted C₆-C₁₀ aryl. In embodiments, R^{7B} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{7B} is independently substituted or

10 unsubstituted C₁-C₄ alkyl. In embodiments, R^{7B} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{7B} is independently substituted or unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{7B} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7B} is independently substituted or unsubstituted phenyl. In embodiments, R^{7B} is independently substituted or

15 unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{7B} is independently substituted C₁-C₄ alkyl. In embodiments, R^{7B} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{7B} is independently substituted C₃-C₆ cycloalkyl. In embodiments, R^{7B} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7B} is independently substituted phenyl. In embodiments, R^{7B} is independently substituted 5 to 6

20 membered heteroaryl. In embodiments, R^{7B} is independently unsubstituted C₁-C₄ alkyl. In embodiments, R^{7B} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{7B} is independently unsubstituted C₃-C₆ cycloalkyl. In embodiments, R^{7B} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7B} is independently unsubstituted phenyl. In embodiments, R^{7B} is independently unsubstituted 5 to

25 6 membered heteroaryl. In embodiments, R^{7B} is independently unsubstituted methyl. In embodiments, R^{7B} is independently unsubstituted ethyl. In embodiments, R^{7B} is independently unsubstituted propyl. In embodiments, R^{7B} is independently unsubstituted isopropyl. In embodiments, R^{7B} is independently unsubstituted tert-butyl.

[0409] In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be

30 joined to form a substituted or unsubstituted heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted

heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 10 membered heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form a substituted 5 to 6 membered heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may be joined to form an unsubstituted 5 to 6 membered heteroaryl.

[0410] In embodiments, R^{7C} is independently hydrogen. In embodiments, R^{7C} is independently $-CX^{7C}_3$. In embodiments, R^{7C} is independently $-CHX^{7C}_2$. In embodiments, R^{7C} is independently $-CH_2X^{7C}$. In embodiments, R^{7C} is independently $-CN$. In embodiments, R^{7C} is independently $-COOH$. In embodiments, R^{7C} is independently $-CONH_2$. In embodiments, R^{7C} is independently substituted or unsubstituted alkyl. In embodiments, R^{7C} is independently substituted or unsubstituted heteroalkyl. In embodiments, R^{7C} is independently substituted or unsubstituted cycloalkyl. In embodiments, R^{7C} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{7C} is independently substituted or unsubstituted aryl. In embodiments, R^{7C} is independently substituted or unsubstituted heteroaryl. In embodiments, R^{7C} is independently substituted alkyl. In

embodiments, R^{7C} is independently substituted heteroalkyl. In embodiments, R^{7C} is independently substituted cycloalkyl. In embodiments, R^{7C} is independently, substituted heterocycloalkyl. In embodiments, R^{7C} is independently substituted aryl. In embodiments, R^{7C} is independently substituted heteroaryl. In embodiments, R^{7C} is independently unsubstituted alkyl. In embodiments, R^{7C} is independently unsubstituted heteroalkyl. In 5 embodiments, R^{7C} is independently unsubstituted cycloalkyl. In embodiments, R^{7C} is independently, unsubstituted heterocycloalkyl. In embodiments, R^{7C} is independently unsubstituted aryl. In embodiments, R^{7C} is independently unsubstituted heteroaryl. In embodiments, R^{7C} is independently substituted or unsubstituted C_1 - C_8 alkyl. In 10 embodiments, R^{7C} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{7C} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{7C} is independently, substituted or unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7C} is independently substituted or unsubstituted C_6 - C_{10} aryl. In embodiments, R^{7C} is independently substituted or unsubstituted 5 to 10 membered 15 heteroaryl. In embodiments, R^{7C} is independently substituted C_1 - C_8 alkyl. In embodiments, R^{7C} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{7C} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{7C} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7C} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{7C} is independently substituted 5 to 10 membered 20 heteroaryl. In embodiments, R^{7C} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{7C} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{7C} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{7C} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7C} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{7C} is independently unsubstituted 25 5 to 10 membered heteroaryl. In embodiments, R^{7C} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{7C} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{7C} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{7C} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7C} is independently 30 substituted or unsubstituted phenyl. In embodiments, R^{7C} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{7C} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{7C} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{7C} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{7C} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7C} is 35 independently substituted phenyl. In embodiments, R^{7C} is independently substituted 5 to 6

membered heteroaryl. In embodiments, R^{7C} is independently unsubstituted C_1 - C_4 alkyl. In
embodiments, R^{7C} is independently unsubstituted 2 to 4 membered heteroalkyl. In
embodiments, R^{7C} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{7C} is
independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7C} is
5 independently unsubstituted phenyl. In embodiments, R^{7C} is independently unsubstituted 5 to
6 membered heteroaryl. In embodiments, R^{7C} is independently unsubstituted methyl. In
embodiments, R^{7C} is independently unsubstituted ethyl. In embodiments, R^{7C} is
independently unsubstituted propyl. In embodiments, R^{7C} is independently unsubstituted
isopropyl. In embodiments, R^{7C} is independently unsubstituted tert-butyl.

10 **[0411]** In embodiments, R^{7D} is independently hydrogen. In embodiments, R^{7D} is
independently $-CX^{7D}_3$. In embodiments, R^{7D} is independently $-CHX^{7D}_2$. In embodiments,
 R^{7D} is independently $-CH_2X^{7D}$. In embodiments, R^{7D} is independently $-CN$. In
embodiments, R^{7D} is independently $-COOH$. In embodiments, R^{7D} is
independently $-CONH_2$. In embodiments, R^{7D} is independently substituted or unsubstituted
15 alkyl. In embodiments, R^{7D} is independently substituted or unsubstituted heteroalkyl. In
embodiments, R^{7D} is independently substituted or unsubstituted cycloalkyl. In embodiments,
 R^{7D} is independently, substituted or unsubstituted heterocycloalkyl. In embodiments, R^{7D} is
independently substituted or unsubstituted aryl. In embodiments, R^{7D} is independently
substituted or unsubstituted heteroaryl. In embodiments, R^{7D} is independently substituted
20 alkyl. In embodiments, R^{7D} is independently substituted heteroalkyl. In embodiments, R^{7D} is
independently substituted cycloalkyl. In embodiments, R^{7D} is independently, substituted
heterocycloalkyl. In embodiments, R^{7D} is independently substituted aryl. In embodiments,
 R^{7D} is independently substituted heteroaryl. In embodiments, R^{7D} is independently
unsubstituted alkyl. In embodiments, R^{7D} is independently unsubstituted heteroalkyl. In
25 embodiments, R^{7D} is independently unsubstituted cycloalkyl. In embodiments, R^{7D} is
independently, unsubstituted heterocycloalkyl. In embodiments, R^{7D} is independently
unsubstituted aryl. In embodiments, R^{7D} is independently unsubstituted heteroaryl. In
embodiments, R^{7D} is independently substituted or unsubstituted C_1 - C_8 alkyl. In
embodiments, R^{7D} is independently substituted or unsubstituted 2 to 8 membered heteroalkyl.
30 In embodiments, R^{7D} is independently substituted or unsubstituted C_3 - C_8 cycloalkyl. In
embodiments, R^{7D} is independently, substituted or unsubstituted 3 to 8 membered
heterocycloalkyl. In embodiments, R^{7D} is independently substituted or unsubstituted C_6 - C_{10}
aryl. In embodiments, R^{7D} is independently substituted or unsubstituted 5 to 10 membered
heteroaryl. In embodiments, R^{7D} is independently substituted C_1 - C_8 alkyl. In embodiments,

R^{7D} is independently substituted 2 to 8 membered heteroalkyl. In embodiments, R^{7D} is independently substituted C_3 - C_8 cycloalkyl. In embodiments, R^{7D} is independently, substituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7D} is independently substituted C_6 - C_{10} aryl. In embodiments, R^{7D} is independently substituted 5 to 10 membered heteroaryl. In embodiments, R^{7D} is independently unsubstituted C_1 - C_8 alkyl. In embodiments, R^{7D} is independently unsubstituted 2 to 8 membered heteroalkyl. In embodiments, R^{7D} is independently unsubstituted C_3 - C_8 cycloalkyl. In embodiments, R^{7D} is independently, unsubstituted 3 to 8 membered heterocycloalkyl. In embodiments, R^{7D} is independently unsubstituted C_6 - C_{10} aryl. In embodiments, R^{7D} is independently unsubstituted 5 to 10 membered heteroaryl. In embodiments, R^{7D} is independently substituted or unsubstituted C_1 - C_4 alkyl. In embodiments, R^{7D} is independently substituted or unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{7D} is independently substituted or unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{7D} is independently, substituted or unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7D} is independently substituted or unsubstituted phenyl. In embodiments, R^{7D} is independently substituted or unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{7D} is independently substituted C_1 - C_4 alkyl. In embodiments, R^{7D} is independently substituted 2 to 4 membered heteroalkyl. In embodiments, R^{7D} is independently substituted C_3 - C_6 cycloalkyl. In embodiments, R^{7D} is independently, substituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7D} is independently substituted phenyl. In embodiments, R^{7D} is independently substituted 5 to 6 membered heteroaryl. In embodiments, R^{7D} is independently unsubstituted C_1 - C_4 alkyl. In embodiments, R^{7D} is independently unsubstituted 2 to 4 membered heteroalkyl. In embodiments, R^{7D} is independently unsubstituted C_3 - C_6 cycloalkyl. In embodiments, R^{7D} is independently unsubstituted 3 to 6 membered heterocycloalkyl. In embodiments, R^{7D} is independently unsubstituted phenyl. In embodiments, R^{7D} is independently unsubstituted 5 to 6 membered heteroaryl. In embodiments, R^{7D} is independently unsubstituted methyl. In embodiments, R^{7D} is independently unsubstituted ethyl. In embodiments, R^{7D} is independently unsubstituted propyl. In embodiments, R^{7D} is independently unsubstituted isopropyl. In embodiments, R^{7D} is independently unsubstituted tert-butyl.

[0412] In embodiments, R^7 is independently hydrogen, halogen, $-CX^7_3$, $-CHX^7_2$, $-CH_2X^7$, $-OCX^7_3$, $-OCH_2X^7$, $-OCHX^7_2$, $-CN$, $-SO_{n7}R^{7D}$, $-SO_{v7}NR^{7A}R^{7B}$, $-NHC(O)NR^{7A}R^{7B}$, $-N(O)_{m7}$, $-NR^{7A}R^{7B}$, $-C(O)R^{7C}$, $-C(O)OR^{7C}$, $-C(O)NR^{7A}R^{7B}$, $-OR^{7D}$, $-NR^{7A}SO_2R^{7D}$, $-NR^{7A}C(O)R^{7C}$, $-NR^{7A}C(O)OR^{7C}$, $-NR^{7A}OR^{7C}$, R^{38} -substituted or unsubstituted alkyl, R^{38} -substituted or unsubstituted heteroalkyl, R^{38} -substituted or unsubstituted

cycloalkyl, R^{38} -substituted or unsubstituted heterocycloalkyl, R^{38} -substituted or unsubstituted aryl, or R^{38} -substituted or unsubstituted heteroaryl. In embodiments, R^7 is independently halogen, $-CX^7_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^7_3$, $-OCHX^7_2$, R^{38} -substituted or unsubstituted alkyl, R^{38} -substituted or unsubstituted heteroalkyl, R^{38} -substituted or unsubstituted cycloalkyl, R^{38} -substituted or unsubstituted heterocycloalkyl, R^{38} -substituted or unsubstituted aryl, or R^{38} -substituted or unsubstituted heteroaryl. In embodiments, R^7 is independently halogen, $-CX^7_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^7_3$, $-OCHX^7_2$, R^{38} -substituted or unsubstituted C_1 - C_8 alkyl, R^{38} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{38} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{38} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{38} -substituted or unsubstituted phenyl, or R^{38} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^7 is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^7 is independently hydrogen. In embodiments, R^7 is independently methyl. In embodiments, R^7 is independently ethyl.

[0413] R^{38} is independently oxo, halogen, $-CX^{38}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38}_3$, $-OCHX^{38}_2$, R^{39} -substituted or unsubstituted alkyl, R^{39} -substituted or unsubstituted heteroalkyl, R^{39} -substituted or unsubstituted cycloalkyl, R^{39} -substituted or unsubstituted heterocycloalkyl, R^{39} -substituted or unsubstituted aryl, or R^{39} -substituted or unsubstituted heteroaryl. In embodiments, R^{38} is independently oxo, halogen, $-CX^{38}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38}_3$, $-OCHX^{38}_2$, R^{39} -substituted or unsubstituted C_1 - C_8 alkyl, R^{39} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{39} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{39} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{39} -substituted or unsubstituted phenyl, or R^{39} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{38} is $-F$, $-Cl$, $-Br$, or $-I$.

[0414] R^{39} is independently oxo, halogen, $-CX^{39}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39}_3$, $-OCHX^{39}_2$, R^{40} -substituted or unsubstituted alkyl, R^{40} -substituted or

unsubstituted heteroalkyl, R^{40} -substituted or unsubstituted cycloalkyl, R^{40} -substituted or unsubstituted heterocycloalkyl, R^{40} -substituted or unsubstituted aryl, or R^{40} -substituted or unsubstituted heteroaryl. In embodiments, R^{39} is independently oxo, halogen, $-CX^{39}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39}_3$, $-OCHX^{39}_2$, R^{40} -substituted or unsubstituted C_1 - C_8 alkyl, R^{40} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{40} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{40} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{40} -substituted or unsubstituted phenyl, or R^{40} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{39} is $-F$, $-Cl$, $-Br$, or $-I$.

[0415] In embodiments, R^{7A} is independently

hydrogen, $-CX^{7A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{7A}_2$, $-CH_2X^{7A}$, R^{38A} -substituted or unsubstituted alkyl, R^{38A} -substituted or unsubstituted heteroalkyl, R^{38A} -substituted or unsubstituted cycloalkyl, R^{38A} -substituted or unsubstituted heterocycloalkyl, R^{38A} -substituted or unsubstituted aryl, or R^{38A} -substituted or unsubstituted heteroaryl. In embodiments, R^{7A} is independently hydrogen, $-CX^{7A}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{7A}_2$, $-CH_2X^{7A}$, R^{38A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{38A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{38A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{38A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{38A} -substituted or unsubstituted phenyl, or R^{38A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{7A} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{7A} is independently hydrogen. In embodiments, R^{7A} is independently methyl. In embodiments, R^{7A} is independently ethyl.

[0416] In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{38A} -substituted or unsubstituted heterocycloalkyl or R^{38A} -

substituted or unsubstituted heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{38A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{38A} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0417] R^{38A} is independently oxo,

halogen, $-CX^{38A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38A}_3$, $-OCHX^{38A}_2$, R^{39A} -substituted or unsubstituted alkyl, R^{39A} -substituted or unsubstituted heteroalkyl, R^{39A} -substituted or unsubstituted cycloalkyl, R^{39A} -substituted or

unsubstituted heterocycloalkyl, R^{39A} -substituted or unsubstituted aryl, or R^{39A} -substituted or unsubstituted heteroaryl. In embodiments, R^{38A} is independently oxo, halogen, $-CX^{38A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38A}_3$, $-OCHX^{38A}_2$, R^{39A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{39A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{39A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{39A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{39A} -substituted or unsubstituted phenyl, or R^{39A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{38A} is $-F$, $-Cl$, $-Br$, or $-I$.

10 **[0418]** R^{39A} is independently oxo, halogen, $-CX^{39A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39A}_3$, $-OCHX^{39A}_2$, R^{40A} -substituted or unsubstituted alkyl, R^{40A} -substituted or unsubstituted heteroalkyl, R^{40A} -substituted or unsubstituted cycloalkyl, R^{40A} -substituted or unsubstituted heterocycloalkyl, R^{40A} -substituted or unsubstituted aryl, or R^{40A} -substituted or unsubstituted heteroaryl. In embodiments, R^{39A} is independently oxo, halogen, $-CX^{39A}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39A}_3$, $-OCHX^{39A}_2$, R^{40A} -substituted or unsubstituted C_1 - C_8 alkyl, R^{40A} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{40A} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{40A} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{40A} -substituted or unsubstituted phenyl, or R^{40A} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{39A} is $-F$, $-Cl$, $-Br$, or $-I$.

[0419] In embodiments, R^{7B} is independently hydrogen, $-CX^{7B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{7B}_2$, $-CH_2X^{7B}$, R^{38B} -substituted or unsubstituted alkyl, R^{38B} -substituted or unsubstituted heteroalkyl, R^{38B} -substituted or unsubstituted cycloalkyl, R^{38B} -substituted or unsubstituted heterocycloalkyl, R^{38B} -substituted or unsubstituted aryl, or R^{38B} -substituted or unsubstituted heteroaryl. In embodiments, R^{7B} is independently hydrogen, $-CX^{7B}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{7B}_2$, $-CH_2X^{7B}$, R^{38B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{38B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{38B} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{38B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{38B} -substituted or unsubstituted phenyl, or R^{38B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{7B} is $-F$, $-Cl$, $-Br$, or $-I$. In

embodiments, R^{7B} is independently hydrogen. In embodiments, R^{7B} is independently methyl. In embodiments, R^{7B} is independently ethyl.

[0420] In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{38B} -substituted or unsubstituted heterocycloalkyl or R^{38B} -

5 substituted or unsubstituted heteroaryl. In embodiments, R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may optionally be joined to form a R^{38B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl or R^{38B} -substituted or unsubstituted 5 to 6 membered heteroaryl.

[0421] R^{38B} is independently oxo,

10 halogen, $-CX^{38B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38B}_3$, $-OCHX^{38B}_2$, R^{39B} -substituted or unsubstituted alkyl, R^{39B} -substituted or unsubstituted heteroalkyl, R^{39B} -substituted or unsubstituted cycloalkyl, R^{39B} -substituted or unsubstituted heterocycloalkyl, R^{39B} -substituted or unsubstituted aryl, or R^{39B} -substituted or unsubstituted heteroaryl. In embodiments, R^{38B} is independently oxo,

15 halogen, $-CX^{38B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38B}_3$, $-OCHX^{38B}_2$, R^{39B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{39B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{39B} -substituted or unsubstituted

20 C_3 - C_8 cycloalkyl, R^{39B} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{39B} -substituted or unsubstituted phenyl, or R^{39B} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{38B} is $-F$, $-Cl$, $-Br$, or $-I$.

[0422] R^{39B} is independently oxo,

halogen, $-CX^{39B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39B}_3$, $-OCHX^{39B}_2$, R^{40B} -substituted or unsubstituted alkyl, R^{40B} -substituted or unsubstituted heteroalkyl, R^{40B} -substituted or unsubstituted cycloalkyl, R^{40B} -substituted or unsubstituted heterocycloalkyl, R^{40B} -substituted or unsubstituted aryl, or R^{40B} -substituted or unsubstituted heteroaryl. In embodiments, R^{39B} is independently oxo,

25 halogen, $-CX^{39B}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39B}_3$, $-OCHX^{39B}_2$, R^{40B} -substituted or unsubstituted C_1 - C_8 alkyl, R^{40B} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{40B} -substituted or unsubstituted

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C₃-C₈ cycloalkyl, R^{40B}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{40B}-substituted or unsubstituted phenyl, or R^{40B}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{39B} is -F, -Cl, -Br, or -I.

[0423] In embodiments, R^{7C} is independently

- 5 hydrogen, -CX^{7C}₃, -CN, -COOH, -CONH₂, -CHX^{7C}₂, -CH₂X^{7C}, R^{38C}-substituted or unsubstituted alkyl, R^{38C}-substituted or unsubstituted heteroalkyl, R^{38C}-substituted or unsubstituted cycloalkyl, R^{38C}-substituted or unsubstituted heterocycloalkyl, R^{38C}-substituted or unsubstituted aryl, or R^{38C}-substituted or unsubstituted heteroaryl. In embodiments, R^{7C} is independently hydrogen, -CX^{7C}₃, -CN, -COOH, -CONH₂, -CHX^{7C}₂, -CH₂X^{7C}, R^{38C}-substituted or unsubstituted C₁-C₈ alkyl, R^{38C}-substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{38C}-substituted or unsubstituted C₃-C₈ cycloalkyl, R^{38C}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{38C}-substituted or unsubstituted phenyl, or R^{38C}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{7C} is -F, -Cl, -Br, or -I. In embodiments, R^{7C} is independently hydrogen. In embodiments, R^{7C} is independently methyl.
- 10
- 15 In embodiments, R^{7C} is independently ethyl.

[0424] R^{38C} is independently oxo,

- halogen, -CX^{38C}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{38C}₃, -OCHX^{38C}₂, R^{39C}-substituted or unsubstituted alkyl, R^{39C}-substituted or unsubstituted heteroalkyl, R^{39C}-substituted or unsubstituted cycloalkyl, R^{39C}-substituted or unsubstituted heterocycloalkyl, R^{39C}-substituted or unsubstituted aryl, or R^{39C}-substituted or unsubstituted heteroaryl. In embodiments, R^{38C} is independently oxo,
- 20 halogen, -CX^{38C}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,
- 25 -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{38C}₃, -OCHX^{38C}₂, R^{39C}-substituted or unsubstituted C₁-C₈ alkyl, R^{39C}-substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{39C}-substituted or unsubstituted C₃-C₈ cycloalkyl, R^{39C}-substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{39C}-substituted or unsubstituted phenyl, or R^{39C}-substituted or unsubstituted 5 to 6 membered heteroaryl. X^{38C} is -F, -Cl, -Br, or -I.

30 **[0425]** R^{39C} is independently oxo,

halogen, -CX^{39C}₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCX^{39C}₃, -OCHX^{39C}₂, R^{40C}-substituted or unsubstituted alkyl, R^{40C}-substituted or

unsubstituted heteroalkyl, R^{40C} -substituted or unsubstituted cycloalkyl, R^{40C} -substituted or unsubstituted heterocycloalkyl, R^{40C} -substituted or unsubstituted aryl, or R^{40C} -substituted or unsubstituted heteroaryl. In embodiments, R^{39C} is independently oxo, halogen, $-CX^{39C}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{39C}_3$, $-OCHX^{39C}_2$, R^{40C} -substituted or unsubstituted C_1 - C_8 alkyl, R^{40C} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{40C} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{40C} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{40C} -substituted or unsubstituted phenyl, or R^{40C} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{39C} is $-F$, $-Cl$, $-Br$, or $-I$.

[0426] In embodiments, R^{7D} is independently hydrogen, $-CX^{7D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{7D}_2$, $-CH_2X^{7D}$, R^{38D} -substituted or unsubstituted alkyl, R^{38D} -substituted or unsubstituted heteroalkyl, R^{38D} -substituted or unsubstituted cycloalkyl, R^{38D} -substituted or unsubstituted heterocycloalkyl, R^{38D} -substituted or unsubstituted aryl, or R^{38D} -substituted or unsubstituted heteroaryl. In embodiments, R^{7D} is independently hydrogen, $-CX^{7D}_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX^{7D}_2$, $-CH_2X^{7D}$, R^{38D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{38D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{38D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{38D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{38D} -substituted or unsubstituted phenyl, or R^{38D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{7D} is $-F$, $-Cl$, $-Br$, or $-I$. In embodiments, R^{7D} is independently hydrogen. In embodiments, R^{7D} is independently methyl. In embodiments, R^{7D} is independently ethyl.

[0427] R^{38D} is independently oxo, halogen, $-CX^{38D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38D}_3$, $-OCHX^{38D}_2$, R^{39D} -substituted or unsubstituted alkyl, R^{39D} -substituted or unsubstituted heteroalkyl, R^{39D} -substituted or unsubstituted cycloalkyl, R^{39D} -substituted or unsubstituted heterocycloalkyl, R^{39D} -substituted or unsubstituted aryl, or R^{39D} -substituted or unsubstituted heteroaryl. In embodiments, R^{38D} is independently oxo, halogen, $-CX^{38D}_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCX^{38D}_3$, $-OCHX^{38D}_2$, R^{39D} -substituted or unsubstituted C_1 - C_8 alkyl, R^{39D} -substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{39D} -substituted or unsubstituted C_3 - C_8 cycloalkyl, R^{39D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{39D} -

substituted or unsubstituted phenyl, or R^{39D} -substituted or unsubstituted 5 to 6 membered heteroaryl. X^{38D} is -F, -Cl, -Br, or -I.

[0428] R^{39D} is independently oxo,

halogen, $-CX^{39D}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 5 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, $-OCX^{39D}_3$, $-OCHX^{39D}_2$, R^{40D} -substituted or unsubstituted alkyl, R^{40D} -substituted or
 unsubstituted heteroalkyl, R^{40D} -substituted or unsubstituted cycloalkyl, R^{40D} -substituted or
 unsubstituted heterocycloalkyl, R^{40D} -substituted or unsubstituted aryl, or R^{40D} -substituted or
 unsubstituted heteroaryl. In embodiments, R^{39D} is independently oxo,

10 halogen, $-CX^{39D}_3$, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, $-OCX^{39D}_3$, $-OCHX^{39D}_2$, R^{40D} -substituted or unsubstituted C₁-C₈ alkyl, R^{40D} -
 substituted or unsubstituted 2 to 8 membered heteroalkyl, R^{40D} -substituted or unsubstituted
 C₃-C₈ cycloalkyl, R^{40D} -substituted or unsubstituted 3 to 6 membered heterocycloalkyl, R^{40D} -
 15 substituted or unsubstituted phenyl, or R^{40D} -substituted or unsubstituted 5 to 6 membered
 heteroaryl. X^{39D} is -F, -Cl, -Br, or -I.

[0429] R^{40} , R^{40A} , R^{40B} , R^{40C} , and R^{40D} are independently hydrogen, oxo,

halogen, -CCl₃, -CBr₃, -CF₃, -CI₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -S
 O₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,

20 -NHC(O)NH₂, -NHSO₂H, -NHC(O)H,

-NHC(O)OH, -NHOH, -OCCl₃, -OCF₃, -OCBr₃, -OCI₃, -OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF
 2, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted
 heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{40} , R^{40A} ,
 R^{40B} , R^{40C} , and R^{40D} are independently oxo,

25 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCF₃, -OCHF₂, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted
 cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In
 embodiments, R^{40} , R^{40A} , R^{40B} , R^{40C} , and R^{40D} are independently oxo,

30 halogen, -CF₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂,
 -NHNH₂, -ONH₂, -NHC(O)NHNH₂, -NHC(O)NH₂, -NHSO₂H, -NHC(O)H, -NHC(O)OH,
 -NHOH, -OCF₃, -OCHF₂, unsubstituted C₁-C₈ alkyl, unsubstituted 2 to 8 membered

heteroalkyl, unsubstituted C₃-C₈ cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

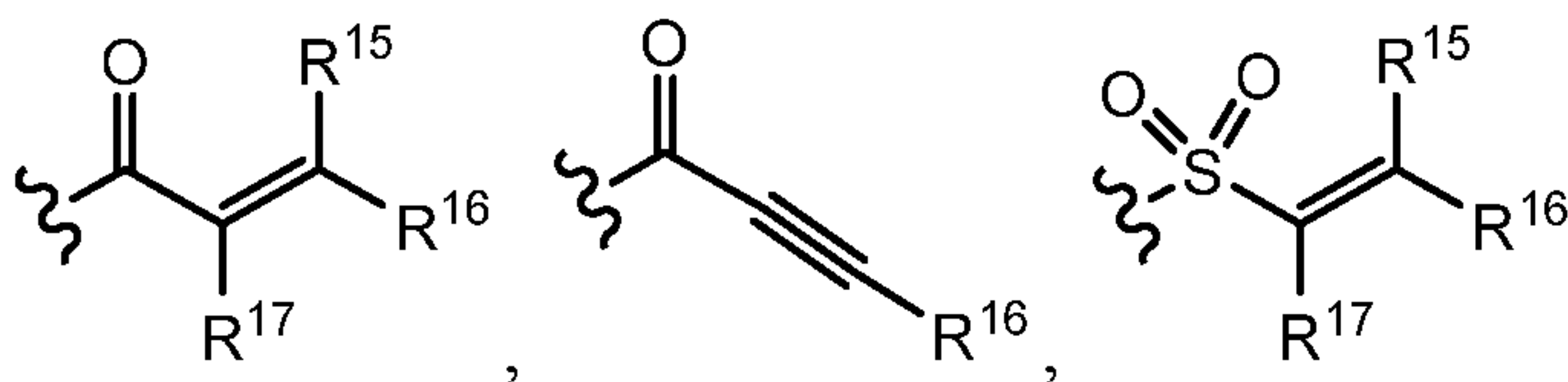
[0430] In embodiments, X is -F. In embodiments, X is -Cl. In embodiments, X is -Br. In
embodiments, X is -I. In embodiments, X¹ is -F. In embodiments, X¹ is -Cl. In
5 embodiments, X¹ is -Br. In embodiments, X¹ is -I. In embodiments, X² is -F. In
embodiments, X² is -Cl. In embodiments, X² is -Br. In embodiments, X² is -I. In
embodiments, X⁴ is -F. In embodiments, X⁴ is -Cl. In embodiments, X⁴ is -Br. In
embodiments, X⁴ is -I. In embodiments, X⁵ is -F. In embodiments, X⁵ is -Cl. In
embodiments, X⁵ is -Br. In embodiments, X⁵ is -I. In embodiments, X⁶ is -F. In
10 embodiments, X⁶ is -Cl. In embodiments, X⁶ is -Br. In embodiments, X⁶ is -I. In
embodiments, X⁷ is -F. In embodiments, X⁷ is -Cl. In embodiments, X⁷ is -Br. In
embodiments, X⁷ is -I.

[0431] In embodiments, n₁ is 0. In embodiments, n₁ is 1. In embodiments, n₁ is 2. In
embodiments, n₁ is 3. In embodiments, n₁ is 4. In embodiments, n₂ is 0. In embodiments,
15 n₂ is 1. In embodiments, n₂ is 2. In embodiments, n₂ is 3. In embodiments, n₂ is 4. In
embodiments, n₄ is 0. In embodiments, n₄ is 1. In embodiments, n₄ is 2. In embodiments,
n₄ is 3. In embodiments, n₄ is 4. In embodiments, n₅ is 0. In embodiments, n₅ is 1. In
embodiments, n₅ is 2. In embodiments, n₅ is 3. In embodiments, n₅ is 4. In embodiments,
n₆ is 0. In embodiments, n₆ is 1. In embodiments, n₆ is 2. In embodiments, n₆ is 3. In
20 embodiments, n₆ is 4. In embodiments, n₇ is 0. In embodiments, n₇ is 1. In embodiments,
n₇ is 2. In embodiments, n₇ is 3. In embodiments, n₇ is 4. In embodiments, n₁₀₉ is 0. In
embodiments, n₁₀₉ is 1. In embodiments, n₁₀₉ is 2. In embodiments, n₁₀₉ is 3. In
embodiments, n₁₀₉ is 4. In embodiments, n₁₀₁ is 0. In embodiments, n₁₀₁ is 1. In
embodiments, n₁₀₁ is 2. In embodiments, n₁₀₁ is 3. In embodiments, n₁₀₁ is 4.

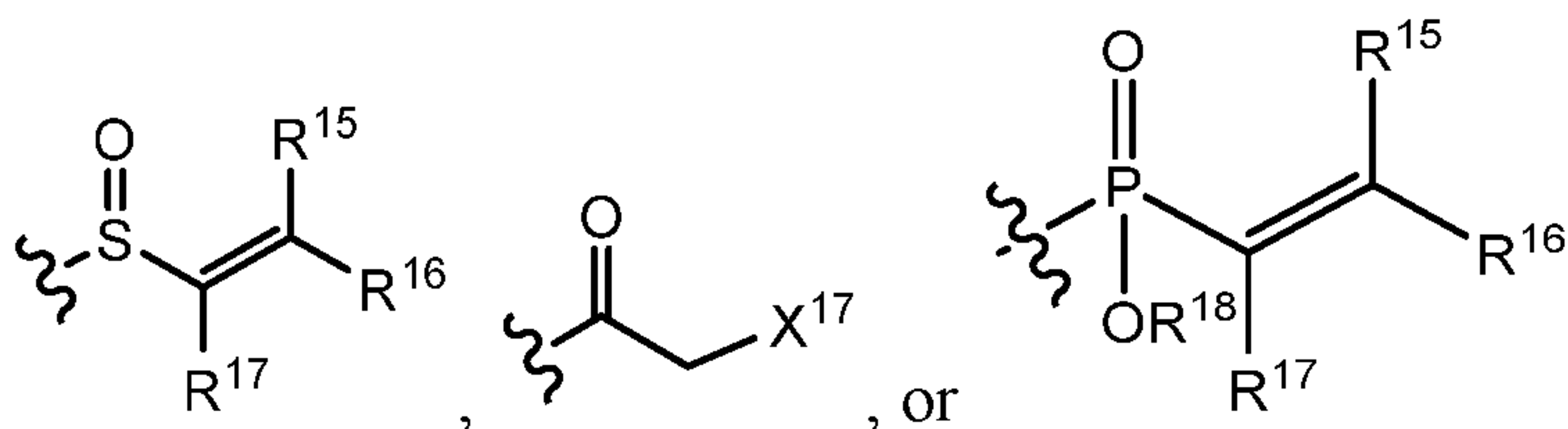
[0432] In embodiments, m₁ is 1. In embodiments, m₁ is 2. In embodiments, m₂ is 1. In
embodiments, m₂ is 2. In embodiments, m₄ is 1. In embodiments, m₄ is 2. In embodiments,
m₅ is 1. In embodiments, m₅ is 2. In embodiments, m₆ is 1. In embodiments, m₆ is 2. In
embodiments, m₇ is 1. In embodiments, m₇ is 2. In embodiments, m₁₀₉ is 1. In
embodiments, m₁₀₉ is 2. In embodiments, m₁₀₁ is 1. In embodiments, m₁₀₁ is 2.

[0433] In embodiments, v₁ is 1. In embodiments, v₁ is 2. In embodiments, v₂ is 1. In
embodiments, v₂ is 2. In embodiments, v₄ is 1. In embodiments, v₄ is 2. In embodiments,
v₅ is 1. In embodiments, v₅ is 2. In embodiments, v₆ is 1. In embodiments, v₆ is 2. In

[0434] In embodiments, E is a covalent cysteine modifier moiety.



[0435] In embodiments, E is:

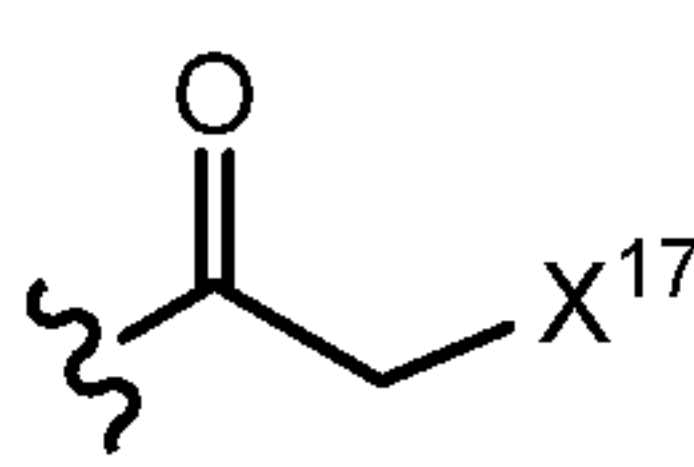

$$\begin{aligned} &\text{CH}_2\text{X}^{15}, -\text{CN}, -\text{SO}_{\text{ml}5}\text{R}^{15\text{D}}, -\text{SO}_{\text{vl}5}\text{NR}^{15\text{A}}\text{R}^{15\text{B}}, -\text{NHNr}^{15\text{A}}\text{R}^{15\text{B}}, -\text{ONR}^{15\text{A}}\text{R}^{15\text{B}}, \\ &-\text{NHC}=\text{(O)}\text{NHNr}^{15\text{A}}\text{R}^{15\text{B}}, -\text{NHC}(\text{O})\text{NR}^{15\text{A}}\text{R}^{15\text{B}}, -\text{N}(\text{O})_{\text{ml}5}, -\text{NR}^{15\text{A}}\text{R}^{15\text{B}}, -\text{C}(\text{O})\text{R}^{15\text{C}}, \\ &-\text{C}(\text{O})-\text{OR}^{15\text{C}}, -\text{C}(\text{O})\text{NR}^{15\text{A}}\text{R}^{15\text{B}}, -\text{OR}^{15\text{D}}, -\text{NR}^{15\text{A}}\text{SO}_2\text{R}^{15\text{D}}, -\text{NR}^{15\text{A}}\text{C}(\text{O})\text{R}^{15\text{C}}, - \end{aligned}$$

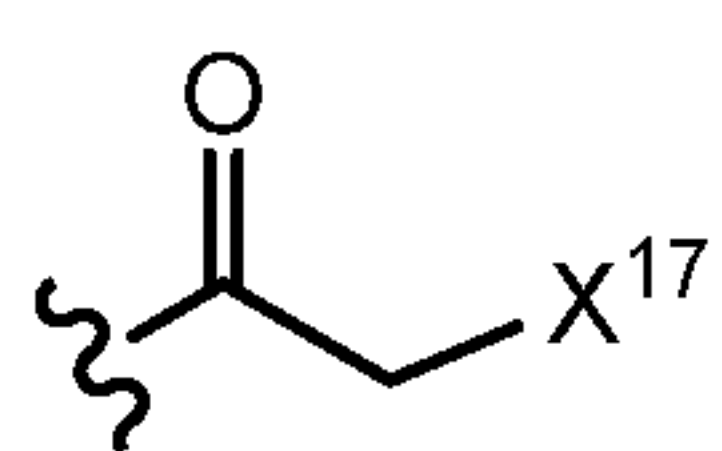
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unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl.

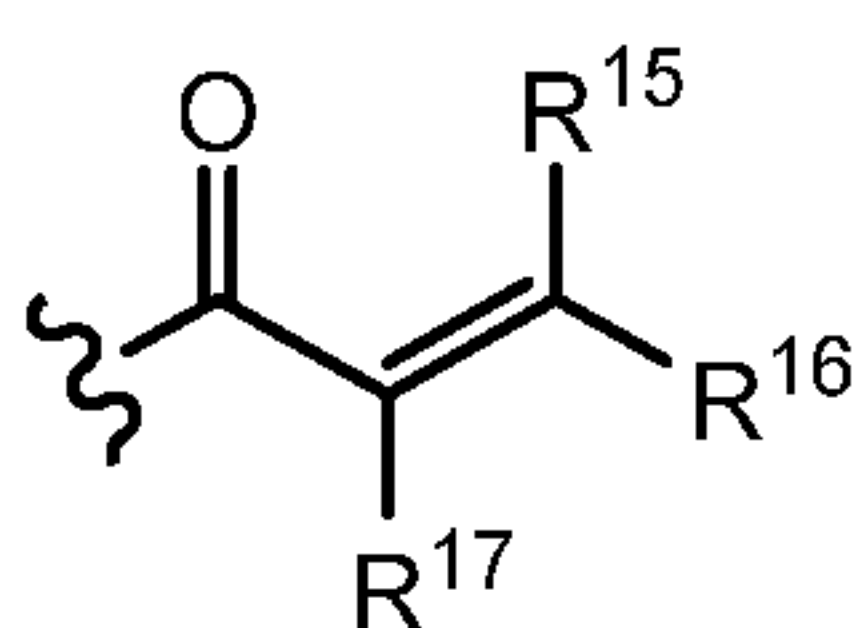
[0437] Each R^{15A} , R^{15B} , R^{15C} , R^{15D} , R^{16A} , R^{16B} , R^{16C} , R^{16D} , R^{17A} , R^{17B} , R^{17C} , R^{17D} , R^{18A} , R^{18B} , R^{18C} , R^{18D} , is independently hydrogen, $-CX_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX_2$, $-CH_2X$,

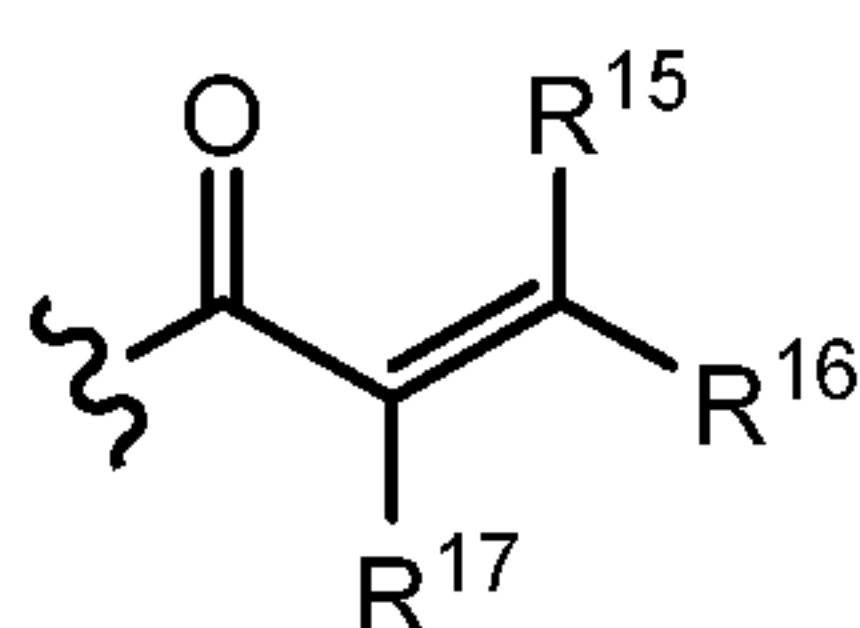
substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{15A} and R^{15B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{16A} and R^{16B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{17A} and R^{17B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{18A} and R^{18B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl. Each X , X^{15} , X^{16} , X^{17} and X^{18} is independently $-F$, $-Cl$, $-Br$, or $-I$. The symbols n_{15} , n_{16} , n_{17} , v_{15} , v_{16} , and v_{17} , are independently and integer from 0 to 4. The symbols m_{15} , m_{16} , and m_{17} are independently and integer between 1 and 2.

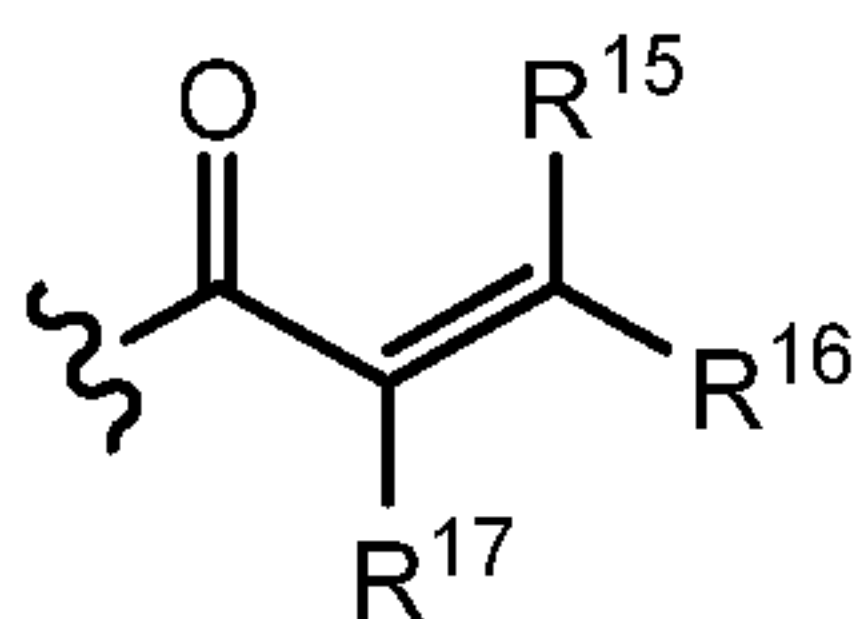
[0438] In embodiments, E is:  and X^{17} is $-Cl$. In embodiments, E is:



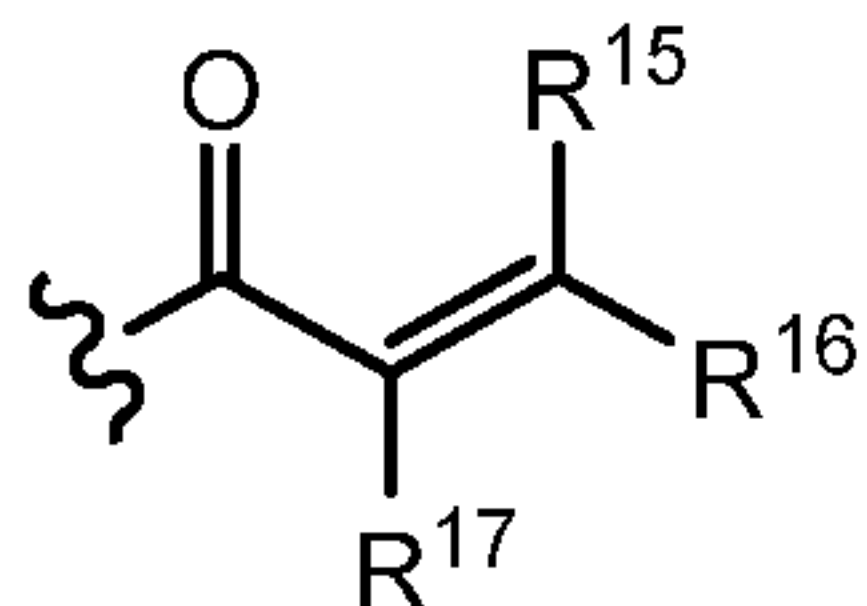
. In embodiments, X^{17} is $-Cl$.

[0439] In embodiments, E is:  and R^{15} , R^{16} , and R^{17} are independently

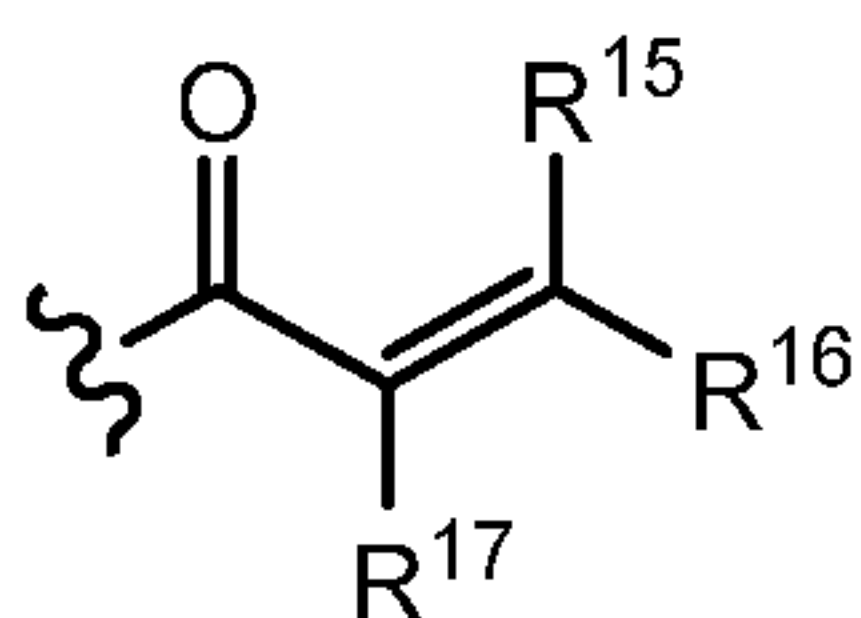
hydrogen. In embodiments, E is:  . In embodiments, R^{15} , R^{16} , and R^{17} are independently hydrogen.



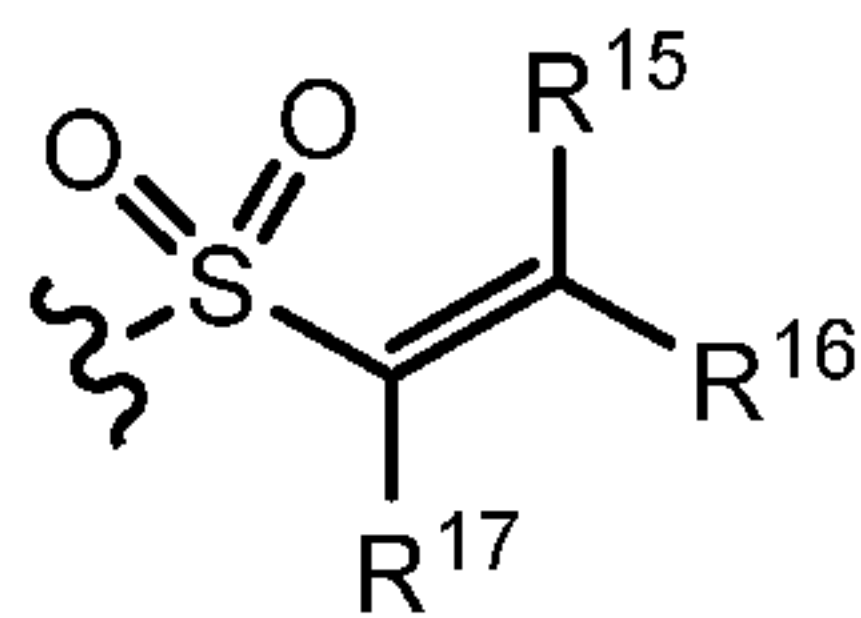
[0440] In embodiments, E is: ; R^{15} is independently hydrogen; R^{16} is independently hydrogen or $-\text{CH}_2\text{NR}^{16\text{A}}\text{R}^{16\text{B}}$; R^{17} is independently hydrogen; and $R^{16\text{A}}$ and $R^{16\text{B}}$ are independently hydrogen or unsubstituted alkyl. In embodiments, E is:



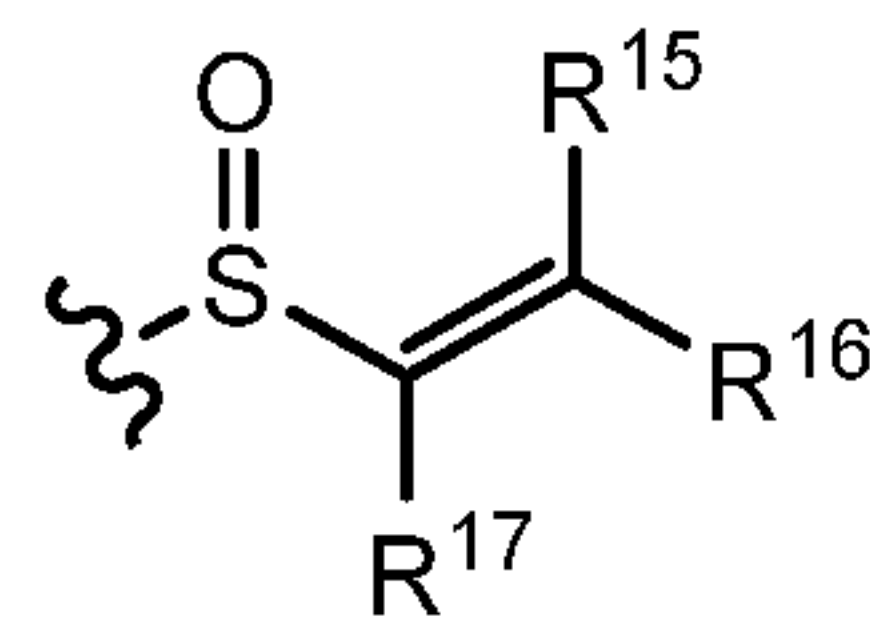
. In embodiments, R^{15} is independently hydrogen. In embodiments, R^{16} is independently hydrogen or $-\text{CH}_2\text{NR}^{16\text{A}}\text{R}^{16\text{B}}$. In embodiments, R^{17} is independently hydrogen. In embodiments, $R^{16\text{A}}$ and $R^{16\text{B}}$ are independently hydrogen or unsubstituted alkyl. In embodiments, $R^{16\text{A}}$ and $R^{16\text{B}}$ are independently unsubstituted methyl.



[0441] In embodiments, E is: . In embodiments, E is: . In



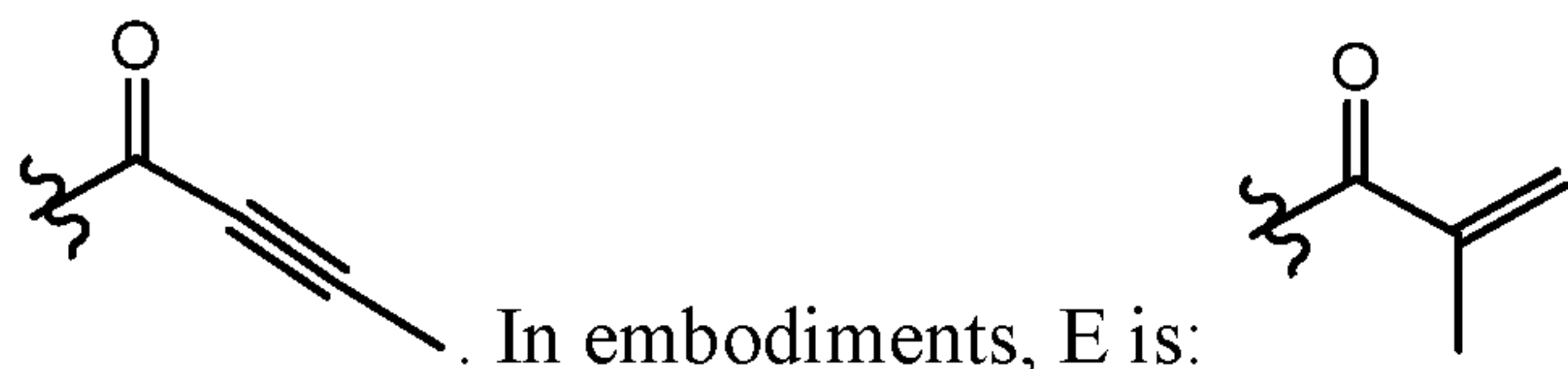
embodiments, E is: . In embodiments, E is: . In



embodiments, E is: . In embodiments, E is: . In



embodiments, E is: . In embodiments, E is: .



embodiments, E is: . In embodiments, E is: .

[0442] X may independently be $-\text{F}$. X may independently be $-\text{Cl}$. X may independently be $-\text{Br}$. X may independently be $-\text{I}$. X^{15} may independently be $-\text{F}$. X^{15} may independently be $-\text{Cl}$. X^{15} may independently be $-\text{Br}$. X^{15} may independently be $-\text{I}$. X^{16} may

independently be $-\text{F}$. X^{16} may independently be $-\text{Cl}$. X^{16} may independently be $-\text{Br}$. X^{16} may independently be $-\text{I}$. X^{17} may independently be $-\text{F}$. X^{17} may independently be $-\text{Cl}$. X^{17} may independently be $-\text{Br}$. X^{17} may independently be $-\text{I}$. X^{18} may independently be $-\text{F}$. X^{18} may independently be $-\text{Cl}$. X^{18} may independently be $-\text{Br}$. X^{18} may independently be $-\text{I}$. n_{15} may independently be 0. n_{15} may independently be 1. n_{15} may independently be 2. n_{15} may independently be 3. n_{15} may independently be 4. n_{16} may independently be 0.

- n16 may independently be 1. n16 may independently be 2. n16 may independently be 3.
 n16 may independently be 4. n17 may independently be 0. n17 may independently be 1.
 n17 may independently be 2. n17 may independently be 3. n17 may independently be 4.
 v15 may independently be 0. v15 may independently be 1. v15 may independently be 2.
 5 v15 may independently be 3. v15 may independently be 4. v16 may independently be 0.
 v16 may independently be 1. v16 may independently be 2. v16 may independently be 3.
 v16 may independently be 4. m15 may independently be 1. m15 may independently be 2.
 m16 may independently be 1. m16 may independently be 2. m17 may independently be 1.
 m17 may independently be 2.
- 10 **[0443]** In embodiments, R^{15} is hydrogen. In embodiments, R^{15} is halogen. In
 embodiments, R^{15} is CX^{15}_3 . In embodiments, R^{15} is $-CHX^{15}_2$. In embodiments, R^{15} is -
 CH_2X^{15} . In embodiments, R^{15} is $-CN$. In embodiments, R^{15} is $-SO_{n15}R^{15D}$. In embodiments,
 R^{15} is $-SO_{v15}NR^{15A}R^{15B}$. In embodiments, R^{15} is $-NHN R^{15A}R^{15B}$. In embodiments, R^{15} is
 $-ONR^{15A}R^{15B}$. In embodiments, R^{15} is $-NHC(=O)NHN R^{15A}R^{15B}$. In embodiments, R^{15} is
 15 $-NHC(O)NR^{15A}R^{15B}$. In embodiments, R^{15} is $-N(O)_{m15}$. In embodiments, R^{15} is $-NR^{15A}R^{15B}$.
 In embodiments, R^{15} is $-C(O)R^{15C}$. In embodiments, R^{15} is $-C(O)-OR^{15C}$. In embodiments,
 R^{15} is $-C(O)NR^{15A}R^{15B}$. In embodiments, R^{15} is $-OR^{15D}$. In embodiments, R^{15} is -
 $NR^{15A}SO_2R^{15D}$. In embodiments, R^{15} is $-NR^{15A}C(O)R^{15C}$. In embodiments, R^{15} is -
 $NR^{15A}C(O)OR^{15C}$. In embodiments, R^{15} is $-NR^{15A}OR^{15C}$. In embodiments, R^{15} is $-OCX^{15}_3$.
 20 In embodiments, R^{15} is $-OCHX^{15}_2$. In embodiments, R^{15} is substituted or unsubstituted alkyl.
 In embodiments, R^{15} is substituted or unsubstituted heteroalkyl. In embodiments, R^{15} is
 substituted or unsubstituted cycloalkyl. In embodiments, R^{15} is substituted or unsubstituted
 heterocycloalkyl. In embodiments, R^{15} is substituted or unsubstituted aryl. In embodiments,
 R^{15} is substituted or unsubstituted heteroaryl. In embodiments, R^{15} is substituted alkyl. In
 25 embodiments, R^{15} is substituted heteroalkyl. In embodiments, R^{15} is substituted cycloalkyl.
 In embodiments, R^{15} is substituted heterocycloalkyl. In embodiments, R^{15} is substituted aryl.
 In embodiments, R^{15} is substituted heteroaryl. In embodiments, R^{15} is unsubstituted alkyl. In
 embodiments, R^{15} is unsubstituted heteroalkyl. In embodiments, R^{15} is unsubstituted
 cycloalkyl. In embodiments, R^{15} is unsubstituted heterocycloalkyl. In embodiments, R^{15} is
 30 unsubstituted aryl. In embodiments, R^{15} is unsubstituted heteroaryl. In embodiments, R^{15} is
 unsubstituted methyl. In embodiments, R^{15} is unsubstituted ethyl. In embodiments, R^{15} is
 unsubstituted propyl. In embodiments, R^{15} is unsubstituted isopropyl. In embodiments, R^{15}
 is unsubstituted butyl. In embodiments, R^{15} is unsubstituted tert-butyl.

[0444] In embodiments, R^{15A} is hydrogen. In embodiments, R^{15A} is $-CX_3$. In
embodiments, R^{15A} is $-CN$. In embodiments, R^{15A} is $-COOH$. In embodiments, R^{15A}
is $-CONH_2$. In embodiments, R^{15A} is $-CHX_2$. In embodiments, R^{15A} is $-CH_2X$. In
embodiments, R^{15A} is unsubstituted methyl. In embodiments, R^{15A} is unsubstituted ethyl. In
5 embodiments, R^{15A} is unsubstituted propyl. In embodiments, R^{15A} is unsubstituted isopropyl.
In embodiments, R^{15A} is unsubstituted butyl. In embodiments, R^{15A} is unsubstituted tert-
butyl.

[0445] In embodiments, R^{15B} is hydrogen. In embodiments, R^{15B} is $-CX_3$. In
embodiments, R^{15B} is $-CN$. In embodiments, R^{15B} is $-COOH$. In embodiments, R^{15B}
10 is $-CONH_2$. In embodiments, R^{15B} is $-CHX_2$. In embodiments, R^{15B} is $-CH_2X$. In
embodiments, R^{15B} is unsubstituted methyl. In embodiments, R^{15B} is unsubstituted ethyl. In
embodiments, R^{15B} is unsubstituted propyl. In embodiments, R^{15B} is unsubstituted isopropyl.
In embodiments, R^{15B} is unsubstituted butyl. In embodiments, R^{15B} is unsubstituted tert-
butyl.

[0446] In embodiments, R^{15C} is hydrogen. In embodiments, R^{15C} is $-CX_3$. In
embodiments, R^{15C} is $-CN$. In embodiments, R^{15C} is $-COOH$. In embodiments, R^{15C}
15 is $-CONH_2$. In embodiments, R^{15C} is $-CHX_2$. In embodiments, R^{15C} is $-CH_2X$. In
embodiments, R^{15C} is unsubstituted methyl. In embodiments, R^{15C} is unsubstituted ethyl. In
embodiments, R^{15C} is unsubstituted propyl. In embodiments, R^{15C} is unsubstituted isopropyl.
20 In embodiments, R^{15C} is unsubstituted butyl. In embodiments, R^{15C} is unsubstituted tert-
butyl.

[0447] In embodiments, R^{15D} is hydrogen. In embodiments, R^{15D} is $-CX_3$. In
embodiments, R^{15D} is $-CN$. In embodiments, R^{15D} is $-COOH$. In embodiments, R^{15D}
25 is $-CONH_2$. In embodiments, R^{15D} is $-CHX_2$. In embodiments, R^{15D} is $-CH_2X$. In
embodiments, R^{15D} is unsubstituted methyl. In embodiments, R^{15D} is unsubstituted ethyl. In
embodiments, R^{15D} is unsubstituted propyl. In embodiments, R^{15D} is unsubstituted isopropyl.
In embodiments, R^{15D} is unsubstituted butyl. In embodiments, R^{15D} is unsubstituted tert-
butyl.

[0448] In embodiments, R^{15} is independently hydrogen, oxo,
30 halogen, $-CX^{15}_3$, $-CHX^{15}_2$, $-OCH_2X^{15}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-$
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-$
 $NHSO_2H$, $-NHC(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{15}_3$, $-OCHX^{15}_2$, R^{72} -substituted or
unsubstituted alkyl, R^{72} -substituted or unsubstituted heteroalkyl, R^{72} -substituted or

unsubstituted cycloalkyl, R^{72} -substituted or unsubstituted heterocycloalkyl, R^{72} -substituted or unsubstituted aryl, or R^{72} -substituted or unsubstituted heteroaryl. X^{15} is halogen. In embodiments, X^{15} is F.

[0449] R^{72} is independently oxo,

5 halogen, $-CX^{72}_3$, $-CHX^{72}_2$, $-OCH_2X^{72}$, $-OCHX^{72}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{72}_3$, $-OCHX^{72}_2$, R^{73} -substituted or unsubstituted alkyl, R^{73} -substituted or unsubstituted heteroalkyl, R^{73} -substituted or unsubstituted cycloalkyl, R^{73} -substituted or unsubstituted heterocycloalkyl, R^{73} -substituted or unsubstituted aryl, or R^{73} -substituted or unsubstituted heteroaryl. X^{72} is halogen. In
10 embodiments, X^{72} is F.

[0450] R^{73} is independently oxo,

halogen, $-CX^{73}_3$, $-CHX^{73}_2$, $-OCH_2X^{73}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{73}_3$, $-OCHX^{73}_2$, R^{74} -substituted or unsubstituted alkyl, R^{74} -substituted or unsubstituted heteroalkyl, R^{74} -substituted or unsubstituted cycloalkyl, R^{74} -substituted or unsubstituted heterocycloalkyl, R^{74} -substituted or unsubstituted aryl, or R^{74} -substituted or unsubstituted heteroaryl. X^{73} is halogen. In
15 embodiments, X^{73} is F.

20 **[0451]** In embodiments, R^{15A} is independently hydrogen, oxo,

halogen, $-CX^{15A}_3$, $-CHX^{15A}_2$, $-OCH_2X^{15A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{15A}_3$, $-OCHX^{15A}_2$, R^{72A} -substituted or unsubstituted alkyl, R^{72A} -substituted or unsubstituted heteroalkyl, R^{72A} -substituted or unsubstituted cycloalkyl, R^{72A} -substituted or unsubstituted heterocycloalkyl, R^{72A} -substituted or unsubstituted aryl, or R^{72A} -substituted or unsubstituted heteroaryl. X^{15A} is halogen. In
25 embodiments, X^{15A} is F.

[0452] R^{72A} is independently oxo,

halogen, $-CX^{72A}_3$, $-CHX^{72A}_2$, $-OCH_2X^{72A}$, $-OCHX^{72A}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{72A}_3$, $-OCHX^{72A}_2$, R^{73A} -substituted or unsubstituted alkyl, R^{73A} -substituted or unsubstituted heteroalkyl, R^{73A} -substituted or unsubstituted cycloalkyl, R^{73A} -substituted or unsubstituted heterocycloalkyl,
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R^{73A} -substituted or unsubstituted aryl, or R^{73A} -substituted or unsubstituted heteroaryl. X^{72A} is halogen. In embodiments, X^{72A} is F.

[0453] R^{73A} is independently oxo,

halogen, $-CX^{73A}_3$, $-CHX^{73A}_2$, $-OCH_2X^{73A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{73A}_3$, $-OCHX^{73A}_2$, R^{74A} -substituted or

unsubstituted alkyl, R^{74A} -substituted or unsubstituted heteroalkyl, R^{74A} -substituted or

unsubstituted cycloalkyl, R^{74A} -substituted or unsubstituted heterocycloalkyl, R^{74A} -substituted

or unsubstituted aryl, or R^{74A} -substituted or unsubstituted heteroaryl. X^{73A} is halogen. In

10 embodiments, X^{73A} is F.

[0454] In embodiments, R^{15B} is independently hydrogen, oxo,

halogen, $-CX^{15B}_3$, $-CHX^{15B}_2$, $-OCH_2X^{15B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{15B}_3$, $-OCHX^{15B}_2$, R^{72B} -substituted or

15 unsubstituted alkyl, R^{72B} -substituted or unsubstituted heteroalkyl, R^{72B} -substituted or

unsubstituted cycloalkyl, R^{72B} -substituted or unsubstituted heterocycloalkyl, R^{72B} -substituted

or unsubstituted aryl, or R^{72B} -substituted or unsubstituted heteroaryl. X^{15B} is halogen. In

embodiments, X^{15B} is F.

[0455] R^{72B} is independently oxo,

20 halogen, $-CX^{72B}_3$, $-CHX^{72B}_2$, $-OCH_2X^{72B}$, $-OCHX^{72B}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,

$-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{72B}_3$, $-OCHX^{72B}_2$,

R^{73B} -substituted or unsubstituted alkyl, R^{73B} -substituted or unsubstituted heteroalkyl, R^{73B} -

substituted or unsubstituted cycloalkyl, R^{73B} -substituted or unsubstituted heterocycloalkyl,

25 R^{73B} -substituted or unsubstituted aryl, or R^{73B} -substituted or unsubstituted heteroaryl. X^{72B} is

halogen. In embodiments, X^{72B} is F.

[0456] R^{73B} is independently oxo,

halogen, $-CX^{73B}_3$, $-CHX^{73B}_2$, $-OCH_2X^{73B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

30 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{73B}_3$, $-OCHX^{73B}_2$, R^{74B} -substituted or

unsubstituted alkyl, R^{74B} -substituted or unsubstituted heteroalkyl, R^{74B} -substituted or

unsubstituted cycloalkyl, R^{74B} -substituted or unsubstituted heterocycloalkyl, R^{74B} -substituted

or unsubstituted aryl, or R^{74B} -substituted or unsubstituted heteroaryl. X^{73B} is halogen. In
embodiments, X^{73B} is F.

[0457] In embodiments, R^{15C} is independently hydrogen, oxo,
halogen, $-CX^{15C}_3$, $-CHX^{15C}_2$, $-OCH_2X^{15C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{15C}_3$, $-OCHX^{15C}_2$, R^{72C} -substituted or
unsubstituted alkyl, R^{72C} -substituted or unsubstituted heteroalkyl, R^{72C} -substituted or
unsubstituted cycloalkyl, R^{72C} -substituted or unsubstituted heterocycloalkyl, R^{72C} -substituted
or unsubstituted aryl, or R^{72C} -substituted or unsubstituted heteroaryl. X^{15C} is halogen. In
10 embodiments, X^{15C} is F.

[0458] R^{72C} is independently oxo,
halogen, $-CX^{72C}_3$, $-CHX^{72C}_2$, $-OCH_2X^{72C}$, $-OCHX^{72C}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -
 NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{72C}_3$, $-OCHX^{72C}_2$,
15 R^{73C} -substituted or unsubstituted alkyl, R^{73C} -substituted or unsubstituted heteroalkyl, R^{73C} -
substituted or unsubstituted cycloalkyl, R^{73C} -substituted or unsubstituted heterocycloalkyl,
 R^{73C} -substituted or unsubstituted aryl, or R^{73C} -substituted or unsubstituted heteroaryl. X^{72C} is
halogen. In embodiments, X^{72C} is F.

[0459] R^{73C} is independently oxo,
20 halogen, $-CX^{73C}_3$, $-CHX^{73C}_2$, $-OCH_2X^{73C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{73C}_3$, $-OCHX^{73C}_2$, R^{74C} -substituted or
unsubstituted alkyl, R^{74C} -substituted or unsubstituted heteroalkyl, R^{74C} -substituted or
unsubstituted cycloalkyl, R^{74C} -substituted or unsubstituted heterocycloalkyl, R^{74C} -substituted
25 or unsubstituted aryl, or R^{74C} -substituted or unsubstituted heteroaryl. X^{73C} is halogen. In
embodiments, X^{73C} is F.

[0460] In embodiments, R^{15D} is independently hydrogen, oxo,
halogen, $-CX^{15D}_3$, $-CHX^{15D}_2$, $-OCH_2X^{15D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
30 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{15D}_3$, $-OCHX^{15D}_2$, R^{72D} -substituted or
unsubstituted alkyl, R^{72D} -substituted or unsubstituted heteroalkyl, R^{72D} -substituted or
unsubstituted cycloalkyl, R^{72D} -substituted or unsubstituted heterocycloalkyl, R^{72D} -substituted

or unsubstituted aryl, or R^{72D} -substituted or unsubstituted heteroaryl. X^{15D} is halogen. In
embodiments, X^{15D} is F.

[0461] R^{72D} is independently oxo,

halogen, $-CX^{72D}_3$, $-CHX^{72D}_2$, $-OCH_2X^{72D}$, $-OCHX^{72D}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

5 NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,

$-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{72D}_3$, $-OCHX^{72D}_2$,

R^{73D} -substituted or unsubstituted alkyl, R^{73D} -substituted or unsubstituted heteroalkyl, R^{73D} -

substituted or unsubstituted cycloalkyl, R^{73D} -substituted or unsubstituted heterocycloalkyl,

R^{73D} -substituted or unsubstituted aryl, or R^{73D} -substituted or unsubstituted heteroaryl. X^{72D} is

10 halogen. In embodiments, X^{72D} is F.

[0462] R^{73D} is independently oxo,

halogen, $-CX^{73D}_3$, $-CHX^{73D}_2$, $-OCH_2X^{73D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{73D}_3$, $-OCHX^{73D}_2$, R^{74D} -substituted or

15 unsubstituted alkyl, R^{74D} -substituted or unsubstituted heteroalkyl, R^{74D} -substituted or

unsubstituted cycloalkyl, R^{74D} -substituted or unsubstituted heterocycloalkyl, R^{74D} -substituted

or unsubstituted aryl, or R^{74D} -substituted or unsubstituted heteroaryl. X^{73D} is halogen. In

embodiments, X^{73D} is F.

[0463] In embodiments, R^{16} is hydrogen. In embodiments, R^{16} is halogen. In

20 embodiments, R^{16} is CX^{16}_3 . In embodiments, R^{16} is $-CHX^{16}_2$. In embodiments, R^{16} is -

CH_2X^{16} . In embodiments, R^{16} is $-CN$. In embodiments, R^{16} is $-SO_{n16}R^{16D}$. In embodiments,

R^{16} is $-SO_{v16}NR^{16A}R^{16B}$. In embodiments, R^{16} is $-NHNR^{16A}R^{16B}$. In embodiments, R^{16} is

$-ONR^{16A}R^{16B}$. In embodiments, R^{16} is $-NHC=(O)NHNR^{16A}R^{16B}$. In embodiments, R^{16} is

$-NHC(O)NR^{16A}R^{16B}$. In embodiments, R^{16} is $-N(O)_{m16}$. In embodiments, R^{16} is $-NR^{16A}R^{16B}$.

25 In embodiments, R^{16} is $-C(O)R^{16C}$. In embodiments, R^{16} is $-C(O)-OR^{16C}$. In embodiments,

R^{16} is $-C(O)NR^{16A}R^{16B}$. In embodiments, R^{16} is $-OR^{16D}$. In embodiments, R^{16} is -

$NR^{16A}SO_2R^{16D}$. In embodiments, R^{16} is $-NR^{16A}C(O)R^{16C}$. In embodiments, R^{16} is -

$NR^{16A}C(O)OR^{16C}$. In embodiments, R^{16} is $-NR^{16A}OR^{16C}$. In embodiments, R^{16} is $-OCX^{16}_3$.

In embodiments, R^{16} is $-OCHX^{16}_2$. In embodiments, R^{16} is substituted or unsubstituted alkyl.

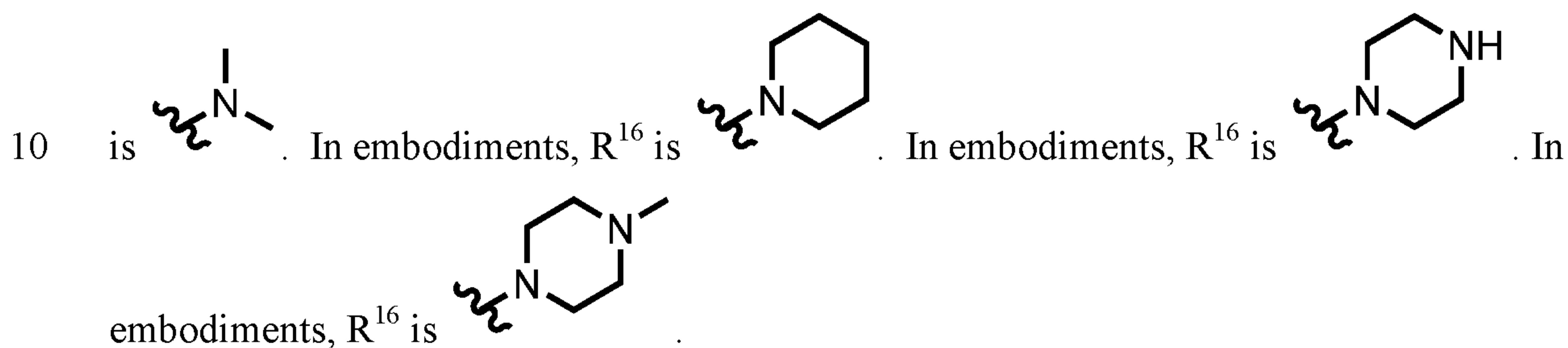
30 In embodiments, R^{16} is substituted or unsubstituted heteroalkyl. In embodiments, R^{16} is

substituted or unsubstituted cycloalkyl. In embodiments, R^{16} is substituted or unsubstituted

heterocycloalkyl. In embodiments, R^{16} is substituted or unsubstituted aryl. In embodiments,

R^{16} is substituted or unsubstituted heteroaryl. In embodiments, R^{16} is substituted alkyl. In

embodiments, R^{16} is substituted heteroalkyl. In embodiments, R^{16} is substituted cycloalkyl. In embodiments, R^{16} is substituted heterocycloalkyl. In embodiments, R^{16} is substituted aryl. In embodiments, R^{16} is substituted heteroaryl. In embodiments, R^{16} is unsubstituted alkyl. In embodiments, R^{16} is unsubstituted heteroalkyl. In embodiments, R^{16} is unsubstituted cycloalkyl. In embodiments, R^{16} is unsubstituted heterocycloalkyl. In embodiments, R^{16} is unsubstituted aryl. In embodiments, R^{16} is unsubstituted heteroaryl. In embodiments, R^{16} is unsubstituted methyl. In embodiments, R^{16} is unsubstituted ethyl. In embodiments, R^{16} is unsubstituted propyl. In embodiments, R^{16} is unsubstituted isopropyl. In embodiments, R^{16} is unsubstituted butyl. In embodiments, R^{16} is unsubstituted tert-butyl. In embodiments, R^{16}



[0464] In embodiments, R^{16A} is hydrogen. In embodiments, R^{16A} is $-CX_3$. In embodiments, R^{16A} is $-CN$. In embodiments, R^{16A} is $-COOH$. In embodiments, R^{16A} is $-CONH_2$. In embodiments, R^{16A} is $-CHX_2$. In embodiments, R^{16A} is $-CH_2X$. In
15 embodiments, R^{16A} is unsubstituted methyl. In embodiments, R^{16A} is unsubstituted ethyl. In embodiments, R^{16A} is unsubstituted propyl. In embodiments, R^{16A} is unsubstituted isopropyl. In embodiments, R^{16A} is unsubstituted butyl. In embodiments, R^{16A} is unsubstituted tert-butyl.

[0465] In embodiments, R^{16B} is hydrogen. In embodiments, R^{16B} is $-CX_3$. In
20 embodiments, R^{16B} is $-CN$. In embodiments, R^{16B} is $-COOH$. In embodiments, R^{16B} is $-CONH_2$. In embodiments, R^{16B} is $-CHX_2$. In embodiments, R^{16B} is $-CH_2X$. In embodiments, R^{16B} is unsubstituted methyl. In embodiments, R^{16B} is unsubstituted ethyl. In embodiments, R^{16B} is unsubstituted propyl. In embodiments, R^{16B} is unsubstituted isopropyl. In embodiments, R^{16B} is unsubstituted butyl. In embodiments, R^{16B} is unsubstituted tert-
25 butyl.

[0466] In embodiments, R^{16C} is hydrogen. In embodiments, R^{16C} is $-CX_3$. In
embodiments, R^{16C} is $-CN$. In embodiments, R^{16C} is $-COOH$. In embodiments, R^{16C} is $-CONH_2$. In embodiments, R^{16C} is $-CHX_2$. In embodiments, R^{16C} is $-CH_2X$. In
embodiments, R^{16C} is unsubstituted methyl. In embodiments, R^{16C} is unsubstituted ethyl. In
30 embodiments, R^{16C} is unsubstituted propyl. In embodiments, R^{16C} is unsubstituted isopropyl.

In embodiments, R^{16C} is unsubstituted butyl. In embodiments, R^{16C} is unsubstituted tert-butyl.

[0467] In embodiments, R^{16D} is hydrogen. In embodiments, R^{16D} is $-CX_3$. In embodiments, R^{16D} is $-CN$. In embodiments, R^{16D} is $-COOH$. In embodiments, R^{16D} is $-CONH_2$. In embodiments, R^{16D} is $-CHX_2$. In embodiments, R^{16D} is $-CH_2X$. In embodiments, R^{16D} is unsubstituted methyl. In embodiments, R^{16D} is unsubstituted ethyl. In embodiments, R^{16D} is unsubstituted propyl. In embodiments, R^{16D} is unsubstituted isopropyl. In embodiments, R^{16D} is unsubstituted butyl. In embodiments, R^{16D} is unsubstituted tert-butyl.

[0468] In embodiments, R^{16} is independently hydrogen, oxo, halogen, $-CX^{16}_3$, $-CHX^{16}_2$, $-OCH_2X^{16}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{16}_3$, $-OCHX^{16}_2$, R^{75} -substituted or unsubstituted alkyl, R^{75} -substituted or unsubstituted heteroalkyl, R^{75} -substituted or unsubstituted cycloalkyl, R^{75} -substituted or unsubstituted heterocycloalkyl, R^{75} -substituted or unsubstituted aryl, or R^{75} -substituted or unsubstituted heteroaryl. X^{16} is halogen. In embodiments, X^{16} is F.

[0469] R^{75} is independently oxo, halogen, $-CX^{75}_3$, $-CHX^{75}_2$, $-OCH_2X^{75}$, $-OCHX^{75}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{75}_3$, $-OCHX^{75}_2$, R^{76} -substituted or unsubstituted alkyl, R^{76} -substituted or unsubstituted heteroalkyl, R^{76} -substituted or unsubstituted cycloalkyl, R^{76} -substituted or unsubstituted heterocycloalkyl, R^{76} -substituted or unsubstituted aryl, or R^{76} -substituted or unsubstituted heteroaryl. X^{75} is halogen. In embodiments, X^{75} is F.

[0470] R^{76} is independently oxo, halogen, $-CX^{76}_3$, $-CHX^{76}_2$, $-OCH_2X^{76}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{76}_3$, $-OCHX^{76}_2$, R^{77} -substituted or unsubstituted alkyl, R^{77} -substituted or unsubstituted heteroalkyl, R^{77} -substituted or unsubstituted cycloalkyl, R^{77} -substituted or unsubstituted heterocycloalkyl, R^{77} -substituted or unsubstituted aryl, or R^{77} -substituted or unsubstituted heteroaryl. X^{76} is halogen. In embodiments, X^{76} is F.

[0471] In embodiments, R^{16A} is independently hydrogen, oxo, halogen, $-CX^{16A}_3$, $-CHX^{16A}_2$, $-OCH_2X^{16A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{16A}_3$, $-OCHX^{16A}_2$, R^{75A} -substituted or unsubstituted alkyl, R^{75A} -substituted or unsubstituted heteroalkyl, R^{75A} -substituted or unsubstituted cycloalkyl, R^{75A} -substituted or unsubstituted heterocycloalkyl, R^{75A} -substituted or unsubstituted aryl, or R^{75A} -substituted or unsubstituted heteroaryl. X^{16A} is halogen. In embodiments, X^{16A} is F.

[0472] R^{75A} is independently oxo, halogen, $-CX^{75A}_3$, $-CHX^{75A}_2$, $-OCH_2X^{75A}$, $-OCHX^{75A}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{75A}_3$, $-OCHX^{75A}_2$, R^{76A} -substituted or unsubstituted alkyl, R^{76A} -substituted or unsubstituted heteroalkyl, R^{76A} -substituted or unsubstituted cycloalkyl, R^{76A} -substituted or unsubstituted heterocycloalkyl, R^{76A} -substituted or unsubstituted aryl, or R^{76A} -substituted or unsubstituted heteroaryl. X^{75A} is halogen. In embodiments, X^{75A} is F.

[0473] R^{76A} is independently oxo, halogen, $-CX^{76A}_3$, $-CHX^{76A}_2$, $-OCH_2X^{76A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{76A}_3$, $-OCHX^{76A}_2$, R^{77A} -substituted or unsubstituted alkyl, R^{77A} -substituted or unsubstituted heteroalkyl, R^{77A} -substituted or unsubstituted cycloalkyl, R^{77A} -substituted or unsubstituted heterocycloalkyl, R^{77A} -substituted or unsubstituted aryl, or R^{77A} -substituted or unsubstituted heteroaryl. X^{76A} is halogen. In embodiments, X^{76A} is F.

[0474] In embodiments, R^{16B} is independently hydrogen, oxo, halogen, $-CX^{16B}_3$, $-CHX^{16B}_2$, $-OCH_2X^{16B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{16B}_3$, $-OCHX^{16B}_2$, R^{75B} -substituted or unsubstituted alkyl, R^{75B} -substituted or unsubstituted heteroalkyl, R^{75B} -substituted or unsubstituted cycloalkyl, R^{75B} -substituted or unsubstituted heterocycloalkyl, R^{75B} -substituted or unsubstituted aryl, or R^{75B} -substituted or unsubstituted heteroaryl. X^{16B} is halogen. In embodiments, X^{16B} is F.

[0475] R^{75B} is independently oxo,
 halogen, $-CX^{75B}_3$, $-CHX^{75B}_2$, $-OCH_2X^{75B}$, $-OCHX^{75B}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{75B}_3$, $-OCHX^{75B}_2$,
 5 R^{76B} -substituted or unsubstituted alkyl, R^{76B} -substituted or unsubstituted heteroalkyl, R^{76B} -
 substituted or unsubstituted cycloalkyl, R^{76B} -substituted or unsubstituted heterocycloalkyl,
 R^{76B} -substituted or unsubstituted aryl, or R^{76B} -substituted or unsubstituted heteroaryl. X^{75B} is
 halogen. In embodiments, X^{75B} is F.

[0476] R^{76B} is independently oxo,
 10 halogen, $-CX^{76B}_3$, $-CHX^{76B}_2$, $-OCH_2X^{76B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{76B}_3$, $-OCHX^{76B}_2$, R^{77B} -substituted or
 unsubstituted alkyl, R^{77B} -substituted or unsubstituted heteroalkyl, R^{77B} -substituted or
 unsubstituted cycloalkyl, R^{77B} -substituted or unsubstituted heterocycloalkyl, R^{77B} -substituted
 15 or unsubstituted aryl, or R^{77B} -substituted or unsubstituted heteroaryl. X^{76B} is halogen. In
 embodiments, X^{76B} is F.

[0477] In embodiments, R^{16C} is independently hydrogen, oxo,
 halogen, $-CX^{16C}_3$, $-CHX^{16C}_2$, $-OCH_2X^{16C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{16C}_3$, $-OCHX^{16C}_2$, R^{75C} -substituted or
 20 unsubstituted alkyl, R^{75C} -substituted or unsubstituted heteroalkyl, R^{75C} -substituted or
 unsubstituted cycloalkyl, R^{75C} -substituted or unsubstituted heterocycloalkyl, R^{75C} -substituted
 or unsubstituted aryl, or R^{75C} -substituted or unsubstituted heteroaryl. X^{16C} is halogen. In
 embodiments, X^{16C} is F.

[0478] R^{75C} is independently oxo,
 halogen, $-CX^{75C}_3$, $-CHX^{75C}_2$, $-OCH_2X^{75C}$, $-OCHX^{75C}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{75C}_3$, $-OCHX^{75C}_2$,
 R^{76C} -substituted or unsubstituted alkyl, R^{76C} -substituted or unsubstituted heteroalkyl, R^{76C} -
 30 substituted or unsubstituted cycloalkyl, R^{76C} -substituted or unsubstituted heterocycloalkyl,
 R^{76C} -substituted or unsubstituted aryl, or R^{76C} -substituted or unsubstituted heteroaryl. X^{75C} is
 halogen. In embodiments, X^{75C} is F.

[0479] R^{76C} is independently oxo,
 halogen, $-CX^{76C}_3$, $-CHX^{76C}_2$, $-OCH_2X^{76C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{76C}_3$, $-OCHX^{76C}_2$, R^{77C} -substituted or
 5 unsubstituted alkyl, R^{77C} -substituted or unsubstituted heteroalkyl, R^{77C} -substituted or unsubstituted cycloalkyl, R^{77C} -substituted or unsubstituted heterocycloalkyl, R^{77C} -substituted or unsubstituted aryl, or R^{77C} -substituted or unsubstituted heteroaryl. X^{76C} is halogen. In embodiments, X^{76C} is F.

[0480] In embodiments, R^{16D} is independently hydrogen, oxo,
 10 halogen, $-CX^{16D}_3$, $-CHX^{16D}_2$, $-OCH_2X^{16D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{16D}_3$, $-OCHX^{16D}_2$, R^{75D} -substituted or unsubstituted alkyl, R^{75D} -substituted or unsubstituted heteroalkyl, R^{75D} -substituted or unsubstituted cycloalkyl, R^{75D} -substituted or unsubstituted heterocycloalkyl, R^{75D} -substituted
 15 or unsubstituted aryl, or R^{75D} -substituted or unsubstituted heteroaryl. X^{16D} is halogen. In embodiments, X^{16D} is F.

[0481] R^{75D} is independently oxo,
 halogen, $-CX^{75D}_3$, $-CHX^{75D}_2$, $-OCH_2X^{75D}$, $-OCHX^{75D}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 20 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{75D}_3$, $-OCHX^{75D}_2$, R^{76D} -substituted or unsubstituted alkyl, R^{76D} -substituted or unsubstituted heteroalkyl, R^{76D} -substituted or unsubstituted cycloalkyl, R^{76D} -substituted or unsubstituted heterocycloalkyl, R^{76D} -substituted or unsubstituted aryl, or R^{76D} -substituted or unsubstituted heteroaryl. X^{75D} is halogen. In embodiments, X^{75D} is F.

[0482] R^{76D} is independently oxo,
 halogen, $-CX^{76D}_3$, $-CHX^{76D}_2$, $-OCH_2X^{76D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{76D}_3$, $-OCHX^{76D}_2$, R^{77D} -substituted or
 25 unsubstituted alkyl, R^{77D} -substituted or unsubstituted heteroalkyl, R^{77D} -substituted or unsubstituted cycloalkyl, R^{77D} -substituted or unsubstituted heterocycloalkyl, R^{77D} -substituted or unsubstituted aryl, or R^{77D} -substituted or unsubstituted heteroaryl. X^{76D} is halogen. In
 30 embodiments, X^{76D} is F.

[0483] In embodiments, R^{17} is hydrogen. In embodiments, R^{17} is halogen. In
embodiments, R^{17} is CX^{17}_3 . In embodiments, R^{17} is $-CHX^{17}_2$. In embodiments, R^{17} is -
 CH_2X^{17} . In embodiments, R^{17} is $-CN$. In embodiments, R^{17} is $-SO_{n17}R^{17D}$. In embodiments,
 R^{17} is $-SO_{v17}NR^{17A}R^{17B}$. In embodiments, R^{17} is $-NHNr^{17A}R^{17B}$. In embodiments, R^{17} is
5 $-ONR^{17A}R^{17B}$. In embodiments, R^{17} is $-NHC(O)NHNr^{17A}R^{17B}$. In embodiments, R^{17} is
 $-NHC(O)NR^{17A}R^{17B}$. In embodiments, R^{17} is $-N(O)_{m17}$. In embodiments, R^{17} is $-NR^{17A}R^{17B}$.
In embodiments, R^{17} is $-C(O)R^{17C}$. In embodiments, R^{17} is $-C(O)-OR^{17C}$. In embodiments,
 R^{17} is $-C(O)NR^{17A}R^{17B}$. In embodiments, R^{17} is $-OR^{17D}$. In embodiments, R^{17} is -
 $NR^{17A}SO_2R^{17D}$. In embodiments, R^{17} is $-NR^{17A}C(O)R^{17C}$. In embodiments, R^{17} is -
10 $NR^{17A}C(O)OR^{17C}$. In embodiments, R^{17} is $-NR^{17A}OR^{17C}$. In embodiments, R^{17} is $-OCX^{17}_3$.
In embodiments, R^{17} is $-OCHX^{17}_2$. In embodiments, R^{17} is substituted or unsubstituted alkyl.
In embodiments, R^{17} is substituted or unsubstituted heteroalkyl. In embodiments, R^{17} is
substituted or unsubstituted cycloalkyl. In embodiments, R^{17} is substituted or unsubstituted
heterocycloalkyl. In embodiments, R^{17} is substituted or unsubstituted aryl. In embodiments,
15 R^{17} is substituted or unsubstituted heteroaryl. In embodiments, R^{17} is substituted alkyl. In
embodiments, R^{17} is substituted heteroalkyl. In embodiments, R^{17} is substituted cycloalkyl.
In embodiments, R^{17} is substituted heterocycloalkyl. In embodiments, R^{17} is substituted aryl.
In embodiments, R^{17} is substituted heteroaryl. In embodiments, R^{17} is unsubstituted alkyl. In
embodiments, R^{17} is unsubstituted heteroalkyl. In embodiments, R^{17} is unsubstituted
20 cycloalkyl. In embodiments, R^{17} is unsubstituted heterocycloalkyl. In embodiments, R^{17} is
unsubstituted aryl. In embodiments, R^{17} is unsubstituted heteroaryl. In embodiments, R^{17} is
unsubstituted methyl. In embodiments, R^{17} is unsubstituted ethyl. In embodiments, R^{17} is
unsubstituted propyl. In embodiments, R^{17} is unsubstituted isopropyl. In embodiments, R^{17}
is unsubstituted butyl. In embodiments, R^{17} is unsubstituted tert-butyl.

25 **[0484]** In embodiments, R^{17A} is hydrogen. In embodiments, R^{17A} is $-CX_3$. In
embodiments, R^{17A} is $-CN$. In embodiments, R^{17A} is $-COOH$. In embodiments, R^{17A}
is $-CONH_2$. In embodiments, R^{17A} is $-CHX_2$. In embodiments, R^{17A} is $-CH_2X$. In
embodiments, R^{17A} is unsubstituted methyl. In embodiments, R^{17A} is unsubstituted ethyl. In
embodiments, R^{17A} is unsubstituted propyl. In embodiments, R^{17A} is unsubstituted isopropyl.
30 In embodiments, R^{17A} is unsubstituted butyl. In embodiments, R^{17A} is unsubstituted tert-
butyl.

[0485] In embodiments, R^{17B} is hydrogen. In embodiments, R^{17B} is $-CX_3$. In
embodiments, R^{17B} is $-CN$. In embodiments, R^{17B} is $-COOH$. In embodiments, R^{17B}
is $-CONH_2$. In embodiments, R^{17B} is $-CHX_2$. In embodiments, R^{17B} is $-CH_2X$. In

embodiments, R^{17B} is unsubstituted methyl. In embodiments, R^{17B} is unsubstituted ethyl. In embodiments, R^{17B} is unsubstituted propyl. In embodiments, R^{17B} is unsubstituted isopropyl. In embodiments, R^{17B} is unsubstituted butyl. In embodiments, R^{17B} is unsubstituted tert-butyl.

- 5 **[0486]** In embodiments, R^{17C} is hydrogen. In embodiments, R^{17C} is $-CX_3$. In embodiments, R^{17C} is $-CN$. In embodiments, R^{17C} is $-COOH$. In embodiments, R^{17C} is $-CONH_2$. In embodiments, R^{17C} is $-CHX_2$. In embodiments, R^{17C} is $-CH_2X$. In embodiments, R^{17C} is unsubstituted methyl. In embodiments, R^{17C} is unsubstituted ethyl. In embodiments, R^{17C} is unsubstituted propyl. In embodiments, R^{17C} is unsubstituted isopropyl.
- 10 In embodiments, R^{17C} is unsubstituted butyl. In embodiments, R^{17C} is unsubstituted tert-butyl.

- [0487]** In embodiments, R^{17D} is hydrogen. In embodiments, R^{17D} is $-CX_3$. In embodiments, R^{17D} is $-CN$. In embodiments, R^{17D} is $-COOH$. In embodiments, R^{17D} is $-CONH_2$. In embodiments, R^{17D} is $-CHX_2$. In embodiments, R^{17D} is $-CH_2X$. In
- 15 embodiments, R^{17D} is unsubstituted methyl. In embodiments, R^{17D} is unsubstituted ethyl. In embodiments, R^{17D} is unsubstituted propyl. In embodiments, R^{17D} is unsubstituted isopropyl. In embodiments, R^{17D} is unsubstituted butyl. In embodiments, R^{17D} is unsubstituted tert-butyl.

- [0488]** In embodiments, R^{17} is independently hydrogen, oxo,
- 20 halogen, $-CX^{17}_3$, $-CHX^{17}_2$, $-OCH_2X^{17}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(=O)NHNH_2$, $-NHC(=O)NH_2$, $-NHSO_2H$, $-NHC(=O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{17}_3$, $-OCHX^{17}_2$, R^{78} -substituted or unsubstituted alkyl, R^{78} -substituted or unsubstituted heteroalkyl, R^{78} -substituted or unsubstituted cycloalkyl, R^{78} -substituted or unsubstituted heterocycloalkyl, R^{78} -substituted or
- 25 unsubstituted aryl, or R^{78} -substituted or unsubstituted heteroaryl. X^{17} is halogen. In embodiments, X^{17} is F.

- [0489]** R^{78} is independently oxo,
- halogen, $-CX^{78}_3$, $-CHX^{78}_2$, $-OCH_2X^{78}$, $-OCHX^{78}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(=O)NHNH_2$, $-NHC(=O)NH_2$, $-NHSO_2H$, $-NHC(=O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{78}_3$, $-OCHX^{78}_2$, R^{79} -substituted or
- 30 unsubstituted alkyl, R^{79} -substituted or unsubstituted heteroalkyl, R^{79} -substituted or unsubstituted cycloalkyl, R^{79} -substituted or unsubstituted heterocycloalkyl, R^{79} -substituted or

unsubstituted aryl, or R^{79} -substituted or unsubstituted heteroaryl. X^{78} is halogen. In
embodiments, X^{78} is F.

[0490] R^{79} is independently oxo,

halogen, $-CX^{79}_3$, $-CHX^{79}_2$, $-OCH_2X^{79}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{79}_3$, $-OCHX^{79}_2$, R^{80} -substituted or

unsubstituted alkyl, R^{80} -substituted or unsubstituted heteroalkyl, R^{80} -substituted or

unsubstituted cycloalkyl, R^{80} -substituted or unsubstituted heterocycloalkyl, R^{80} -substituted or

unsubstituted aryl, or R^{80} -substituted or unsubstituted heteroaryl. X^{79} is halogen. In

10 embodiments, X^{79} is F.

[0491] In embodiments, R^{17A} is independently hydrogen, oxo,

halogen, $-CX^{17A}_3$, $-CHX^{17A}_2$, $-OCH_2X^{17A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{17A}_3$, $-OCHX^{17A}_2$, R^{78A} -substituted or

15 unsubstituted alkyl, R^{78A} -substituted or unsubstituted heteroalkyl, R^{78A} -substituted or

unsubstituted cycloalkyl, R^{78A} -substituted or unsubstituted heterocycloalkyl, R^{78A} -substituted

or unsubstituted aryl, or R^{78A} -substituted or unsubstituted heteroaryl. X^{17A} is halogen. In

embodiments, X^{17A} is F.

[0492] R^{78A} is independently oxo,

20 halogen, $-CX^{78A}_3$, $-CHX^{78A}_2$, $-OCH_2X^{78A}$, $-OCHX^{78A}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,

$-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{78A}_3$, $-OCHX^{78A}_2$,

R^{79A} -substituted or unsubstituted alkyl, R^{79A} -substituted or unsubstituted heteroalkyl, R^{79A} -

substituted or unsubstituted cycloalkyl, R^{79A} -substituted or unsubstituted heterocycloalkyl,

25 R^{79A} -substituted or unsubstituted aryl, or R^{79A} -substituted or unsubstituted heteroaryl. X^{78A} is

halogen. In embodiments, X^{78A} is F.

[0493] R^{79A} is independently oxo,

halogen, $-CX^{79A}_3$, $-CHX^{79A}_2$, $-OCH_2X^{79A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

30 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{79A}_3$, $-OCHX^{79A}_2$, R^{80A} -substituted or

unsubstituted alkyl, R^{80A} -substituted or unsubstituted heteroalkyl, R^{80A} -substituted or

unsubstituted cycloalkyl, R^{80A} -substituted or unsubstituted heterocycloalkyl, R^{80A} -substituted

or unsubstituted aryl, or R^{80A} -substituted or unsubstituted heteroaryl. X^{79A} is halogen. In
embodiments, X^{79A} is F.

[0494] In embodiments, R^{17B} is independently hydrogen, oxo,
halogen, $-CX^{17B}_3$, $-CHX^{17B}_2$, $-OCH_2X^{17B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{17B}_3$, $-OCHX^{17B}_2$, R^{78B} -substituted or
unsubstituted alkyl, R^{78B} -substituted or unsubstituted heteroalkyl, R^{78B} -substituted or
unsubstituted cycloalkyl, R^{78B} -substituted or unsubstituted heterocycloalkyl, R^{78B} -substituted
or unsubstituted aryl, or R^{78B} -substituted or unsubstituted heteroaryl. X^{17B} is halogen. In
10 embodiments, X^{17B} is F.

[0495] R^{78B} is independently oxo,
halogen, $-CX^{78B}_3$, $-CHX^{78B}_2$, $-OCH_2X^{78B}$, $-OCHX^{78B}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -
 NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{78B}_3$, $-OCHX^{78B}_2$,
15 R^{79B} -substituted or unsubstituted alkyl, R^{79B} -substituted or unsubstituted heteroalkyl, R^{79B} -
substituted or unsubstituted cycloalkyl, R^{79B} -substituted or unsubstituted heterocycloalkyl,
 R^{79B} -substituted or unsubstituted aryl, or R^{79B} -substituted or unsubstituted heteroaryl. X^{78B} is
halogen. In embodiments, X^{78B} is F.

[0496] R^{79B} is independently oxo,
20 halogen, $-CX^{79B}_3$, $-CHX^{79B}_2$, $-OCH_2X^{79B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{79B}_3$, $-OCHX^{79B}_2$, R^{80B} -substituted or
unsubstituted alkyl, R^{80B} -substituted or unsubstituted heteroalkyl, R^{80B} -substituted or
unsubstituted cycloalkyl, R^{80B} -substituted or unsubstituted heterocycloalkyl, R^{80B} -substituted
25 or unsubstituted aryl, or R^{80B} -substituted or unsubstituted heteroaryl. X^{79B} is halogen. In
embodiments, X^{79B} is F.

[0497] In embodiments, R^{17C} is independently hydrogen, oxo,
halogen, $-CX^{17C}_3$, $-CHX^{17C}_2$, $-OCH_2X^{17C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
30 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{17C}_3$, $-OCHX^{17C}_2$, R^{78C} -substituted or
unsubstituted alkyl, R^{78C} -substituted or unsubstituted heteroalkyl, R^{78C} -substituted or
unsubstituted cycloalkyl, R^{78C} -substituted or unsubstituted heterocycloalkyl, R^{78C} -substituted

or unsubstituted aryl, or R^{78C} -substituted or unsubstituted heteroaryl. X^{17C} is halogen. In embodiments, X^{17C} is F.

[0498] R^{78C} is independently oxo,

halogen, $-CX^{78C}_3$, $-CHX^{78C}_2$, $-OCH_2X^{78C}$, $-OCHX^{78C}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

5 NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{78C}_3$, $-OCHX^{78C}_2$,
 R^{79C} -substituted or unsubstituted alkyl, R^{79C} -substituted or unsubstituted heteroalkyl, R^{79C} -
substituted or unsubstituted cycloalkyl, R^{79C} -substituted or unsubstituted heterocycloalkyl,
 R^{79C} -substituted or unsubstituted aryl, or R^{79C} -substituted or unsubstituted heteroaryl. X^{78C} is
10 halogen. In embodiments, X^{78C} is F.

[0499] R^{79C} is independently oxo,

halogen, $-CX^{79C}_3$, $-CHX^{79C}_2$, $-OCH_2X^{79C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{79C}_3$, $-OCHX^{79C}_2$, R^{80C} -substituted or

15 unsubstituted alkyl, R^{80C} -substituted or unsubstituted heteroalkyl, R^{80C} -substituted or
unsubstituted cycloalkyl, R^{80C} -substituted or unsubstituted heterocycloalkyl, R^{80C} -substituted
or unsubstituted aryl, or R^{80C} -substituted or unsubstituted heteroaryl. X^{79C} is halogen. In
embodiments, X^{79C} is F.

[0500] In embodiments, R^{17D} is independently hydrogen, oxo,

20 halogen, $-CX^{17D}_3$, $-CHX^{17D}_2$, $-OCH_2X^{17D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{17D}_3$, $-OCHX^{17D}_2$, R^{78D} -substituted or

unsubstituted alkyl, R^{78D} -substituted or unsubstituted heteroalkyl, R^{78D} -substituted or

unsubstituted cycloalkyl, R^{78D} -substituted or unsubstituted heterocycloalkyl, R^{78D} -substituted

25 or unsubstituted aryl, or R^{78D} -substituted or unsubstituted heteroaryl. X^{17D} is halogen. In
embodiments, X^{17D} is F.

[0501] R^{78D} is independently oxo,

halogen, $-CX^{78D}_3$, $-CHX^{78D}_2$, $-OCH_2X^{78D}$, $-OCHX^{78D}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,

30 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{78D}_3$, $-OCHX^{78D}_2$,

R^{79D} -substituted or unsubstituted alkyl, R^{79D} -substituted or unsubstituted heteroalkyl, R^{79D} -

substituted or unsubstituted cycloalkyl, R^{79D} -substituted or unsubstituted heterocycloalkyl,

R^{79D} -substituted or unsubstituted aryl, or R^{79D} -substituted or unsubstituted heteroaryl. X^{78D} is halogen. In embodiments, X^{78D} is F.

[0502] R^{79D} is independently oxo,

halogen, $-CX^{79D}_3$, $-CHX^{79D}_2$, $-OCH_2X^{79D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, -

$NHSO_2H$, $-NHC(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{79D}_3$, $-OCHX^{79D}_2$, R^{80D} -substituted or

unsubstituted alkyl, R^{80D} -substituted or unsubstituted heteroalkyl, R^{80D} -substituted or

unsubstituted cycloalkyl, R^{80D} -substituted or unsubstituted heterocycloalkyl, R^{80D} -substituted

or unsubstituted aryl, or R^{80D} -substituted or unsubstituted heteroaryl. X^{79D} is halogen. In

10 embodiments, X^{79D} is F.

[0503] In embodiments, R^{18} is hydrogen. In embodiments, R^{18} is halogen. In

embodiments, R^{18} is CX^{18}_3 . In embodiments, R^{18} is $-CHX^{18}_2$. In embodiments, R^{18} is -

CH_2X^{18} . In embodiments, R^{18} is $-CN$. In embodiments, R^{18} is $-SO_{n18}R^{18D}$. In embodiments,

R^{18} is $-SO_{v18}NR^{18A}R^{18B}$. In embodiments, R^{18} is $-NHNR^{18A}R^{18B}$. In embodiments, R^{18} is

15 $-ONR^{18A}R^{18B}$. In embodiments, R^{18} is $-NHC(O)NHNR^{18A}R^{18B}$. In embodiments, R^{18} is

$-NHC(O)NR^{18A}R^{18B}$. In embodiments, R^{18} is $-N(O)_{m18}$. In embodiments, R^{18} is $-NR^{18A}R^{18B}$.

In embodiments, R^{18} is $-C(O)R^{18C}$. In embodiments, R^{18} is $-C(O)-OR^{18C}$. In embodiments,

R^{18} is $-C(O)NR^{18A}R^{18B}$. In embodiments, R^{18} is $-OR^{18D}$. In embodiments, R^{18} is -

$NR^{18A}SO_2R^{18D}$. In embodiments, R^{18} is $-NR^{18A}C(O)R^{18C}$. In embodiments, R^{18} is -

20 $NR^{18A}C(O)OR^{18C}$. In embodiments, R^{18} is $-NR^{18A}OR^{18C}$. In embodiments, R^{18} is $-OCX^{18}_3$.

In embodiments, R^{18} is $-OCHX^{18}_2$. In embodiments, R^{18} is substituted or unsubstituted alkyl.

In embodiments, R^{18} is substituted or unsubstituted heteroalkyl. In embodiments, R^{18} is

substituted or unsubstituted cycloalkyl. In embodiments, R^{18} is substituted or unsubstituted

heterocycloalkyl. In embodiments, R^{18} is substituted or unsubstituted aryl. In embodiments,

25 R^{18} is substituted or unsubstituted heteroaryl. In embodiments, R^{18} is substituted alkyl. In

embodiments, R^{18} is substituted heteroalkyl. In embodiments, R^{18} is substituted cycloalkyl.

In embodiments, R^{18} is substituted heterocycloalkyl. In embodiments, R^{18} is substituted aryl.

In embodiments, R^{18} is substituted heteroaryl. In embodiments, R^{18} is unsubstituted alkyl. In

embodiments, R^{18} is unsubstituted heteroalkyl. In embodiments, R^{18} is unsubstituted

30 cycloalkyl. In embodiments, R^{18} is unsubstituted heterocycloalkyl. In embodiments, R^{18} is

unsubstituted aryl. In embodiments, R^{18} is unsubstituted heteroaryl. In embodiments, R^{18} is

unsubstituted methyl. In embodiments, R^{18} is unsubstituted ethyl. In embodiments, R^{18} is

unsubstituted propyl. In embodiments, R^{18} is unsubstituted isopropyl. In embodiments, R^{18}

is unsubstituted butyl. In embodiments, R^{18} is unsubstituted tert-butyl.

[0504] In embodiments, R^{18A} is hydrogen. In embodiments, R^{18A} is $-CX_3$. In
embodiments, R^{18A} is $-CN$. In embodiments, R^{18A} is $-COOH$. In embodiments, R^{18A}
is $-CONH_2$. In embodiments, R^{18A} is $-CHX_2$. In embodiments, R^{18A} is $-CH_2X$. In
embodiments, R^{18A} is unsubstituted methyl. In embodiments, R^{18A} is unsubstituted ethyl. In
5 embodiments, R^{18A} is unsubstituted propyl. In embodiments, R^{18A} is unsubstituted isopropyl.
In embodiments, R^{18A} is unsubstituted butyl. In embodiments, R^{18A} is unsubstituted tert-
butyl.

[0505] In embodiments, R^{18B} is hydrogen. In embodiments, R^{18B} is $-CX_3$. In
embodiments, R^{18B} is $-CN$. In embodiments, R^{18B} is $-COOH$. In embodiments, R^{18B}
10 is $-CONH_2$. In embodiments, R^{18B} is $-CHX_2$. In embodiments, R^{18B} is $-CH_2X$. In
embodiments, R^{18B} is unsubstituted methyl. In embodiments, R^{18B} is unsubstituted ethyl. In
embodiments, R^{18B} is unsubstituted propyl. In embodiments, R^{18B} is unsubstituted isopropyl.
In embodiments, R^{18B} is unsubstituted butyl. In embodiments, R^{18B} is unsubstituted tert-
butyl.

[0506] In embodiments, R^{18C} is hydrogen. In embodiments, R^{18C} is $-CX_3$. In
embodiments, R^{18C} is $-CN$. In embodiments, R^{18C} is $-COOH$. In embodiments, R^{18C}
15 is $-CONH_2$. In embodiments, R^{18C} is $-CHX_2$. In embodiments, R^{18C} is $-CH_2X$. In
embodiments, R^{18C} is unsubstituted methyl. In embodiments, R^{18C} is unsubstituted ethyl. In
embodiments, R^{18C} is unsubstituted propyl. In embodiments, R^{18C} is unsubstituted isopropyl.
20 In embodiments, R^{18C} is unsubstituted butyl. In embodiments, R^{18C} is unsubstituted tert-
butyl.

[0507] In embodiments, R^{18D} is hydrogen. In embodiments, R^{18D} is $-CX_3$. In
embodiments, R^{18D} is $-CN$. In embodiments, R^{18D} is $-COOH$. In embodiments, R^{18D}
25 is $-CONH_2$. In embodiments, R^{18D} is $-CHX_2$. In embodiments, R^{18D} is $-CH_2X$. In
embodiments, R^{18D} is unsubstituted methyl. In embodiments, R^{18D} is unsubstituted ethyl. In
embodiments, R^{18D} is unsubstituted propyl. In embodiments, R^{18D} is unsubstituted isopropyl.
In embodiments, R^{18D} is unsubstituted butyl. In embodiments, R^{18D} is unsubstituted tert-
butyl.

[0508] In embodiments, R^{18} is independently hydrogen, oxo,
30 halogen, $-CX^{18}_3$, $-CHX^{18}_2$, $-OCH_2X^{18}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-$
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-$
 $NHSO_2H$, $-NHC(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{18}_3$, $-OCHX^{18}_2$, R^{81} -substituted or
unsubstituted alkyl, R^{81} -substituted or unsubstituted heteroalkyl, R^{81} -substituted or

unsubstituted cycloalkyl, R^{81} -substituted or unsubstituted heterocycloalkyl, R^{81} -substituted or unsubstituted aryl, or R^{81} -substituted or unsubstituted heteroaryl. X^{18} is halogen. In embodiments, X^{18} is F.

[0509] R^{81} is independently oxo,

5 halogen, $-CX^{81}_3$, $-CHX^{81}_2$, $-OCH_2X^{81}$, $-OCHX^{81}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{81}_3$, $-OCHX^{81}_2$, R^{82} -substituted or unsubstituted alkyl, R^{82} -substituted or unsubstituted heteroalkyl, R^{82} -substituted or unsubstituted cycloalkyl, R^{82} -substituted or unsubstituted heterocycloalkyl, R^{82} -substituted or
10 unsubstituted aryl, or R^{82} -substituted or unsubstituted heteroaryl. X^{81} is halogen. In embodiments, X^{81} is F.

[0510] R^{82} is independently oxo,

halogen, $-CX^{82}_3$, $-CHX^{82}_2$, $-OCH_2X^{82}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{82}_3$, $-OCHX^{82}_2$, R^{83} -substituted or
15 unsubstituted alkyl, R^{83} -substituted or unsubstituted heteroalkyl, R^{83} -substituted or unsubstituted cycloalkyl, R^{83} -substituted or unsubstituted heterocycloalkyl, R^{83} -substituted or unsubstituted aryl, or R^{83} -substituted or unsubstituted heteroaryl. X^{82} is halogen. In embodiments, X^{82} is F.

20 **[0511]** In embodiments, R^{18A} is independently hydrogen, oxo,

halogen, $-CX^{18A}_3$, $-CHX^{18A}_2$, $-OCH_2X^{18A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{18A}_3$, $-OCHX^{18A}_2$, R^{81A} -substituted or
unsubstituted alkyl, R^{81A} -substituted or unsubstituted heteroalkyl, R^{81A} -substituted or
25 unsubstituted cycloalkyl, R^{81A} -substituted or unsubstituted heterocycloalkyl, R^{81A} -substituted or unsubstituted aryl, or R^{81A} -substituted or unsubstituted heteroaryl. X^{18A} is halogen. In embodiments, X^{18A} is F.

[0512] R^{81A} is independently oxo,

halogen, $-CX^{81A}_3$, $-CHX^{81A}_2$, $-OCH_2X^{81A}$, $-OCHX^{81A}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
30 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{81A}_3$, $-OCHX^{81A}_2$, R^{82A} -substituted or unsubstituted alkyl, R^{82A} -substituted or unsubstituted heteroalkyl, R^{82A} -substituted or unsubstituted cycloalkyl, R^{82A} -substituted or unsubstituted heterocycloalkyl,

R^{82A} -substituted or unsubstituted aryl, or R^{82A} -substituted or unsubstituted heteroaryl. X^{81A} is halogen. In embodiments, X^{81A} is F.

[0513] R^{82A} is independently oxo,

halogen, $-CX^{82A}_3$, $-CHX^{82A}_2$, $-OCH_2X^{82A}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{82A}_3$, $-OCHX^{82A}_2$, R^{83A} -substituted or

unsubstituted alkyl, R^{83A} -substituted or unsubstituted heteroalkyl, R^{83A} -substituted or

unsubstituted cycloalkyl, R^{83A} -substituted or unsubstituted heterocycloalkyl, R^{83A} -substituted

or unsubstituted aryl, or R^{83A} -substituted or unsubstituted heteroaryl. X^{82A} is halogen. In

10 embodiments, X^{82A} is F.

[0514] In embodiments, R^{18B} is independently hydrogen, oxo,

halogen, $-CX^{18B}_3$, $-CHX^{18B}_2$, $-OCH_2X^{18B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{18B}_3$, $-OCHX^{18B}_2$, R^{81B} -substituted or

15 unsubstituted alkyl, R^{81B} -substituted or unsubstituted heteroalkyl, R^{81B} -substituted or

unsubstituted cycloalkyl, R^{81B} -substituted or unsubstituted heterocycloalkyl, R^{81B} -substituted

or unsubstituted aryl, or R^{81B} -substituted or unsubstituted heteroaryl. X^{18B} is halogen. In

embodiments, X^{18B} is F.

[0515] R^{81B} is independently oxo,

20 halogen, $-CX^{81B}_3$, $-CHX^{81B}_2$, $-OCH_2X^{81B}$, $-OCHX^{81B}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,

$-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{81B}_3$, $-OCHX^{81B}_2$,

R^{82B} -substituted or unsubstituted alkyl, R^{82B} -substituted or unsubstituted heteroalkyl, R^{82B} -

substituted or unsubstituted cycloalkyl, R^{82B} -substituted or unsubstituted heterocycloalkyl,

25 R^{82B} -substituted or unsubstituted aryl, or R^{82B} -substituted or unsubstituted heteroaryl. X^{81B} is

halogen. In embodiments, X^{81B} is F.

[0516] R^{82B} is independently oxo,

halogen, $-CX^{82B}_3$, $-CHX^{82B}_2$, $-OCH_2X^{82B}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

30 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{82B}_3$, $-OCHX^{82B}_2$, R^{83B} -substituted or

unsubstituted alkyl, R^{83B} -substituted or unsubstituted heteroalkyl, R^{83B} -substituted or

unsubstituted cycloalkyl, R^{83B} -substituted or unsubstituted heterocycloalkyl, R^{83B} -substituted

or unsubstituted aryl, or R^{83B} -substituted or unsubstituted heteroaryl. X^{82B} is halogen. In
embodiments, X^{82B} is F.

[0517] In embodiments, R^{18C} is independently hydrogen, oxo,
halogen, $-CX^{18C}_3$, $-CHX^{18C}_2$, $-OCH_2X^{18C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
5 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{18C}_3$, $-OCHX^{18C}_2$, R^{81C} -substituted or
unsubstituted alkyl, R^{81C} -substituted or unsubstituted heteroalkyl, R^{81C} -substituted or
unsubstituted cycloalkyl, R^{81C} -substituted or unsubstituted heterocycloalkyl, R^{81C} -substituted
or unsubstituted aryl, or R^{81C} -substituted or unsubstituted heteroaryl. X^{18C} is halogen. In
10 embodiments, X^{18C} is F.

[0518] R^{81C} is independently oxo,
halogen, $-CX^{81C}_3$, $-CHX^{81C}_2$, $-OCH_2X^{81C}$, $-OCHX^{81C}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -
 NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,
 $-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{81C}_3$, $-OCHX^{81C}_2$,
15 R^{82C} -substituted or unsubstituted alkyl, R^{82C} -substituted or unsubstituted heteroalkyl, R^{82C} -
substituted or unsubstituted cycloalkyl, R^{82C} -substituted or unsubstituted heterocycloalkyl,
 R^{82C} -substituted or unsubstituted aryl, or R^{82C} -substituted or unsubstituted heteroaryl. X^{81C} is
halogen. In embodiments, X^{81C} is F.

[0519] R^{82C} is independently oxo,
20 halogen, $-CX^{82C}_3$, $-CHX^{82C}_2$, $-OCH_2X^{82C}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{82C}_3$, $-OCHX^{82C}_2$, R^{83C} -substituted or
unsubstituted alkyl, R^{83C} -substituted or unsubstituted heteroalkyl, R^{83C} -substituted or
unsubstituted cycloalkyl, R^{83C} -substituted or unsubstituted heterocycloalkyl, R^{83C} -substituted
25 or unsubstituted aryl, or R^{83C} -substituted or unsubstituted heteroaryl. X^{82C} is halogen. In
embodiments, X^{82C} is F.

[0520] In embodiments, R^{18D} is independently hydrogen, oxo,
halogen, $-CX^{18D}_3$, $-CHX^{18D}_2$, $-OCH_2X^{18D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -
 SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -
30 $NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{18D}_3$, $-OCHX^{18D}_2$, R^{81D} -substituted or
unsubstituted alkyl, R^{81D} -substituted or unsubstituted heteroalkyl, R^{81D} -substituted or
unsubstituted cycloalkyl, R^{81D} -substituted or unsubstituted heterocycloalkyl, R^{81D} -substituted

or unsubstituted aryl, or R^{81D} -substituted or unsubstituted heteroaryl. X^{18D} is halogen. In embodiments, X^{18D} is F.

[0521] R^{81D} is independently oxo,

halogen, $-CX^{81D}_3$, $-CHX^{81D}_2$, $-OCH_2X^{81D}$, $-OCHX^{81D}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

5 NO_2 , $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$,

$-NHC=(O)NH_2$, $-NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{81D}_3$, $-OCHX^{81D}_2$,

R^{82D} -substituted or unsubstituted alkyl, R^{82D} -substituted or unsubstituted heteroalkyl, R^{82D} -

substituted or unsubstituted cycloalkyl, R^{82D} -substituted or unsubstituted heterocycloalkyl,

R^{82D} -substituted or unsubstituted aryl, or R^{82D} -substituted or unsubstituted heteroaryl. X^{81D} is

10 halogen. In embodiments, X^{81D} is F.

[0522] R^{82D} is independently oxo,

halogen, $-CX^{82D}_3$, $-CHX^{82D}_2$, $-OCH_2X^{82D}$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, -

SO_3H , $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC=(O)NHNH_2$, $-NHC=(O)NH_2$, -

$NHSO_2H$, $-NHC=(O)H$, $-NHC(O)-OH$, $-NHOH$, $-OCX^{82D}_3$, $-OCHX^{82D}_2$, R^{83D} -substituted or

15 unsubstituted alkyl, R^{83D} -substituted or unsubstituted heteroalkyl, R^{83D} -substituted or

unsubstituted cycloalkyl, R^{83D} -substituted or unsubstituted heterocycloalkyl, R^{83D} -substituted

or unsubstituted aryl, or R^{83D} -substituted or unsubstituted heteroaryl. X^{82D} is halogen. In

embodiments, X^{82D} is F.

[0523] R^{74} , R^{77} , R^{80} , R^{83} , R^{74A} , R^{77A} , R^{80A} , R^{83A} , R^{74B} , R^{77B} , R^{80B} , R^{83B} , R^{74C} , R^{77C} , R^{80C} ,

20 R^{83C} , R^{74D} , R^{77D} , R^{80D} , and R^{83D} are independently hydrogen, oxo,

halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-S$

O_4H , $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$,

$-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF$

25 $_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted cycloalkyl, unsubstituted

heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In embodiments, R^{74} , R^{77} ,

R^{80} , R^{83} , R^{74A} , R^{77A} , R^{80A} , R^{83A} , R^{74B} , R^{77B} , R^{80B} , R^{83B} , R^{74C} , R^{77C} , R^{80C} , R^{83C} , R^{74D} , R^{77D} ,

R^{80D} , and R^{83D} are independently oxo,

halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$,

30 $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$,

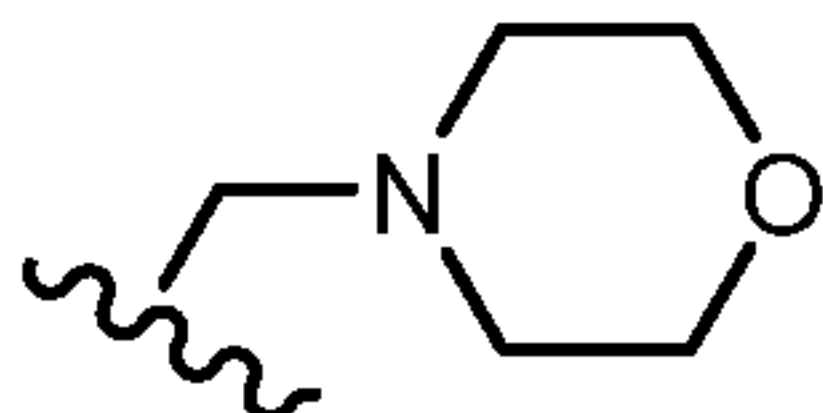
$-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted

cycloalkyl, unsubstituted heterocycloalkyl, unsubstituted aryl, or unsubstituted heteroaryl. In

embodiments, R^{74} , R^{77} , R^{80} , R^{83} , R^{74A} , R^{77A} , R^{80A} , R^{83A} , R^{74B} , R^{77B} , R^{80B} , R^{83B} , R^{74C} , R^{77C} ,

R^{80C} , R^{83C} , R^{74D} , R^{77D} , R^{80D} , R^{83D} , and R^{86} are independently oxo, halogen, $-CF_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCF_3$, $-OCHF_2$, unsubstituted C_1 - C_8 alkyl, unsubstituted 2 to 8 membered
 5 heteroalkyl, unsubstituted C_3 - C_8 cycloalkyl, unsubstituted 3 to 6 membered heterocycloalkyl, unsubstituted phenyl, or unsubstituted 5 to 6 membered heteroaryl.

[0524] In embodiments, R^{15} , R^{16} , R^{17} , and R^{18} are hydrogen. In embodiments, R^{15} is

hydrogen. In embodiments, R^{16} is hydrogen, $-CH_3$, $-CH_2NR^{16A}R^{16B}$, or . In

embodiments, R^{17} is hydrogen. In embodiments, R^{16A} and R^{16B} are independently hydrogen

10 or unsubstituted alkyl. In embodiments, R^{16A} and R^{16B} are independently unsubstituted

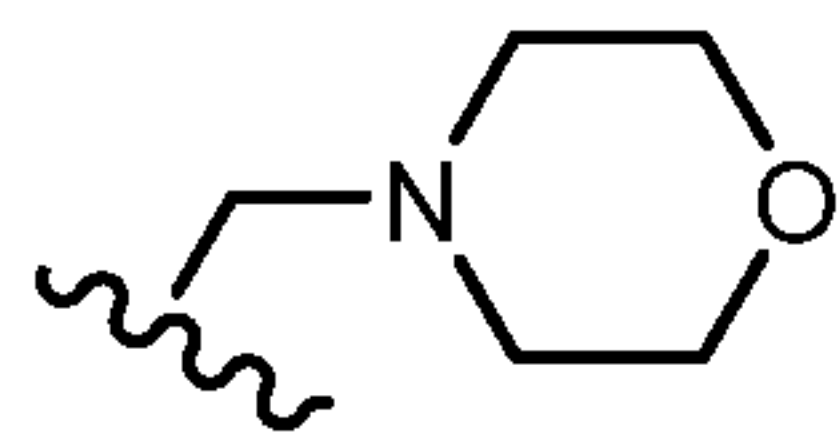
methyl. In embodiments, R^{16A} is independently hydrogen. In embodiments, R^{16A} is

independently unsubstituted alkyl. In embodiments, R^{16B} is independently hydrogen. In

embodiments, R^{16B} is independently unsubstituted alkyl. In embodiments, R^{16A} is

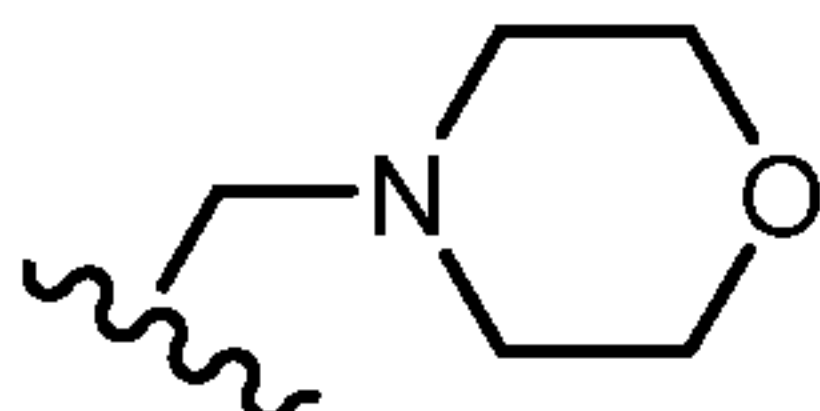
independently unsubstituted methyl. In embodiments, R^{16B} is independently unsubstituted

15 methyl. In embodiments, R^{15} is hydrogen; R^{16} is hydrogen, $-CH_3$, $-CH_2NR^{16A}R^{16B}$, or



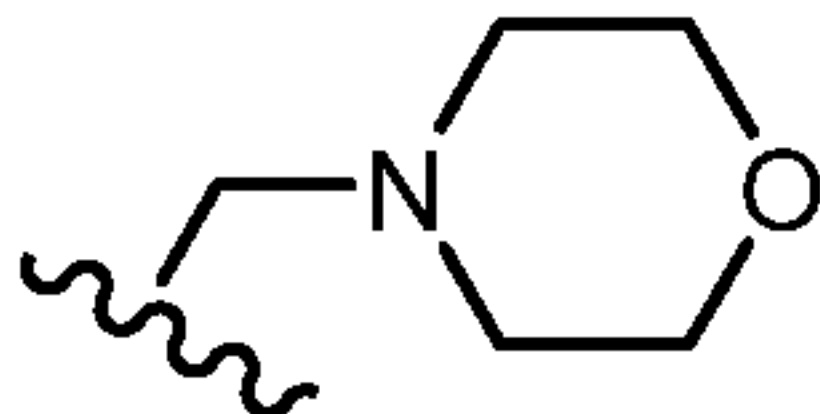
; R^{17} is hydrogen; and R^{16A} and R^{16B} are independently hydrogen or unsubstituted alkyl.

[0525] In embodiments, R^{15} is hydrogen. In embodiments, R^{16} is hydrogen. In

embodiments, R^{17} is hydrogen, $-CH_3$, $-CH_2NR^{17A}R^{17B}$, or . In embodiments,

20 R^{17A} and R^{17B} are independently hydrogen or unsubstituted alkyl. In embodiments, R^{17A} and

R^{17B} are independently unsubstituted methyl. In embodiments, R^{15} is hydrogen; R^{16} is

hydrogen; R^{17} is hydrogen, $-CH_3$, $-CH_2NR^{17A}R^{17B}$, or ; and R^{17A} and R^{17B} are

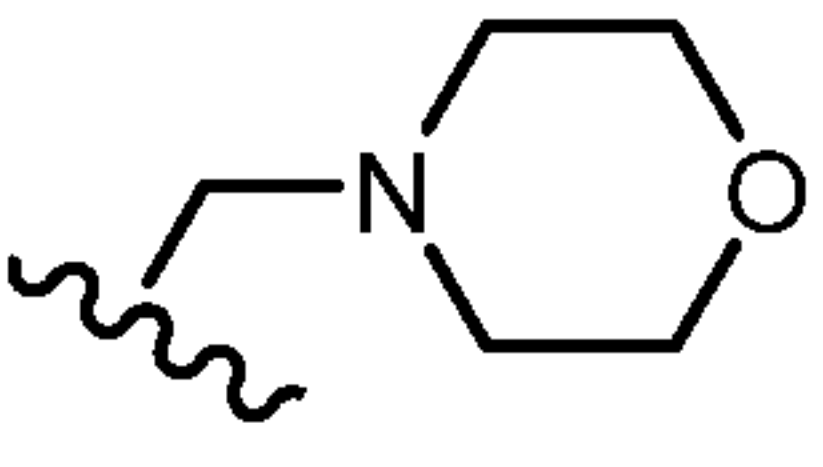
independently hydrogen or unsubstituted alkyl. In embodiments, R^{17A} is independently

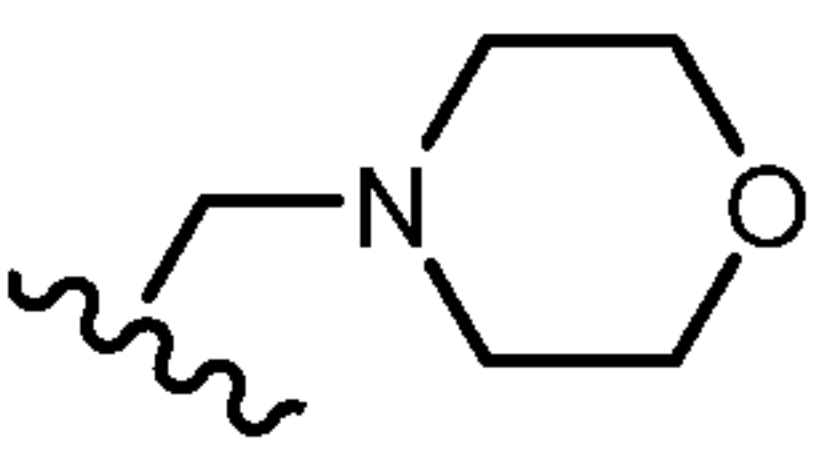
hydrogen. In embodiments, R^{17A} is independently unsubstituted alkyl. In embodiments, R^{17B}

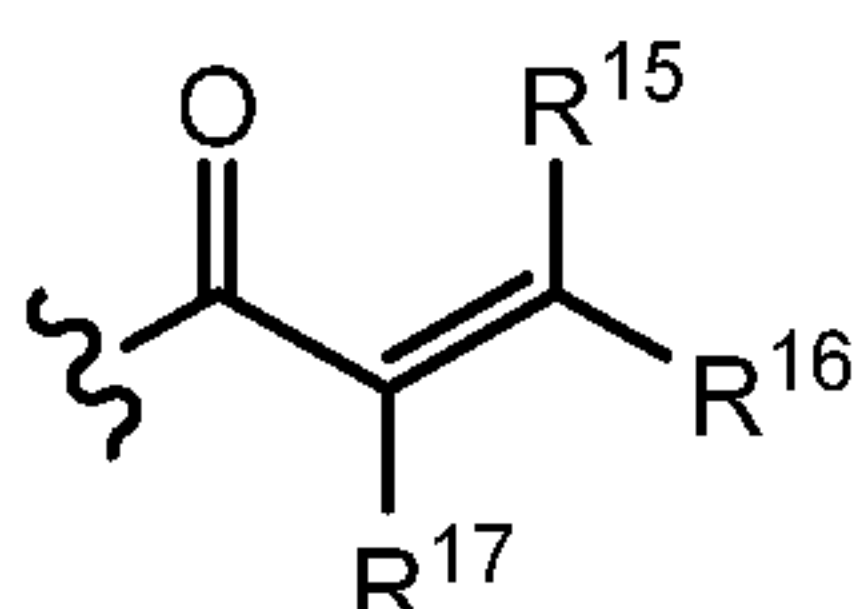
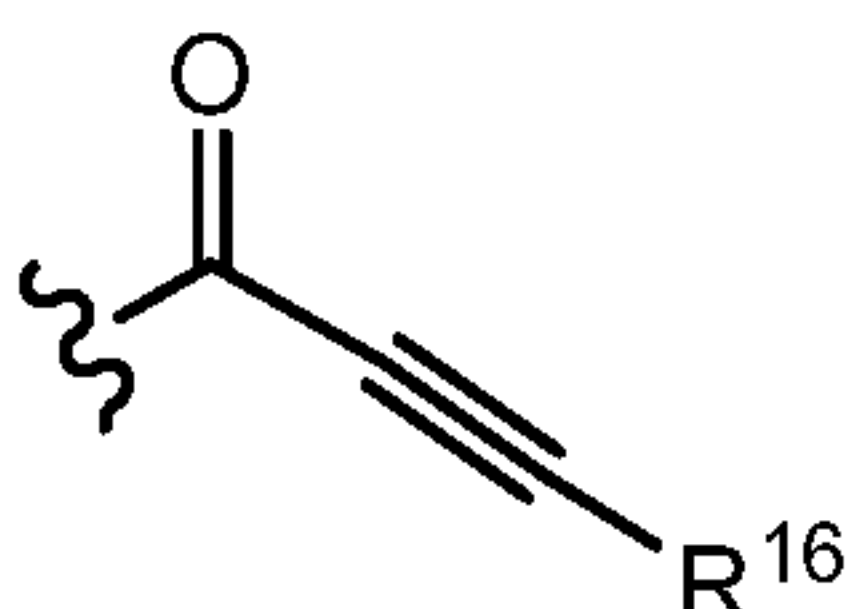
25 is independently hydrogen. In embodiments, R^{17B} is independently unsubstituted alkyl. In

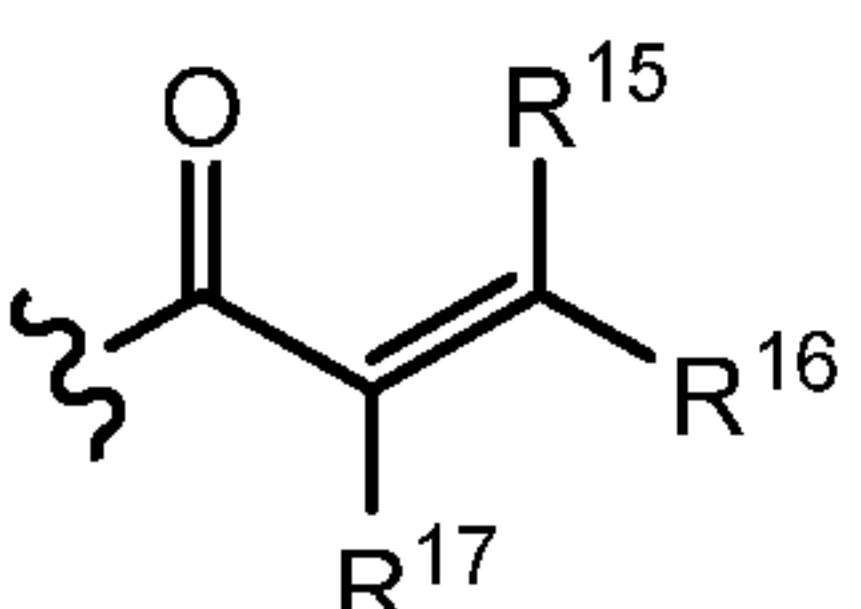
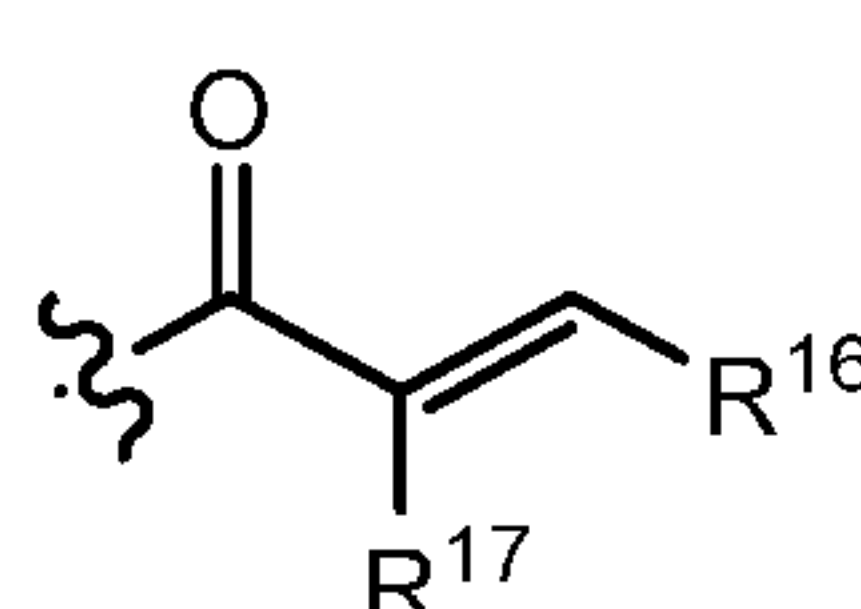
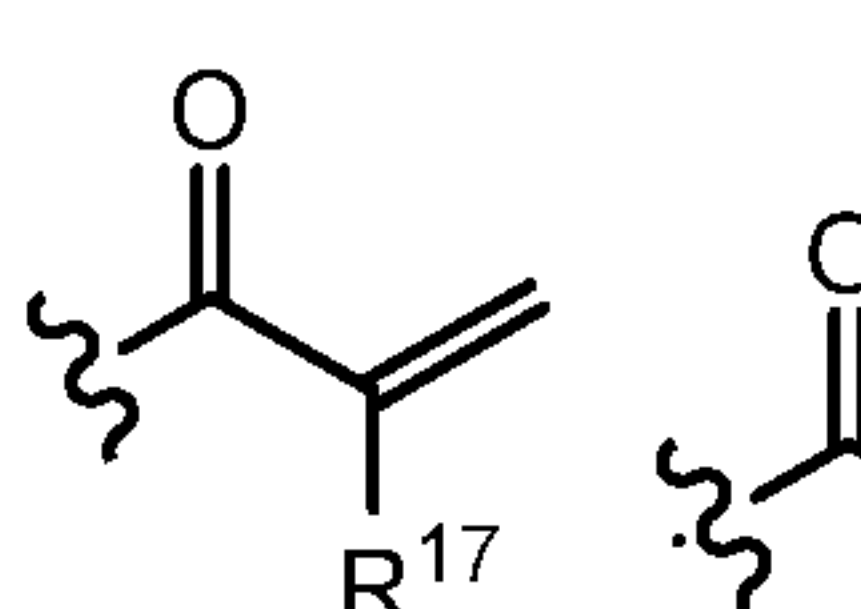
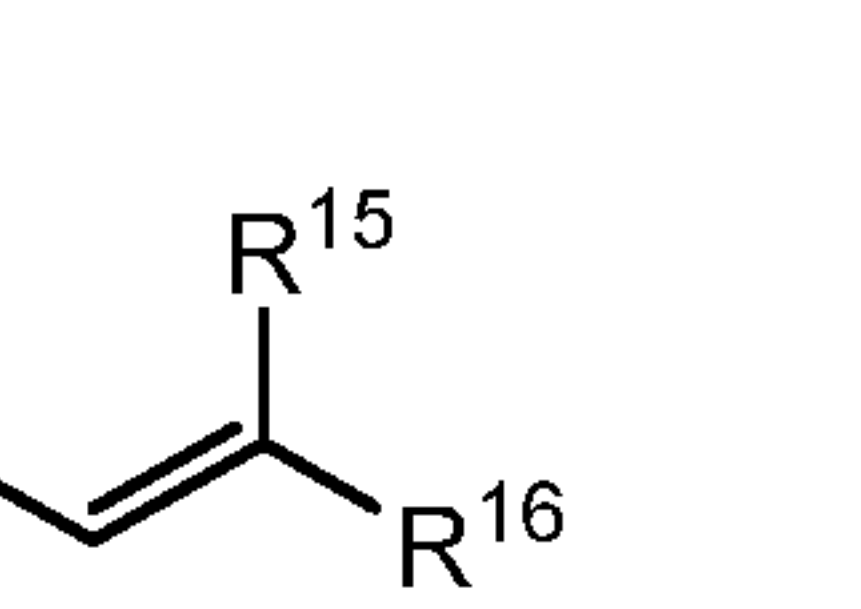
embodiments, R^{17A} is independently unsubstituted methyl. In embodiments, R^{17B} is

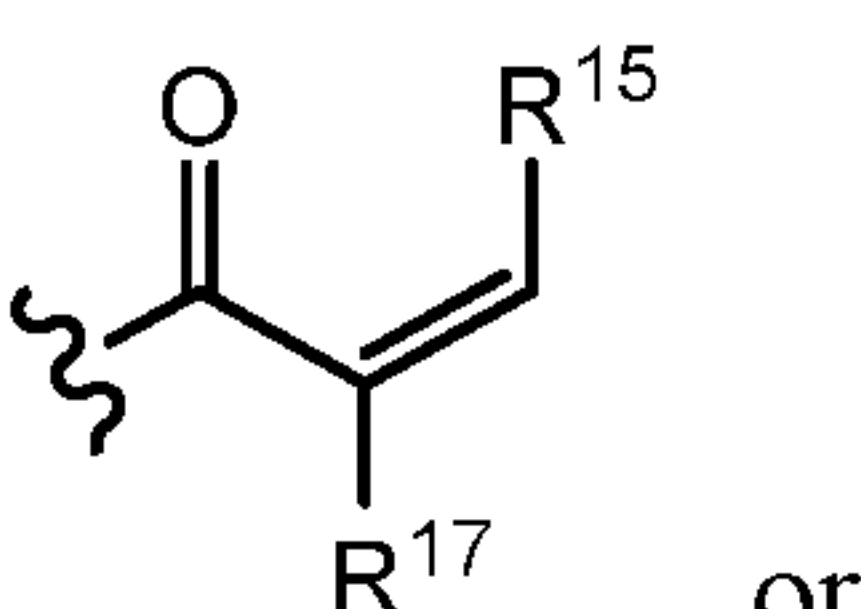
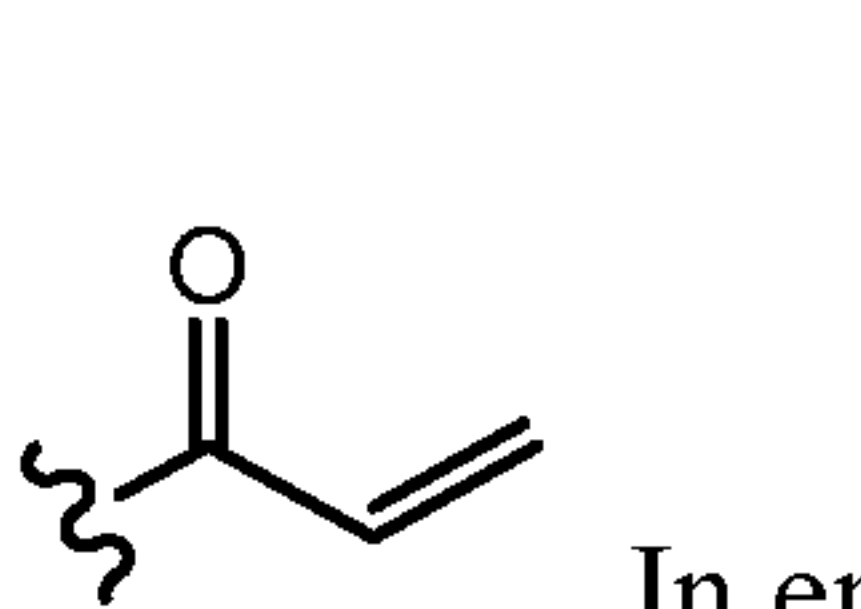
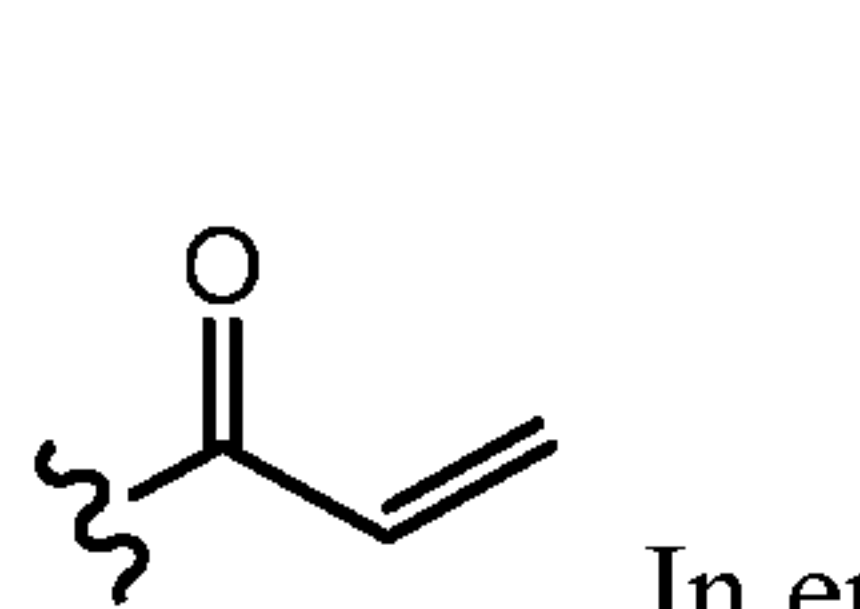
independently unsubstituted methyl.

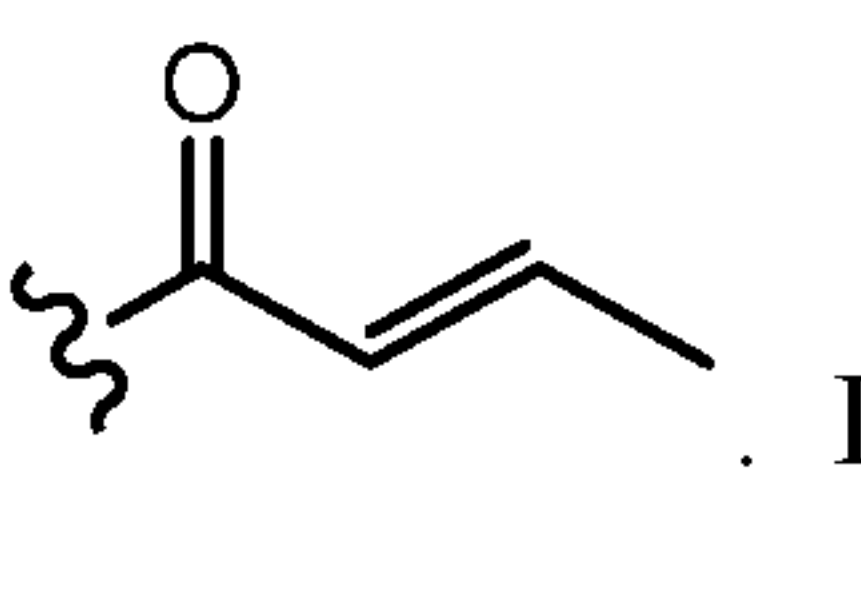
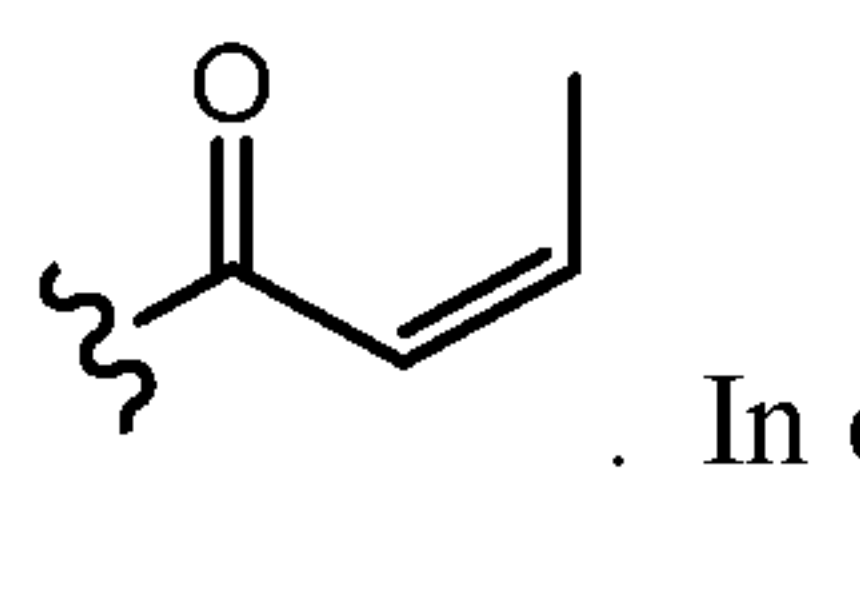
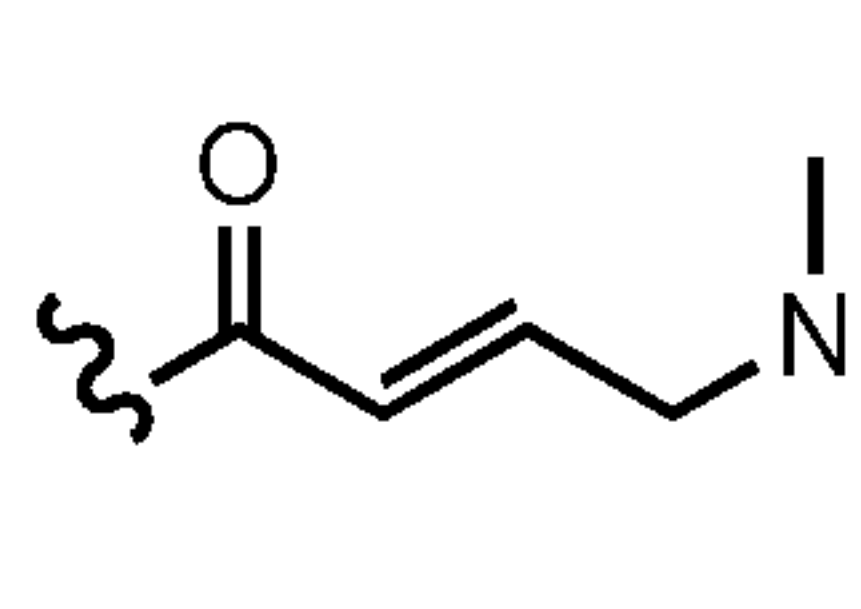
[0526] In embodiments, R^{15} is hydrogen, $-CH_3$, $-CH_2NR^{15A}R^{15B}$, or . In
embodiments, R^{16} is hydrogen. In embodiments, R^{17} is hydrogen. In embodiments, R^{15A} and
 R^{15B} are independently hydrogen or unsubstituted alkyl. In embodiments, R^{15A} and R^{15B} are
independently unsubstituted methyl. In embodiments, R^{15A} is independently hydrogen. In
5 embodiments, R^{15A} is independently unsubstituted alkyl. In embodiments, R^{15B} is
independently hydrogen. In embodiments, R^{15B} is independently unsubstituted alkyl. In
embodiments, R^{15A} is independently unsubstituted methyl. In embodiments, R^{15B} is
independently unsubstituted methyl. In embodiments, R^{15} is hydrogen, $-CH_3$,

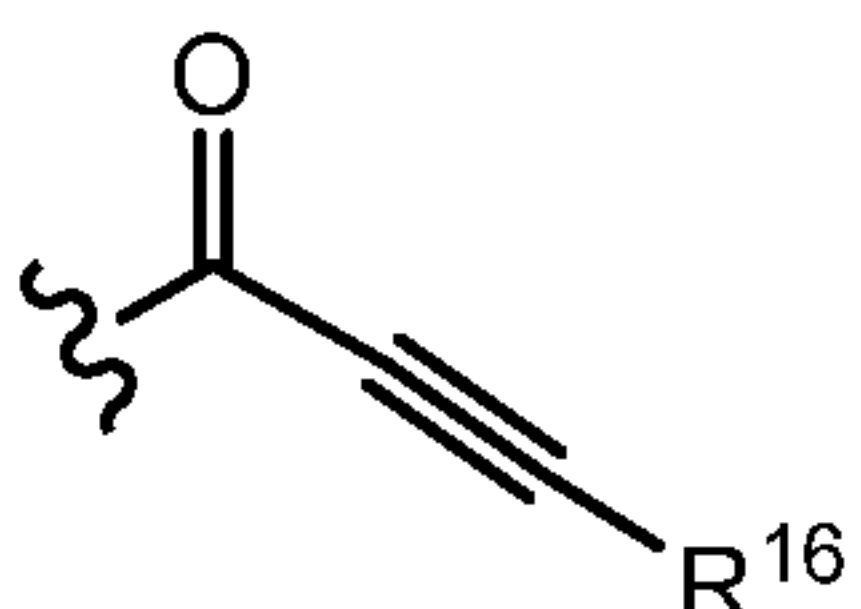
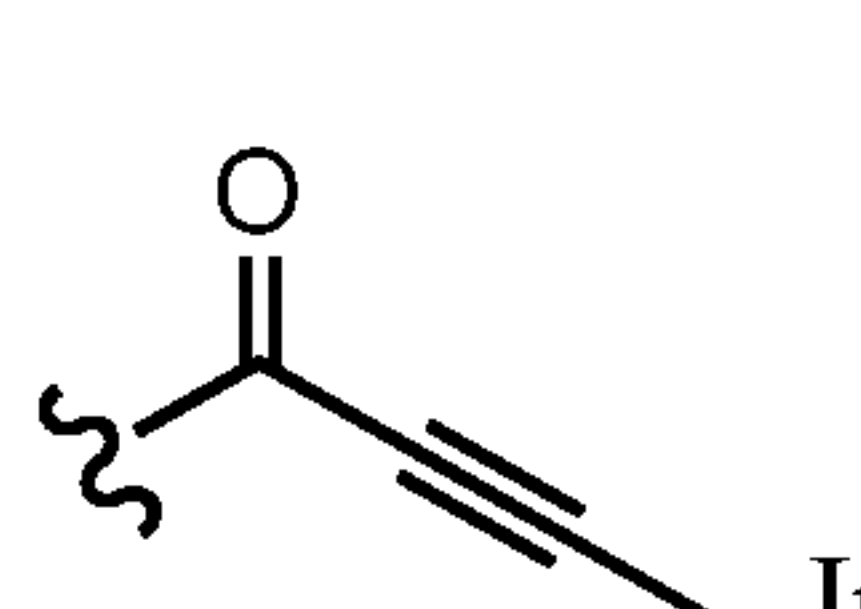
$-CH_2NR^{15A}R^{15B}$, or ; R^{16} is hydrogen; R^{17} is hydrogen; and R^{15A} and R^{15B} are
10 independently hydrogen or unsubstituted alkyl.

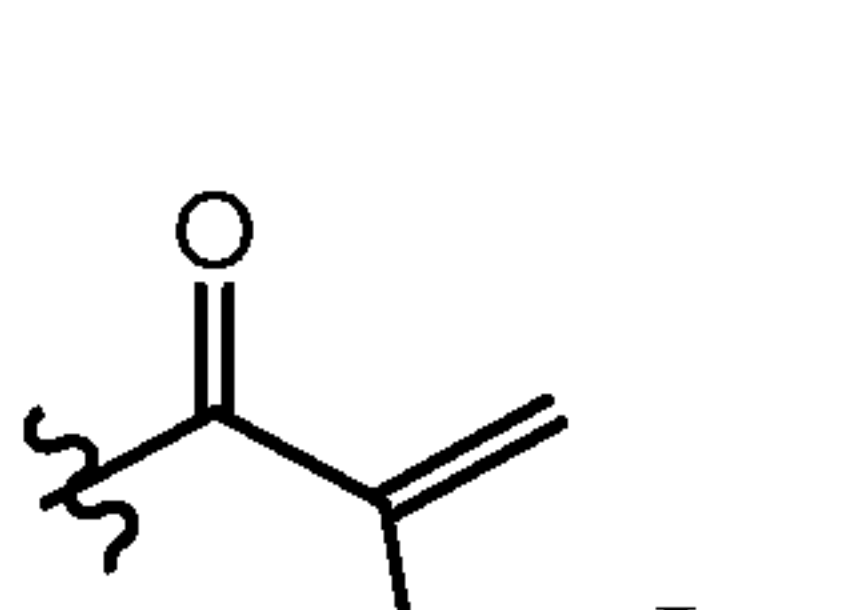
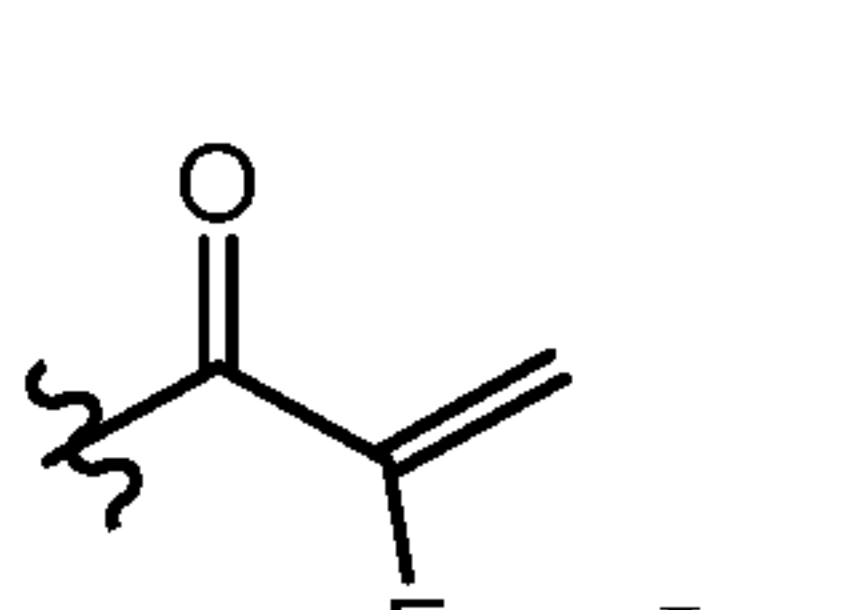
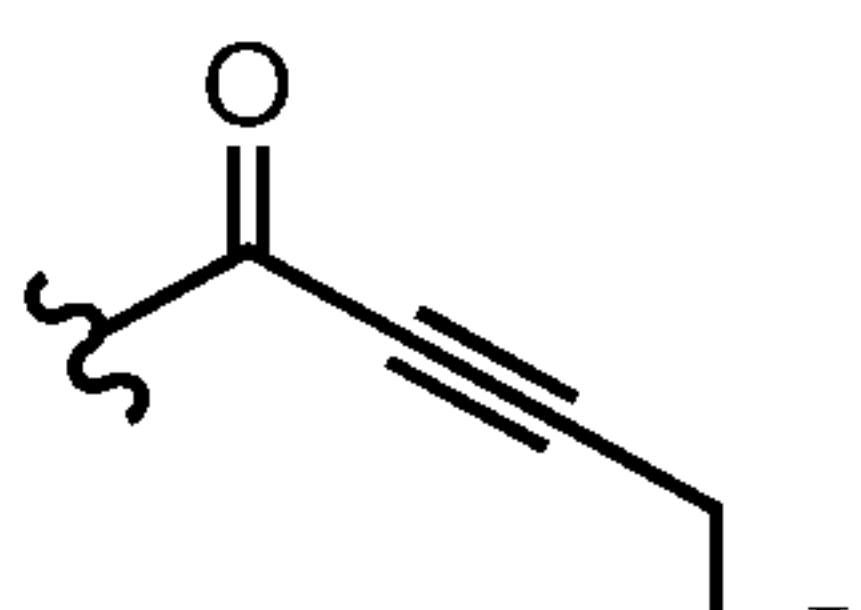
[0527] In embodiments, E is:  or . In embodiments, E is:

. In embodiments, E is: , , ,

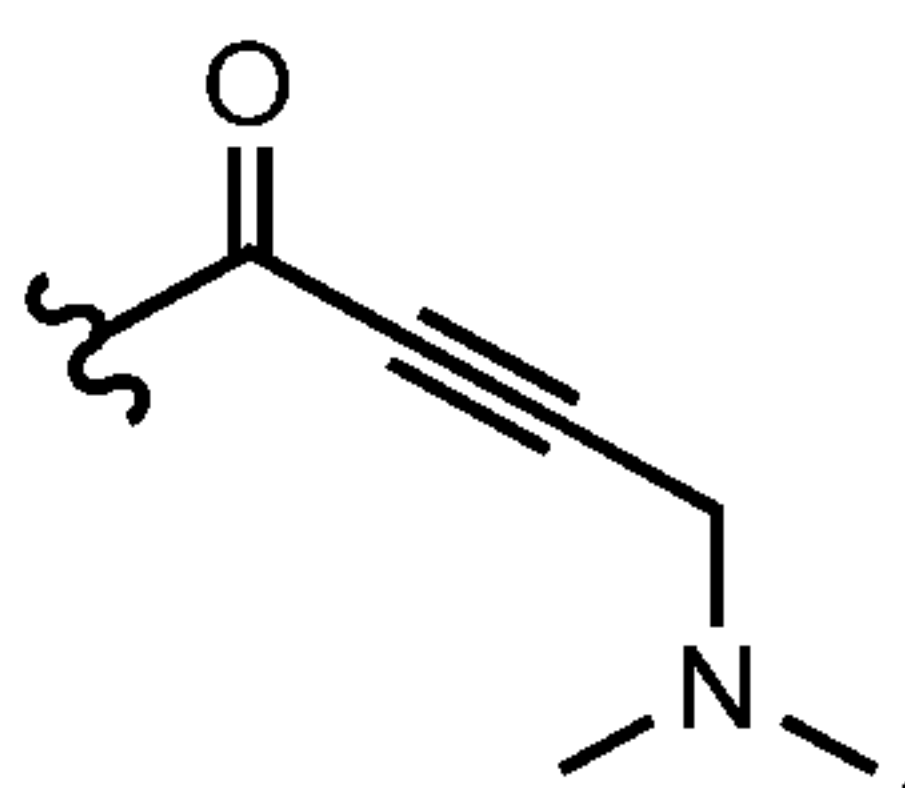
, or . In embodiments, E is: . In embodiments, E is:

. In embodiments, E is: . In embodiments, E is: .

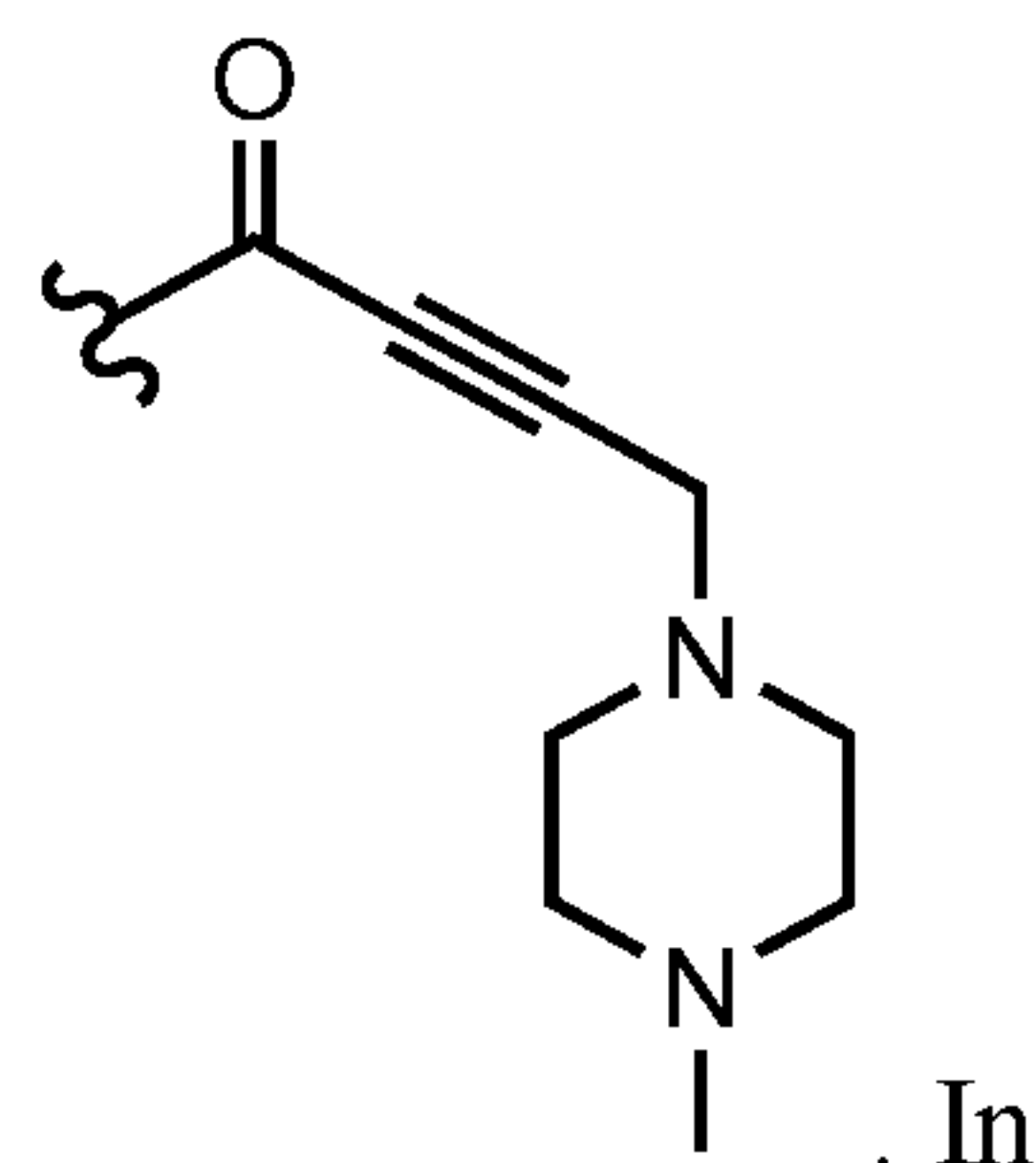
15 In embodiments, E is . In embodiments, E is: . In embodiments,

E is: . In embodiments, E is: . In embodiments, E is: . In

embodiments, E is:

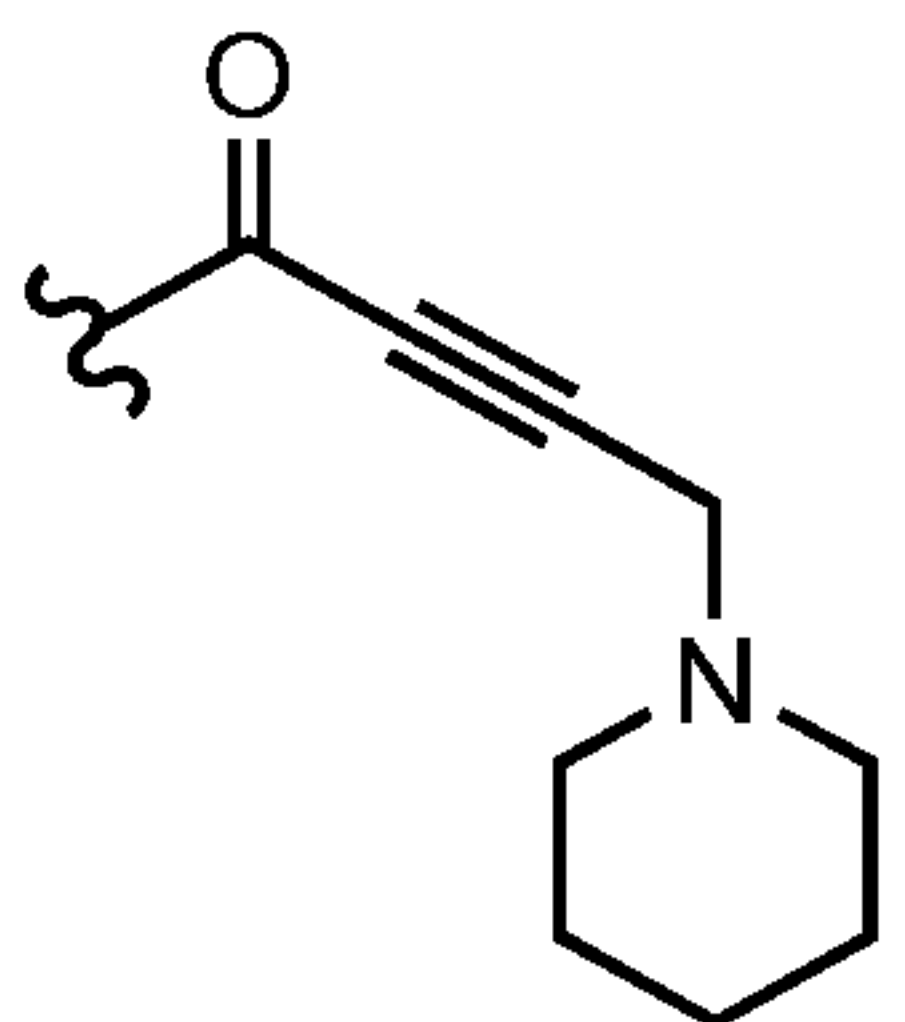


. In embodiments, E is:

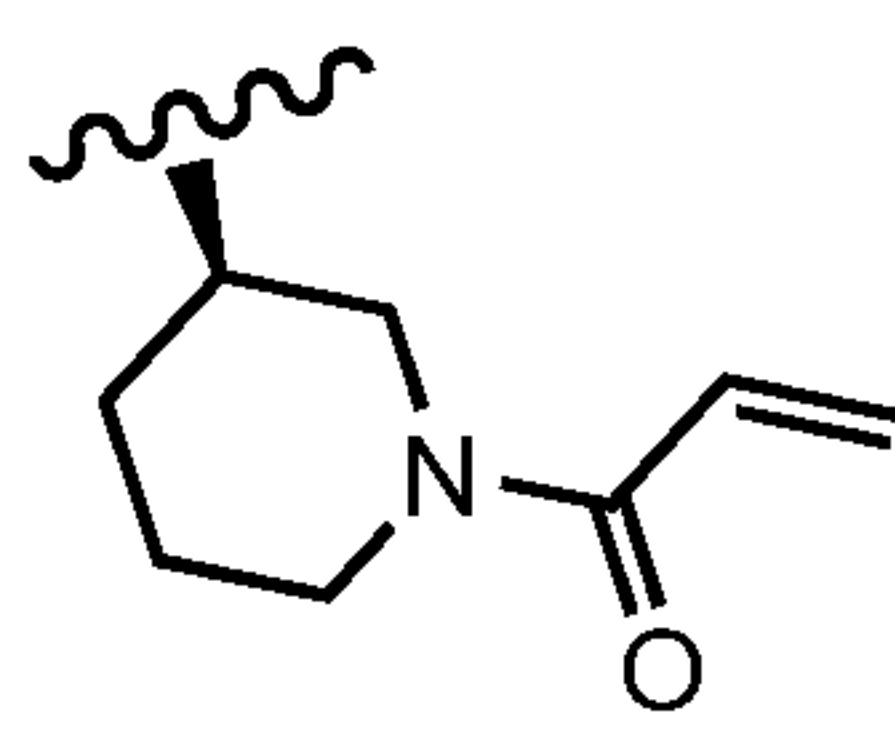


. In

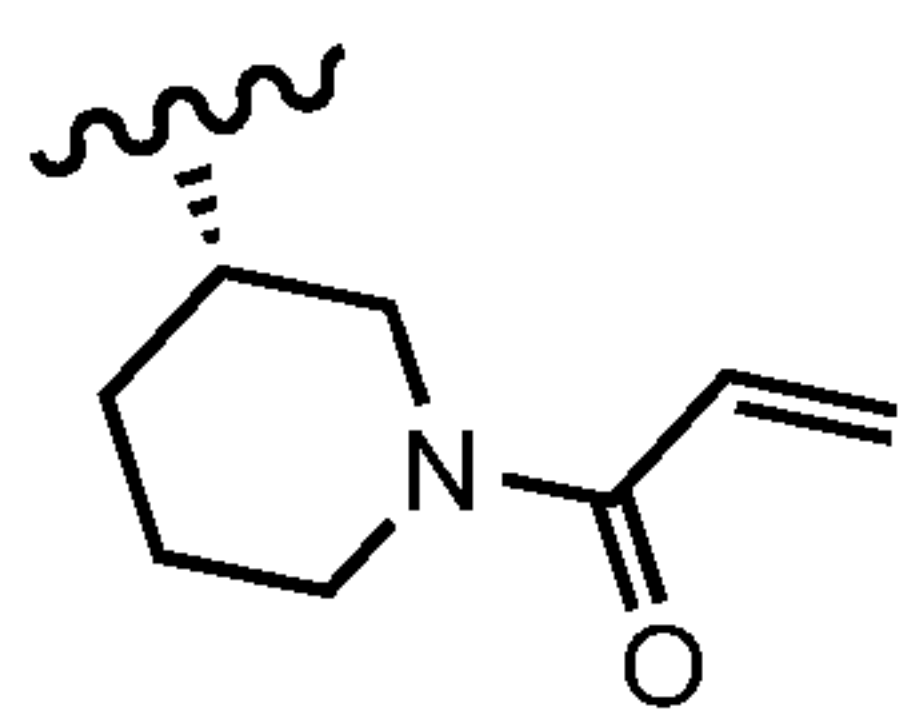
embodiments, E is:



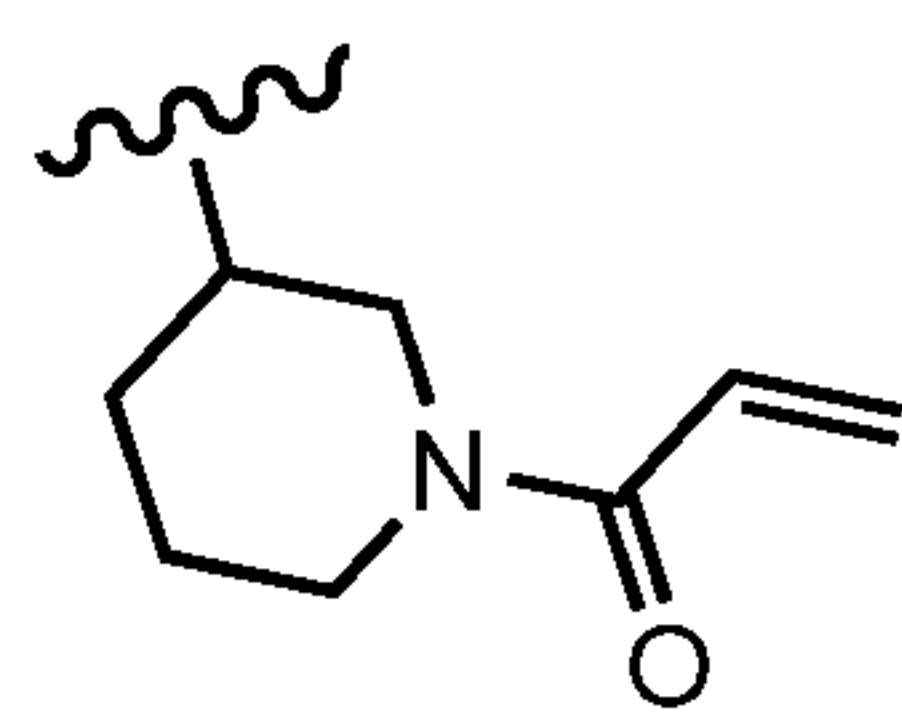
[0528] In embodiments, L¹-L²-E is



. In embodiments, L¹-L²-E is

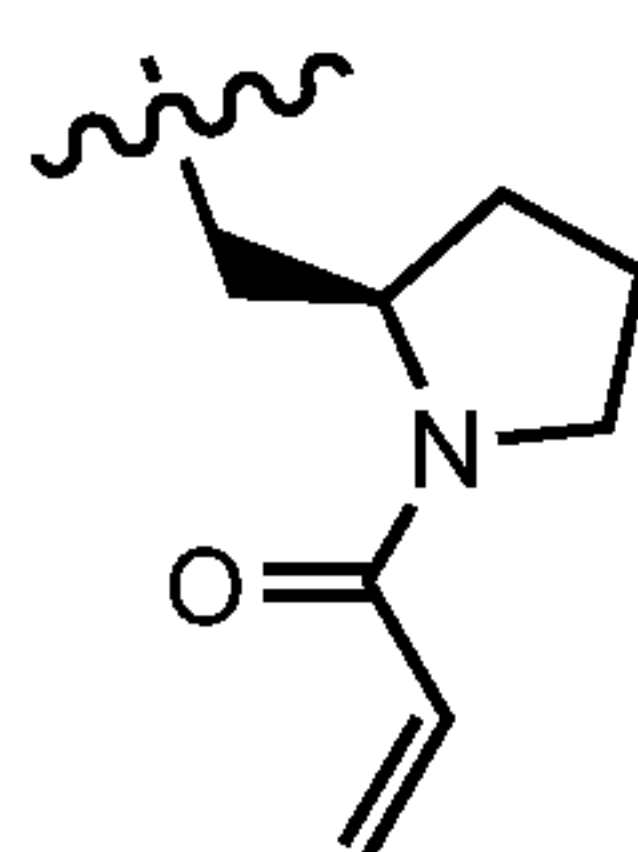


. In embodiments, L¹-L²-E is



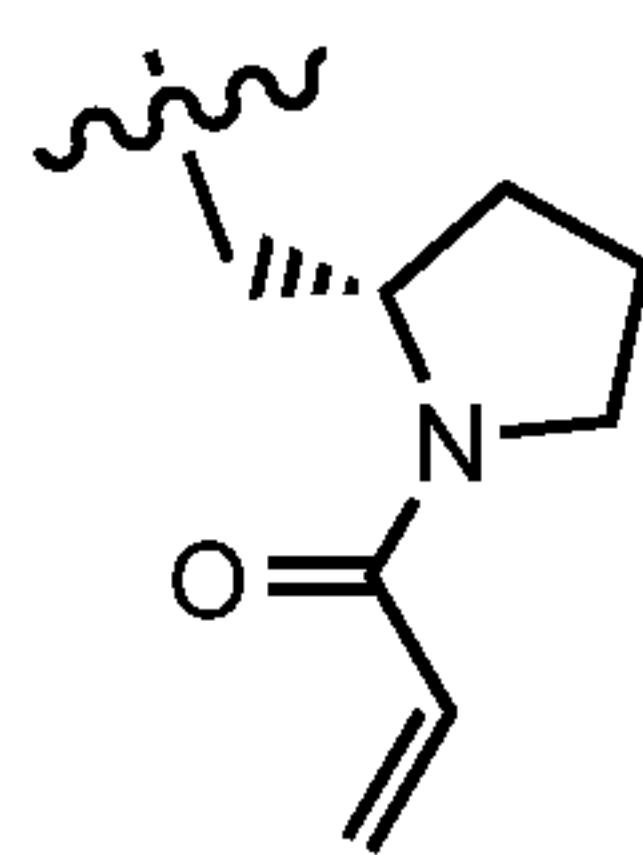
. In embodiments, L¹-L²-E

5 is -CH₂CH₂NHCOCHCH₂. In embodiments, L¹-L²-E is

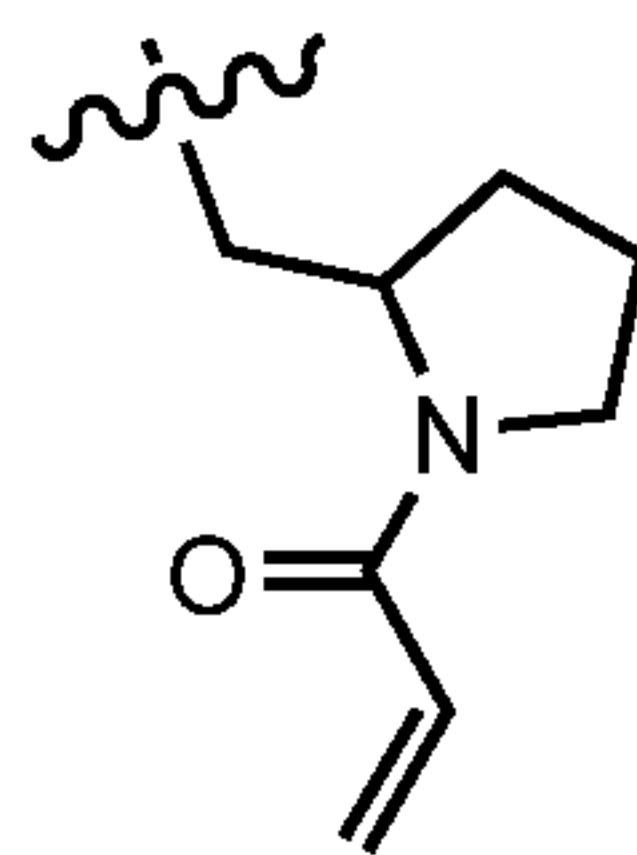


. In embodiments,

L¹-L²-E is

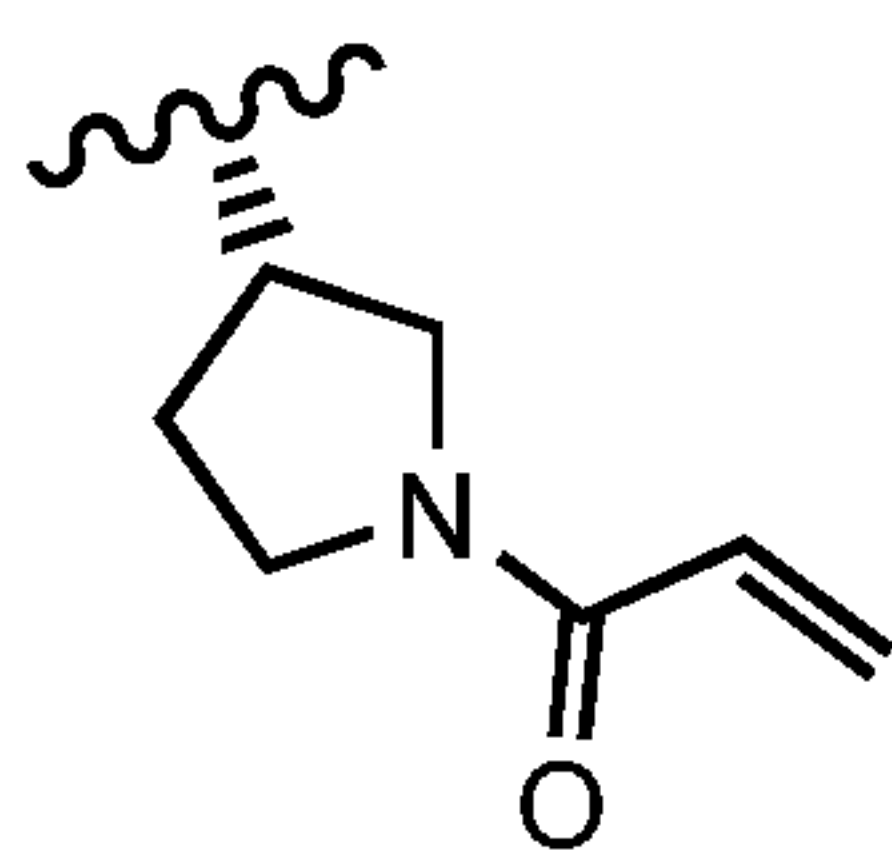


. In embodiments, L¹-L²-E is

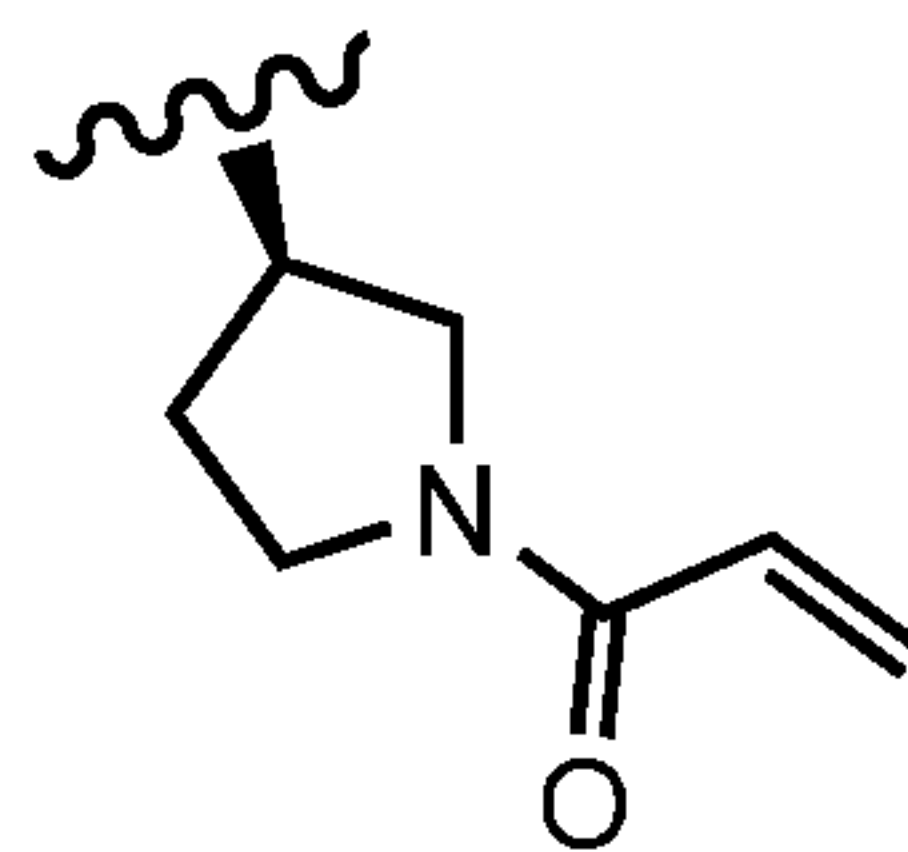


. In embodiments, L¹-L²-E

is

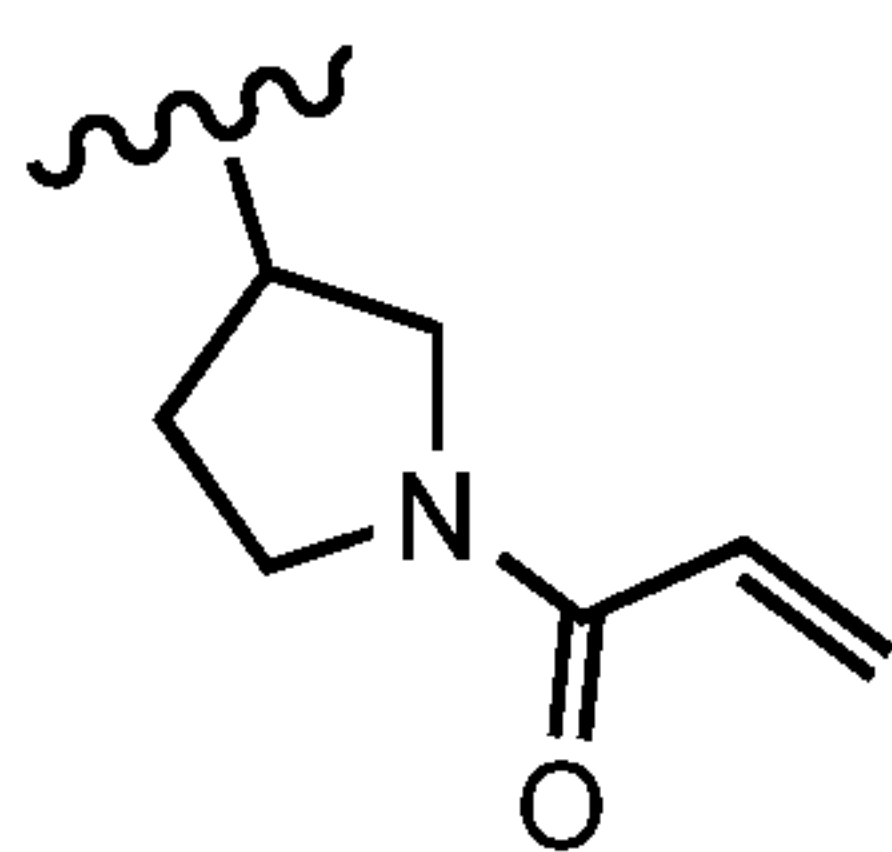


. In embodiments, L¹-L²-E is

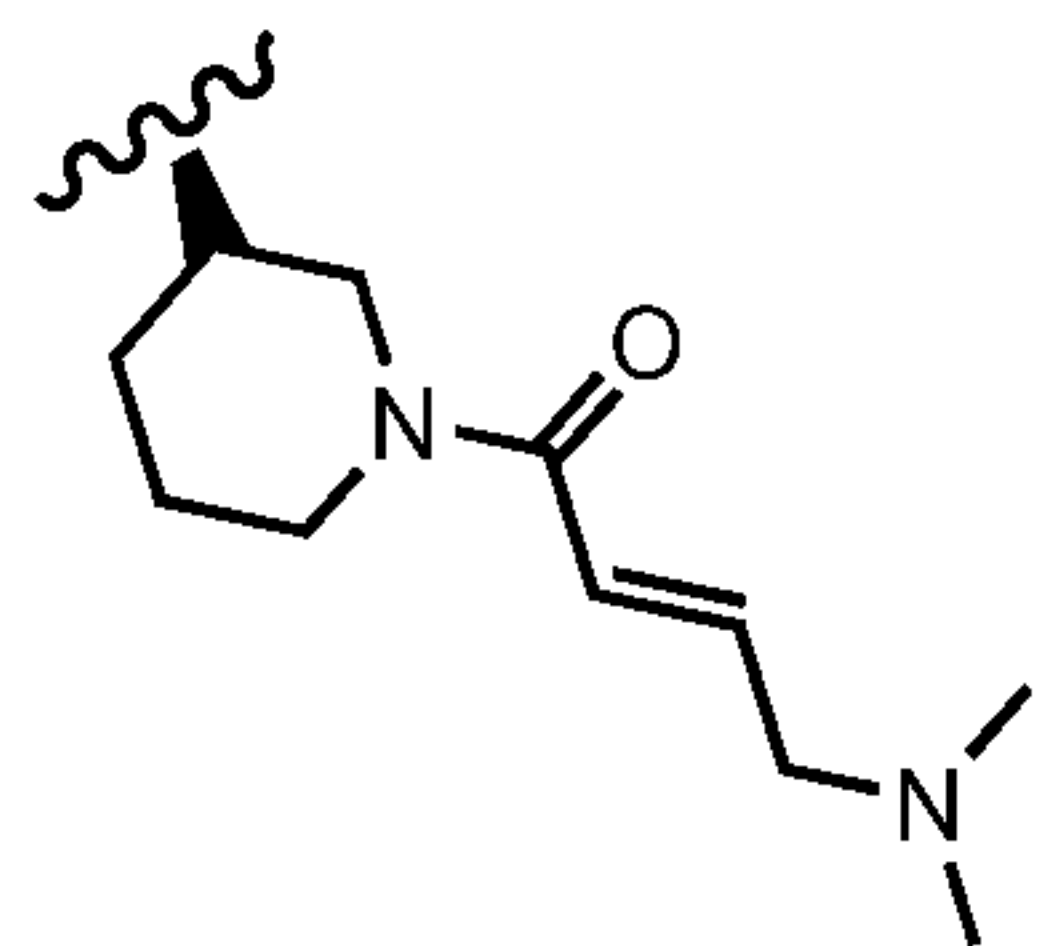


. In embodiments, L¹-L²-E

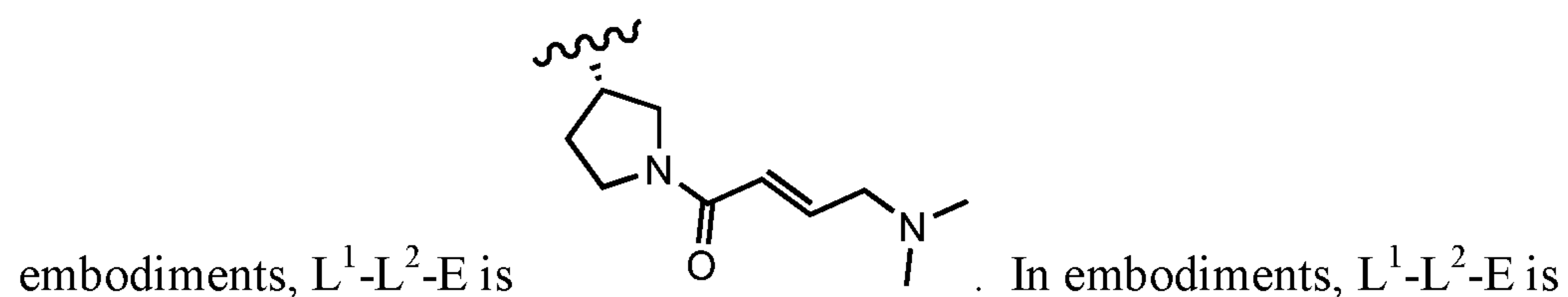
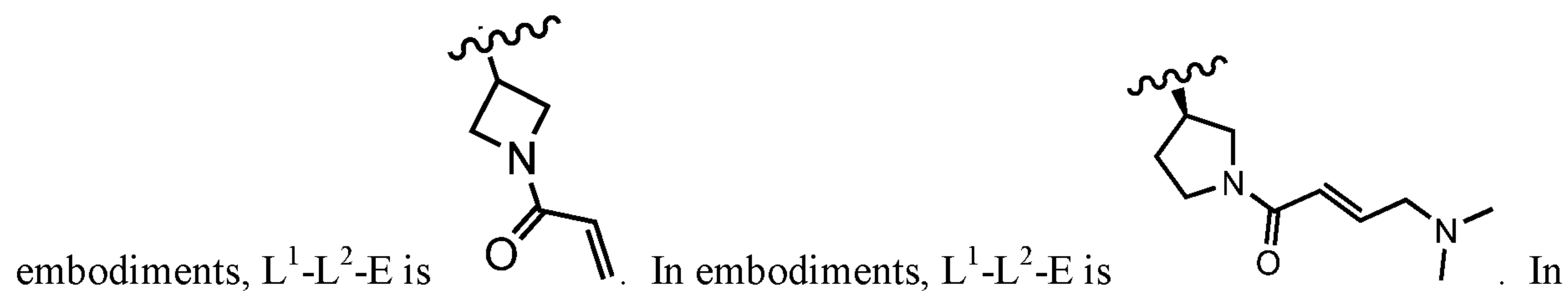
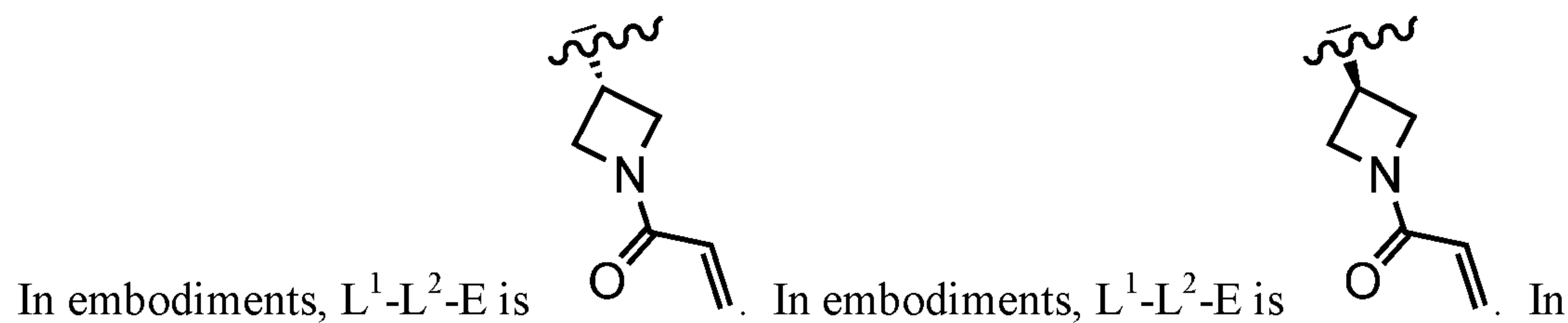
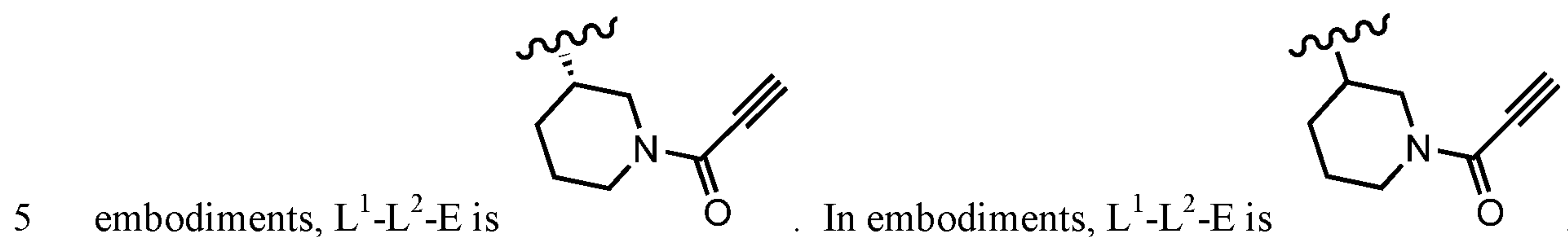
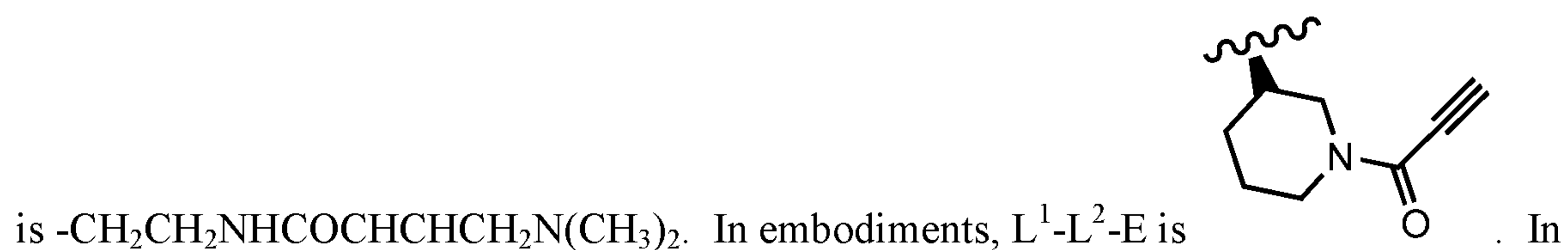
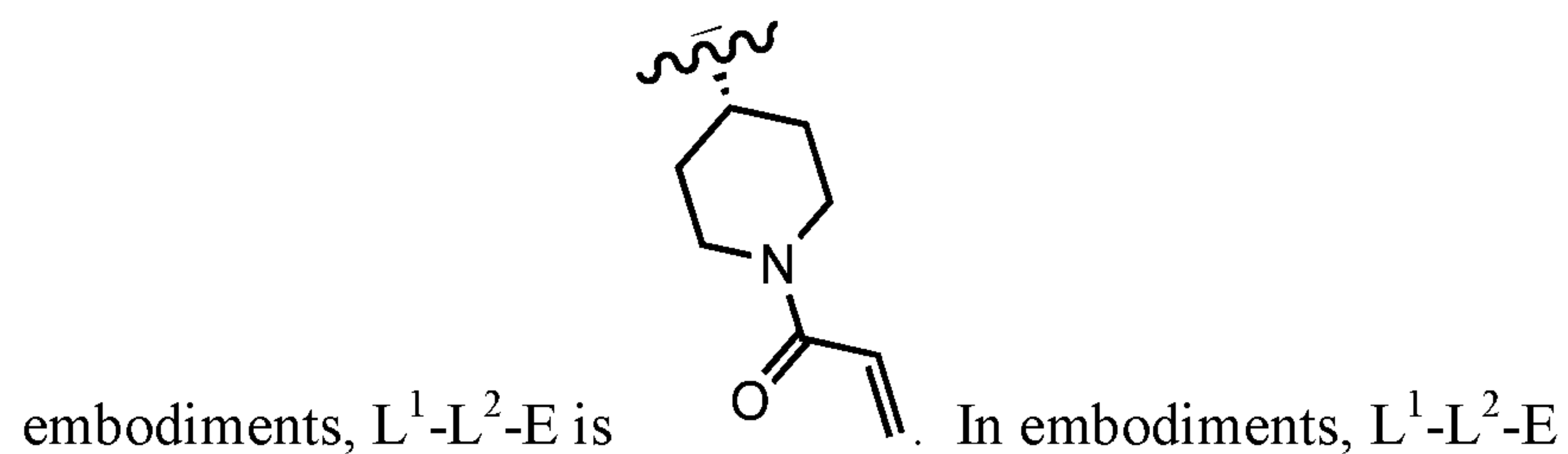
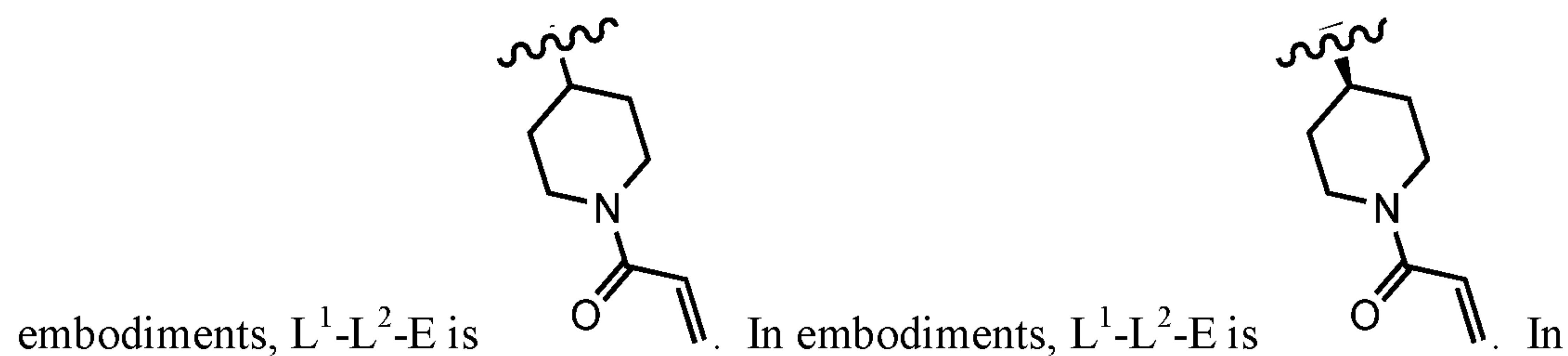
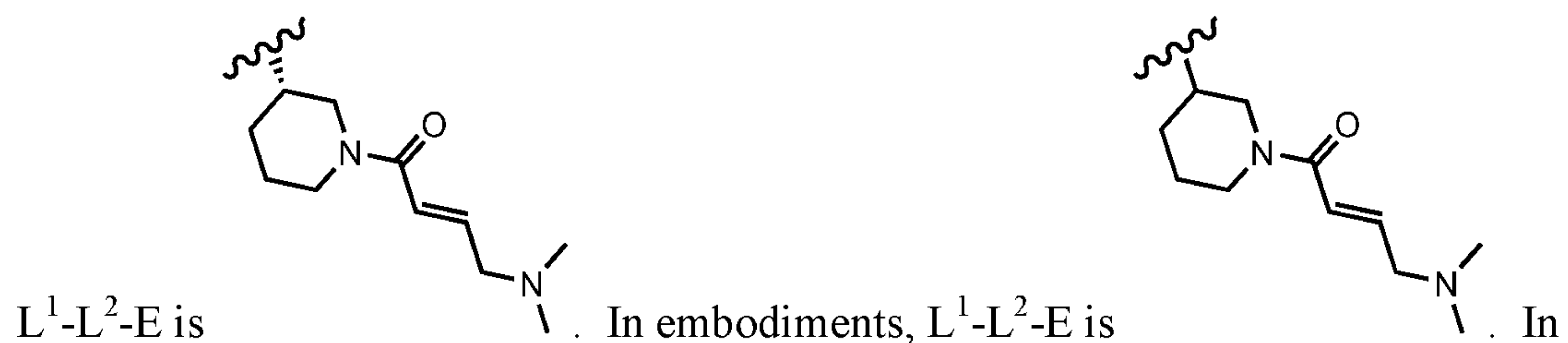
is

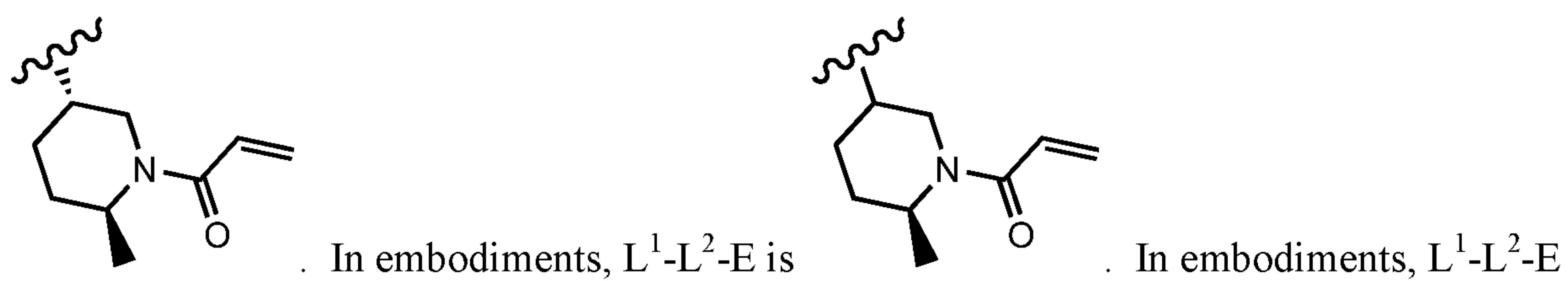
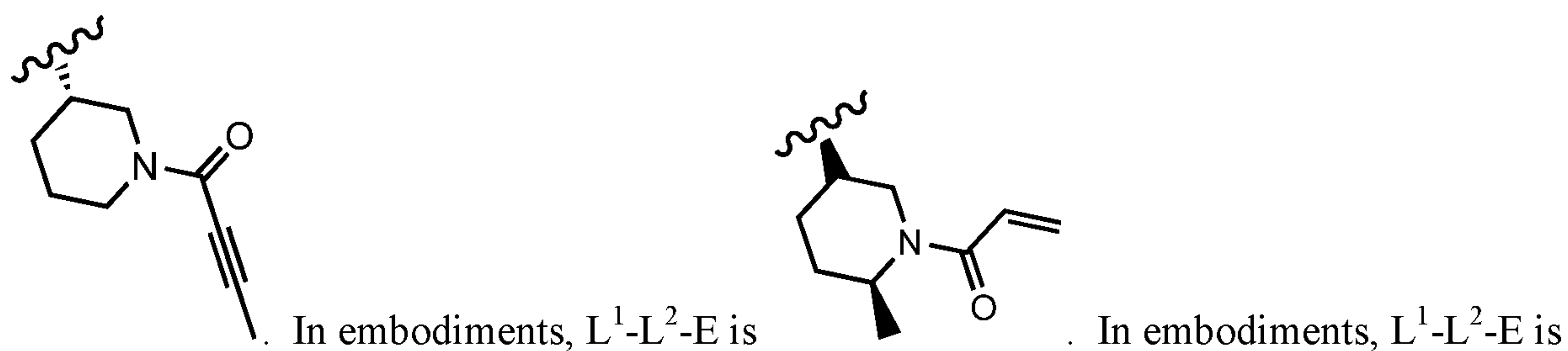
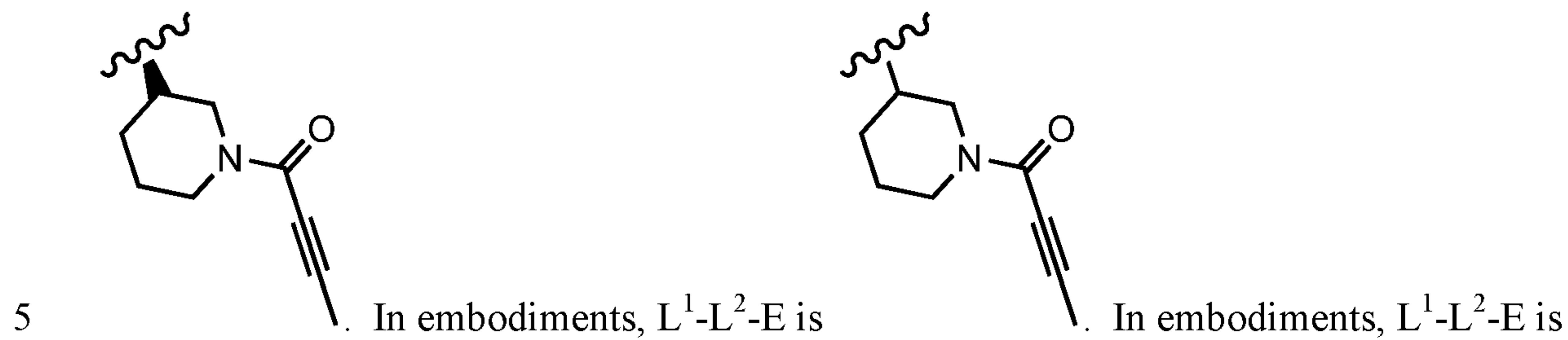
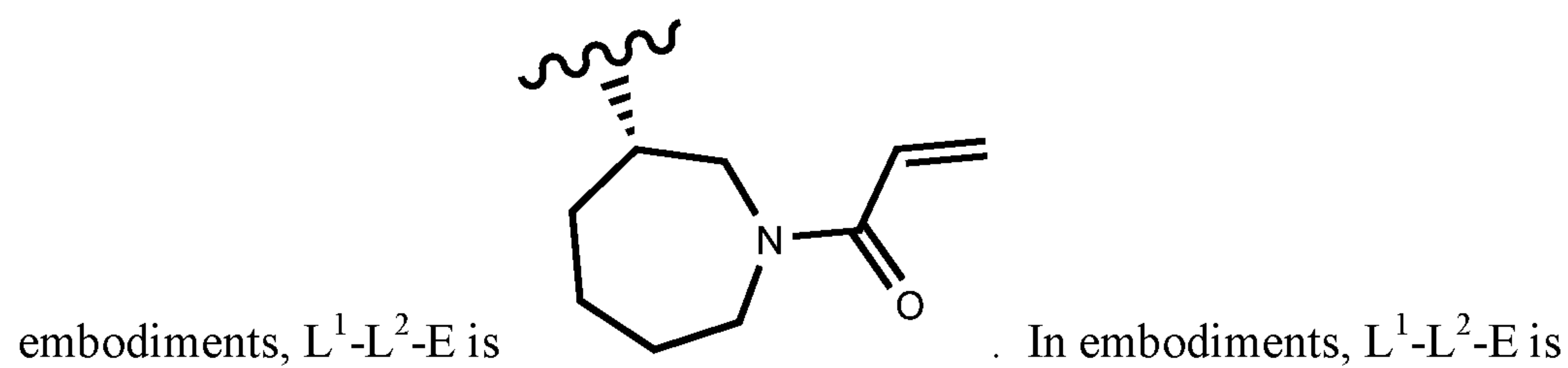
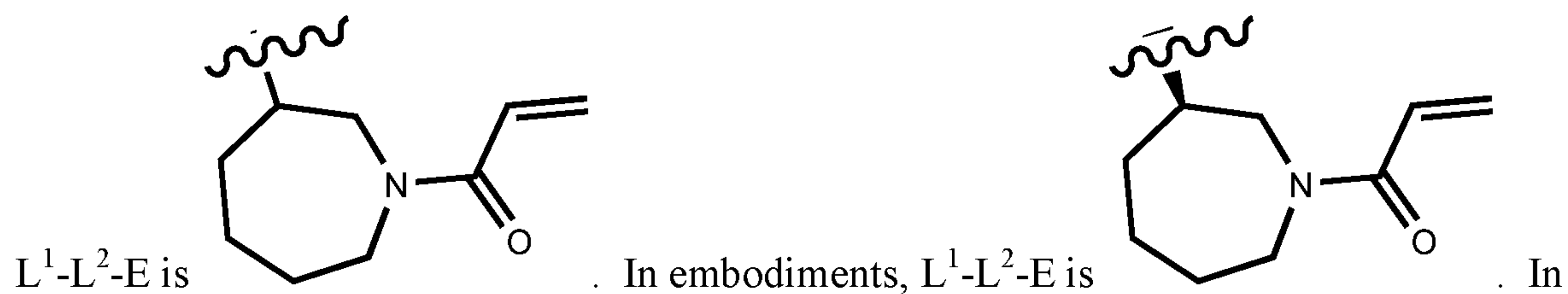
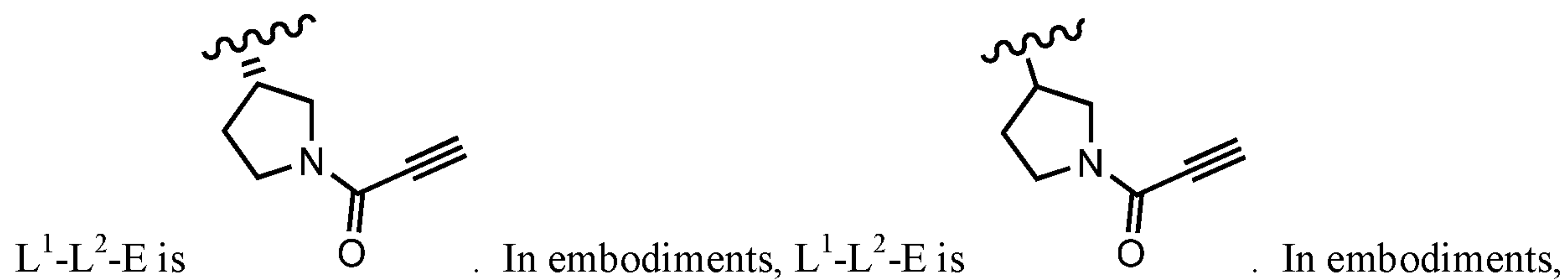
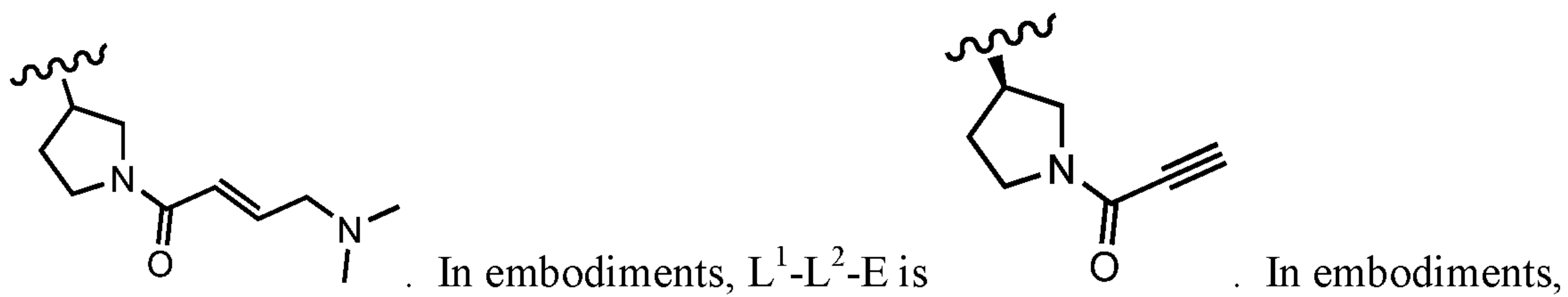


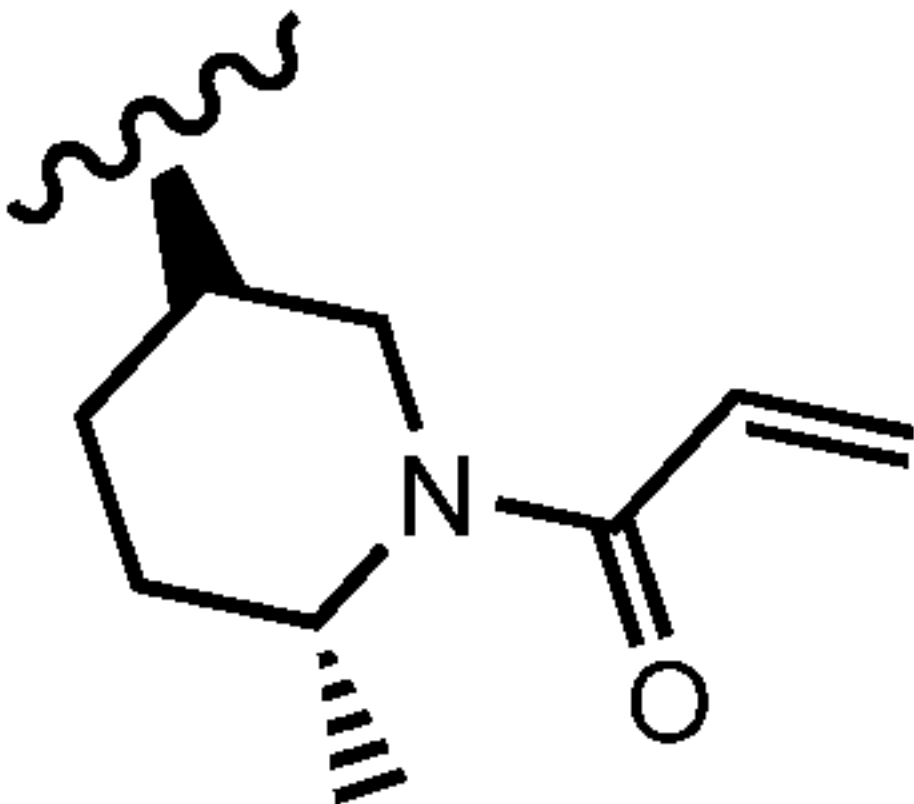
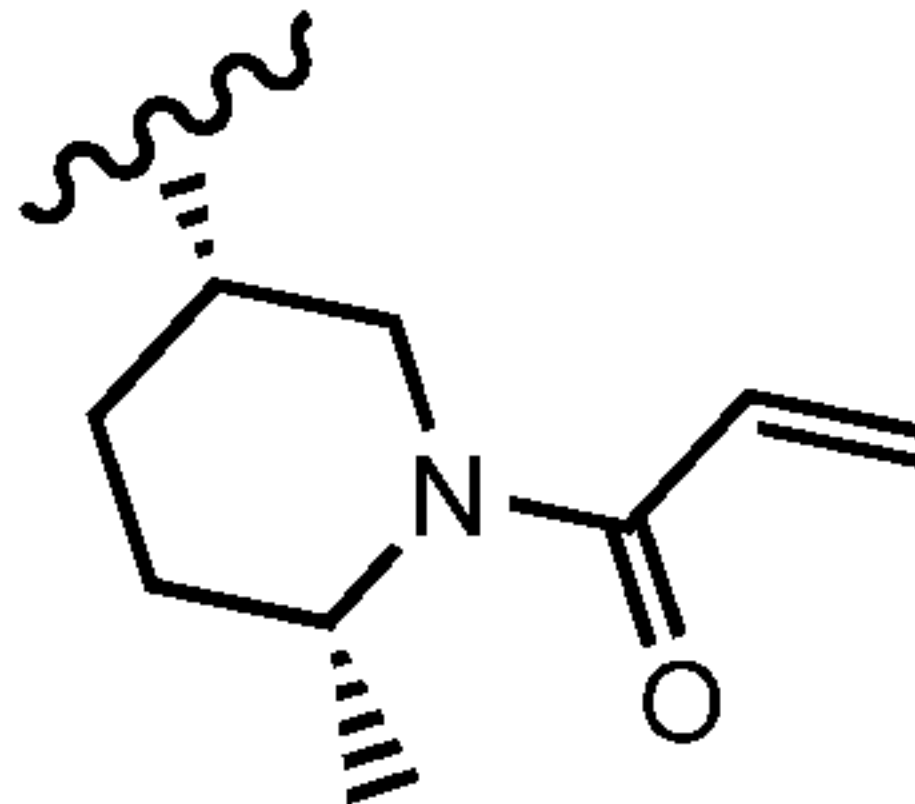
. In embodiments, L¹-L²-E is

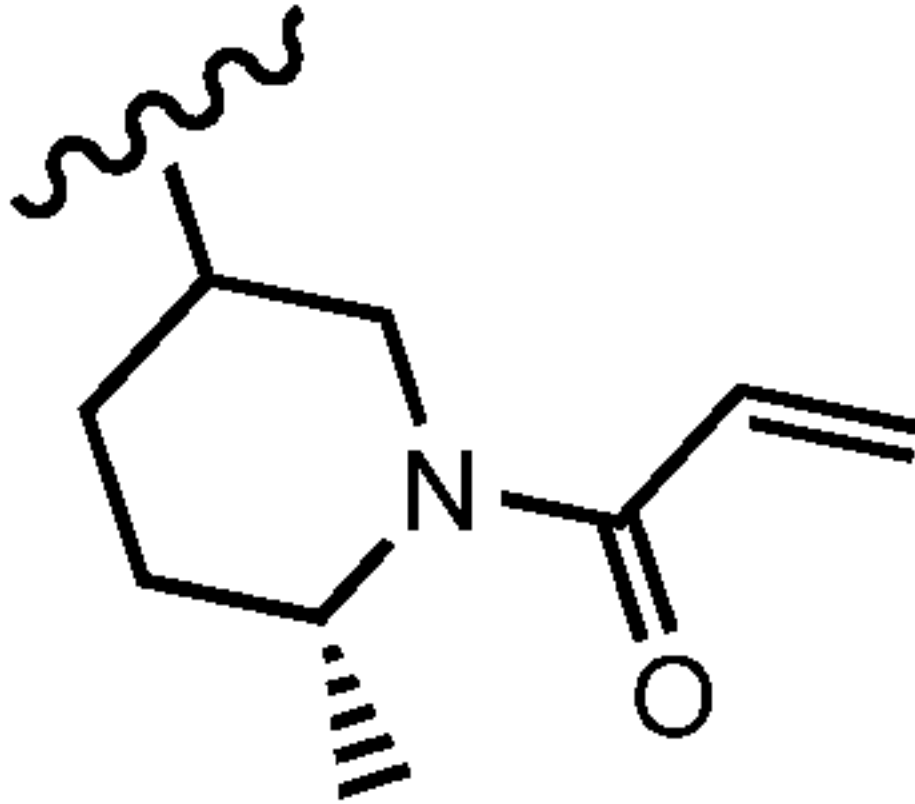
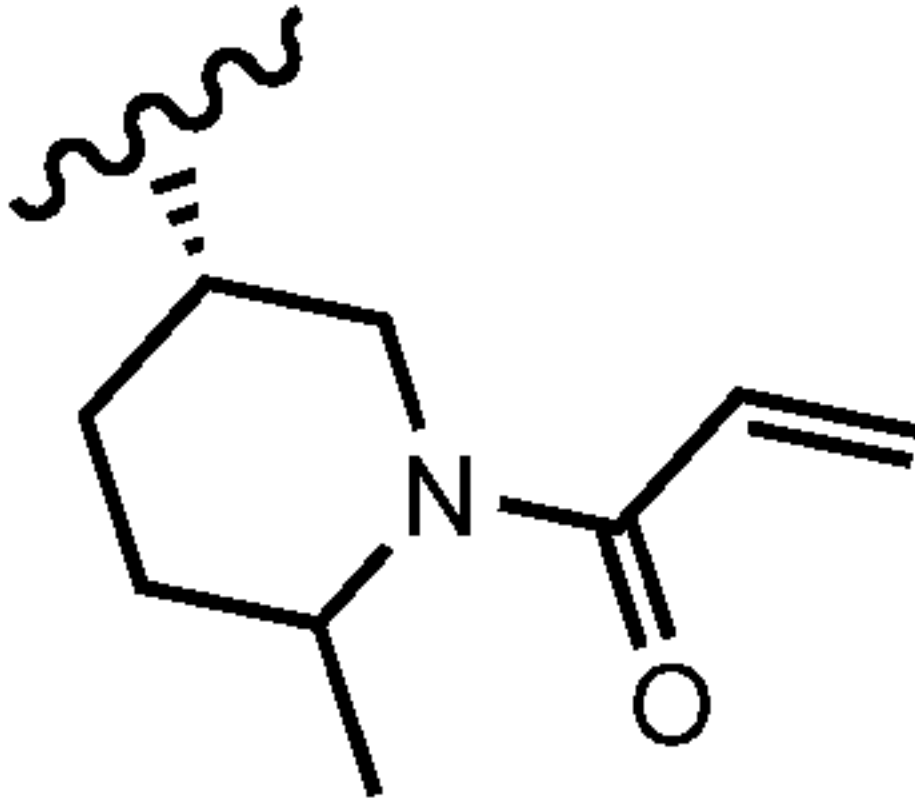


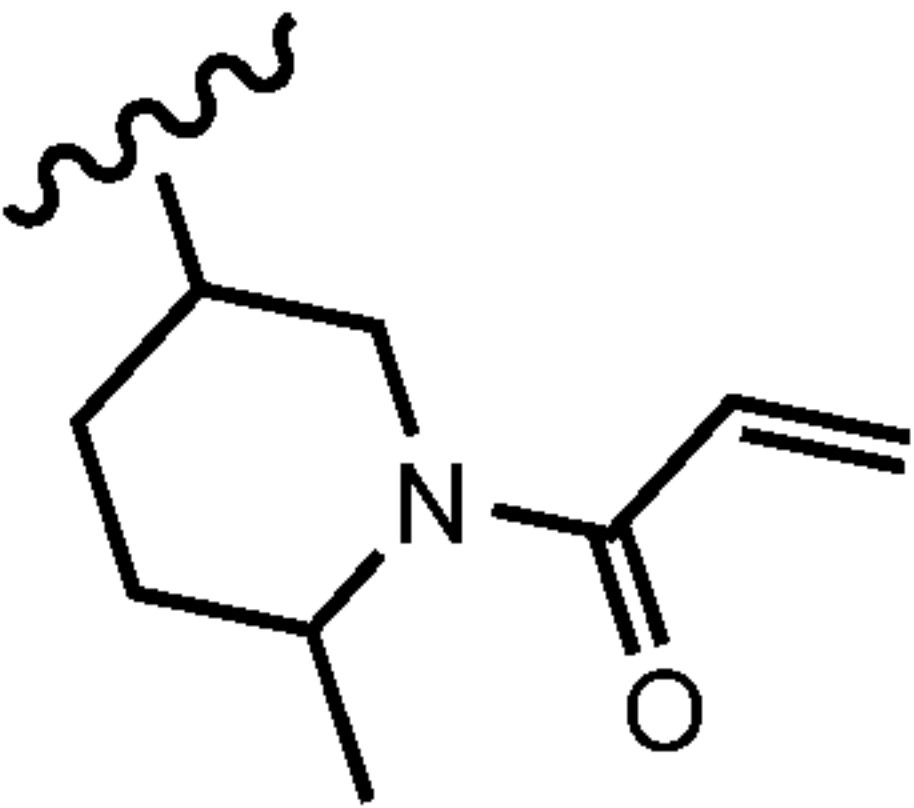
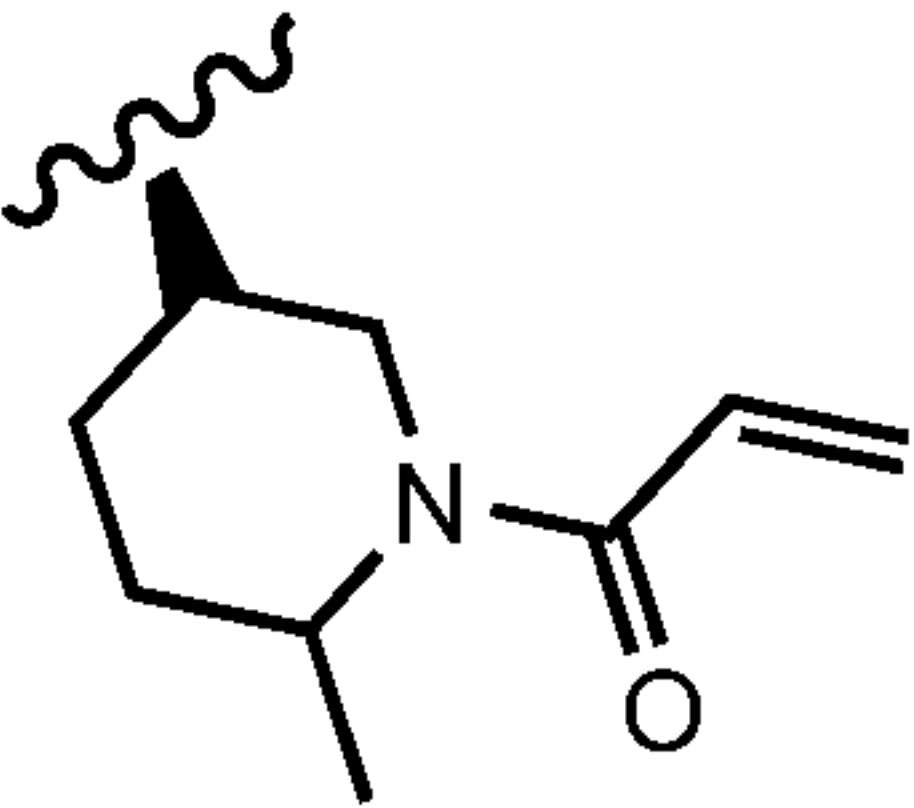
. In embodiments,

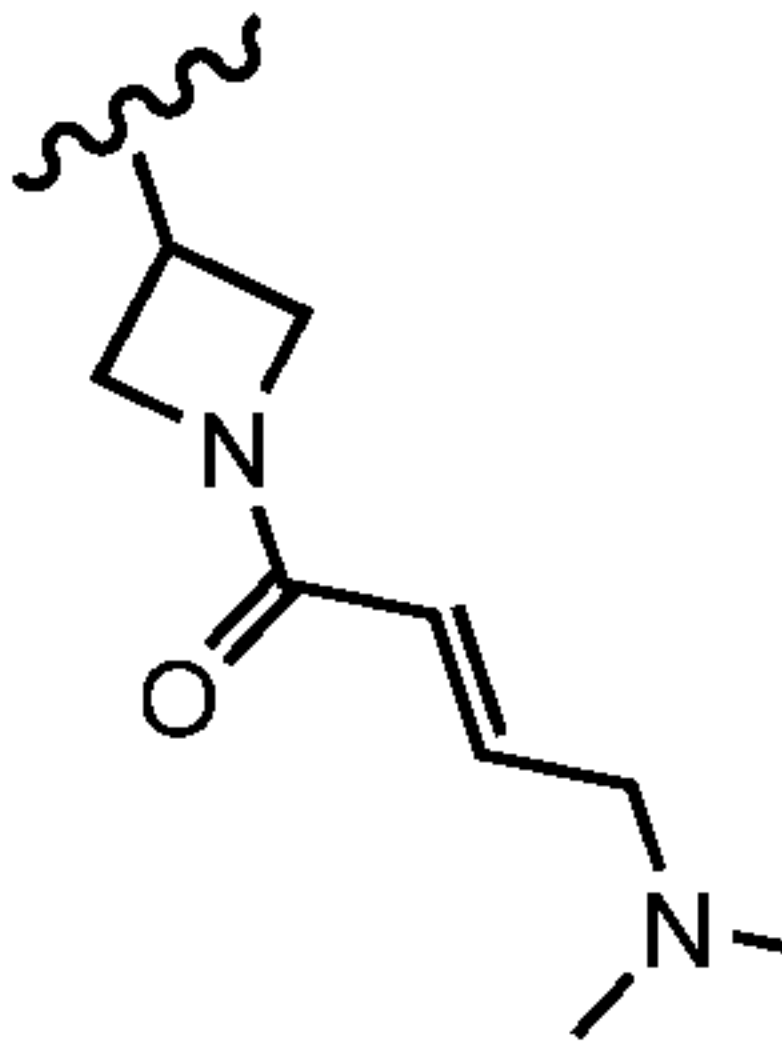
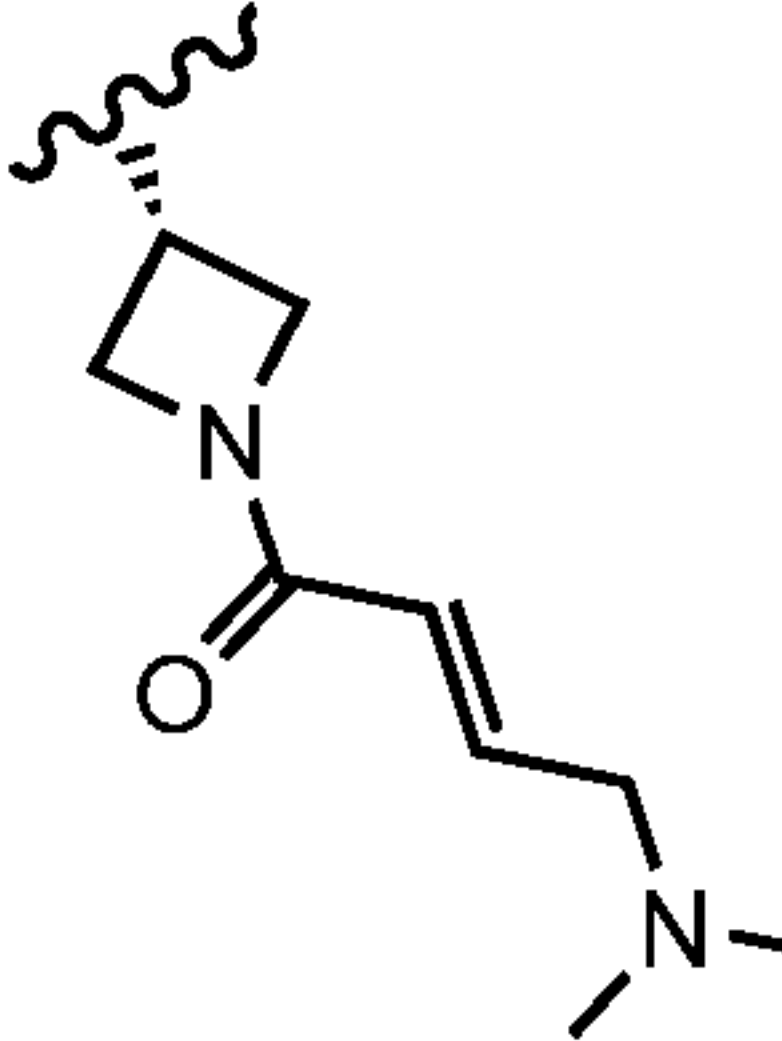


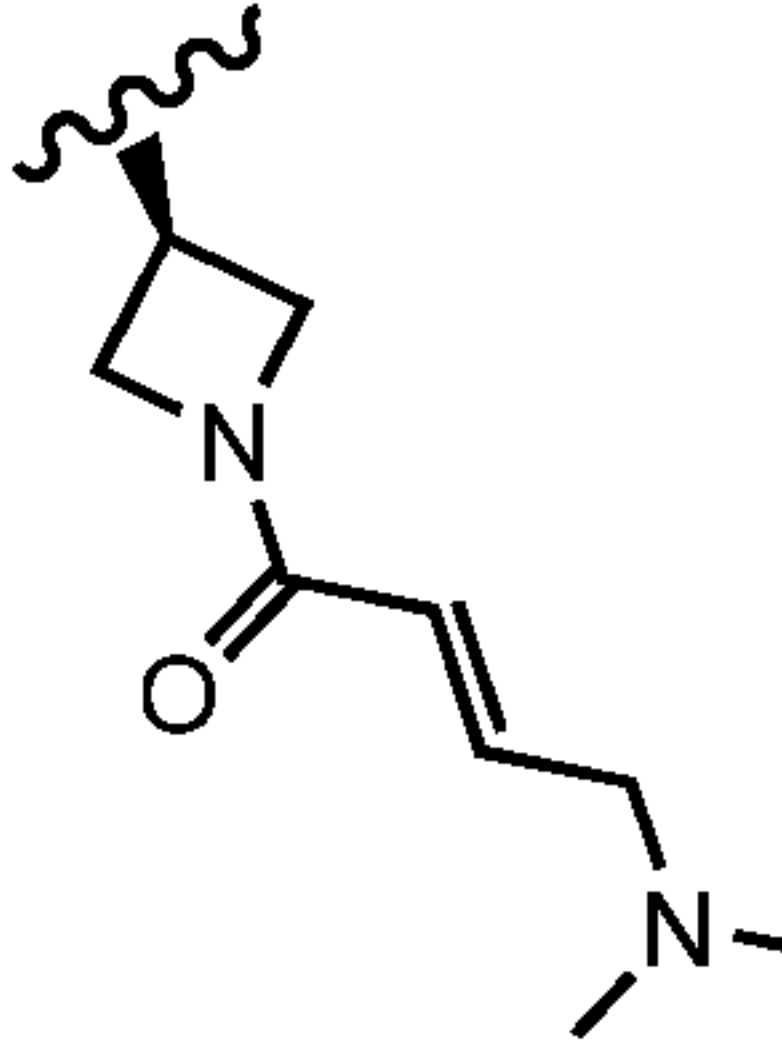
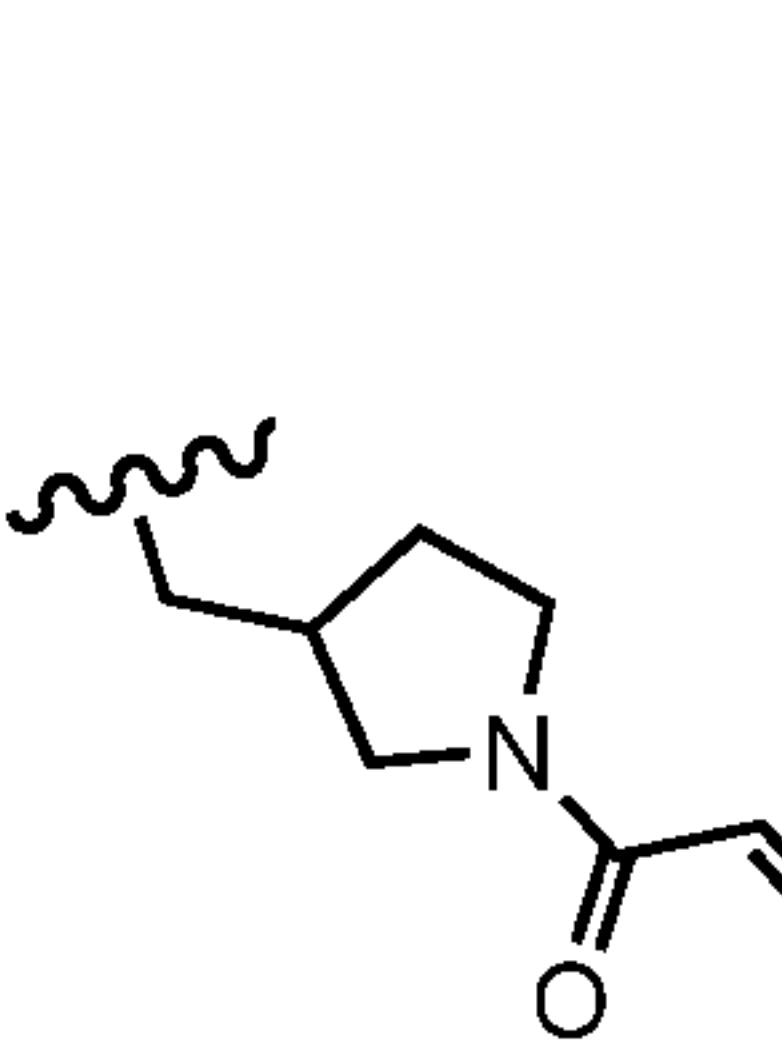


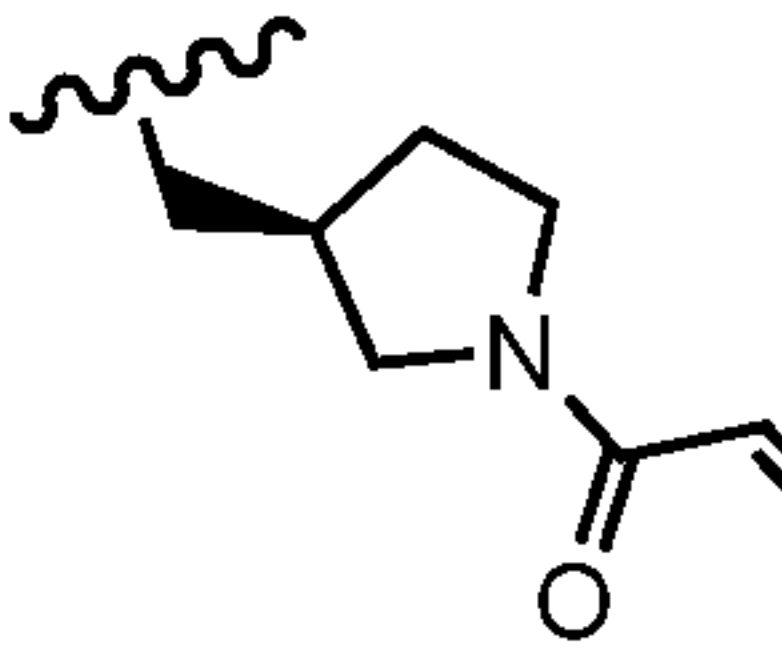
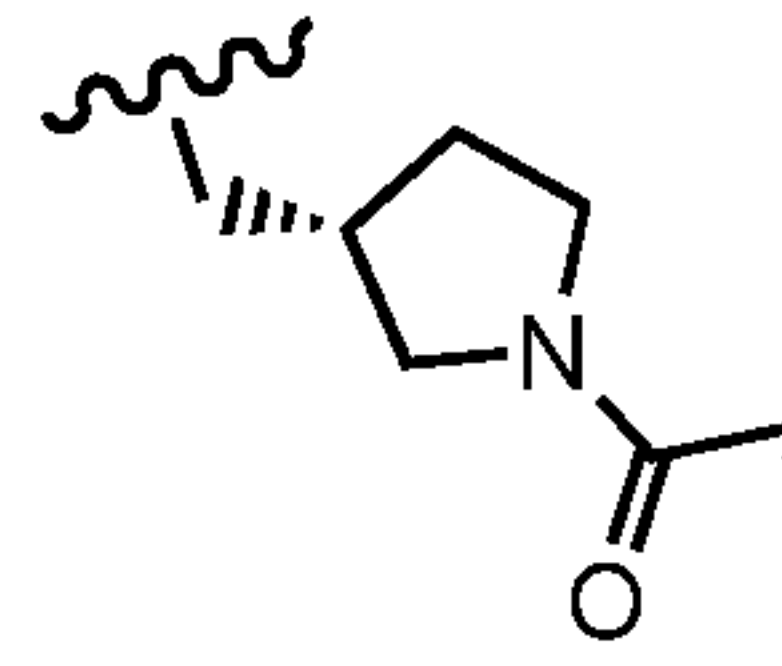
is  . In embodiments, L¹-L²-E is  . In embodiments,

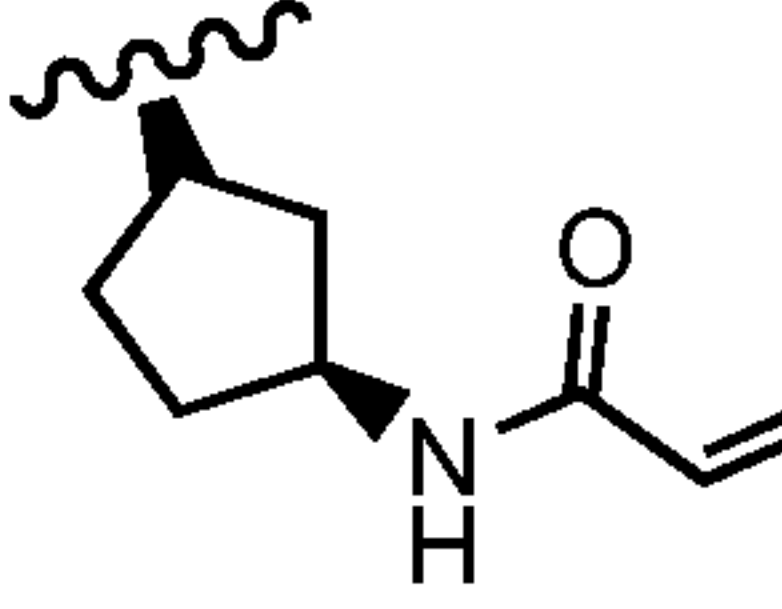
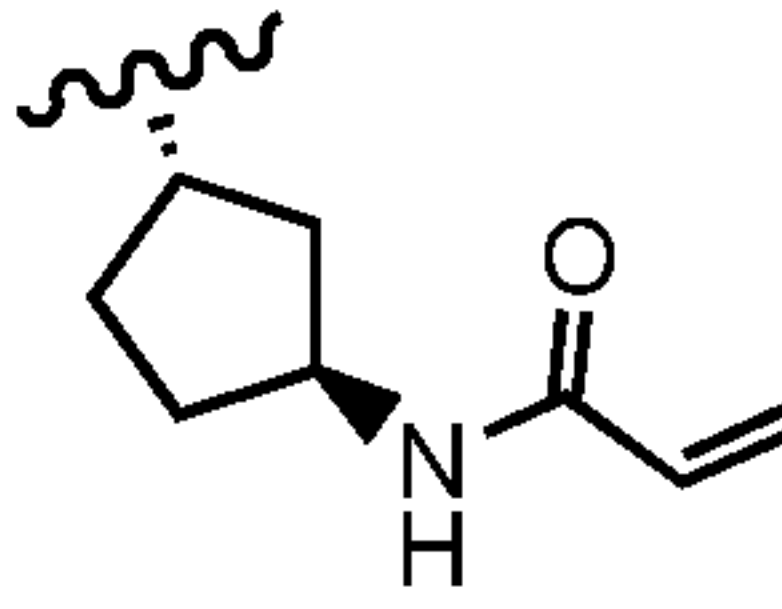
L¹-L²-E is  . In embodiments, L¹-L²-E is  . In

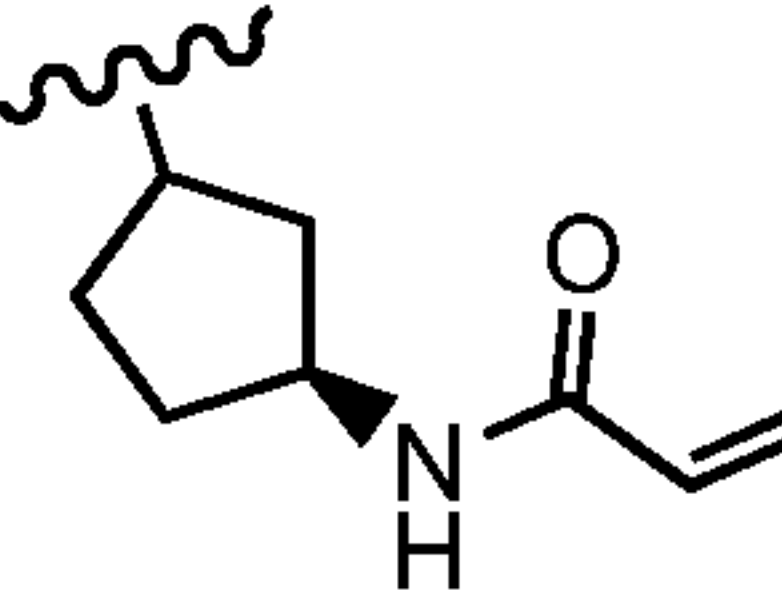
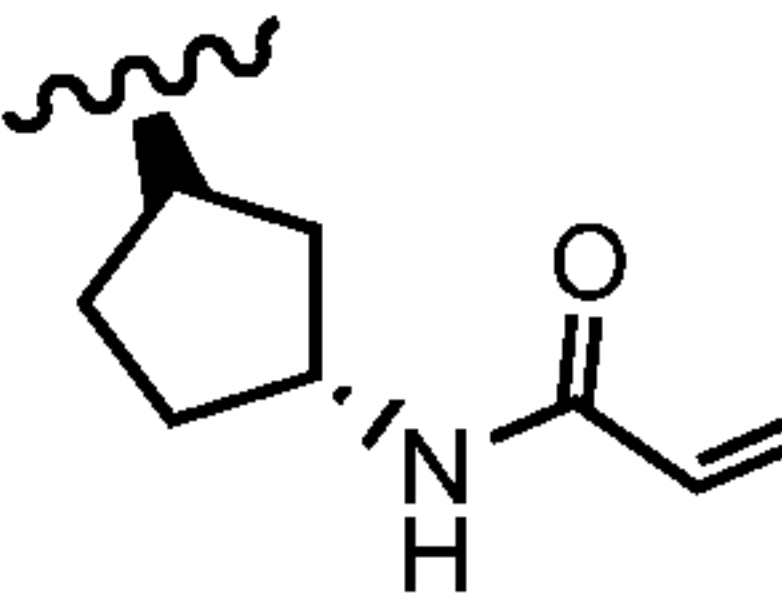
embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  .

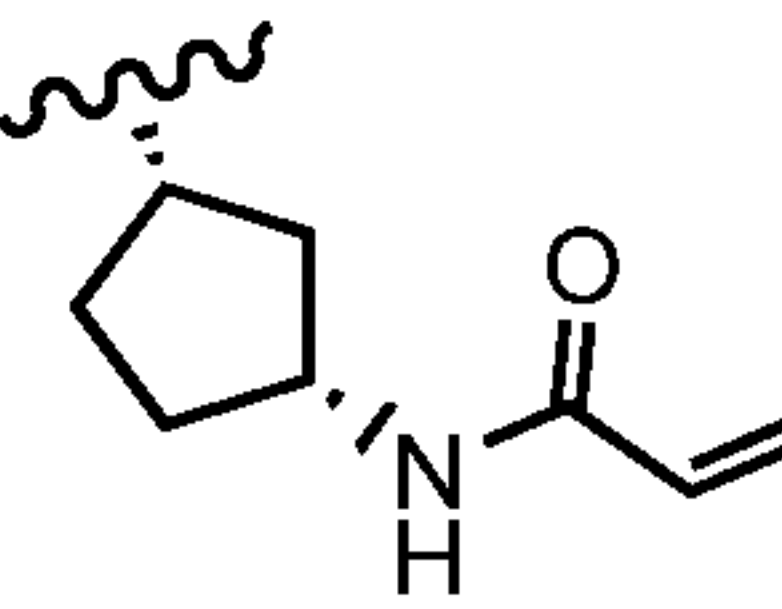
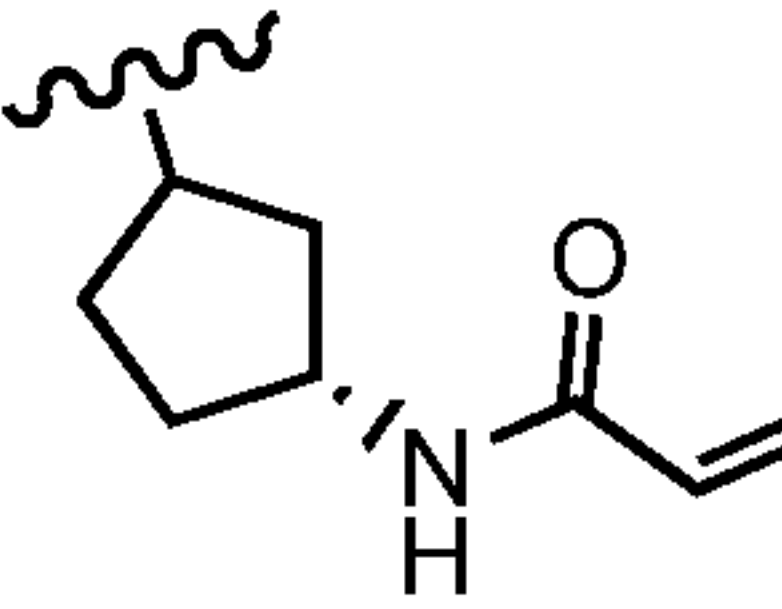
In embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  .

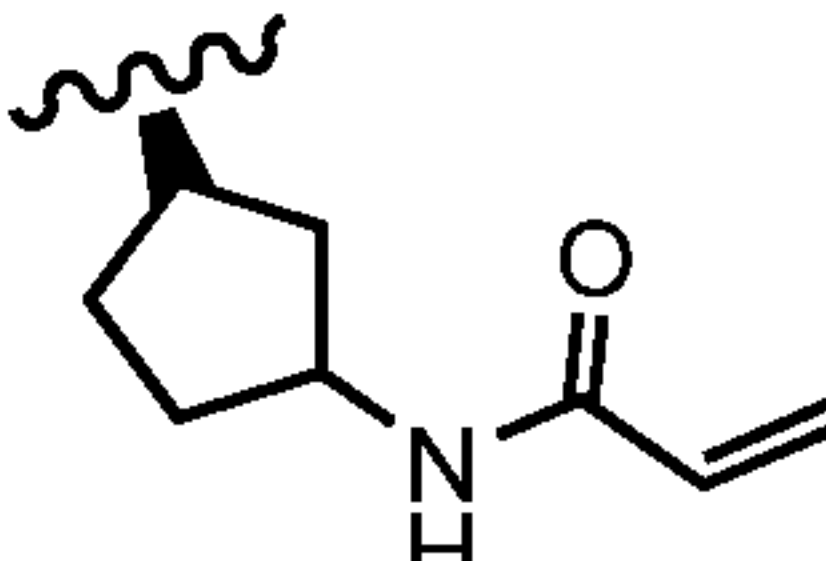
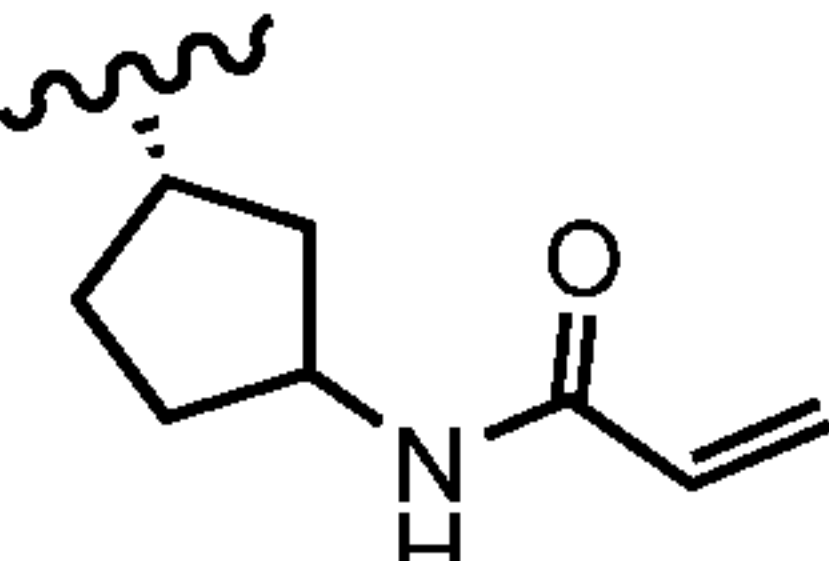
5 In embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  .

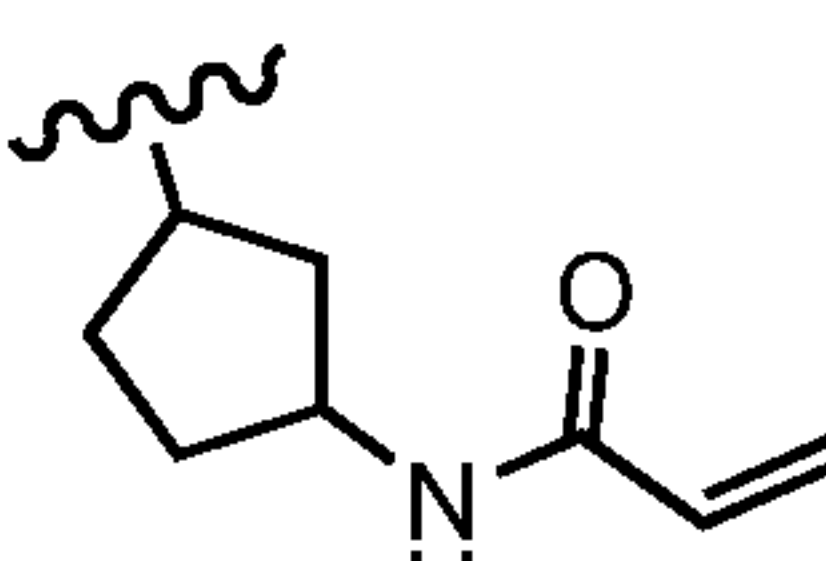
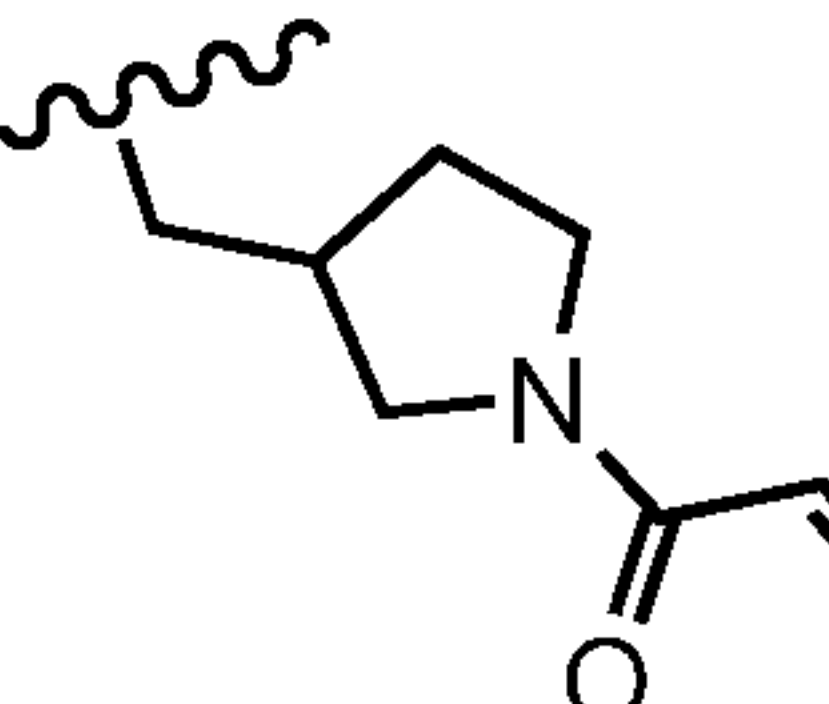
In embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  .

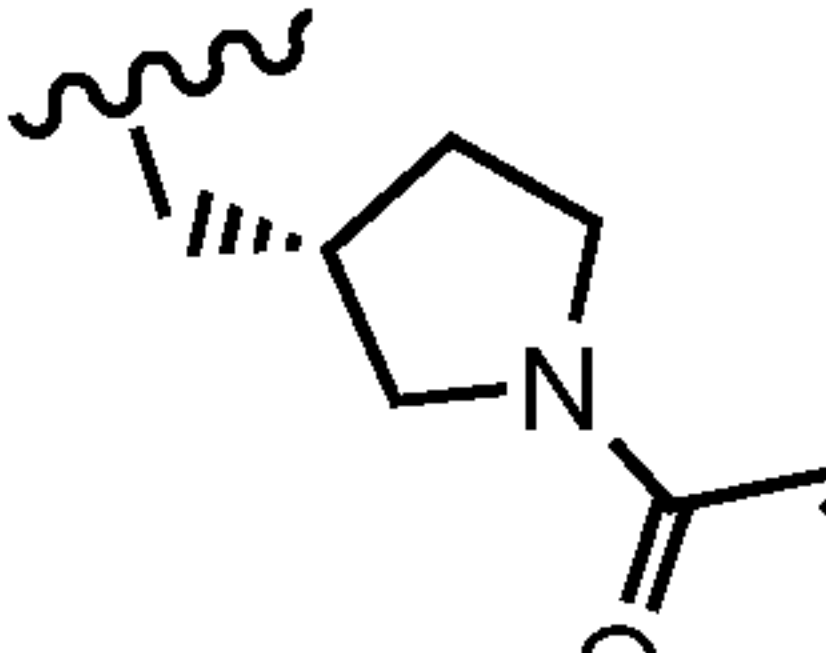
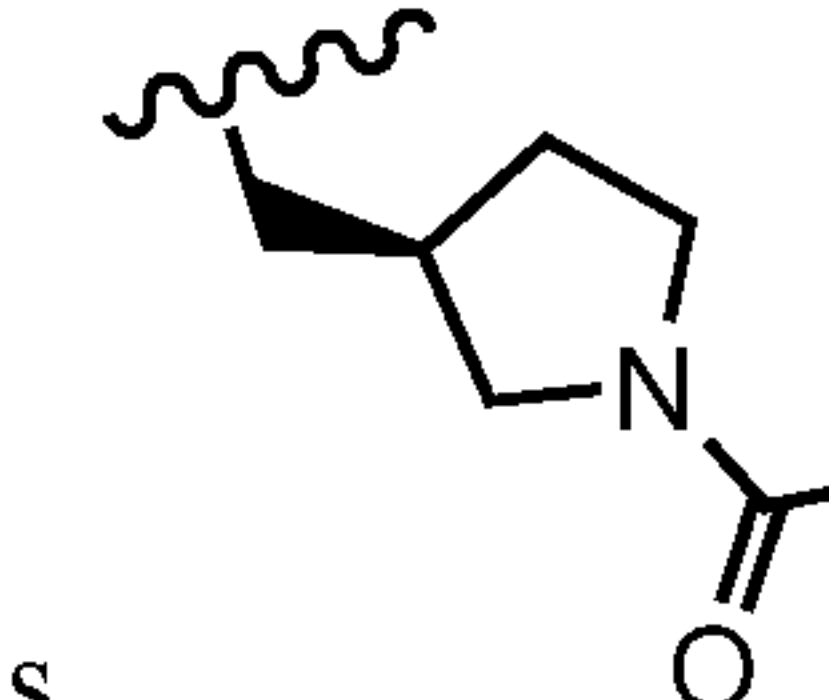
In embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  . In

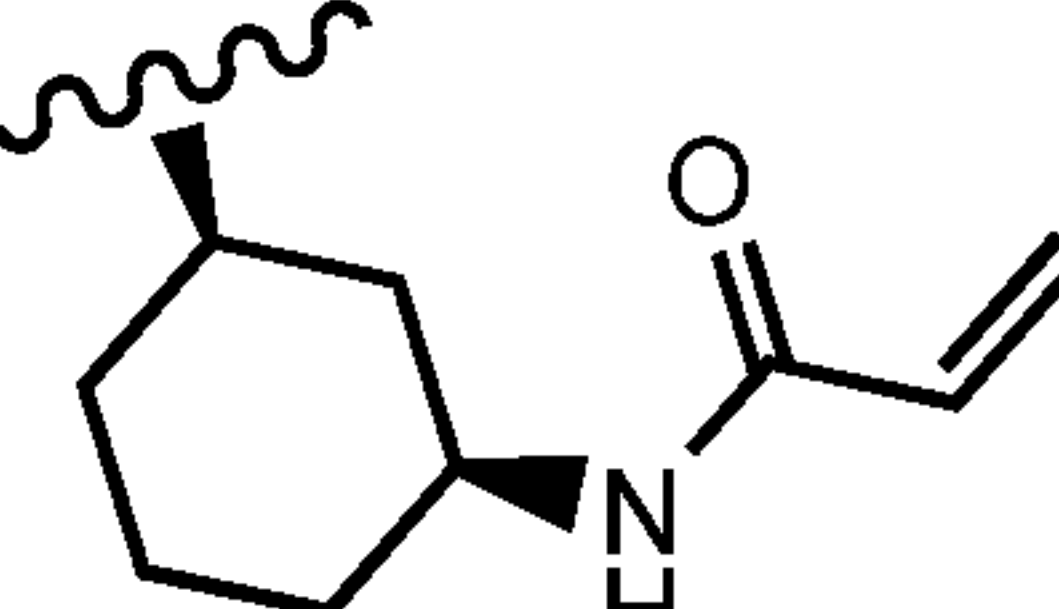
embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  . In

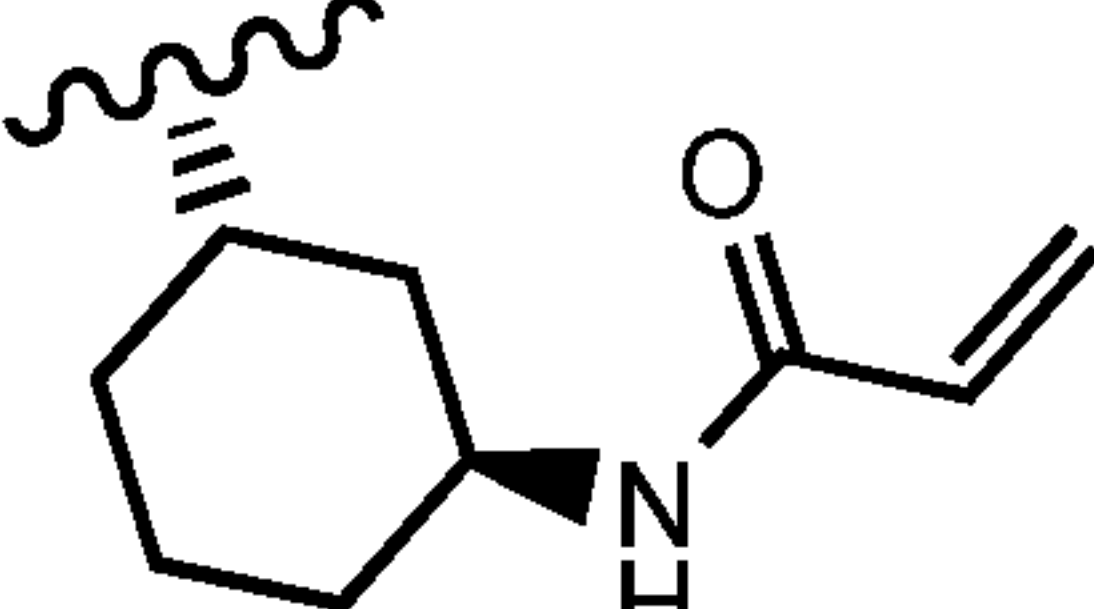
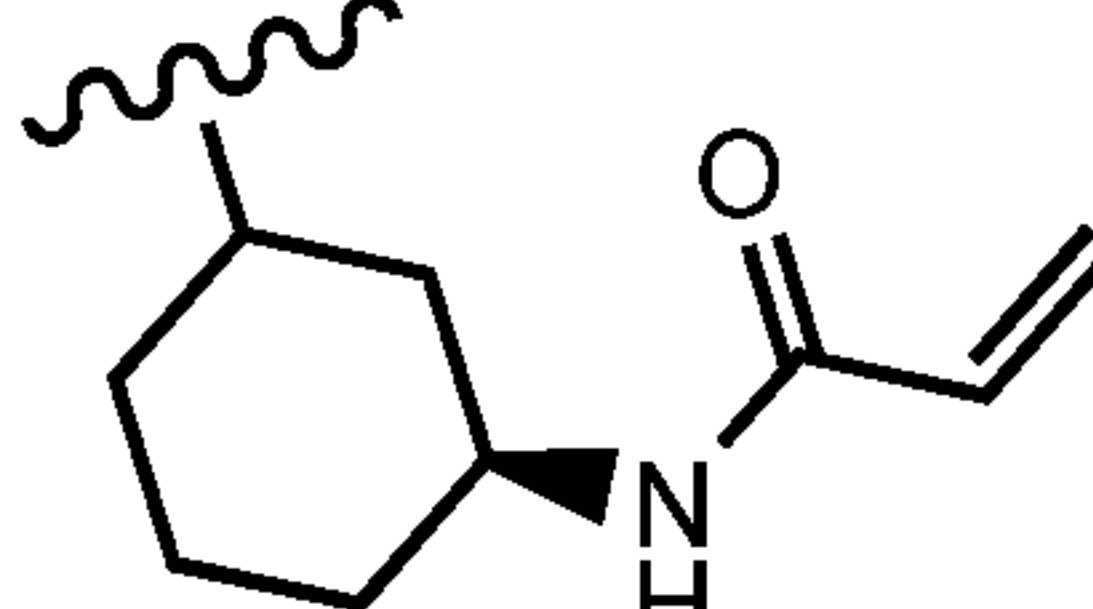
embodiments, L¹-L²-E is  . In embodiments, L¹-L²-E is  . In

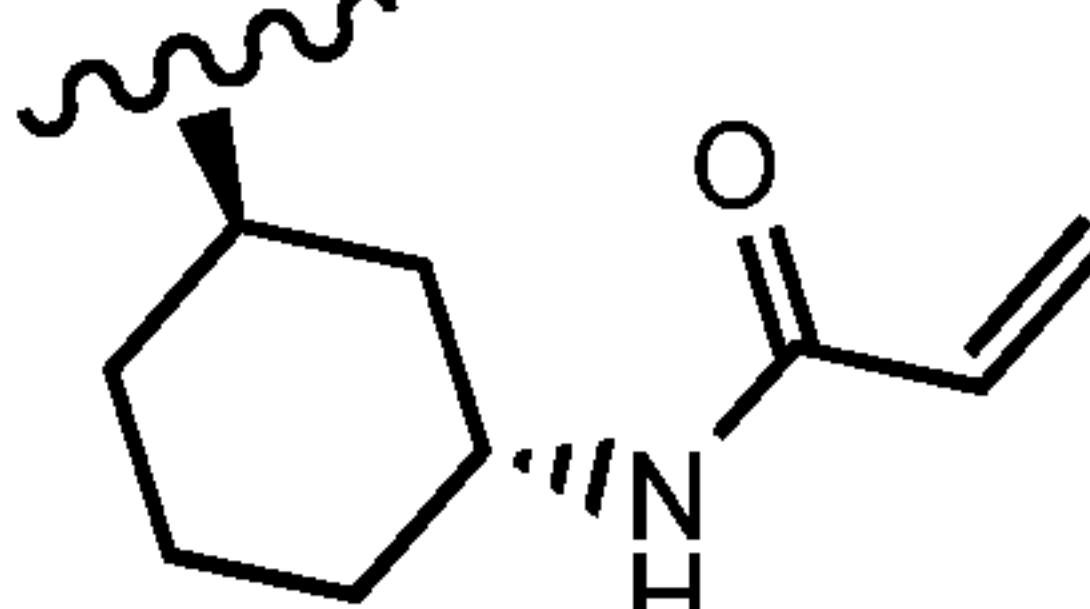
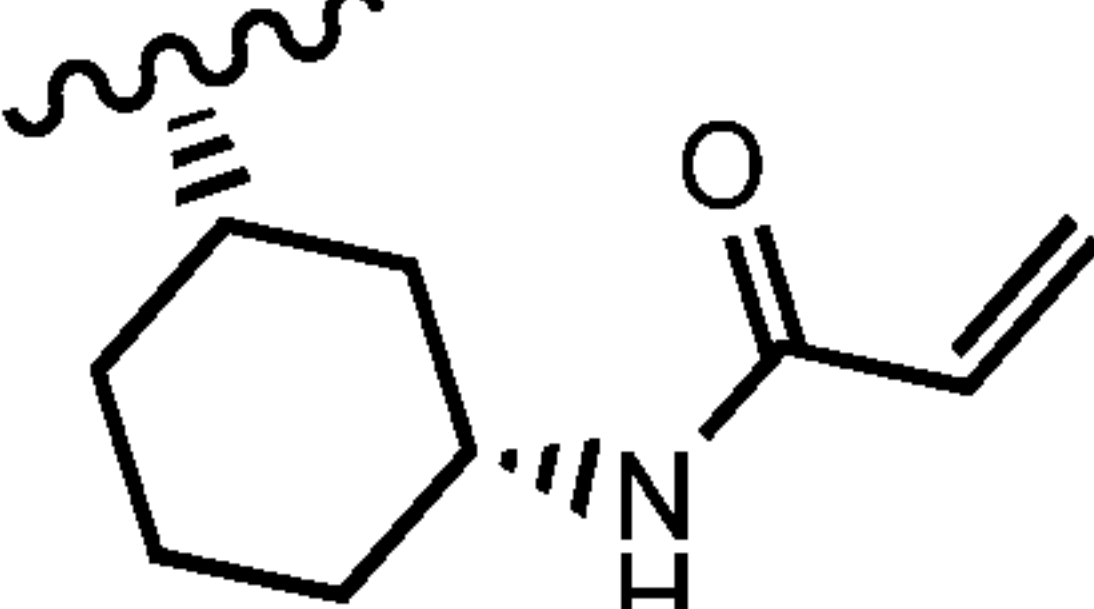
embodiments, L^1-L^2-E is . In embodiments, L^1-L^2-E is . In

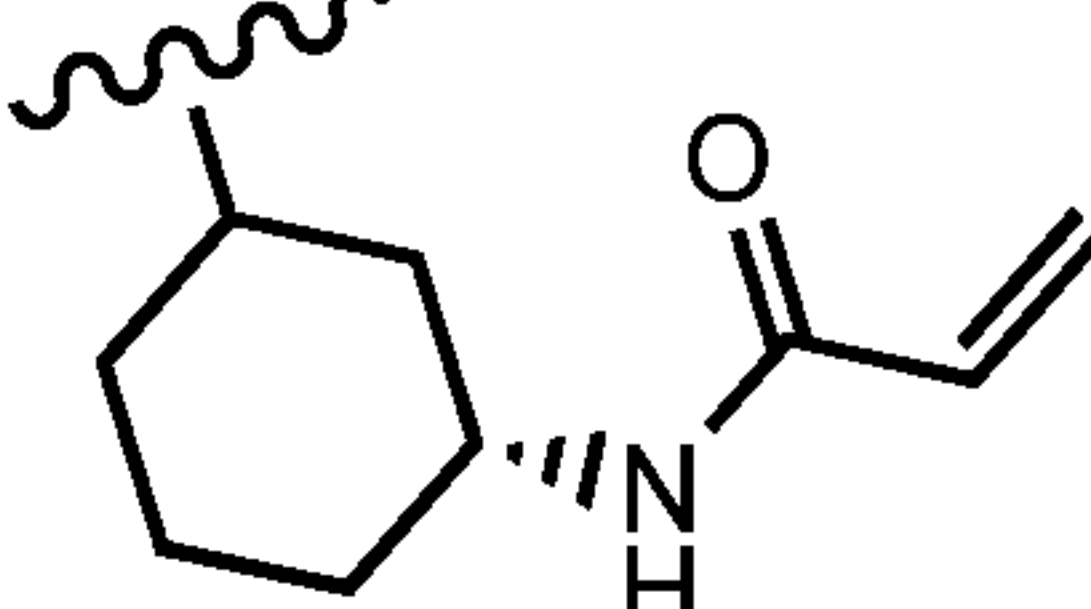
embodiments, L^1-L^2-E is . In embodiments, L^1-L^2-E is . In

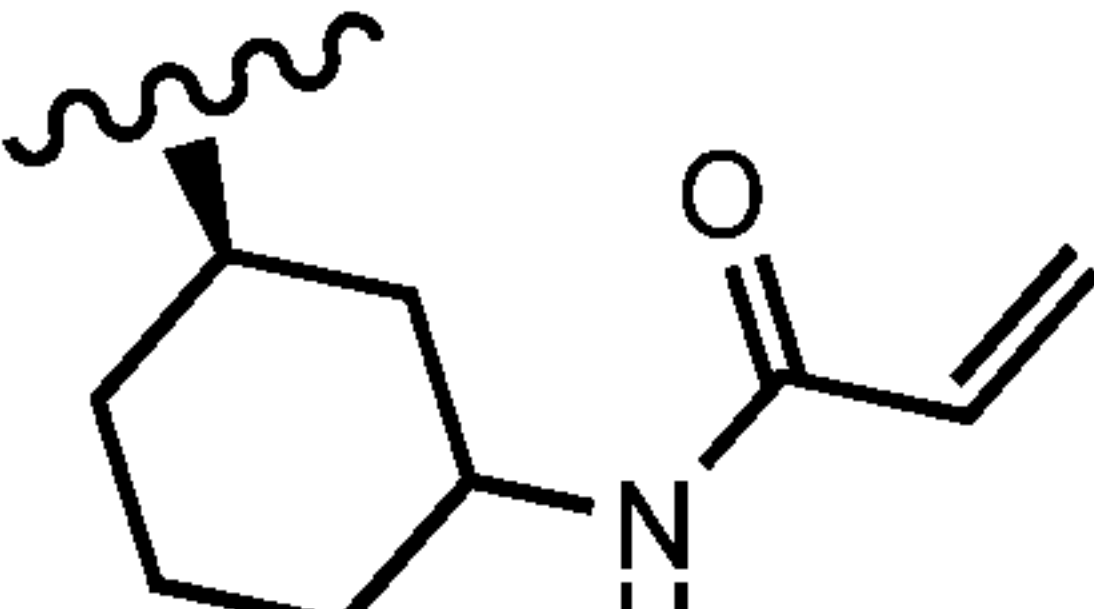
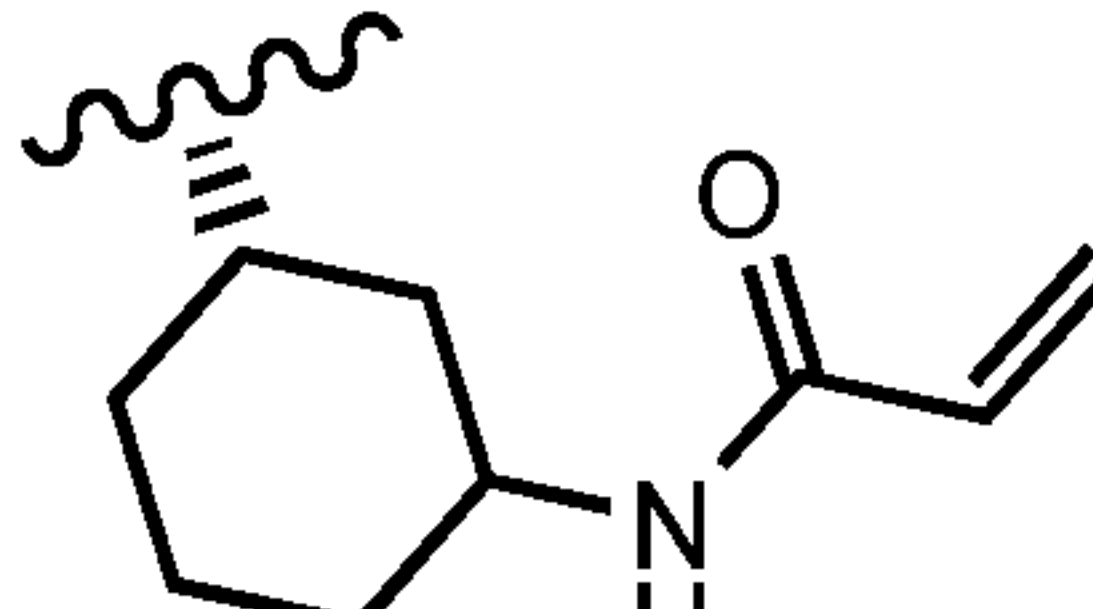
embodiments, L^1-L^2-E is . In embodiments, L^1-L^2-E is . In

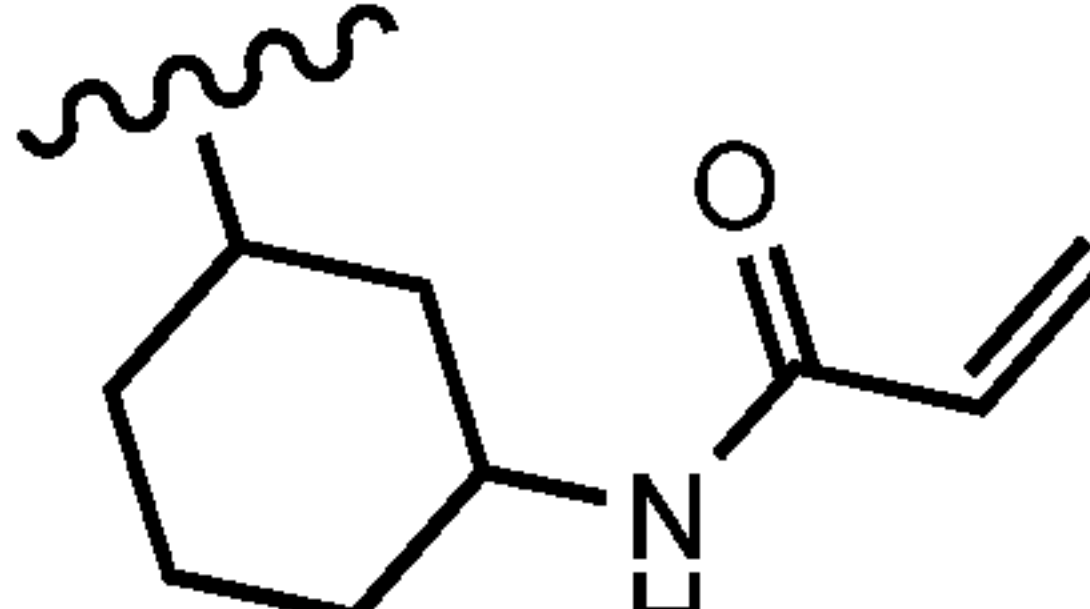
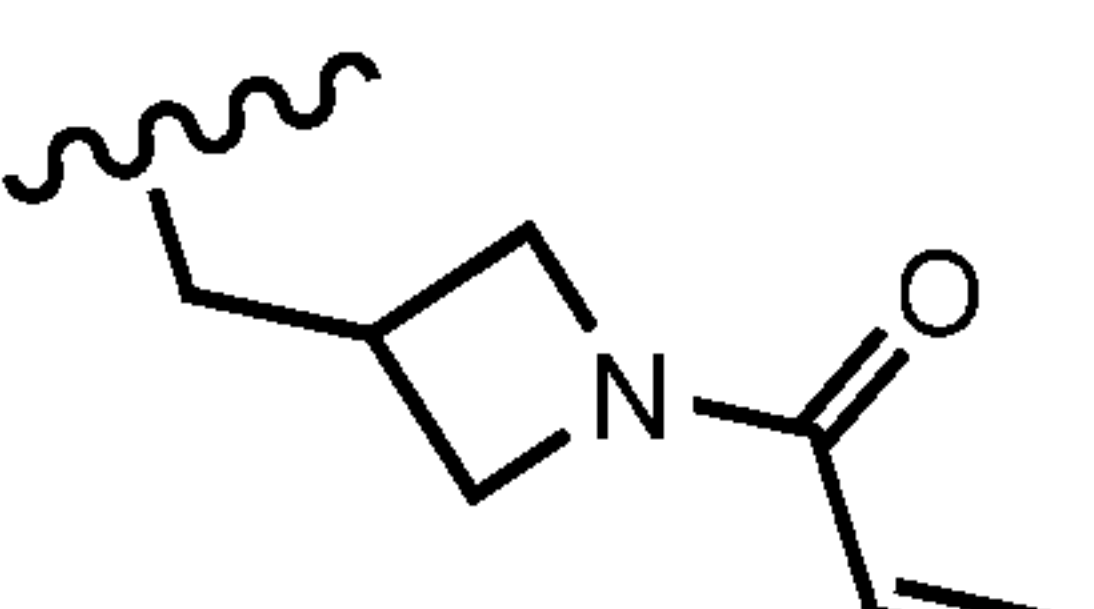
In embodiments, L^1-L^2-E is . In embodiments, L^1-L^2-E is

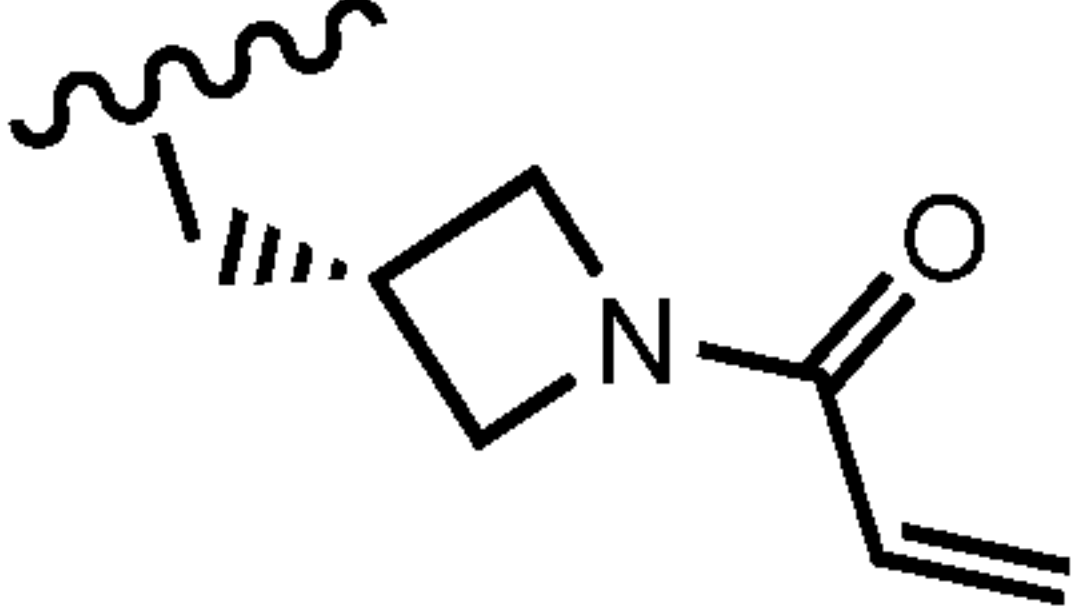
5 . In embodiments, L^1-L^2-E is . In embodiments,

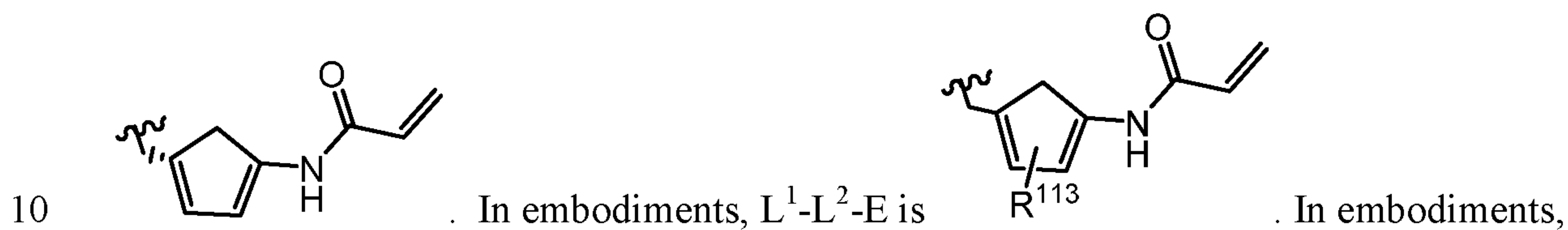
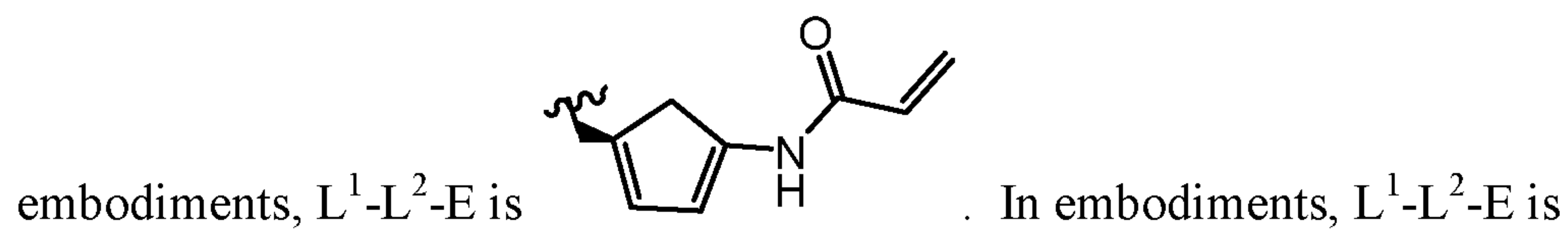
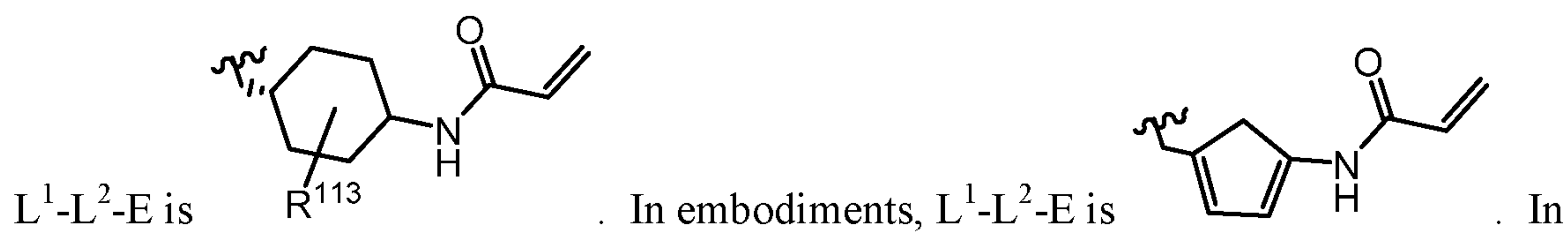
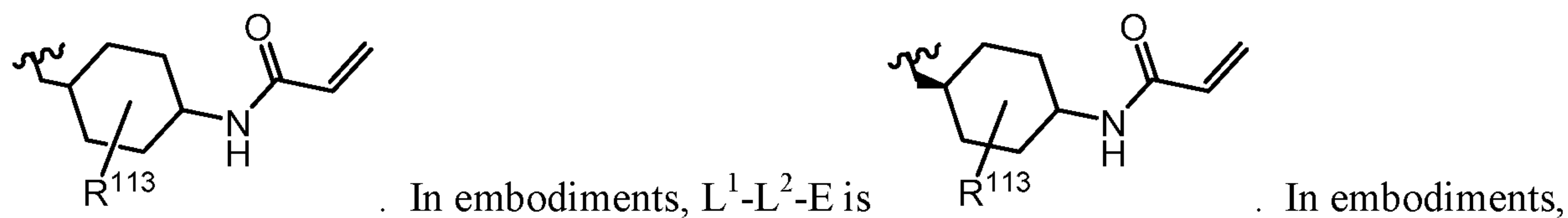
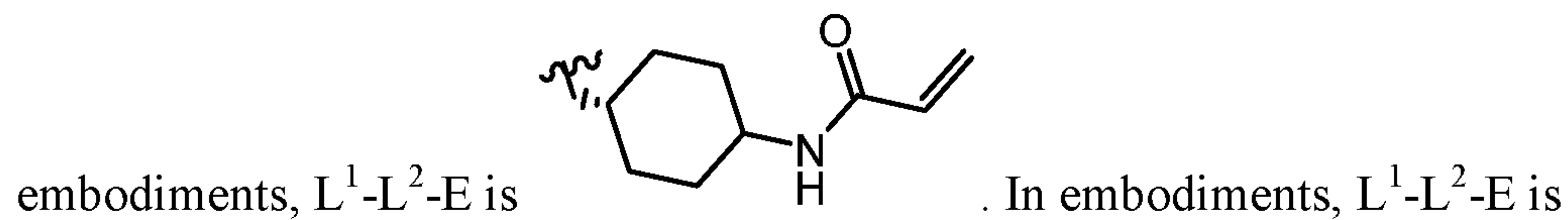
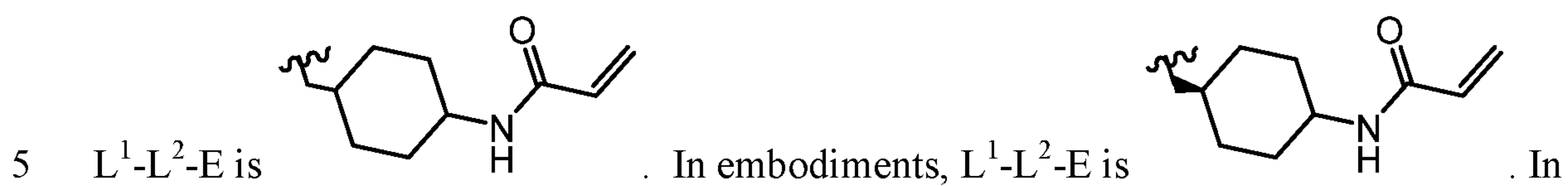
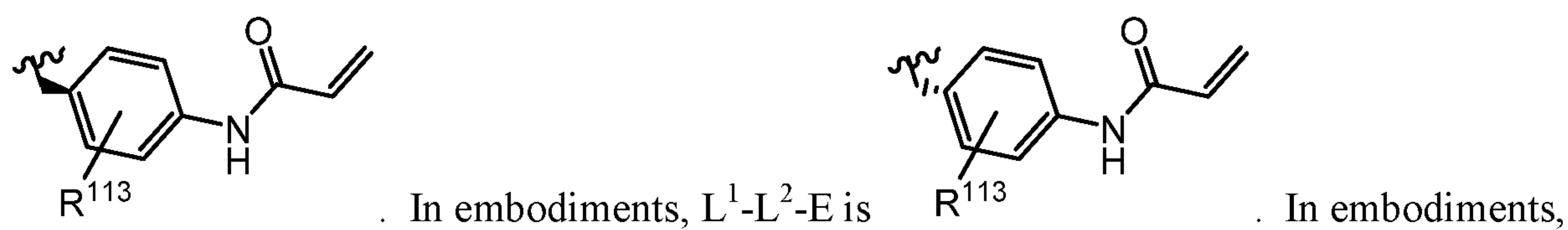
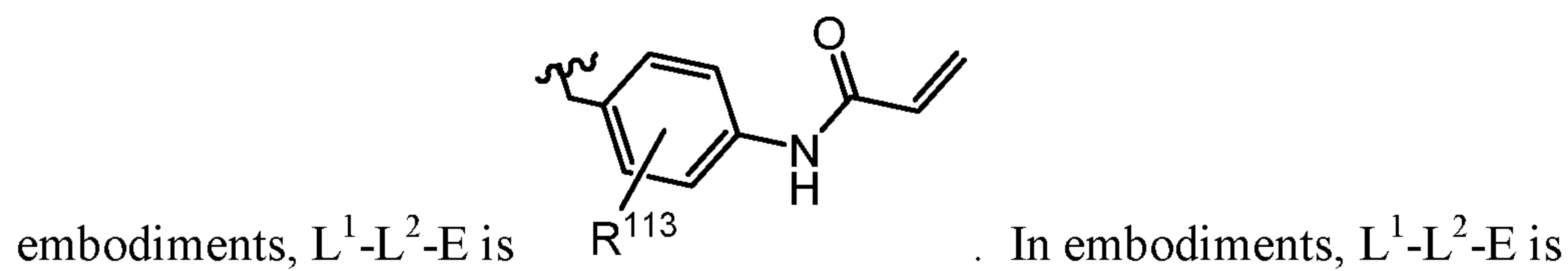
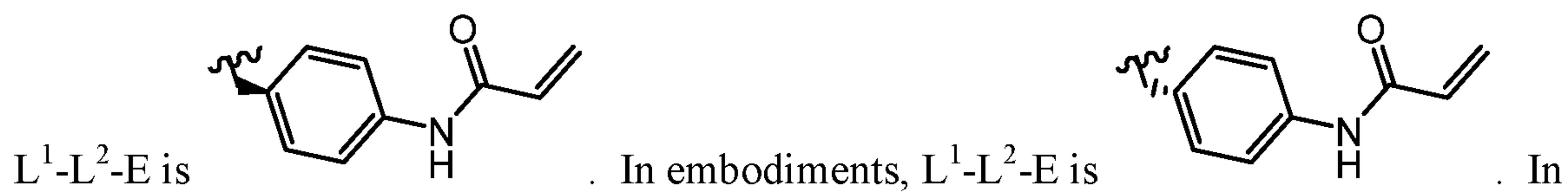
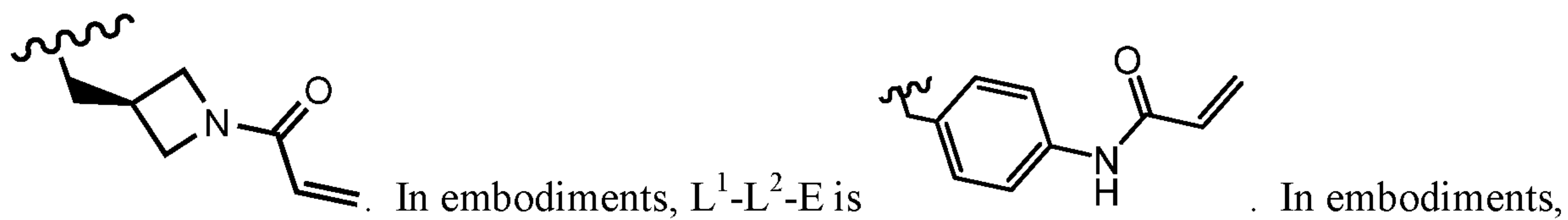
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In

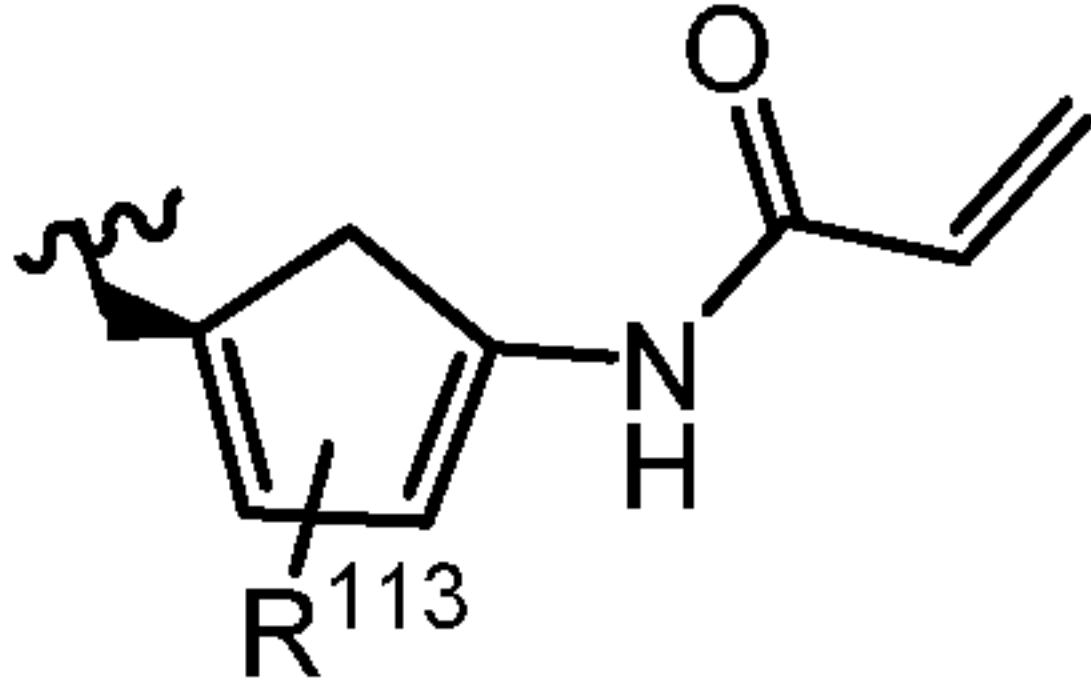
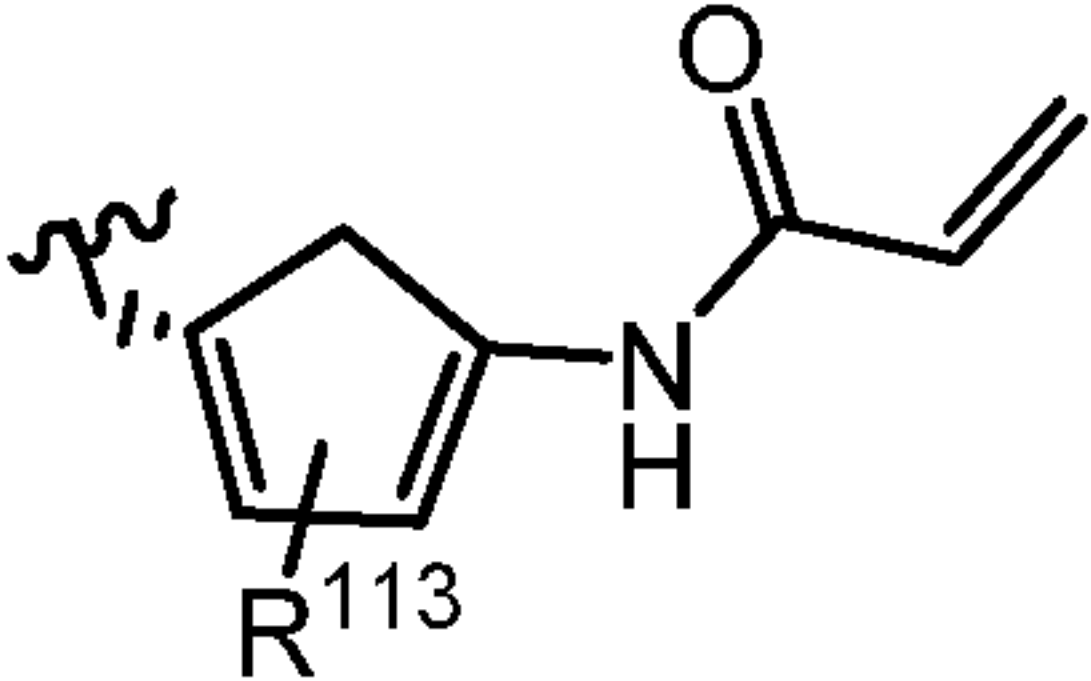
embodiments, L^1-L^2-E is . In embodiments, L^1-L^2-E is

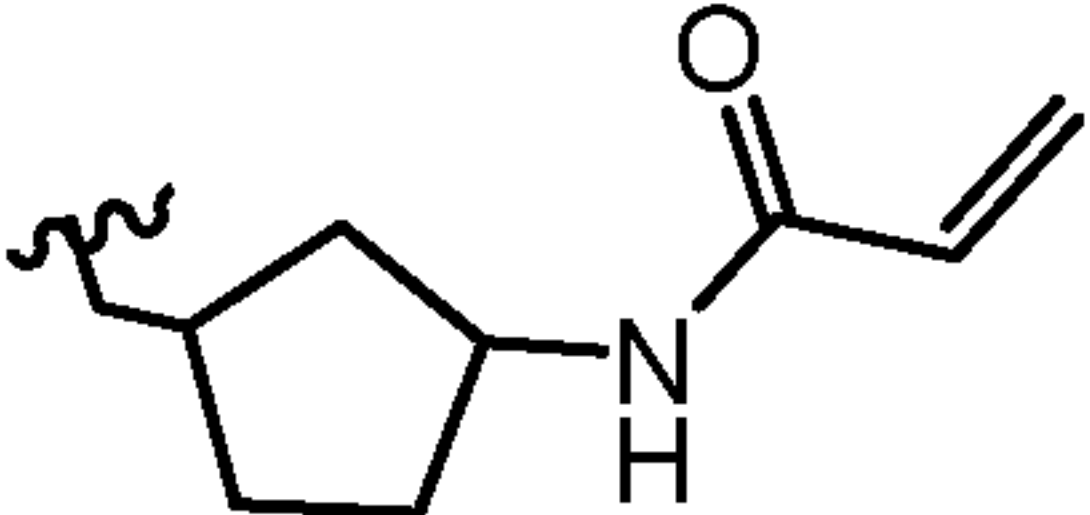
. In embodiments, L^1-L^2-E is . In embodiments,

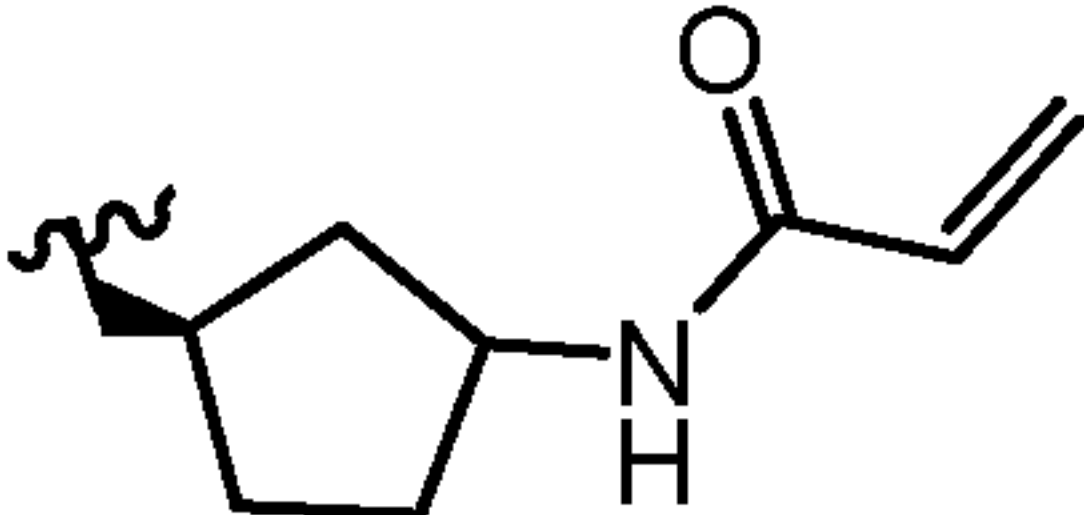
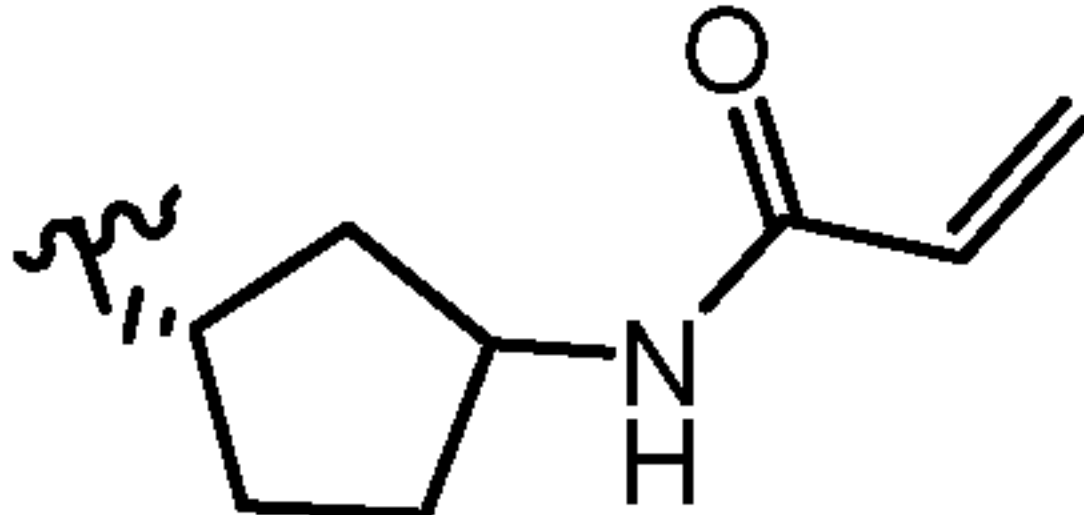
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In

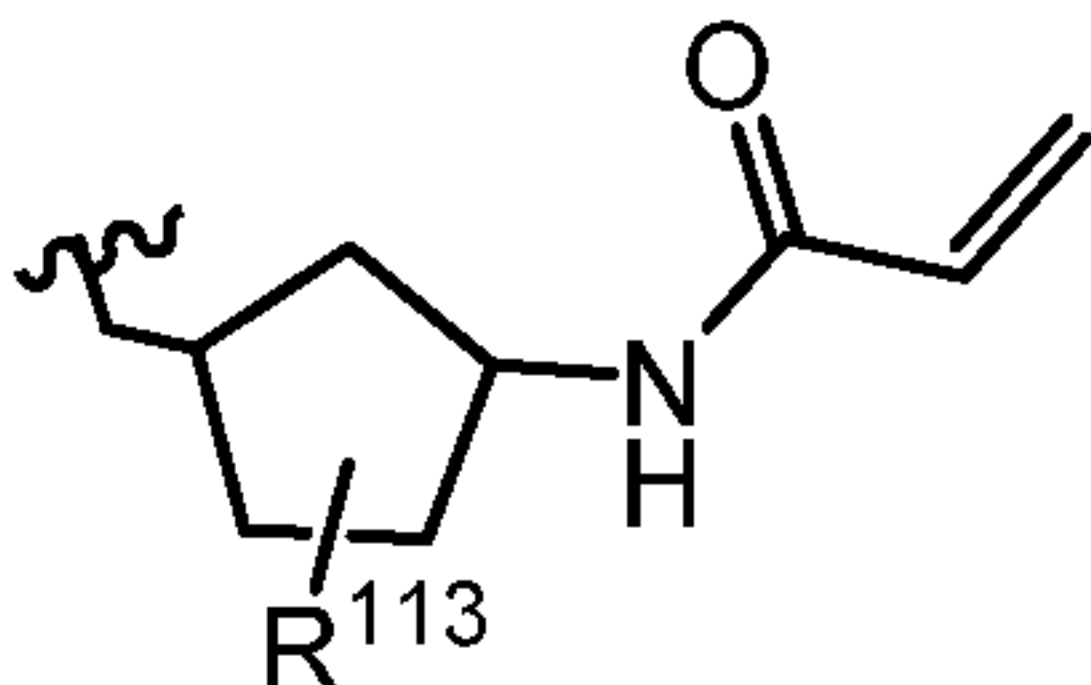
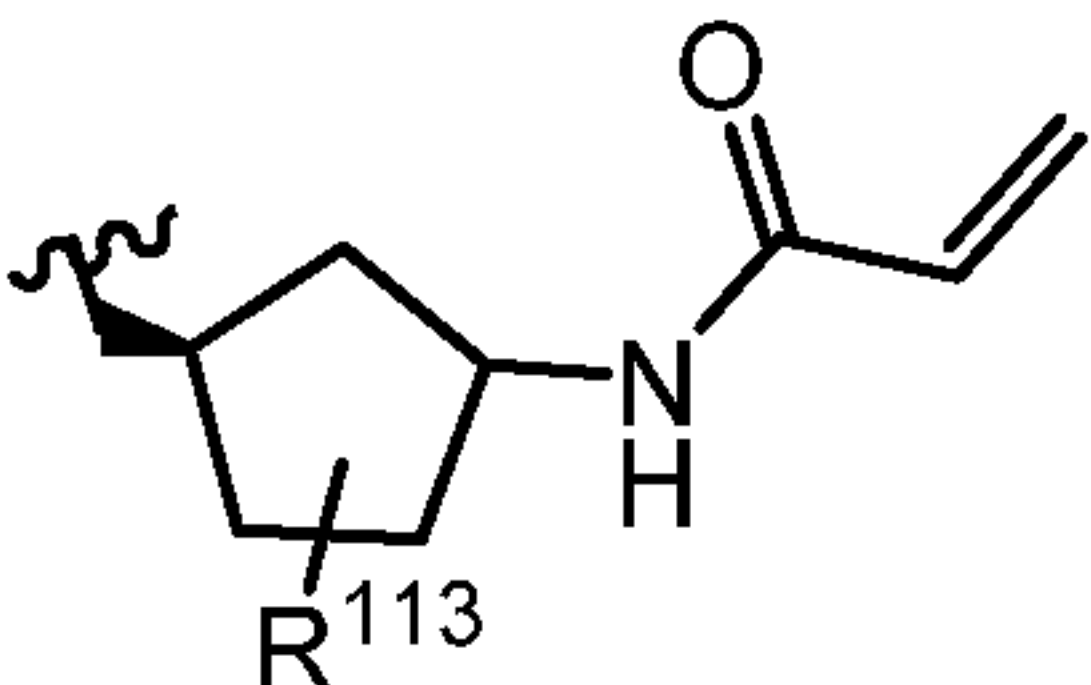
10 . In embodiments, L^1-L^2-E is

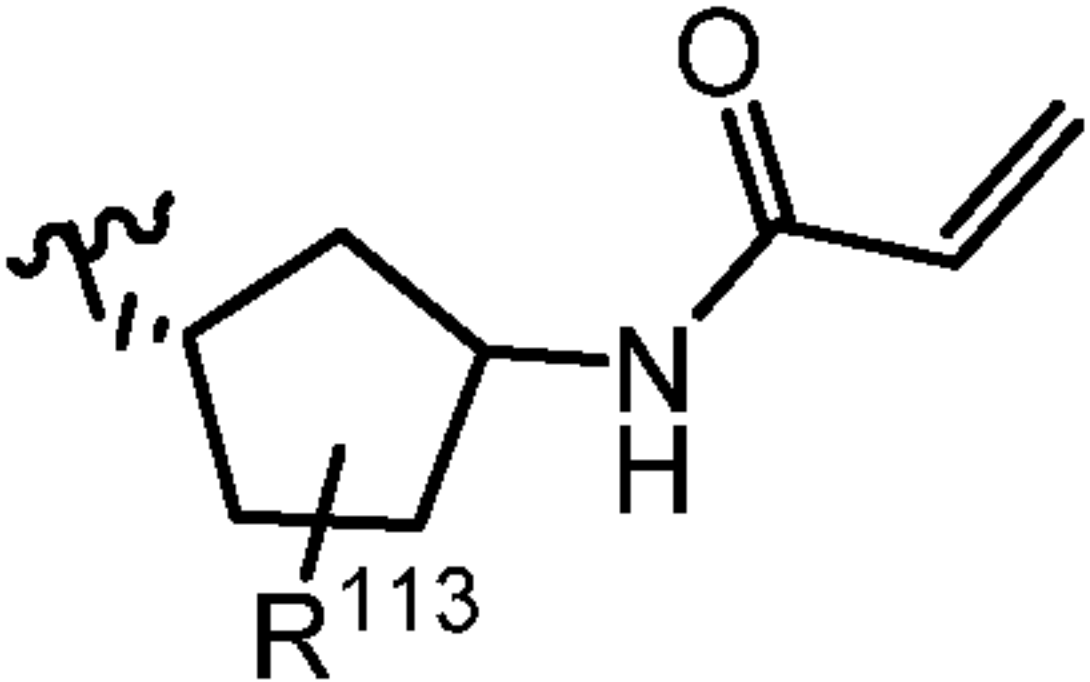


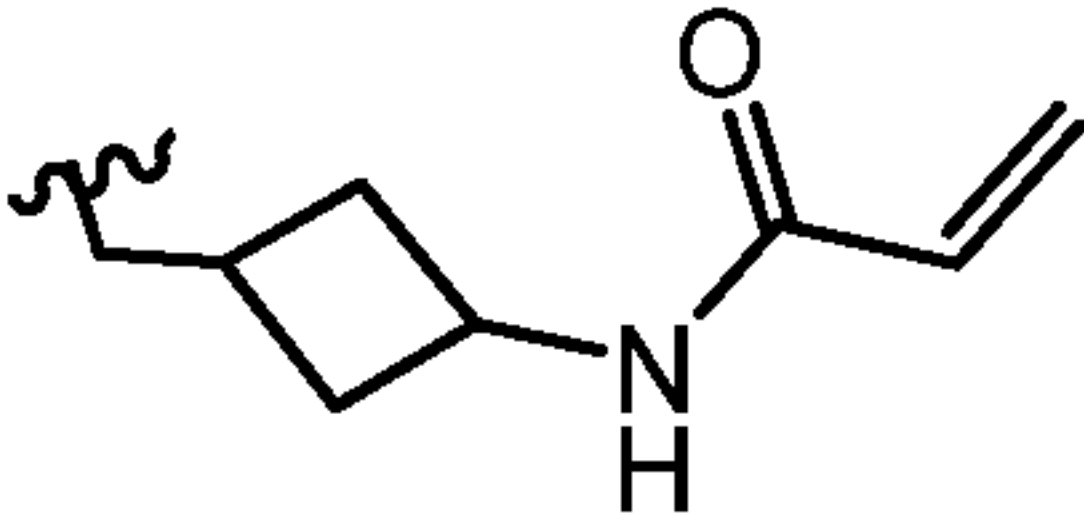
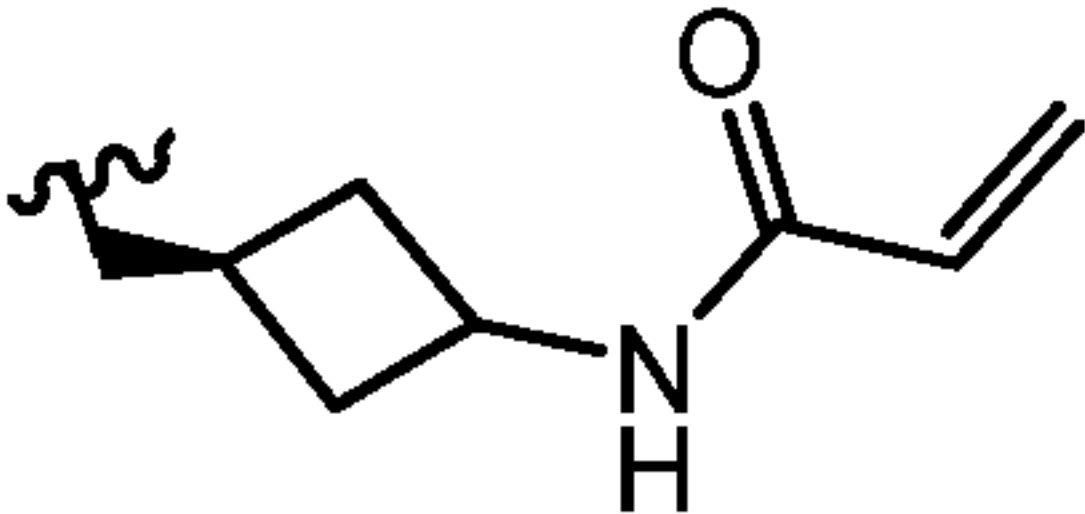
L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is . In

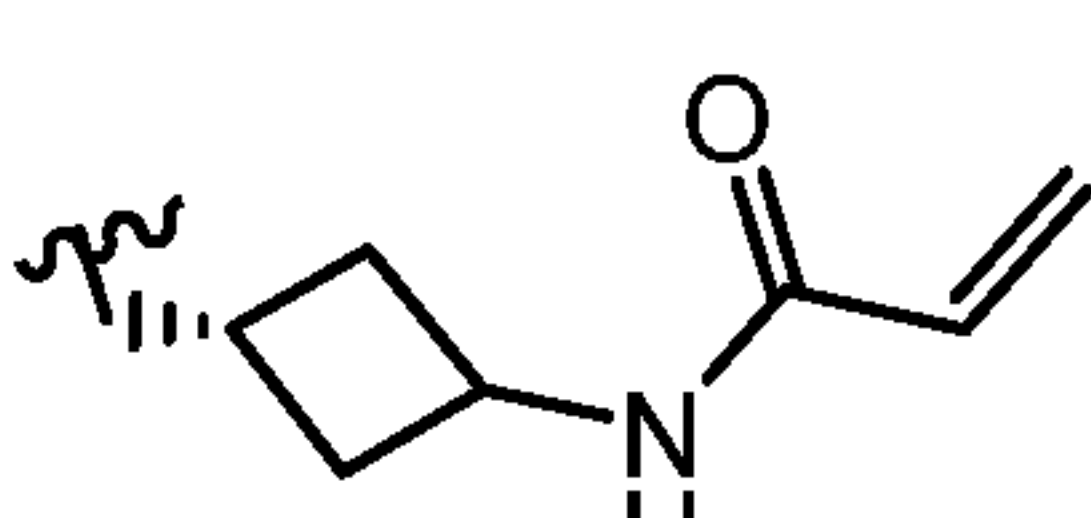
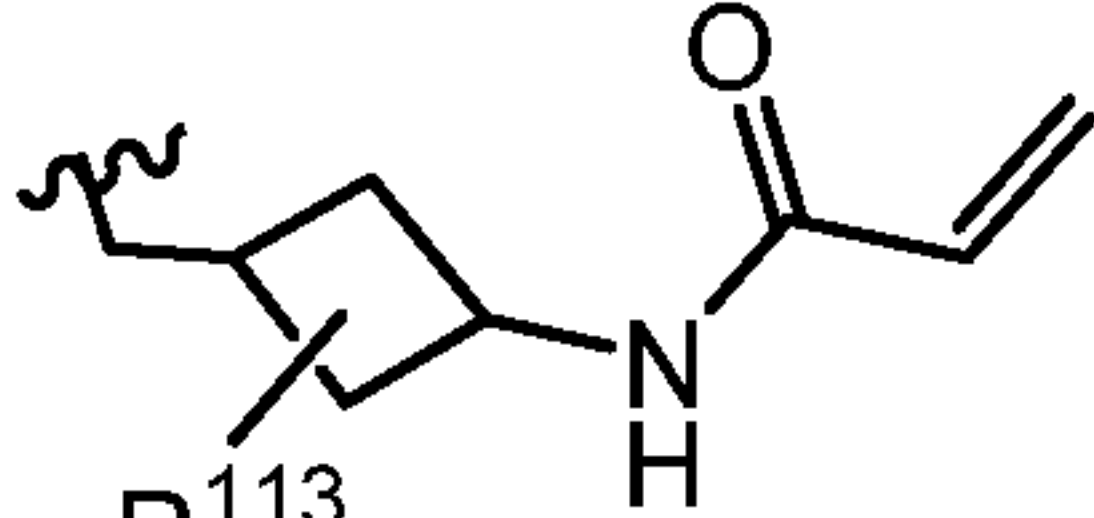
embodiments, L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is

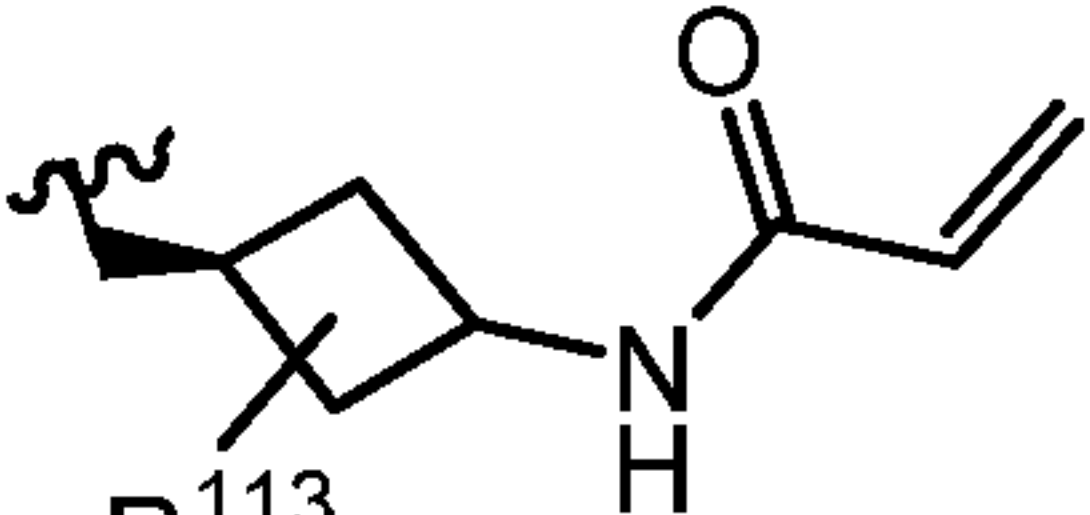
. In embodiments, L^1 - L^2 -E is . In embodiments,

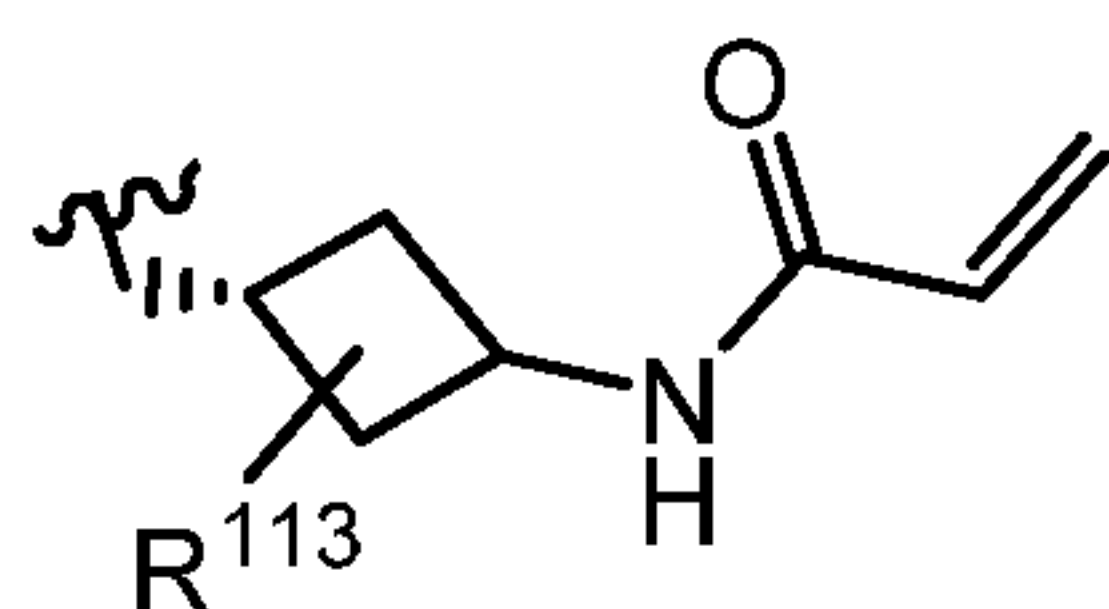
L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is . In

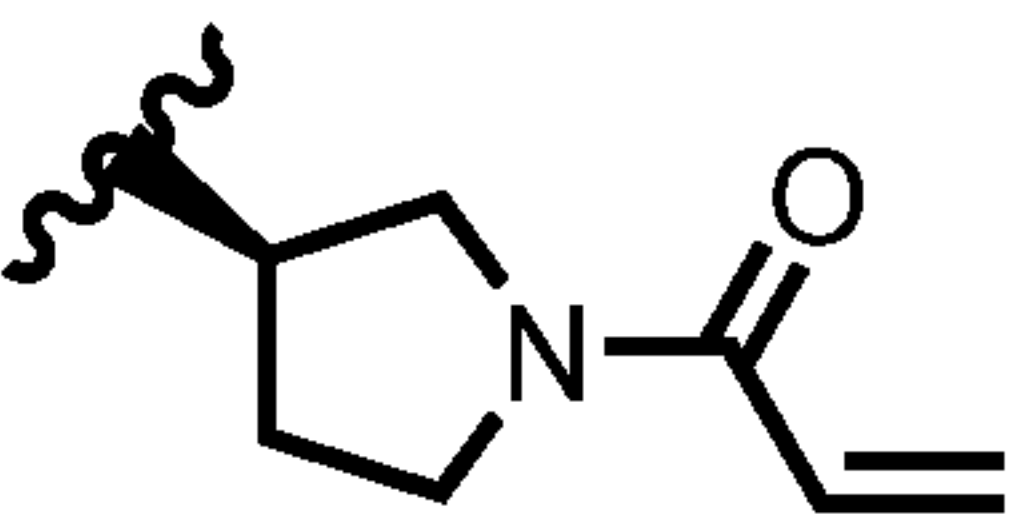
5 L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is

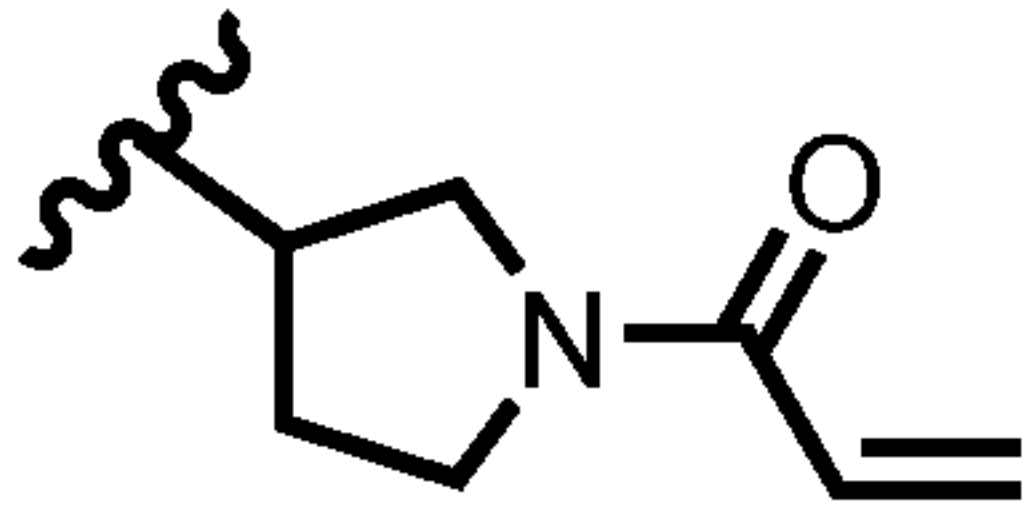
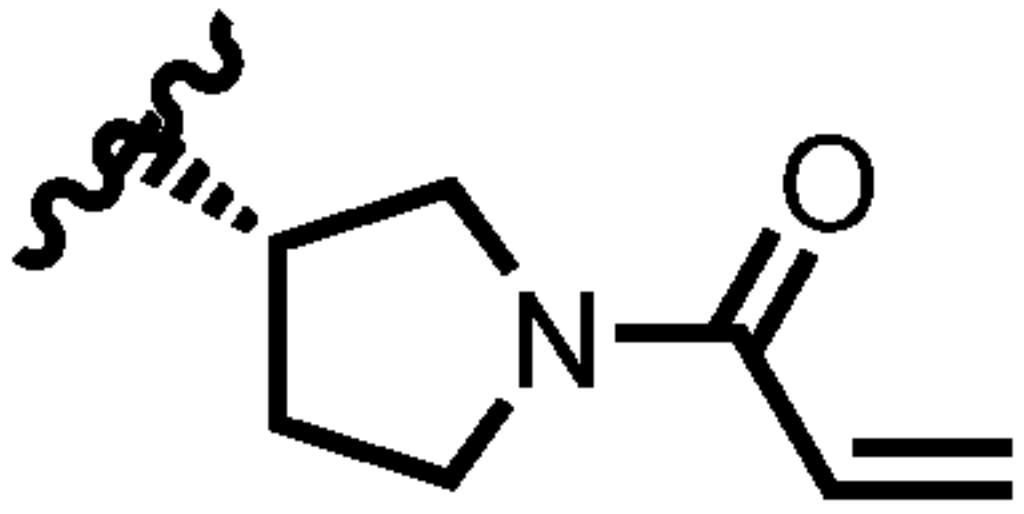
. In embodiments, L^1 - L^2 -E is . In embodiments,

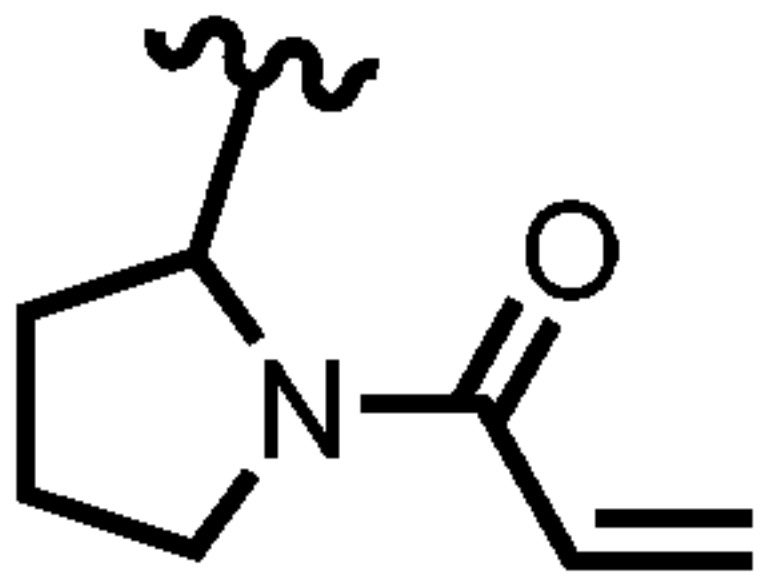
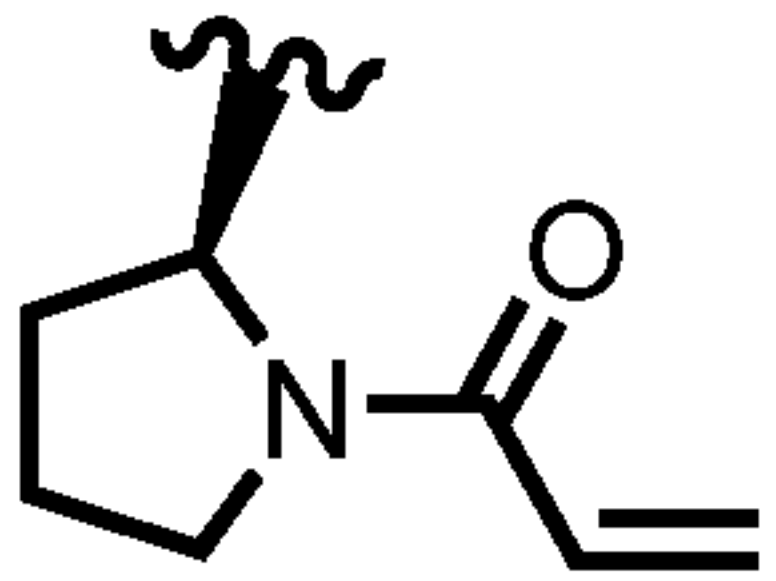
L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is . In

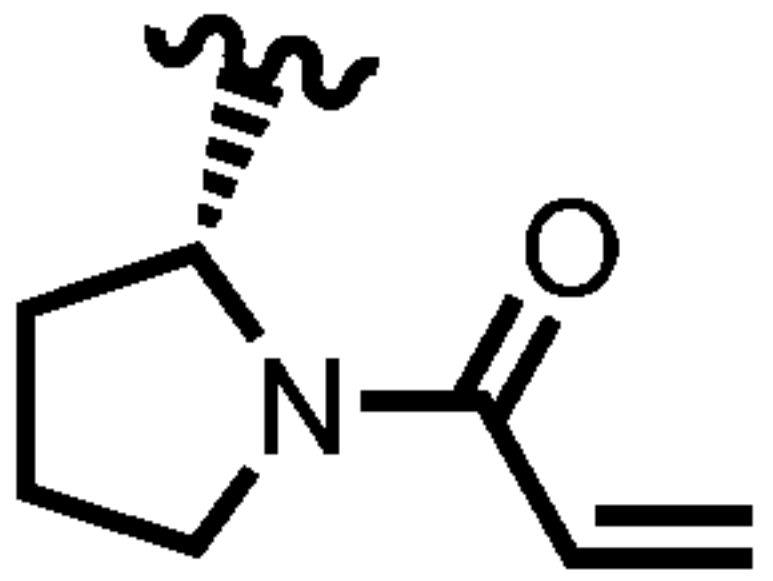
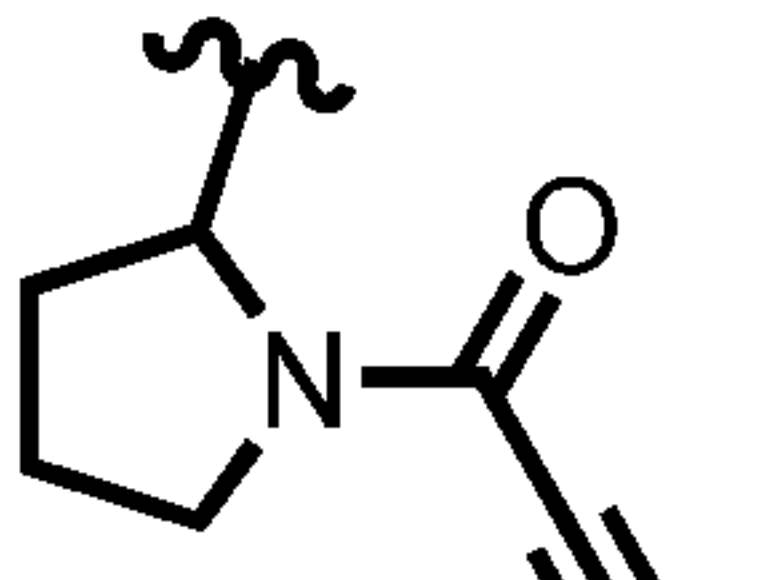
embodiments, L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is

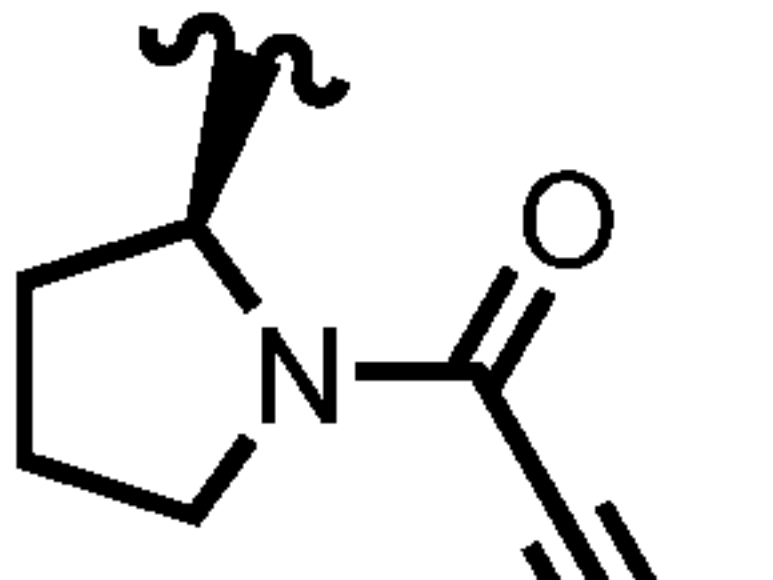
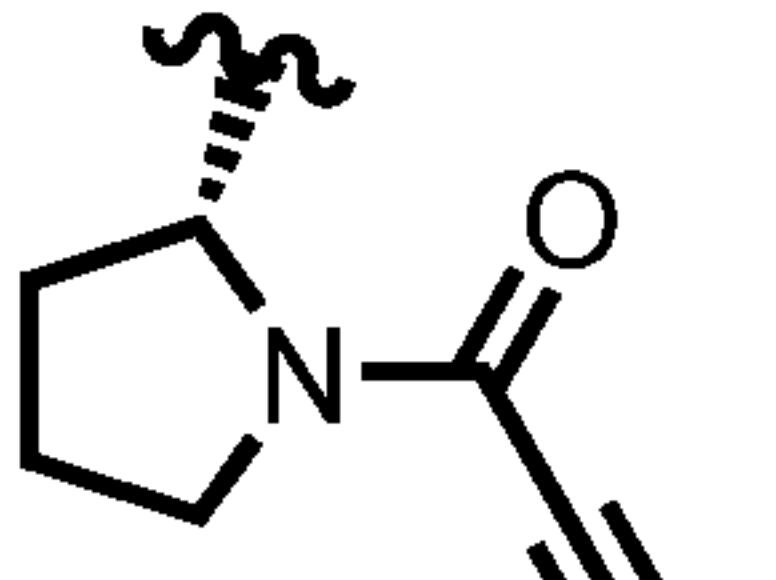


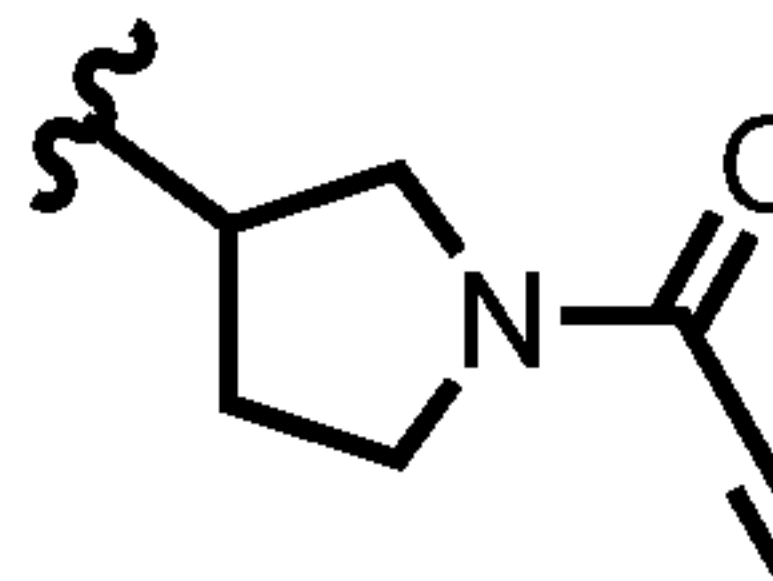
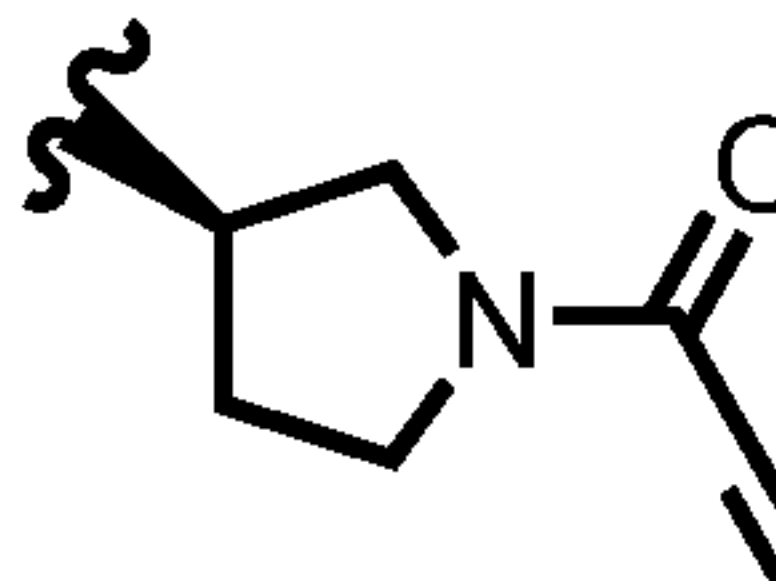
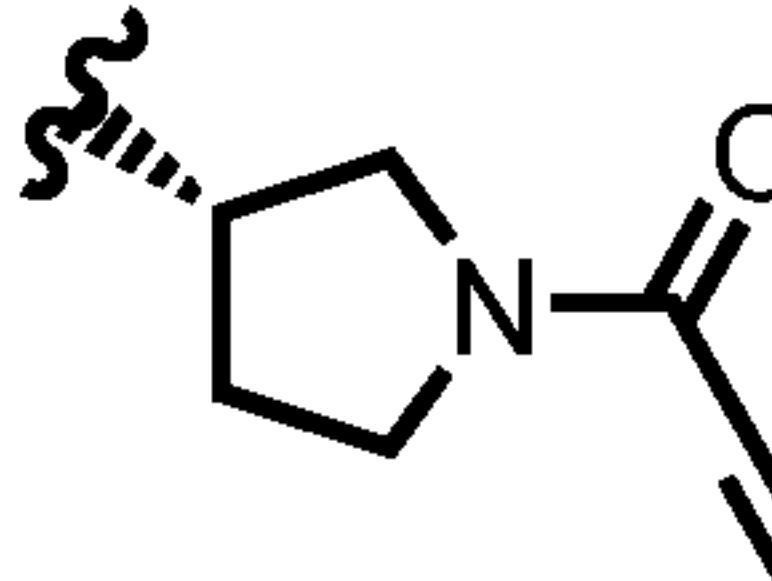
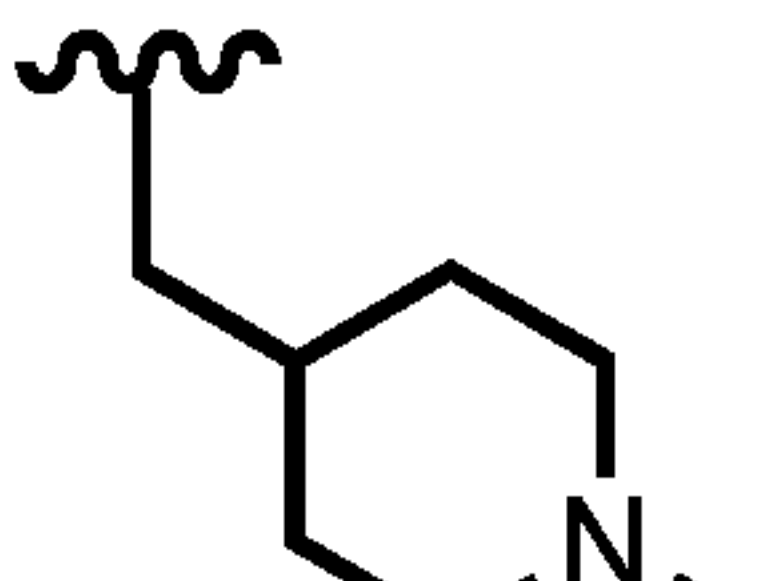
10 [0529] In embodiments, L^1 - L^2 -E is . In embodiments, L^1 - L^2 -E is

. In embodiments, L^1 - L^2 -E is . In embodiments,

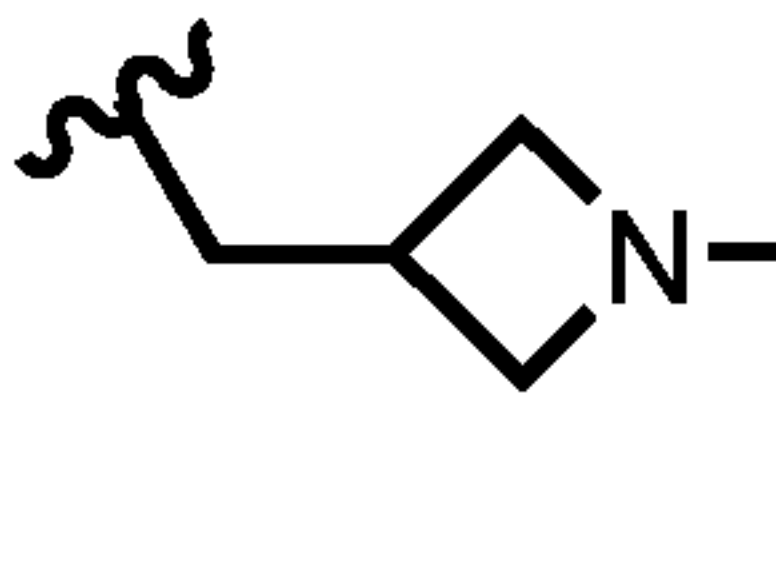
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In embodiments,

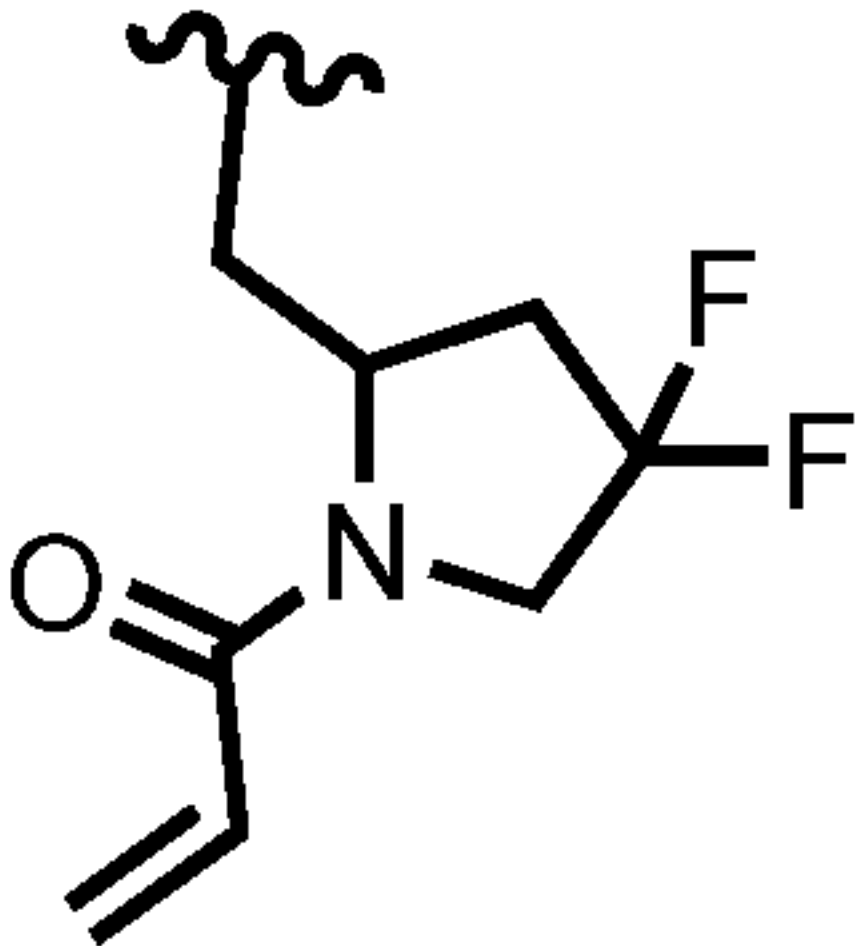
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In embodiments,

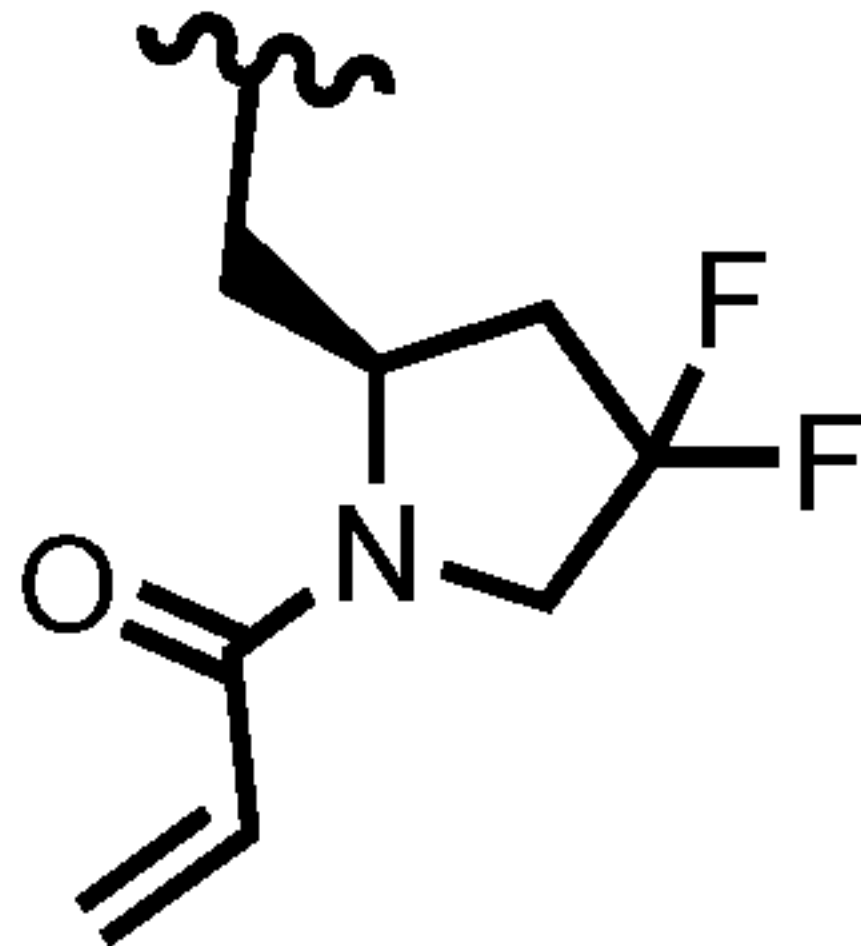
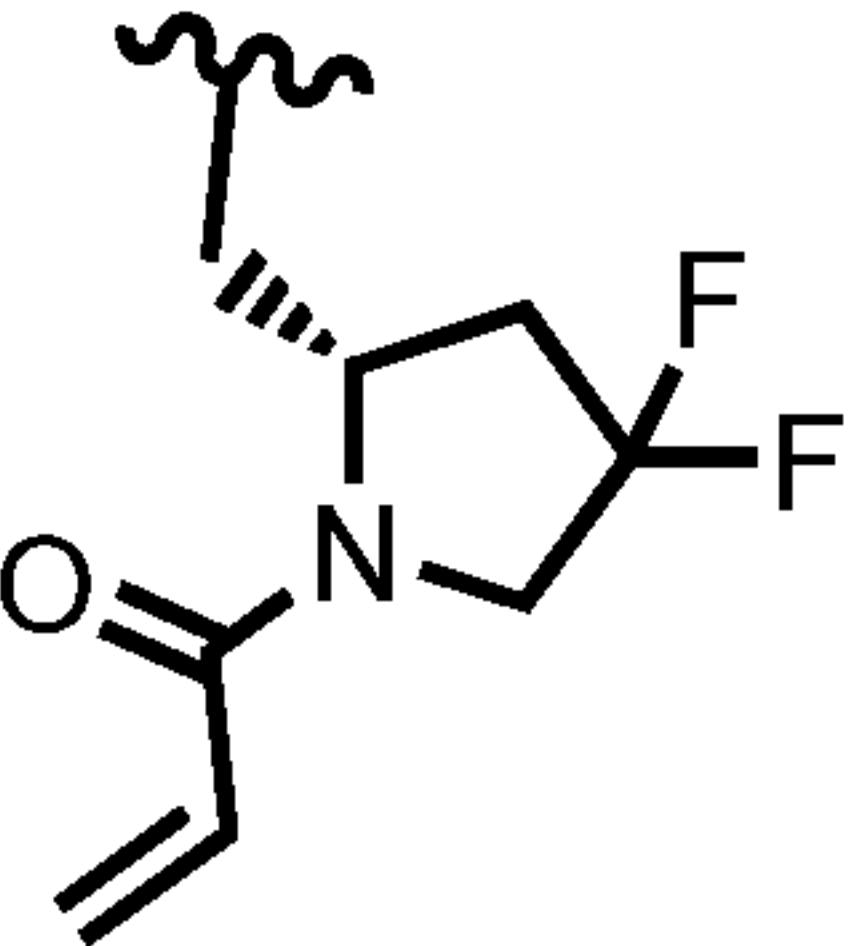
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In embodiments,

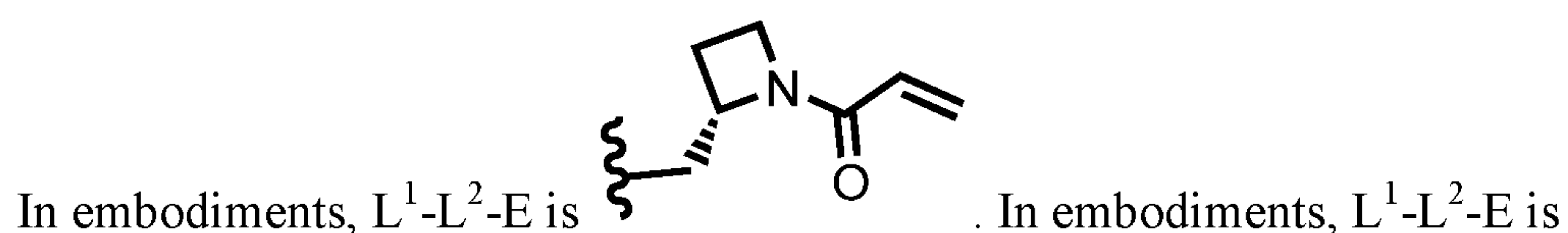
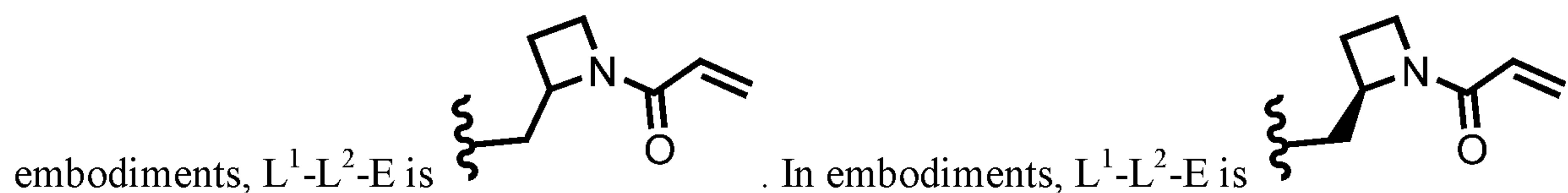
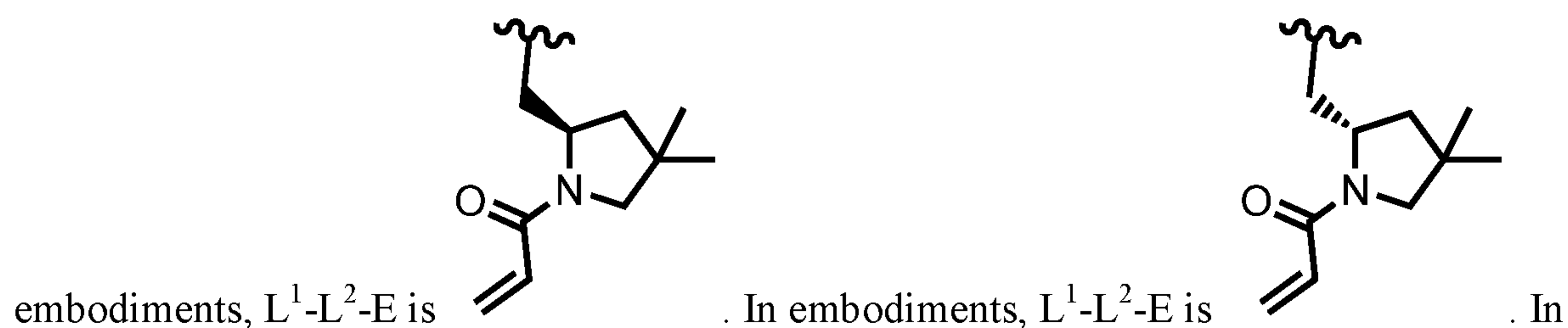
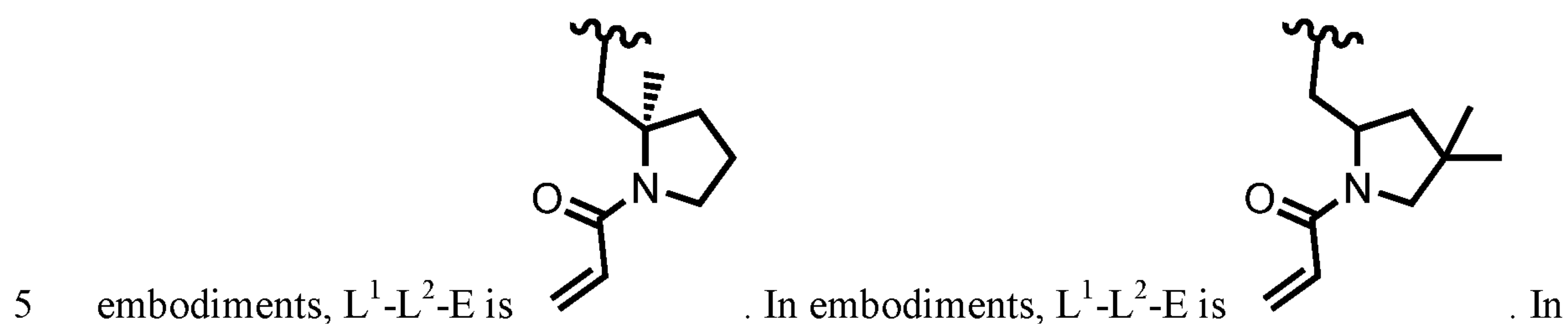
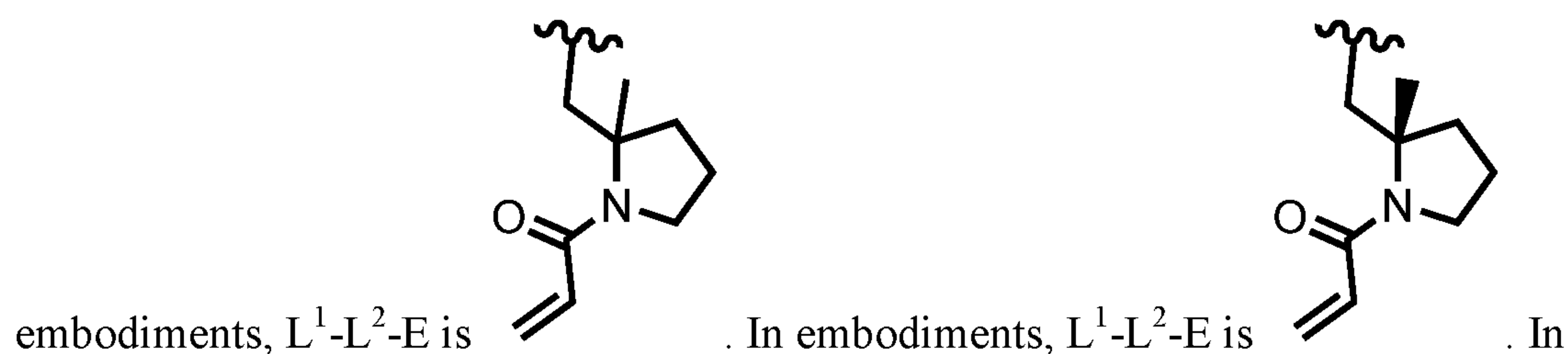
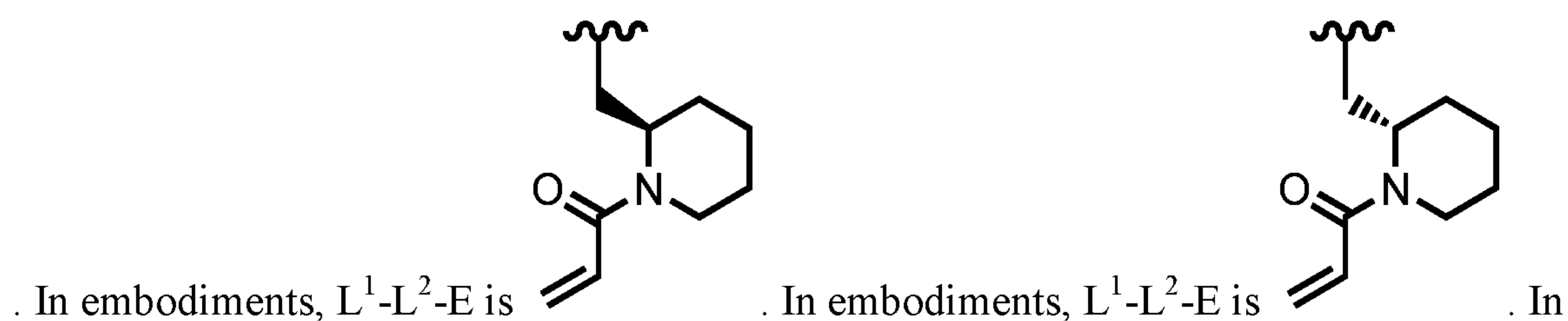
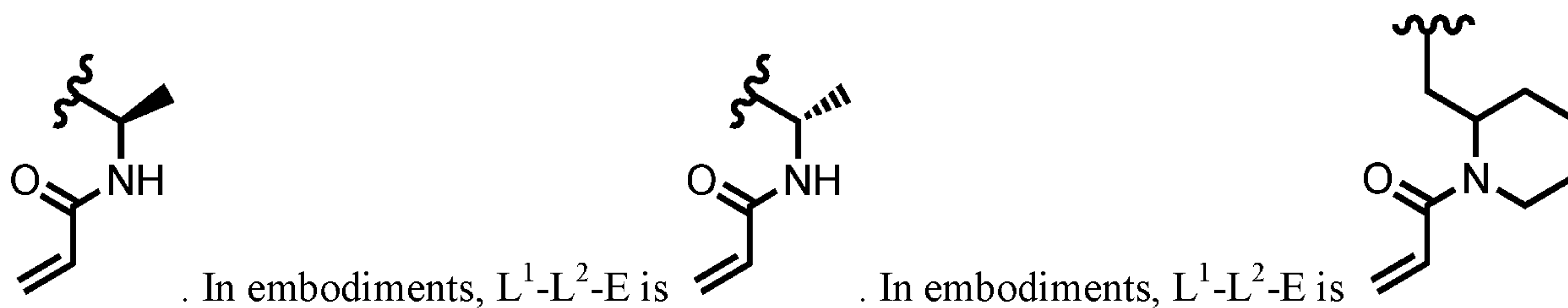
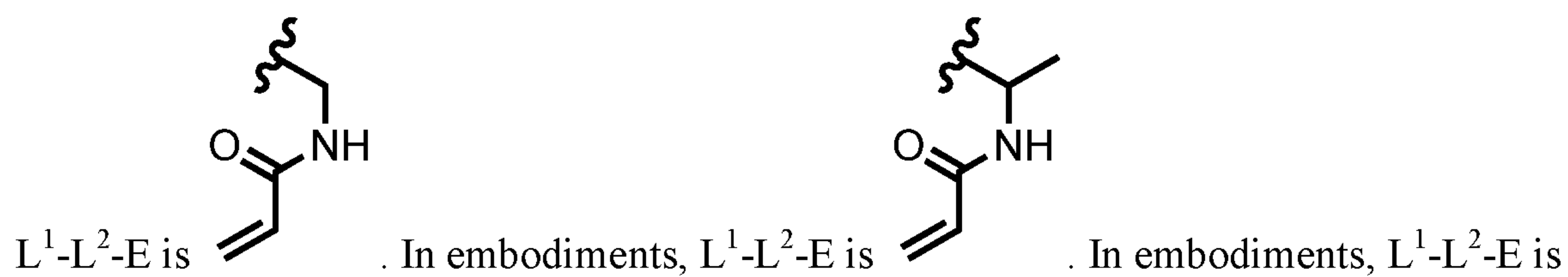
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In
. In embodiments, L^1-L^2-E is .

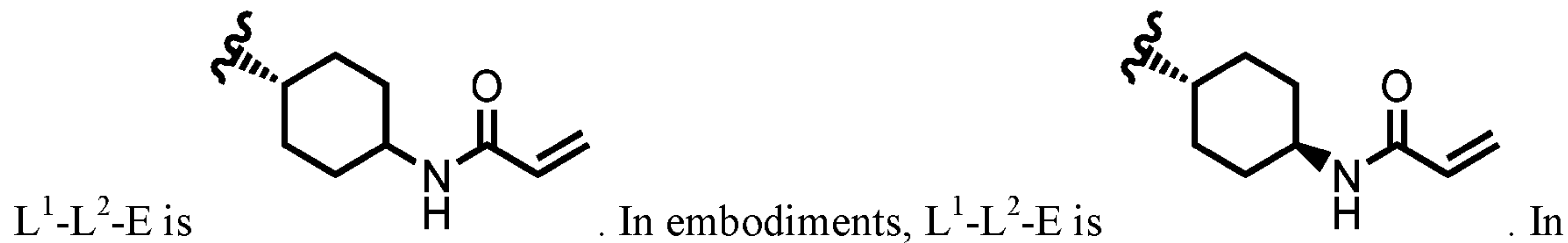
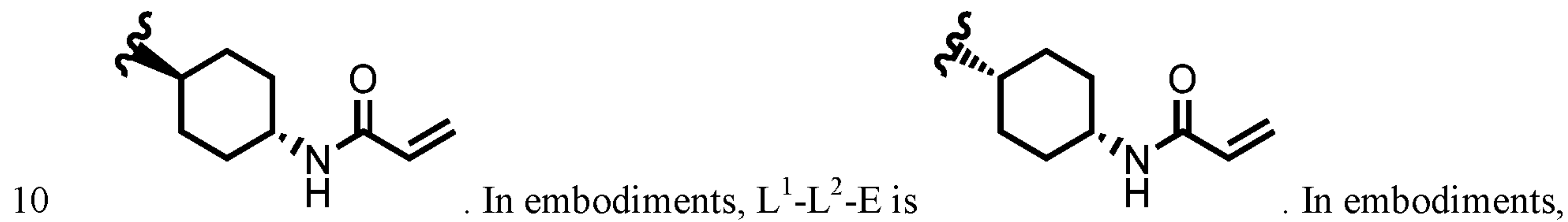
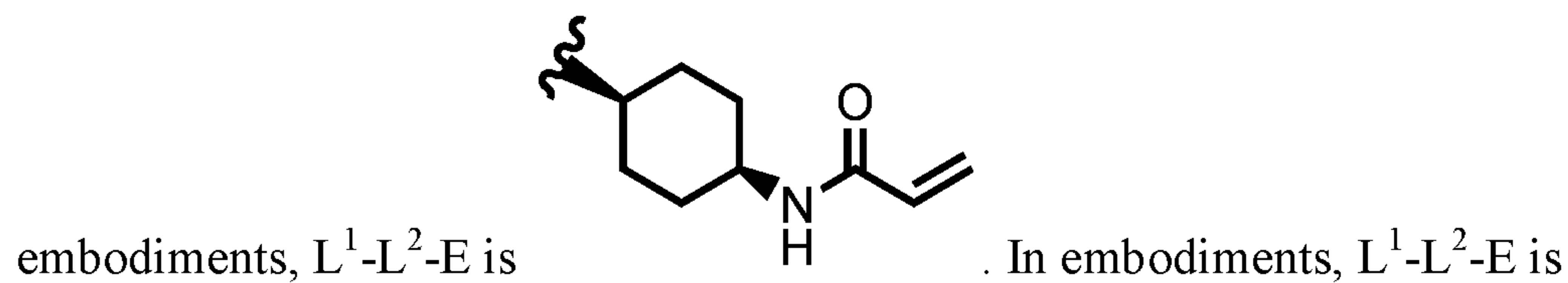
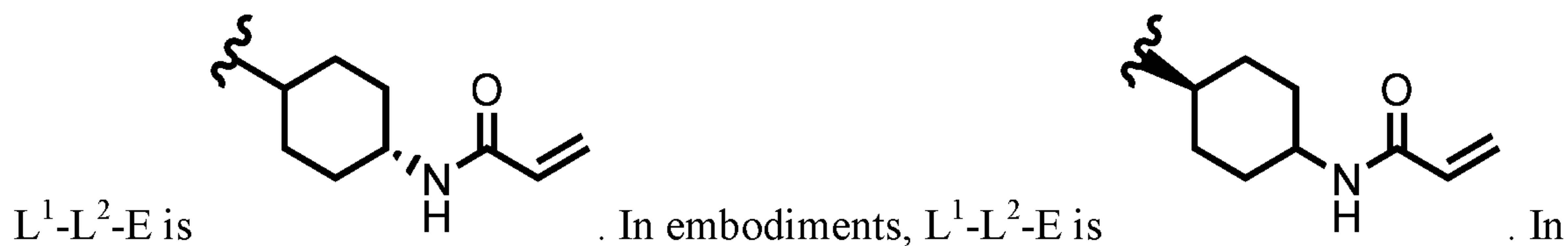
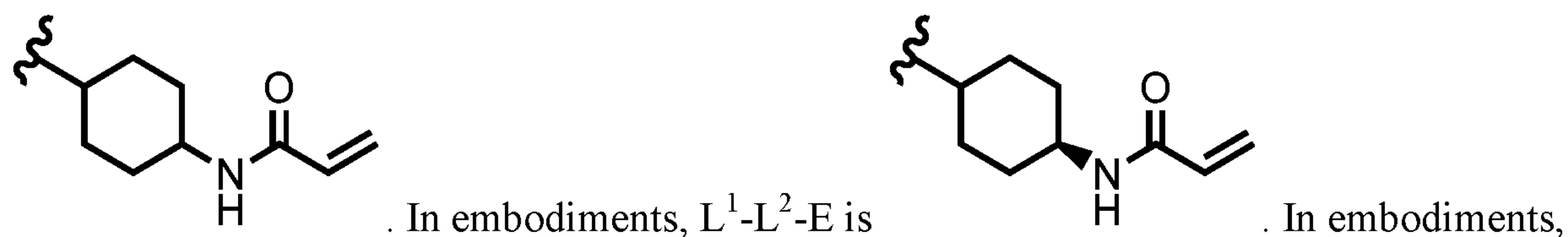
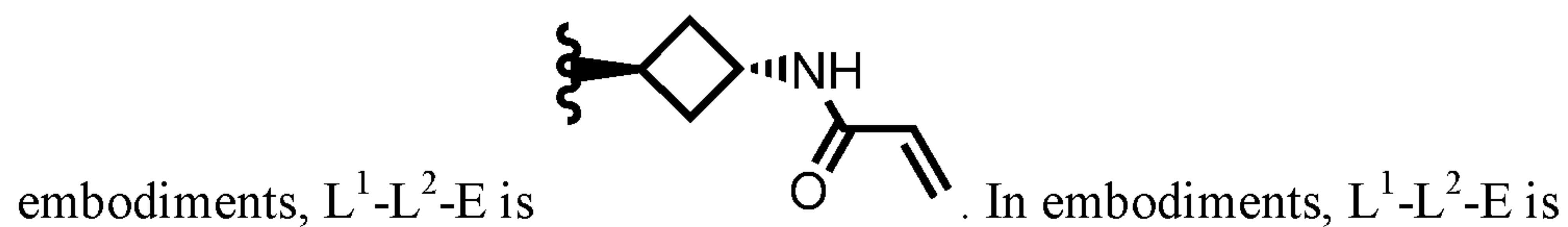
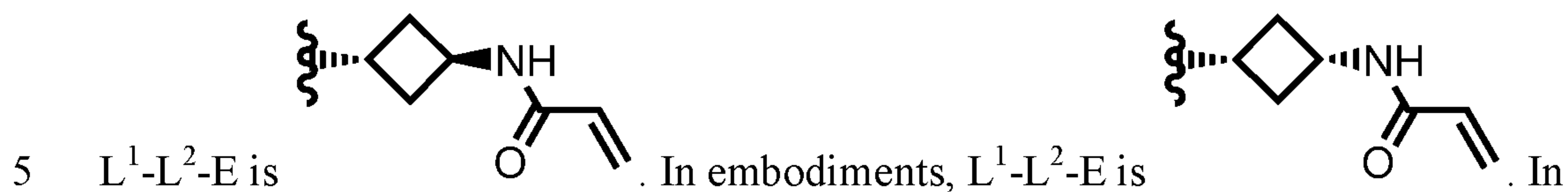
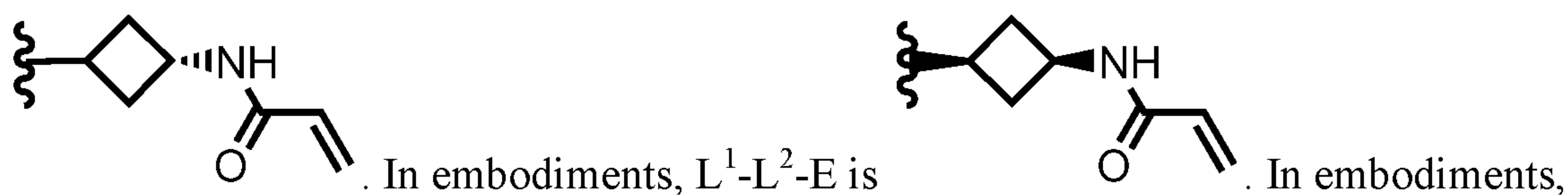
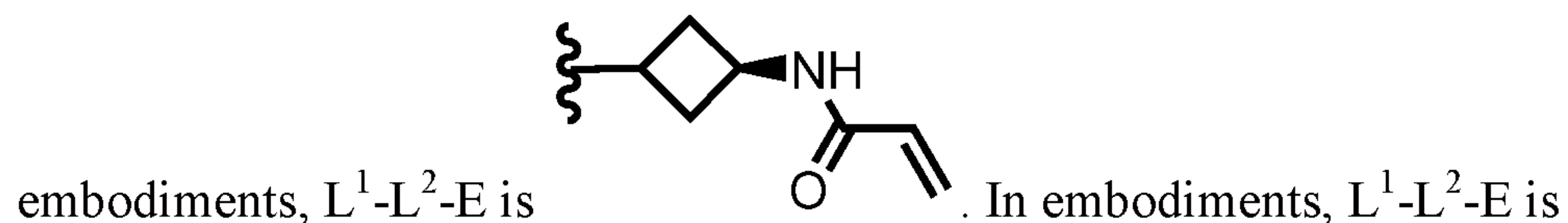
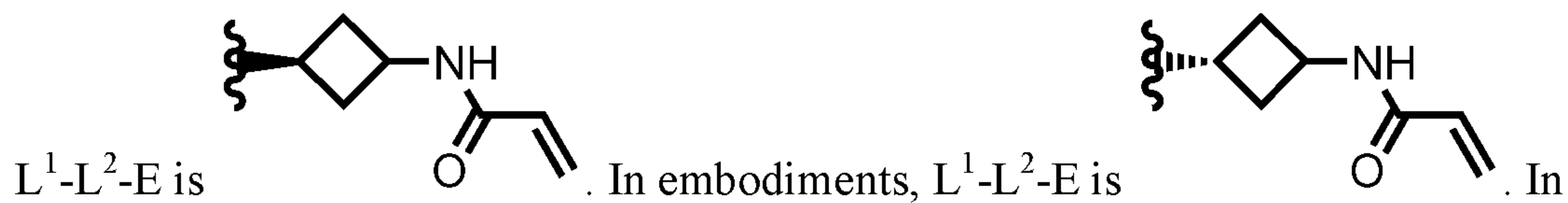
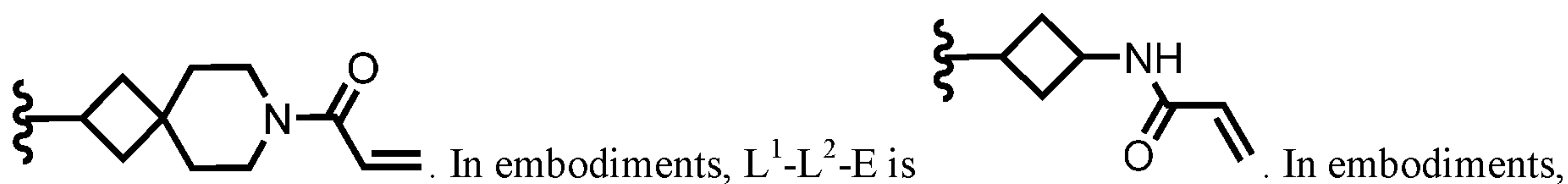
5. In embodiments, L^1-L^2-E is

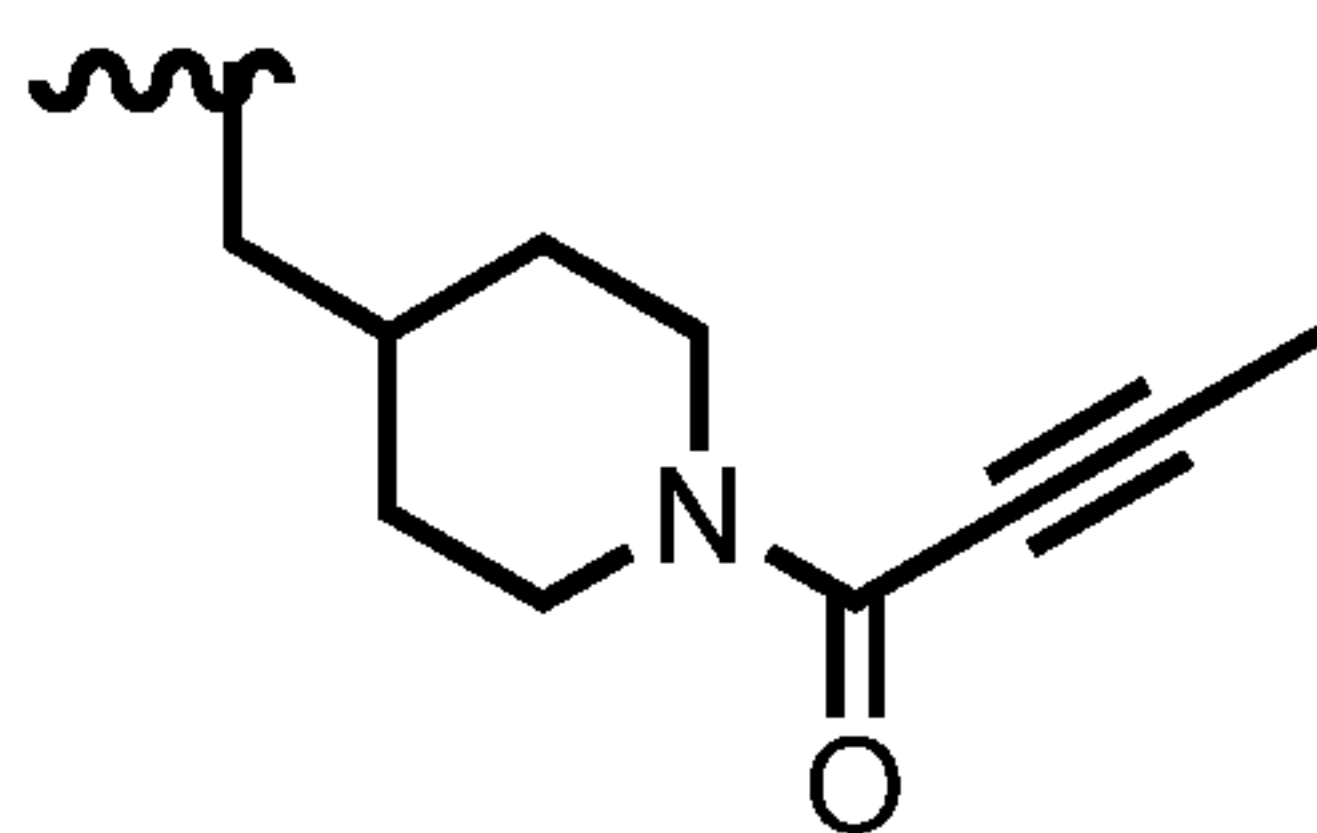
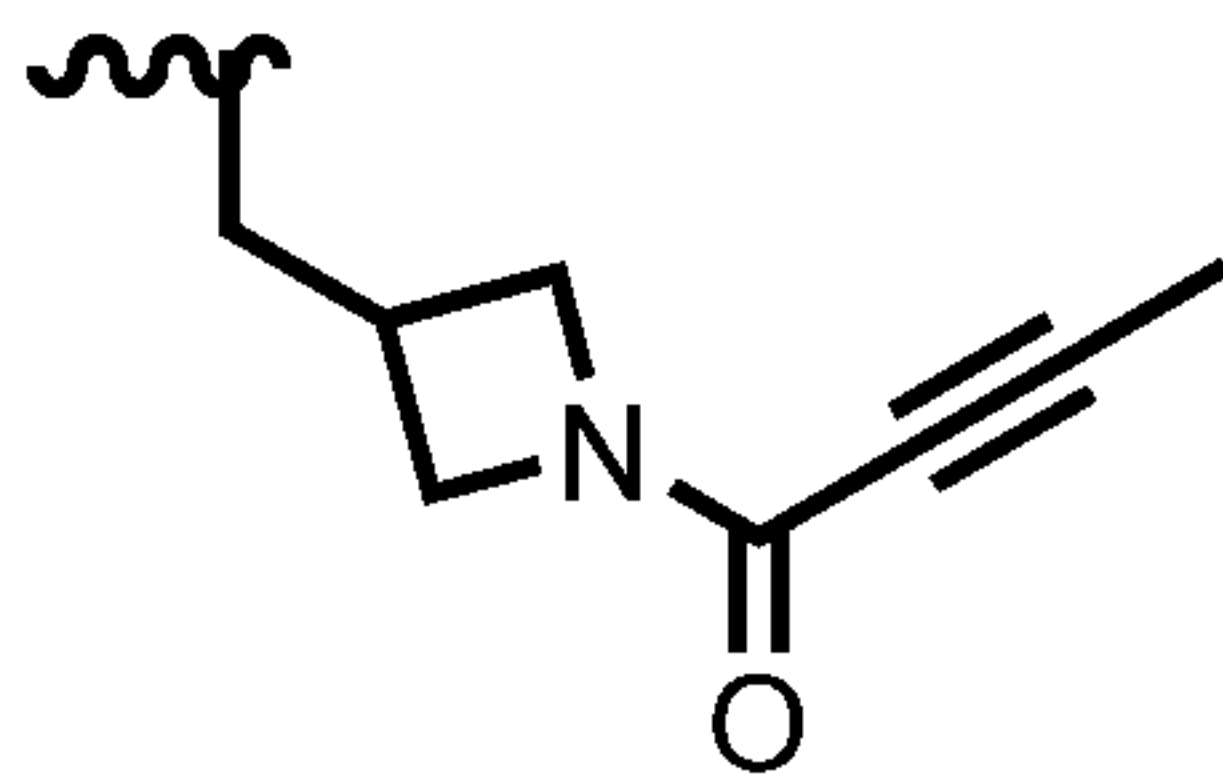
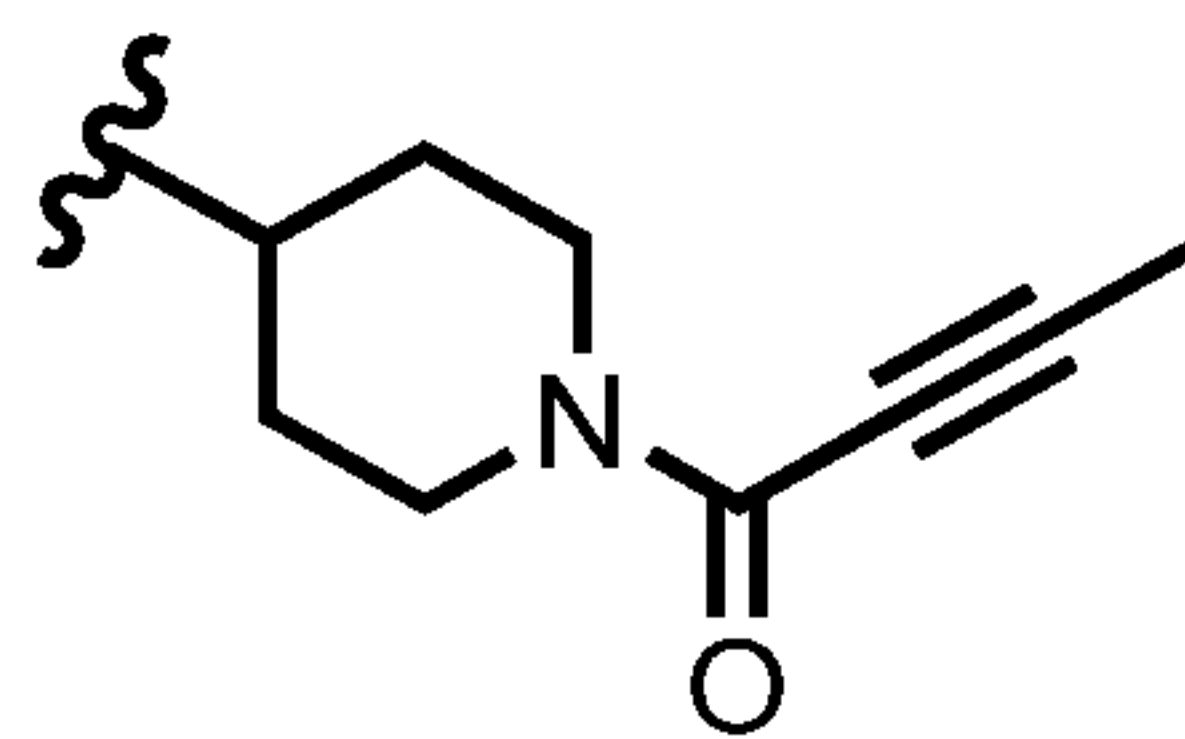
In embodiments, L^1-L^2-E is . In embodiments, L^1-L^2-E is

. In embodiments, L^1-L^2-E is . In embodiments,

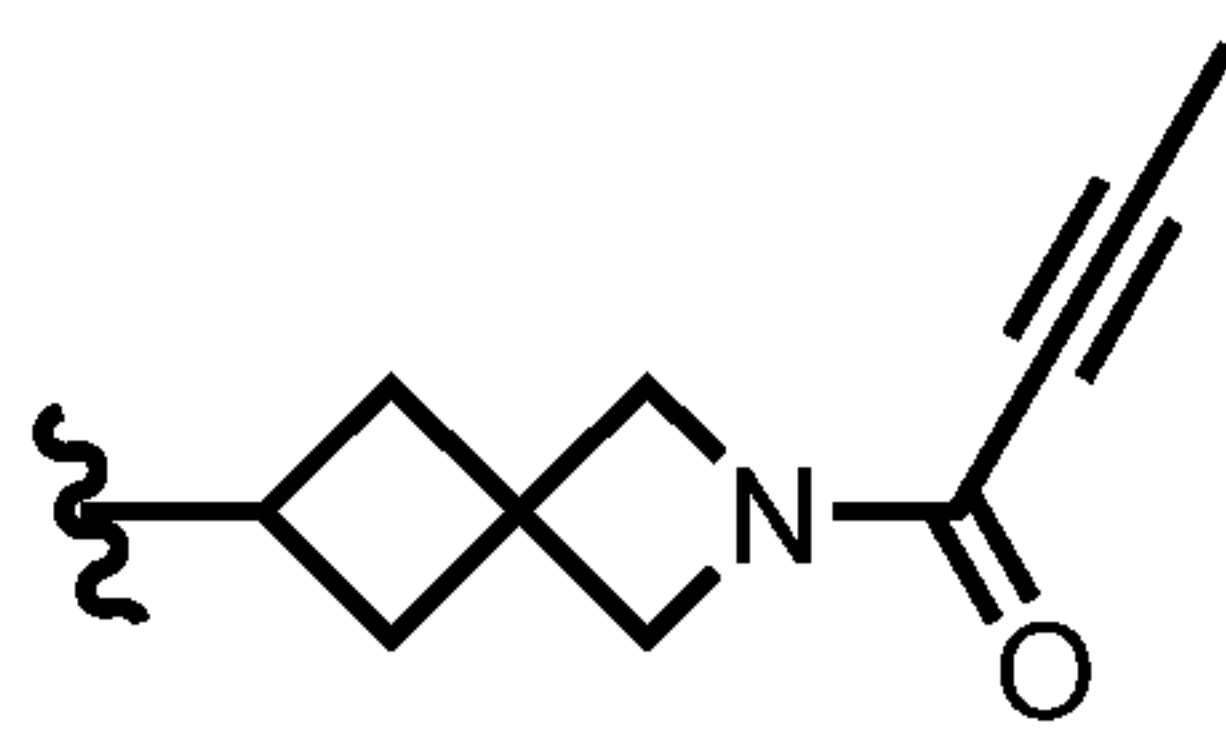
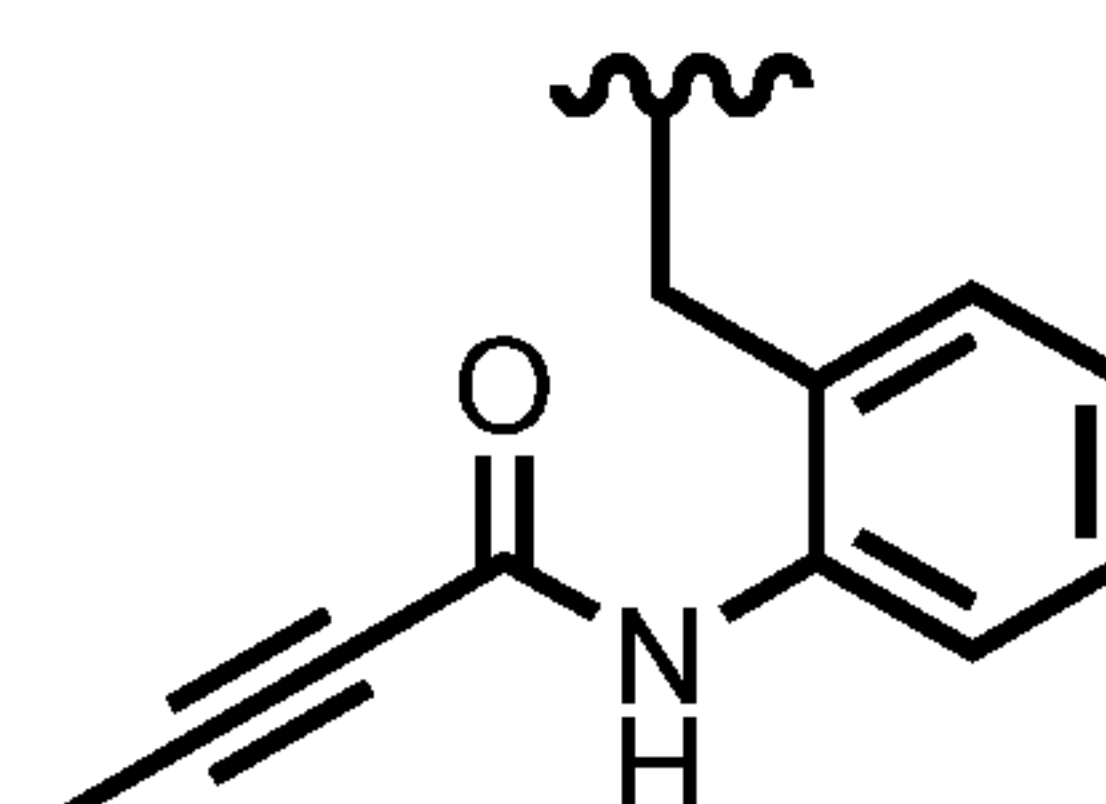
L^1-L^2-E is . In embodiments, L^1-L^2-E is . In embodiments,



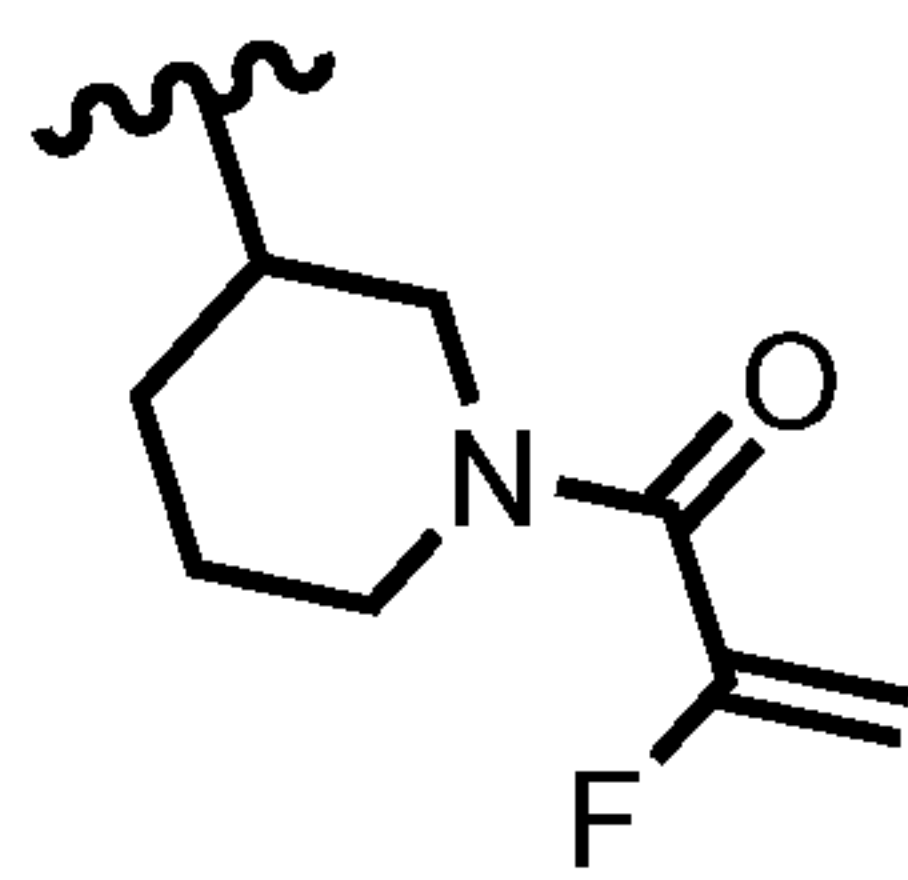
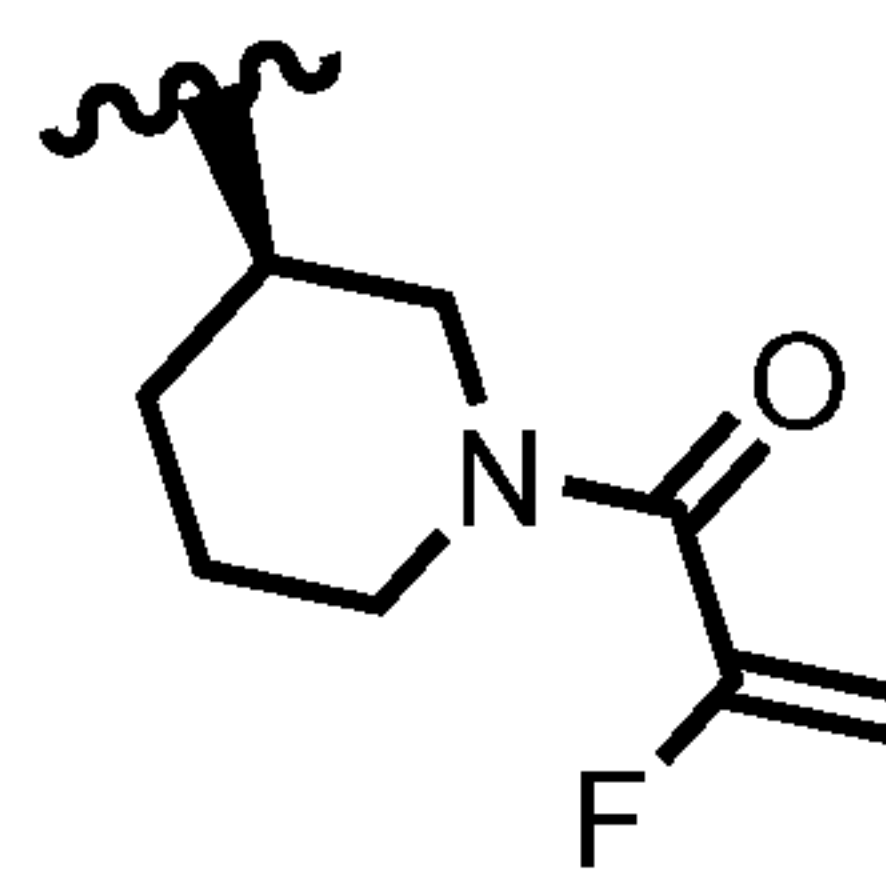


embodiments, L¹-L²-E is. In embodiments, L¹-L²-E is. In embodiments, L¹-L²-E is

. In embodiments,

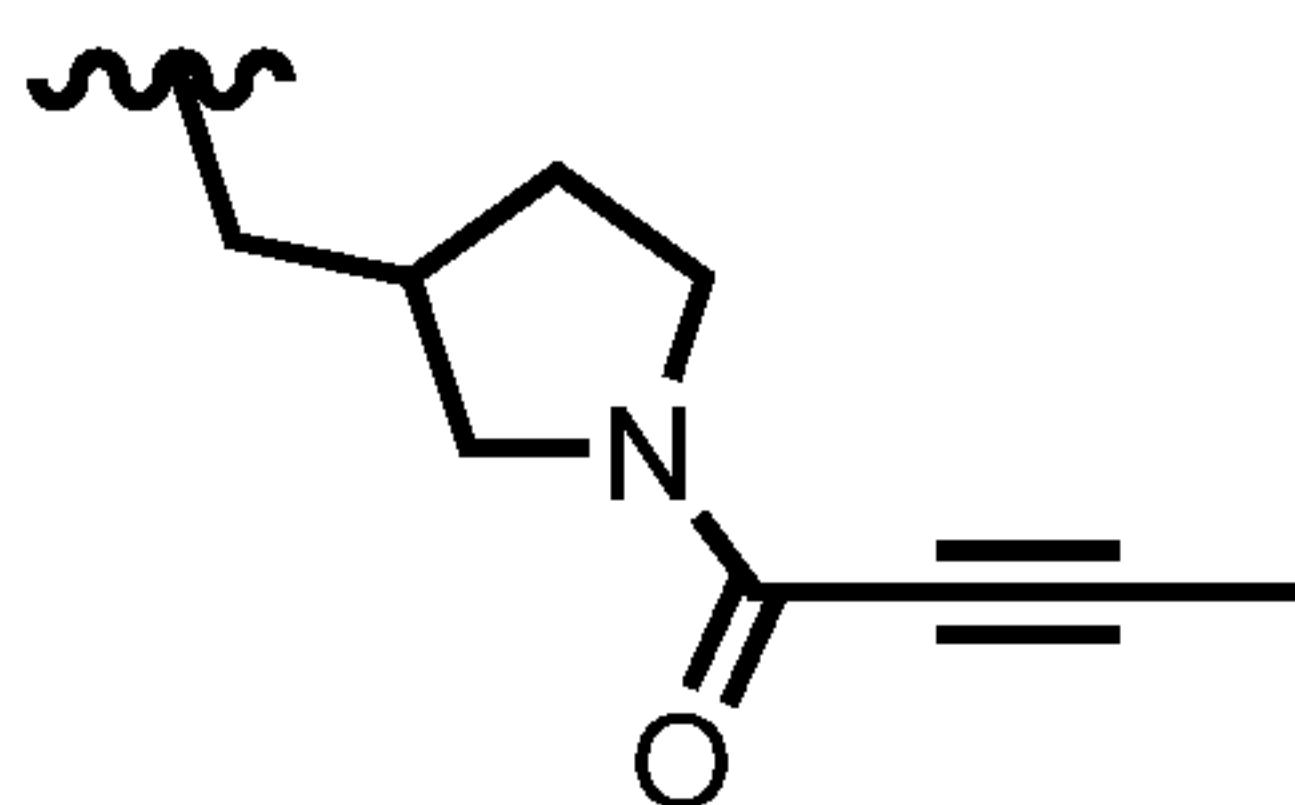
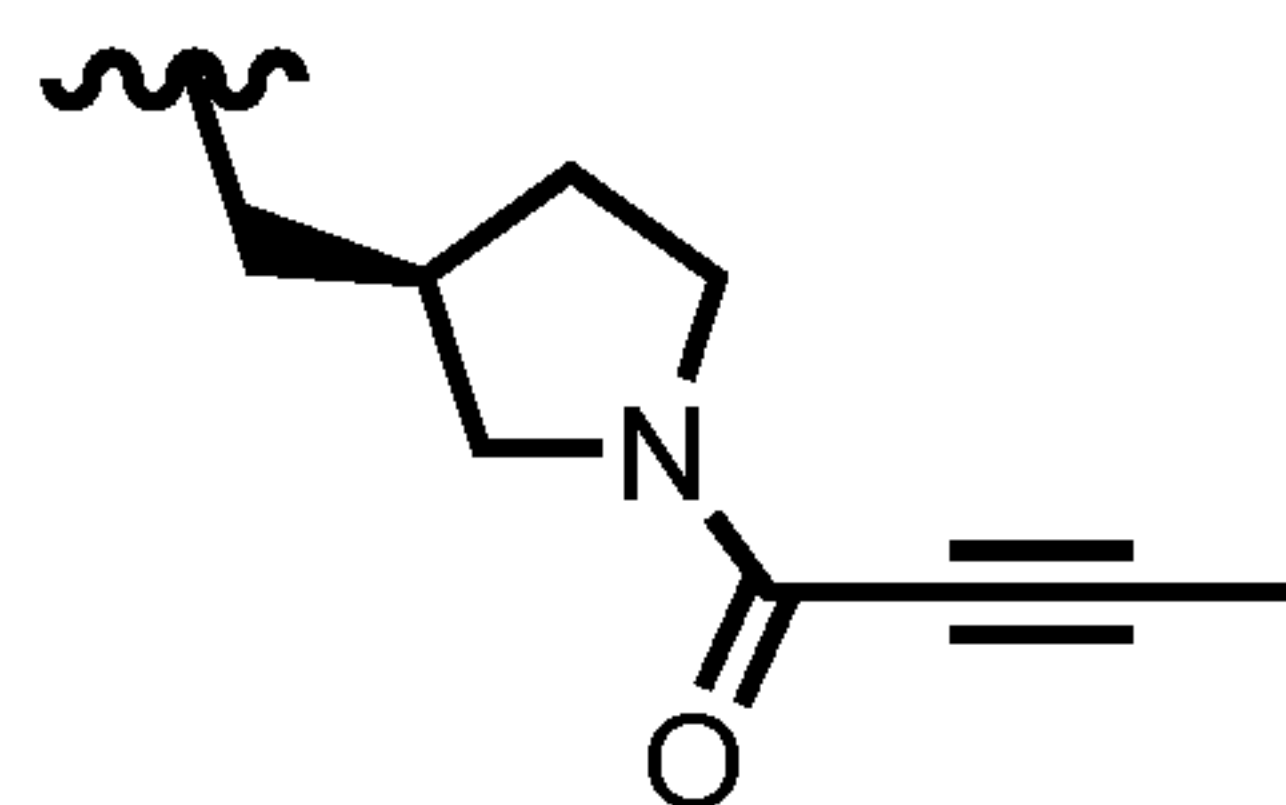
L¹-L²-E is. In embodiments, L¹-L²-E is

. In

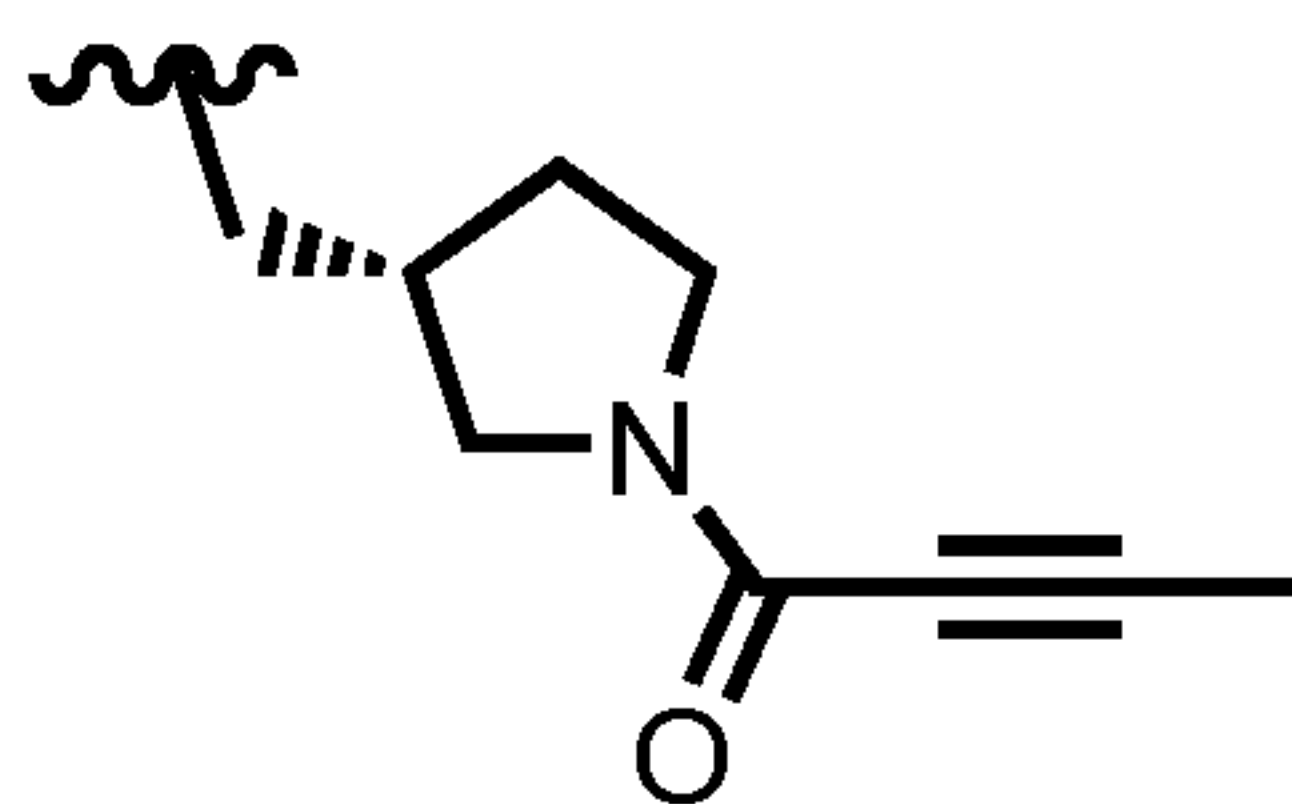
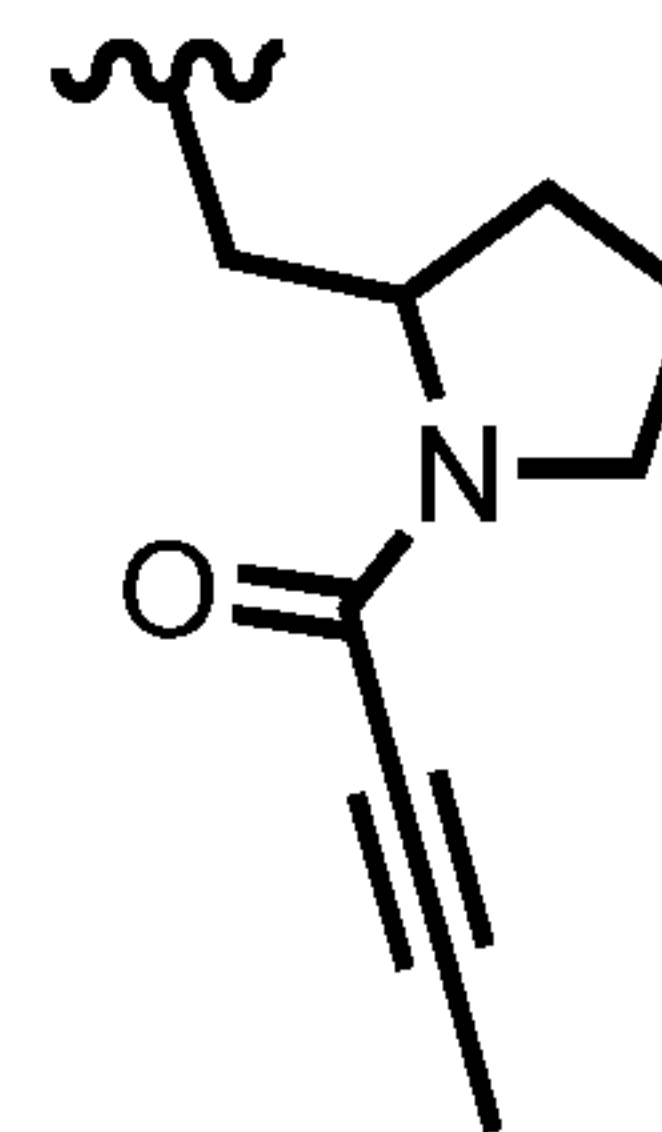
embodiments, L¹-L²-E is. In embodiments, L¹-L²-E is

. In

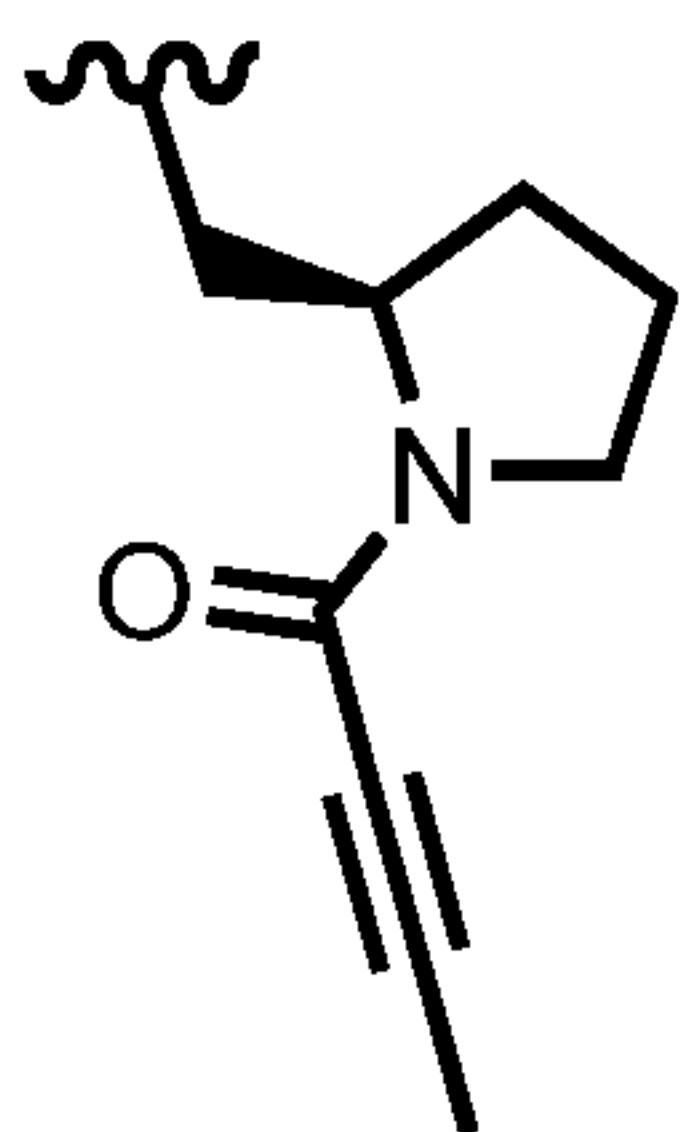
5

embodiments, L¹-L²-E is. In embodiments, L¹-L²-E is. In embodiments, L¹-L²-E is

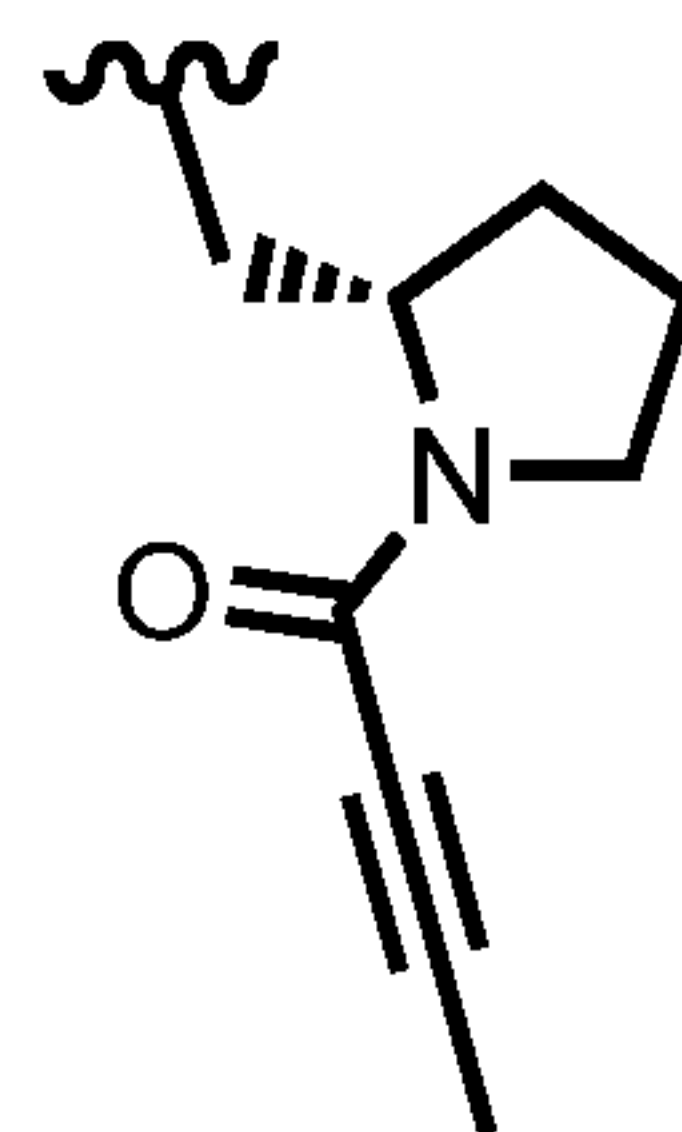
. In

embodiments, L¹-L²-E is. In embodiments, L¹-L²-E is

In embodiments, L^1 - L^2 -E is

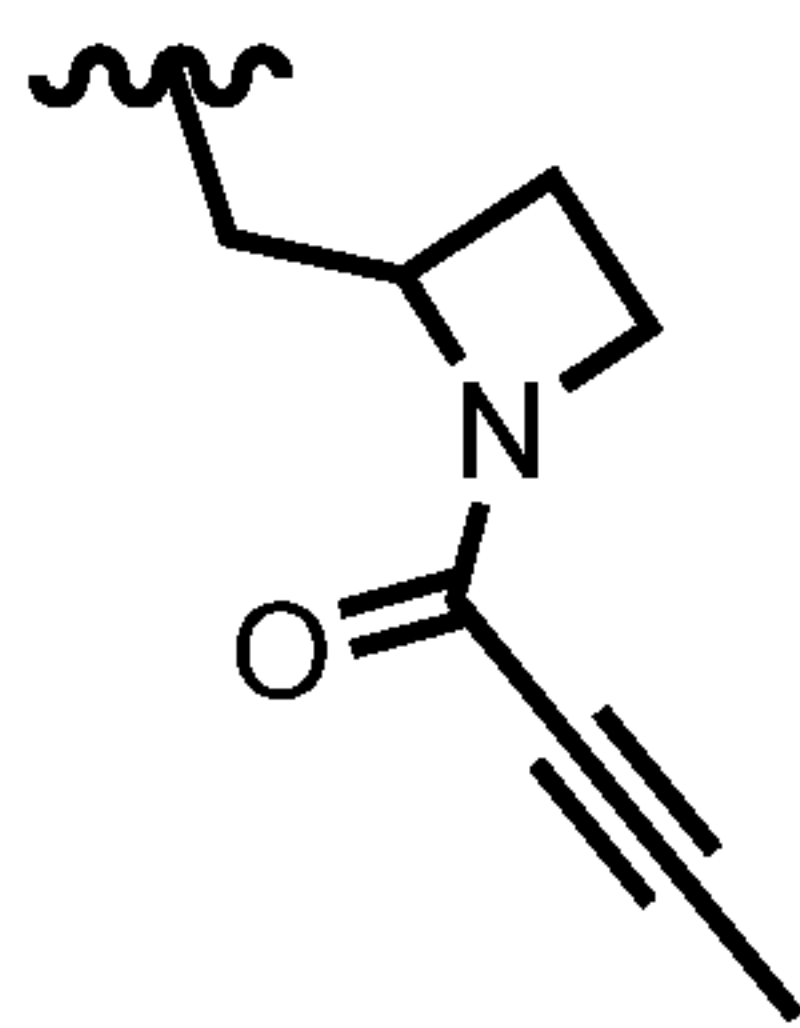


. In embodiments, L^1 - L^2 -E is

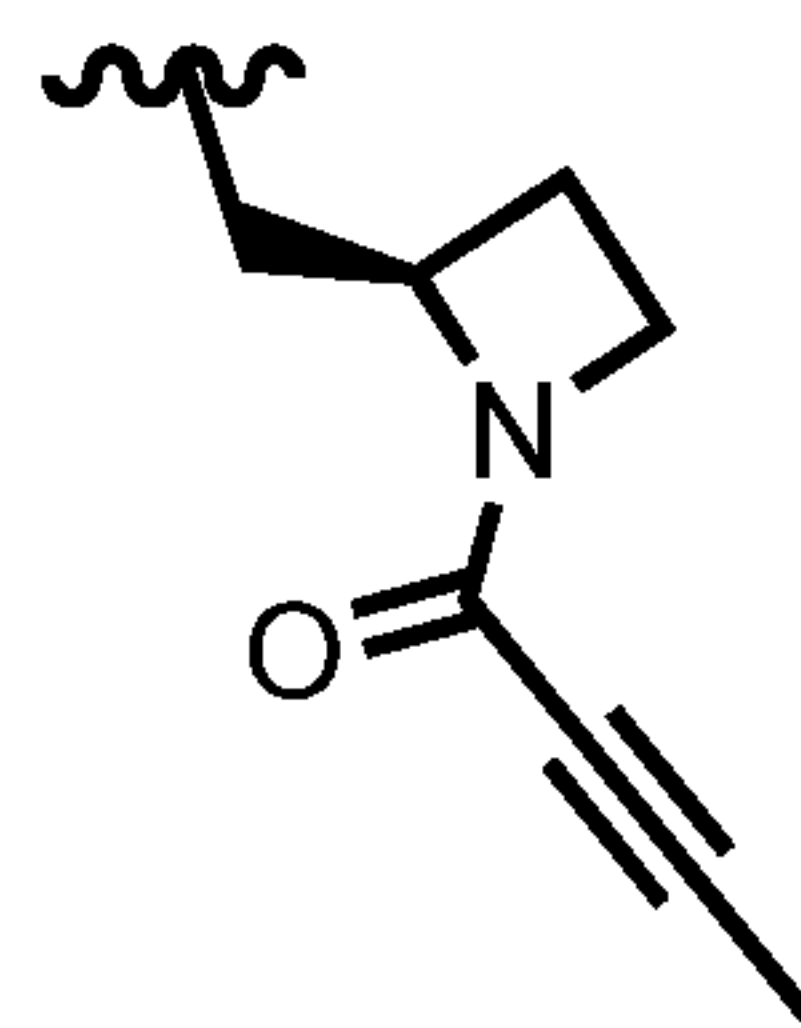


. In

embodiments, L^1 - L^2 -E is

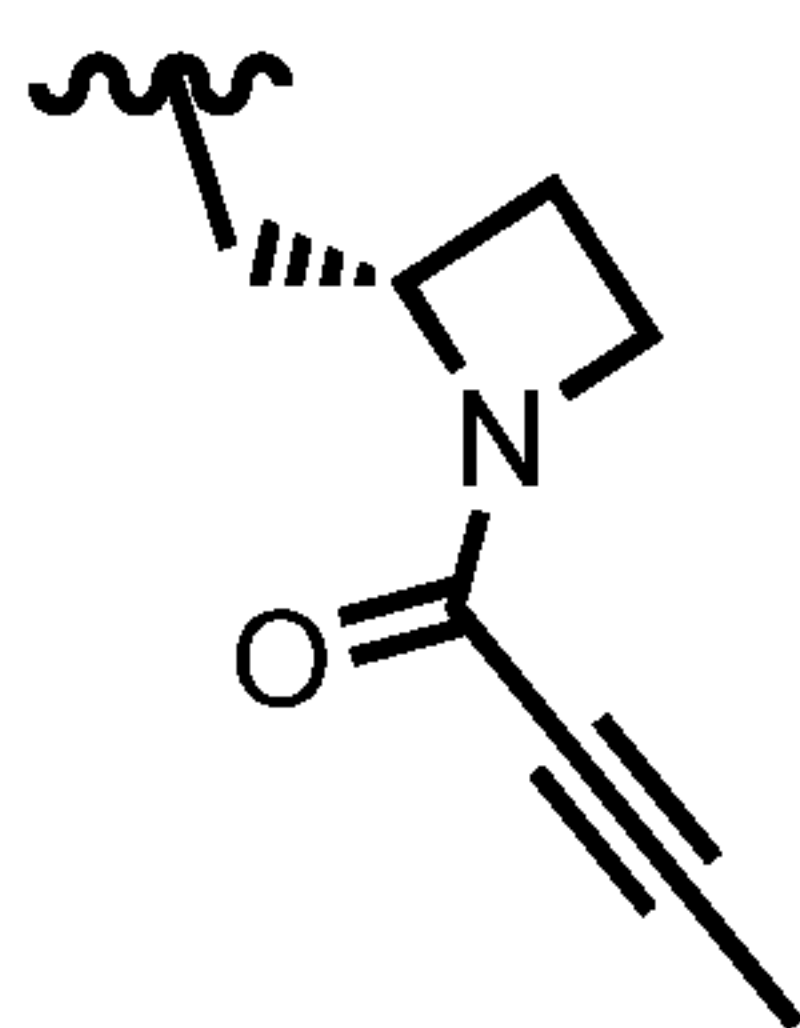


. In embodiments, L^1 - L^2 -E is

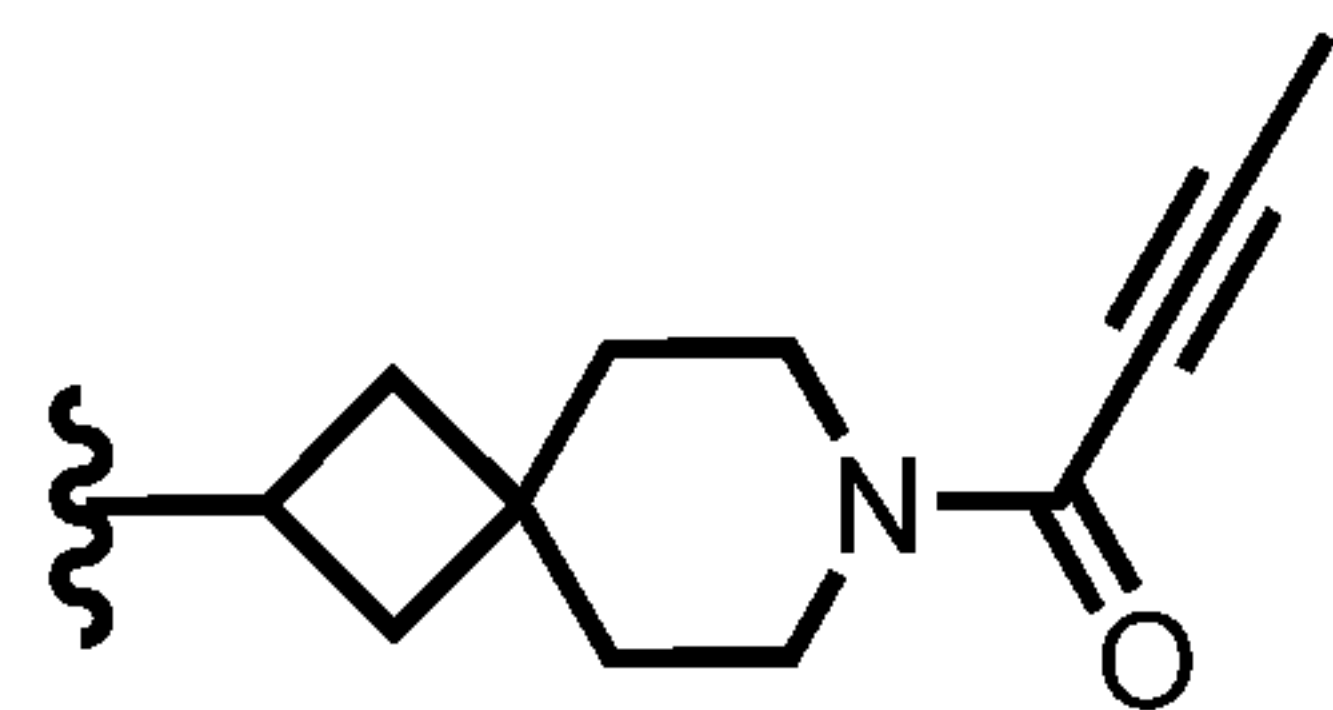


. In

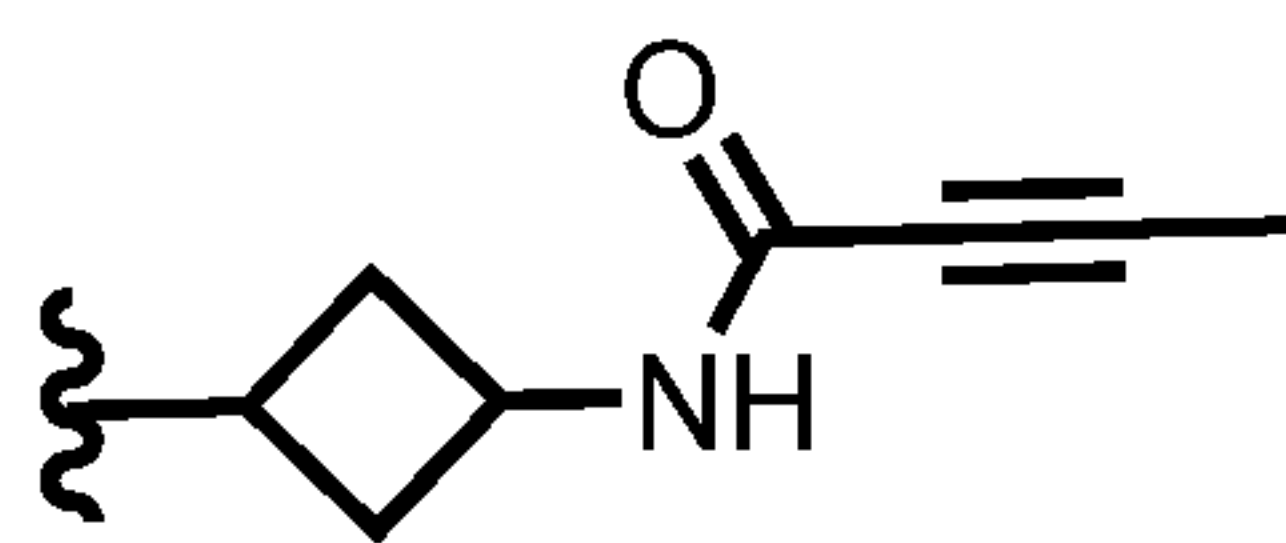
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is



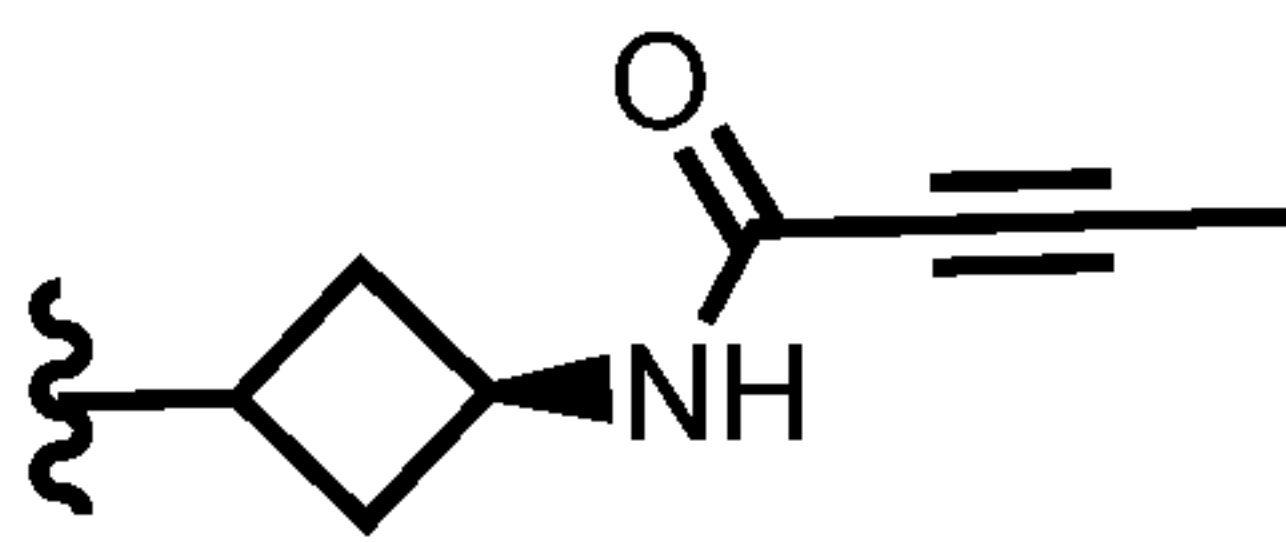
. In embodiments, L^1 - L^2 -E is



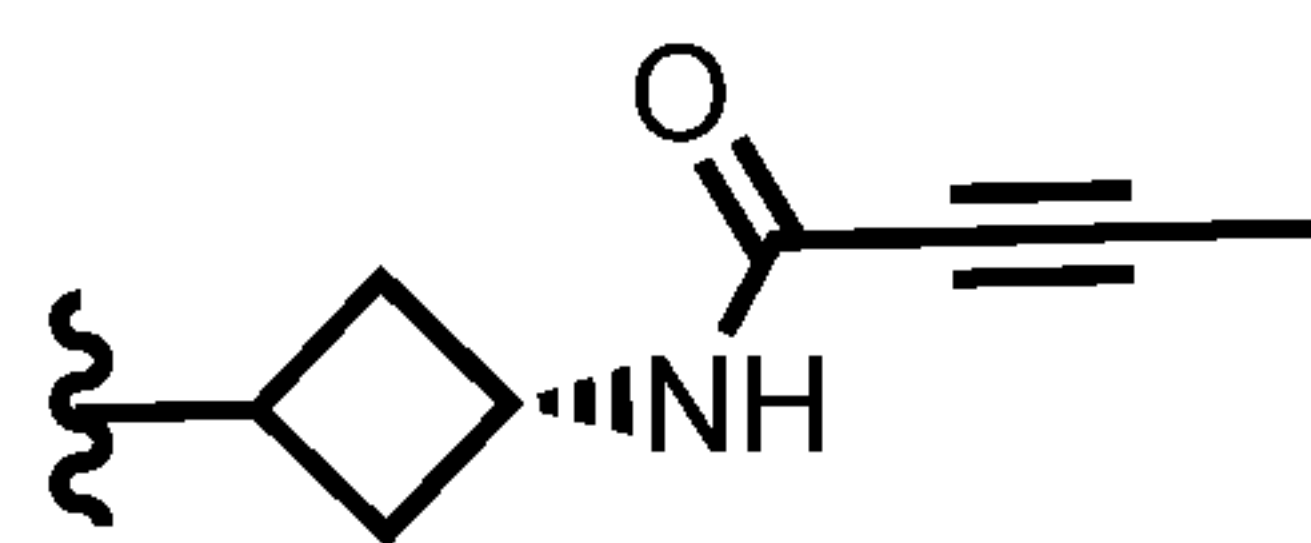
. In

5

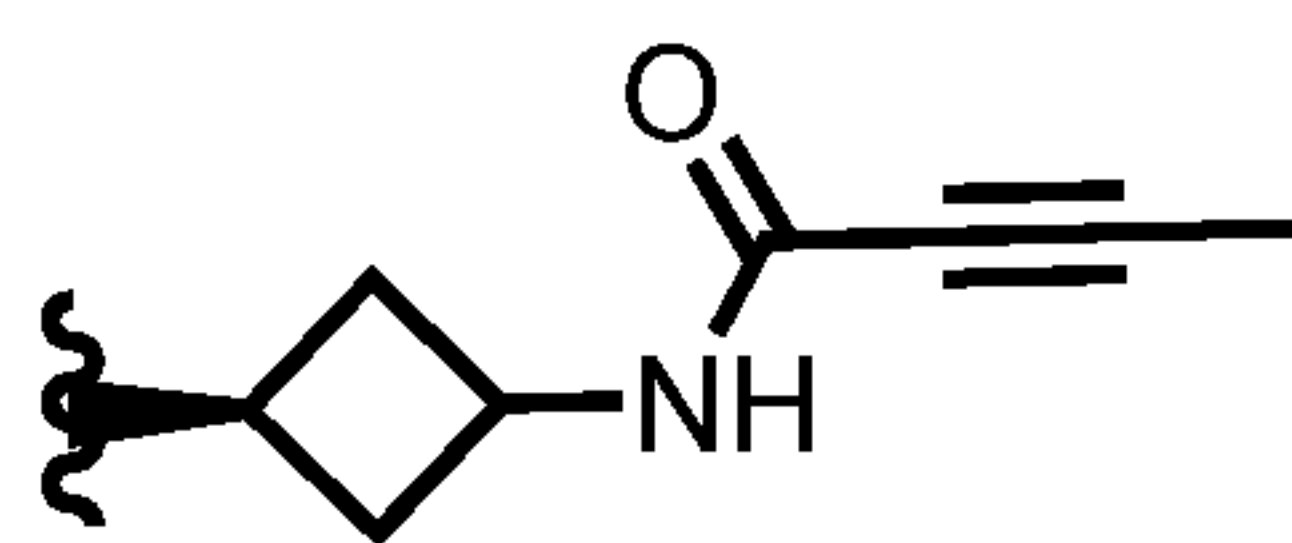
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is

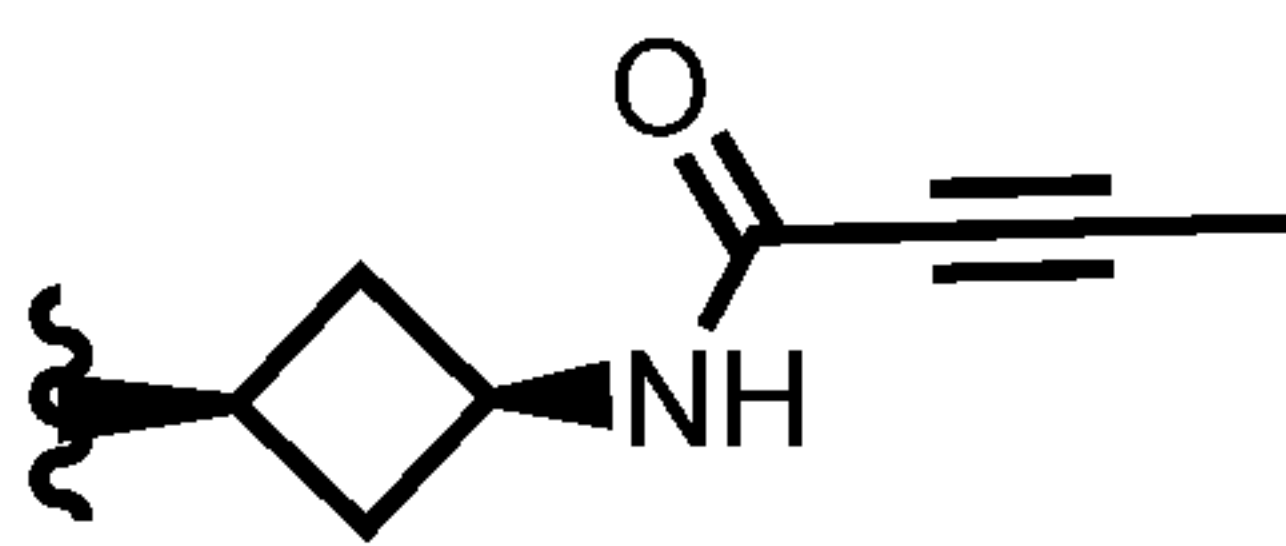


. In embodiments, L^1 - L^2 -E is

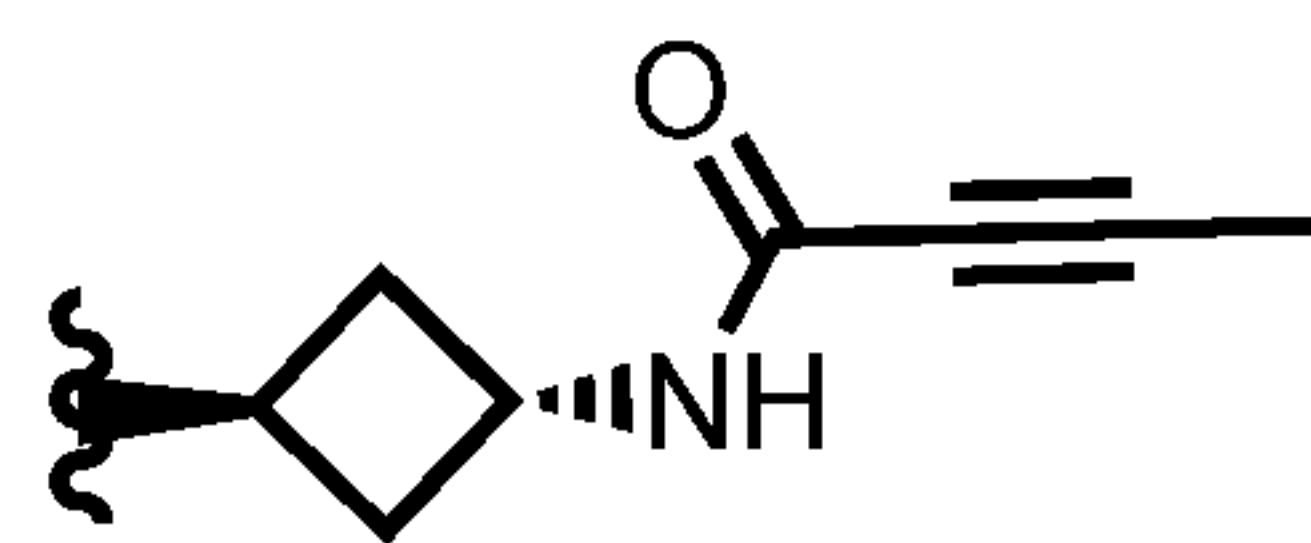


. In

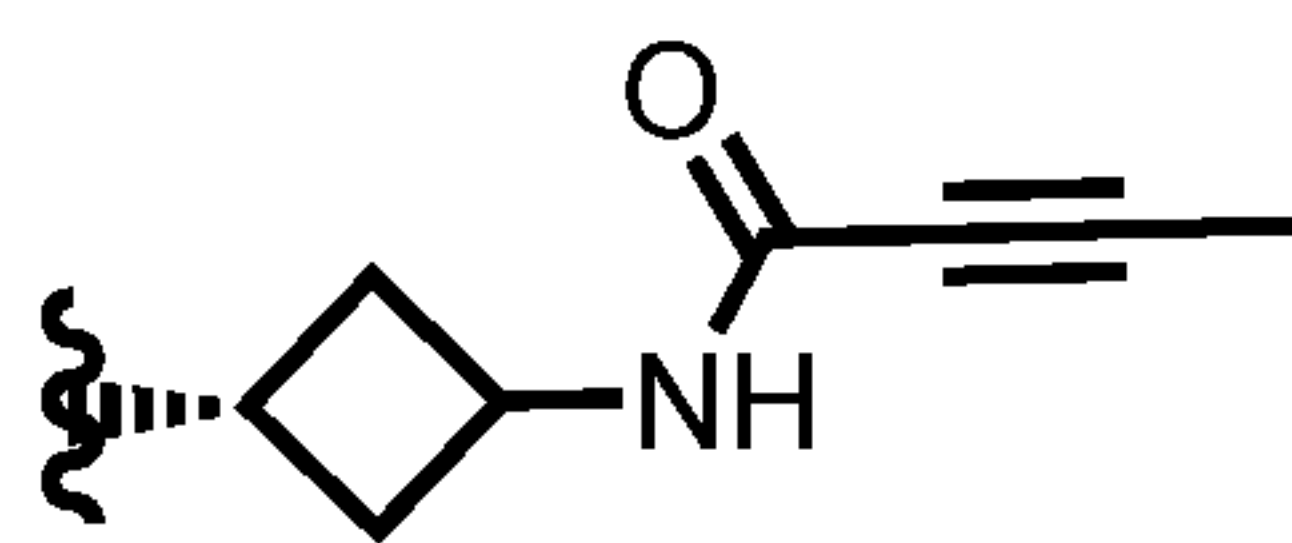
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is

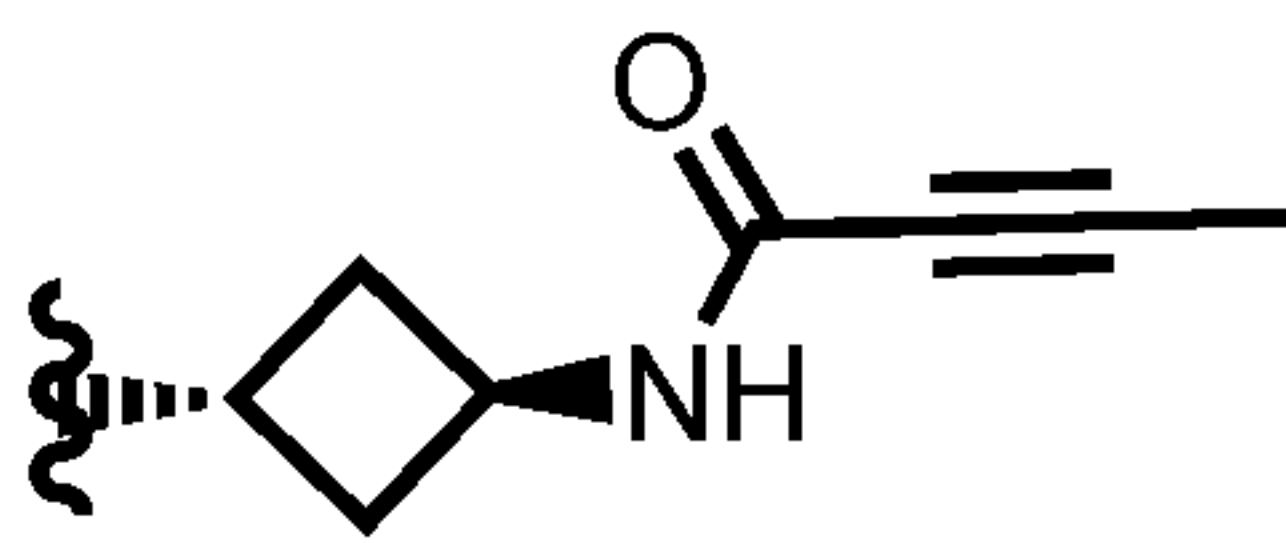


. In embodiments, L^1 - L^2 -E is

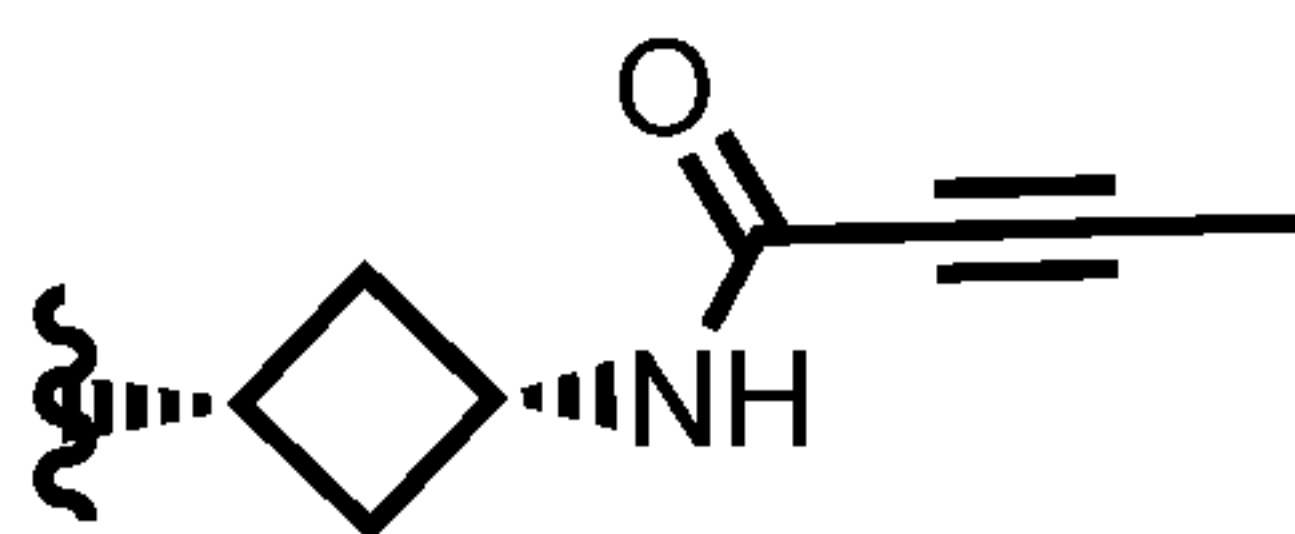


. In

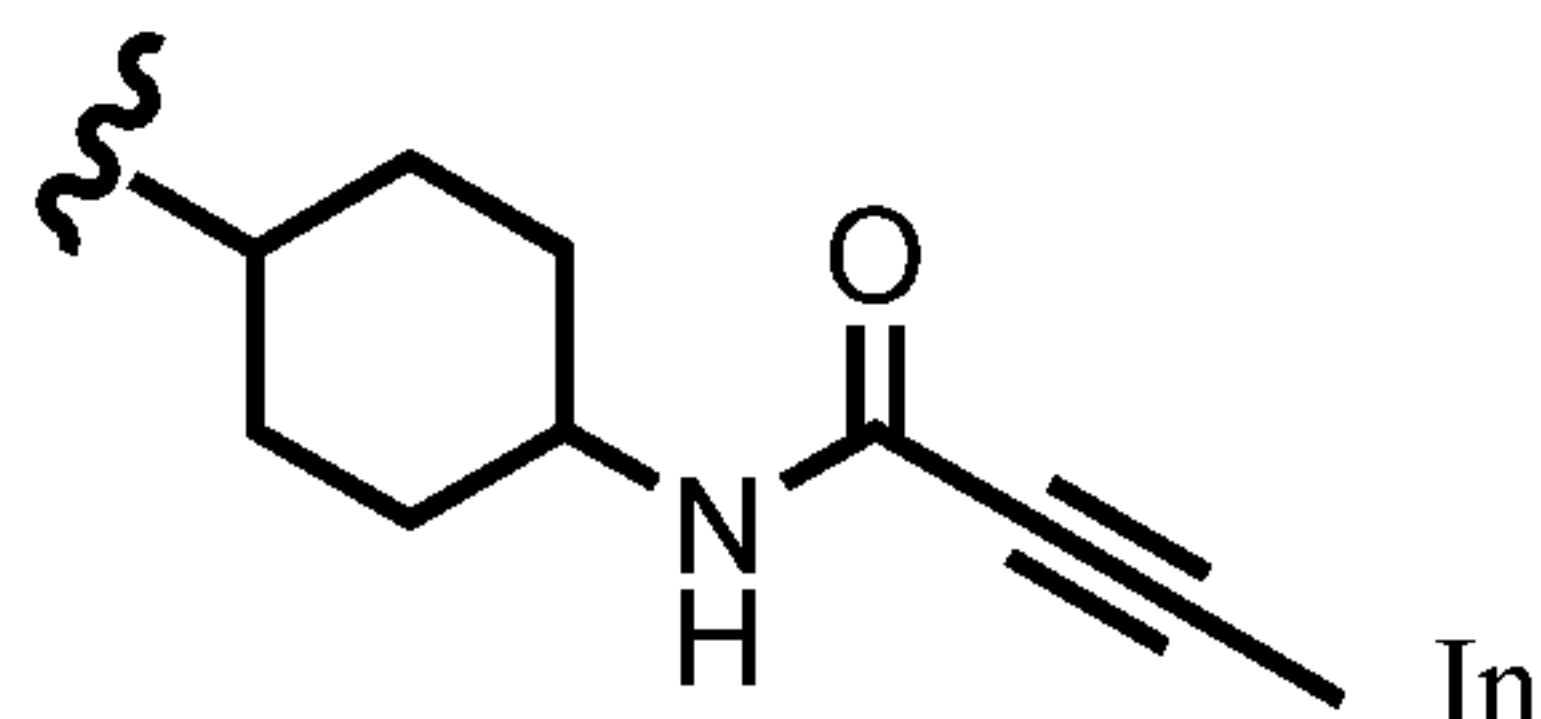
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is

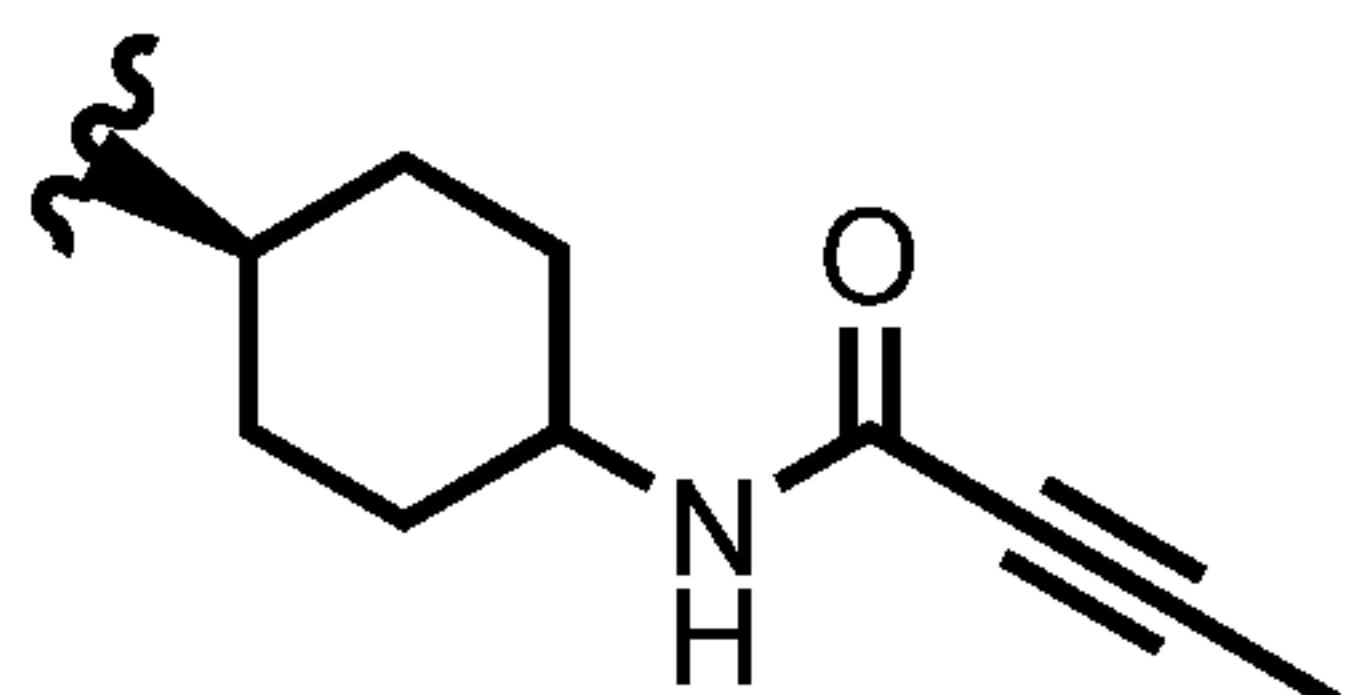


. In embodiments, L^1 - L^2 -E is

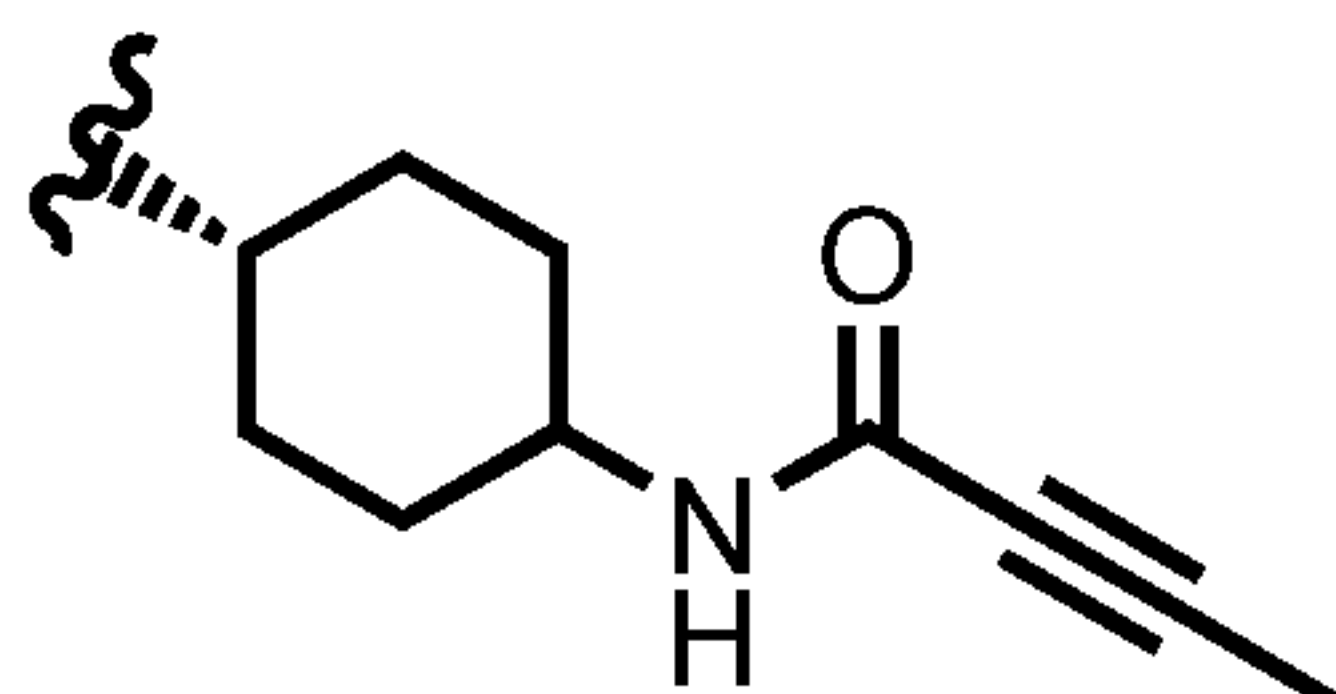


. In

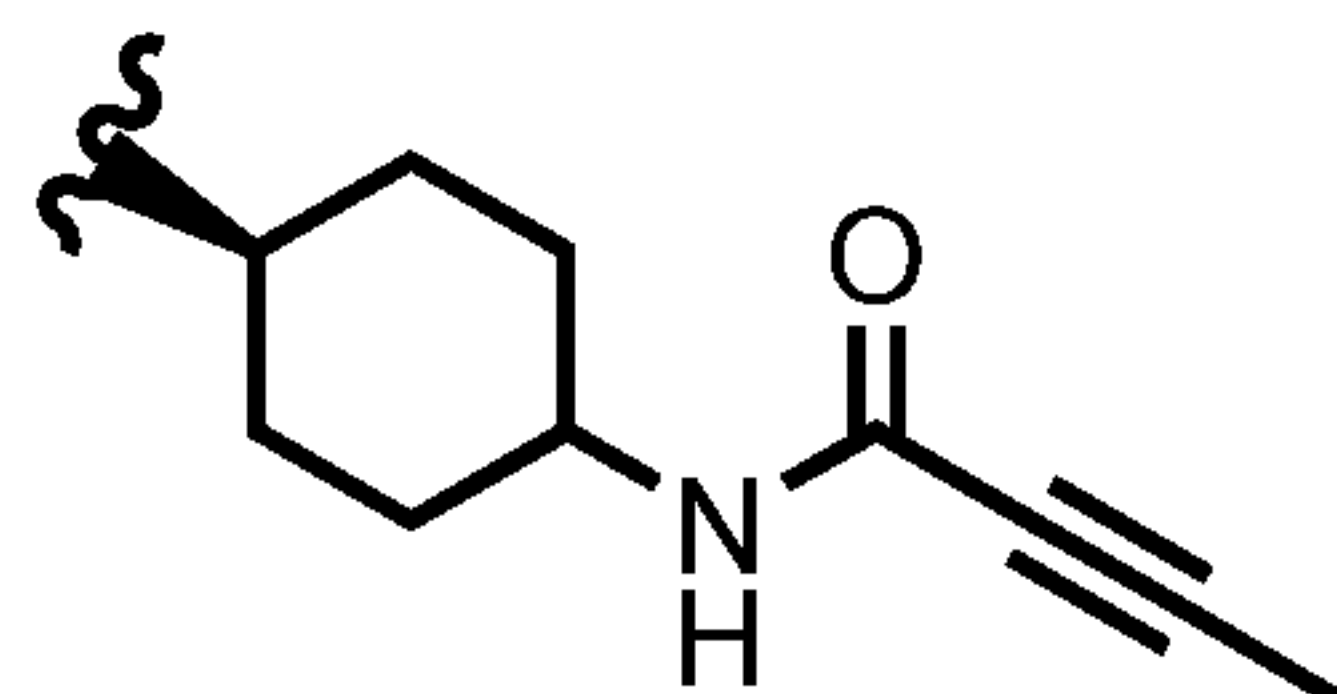
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is

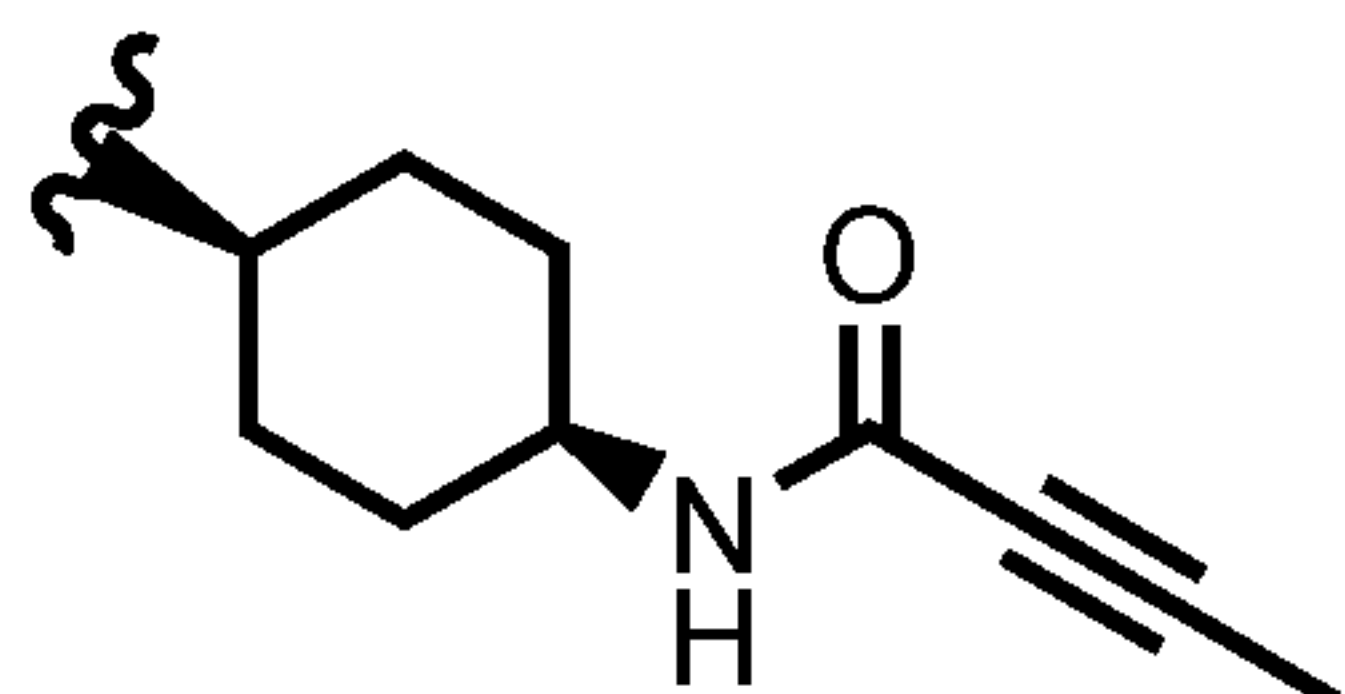


. In embodiments, L^1 - L^2 -E is

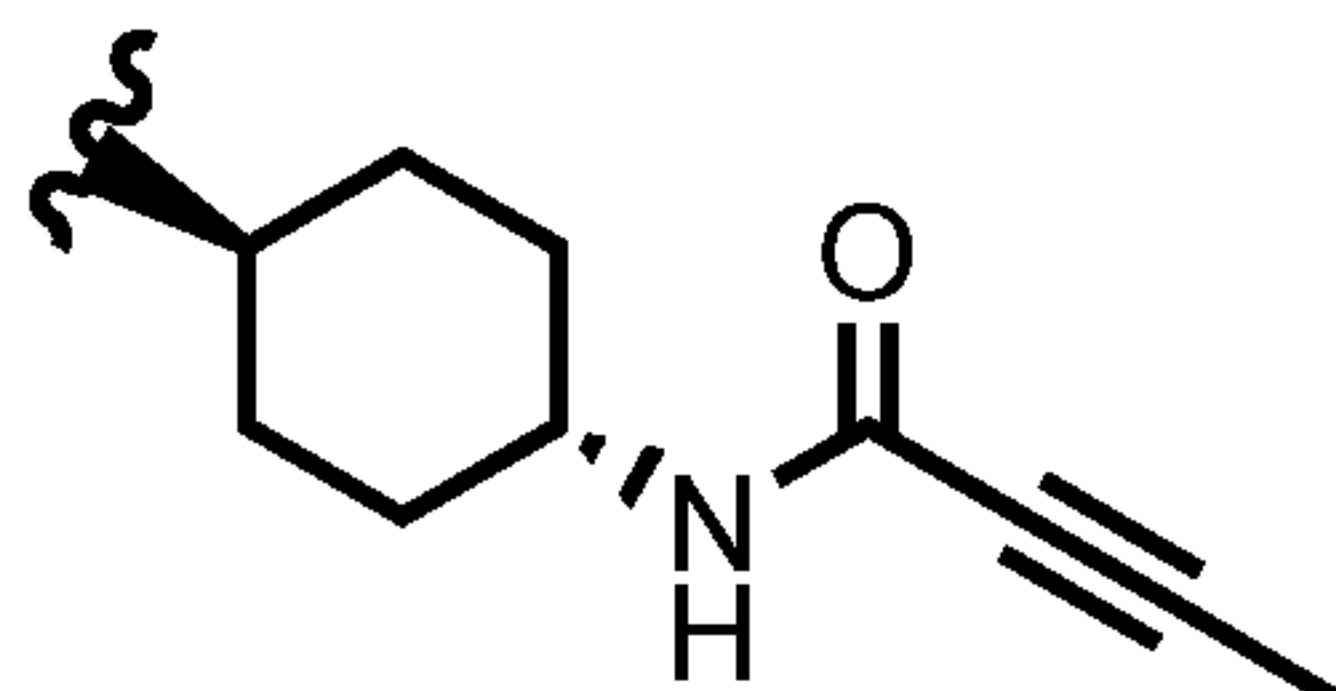


. In

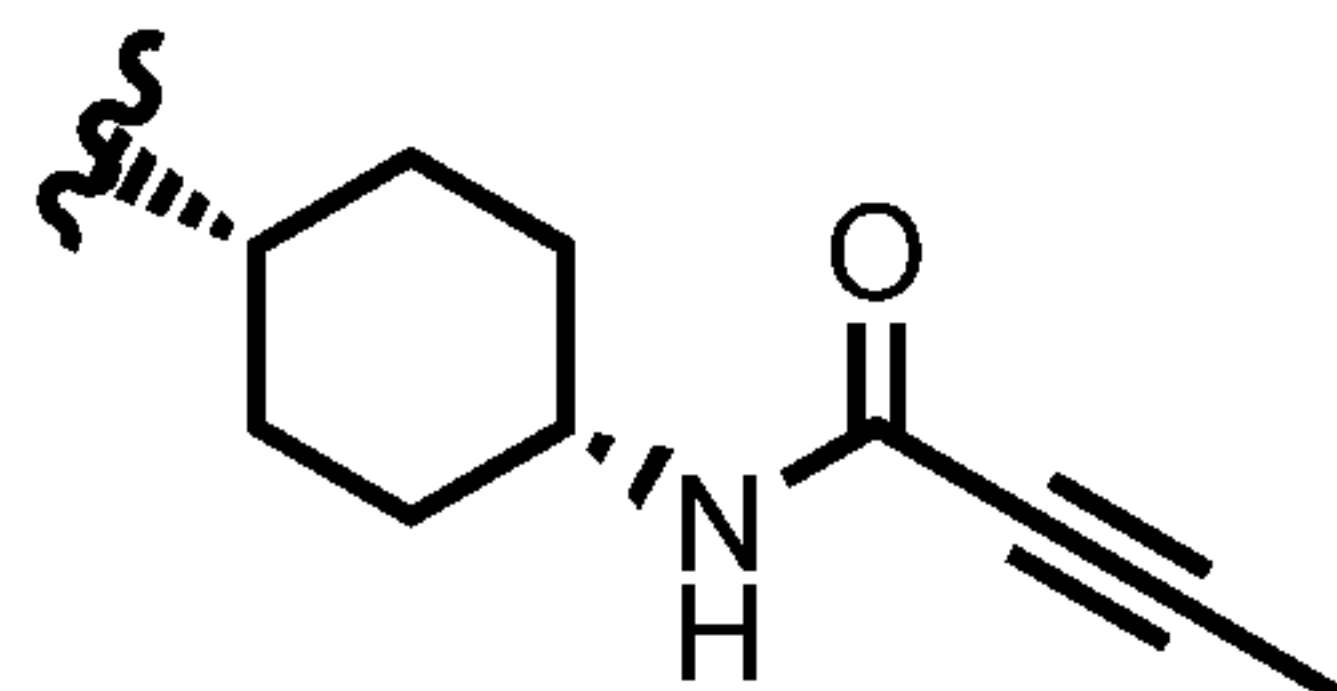
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is

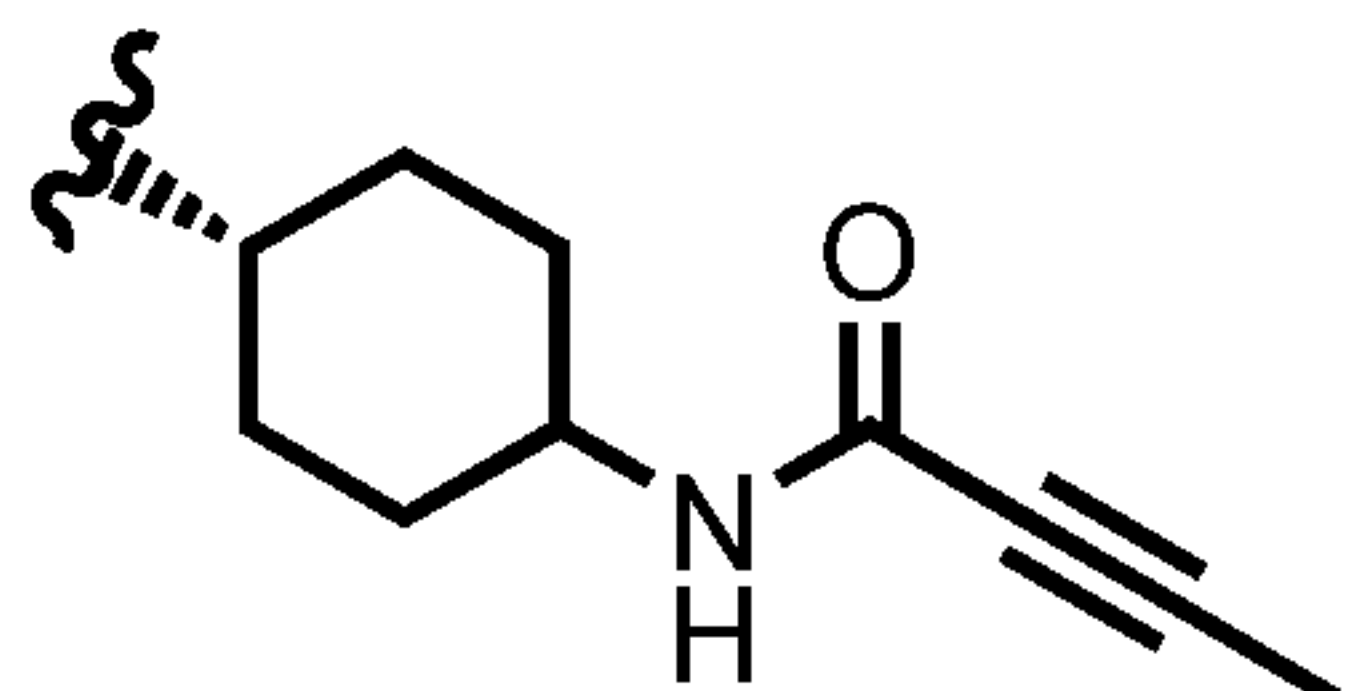


. In embodiments, L^1 - L^2 -E is

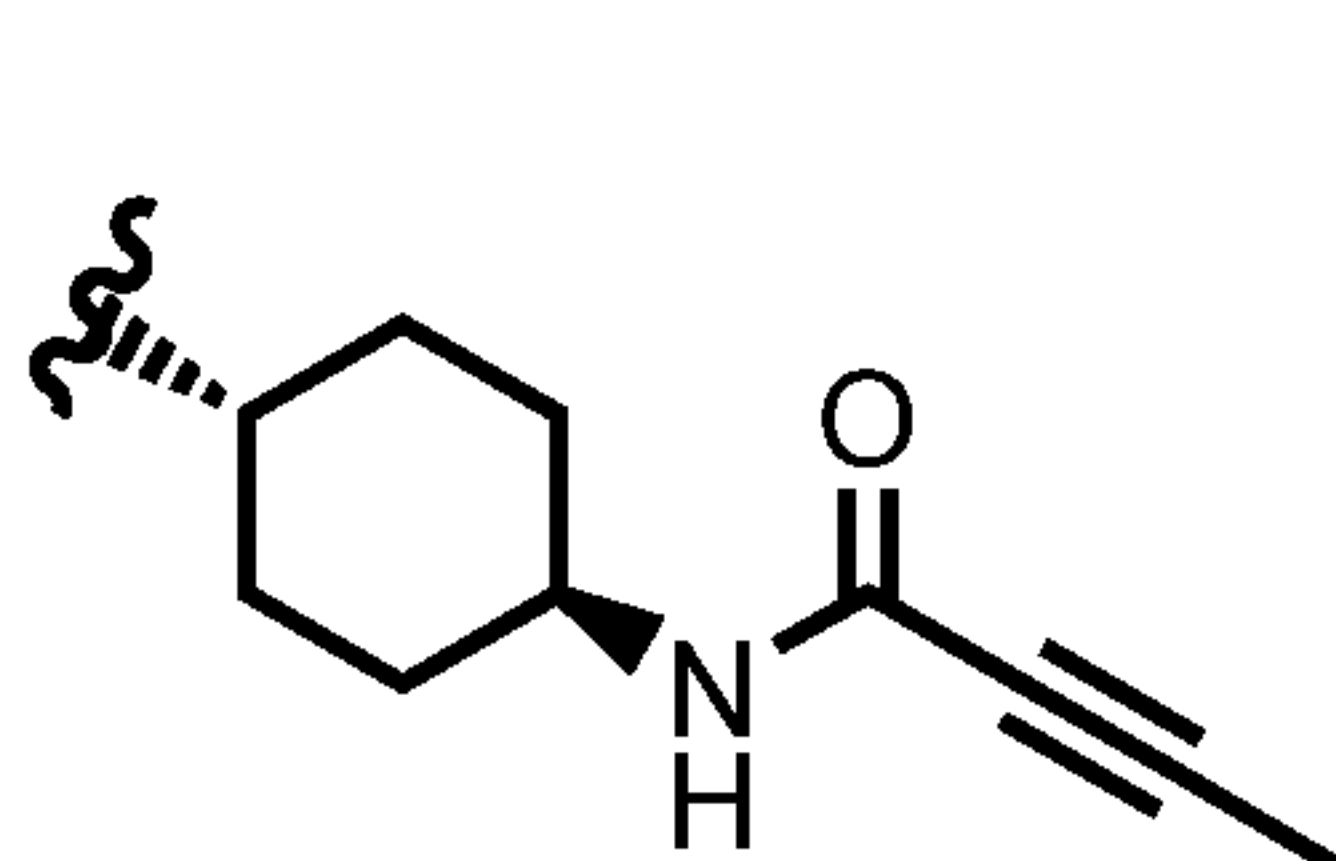


. In

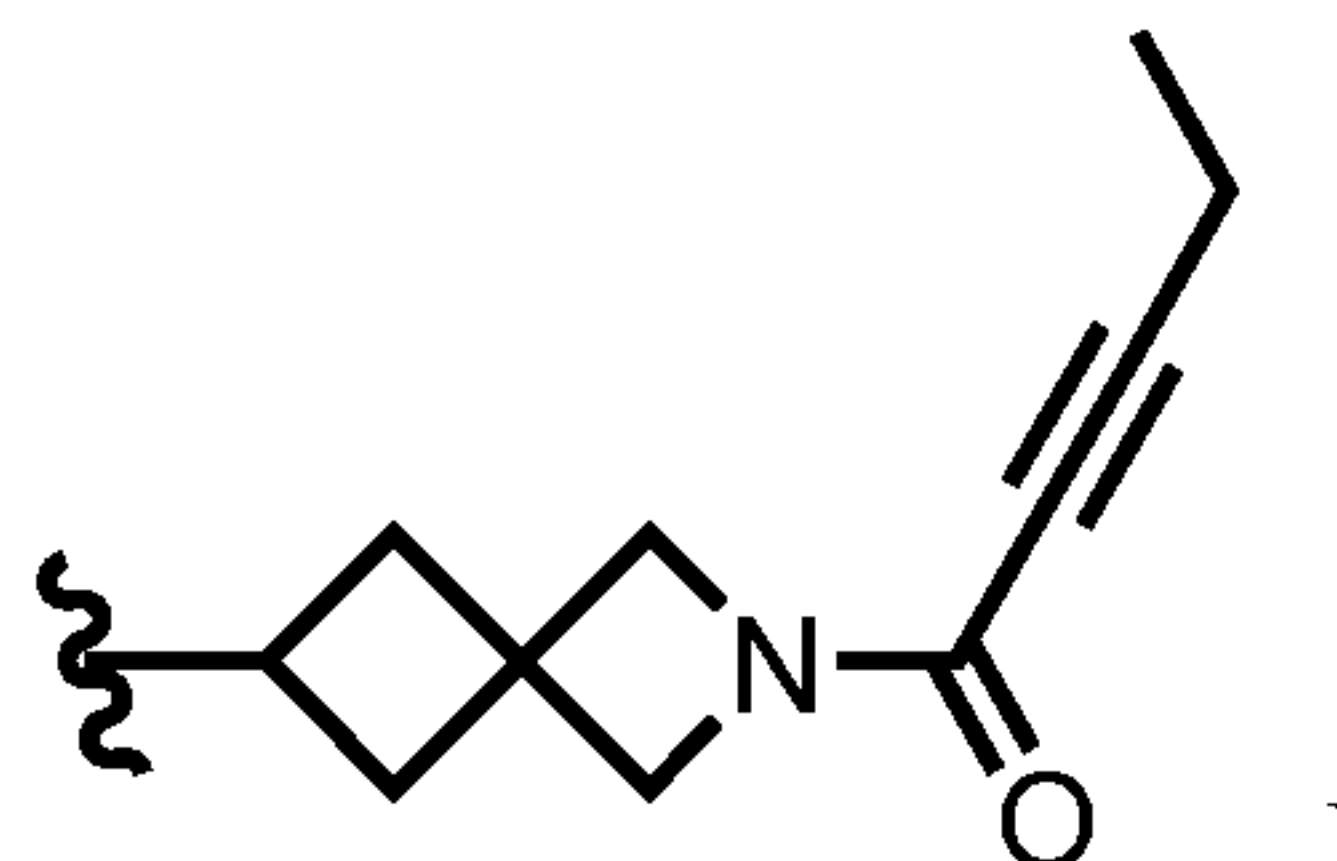
embodiments, L^1 - L^2 -E is



. In embodiments, L^1 - L^2 -E is

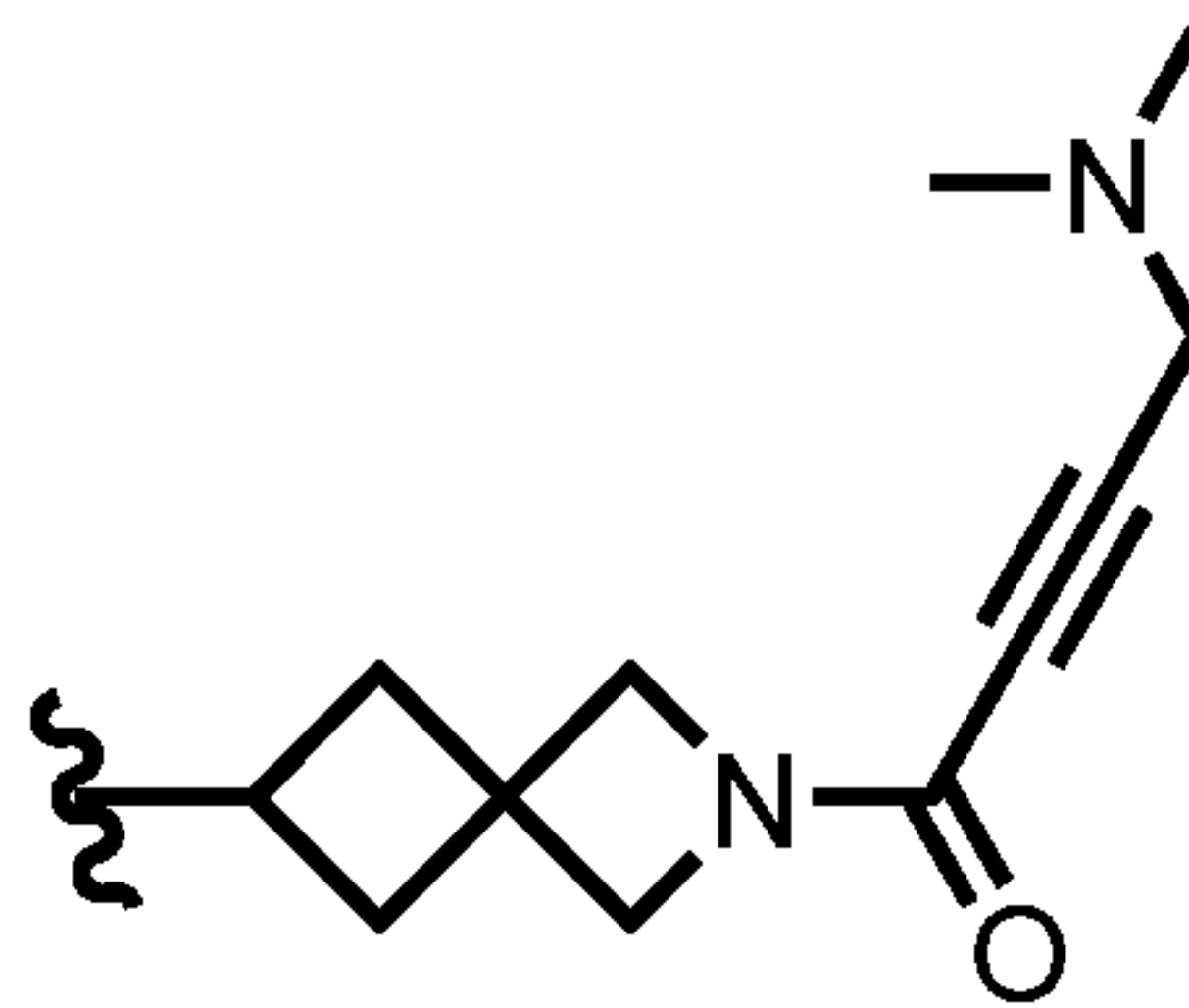


. In embodiments, L^1 - L^2 -E is

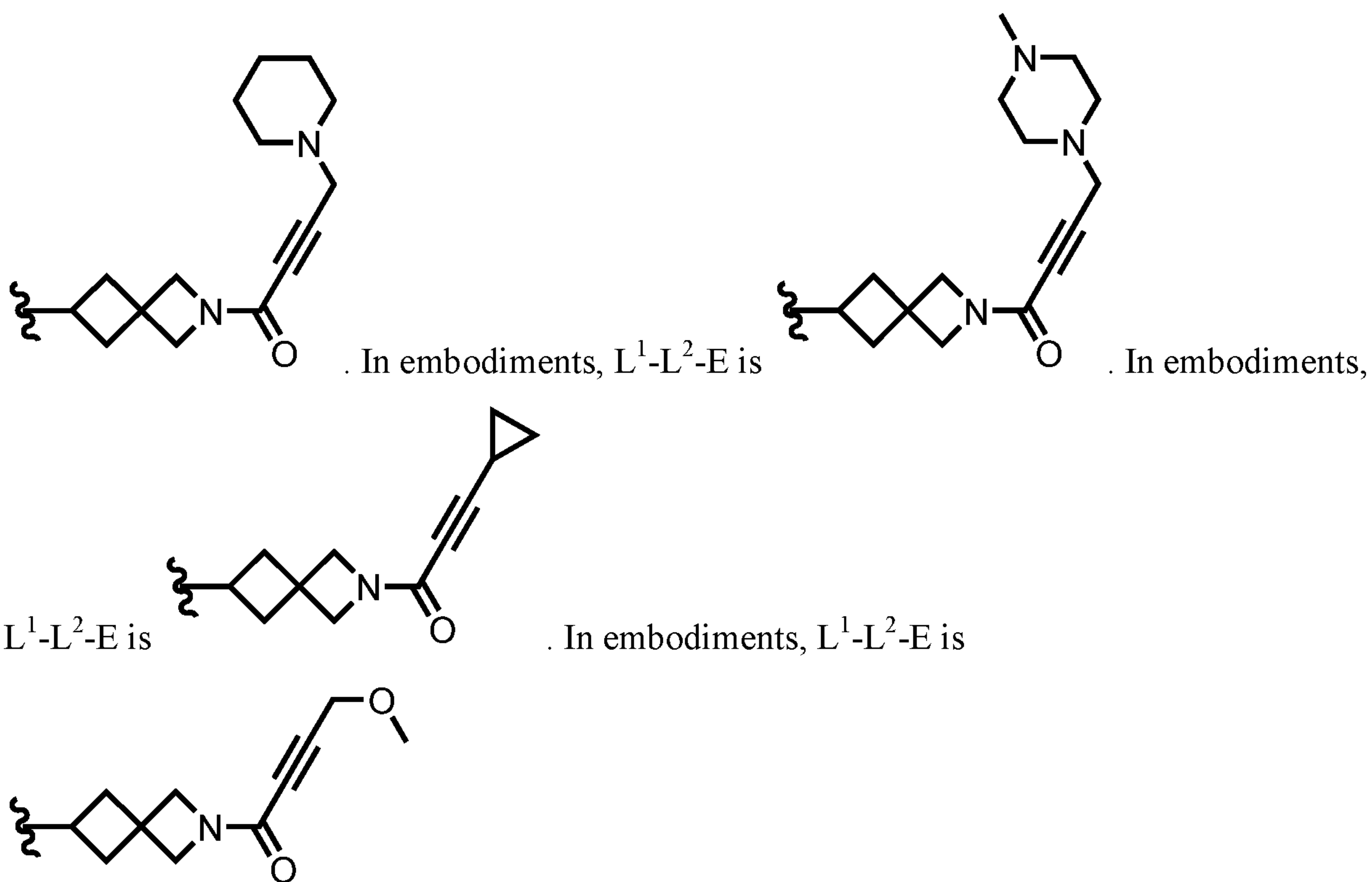


. In

embodiments, L^1 - L^2 -E is

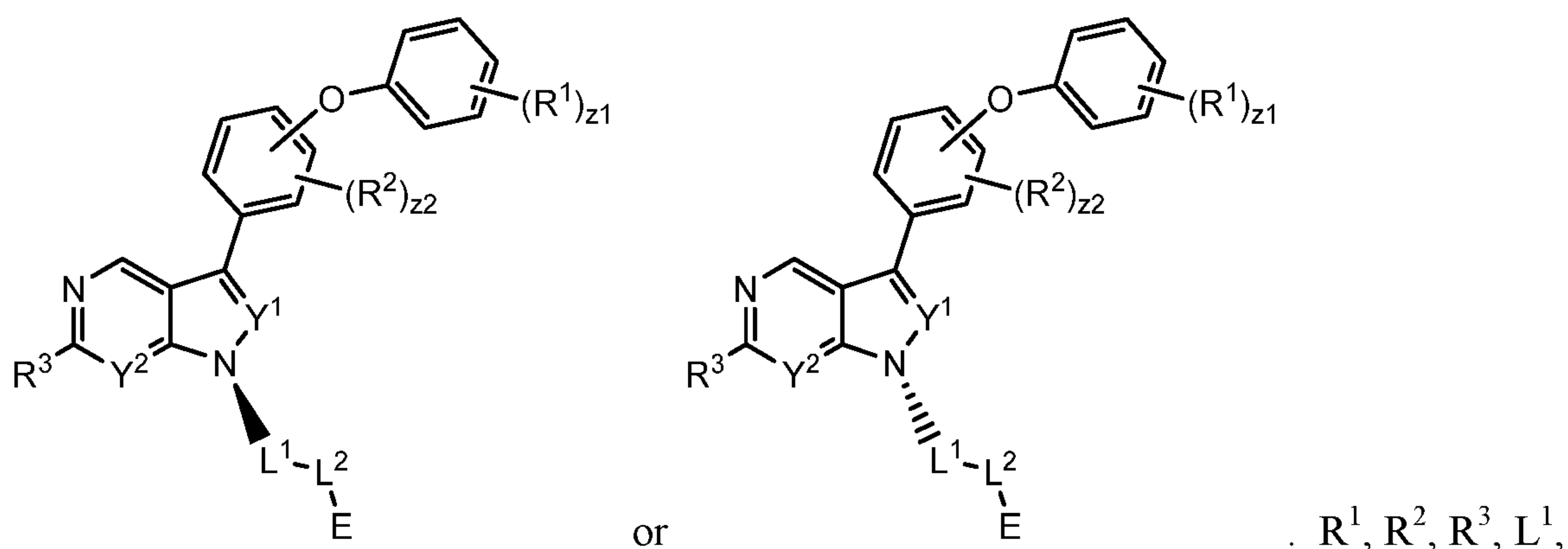


. In embodiments, L^1 - L^2 -E is



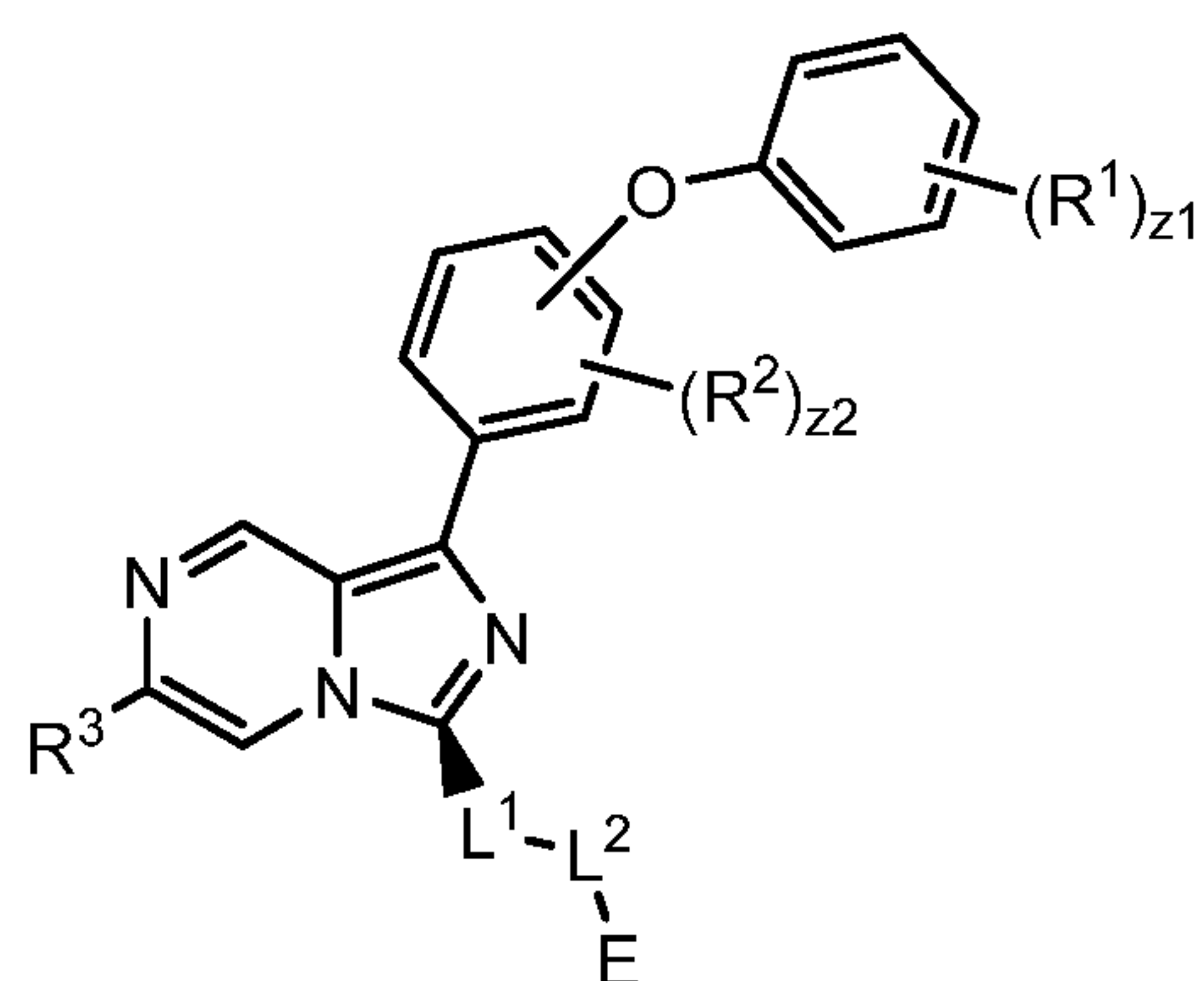
[0530] In embodiments, the compound (e.g., described herein) is capable of entering the
 5 central nervous system of a patient following administration outside of the central nervous
 system (e.g., systemic administration, i.v., or intrarterial). In embodiments, the compound
 (e.g., described herein) is capable of crossing the blood-brain barrier.

[0531] In embodiments, the compound has the formula

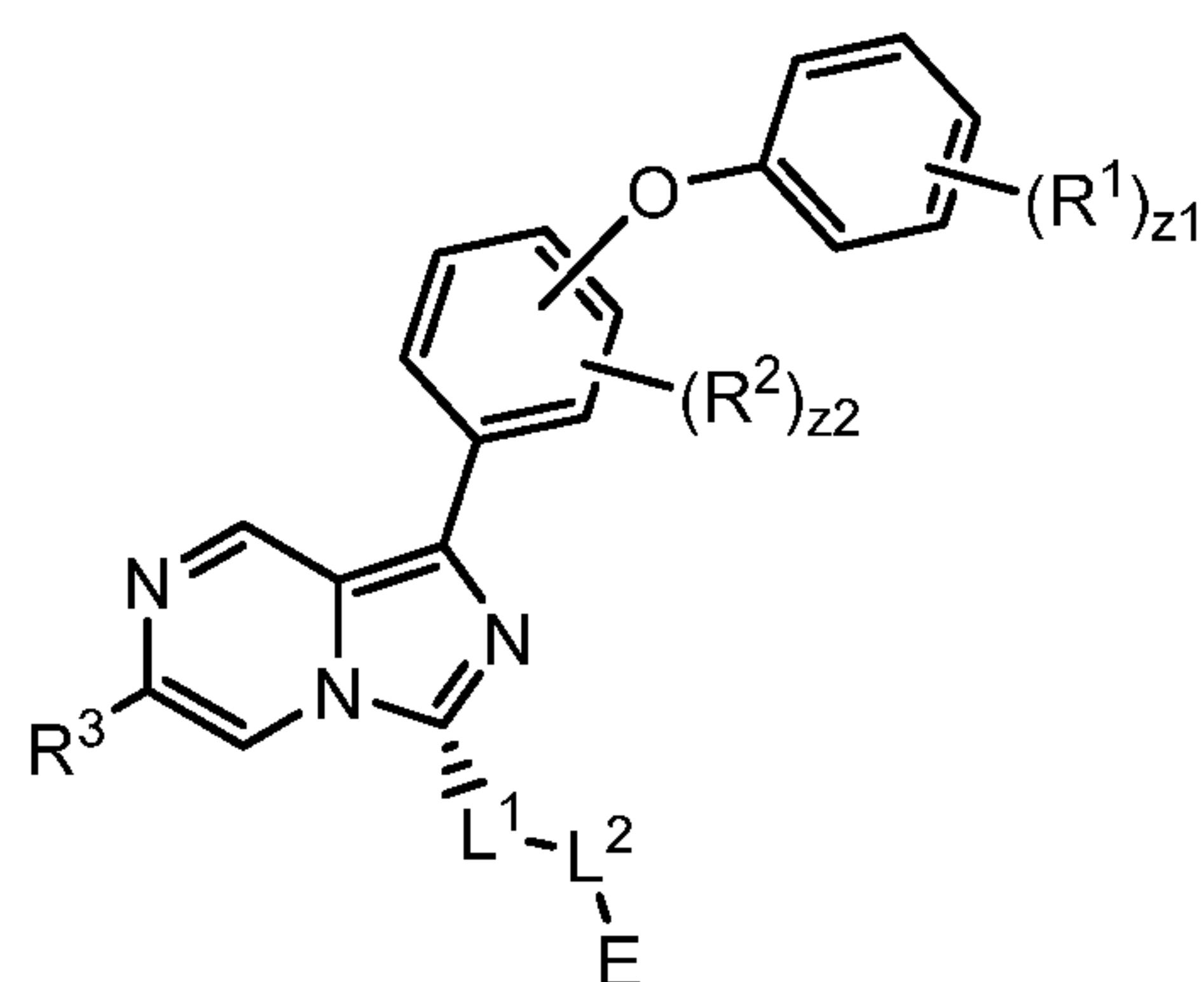


10 L^2 , Y^1 , Y^2 , $z1$, $z2$, and E are as described herein.

[0532] In embodiments, the compound has the formula

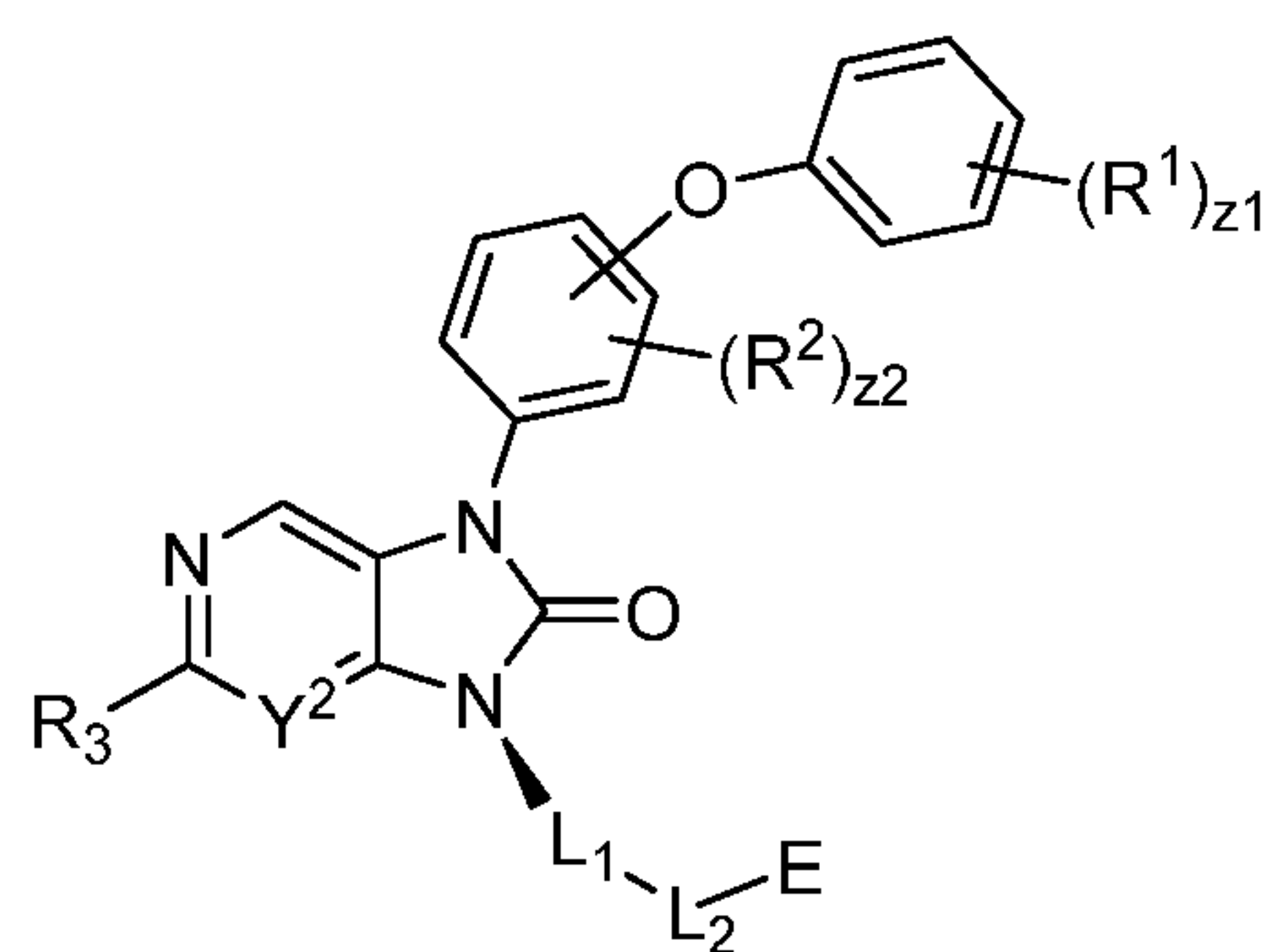


or

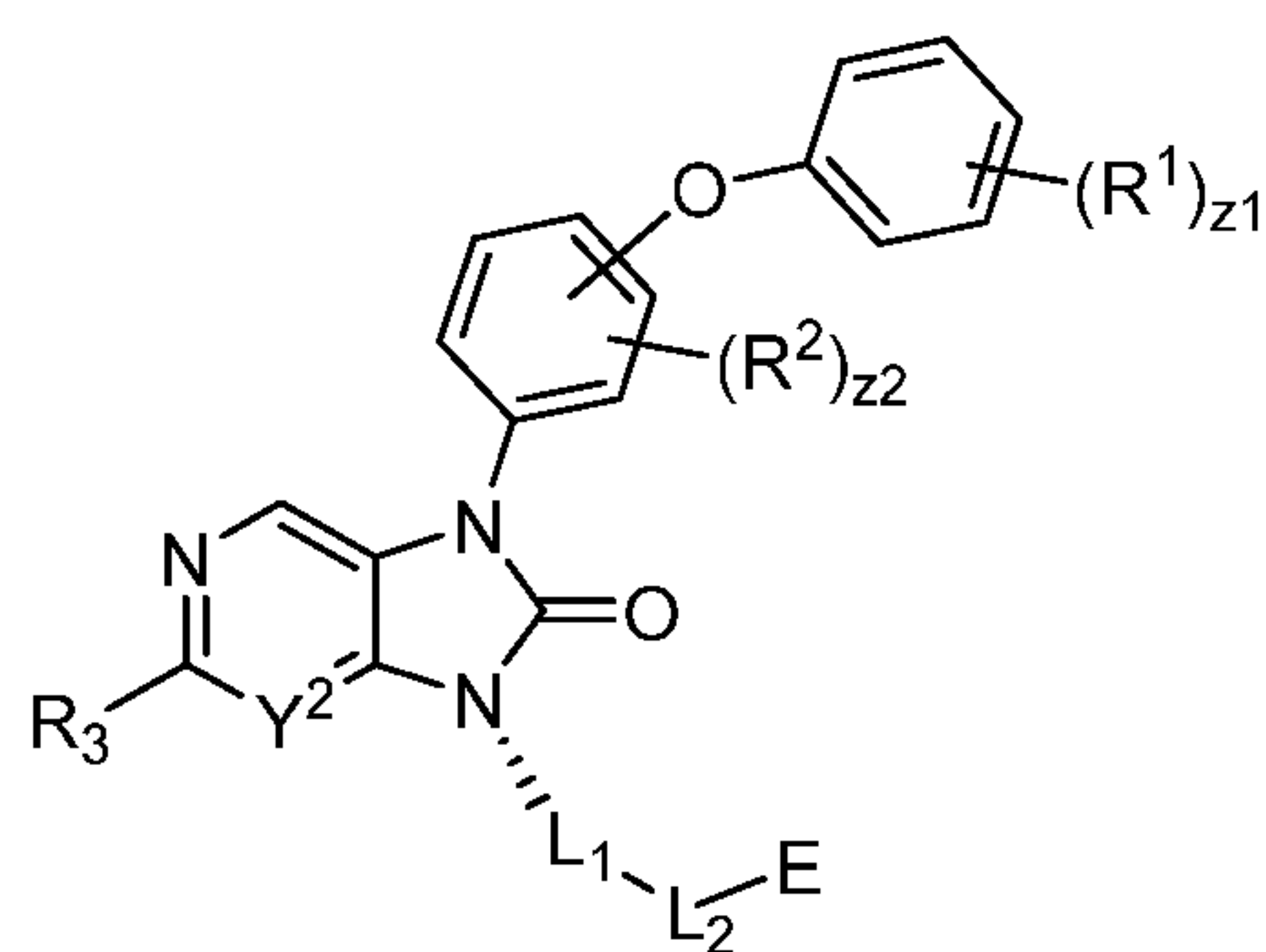
. $R^1, R^2, R^3, L^1,$

$L^2, z1, z2,$ and E are as described herein.

[0533] In embodiments, the compound has the formula

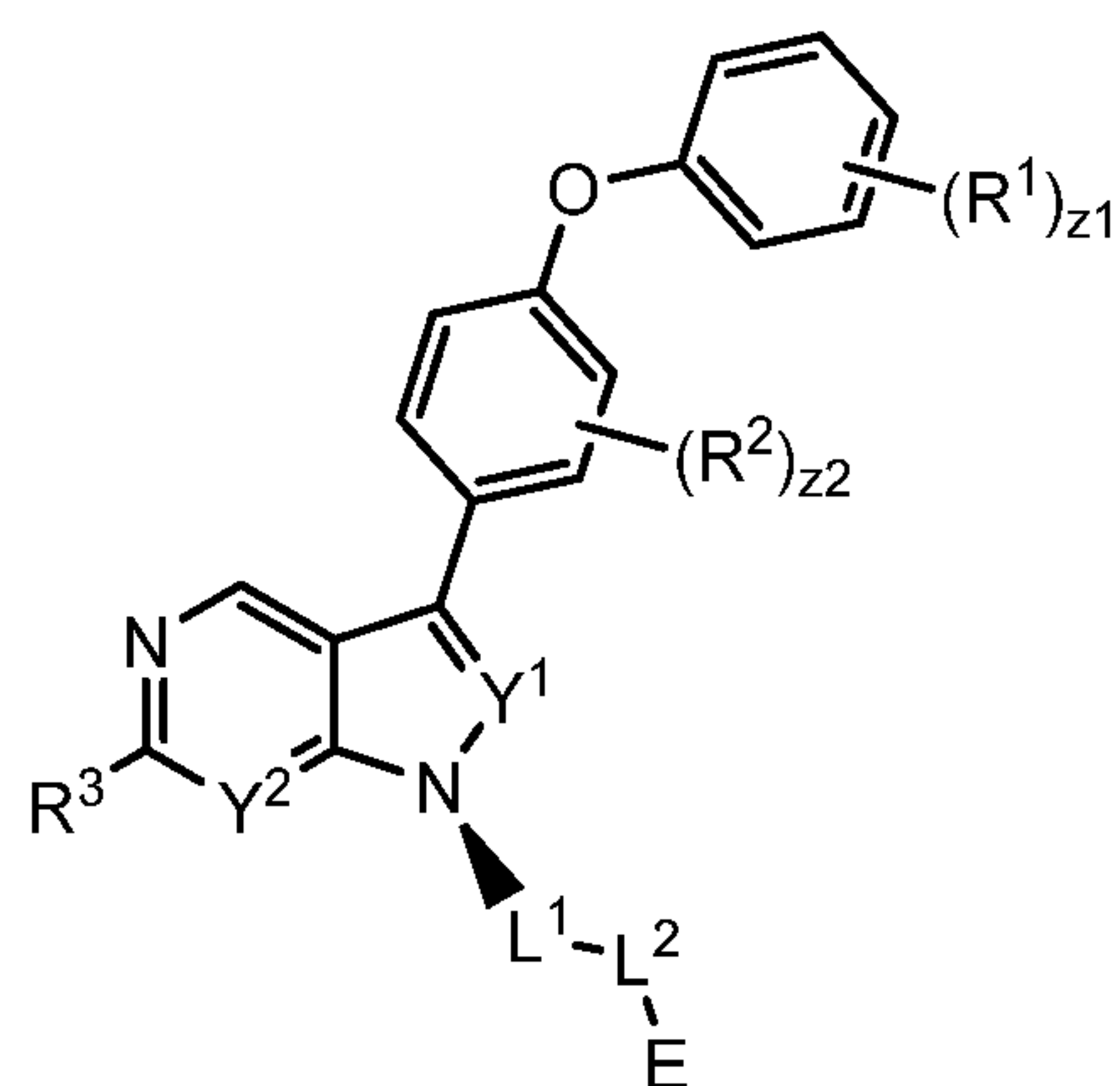


or

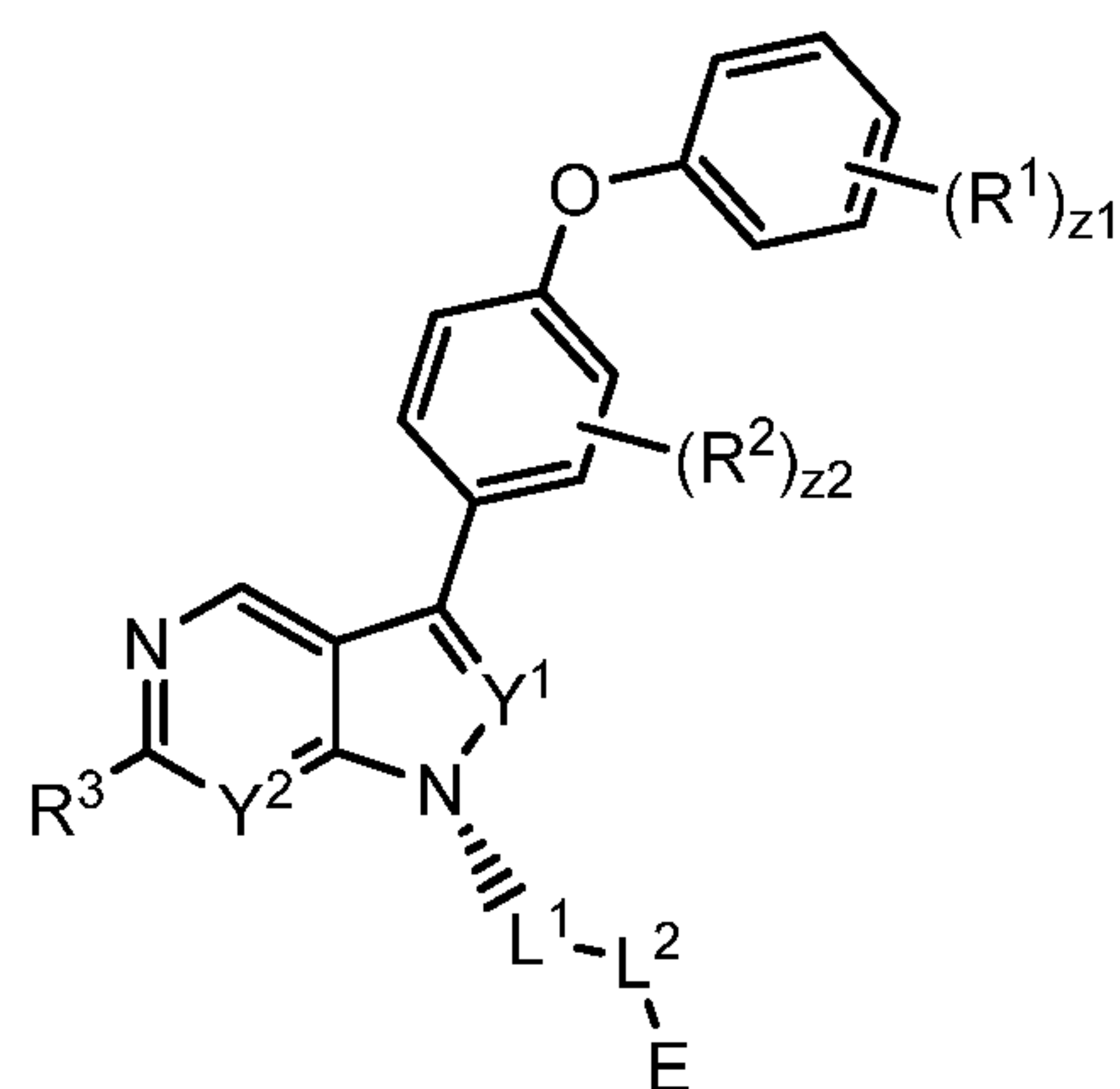
. $R^1, R^2, R^3, L^1, L^2,$

5 $Y^2, z1, z2,$ and E are as described herein.

[0534] In embodiments, the compound has the formula

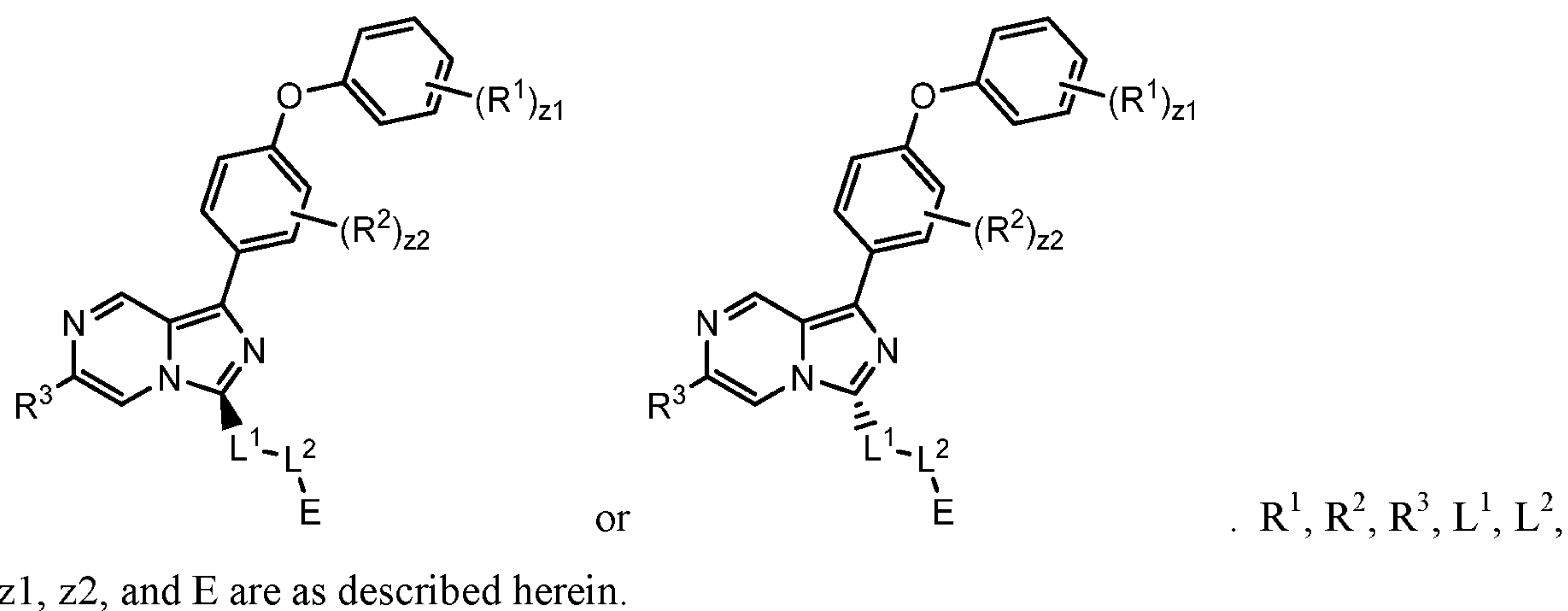


or

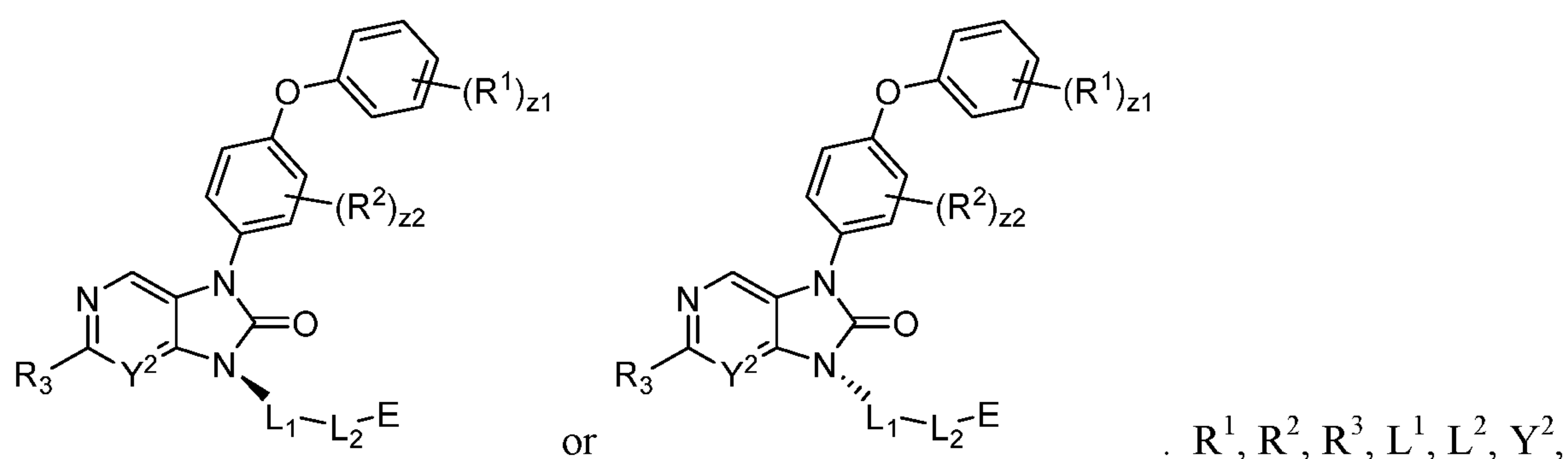
. $R^1, R^2, R^3, L^1, L^2, Y^1,$

$Y^2, z1, z2,$ and E are as described herein.

[0535] In embodiments, the compound has the formula

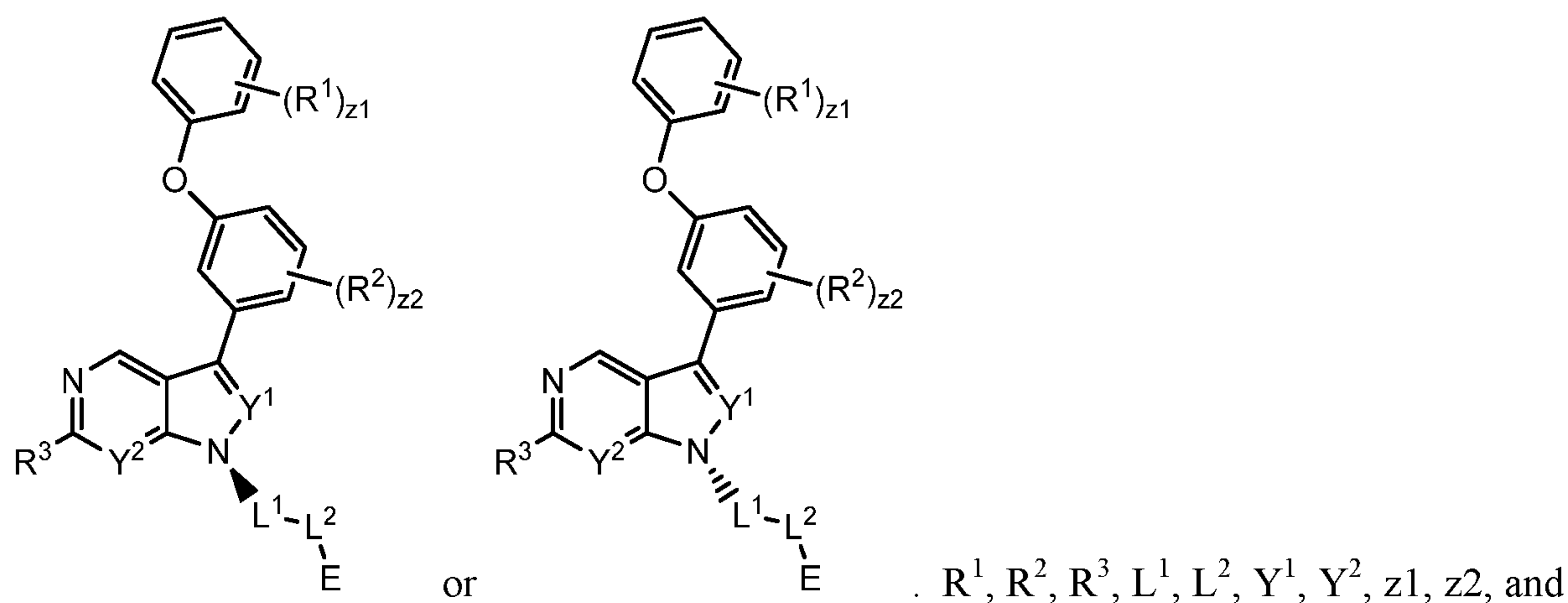


[0536] In embodiments, the compound has the formula

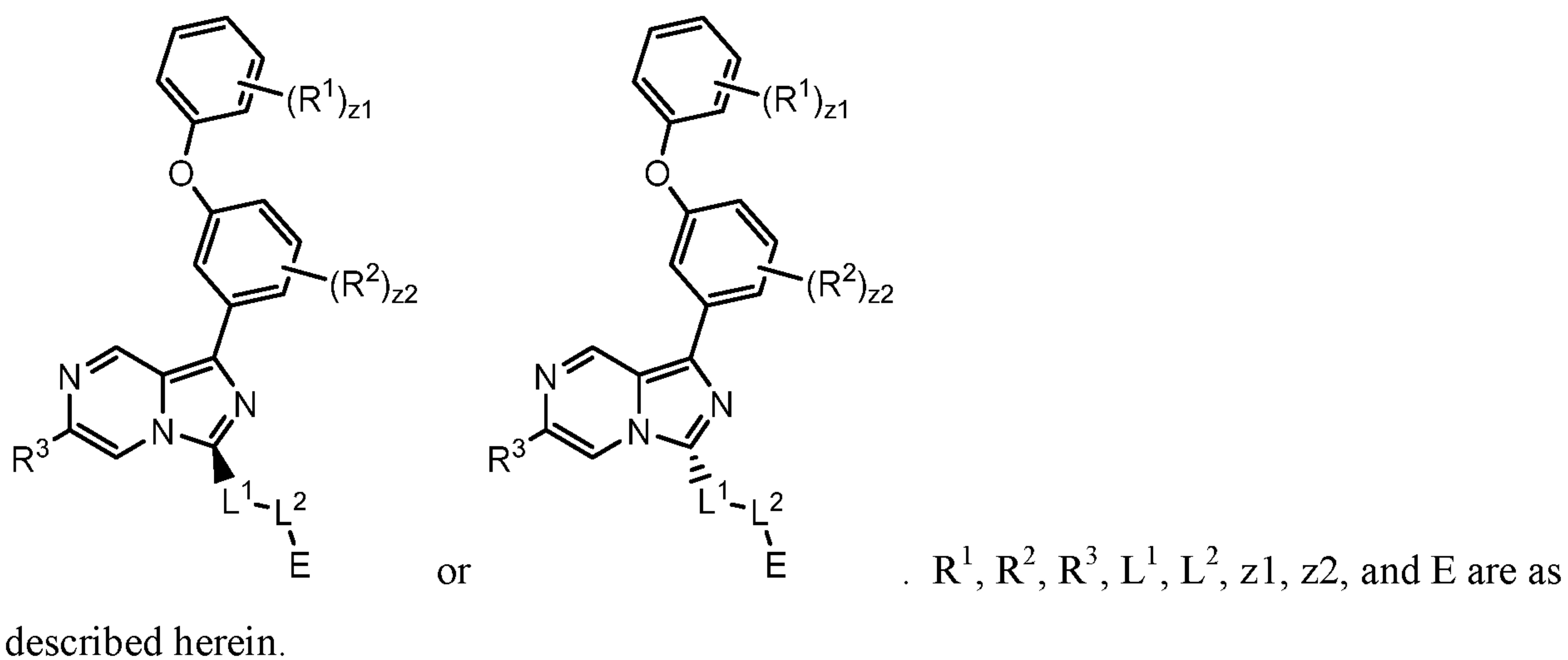


5 $z1, z2,$ and E are as described herein.

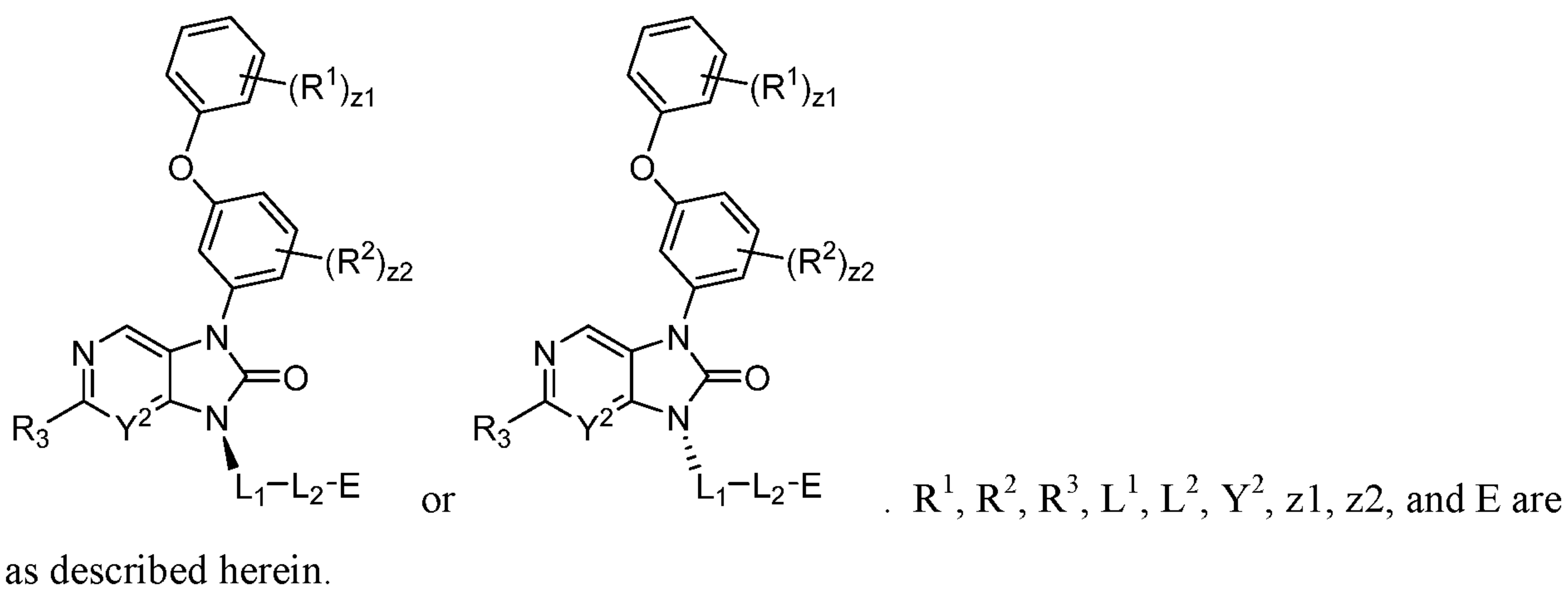
[0537] In embodiments, the compound has the formula



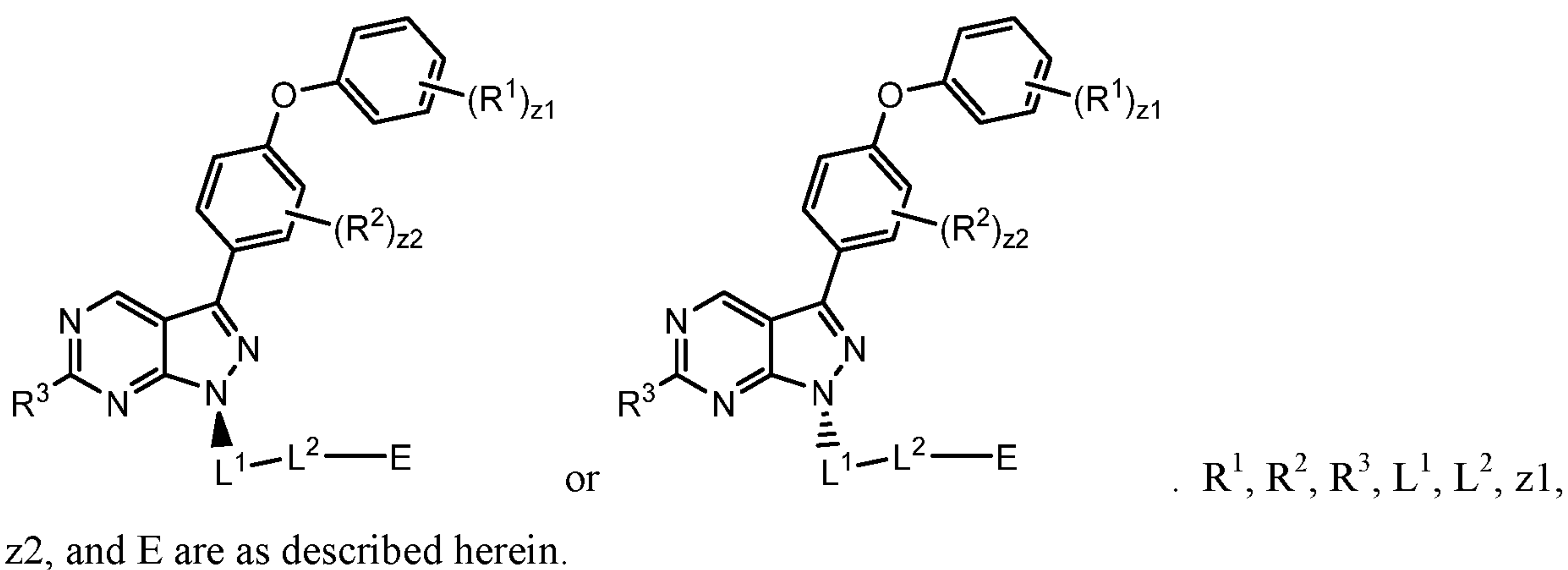
[0538] In embodiments, the compound has the formula



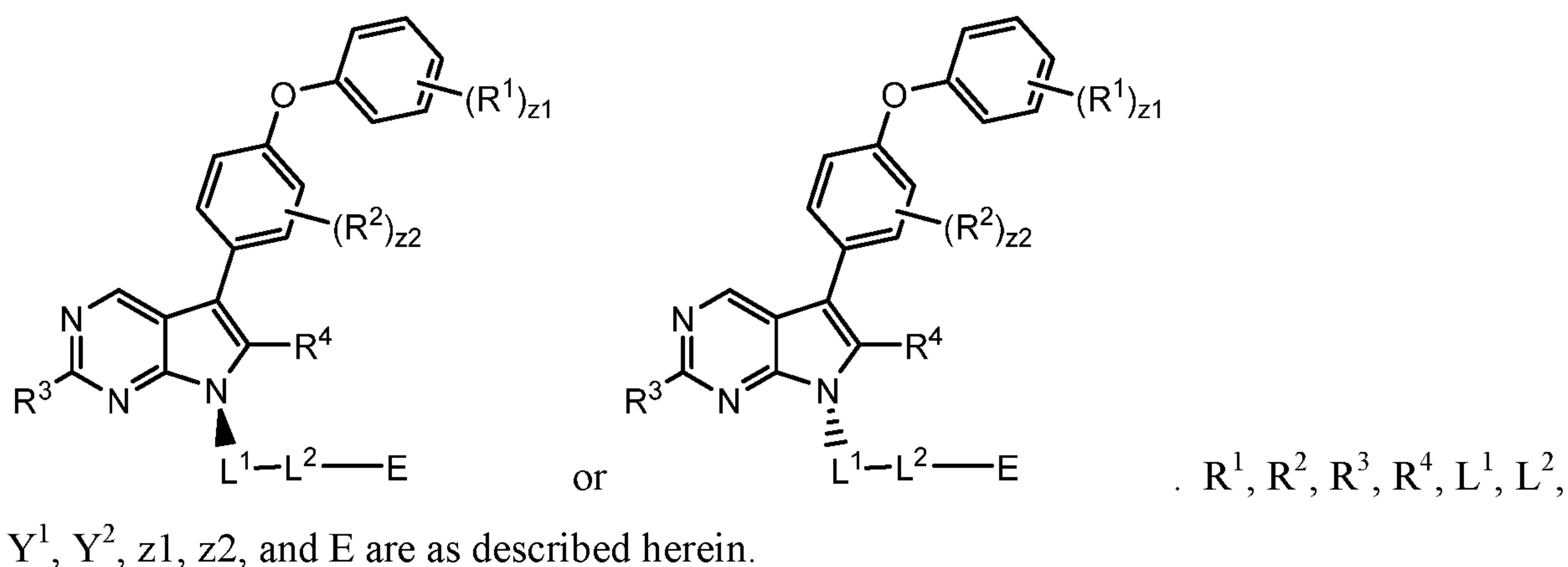
[0539] In embodiments, the compound has the formula



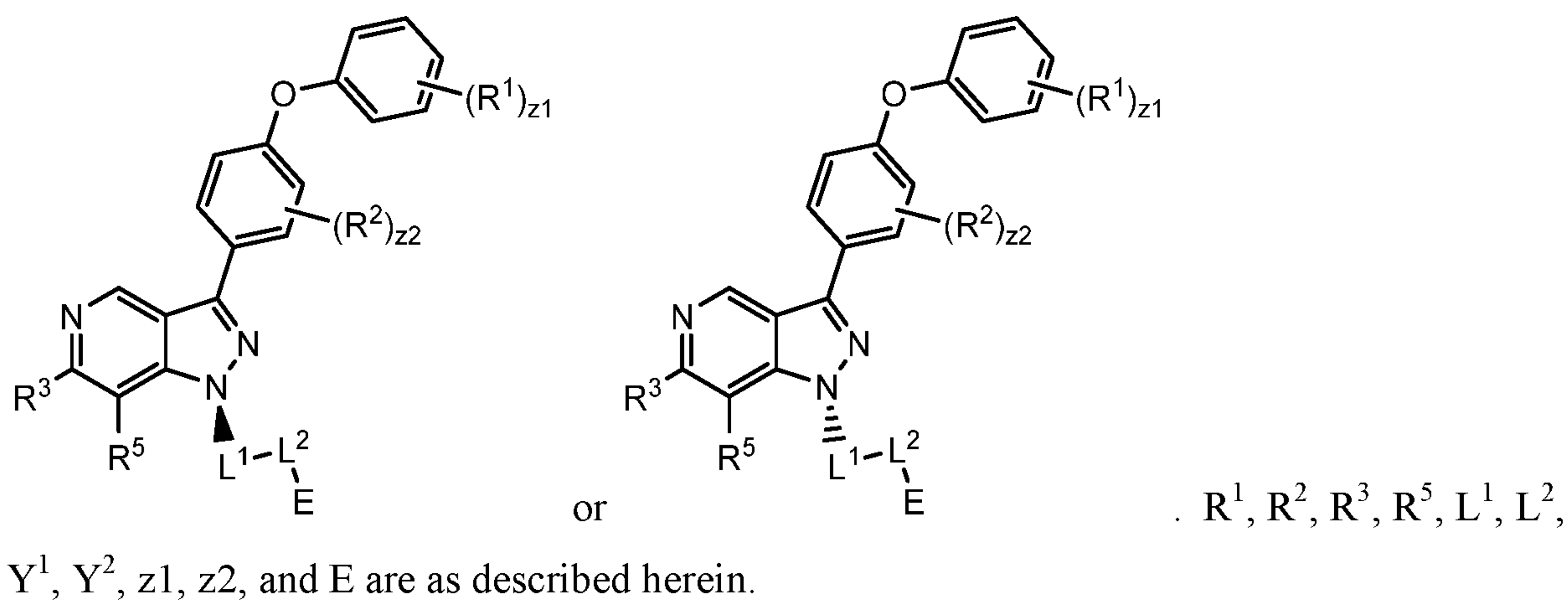
[0540] In embodiments, the compound has the formula



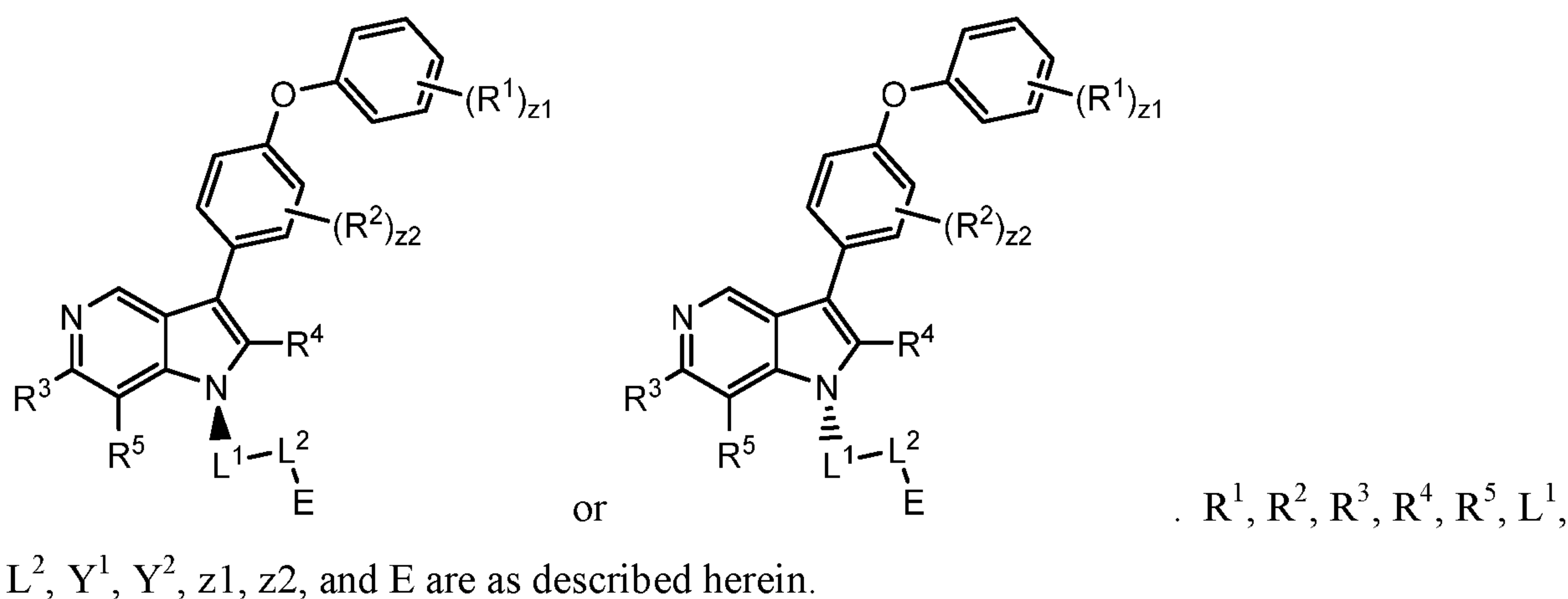
[0541] In embodiments, the compound has the formula



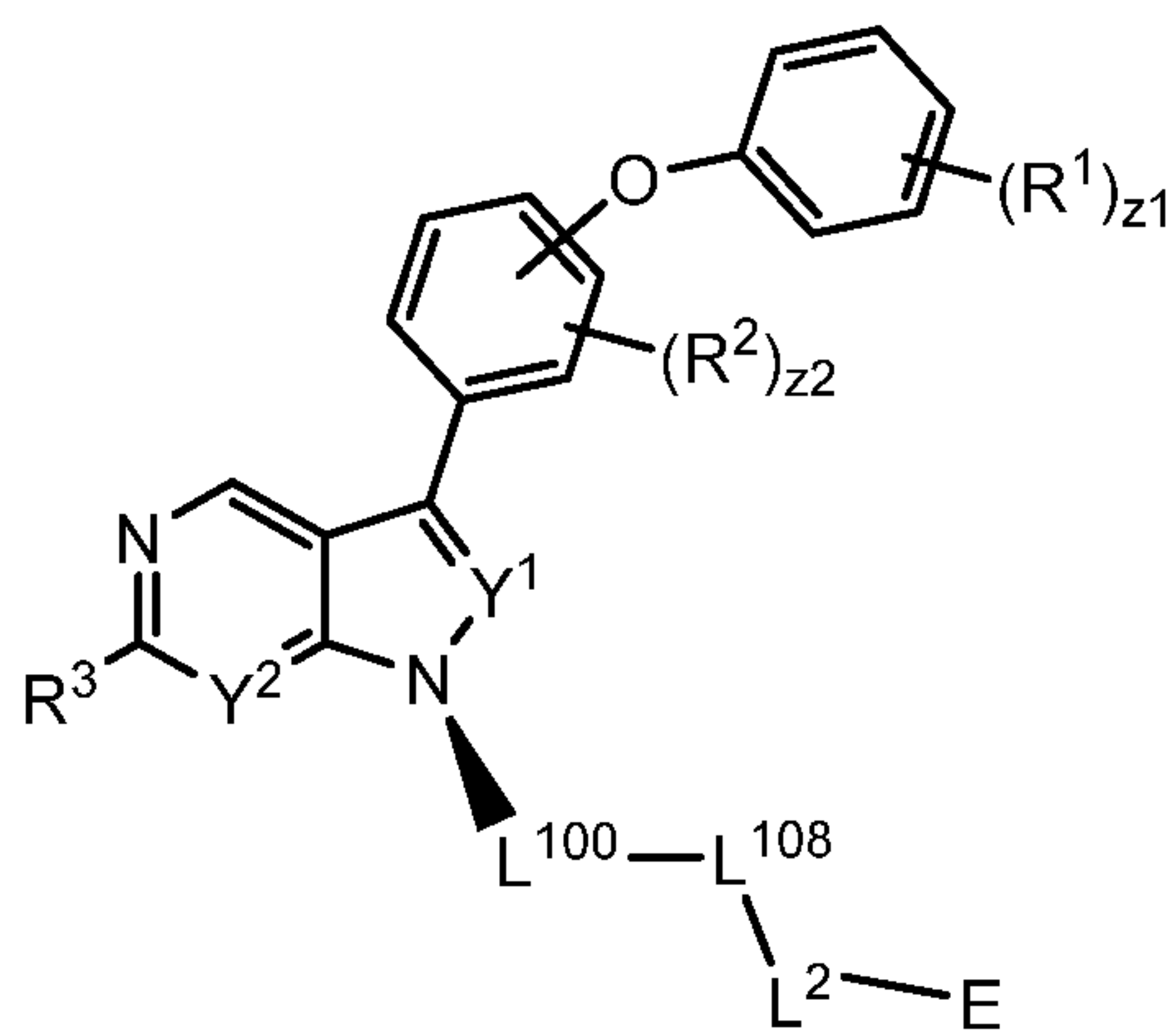
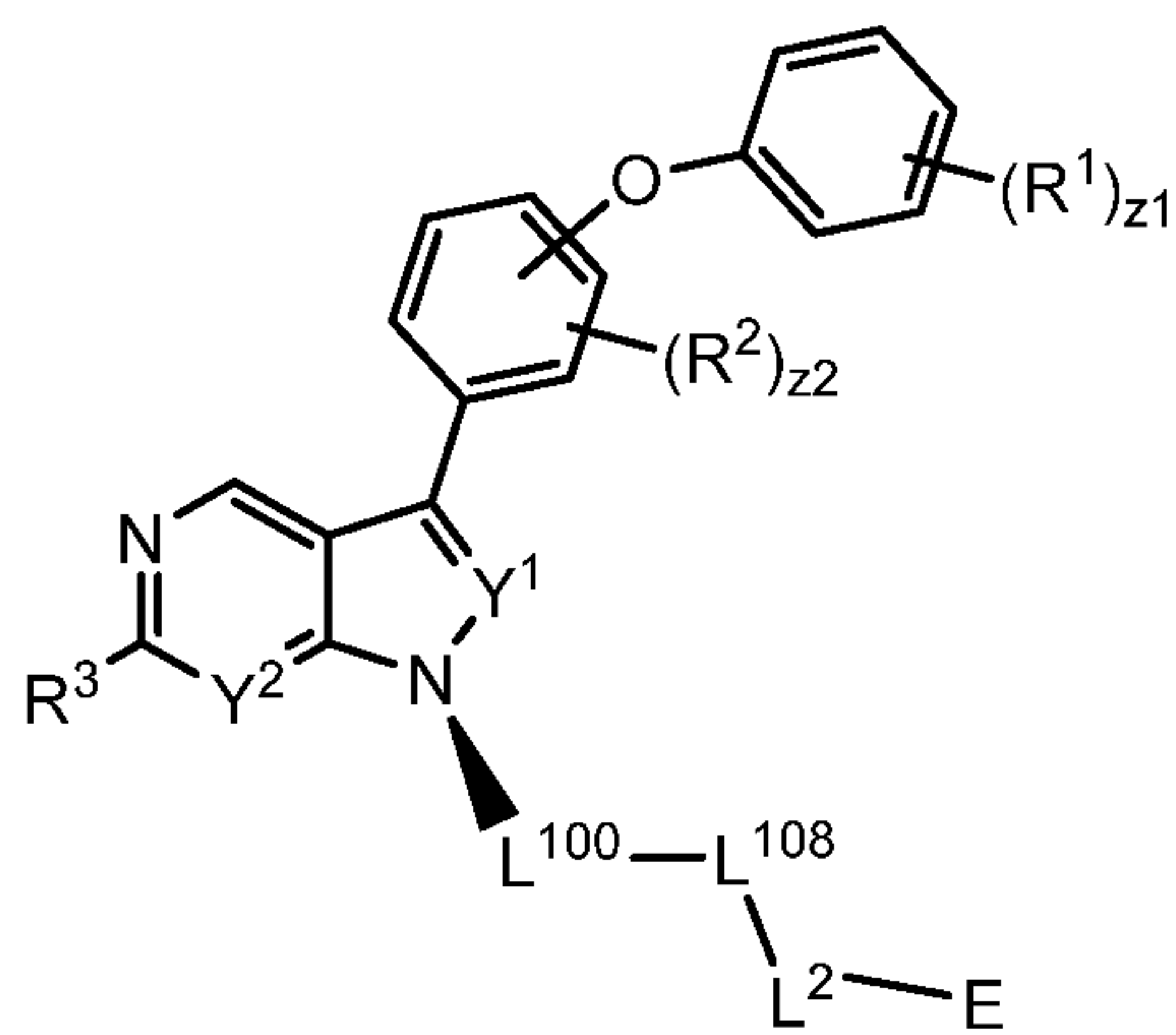
[0542] In embodiments, the compound has the formula



[0543] In embodiments, the compound has the formula

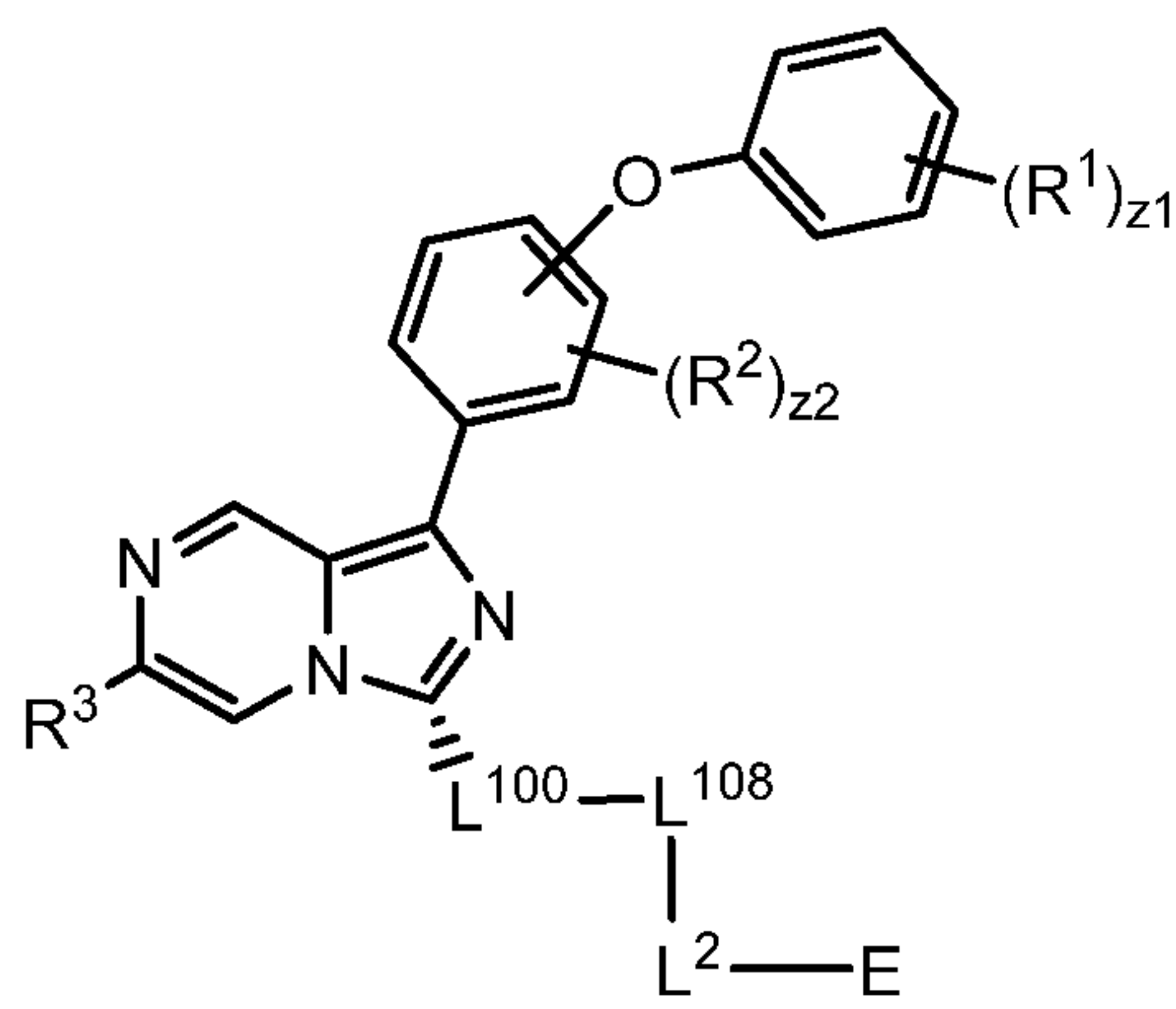
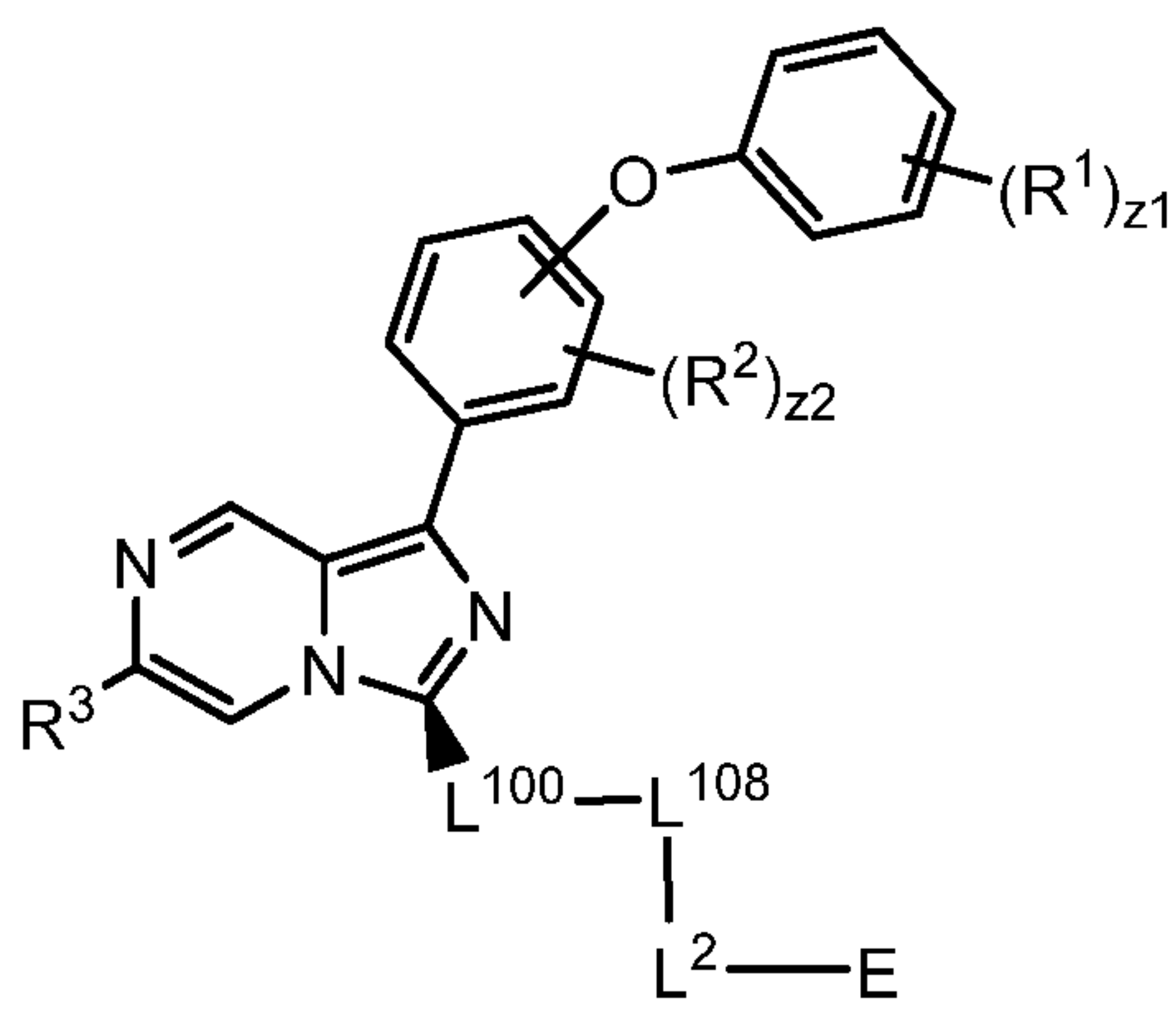


[0544] In embodiments, the compound has the formula



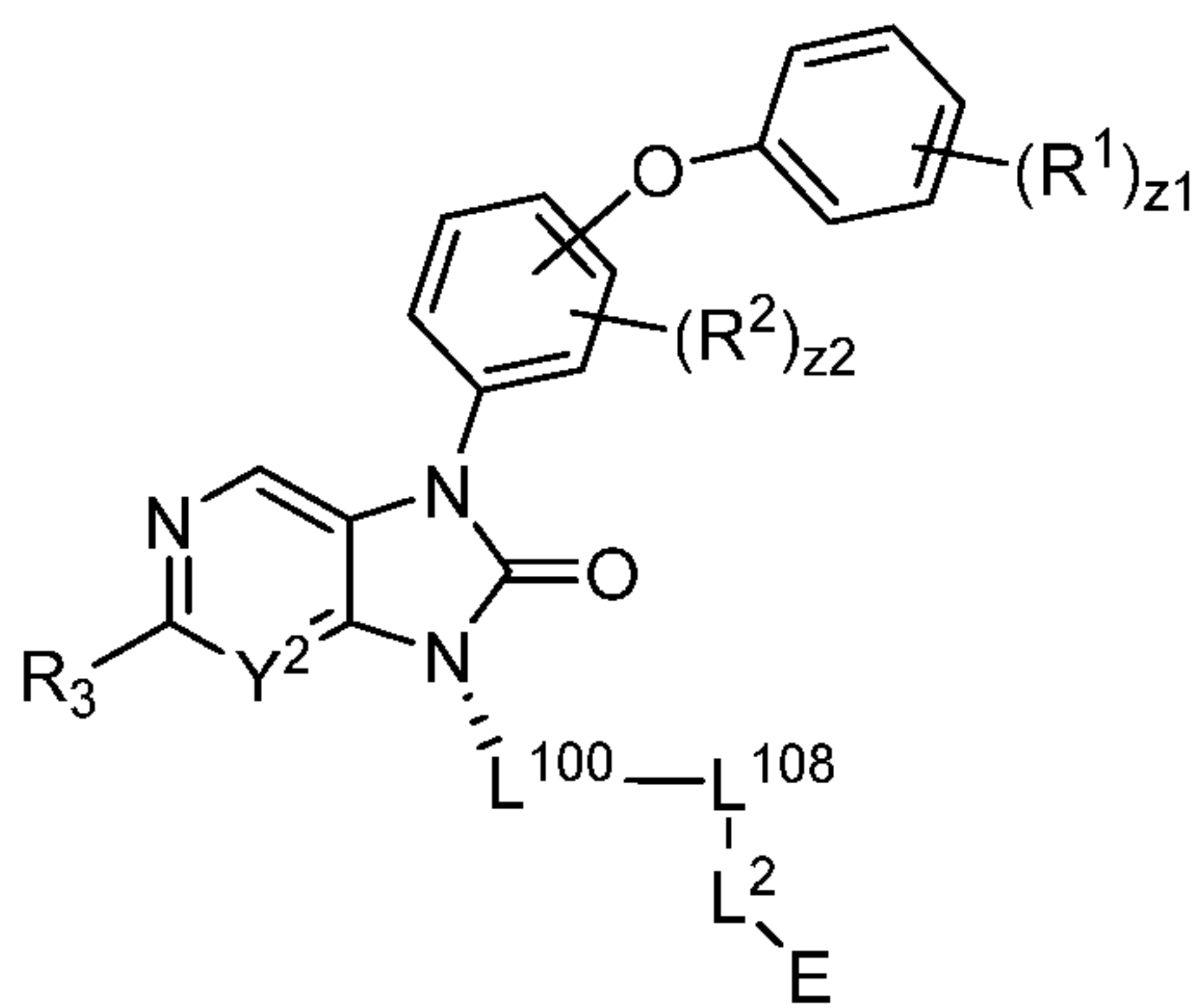
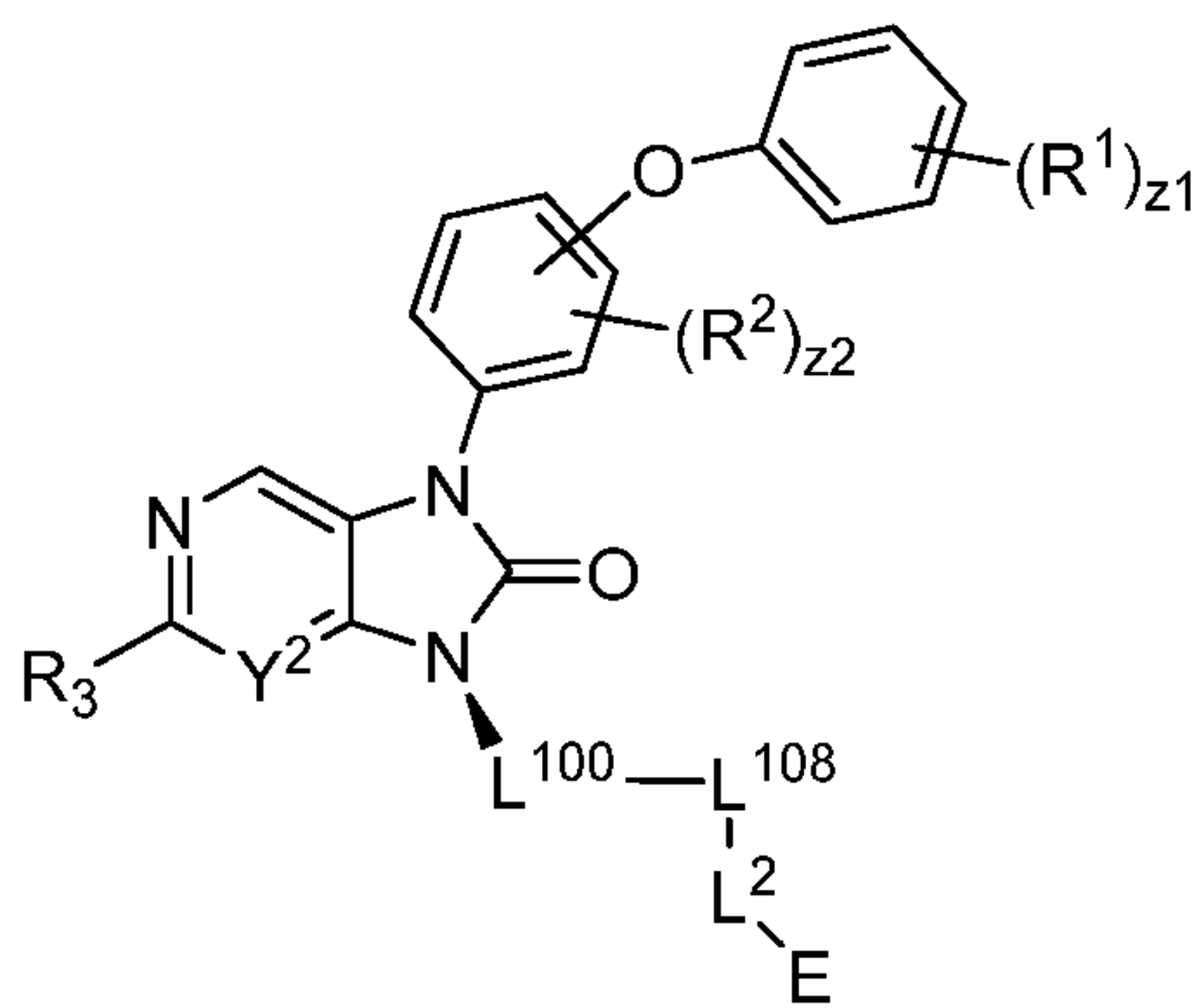
or $R^1, R^2, R^3, L^{100}, L^{108}, L^2, Y^1, Y^2, z1, z2,$ and E are as described herein.

[0545] In embodiments, the compound has the formula



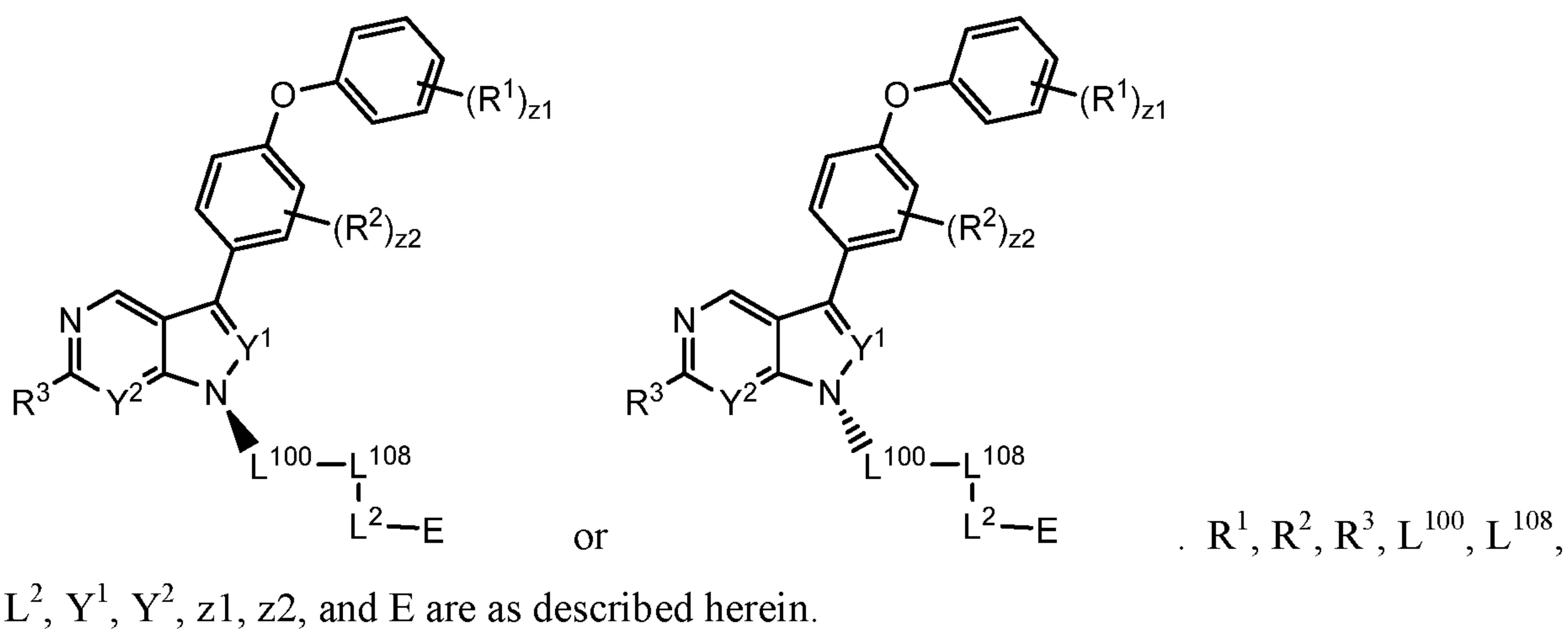
5 $L^{108}, L^2, z1, z2,$ and E are as described herein.

[0546] In embodiments, the compound has the formula

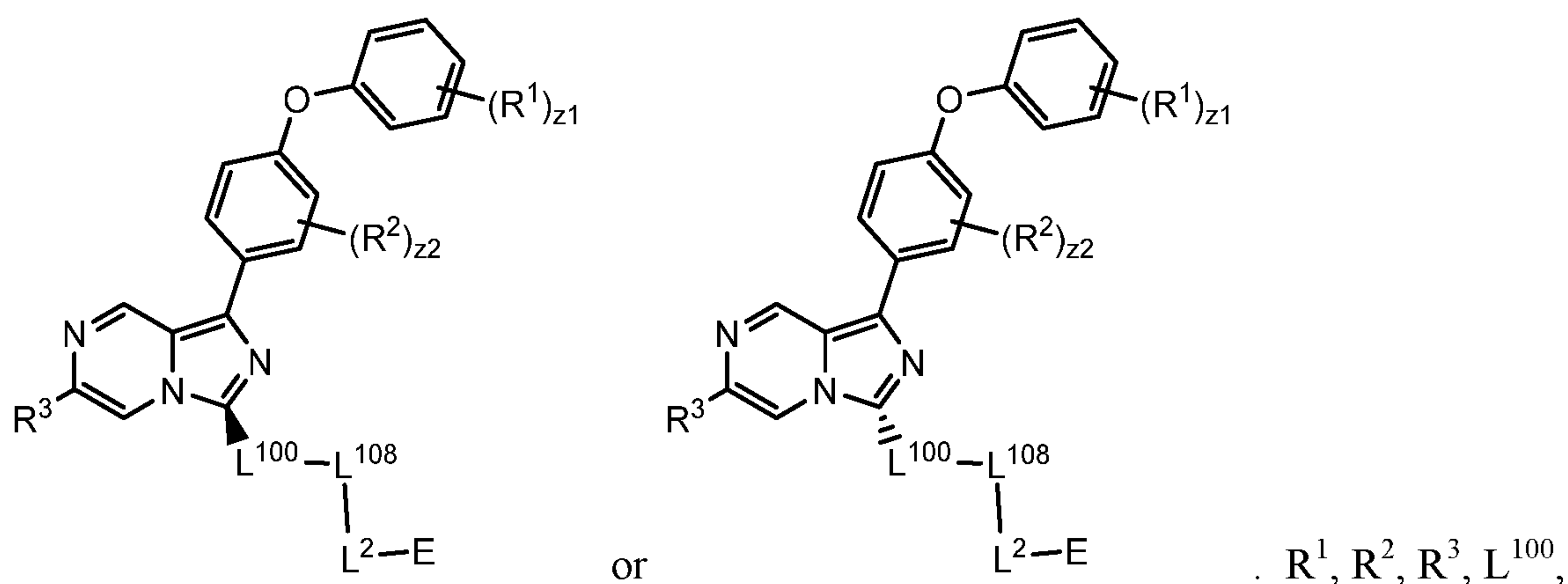


$L^{108}, L^2, Y^2, z1, z2,$ and E are as described herein.

[0547] In embodiments, the compound has the formula

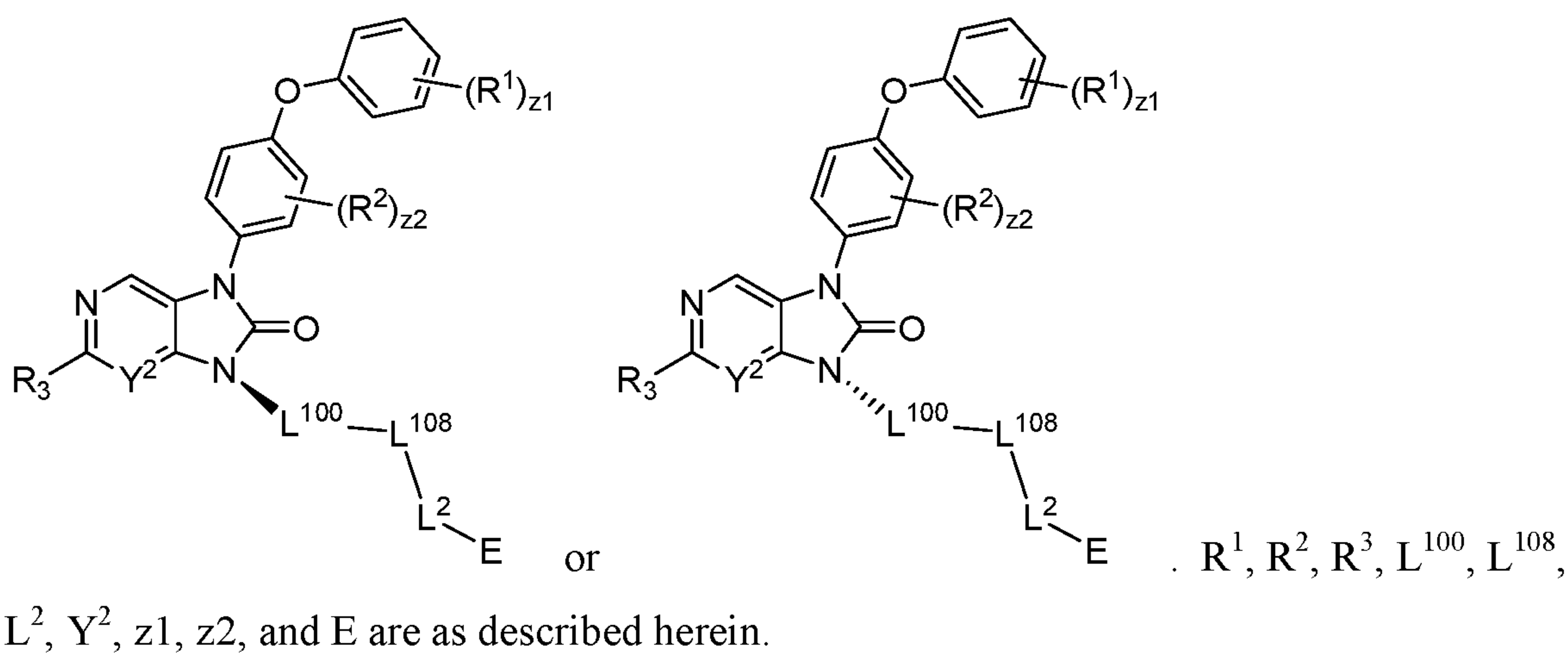


[0548] In embodiments, the compound has the formula

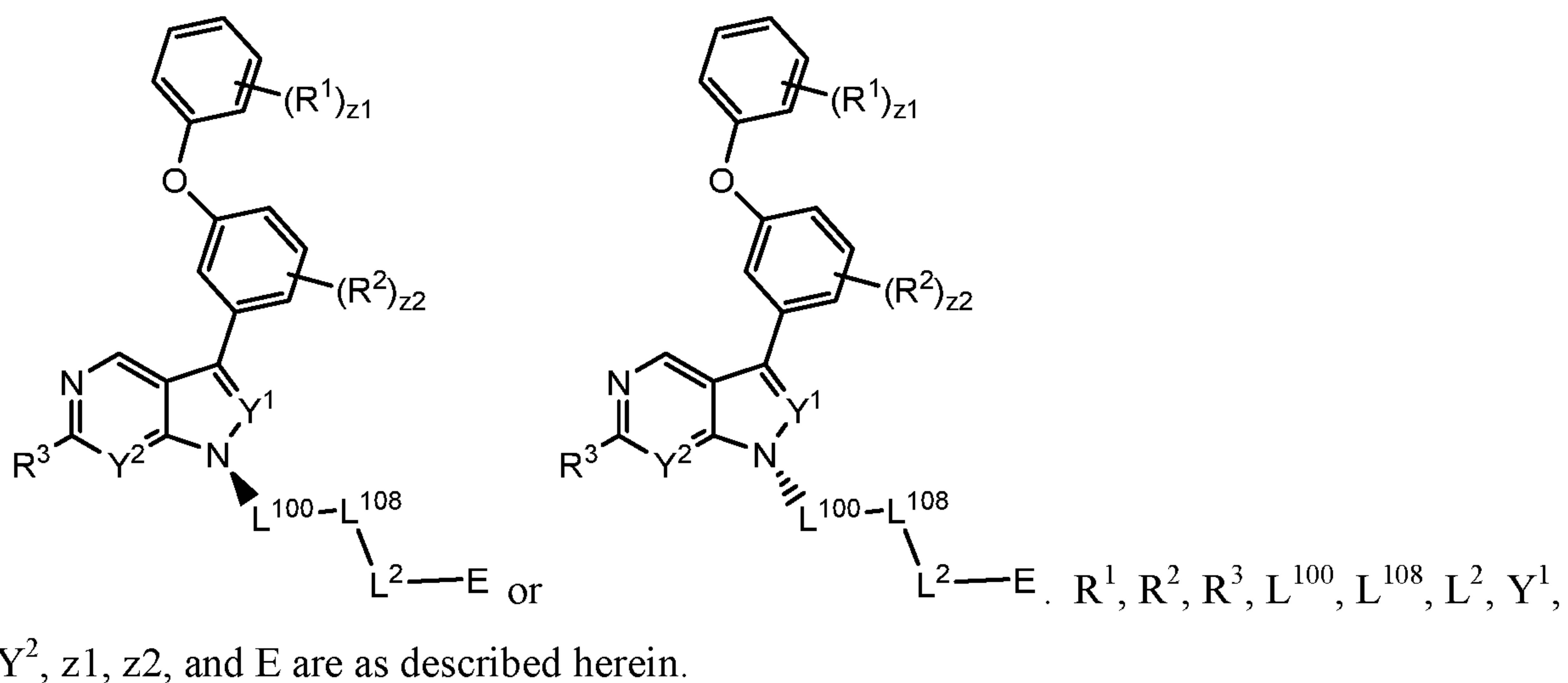


5 $L^{108}, L^2, z1, z2,$ and E are as described herein.

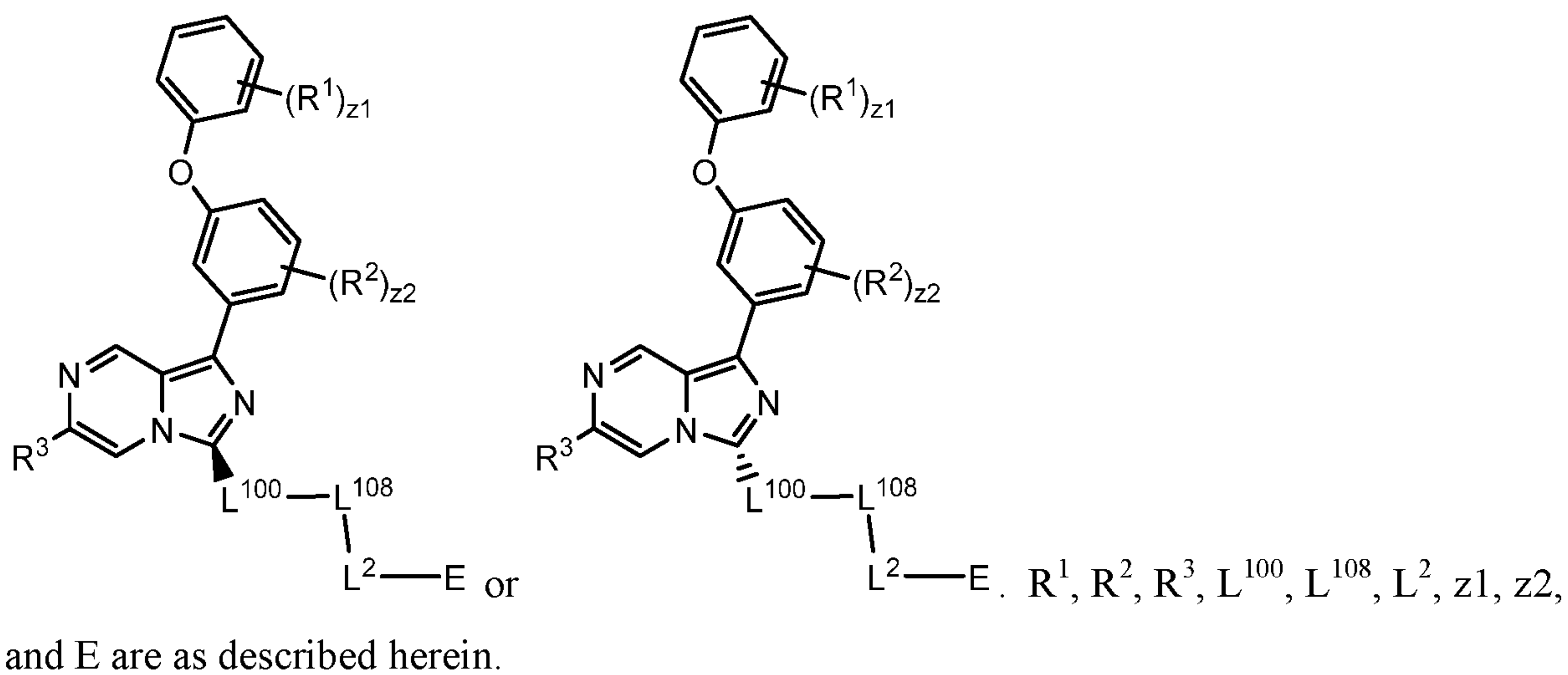
[0549] In embodiments, the compound has the formula



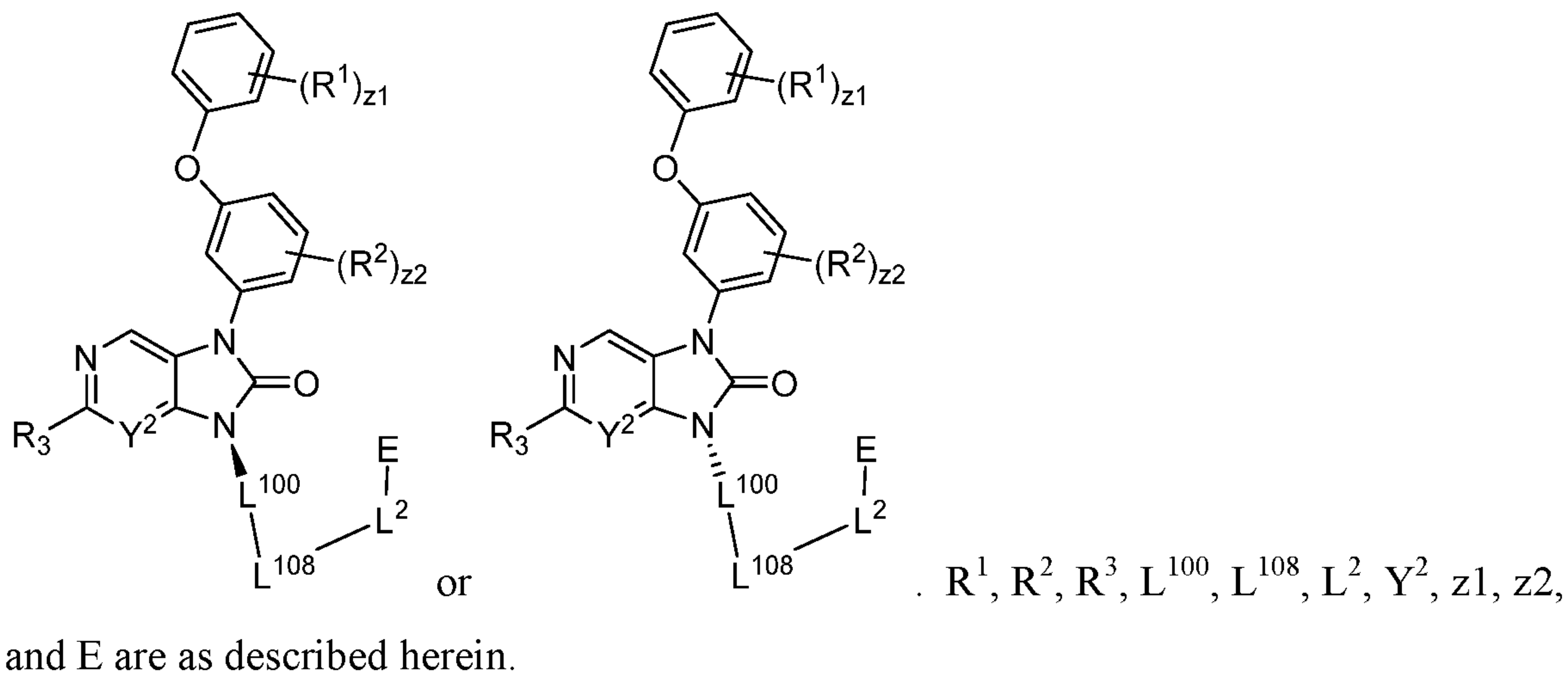
[0550] In embodiments, the compound has the formula



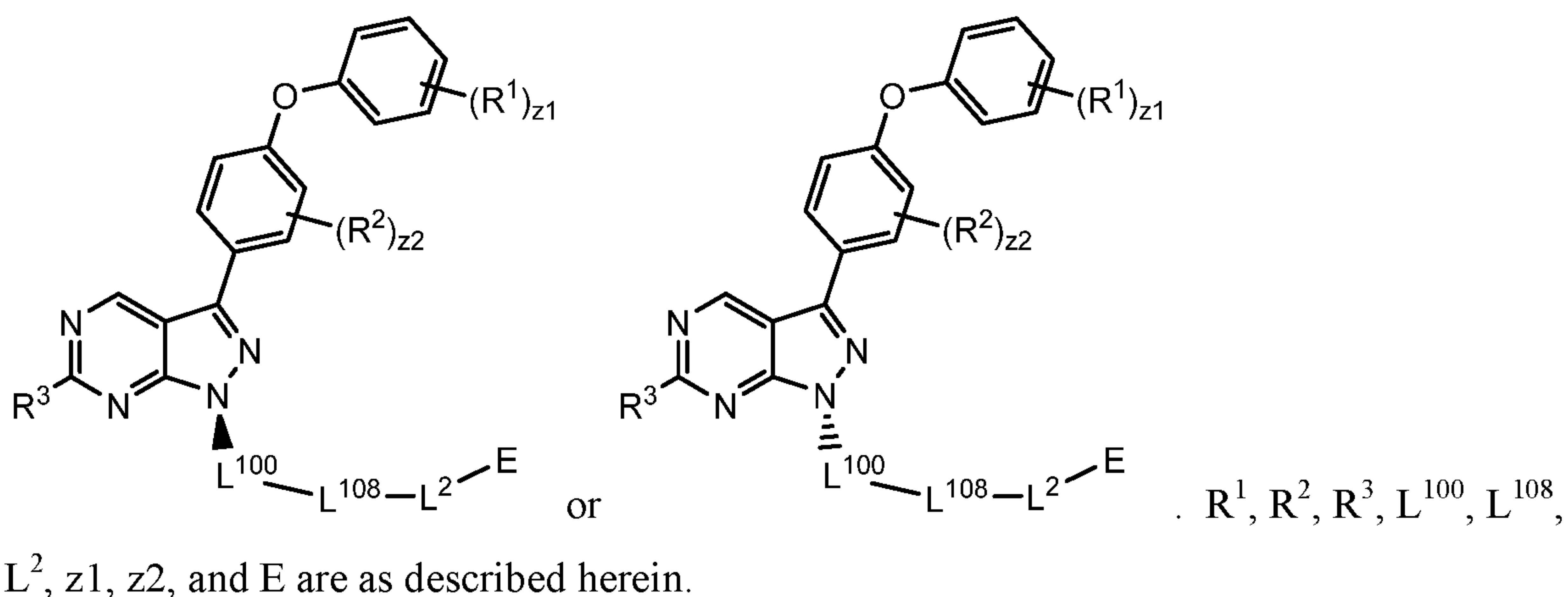
[0551] In embodiments, the compound has the formula



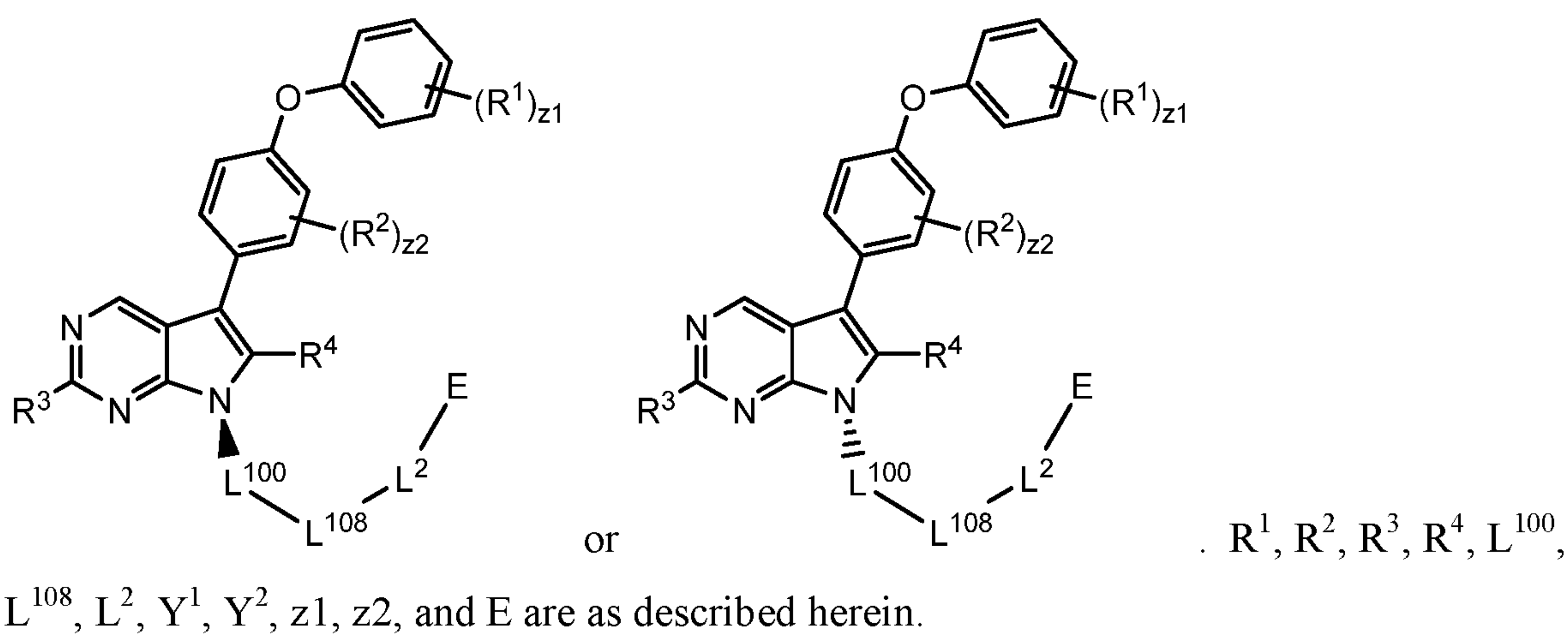
[0552] In embodiments, the compound has the formula



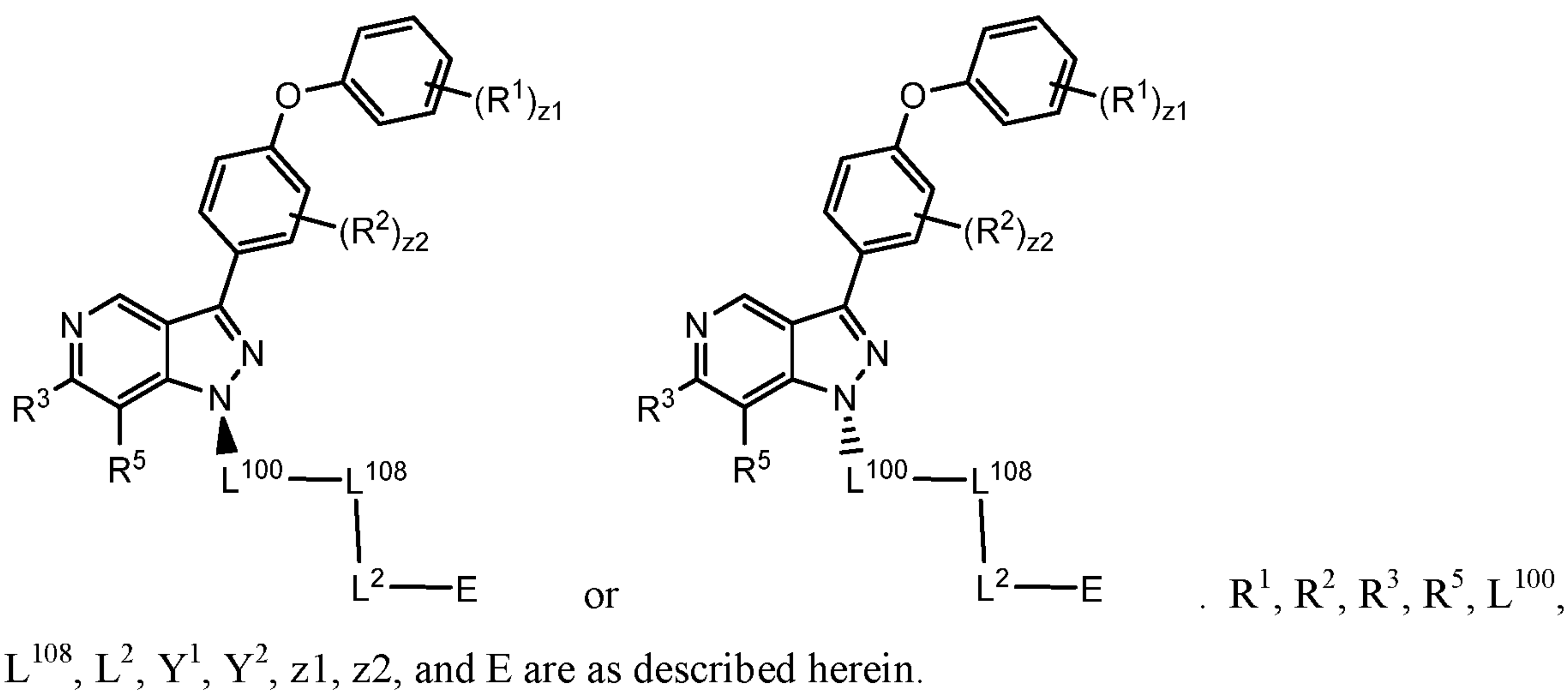
[0553] In embodiments, the compound has the formula



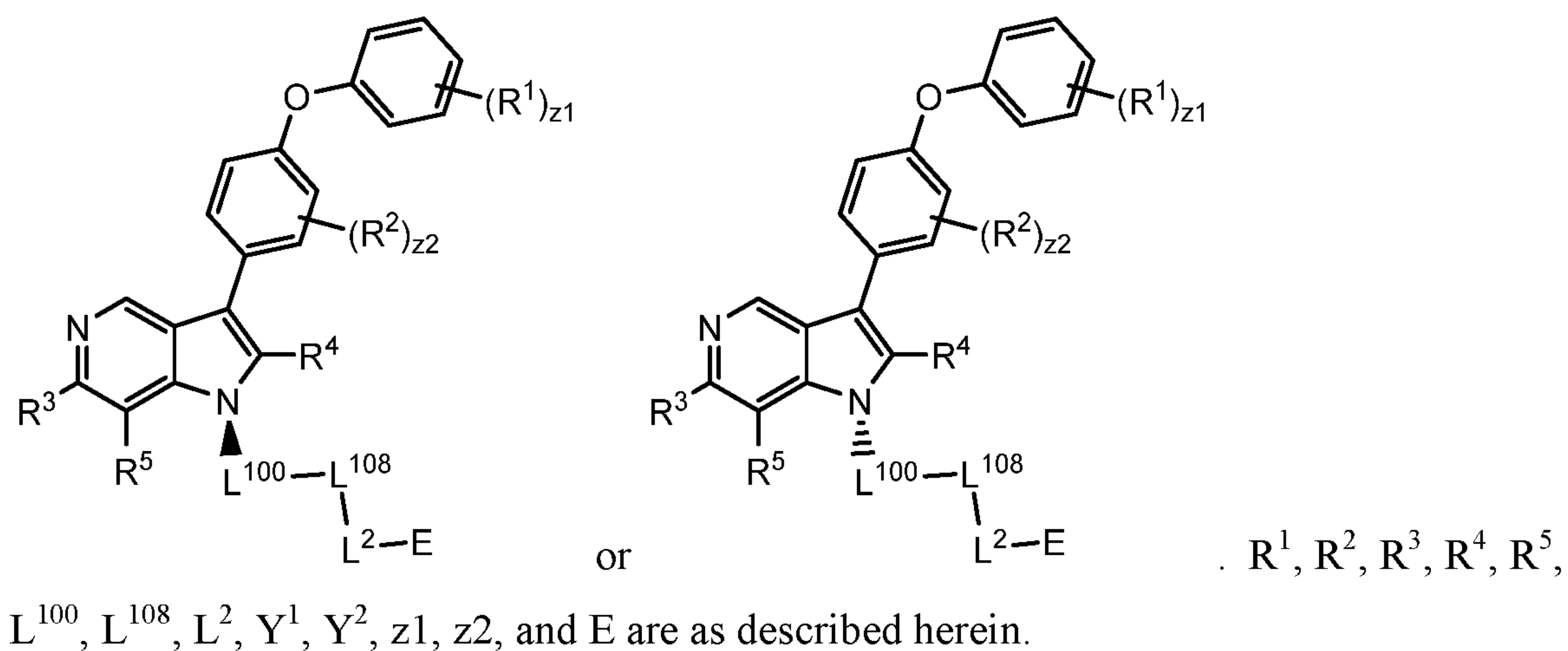
[0554] In embodiments, the compound has the formula



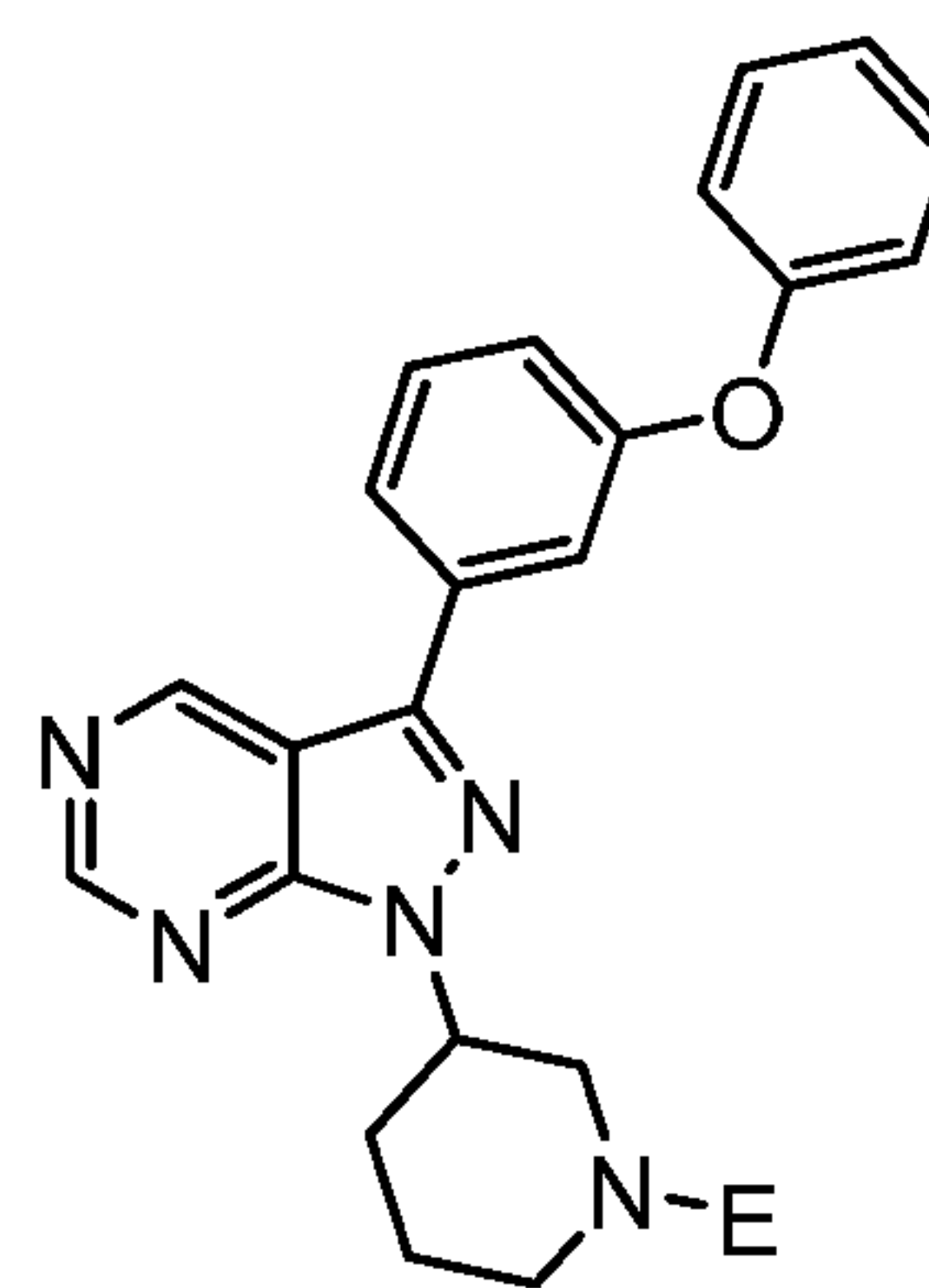
[0555] In embodiments, the compound has the formula



[0556] In embodiments, the compound has the formula

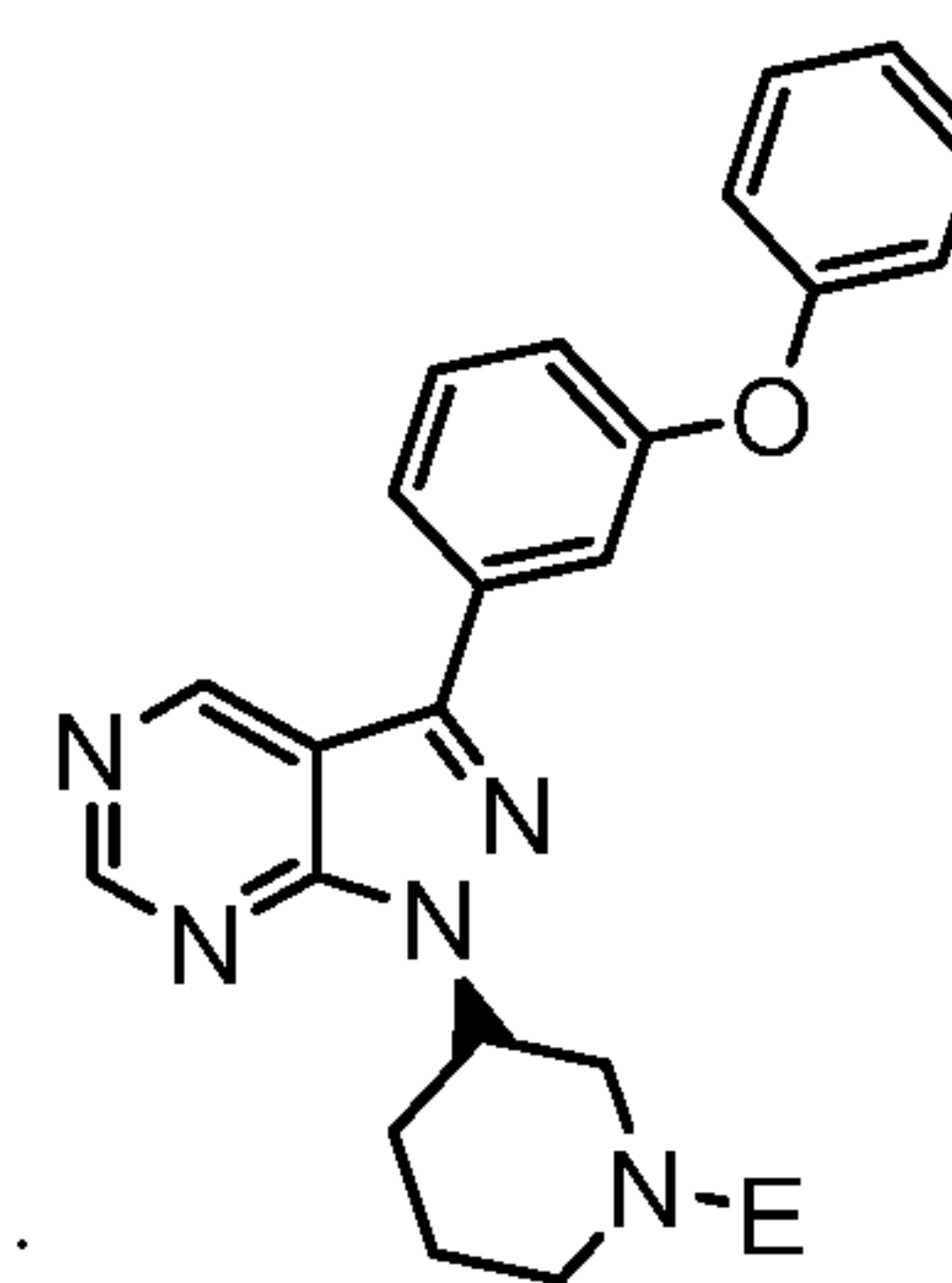


[0557] In embodiments, the compound has the formula:



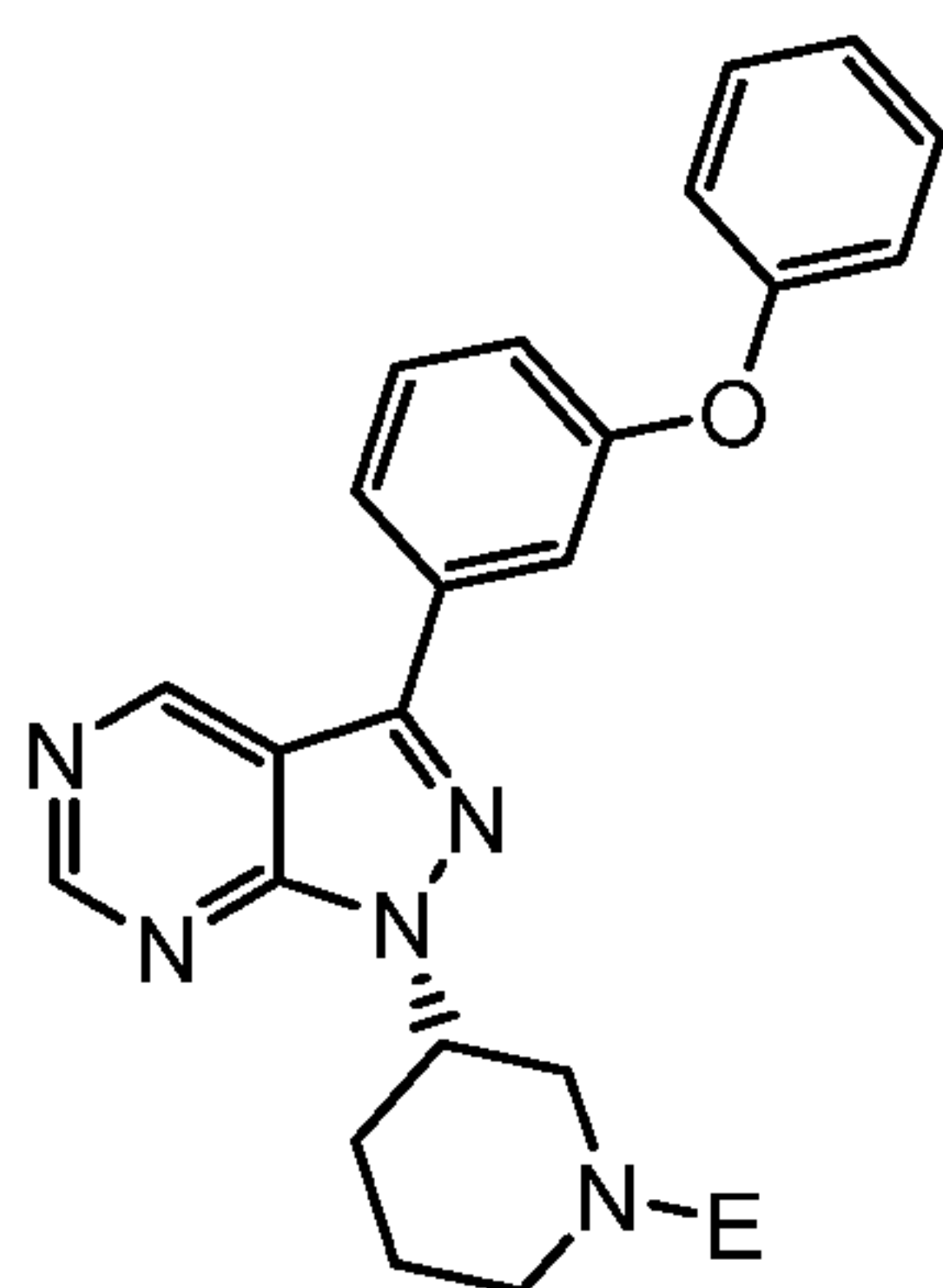
, wherein E is

as described herein. In embodiments, the compound has the formula:

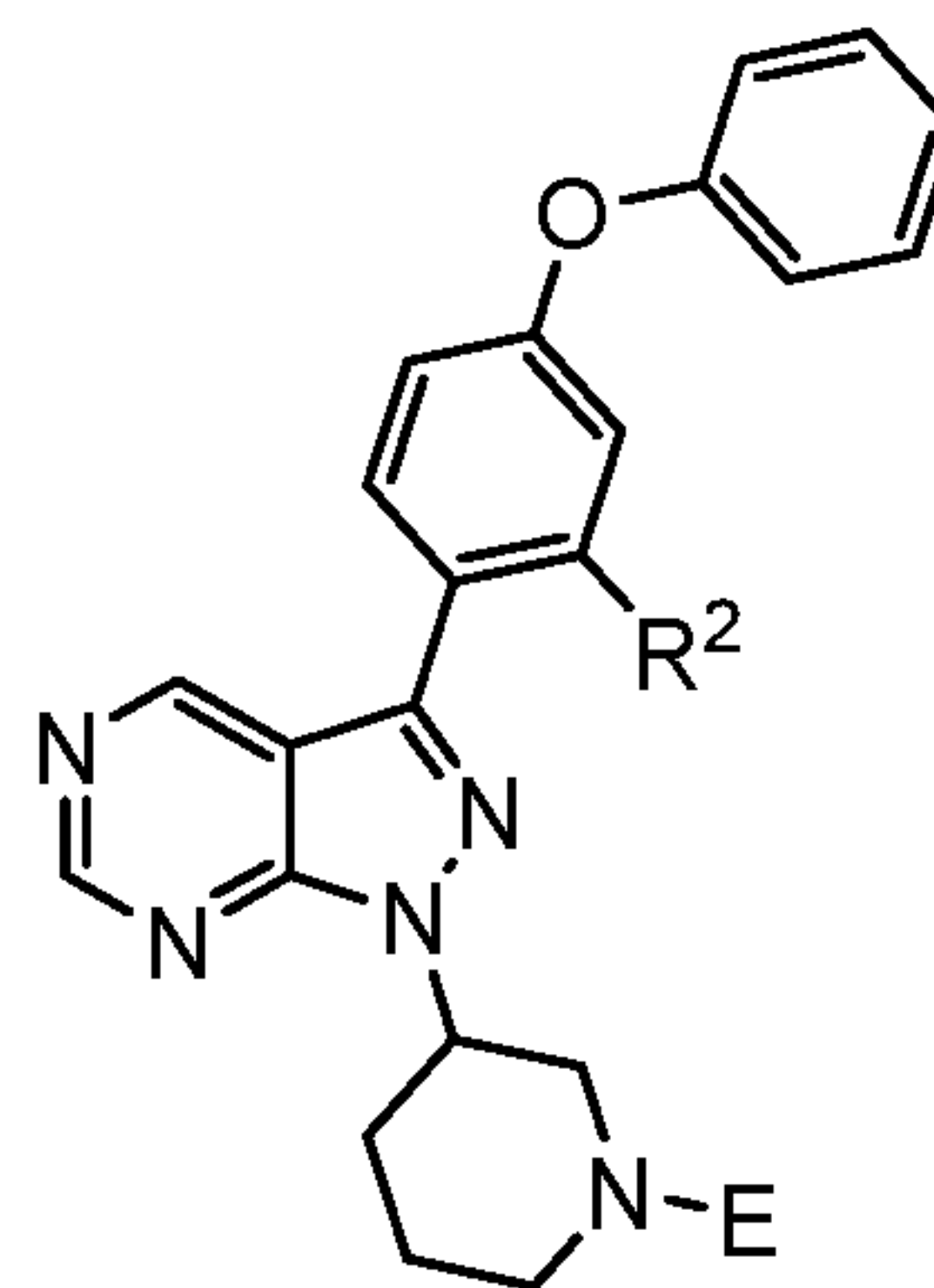


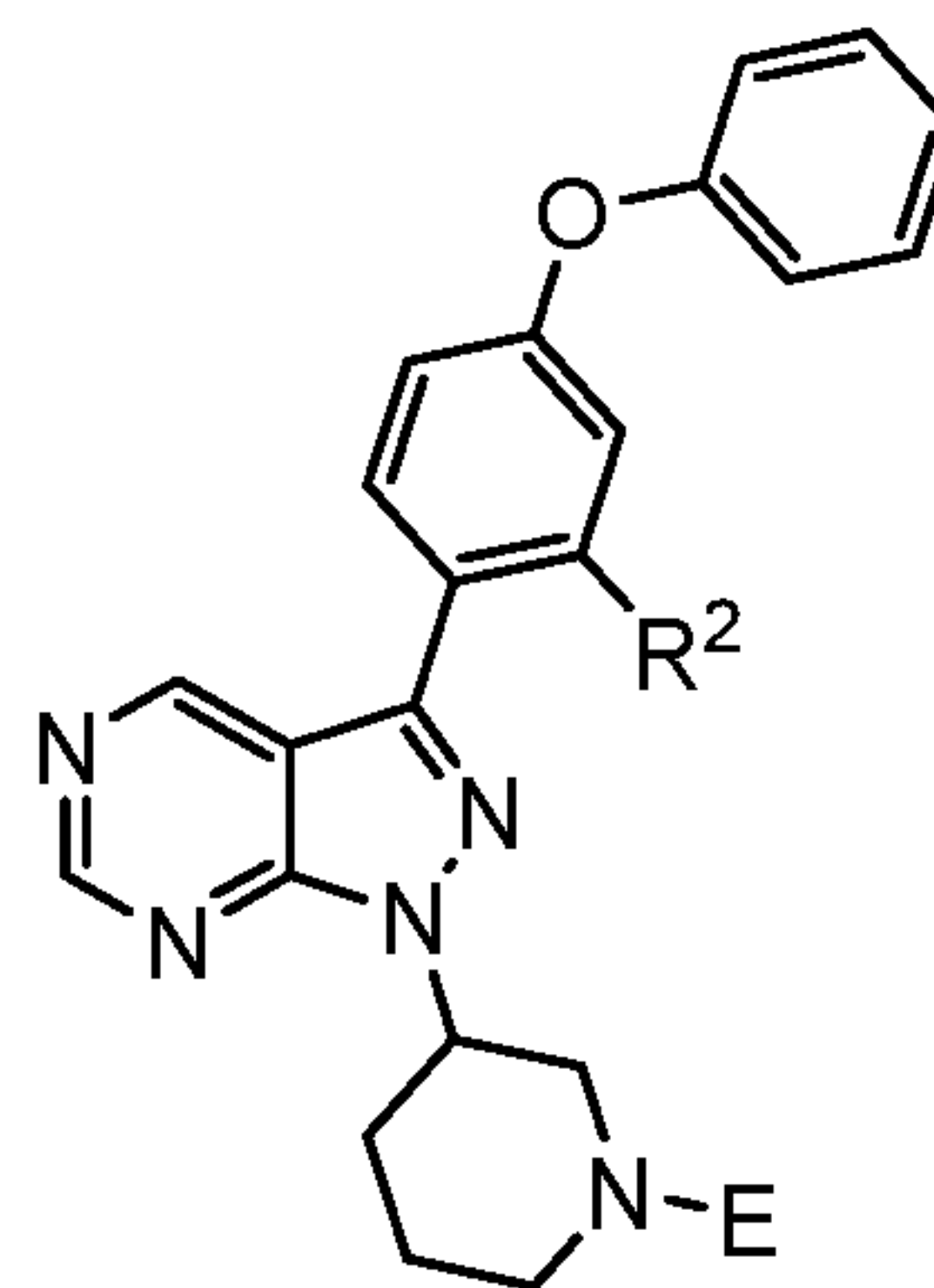
,

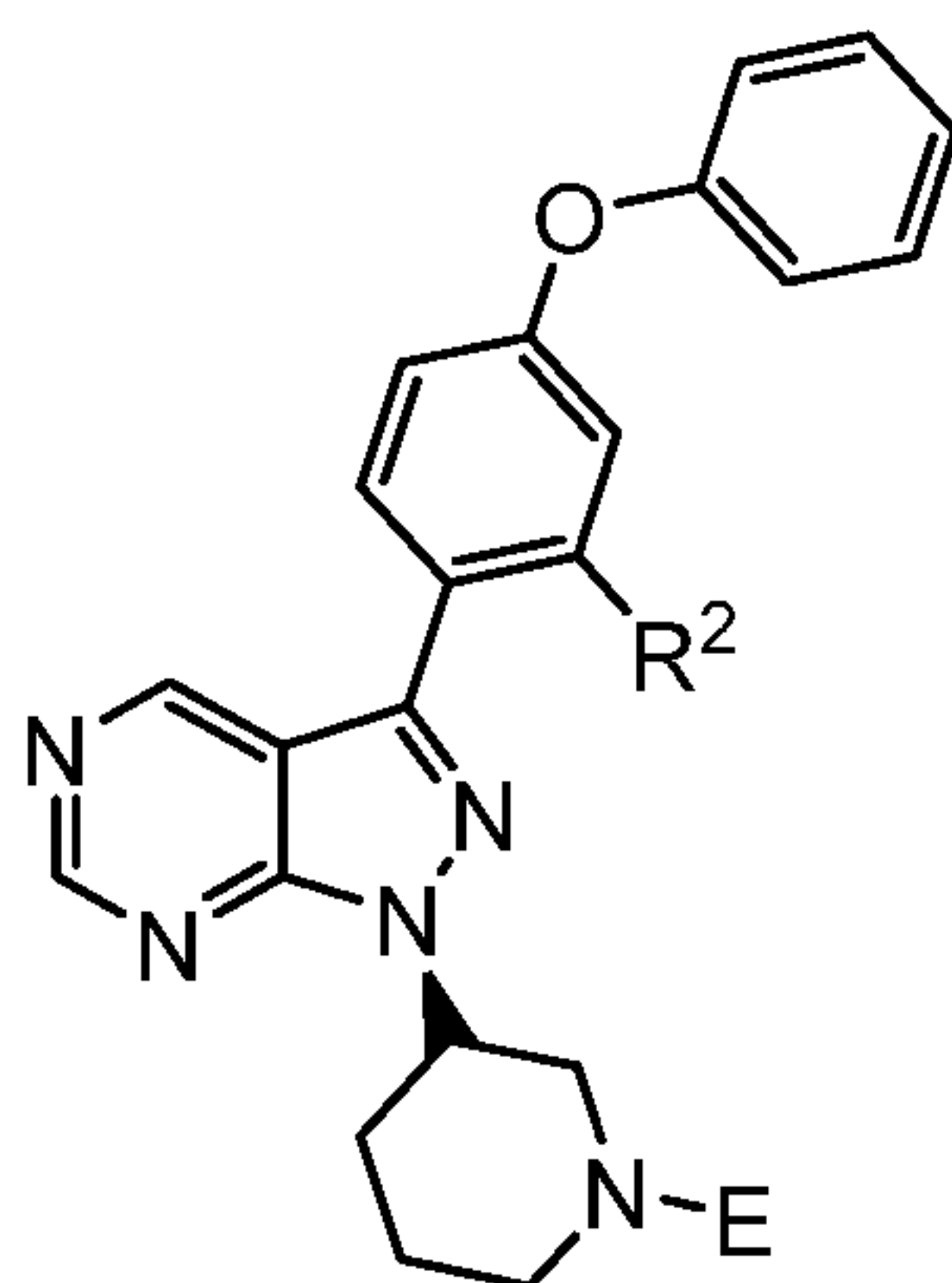
5 wherein E is as described herein. In embodiments, the compound has the formula:



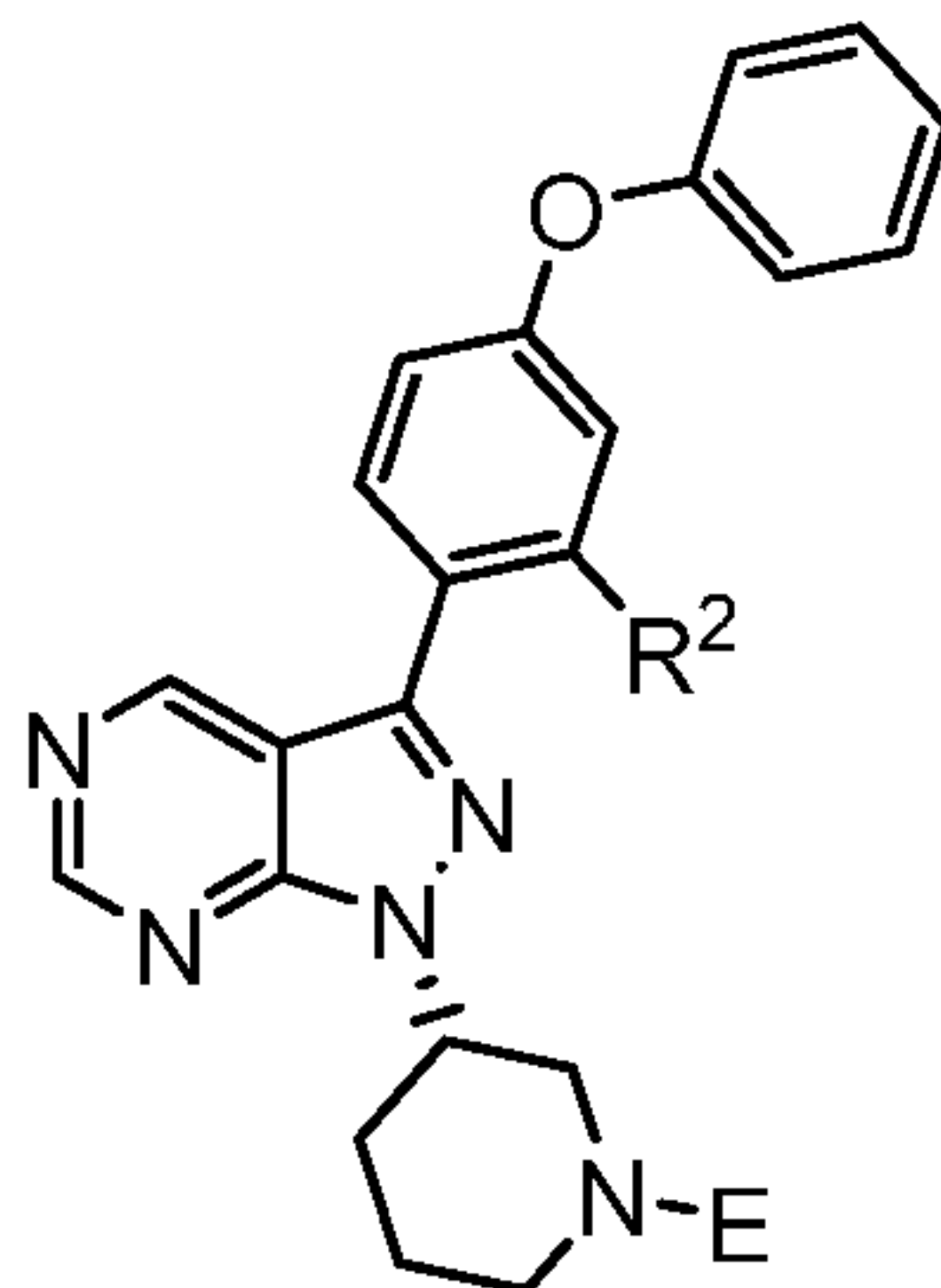
, wherein E is as described herein.

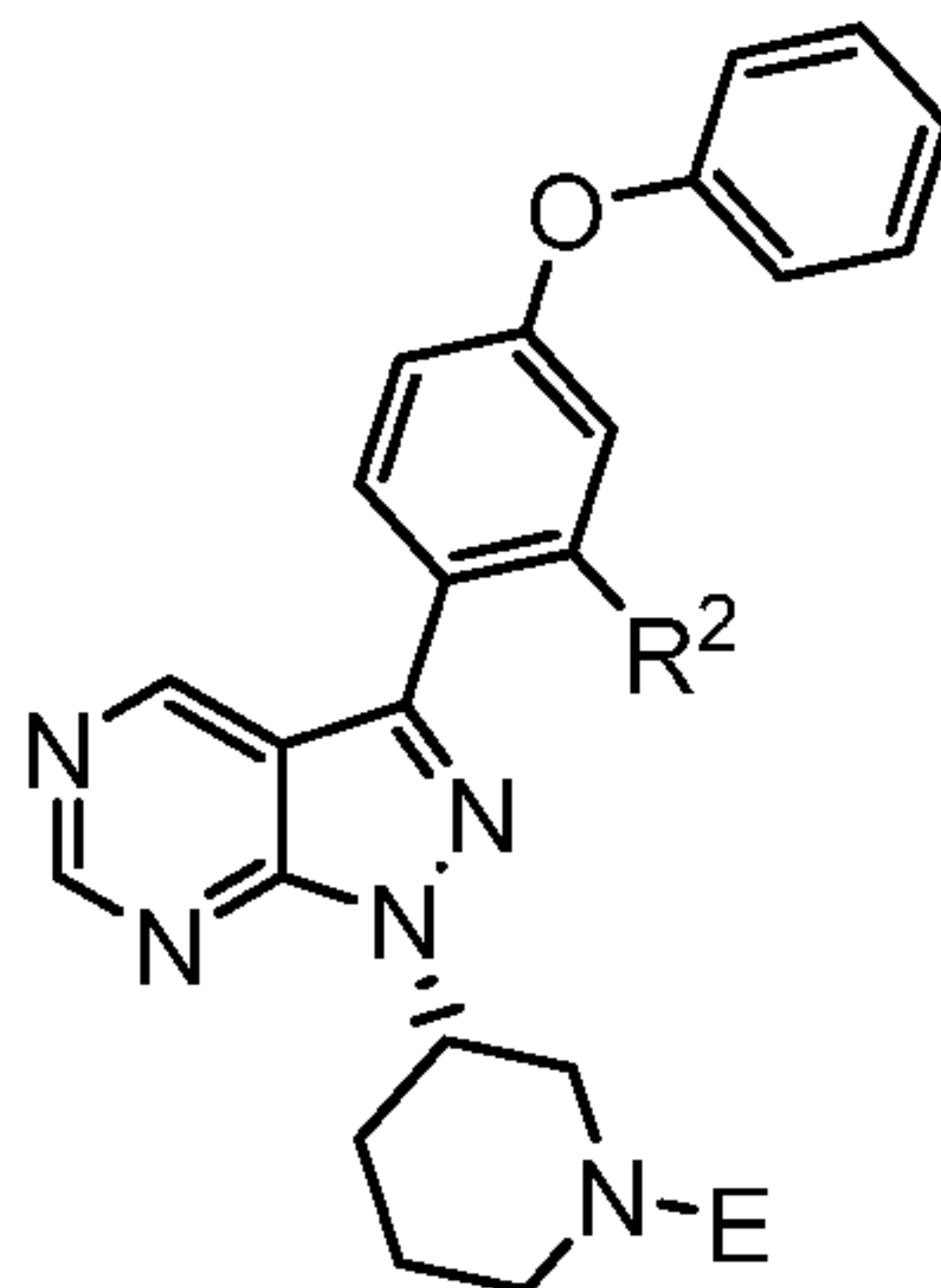


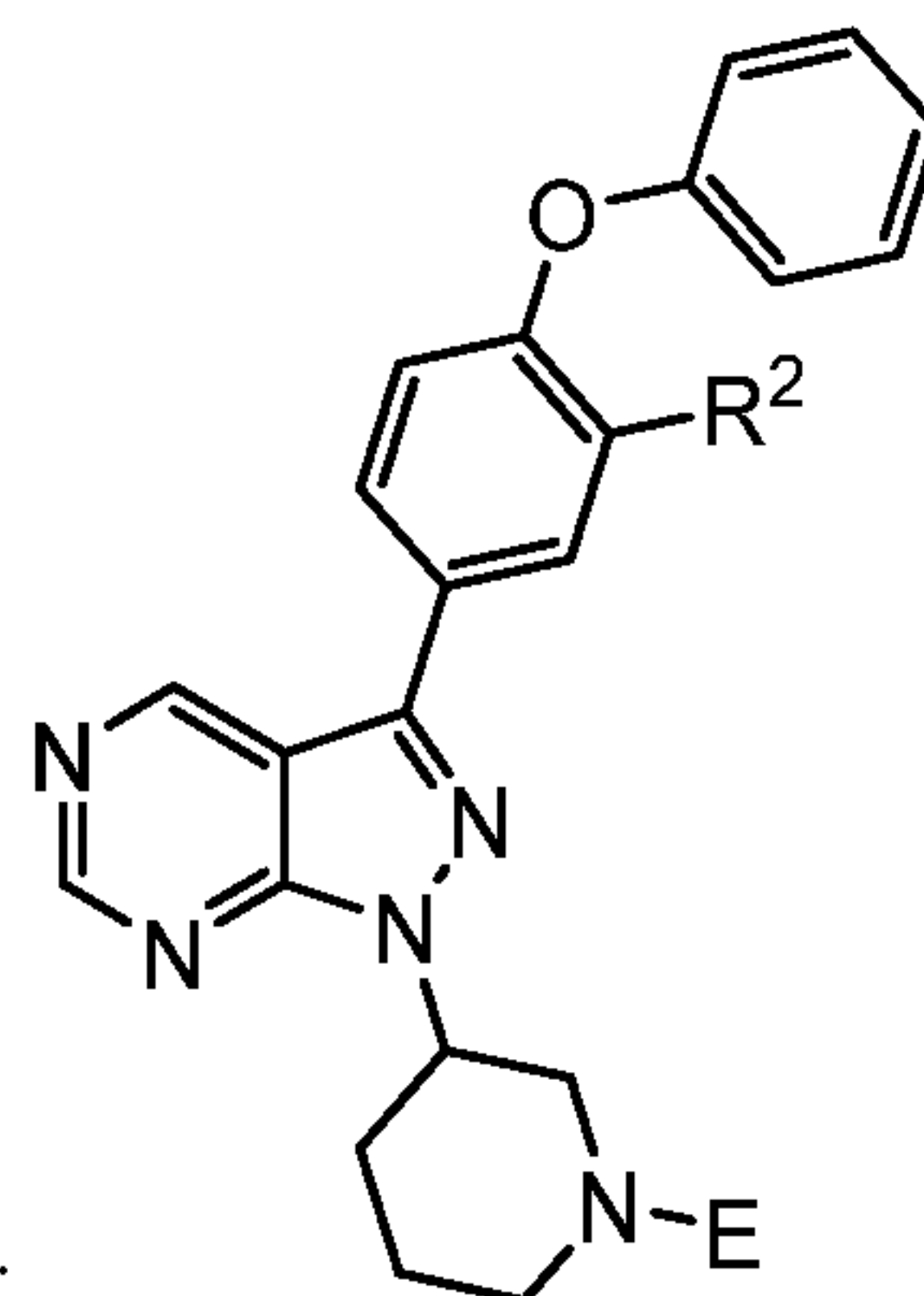
[0558] In embodiments, the compound has the formula: , wherein R² and E are as described herein. In embodiments, the compound has the formula:

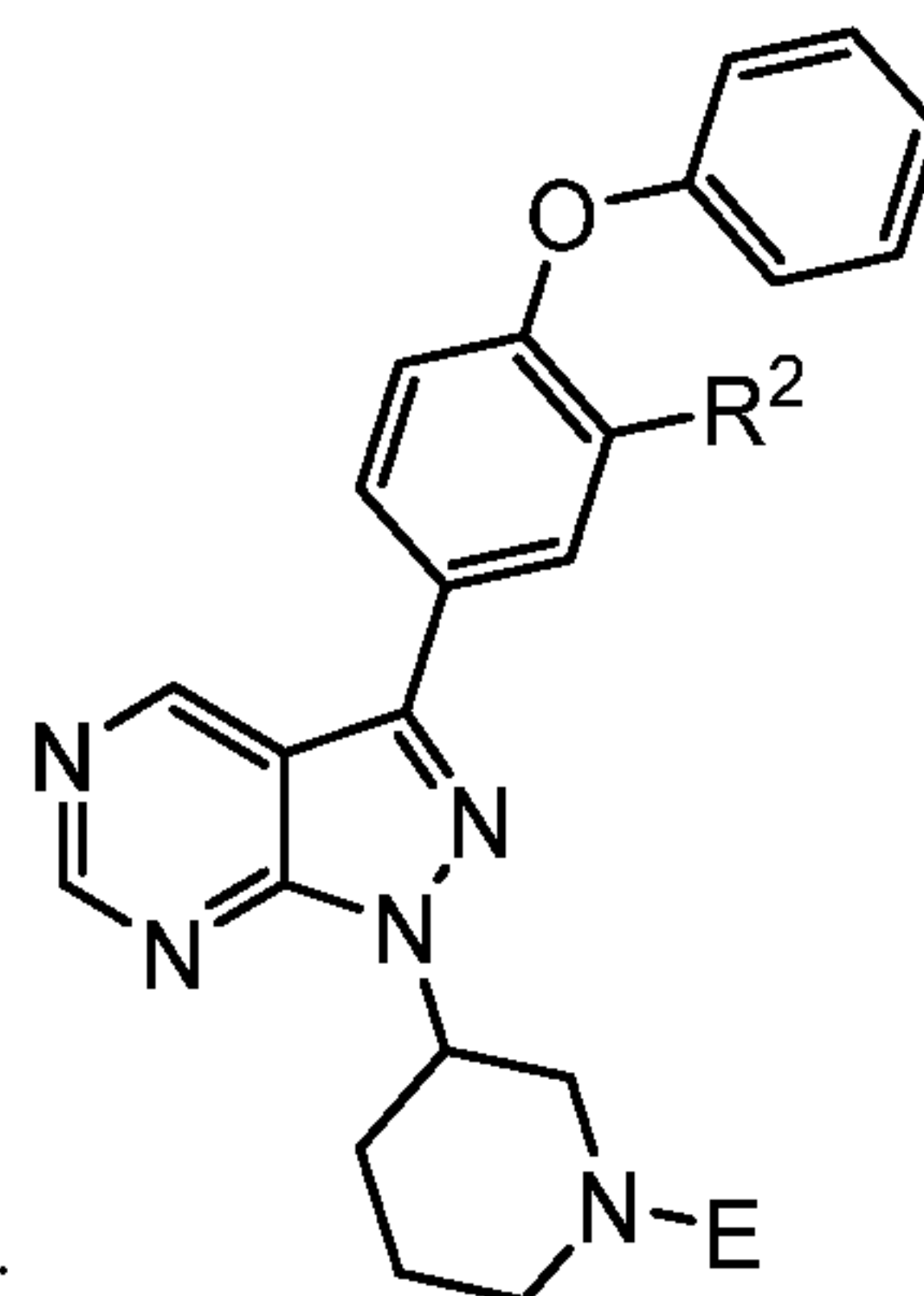


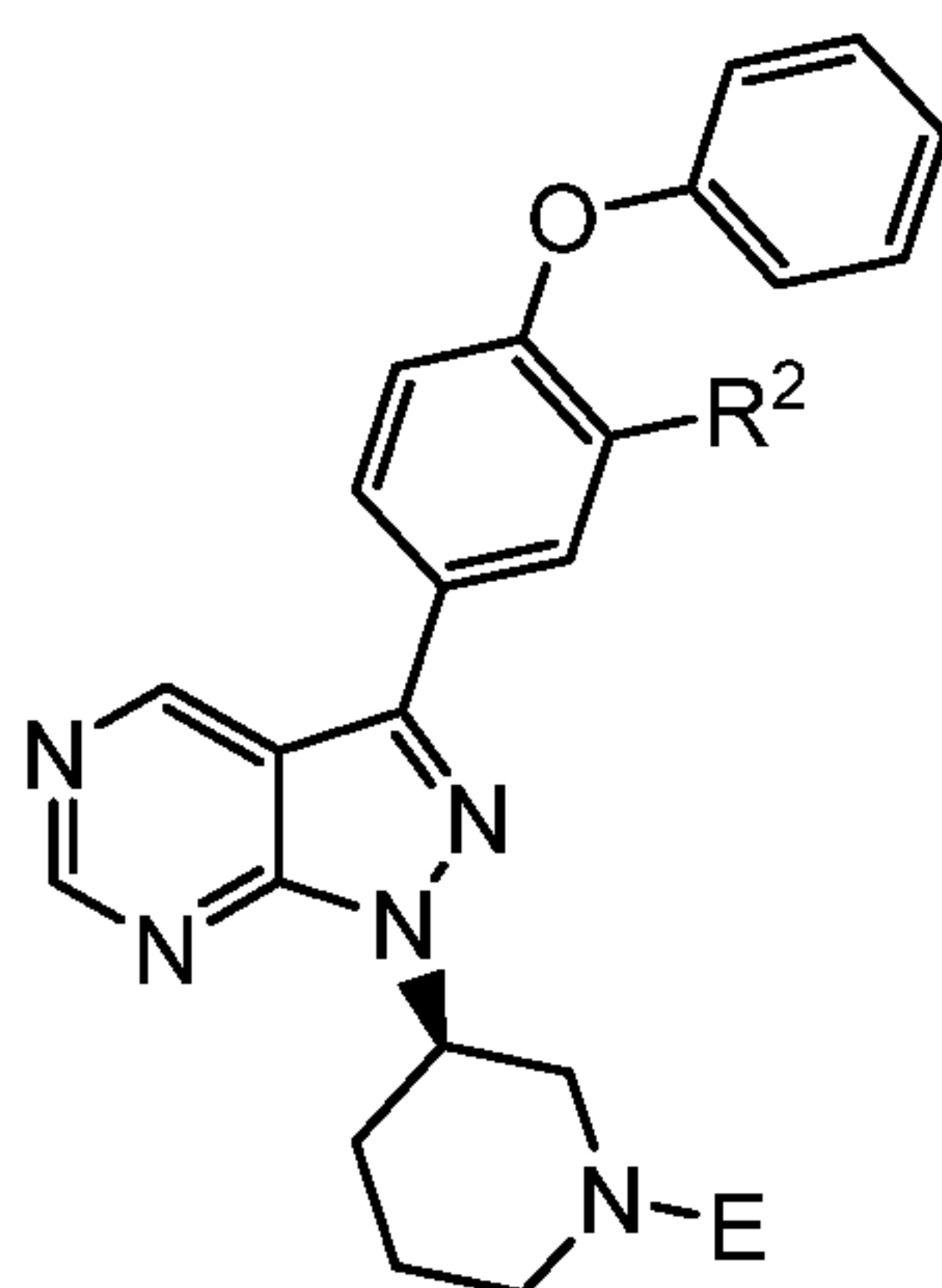
, wherein R² and E are as described herein. In embodiments, the



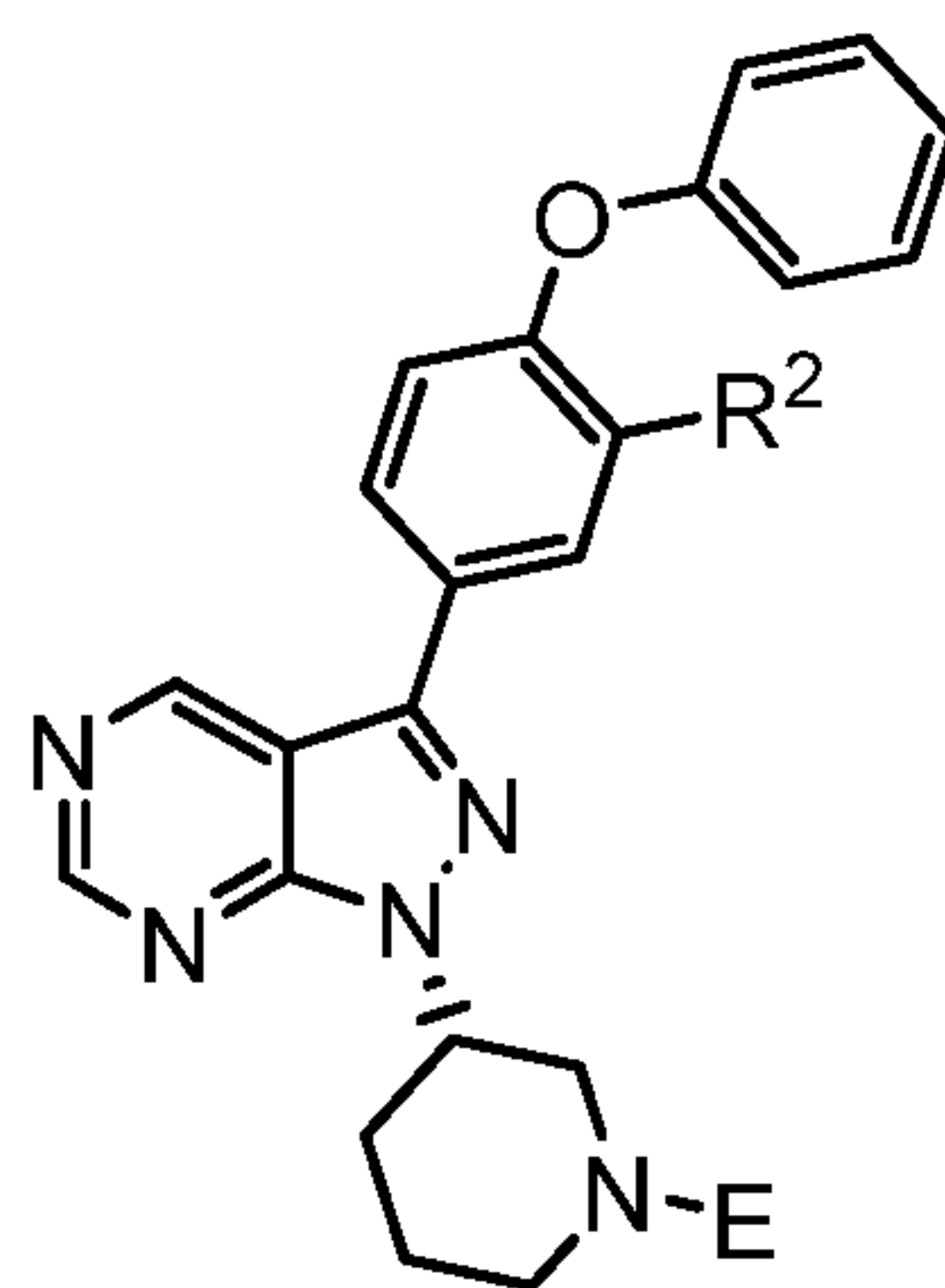
compound has the formula: , wherein R² and E are as described herein.



5 **[0559]** In embodiments, the compound has the formula: , wherein R² and E are as described herein. In embodiments, the compound has the formula:

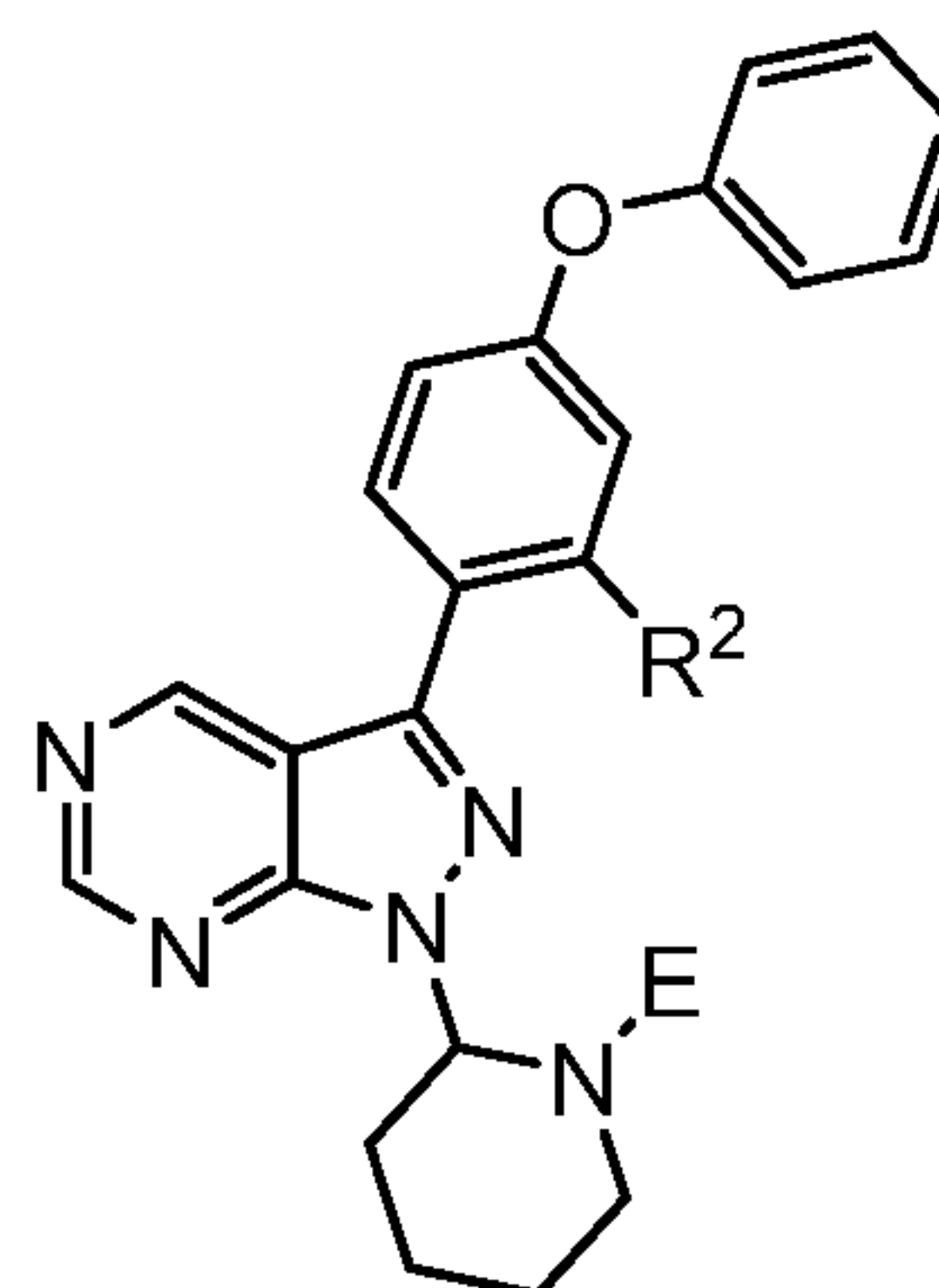


, wherein R^2 and E are as described herein. In embodiments, the



compound has the formula:

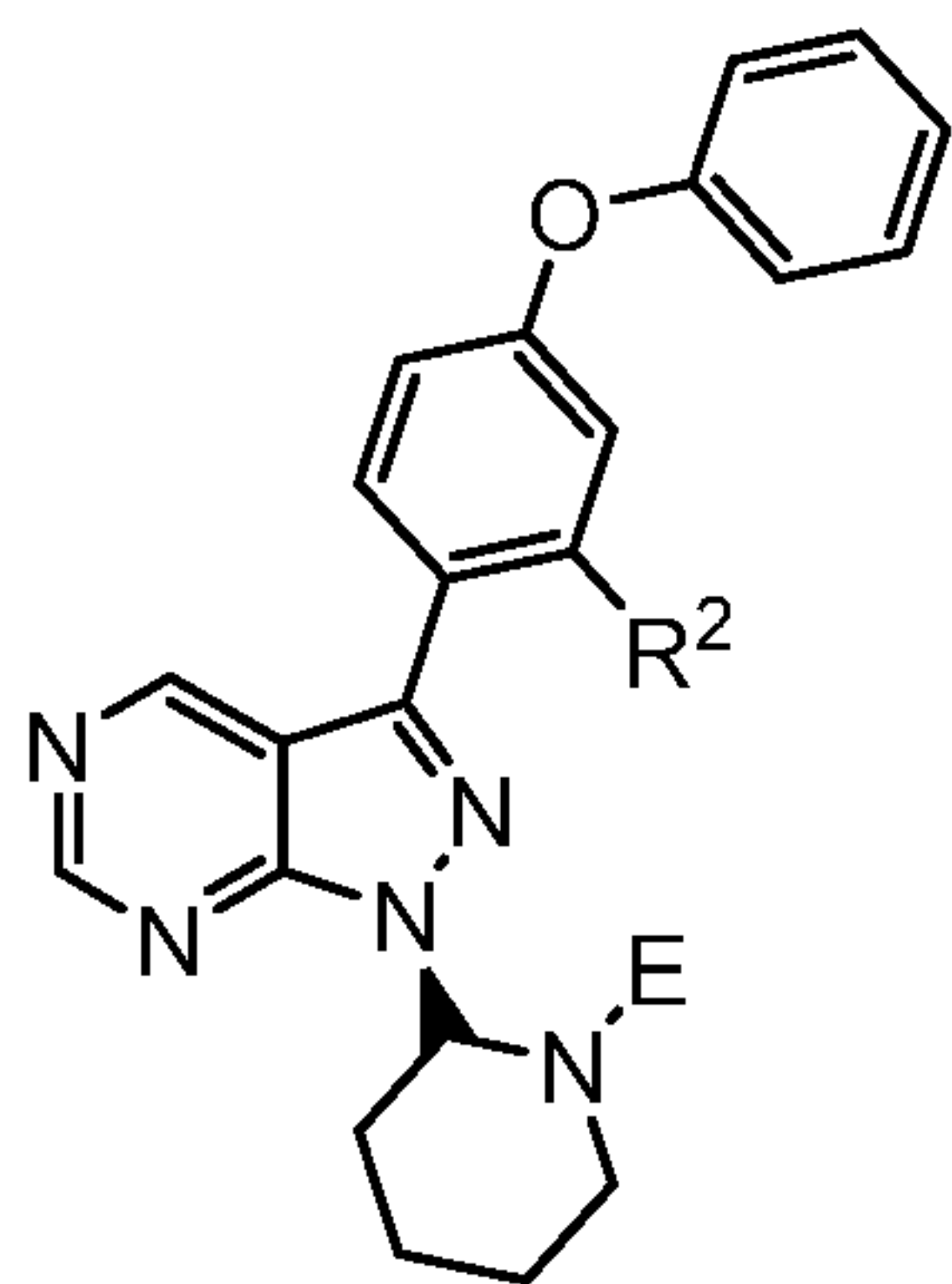
, wherein R^2 and E are as described herein.



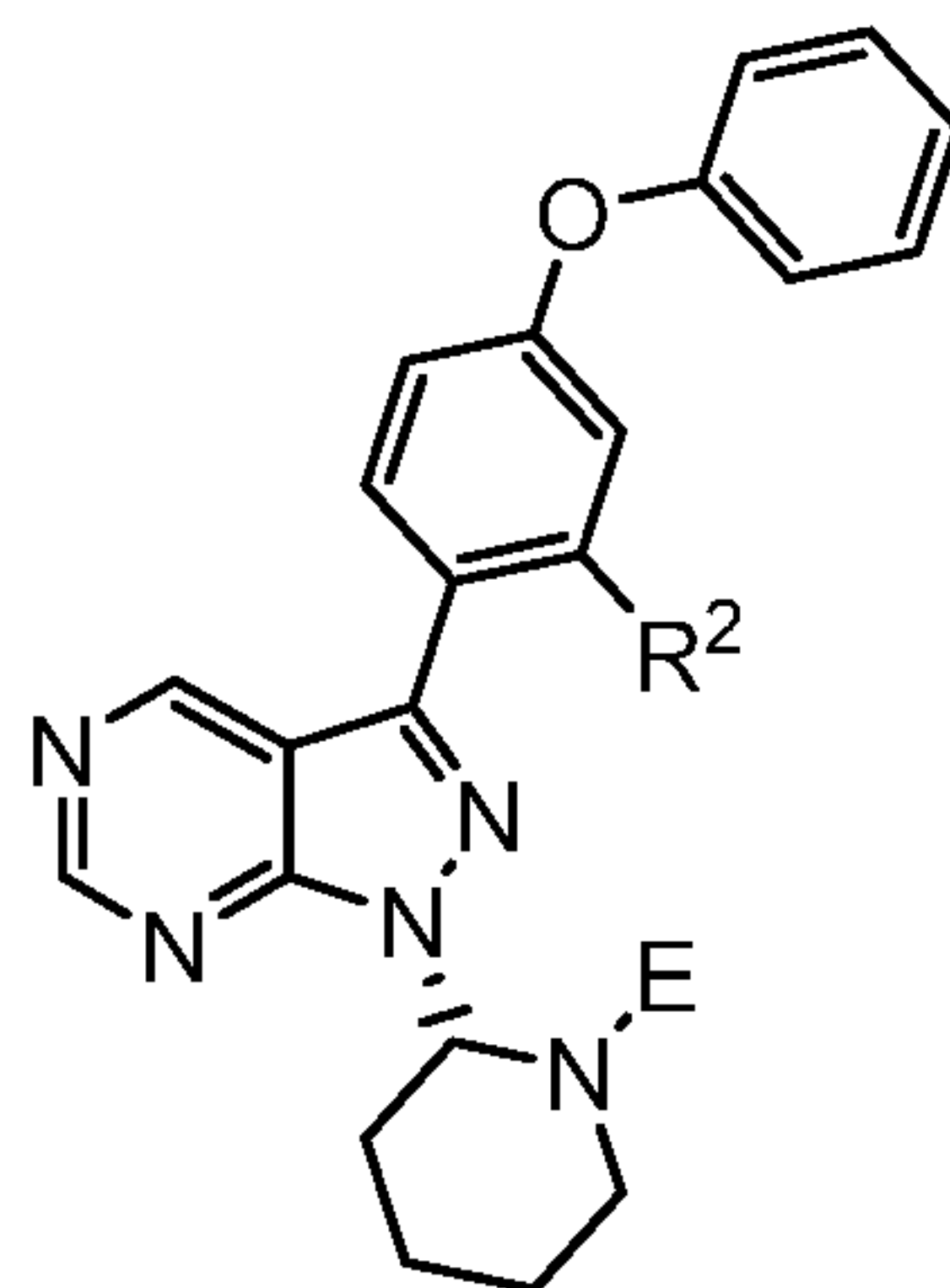
[0560] In embodiments, the compound has the formula:

, wherein R^2

and E are as described herein. In embodiments, the compound has the formula:

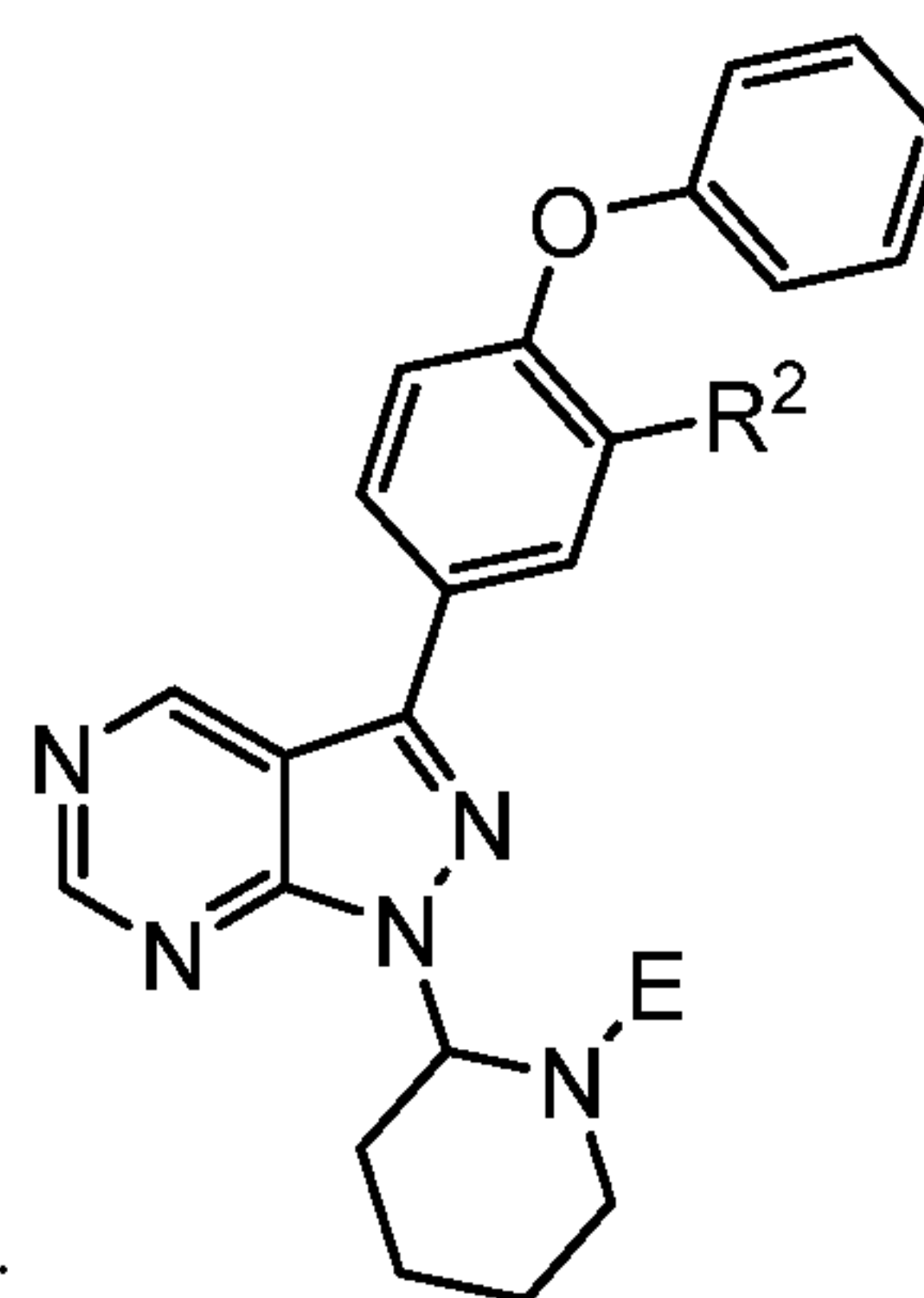


, wherein R^2 and E are as described herein. In embodiments, the



compound has the formula:

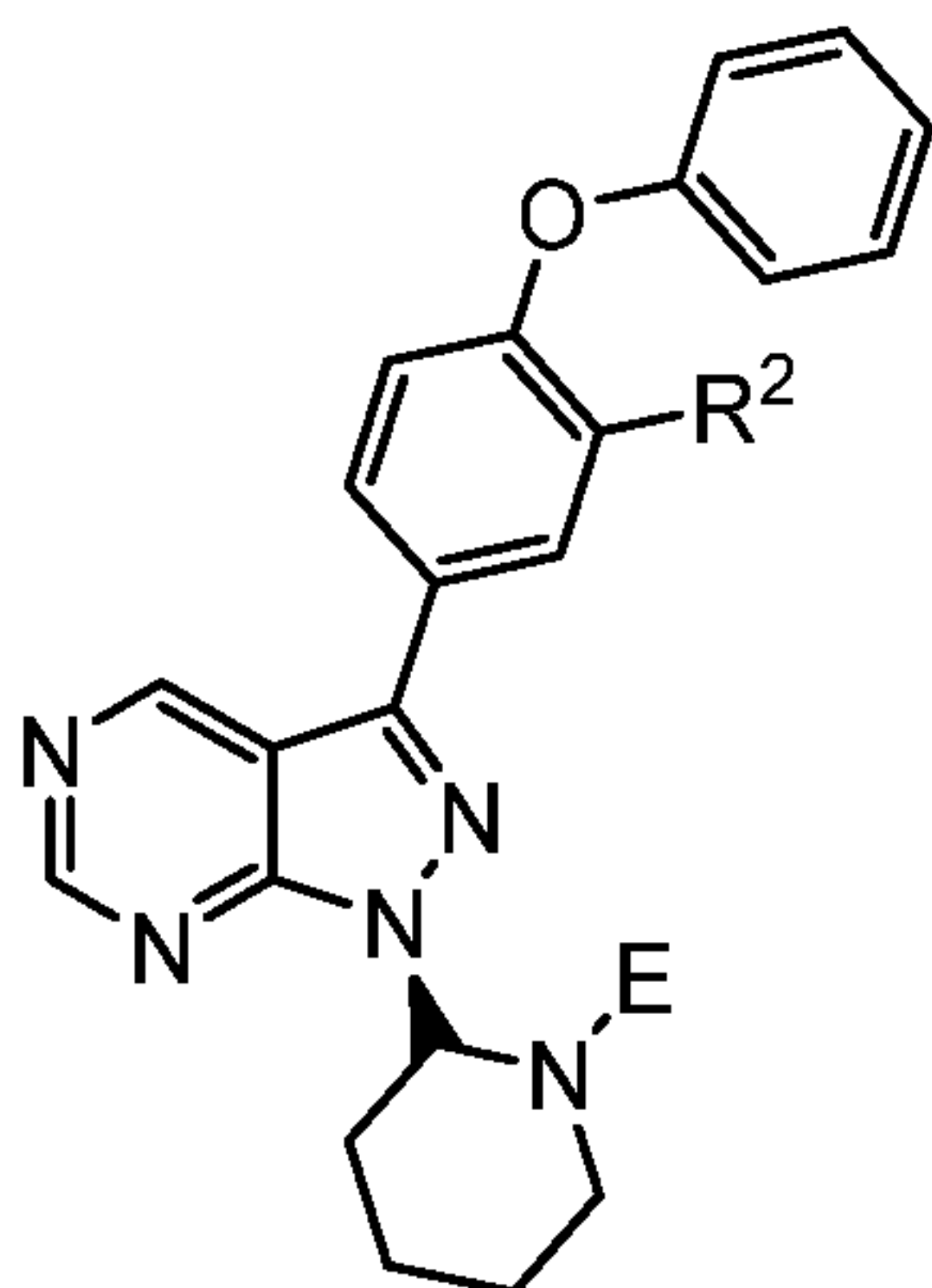
, wherein R^2 and E are as described herein.



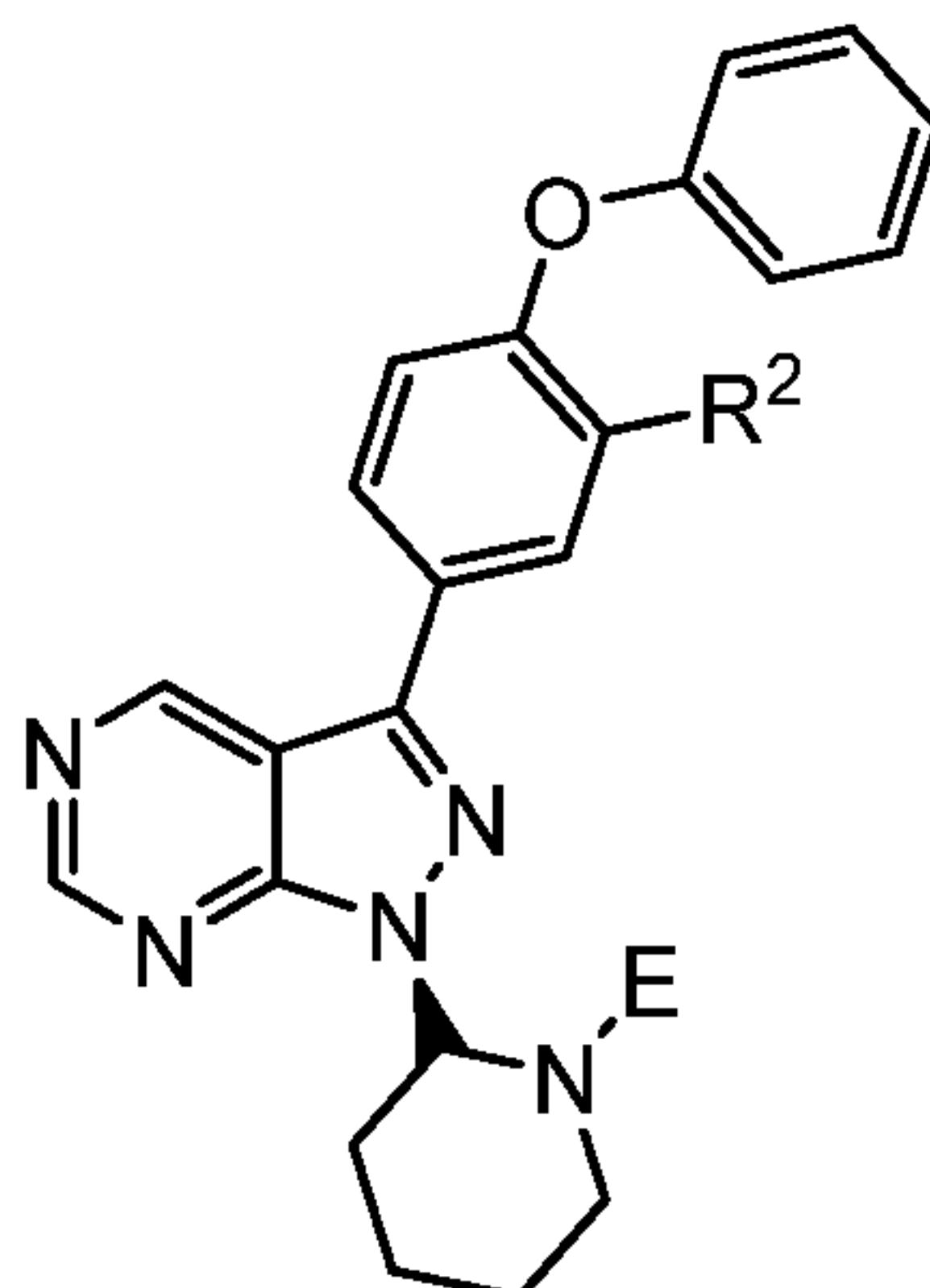
[0561] In embodiments, the compound has the formula:

, wherein R^2

and E are as described herein. In embodiments, the compound has the formula:

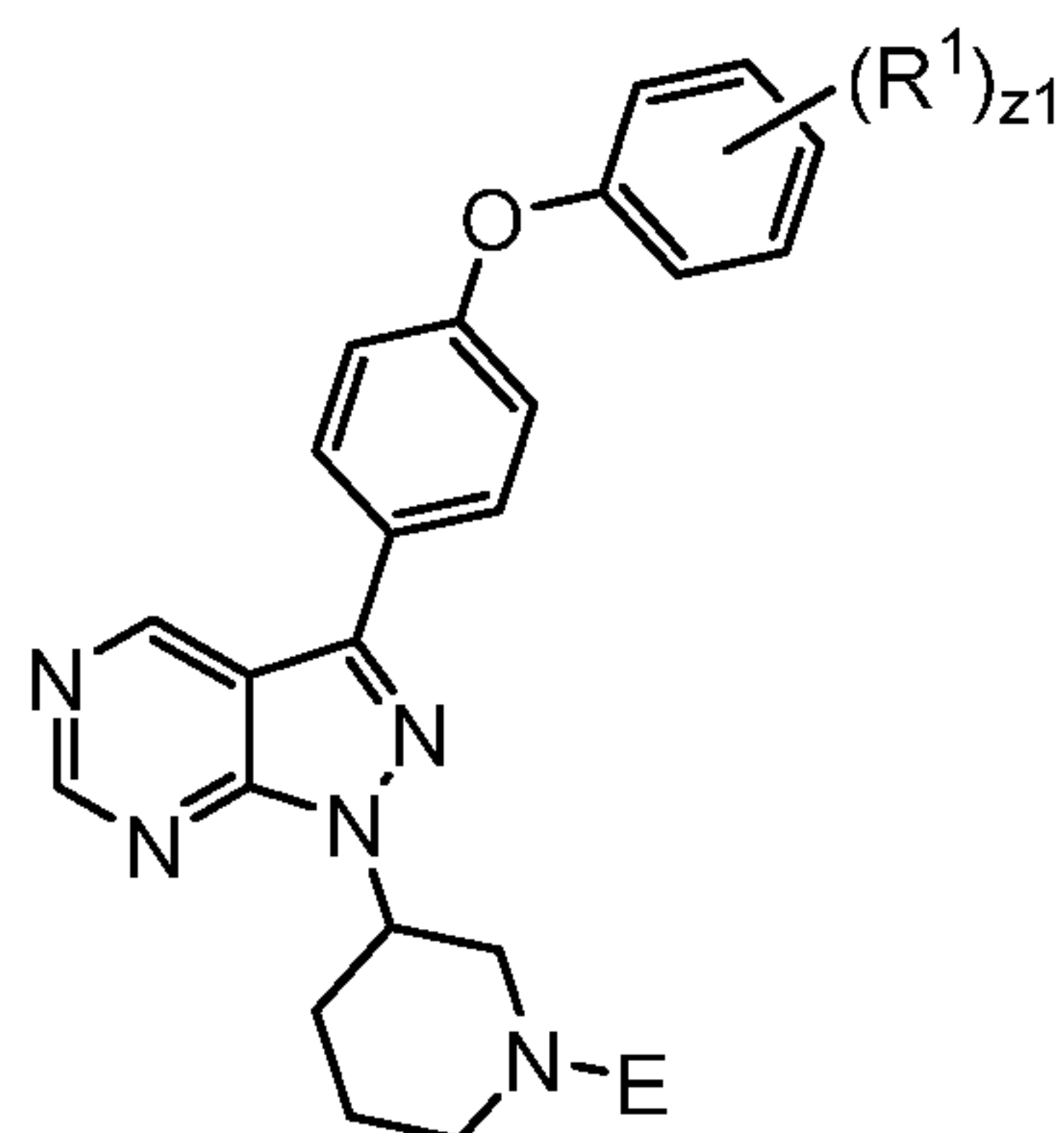


, wherein R^2 and E are as described herein. In embodiments, the



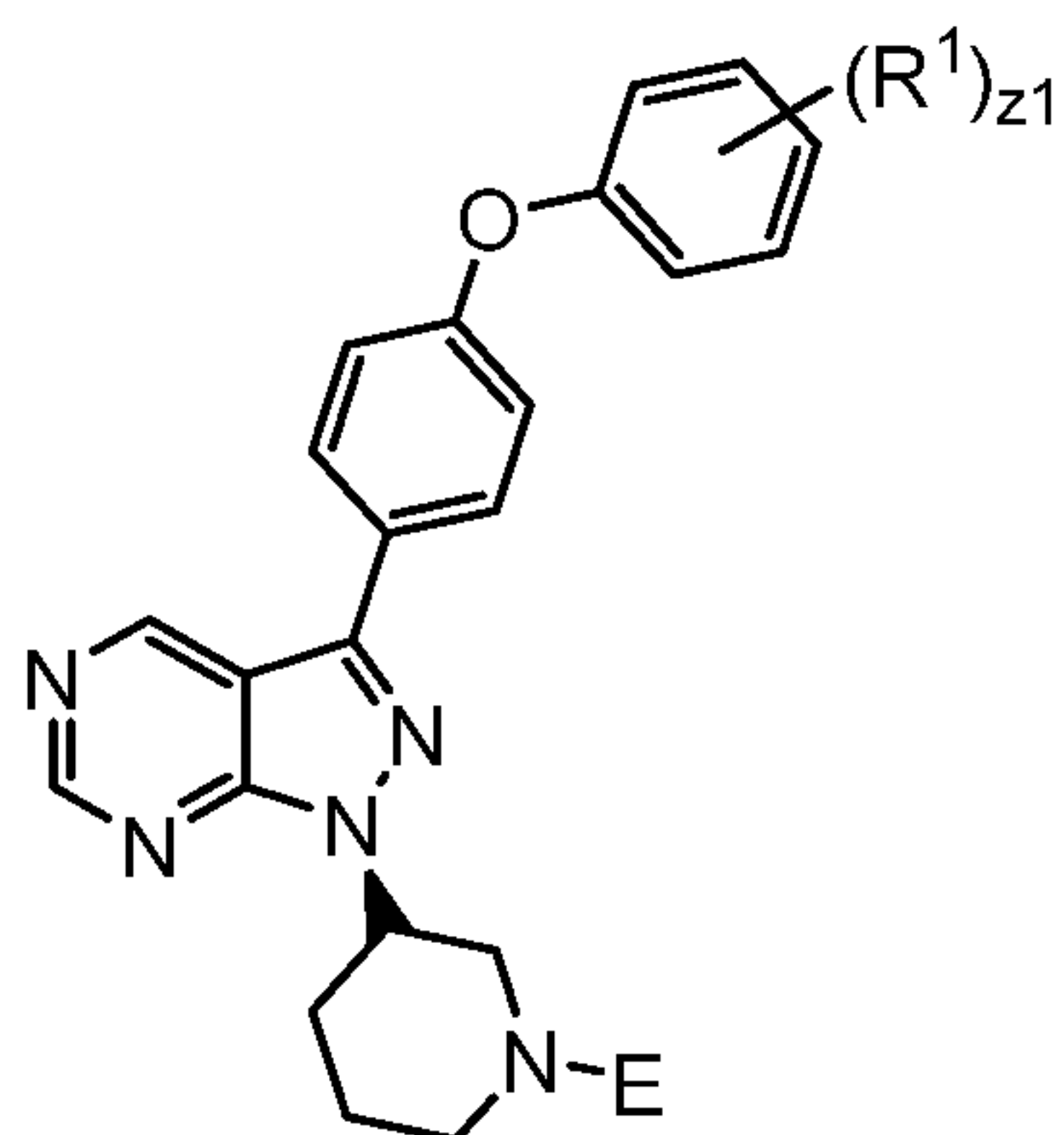
compound has the formula:

, wherein R^2 and E are as described herein.



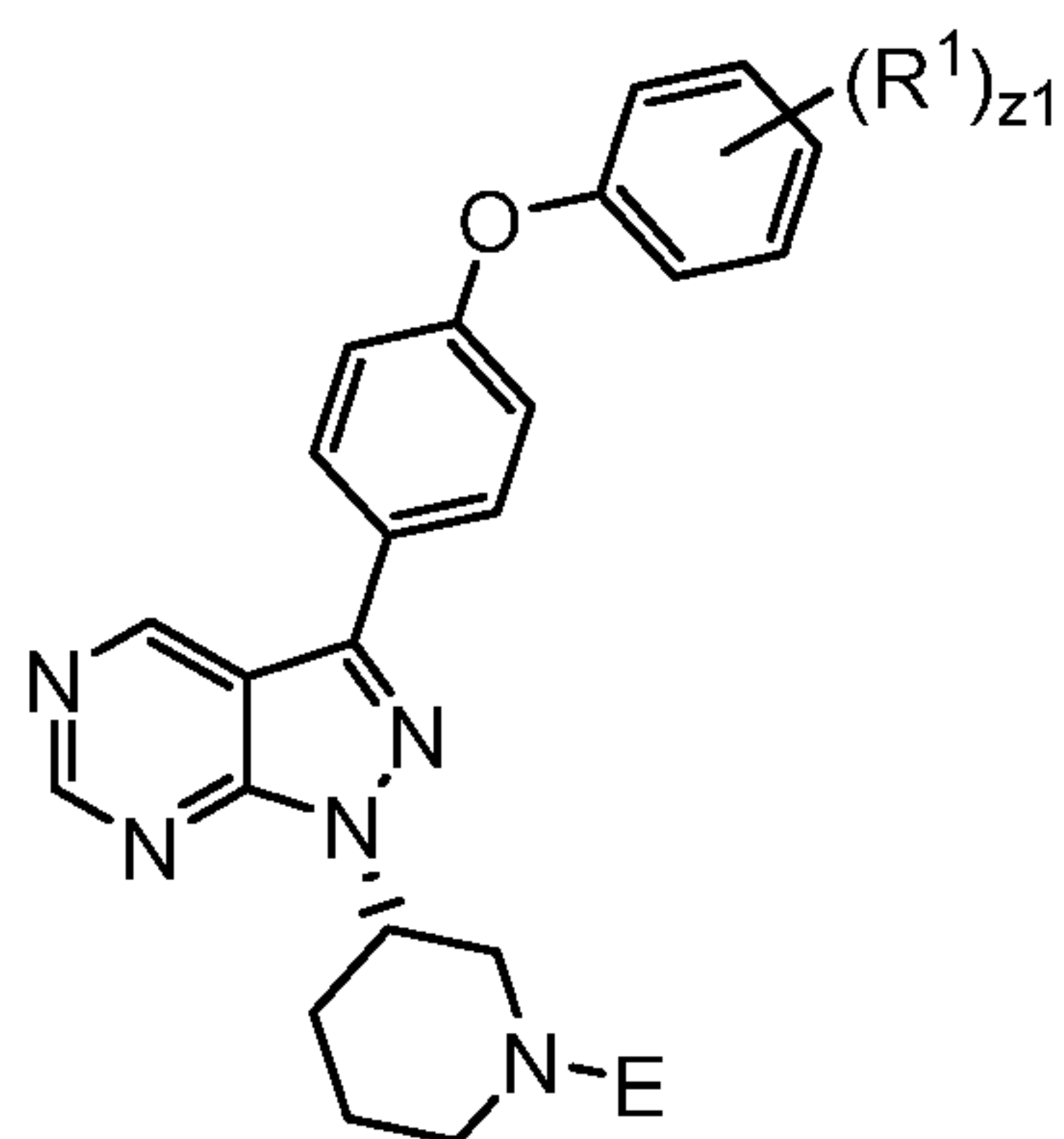
[0562] In embodiments, the compound has the formula:

wherein R^1 , $z1$, and E are as described herein. In embodiments, the compound has the

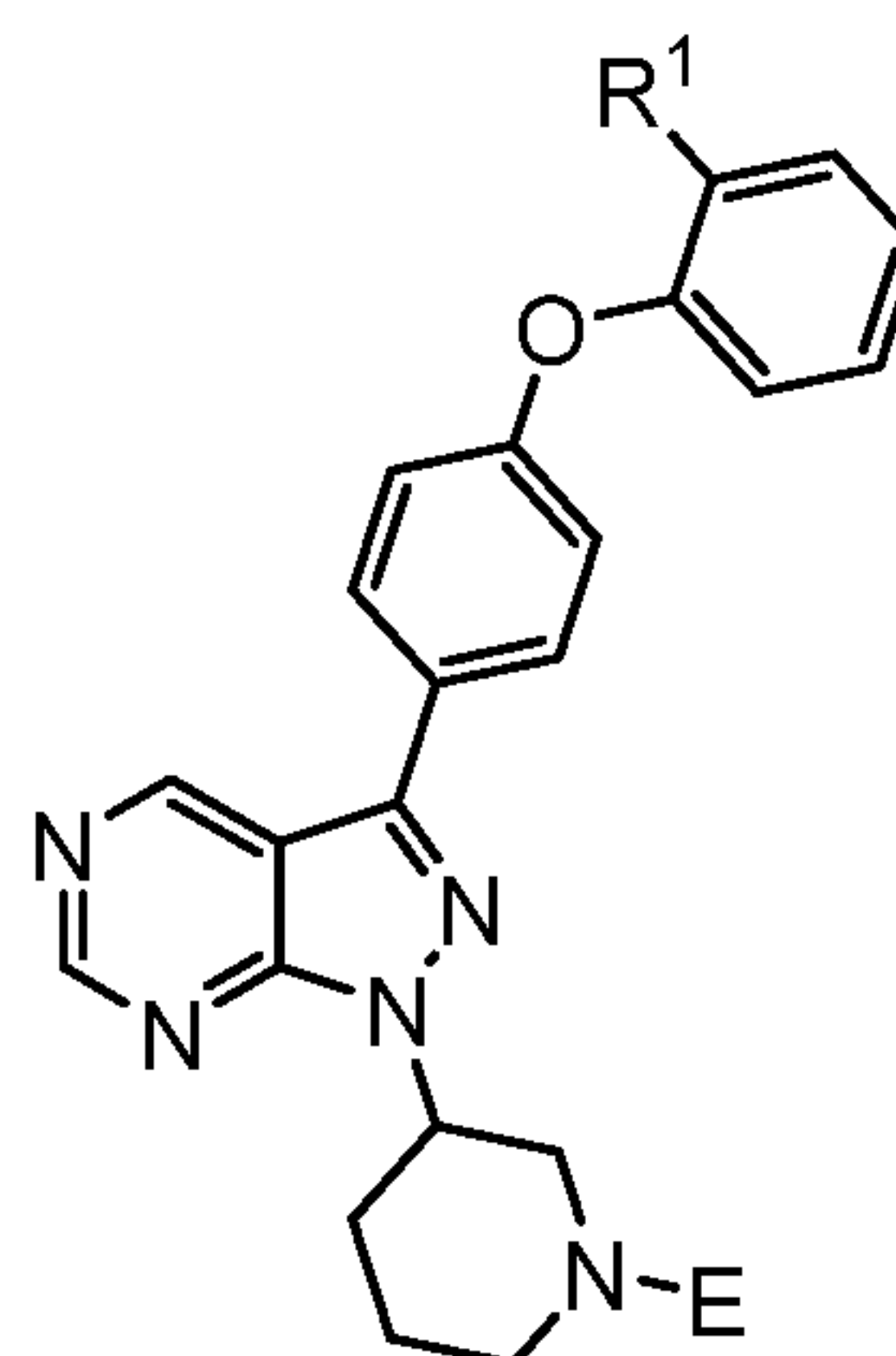


5 formula:

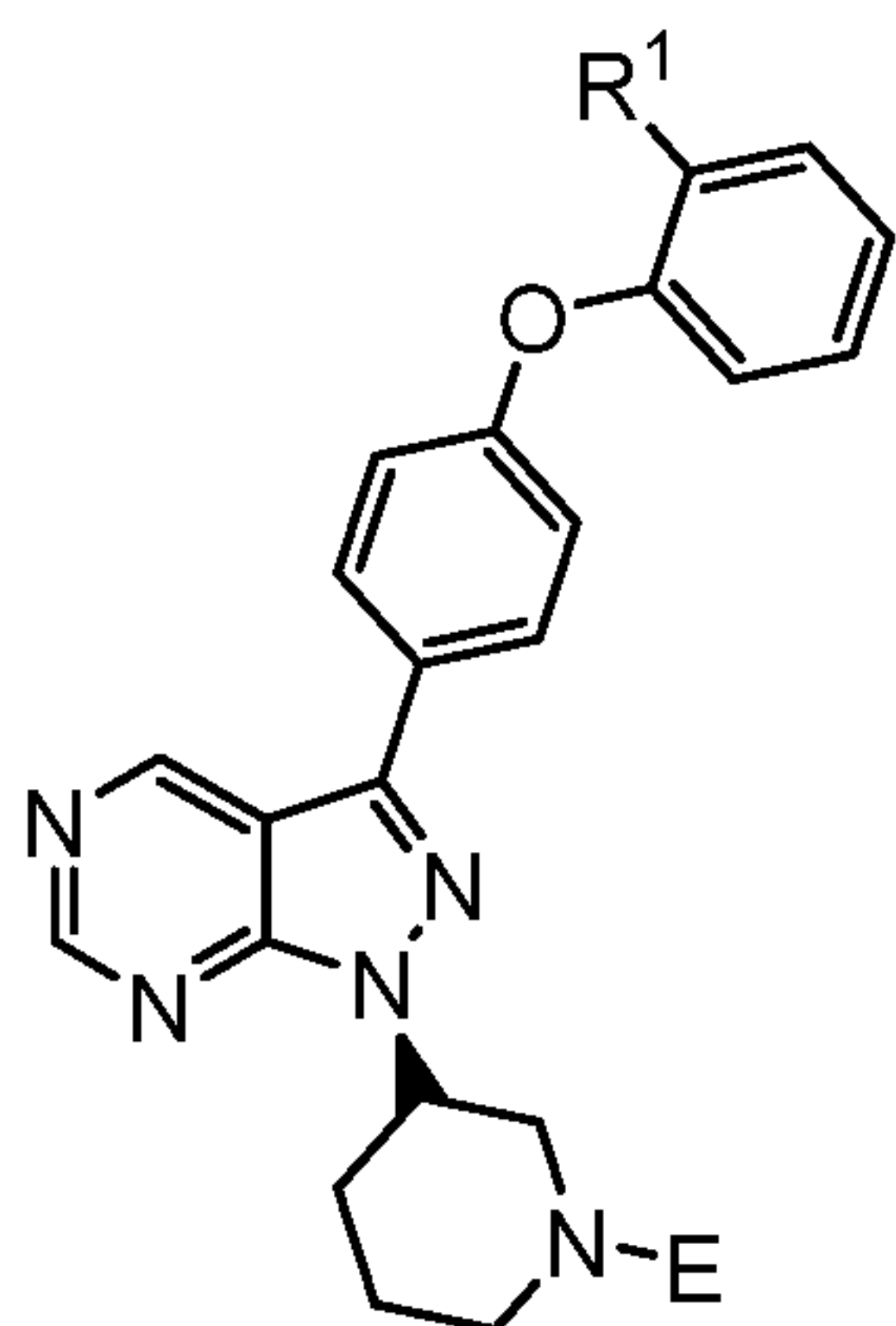
, wherein R^1 , $z1$, and E are as described herein. In



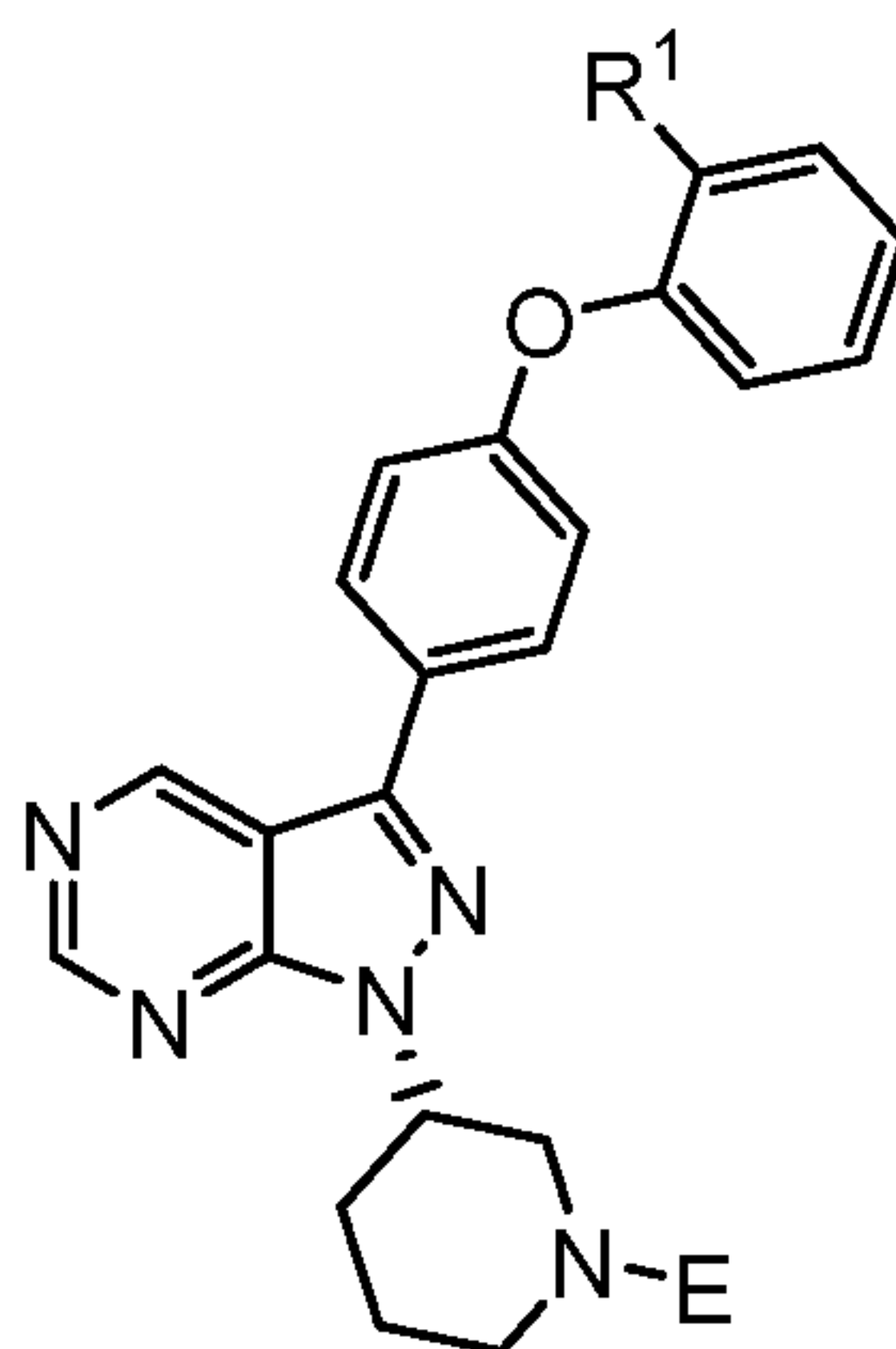
embodiments, the compound has the formula: , wherein R^1 , $z1$, and E are as described herein.



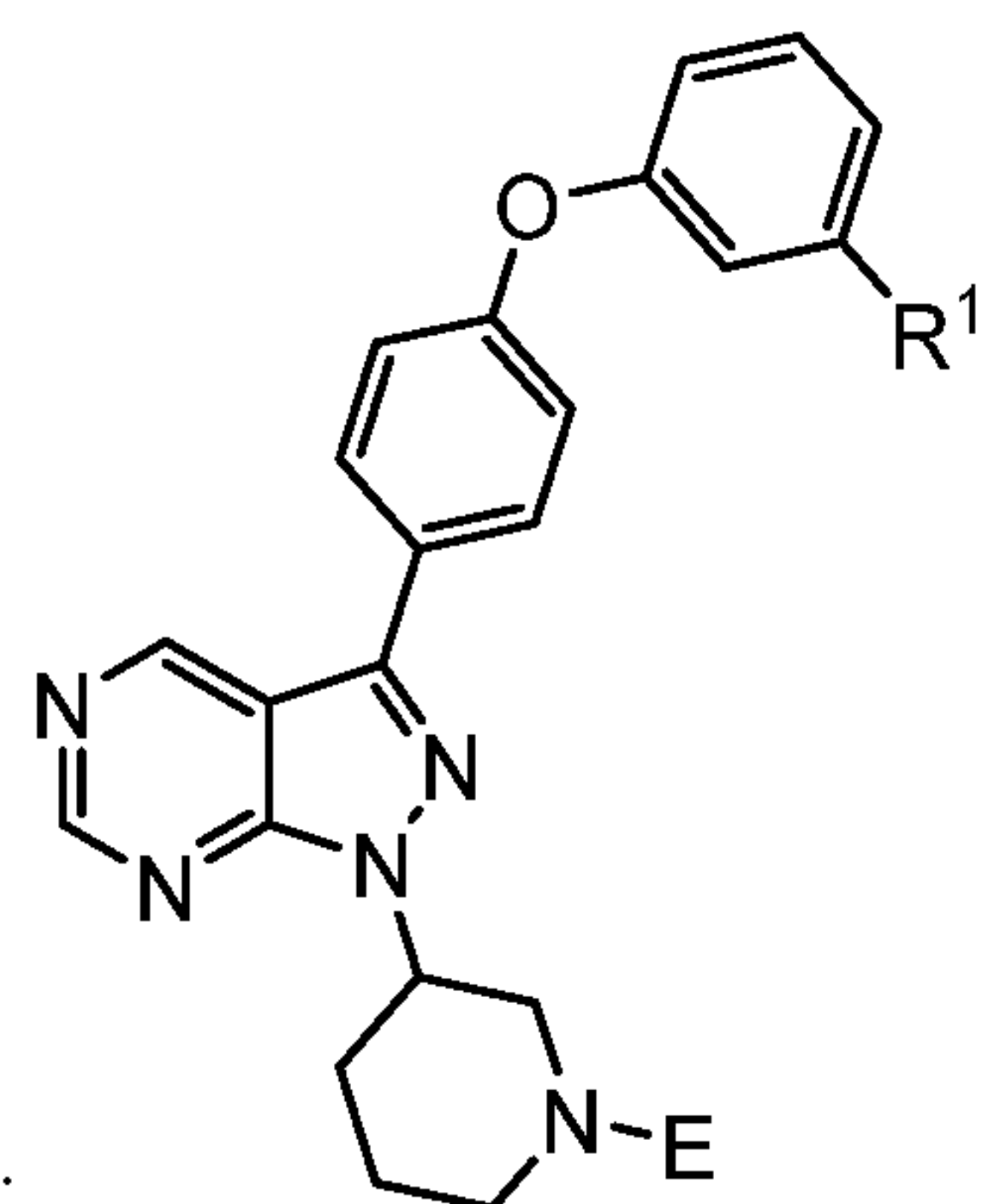
[0563] In embodiments, the compound has the formula: , wherein R^1 and E are as described herein. In embodiments, the compound has the formula:

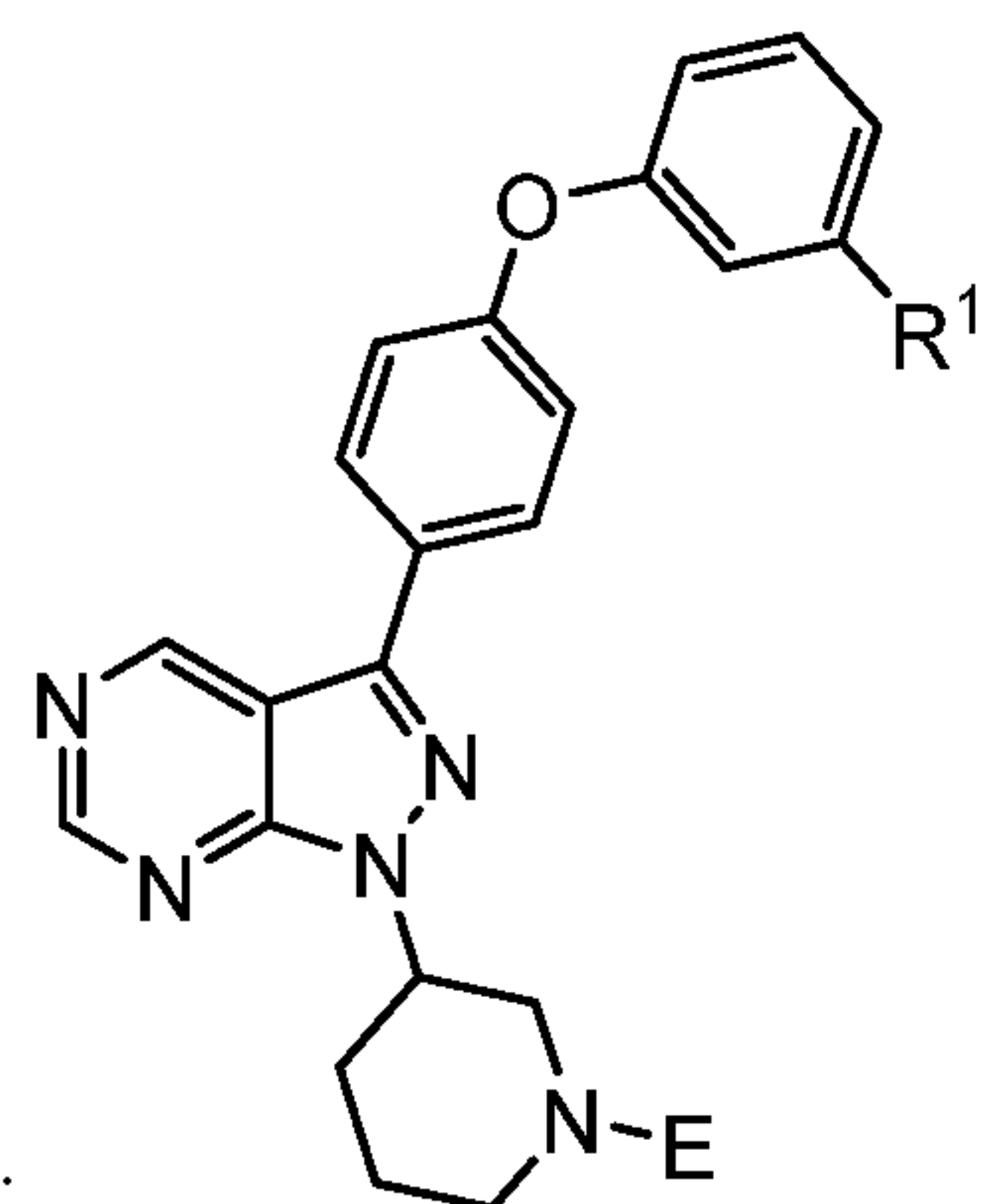


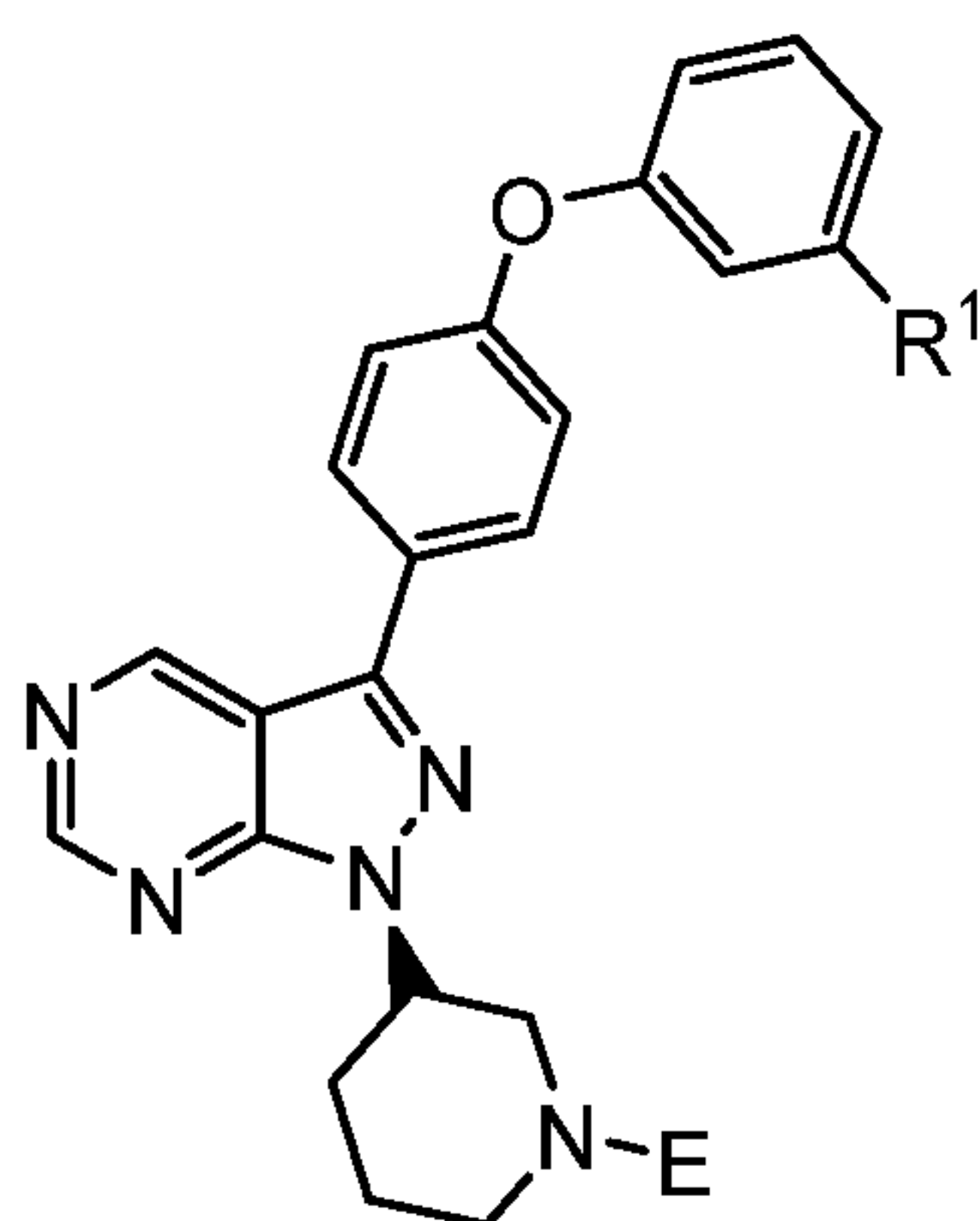
5 , wherein R^1 and E are as described herein. In embodiments, the



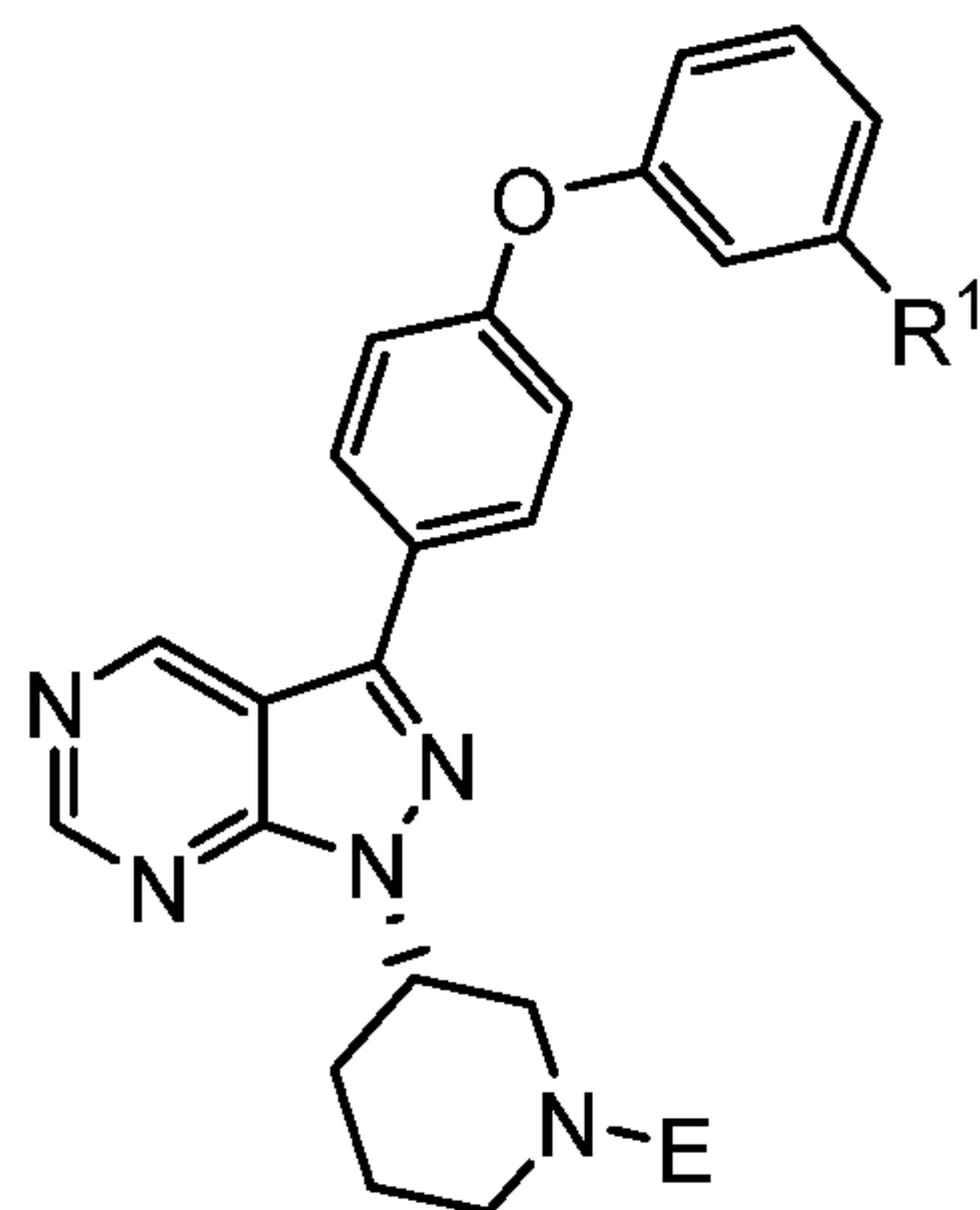
compound has the formula: , wherein R^1 and E are as described herein.



[0564] In embodiments, the compound has the formula: , wherein R¹ and E are as described herein. In embodiments, the compound has the formula:



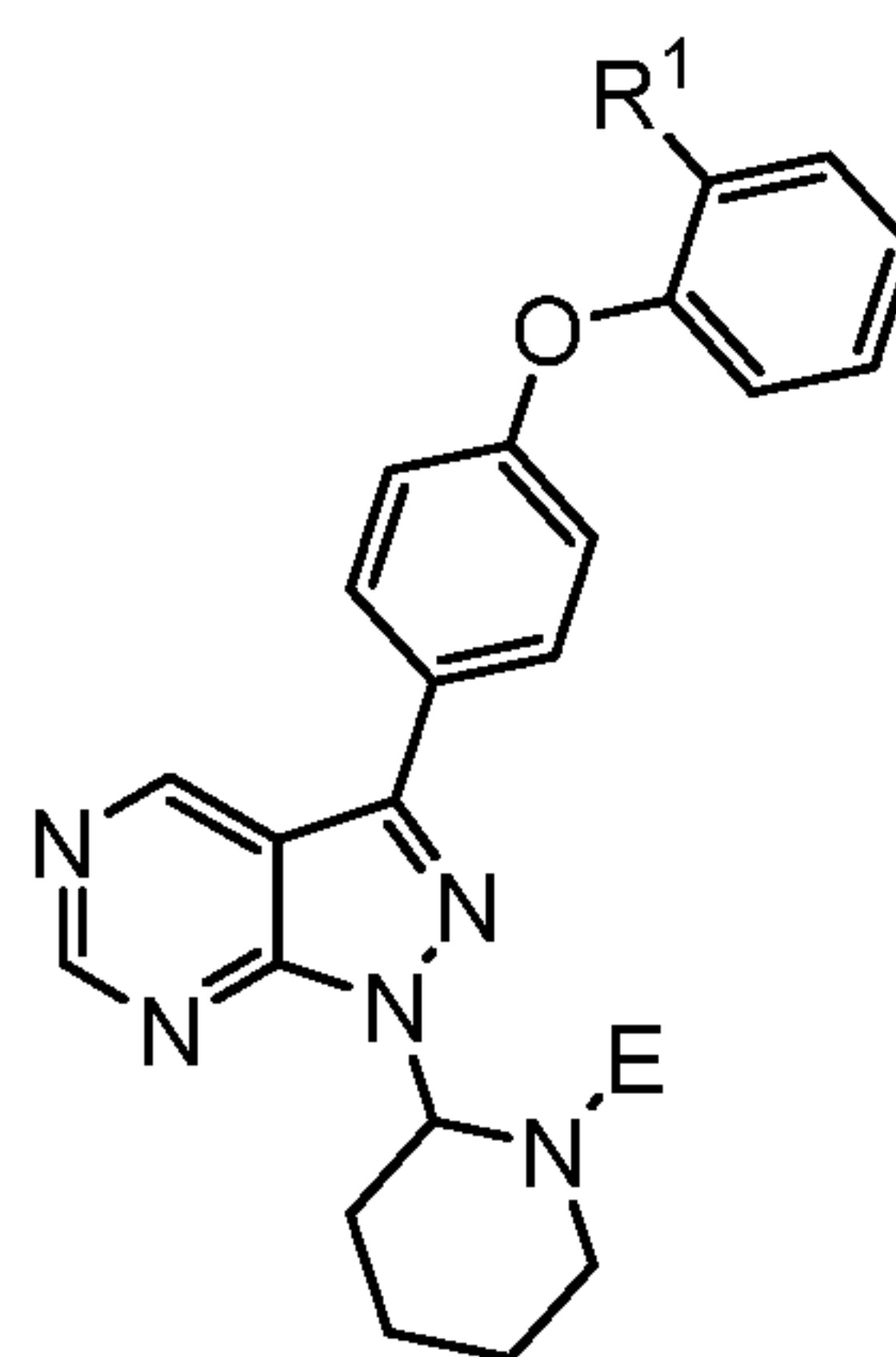
, wherein R¹ and E are as described herein. In embodiments, the

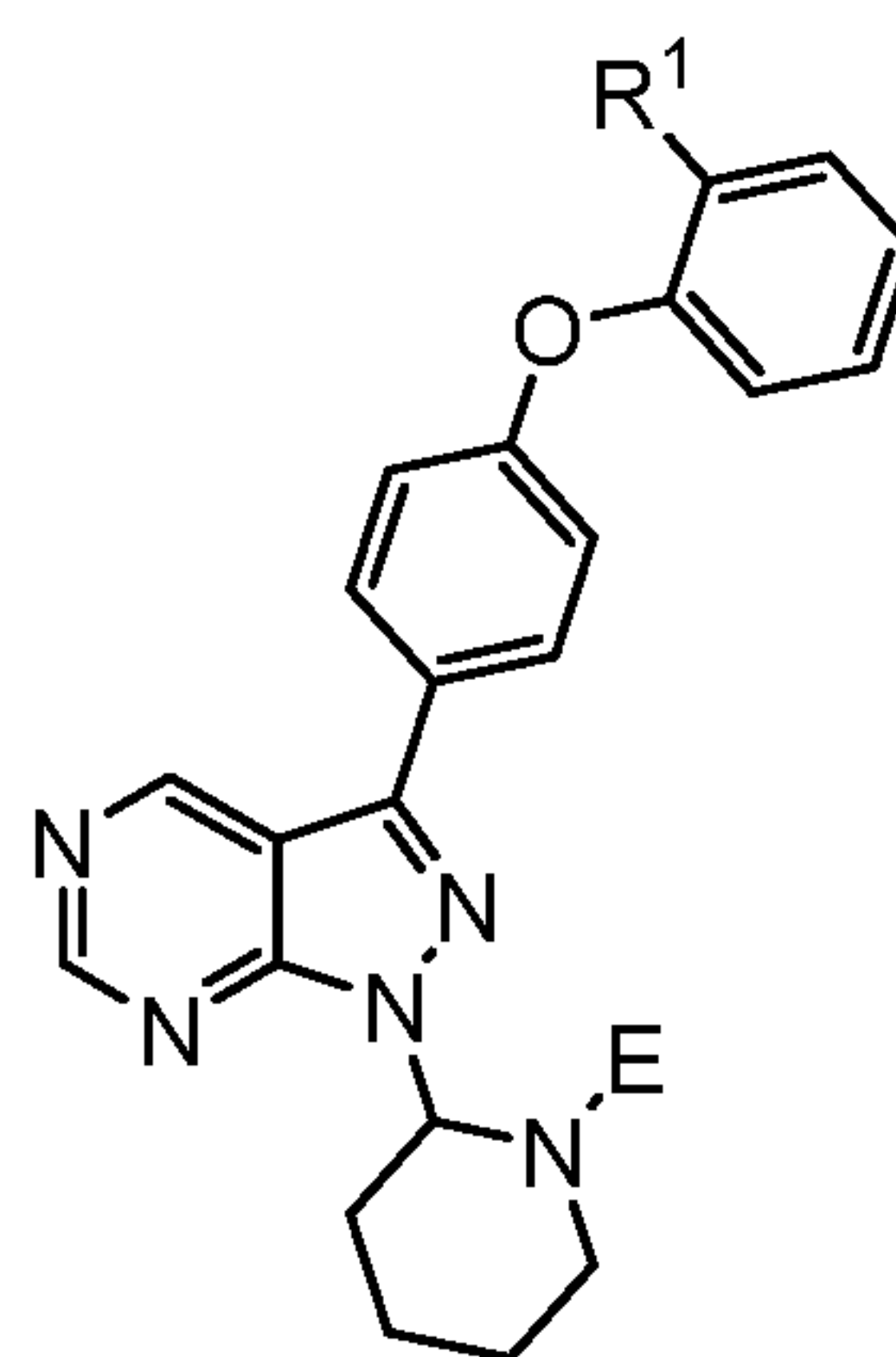


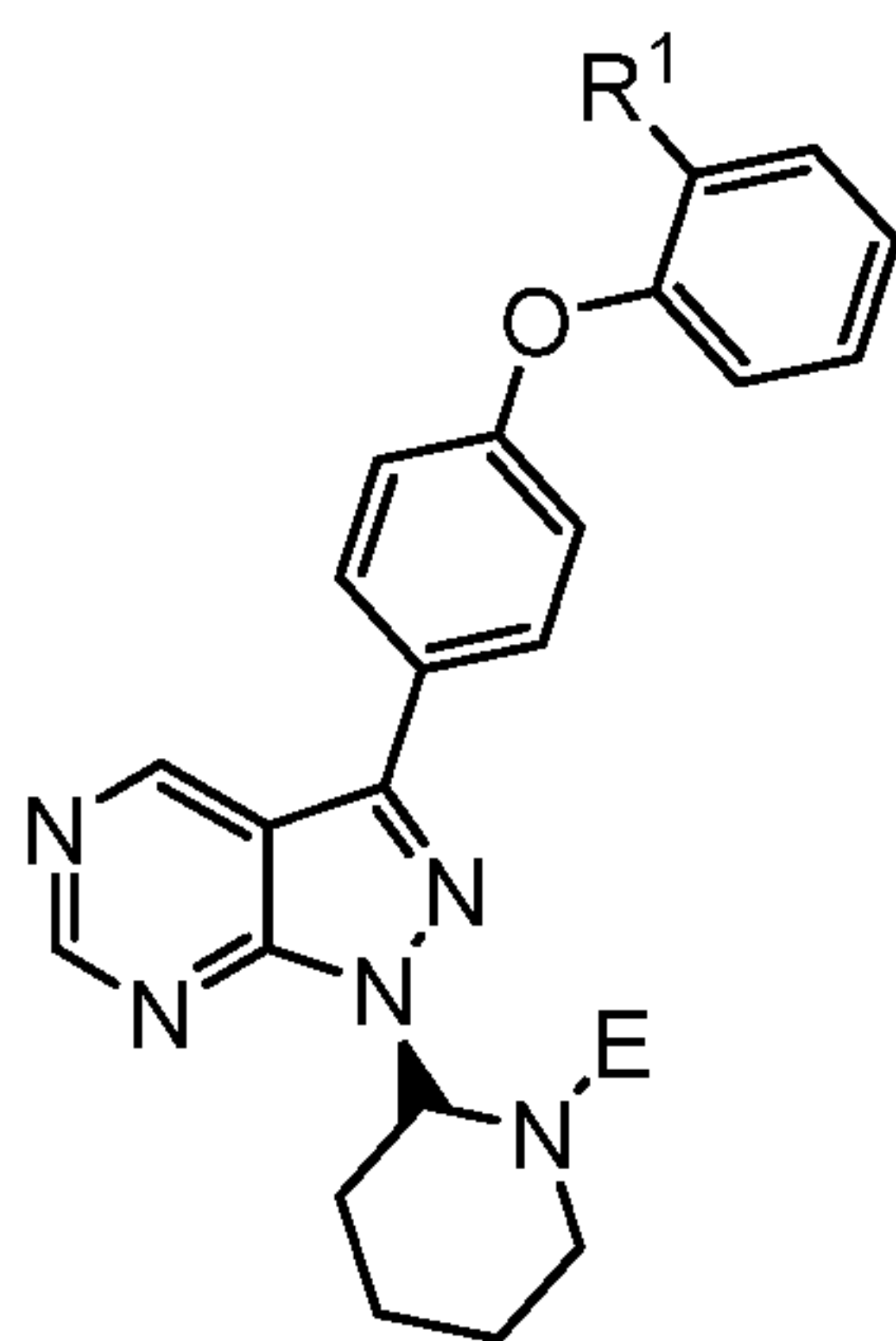
compound has the formula:

, wherein R¹ and E are as described

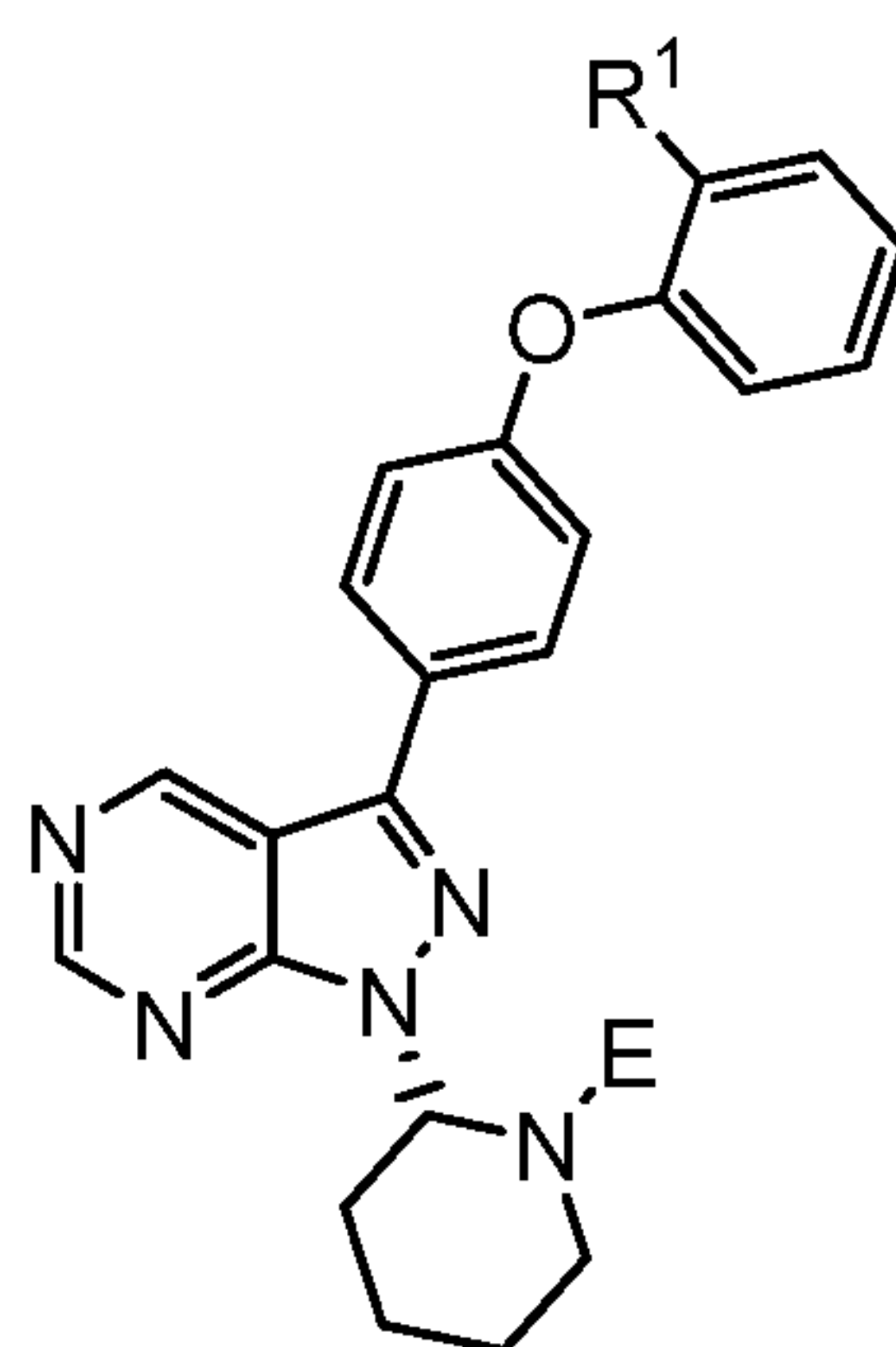
5 herein.



[0565] In embodiments, the compound has the formula: , wherein R¹ and E are as described herein. In embodiments, the compound has the formula:

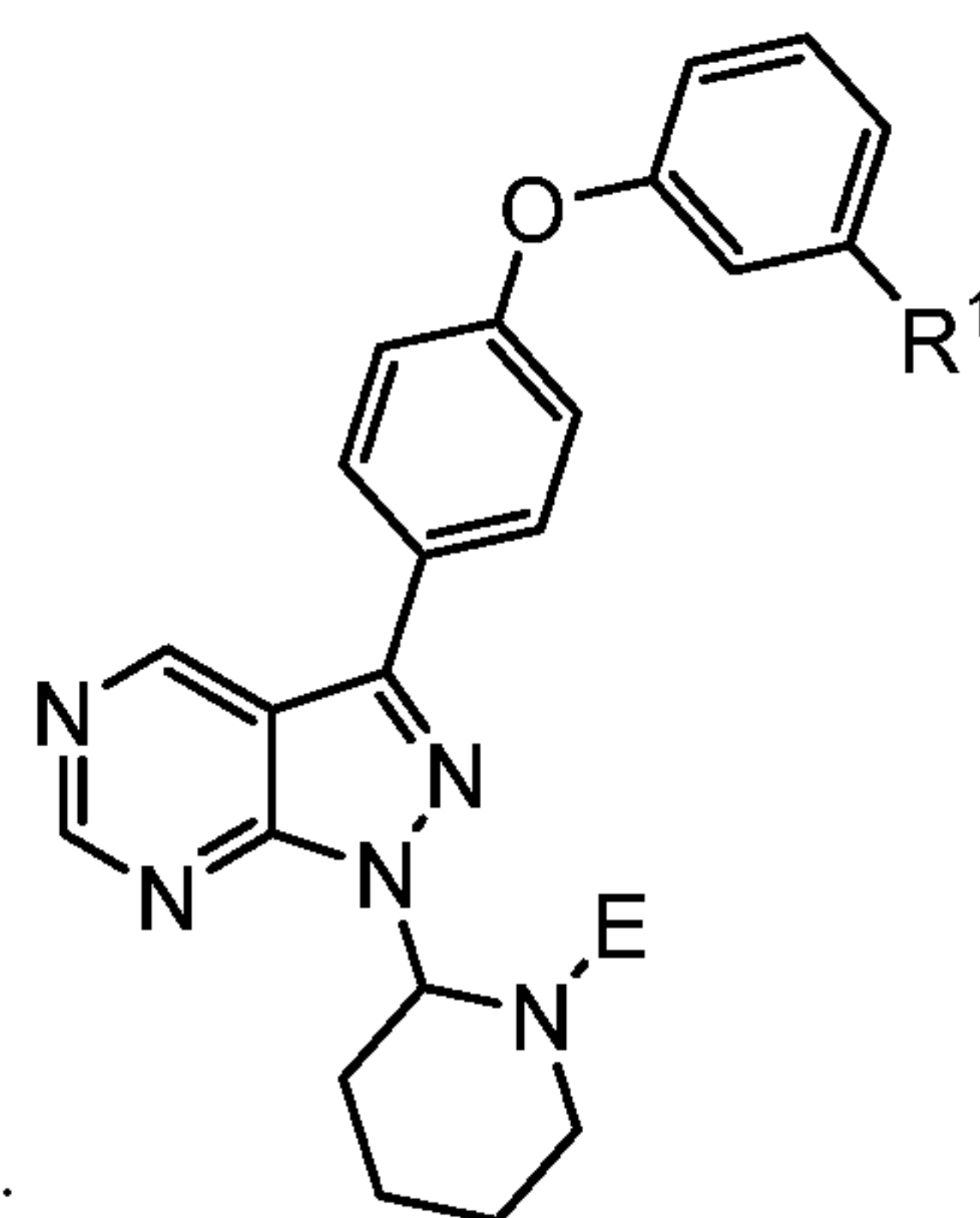


, wherein R¹ and E are as described herein. In embodiments, the



compound has the formula:

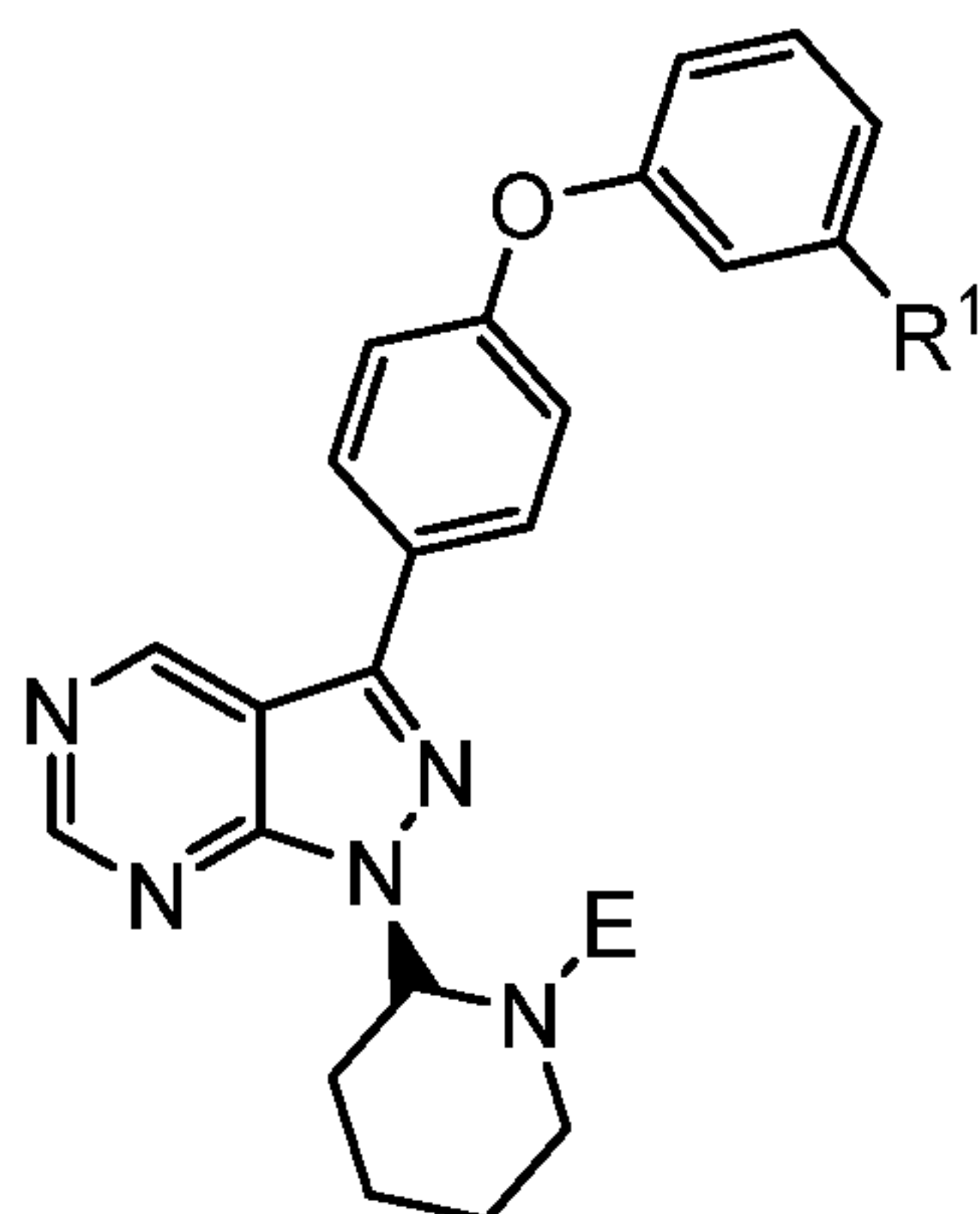
, wherein R¹ and E are as described herein.



[0566] In embodiments, the compound has the formula:

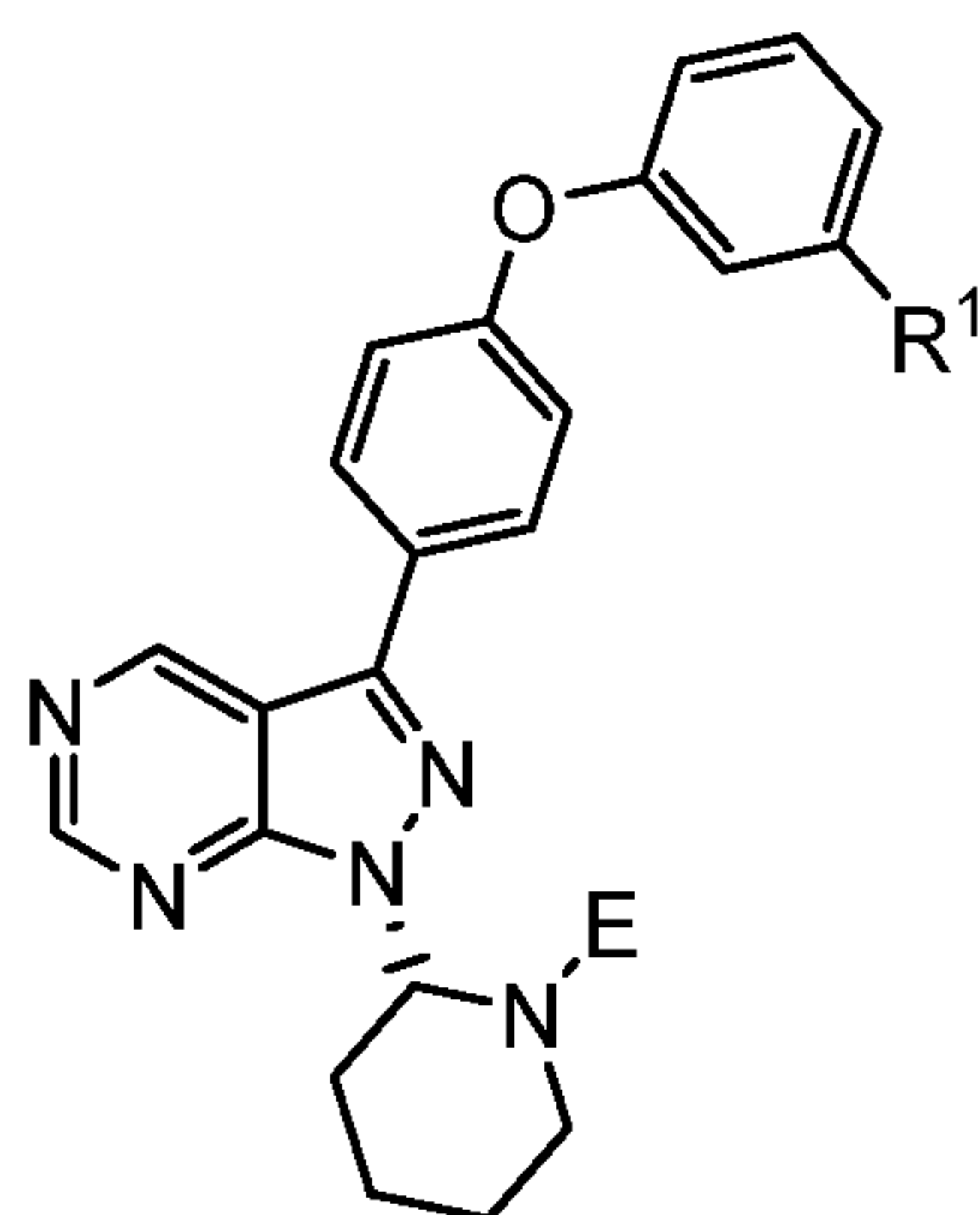
, wherein

R¹ and E are as described herein. In embodiments, the compound has the formula:



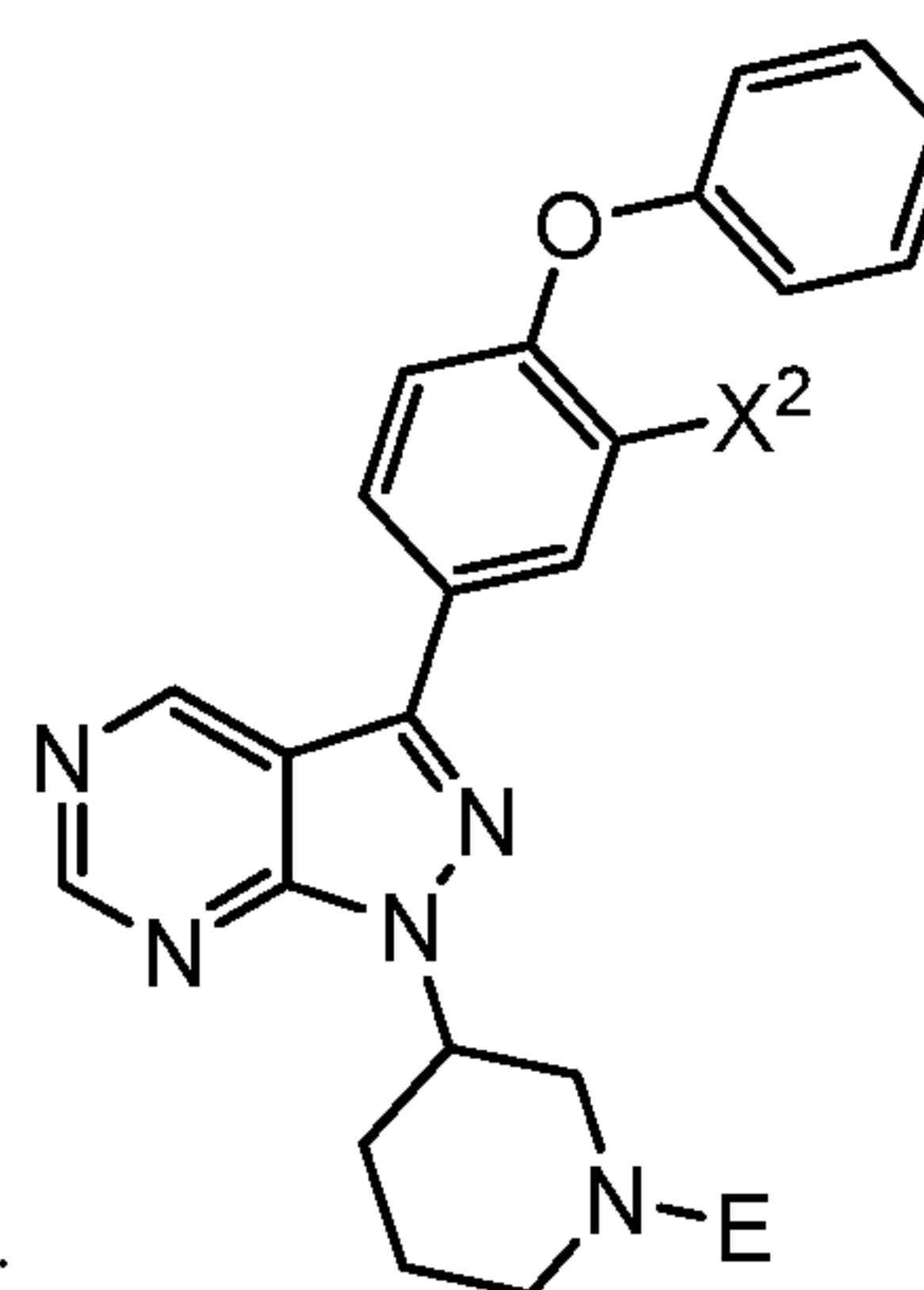
5

, wherein R¹ and E are as described herein. In embodiments, the



compound has the formula:
herein.

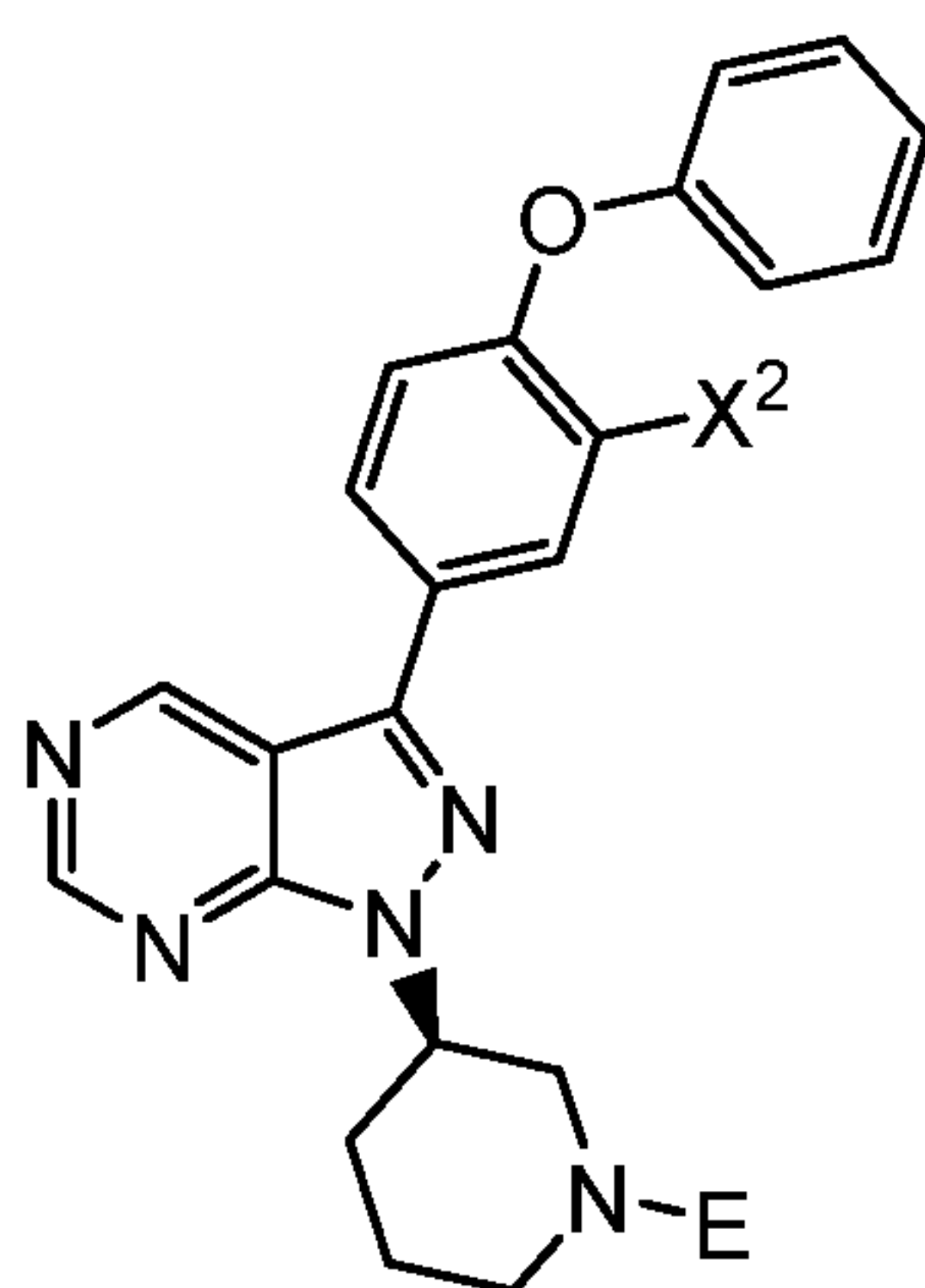
, wherein R^1 and E are as described



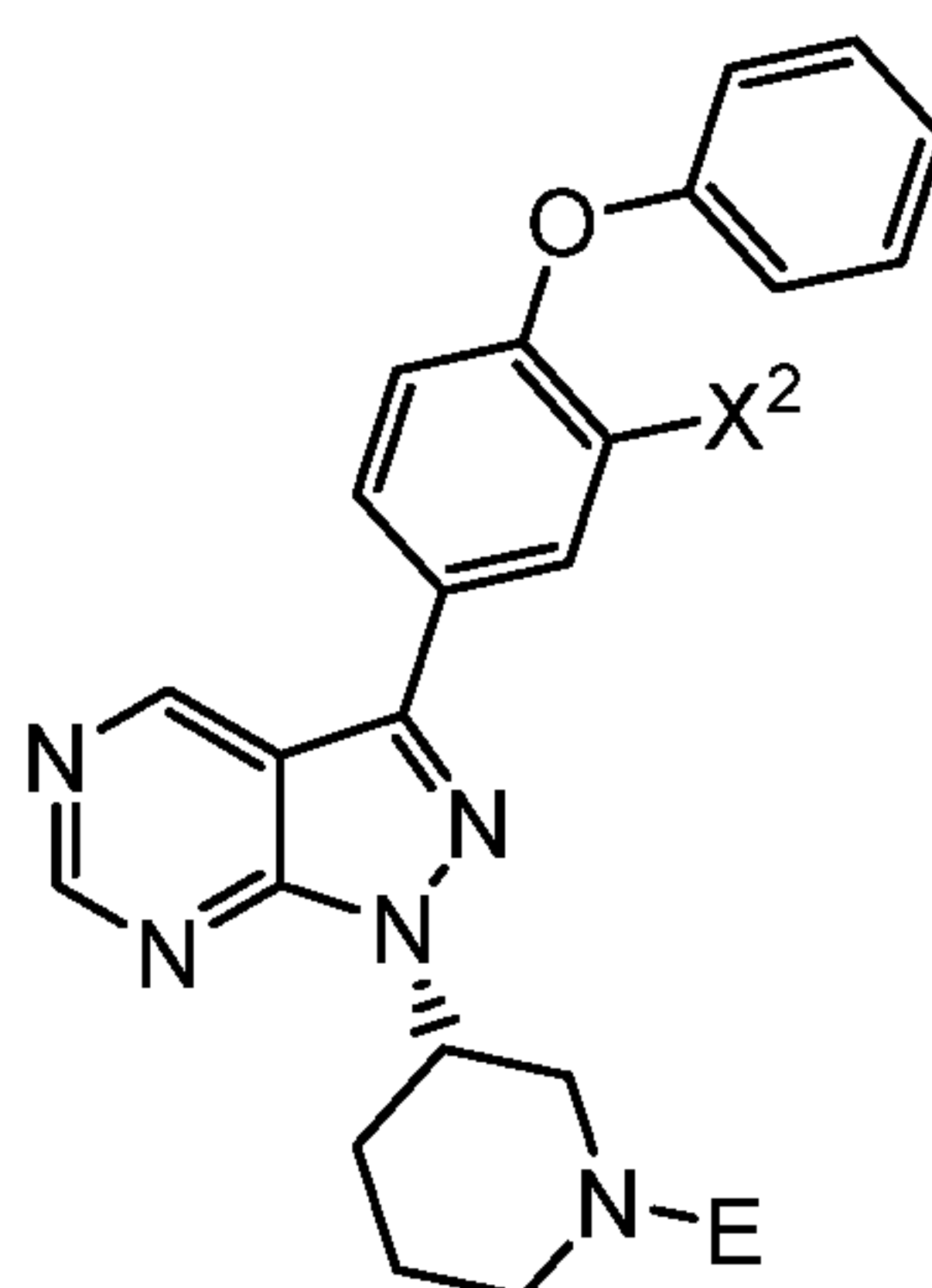
[0567] In embodiments, the compound has the formula:

, wherein X^2

5 and E are as described herein. In embodiments, the compound has the formula:

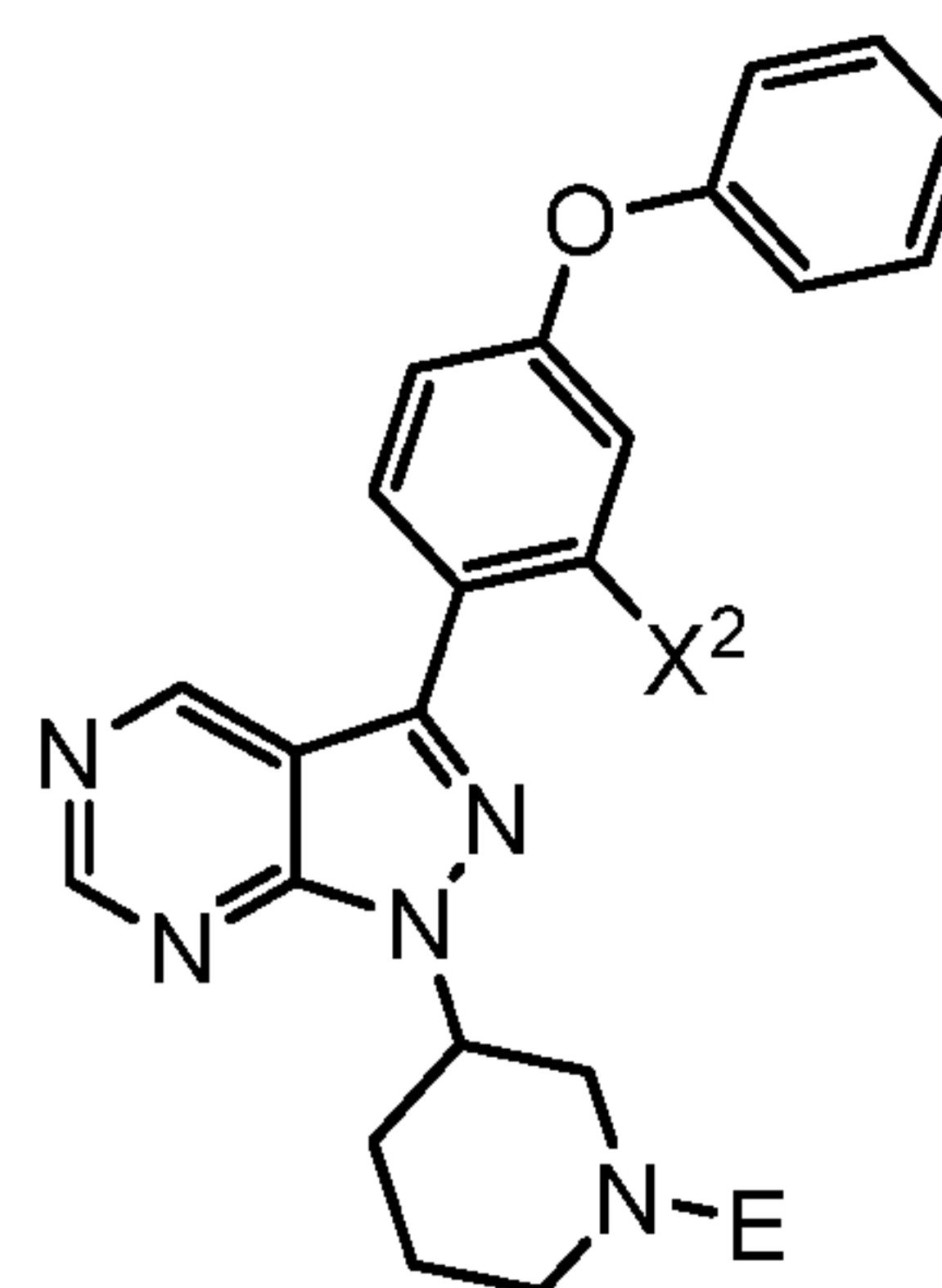


, wherein X^2 and E are as described herein. In embodiments, the

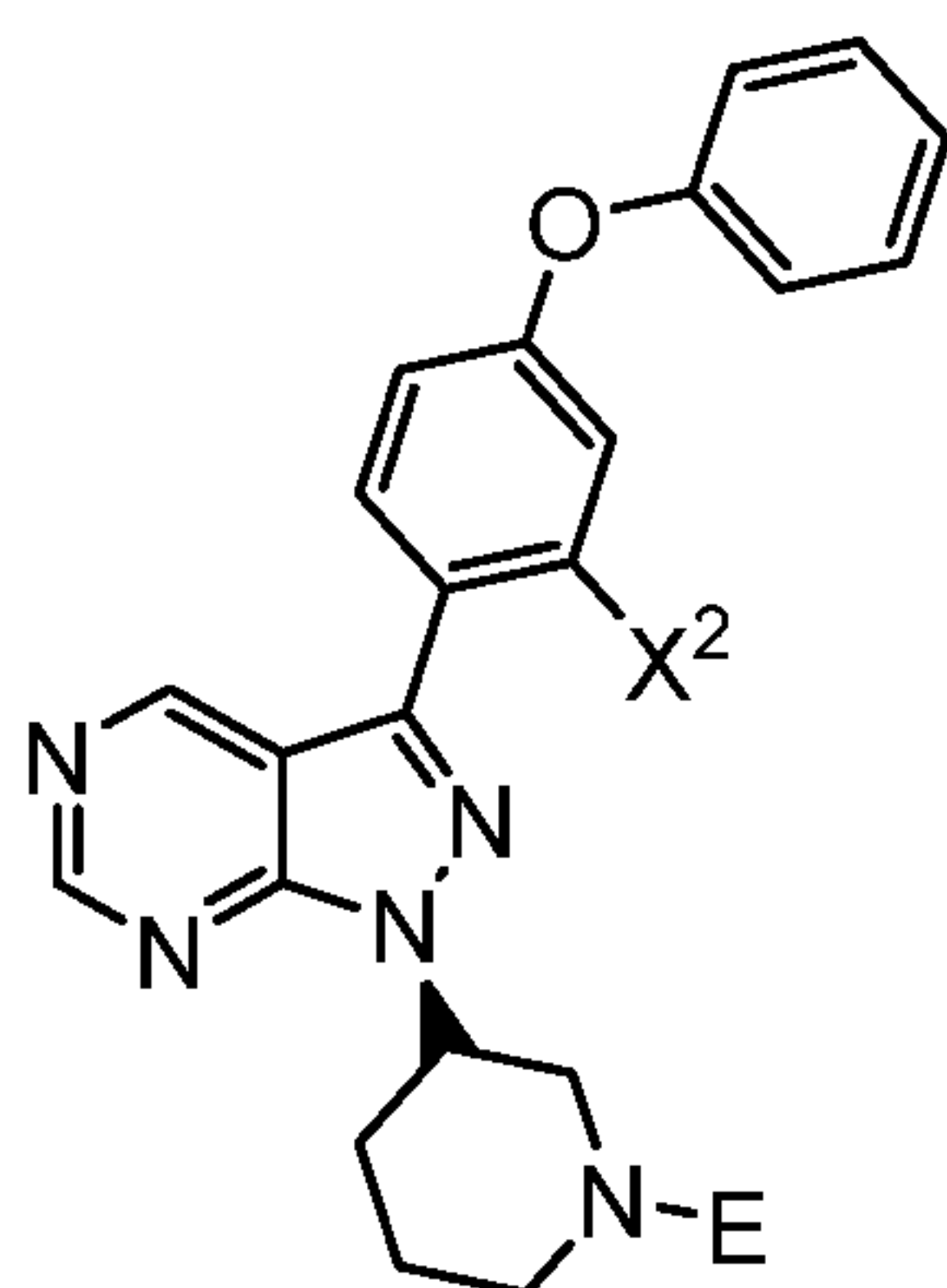


compound has the formula:

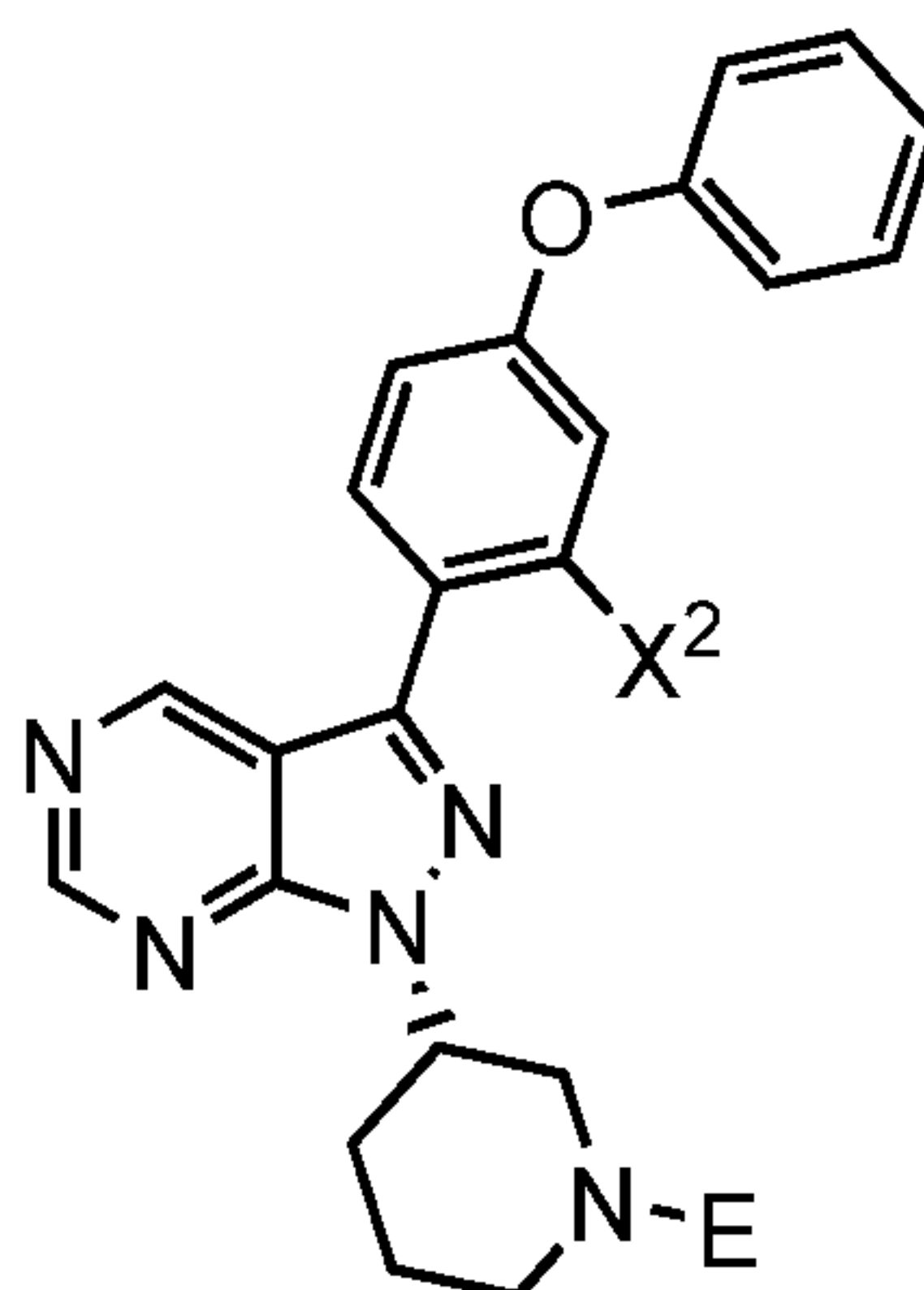
, wherein X^2 and E are as described herein.



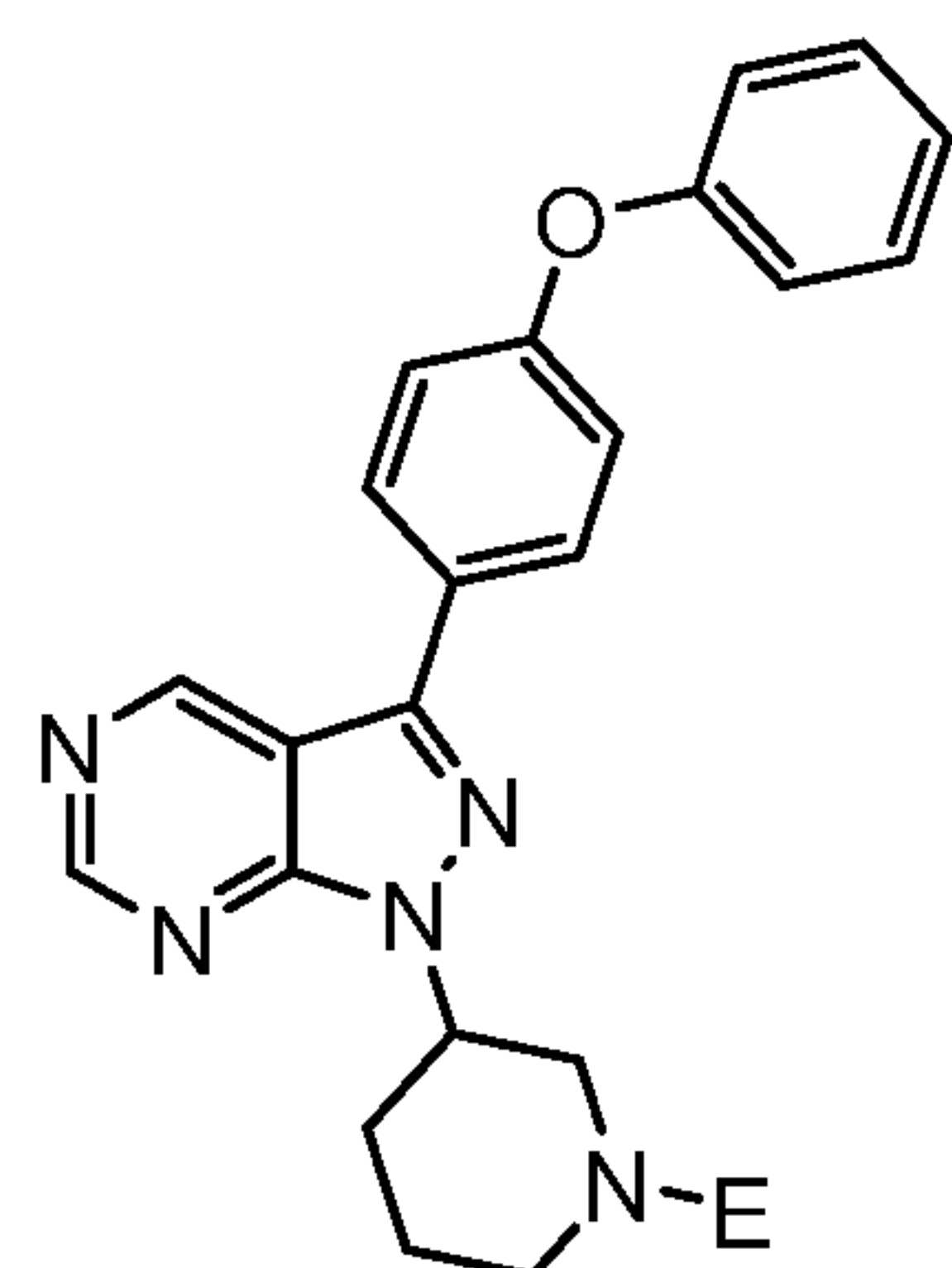
[0568] In embodiments, the compound has the formula: , wherein X^2 and E are as described herein. In embodiments, the compound has the formula:



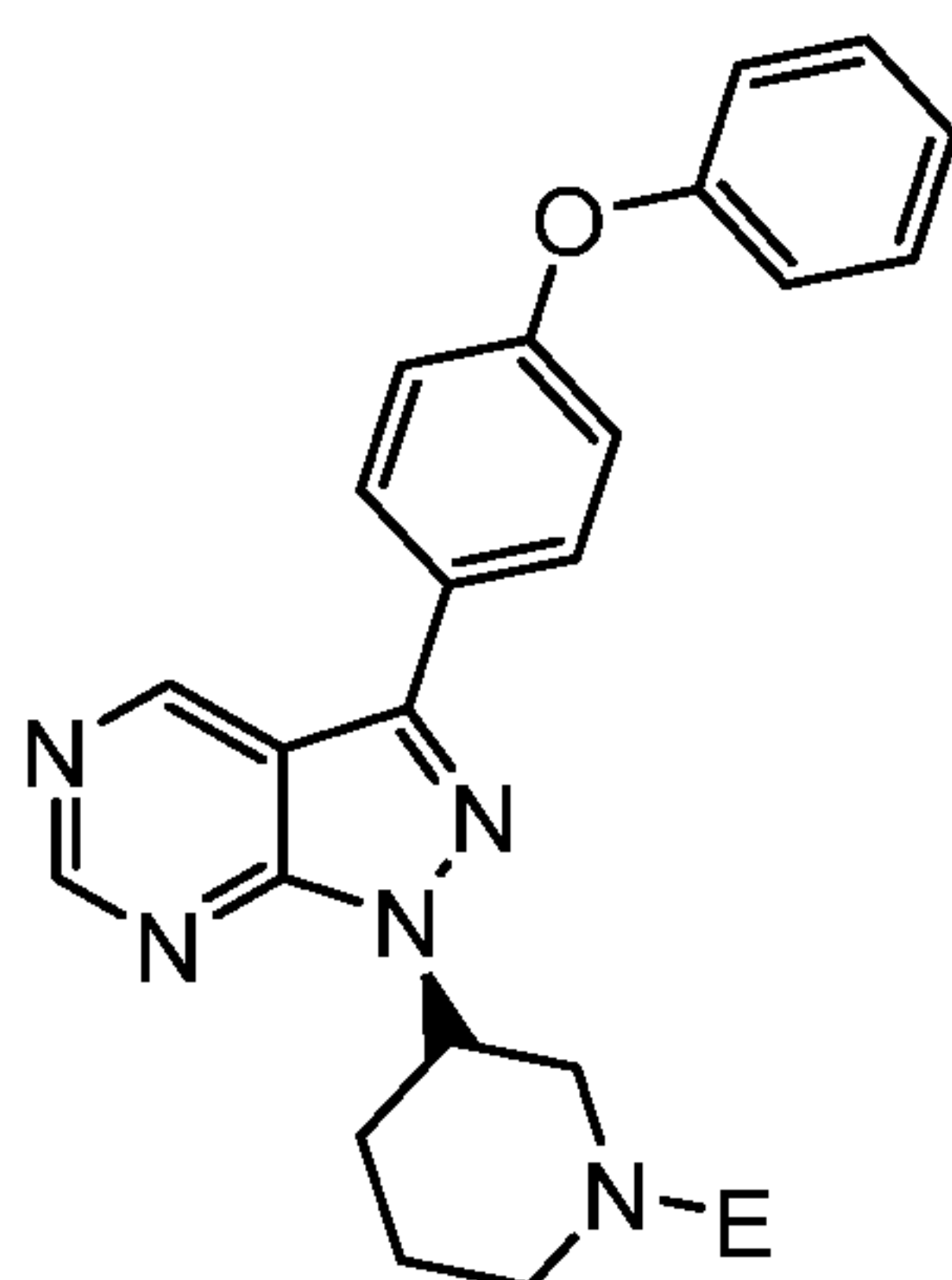
, wherein X^2 and E are as described herein. In embodiments, the



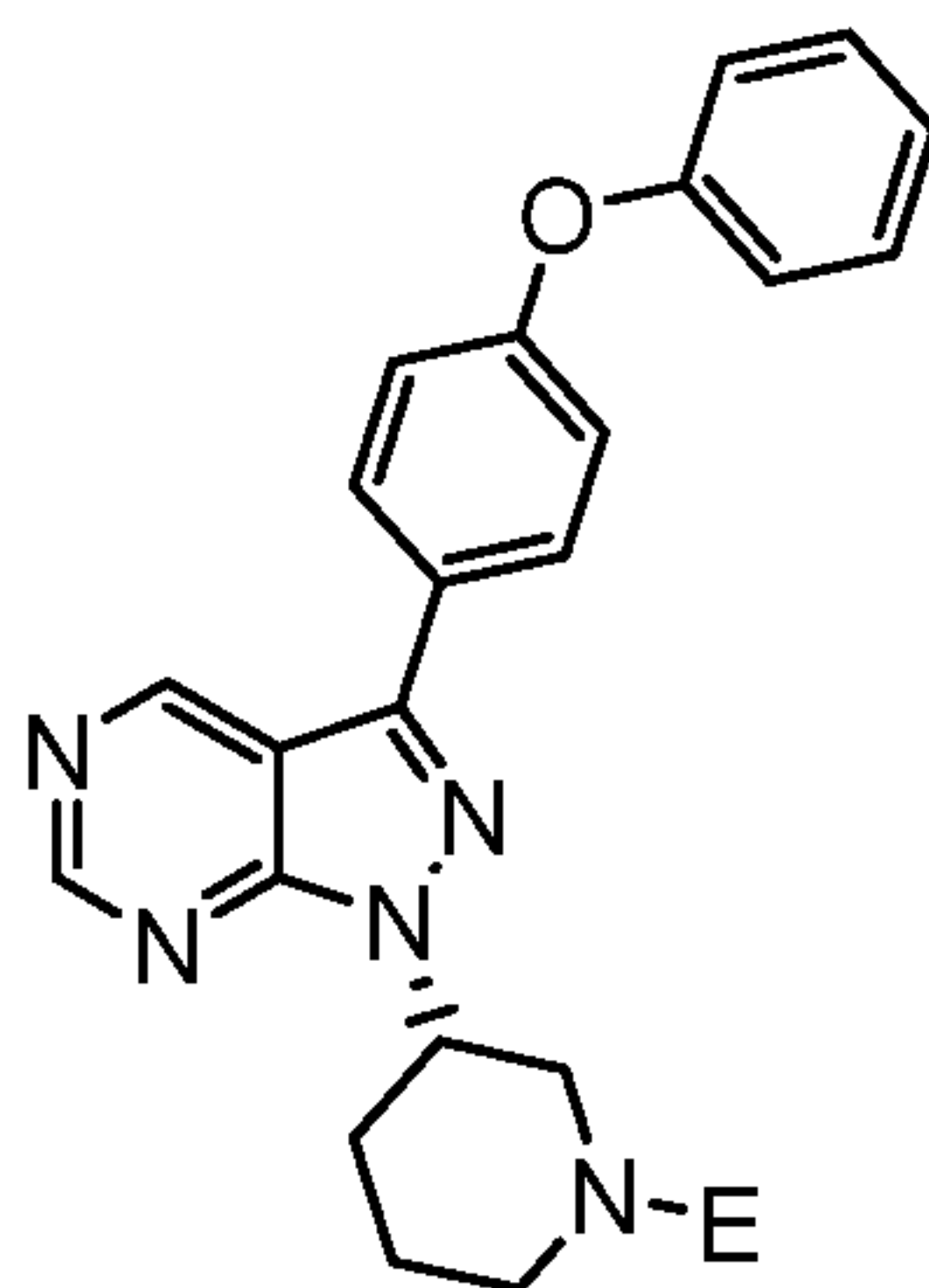
compound has the formula: , wherein X^2 and E are as described herein.



5 **[0569]** In embodiments, the compound has the formula: , wherein R^2 and E are as described herein. In embodiments, the compound has the formula:

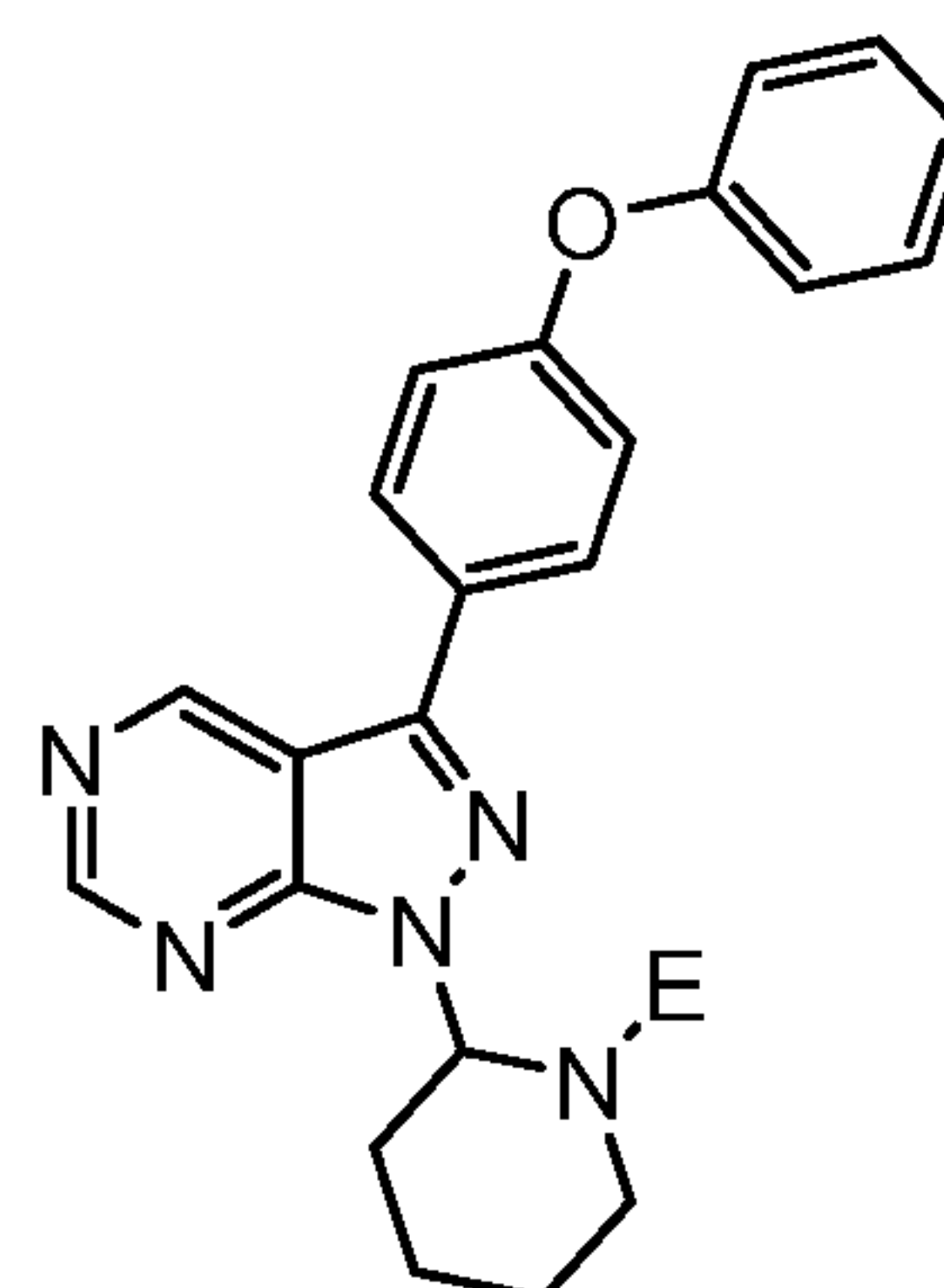


, wherein R^2 and E are as described herein. In embodiments, the



compound has the formula:

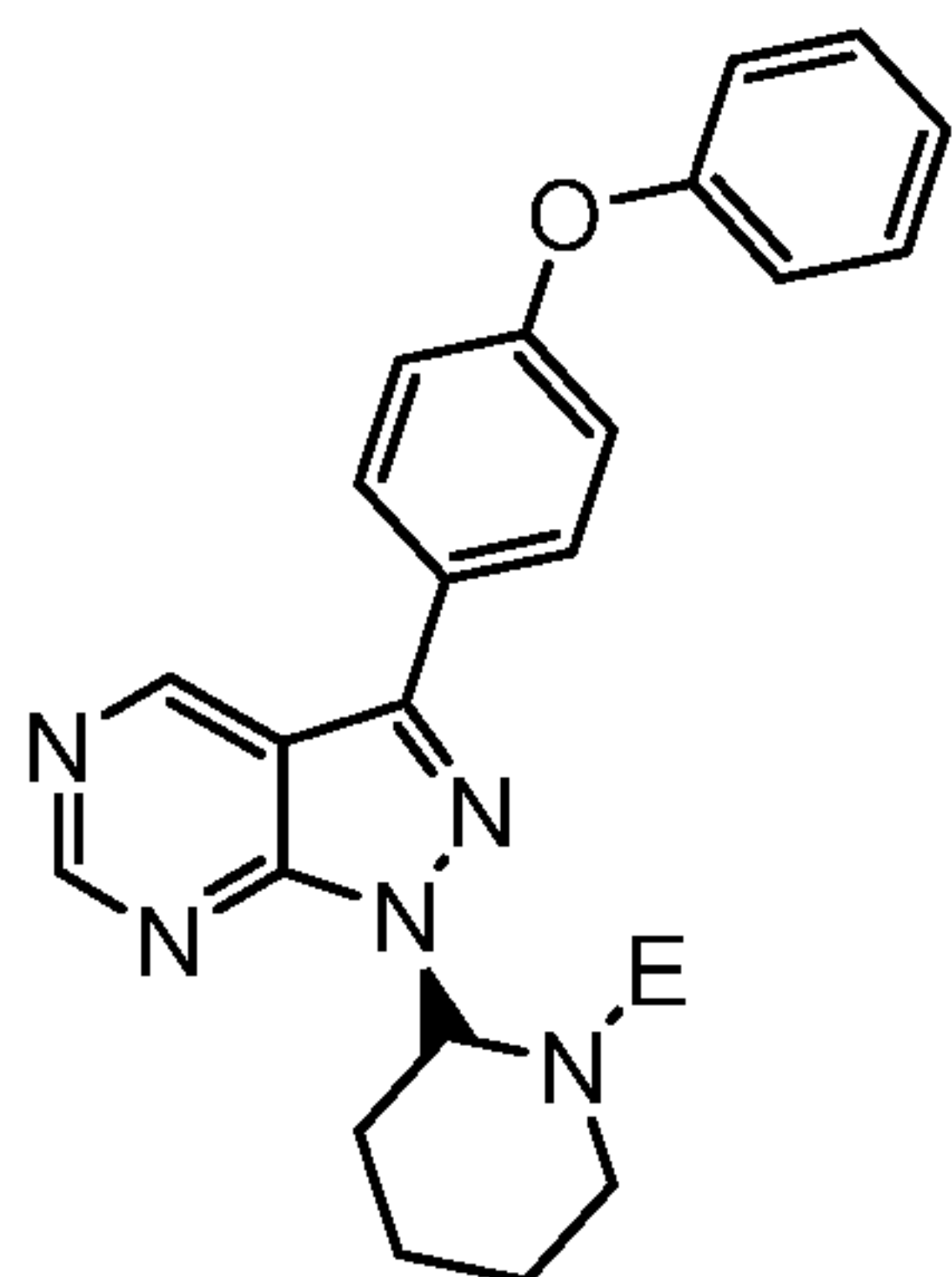
, wherein R^2 and E are as described herein.



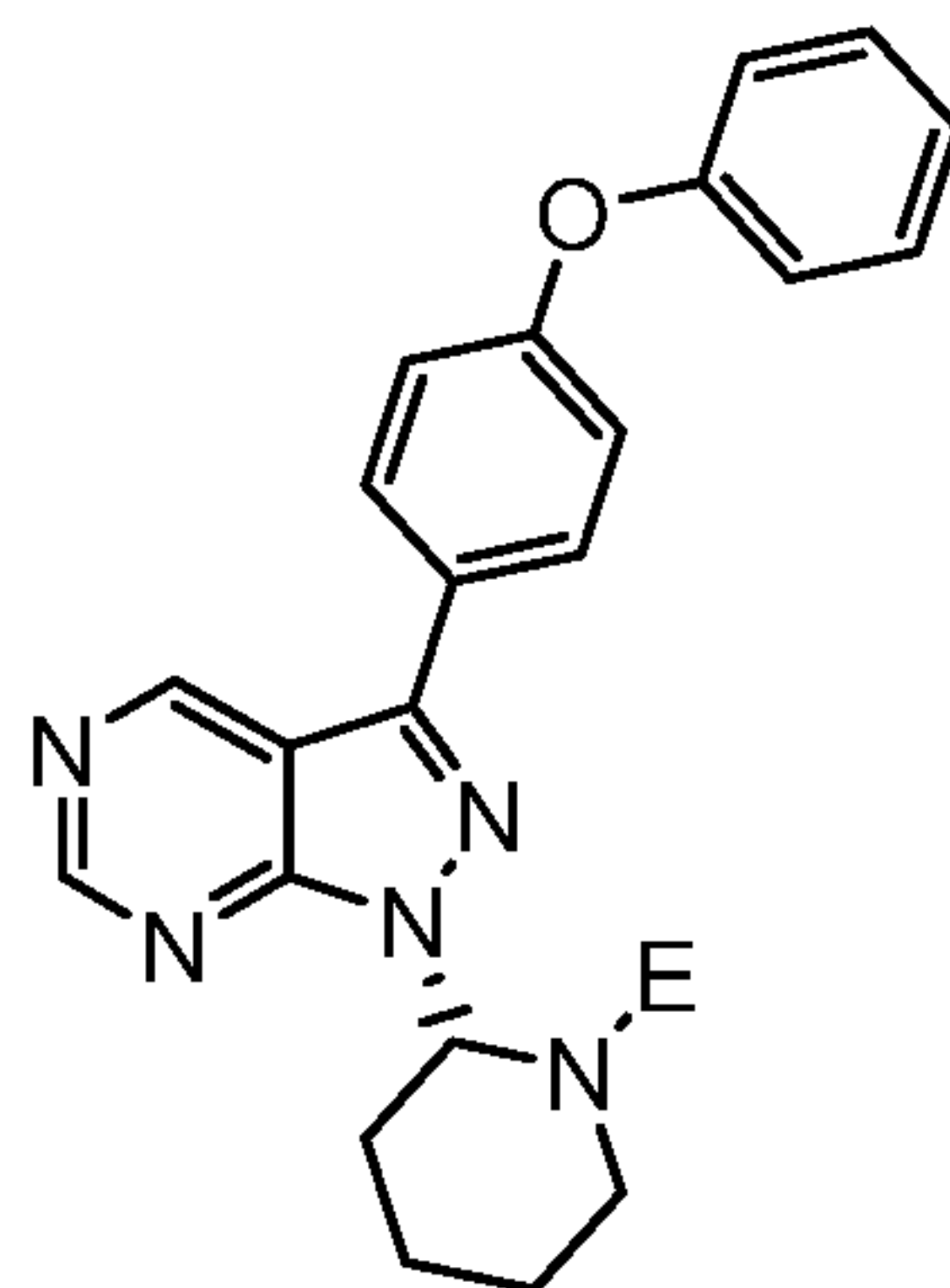
[0570] In embodiments, the compound has the formula:

, wherein R^2

and E are as described herein. In embodiments, the compound has the formula:

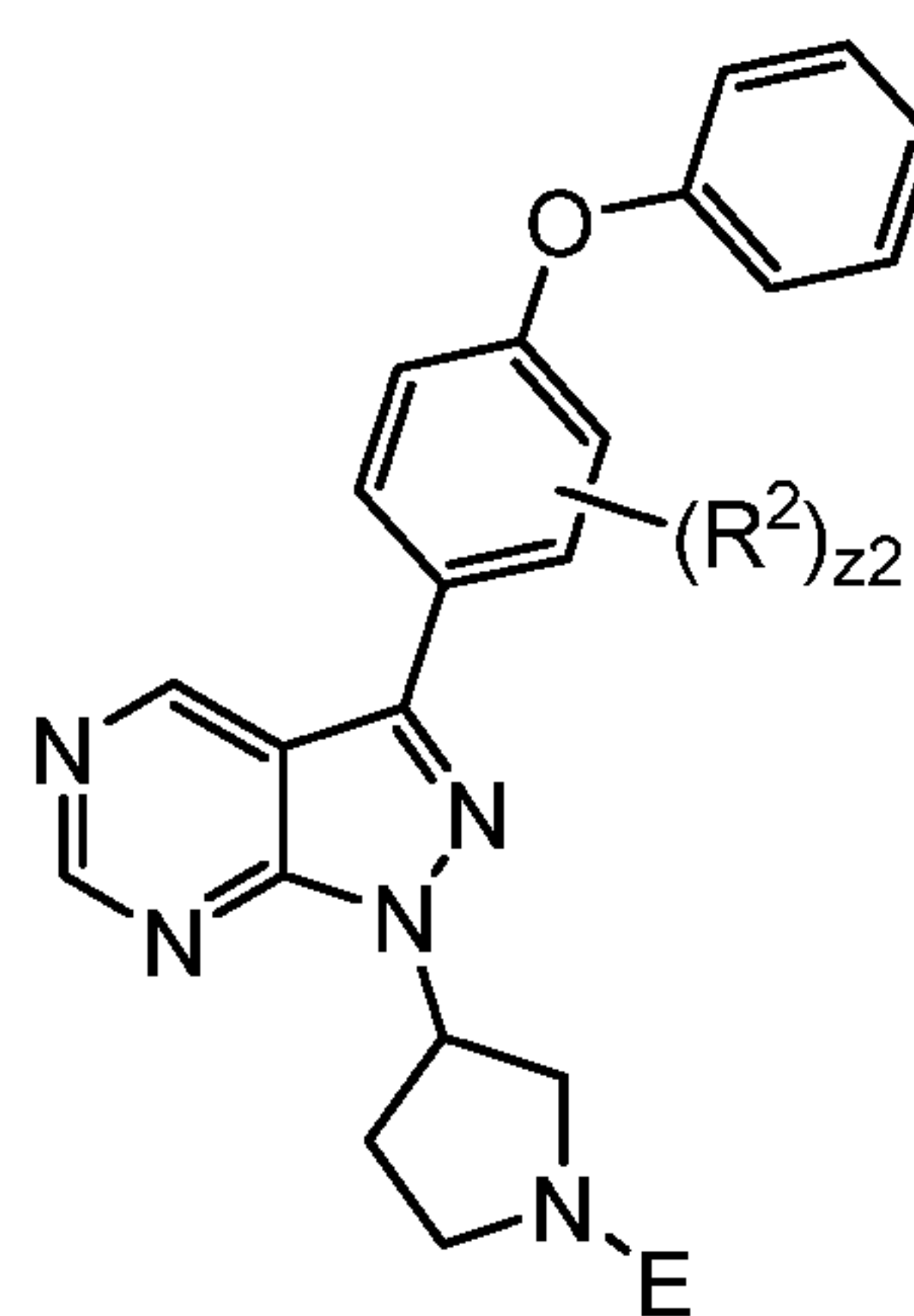


, wherein R^2 and E are as described herein. In embodiments, the

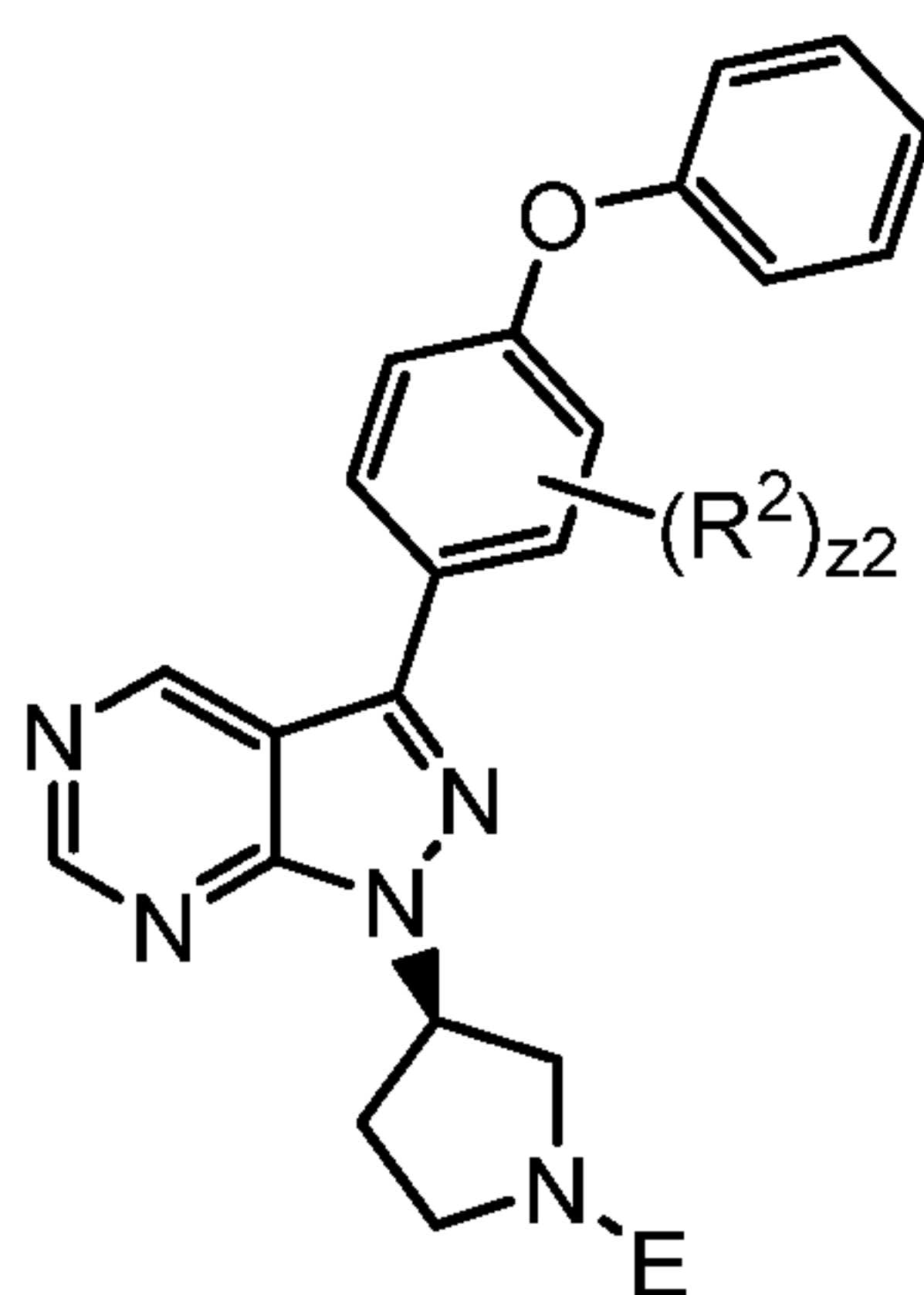


compound has the formula:

, wherein R^2 and E are as described herein.

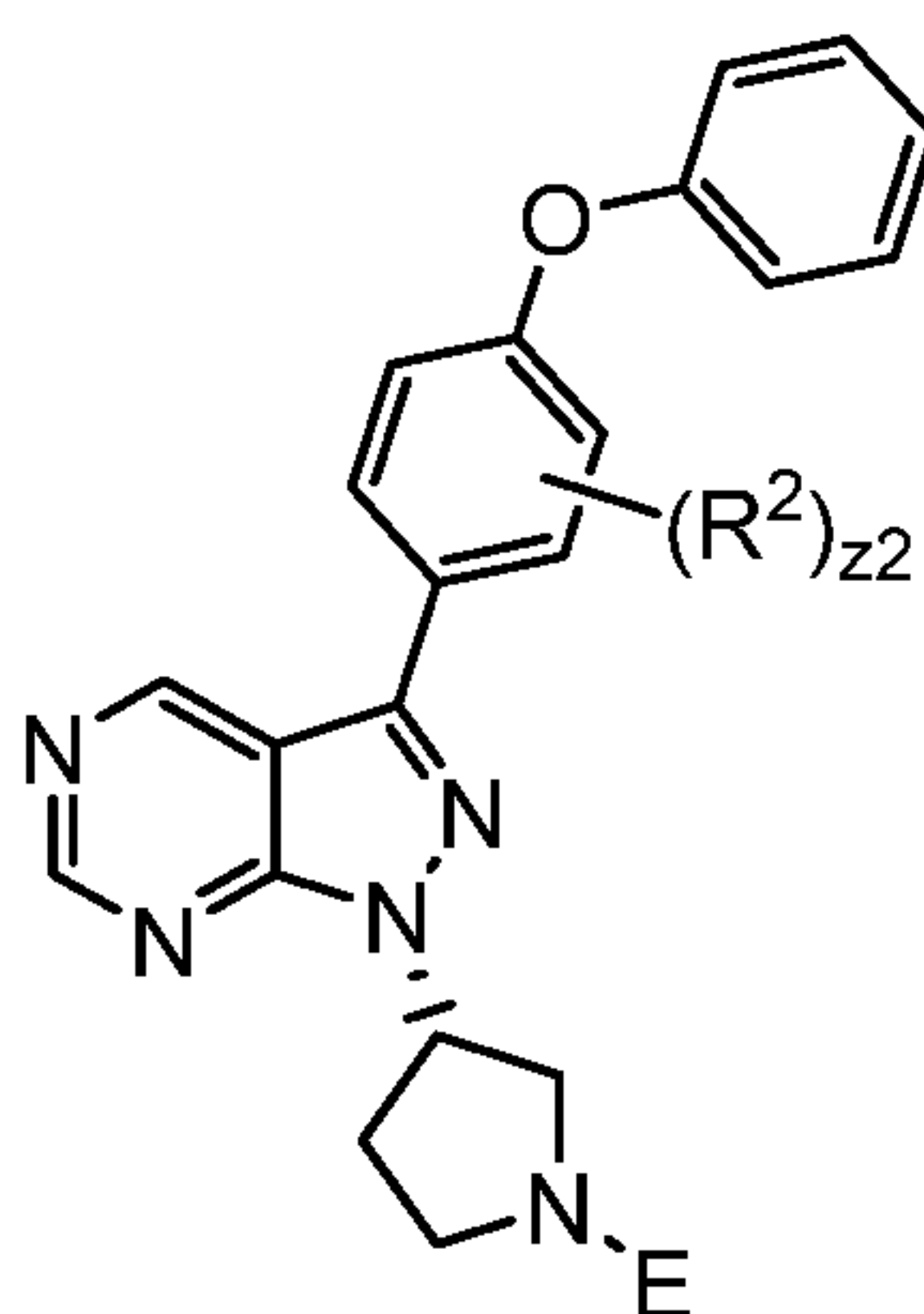


[0571] In embodiments, the compound has the formula: , wherein R^2 , $z2$, and E are as described herein. In embodiments, the compound has the formula:

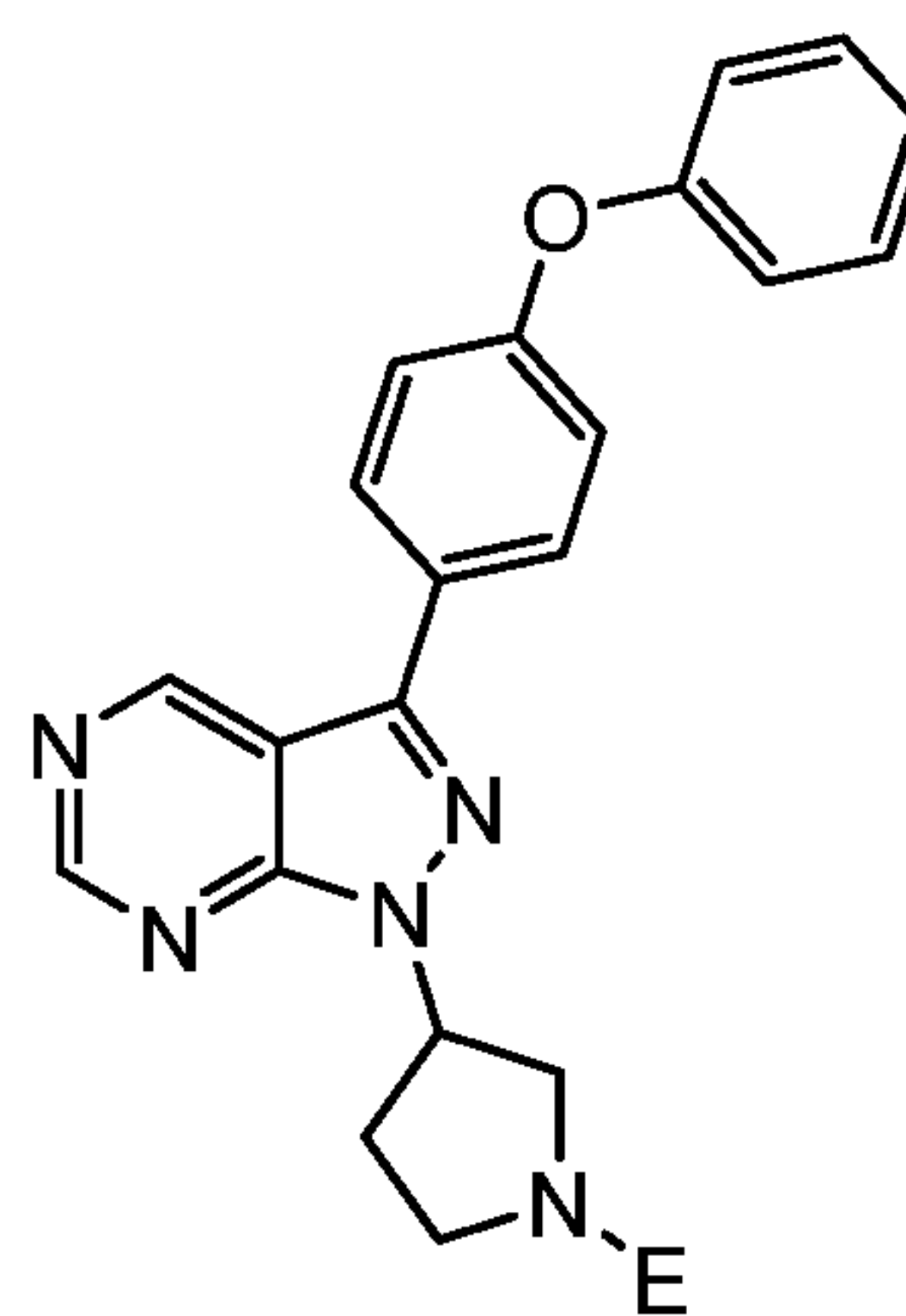


5

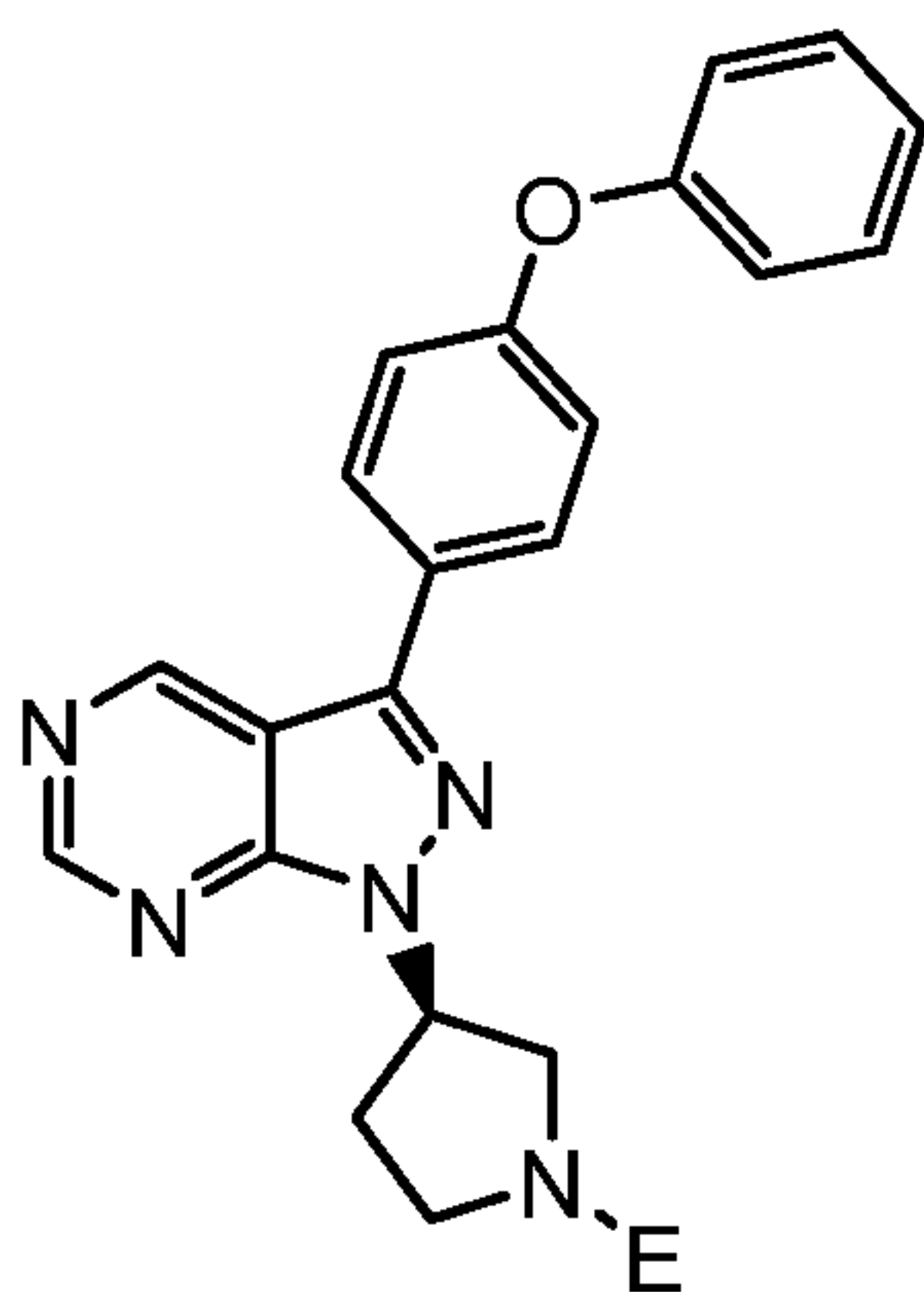
, wherein R^2 , $z2$, and E are as described herein. In embodiments, the



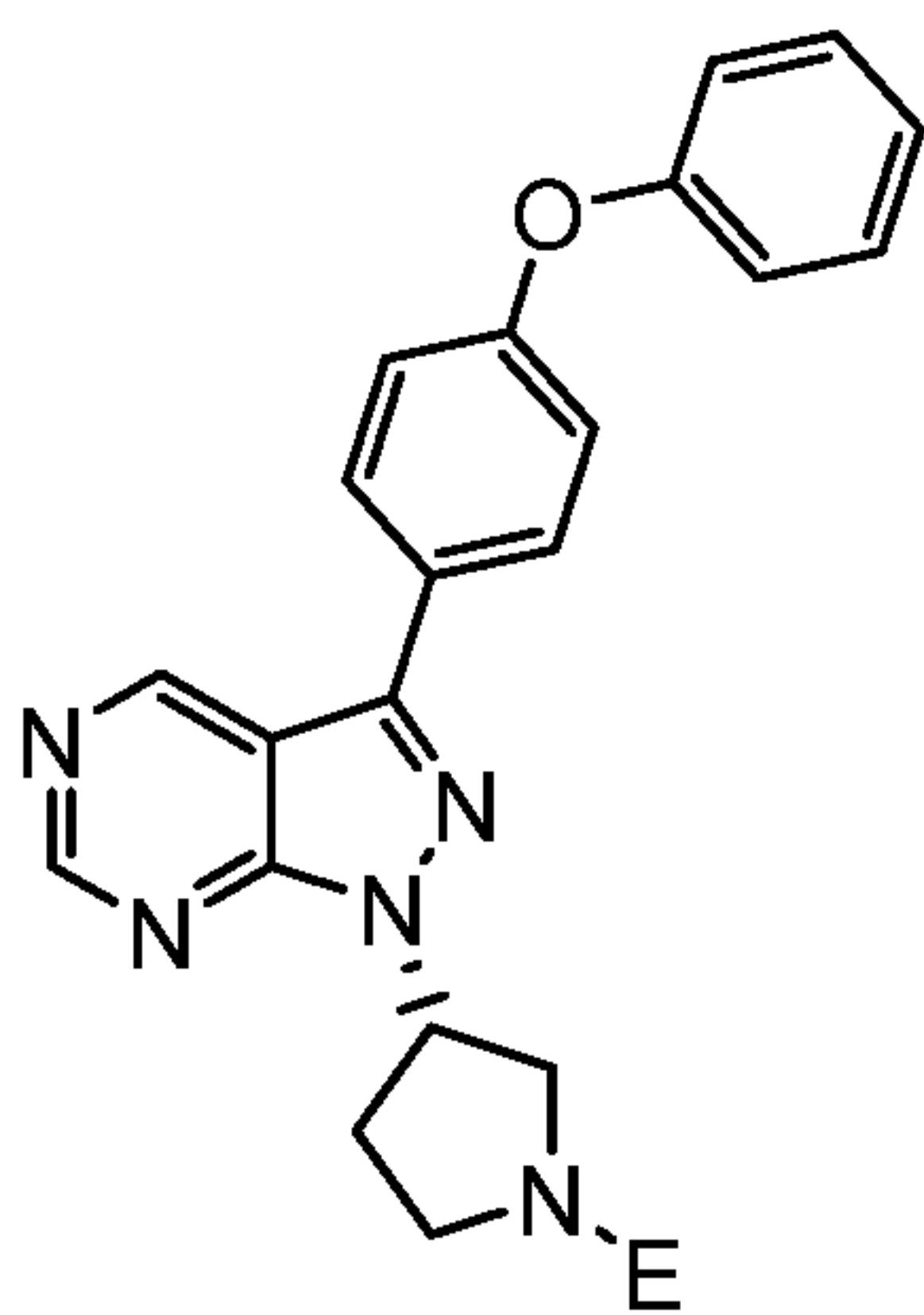
compound has the formula: , wherein R^2 , $z2$, and E are as described herein.



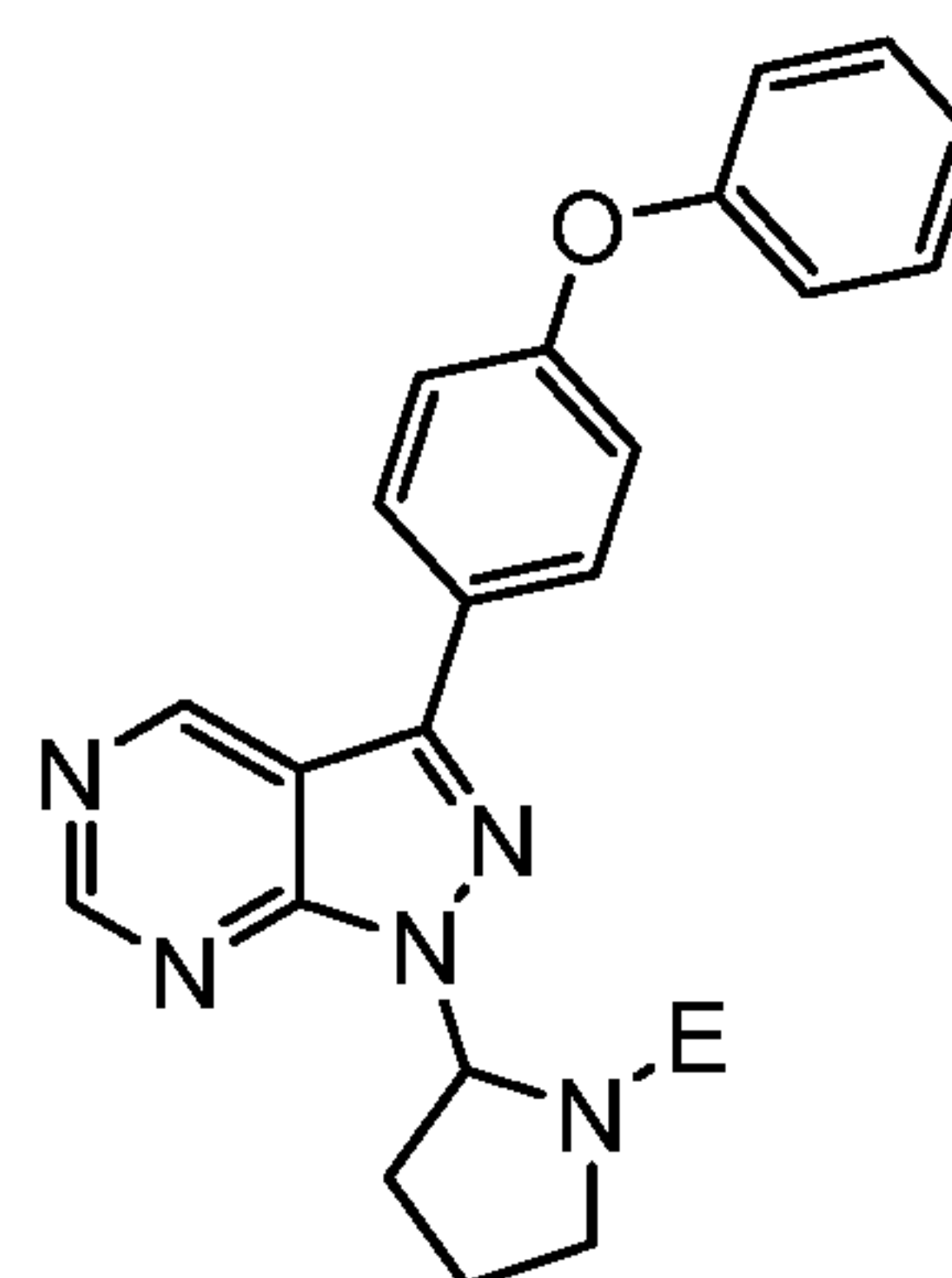
[0572] In embodiments, the compound has the formula: , wherein E is as described herein. In embodiments, the compound has the formula:



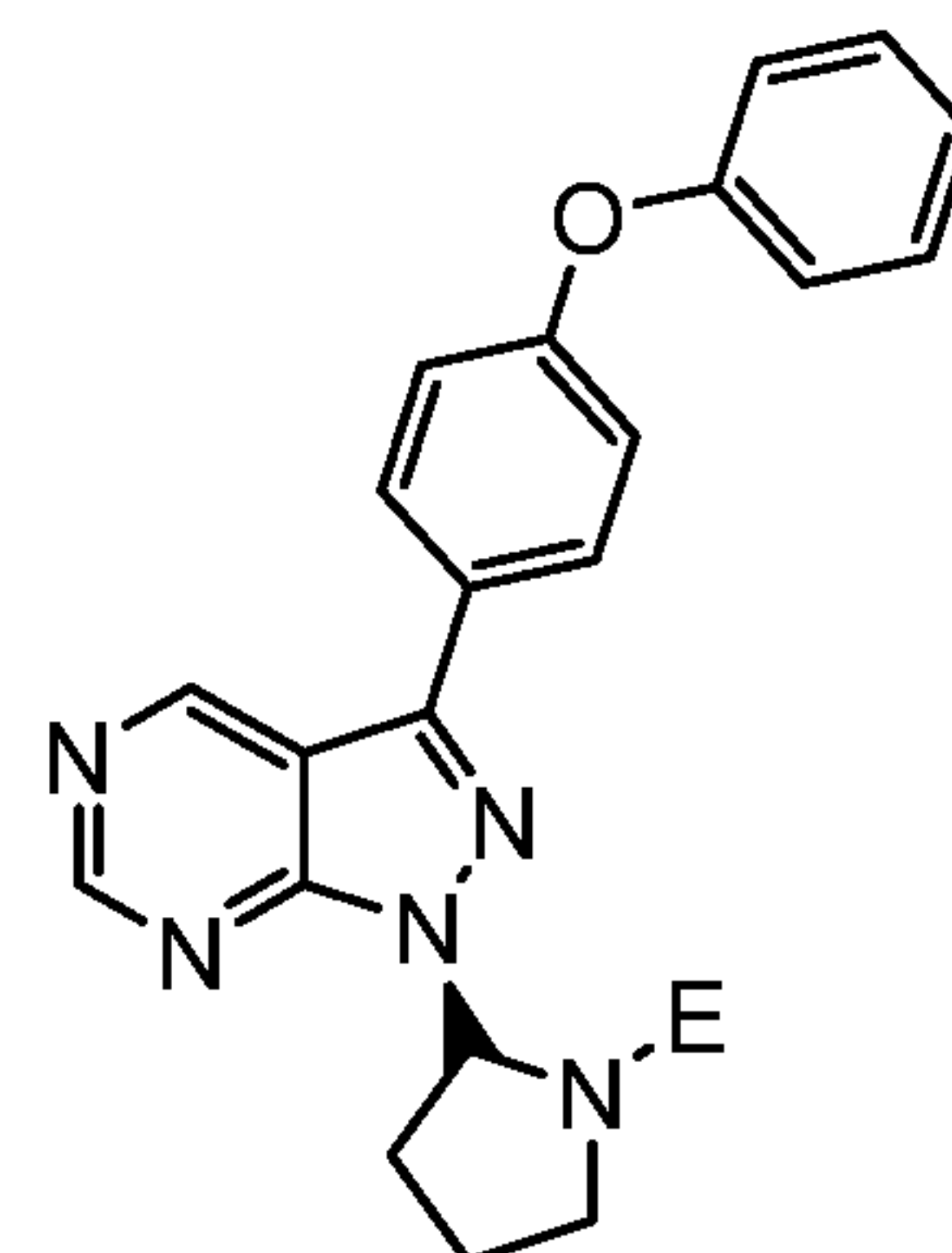
5 , wherein E is as described herein, the compound has the formula:



, wherein E is as described herein.

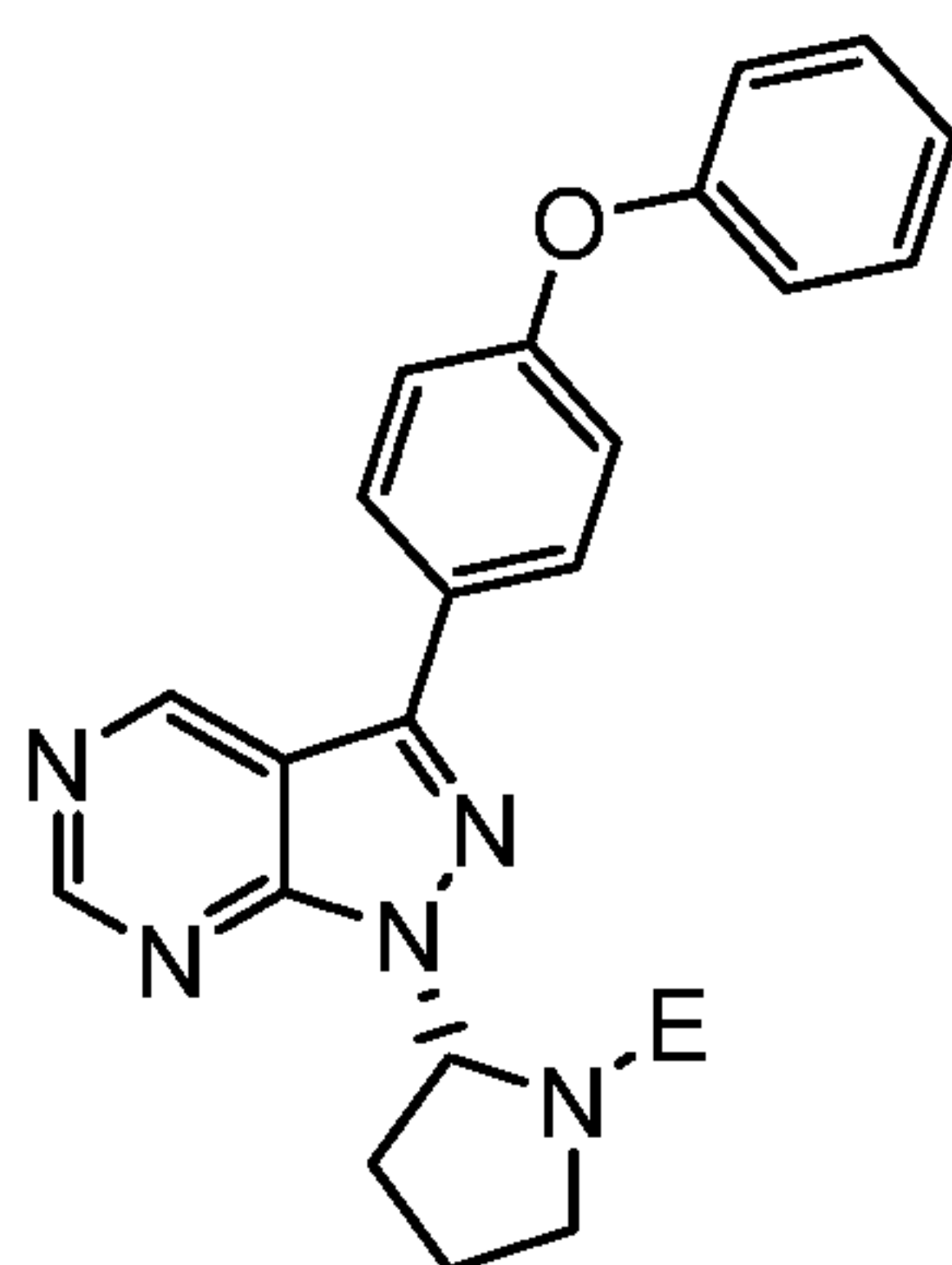


[0573] In embodiments, the compound has the formula: , wherein E

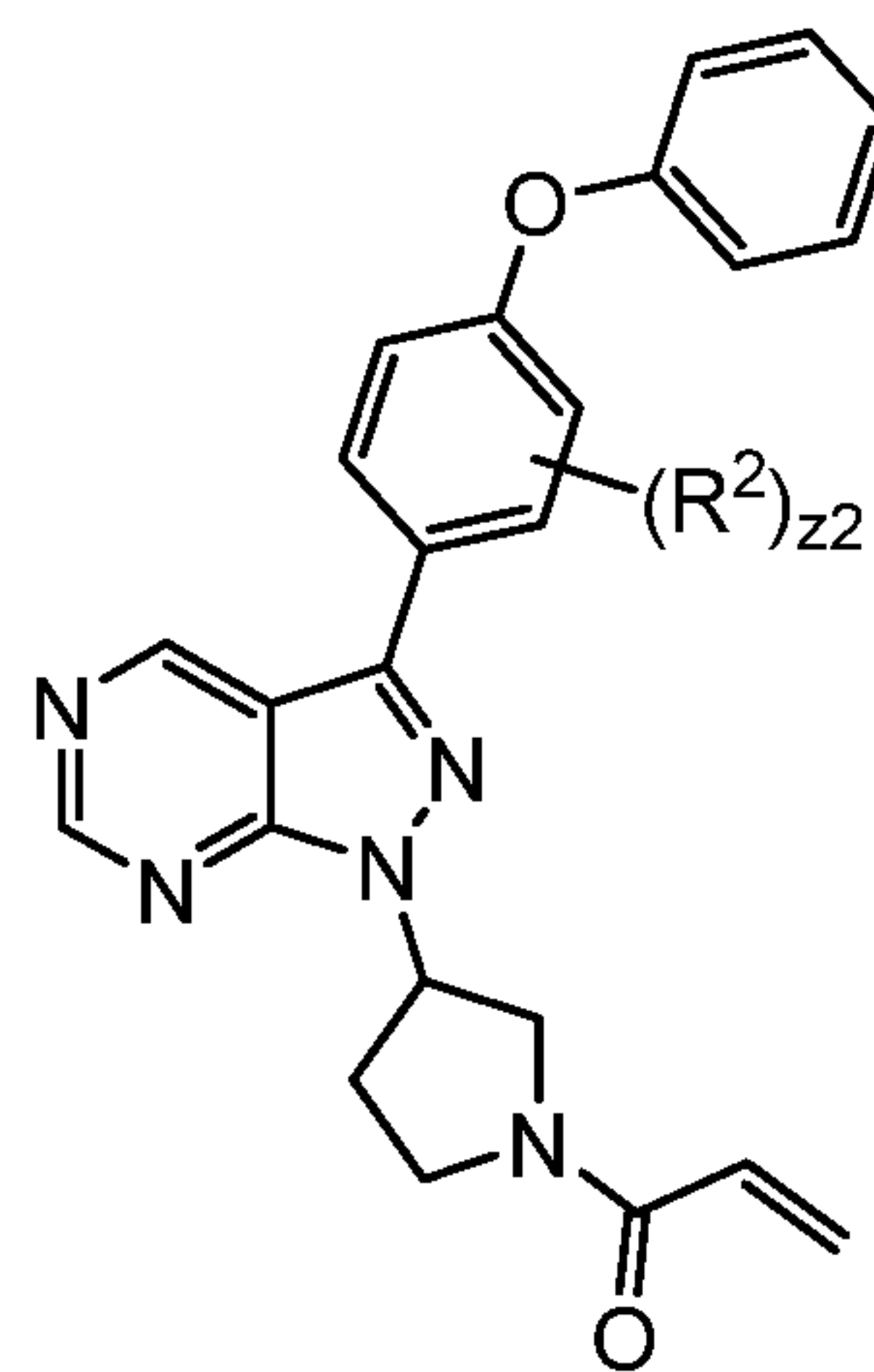


is as described herein. In embodiments, the compound has the formula:

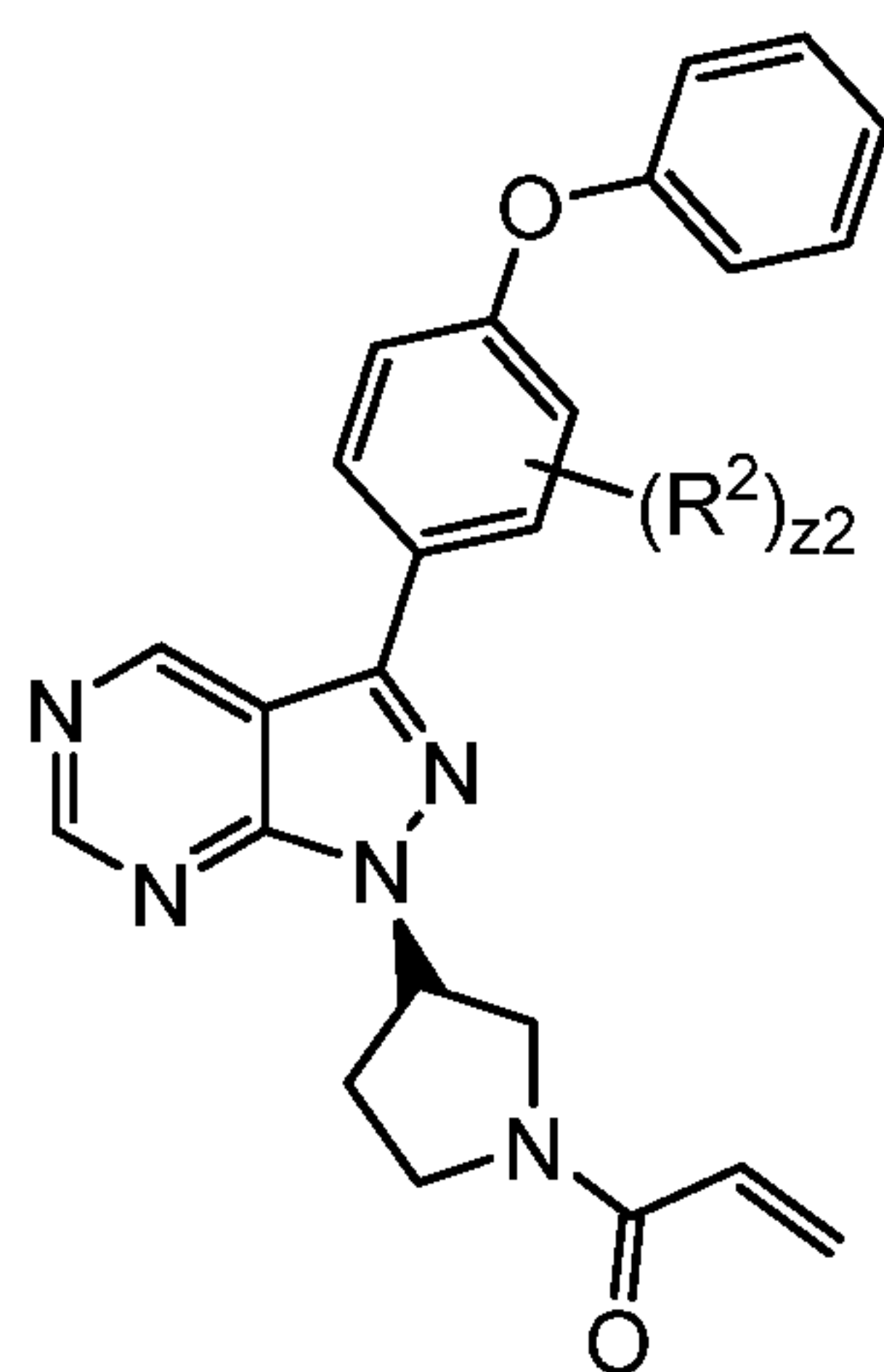
, wherein E is as described herein. In embodiments, the compound has the formula:



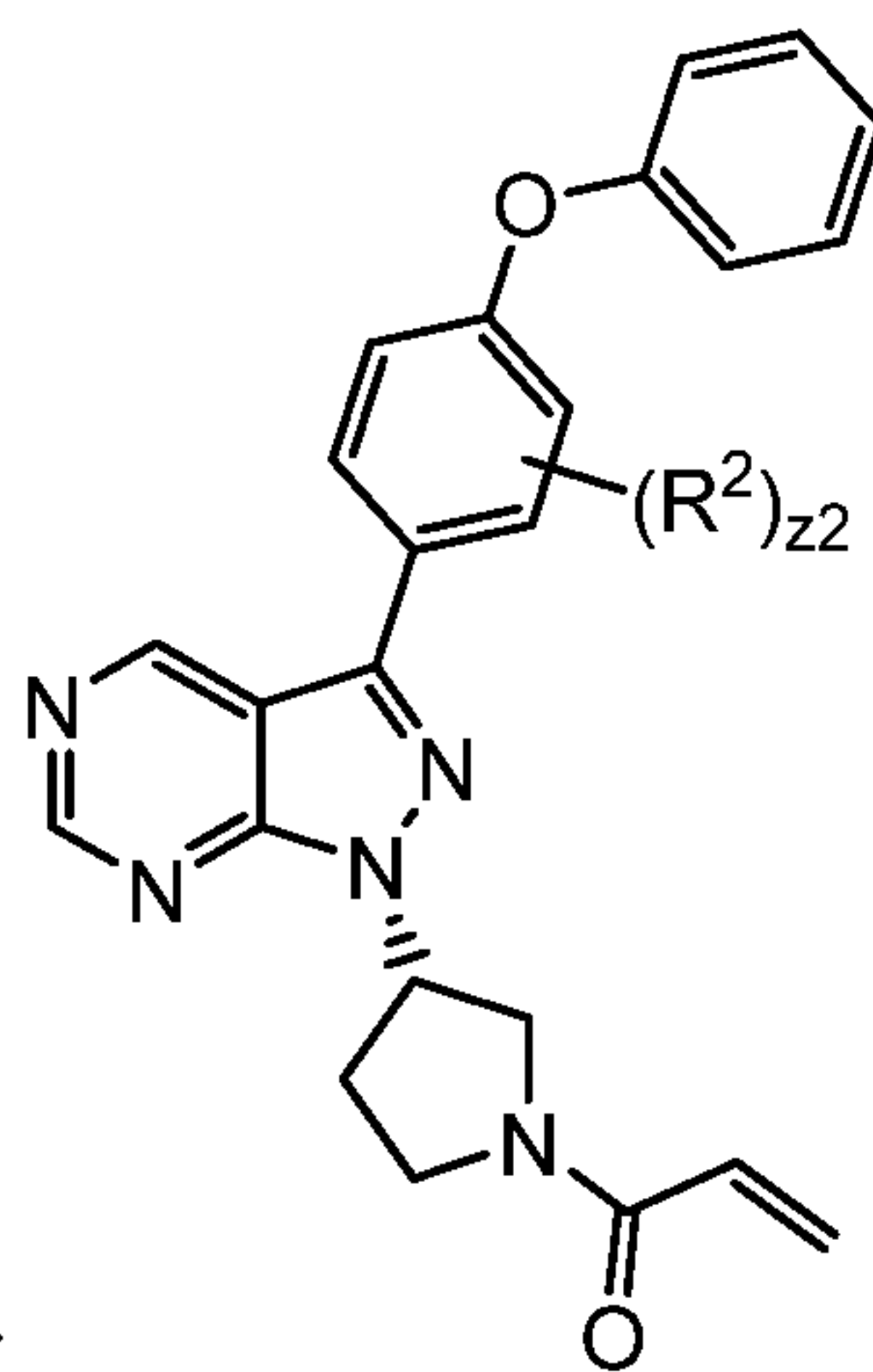
, wherein E is as described herein.



5 [0574] In embodiments, the compound has the formula: , wherein R^2 and z_2 are as described herein. In embodiments, the compound has the formula:



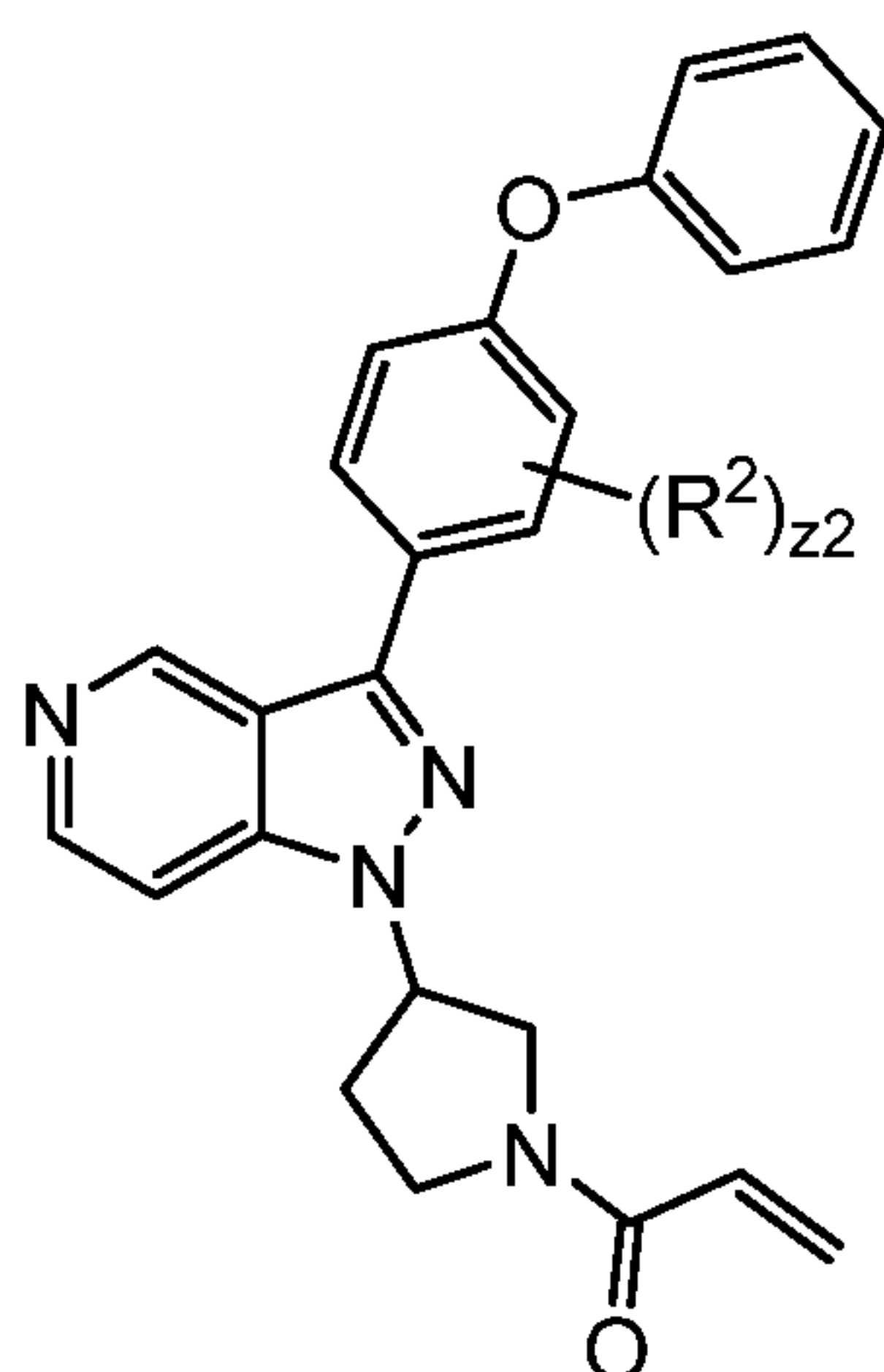
, wherein R^2 and $z2$ are as described herein. In embodiments, the



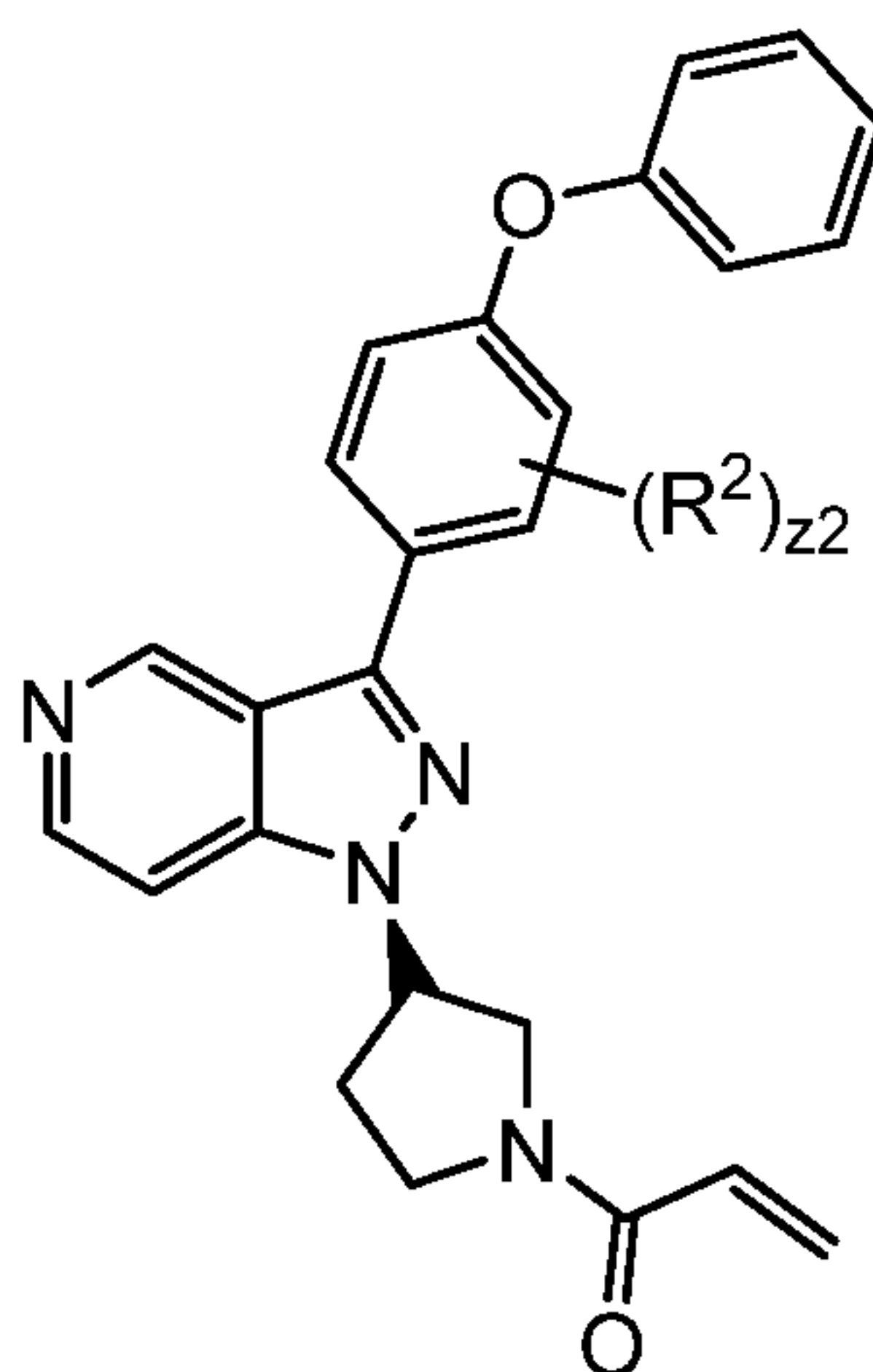
compound has the formula:

, wherein R^2 and $z2$ are as described herein.

[0575] In embodiments, the compound has the formula:

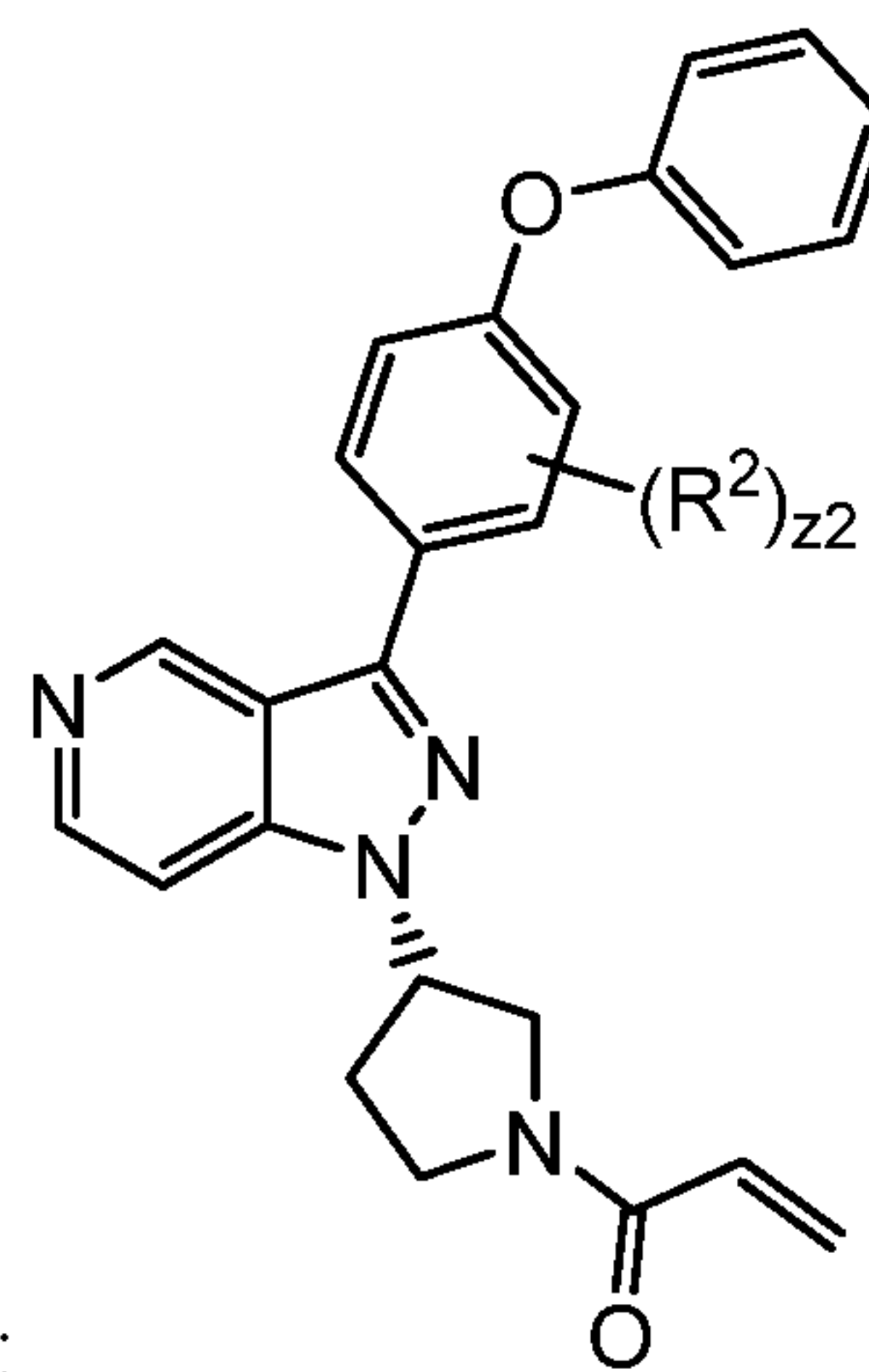


wherein R^2 and $z2$ are as described herein. In embodiments, the



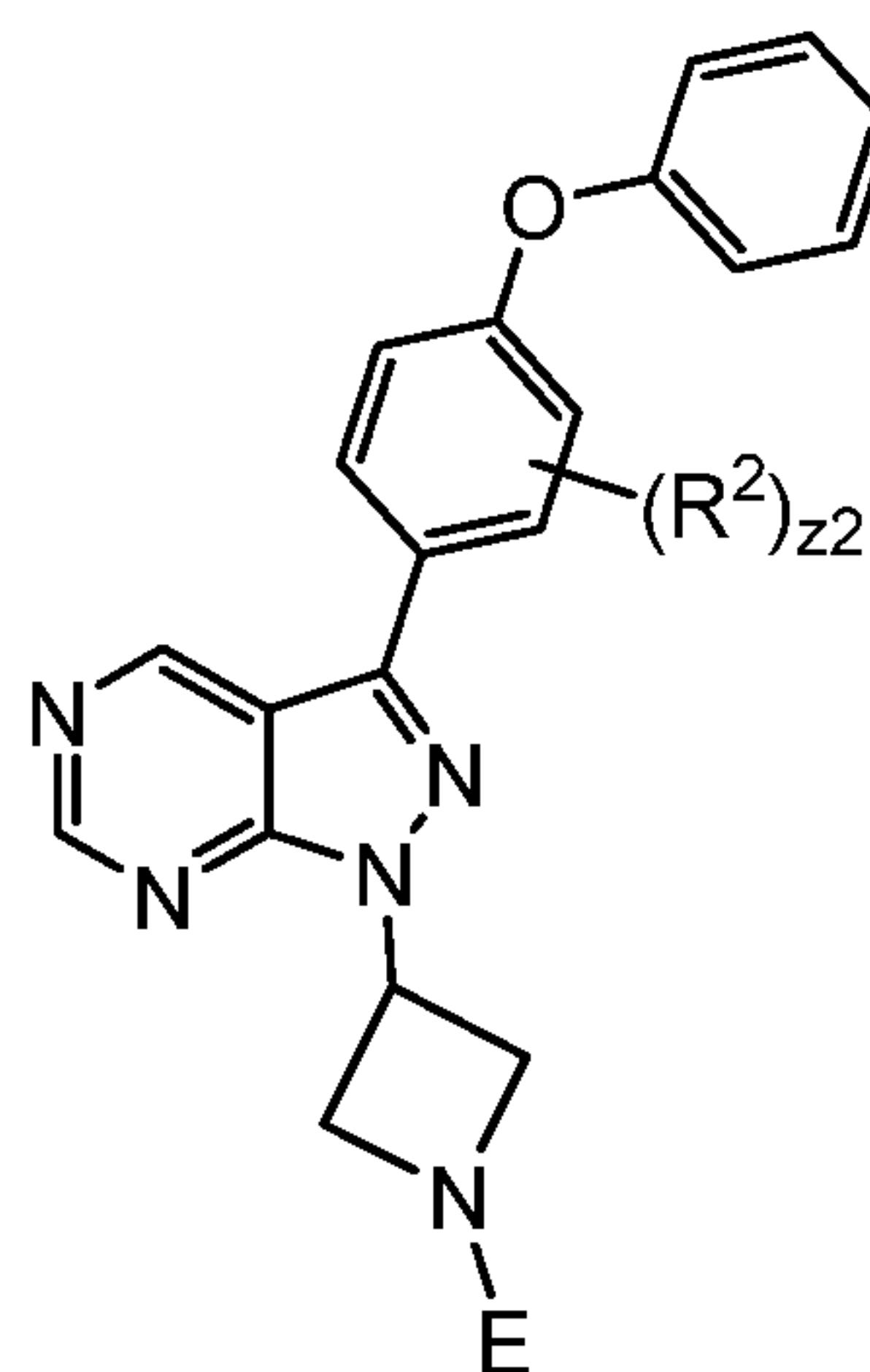
compound has the formula:

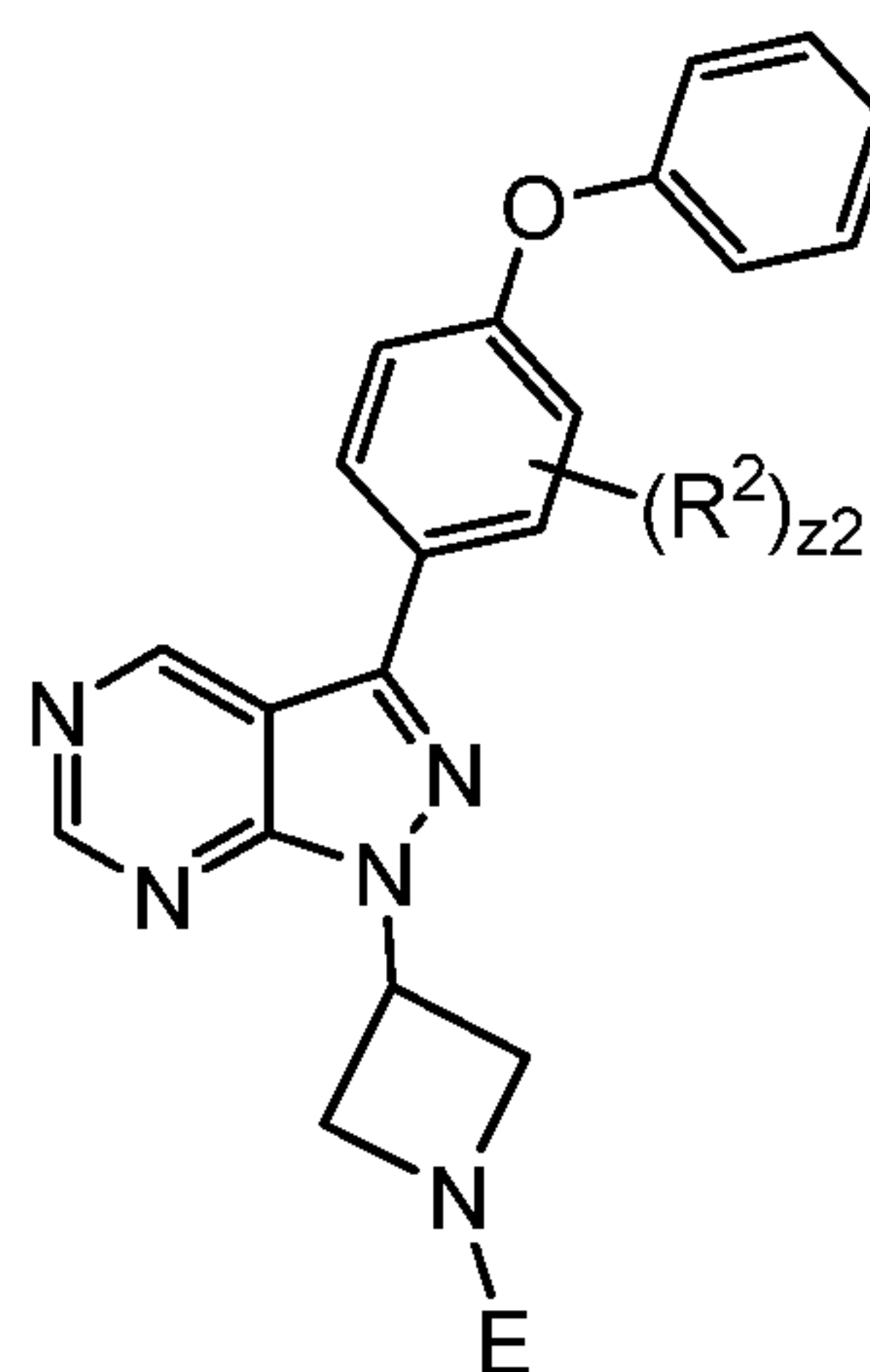
wherein R^2 and $z2$ are as described herein.

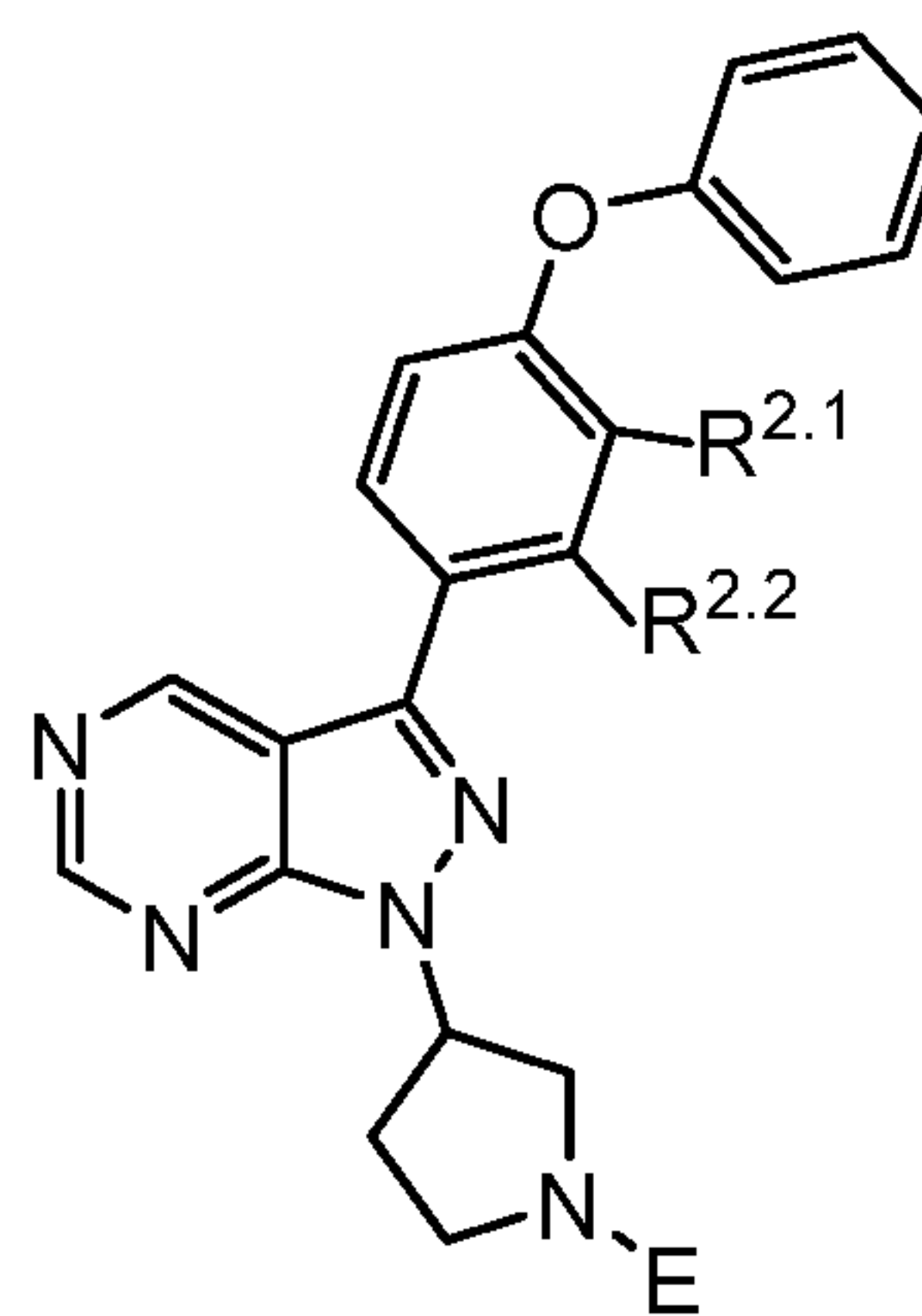


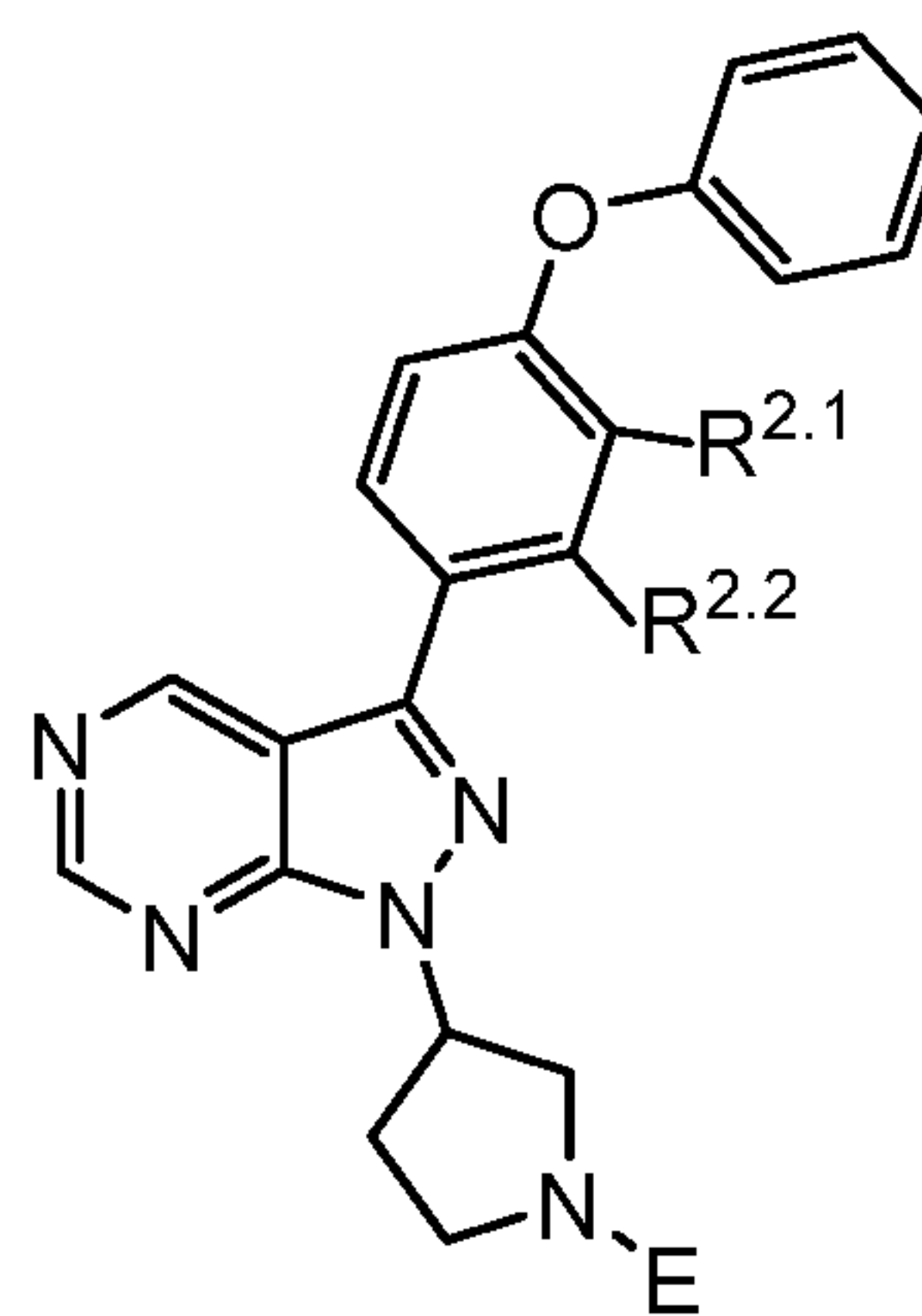
In embodiments, the compound has the formula:
are as described herein.

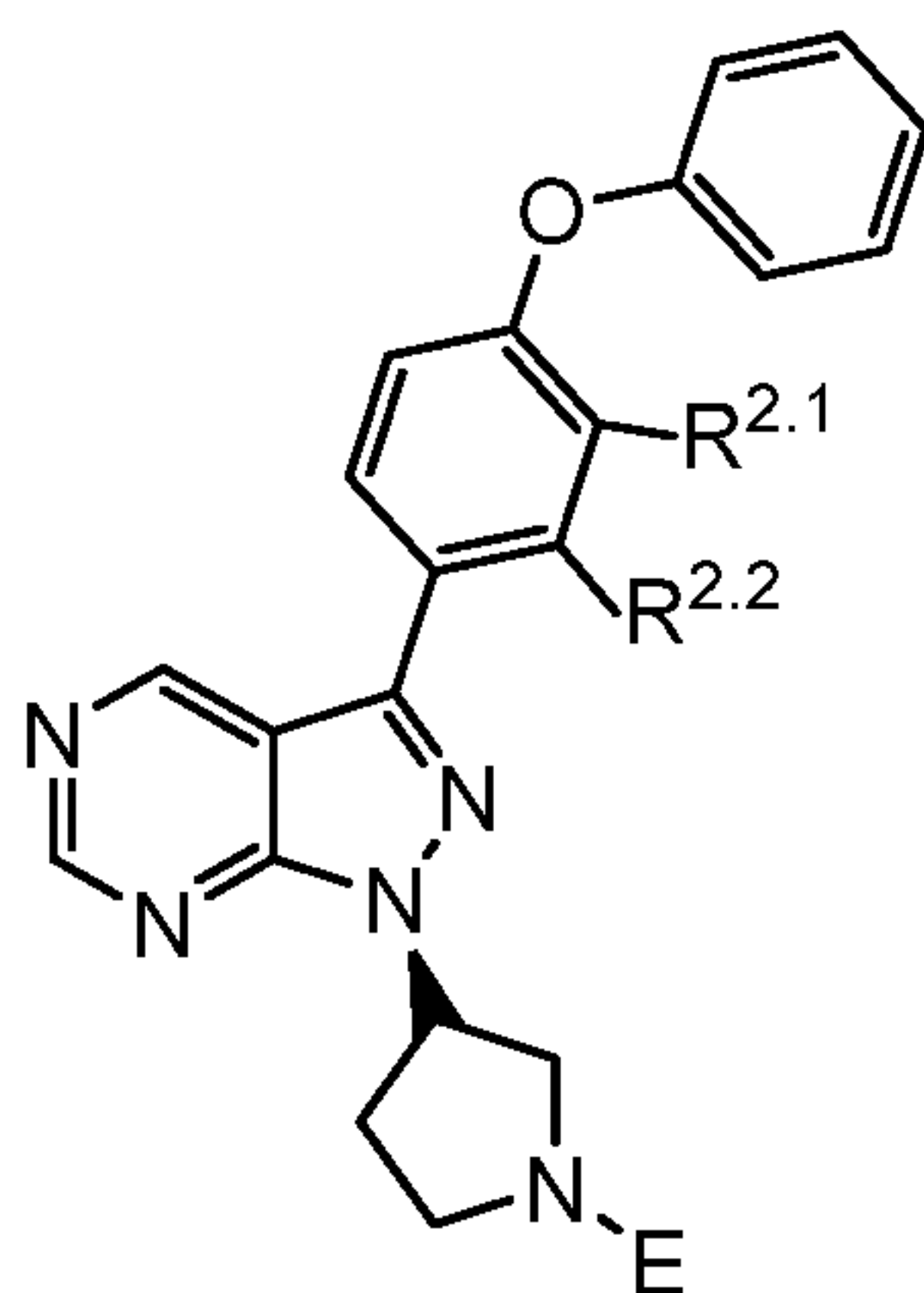
, wherein R^2 and $z2$

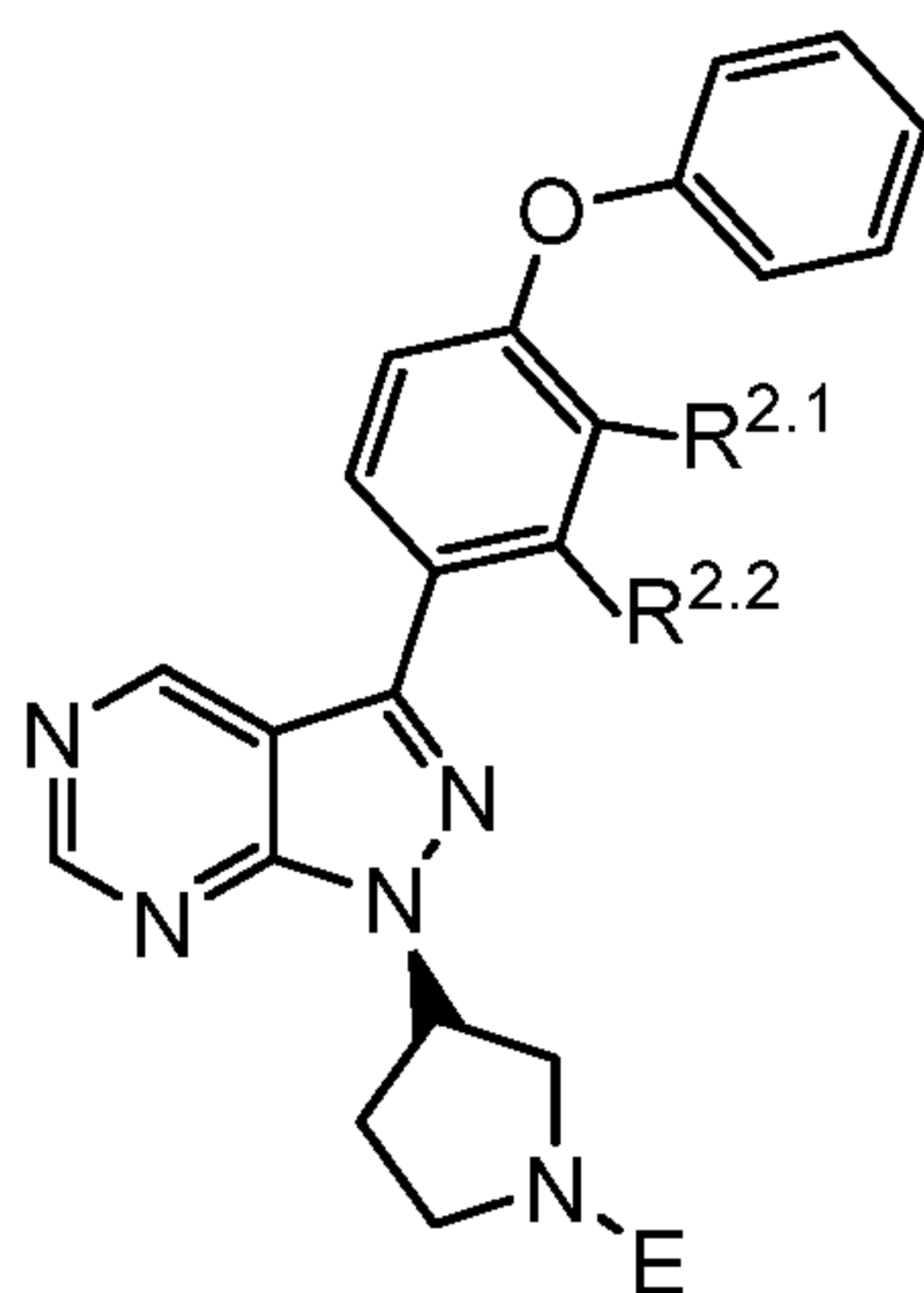


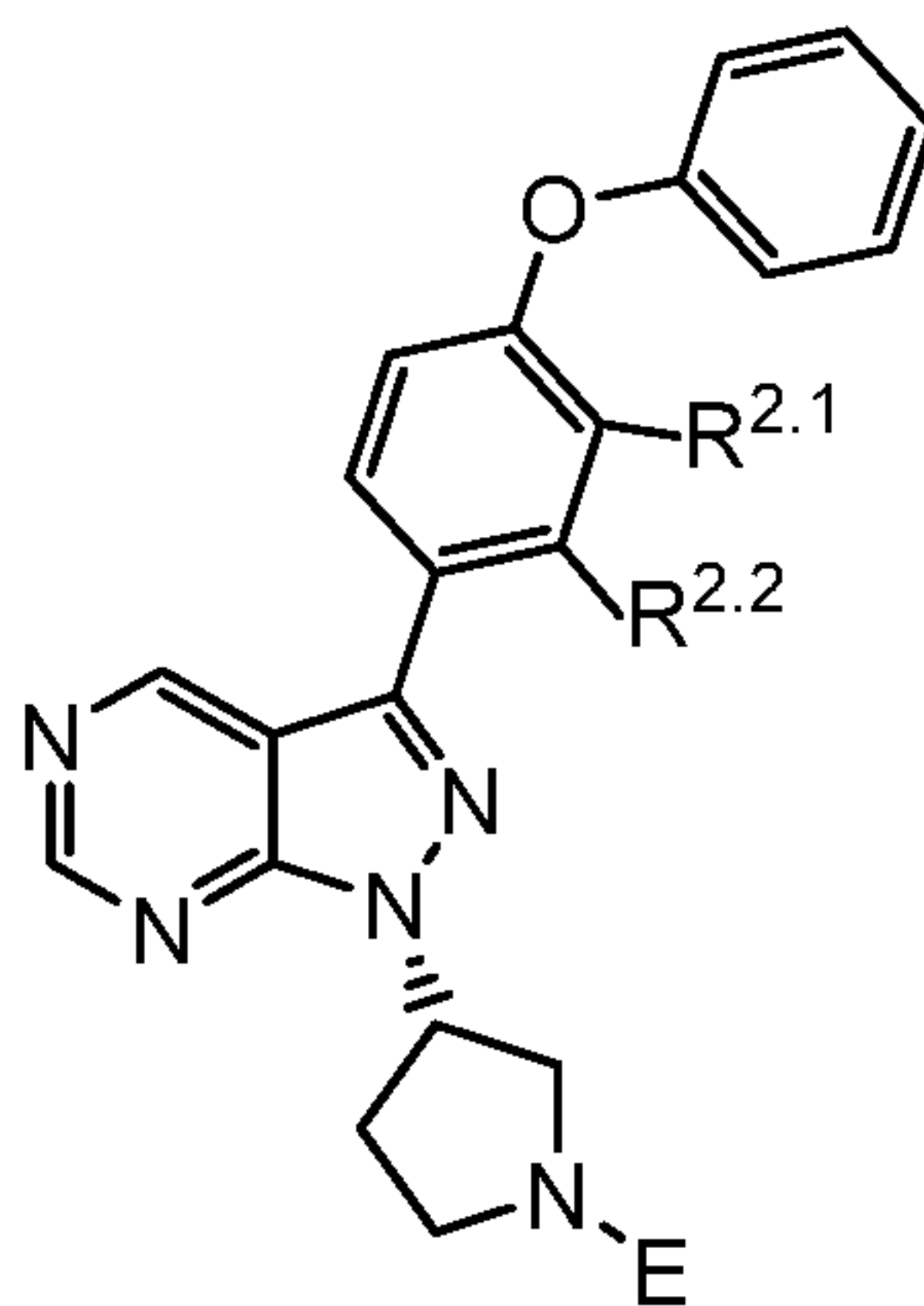
[0576] In embodiments, the compound has the formula: , wherein R^2 , z_2 , and E are as described herein.

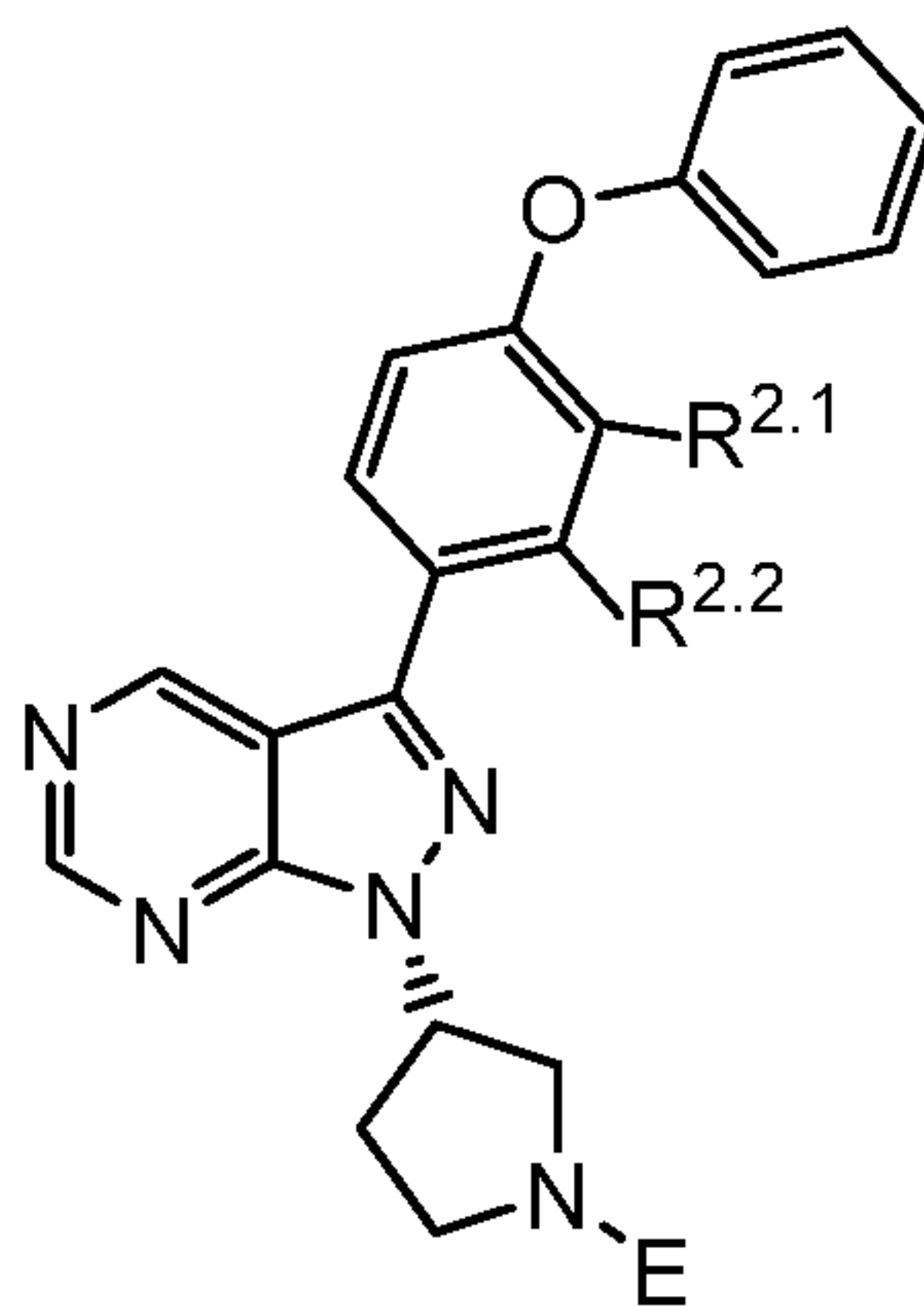


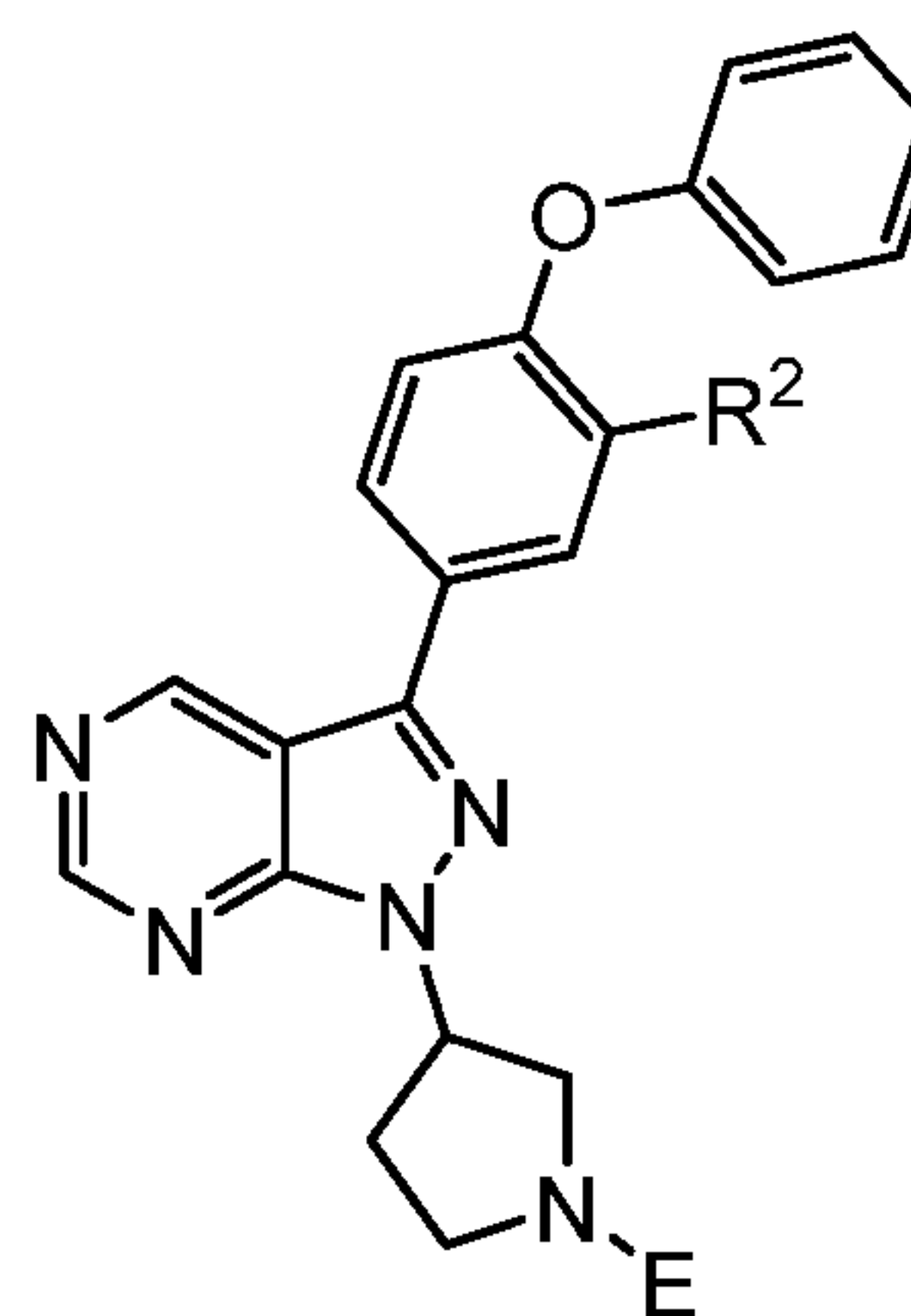
[0577] In embodiments, the compound has the formula: , wherein E is as described herein. $R^{2.1}$ and $R^{2.2}$ are each R^1 at a fixed position on the attached ring. $R^{2.1}$ and $R^{2.2}$ may be any substituent of R^2 described herein, including in any aspect, embodiment, example, figure, or claim. In embodiments, the compound has the formula:

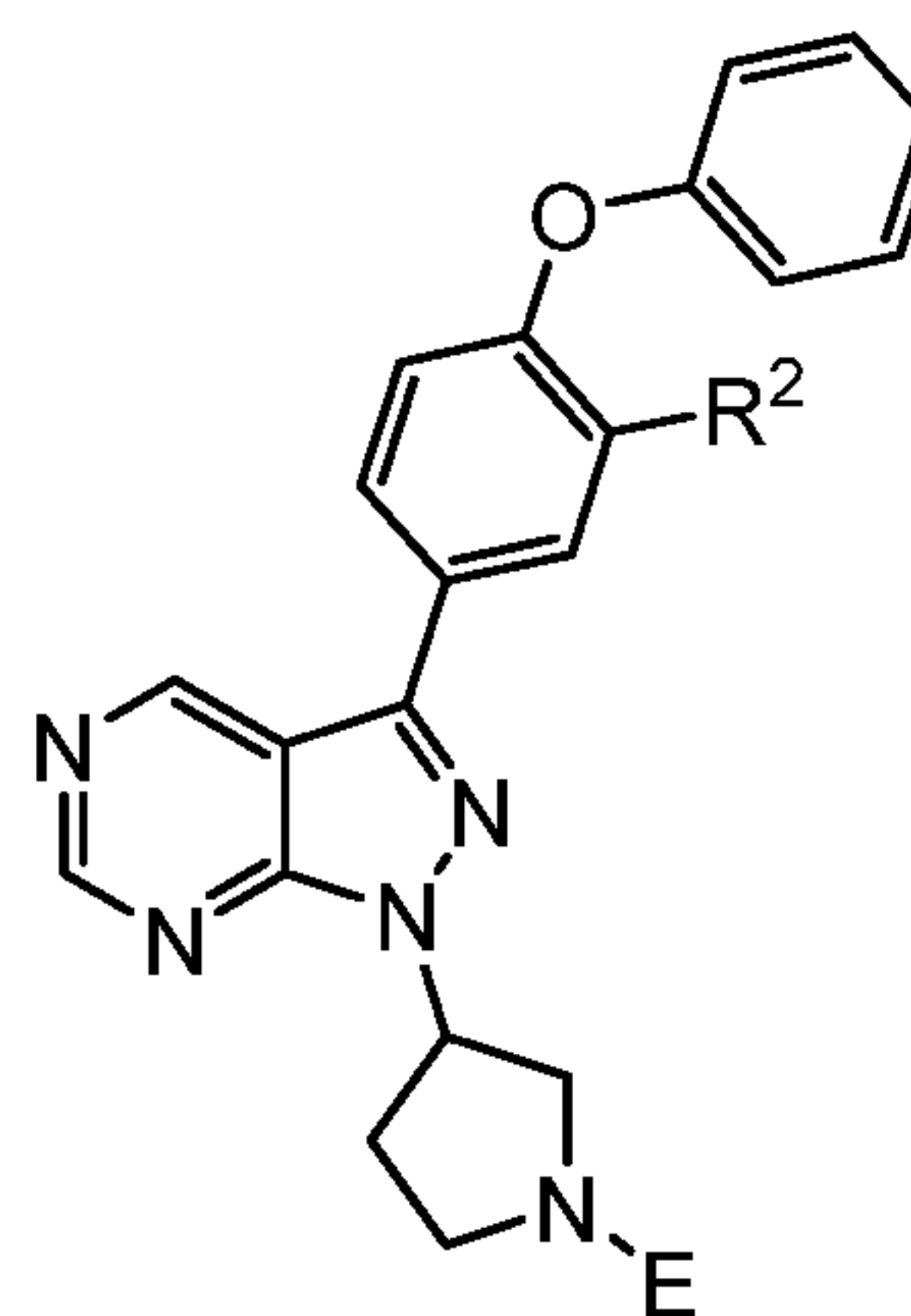


, wherein E is as described herein. $R^{2.1}$ and $R^{2.2}$ are each R^1 at a fixed position on the attached ring. $R^{2.1}$ and $R^{2.2}$ may be any substituent of R^2 described herein, including in any aspect, embodiment, example, figure, or claim. In embodiments, the

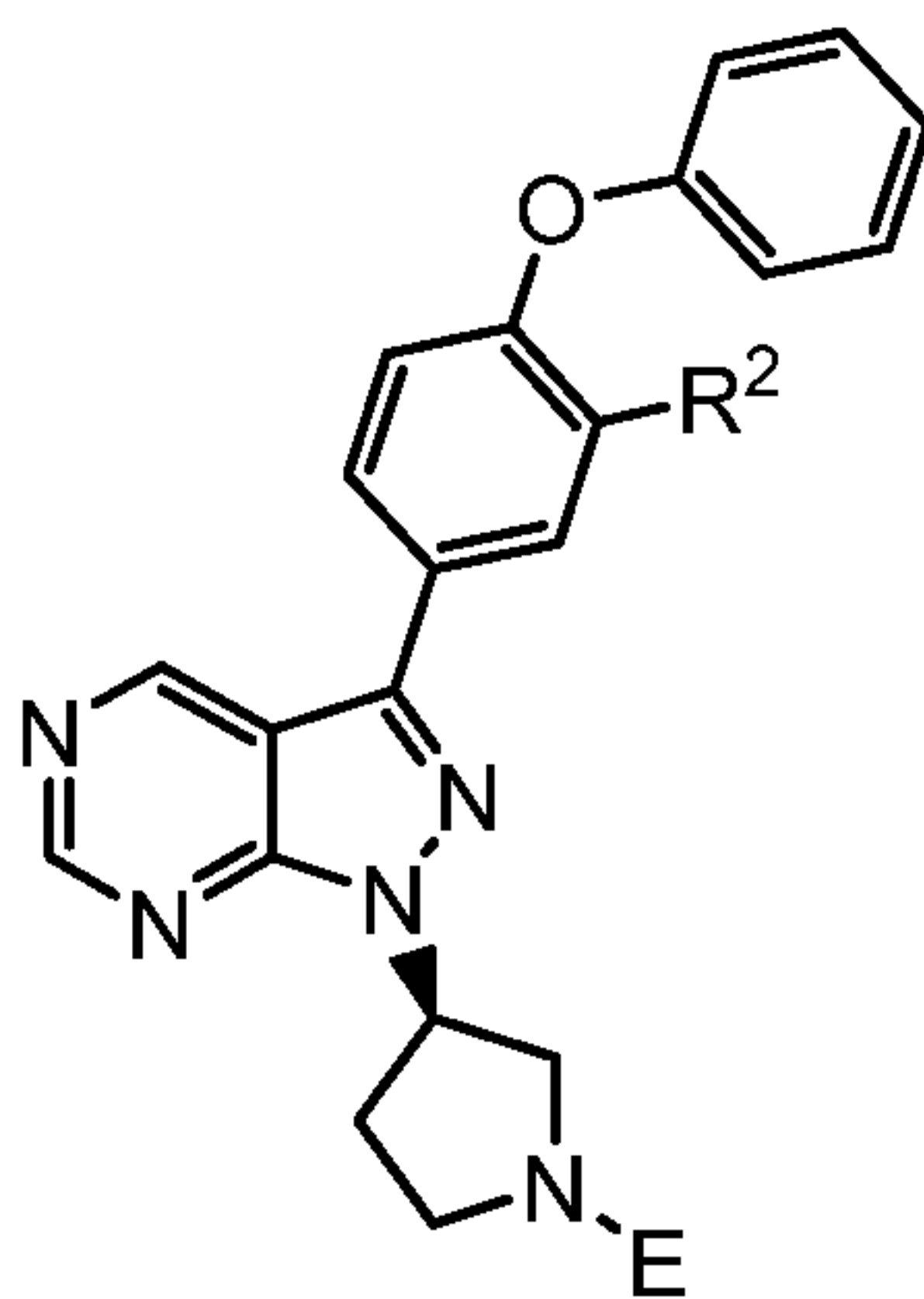


compound has the formula: , wherein E is as described herein. $R^{2.1}$ and $R^{2.2}$ are each R^1 at a fixed position on the attached ring. $R^{2.1}$ and $R^{2.2}$ may be any substituent of R^2 described herein, including in any aspect, embodiment, example, figure, or claim.

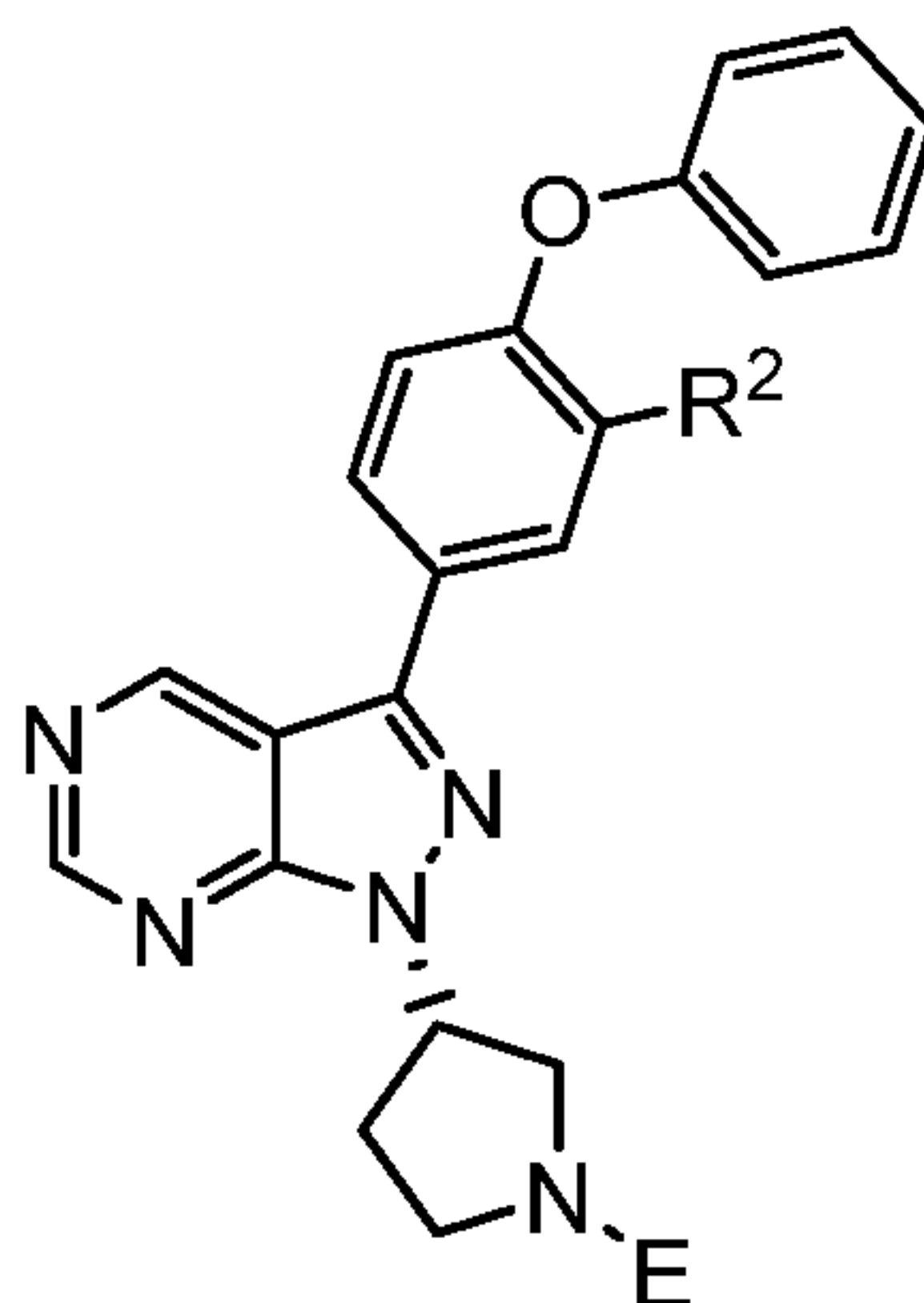


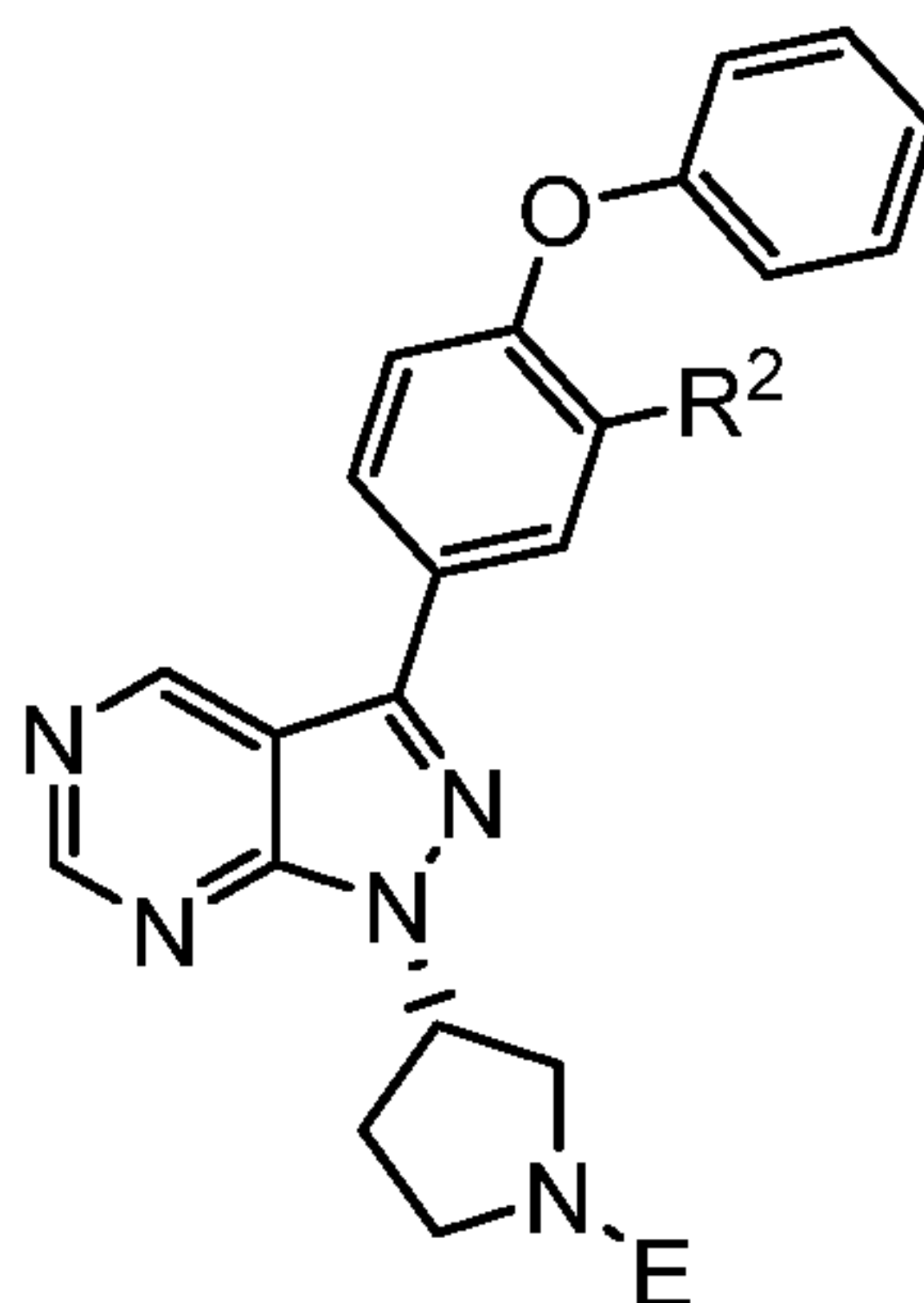
[0578] In embodiments, the compound has the formula: , wherein R^2

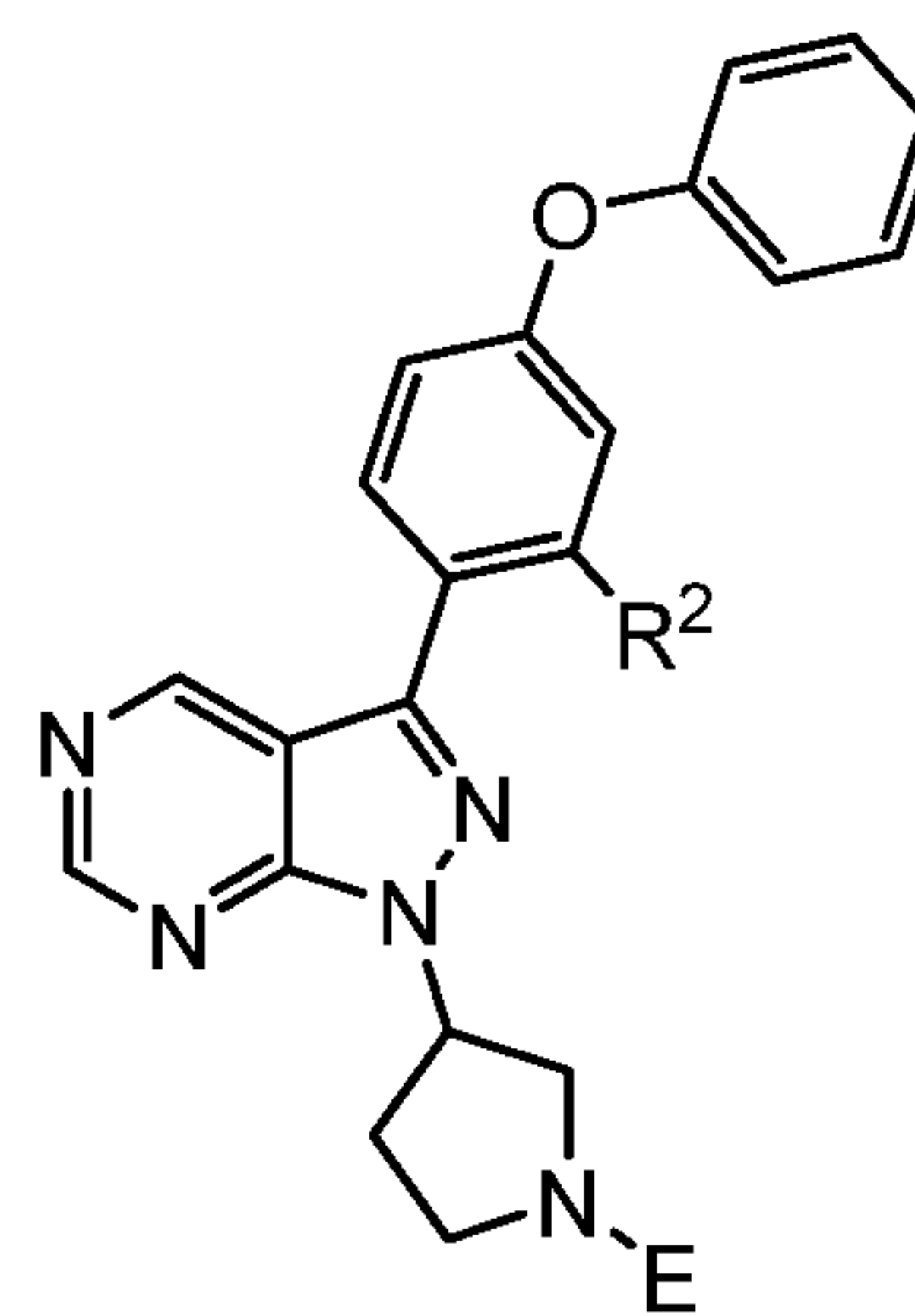
5 and E are as described herein. In embodiments, the compound has the formula:

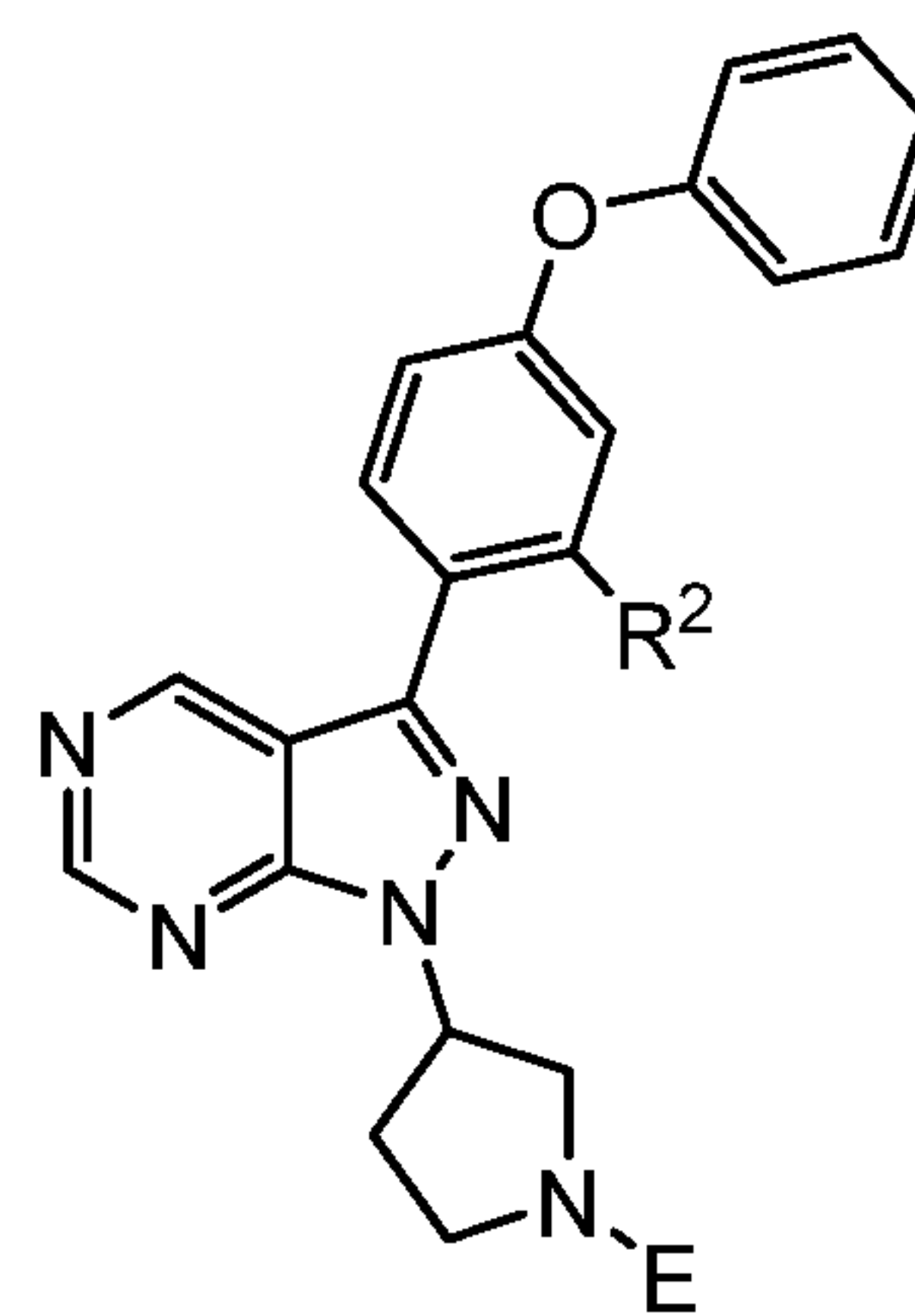


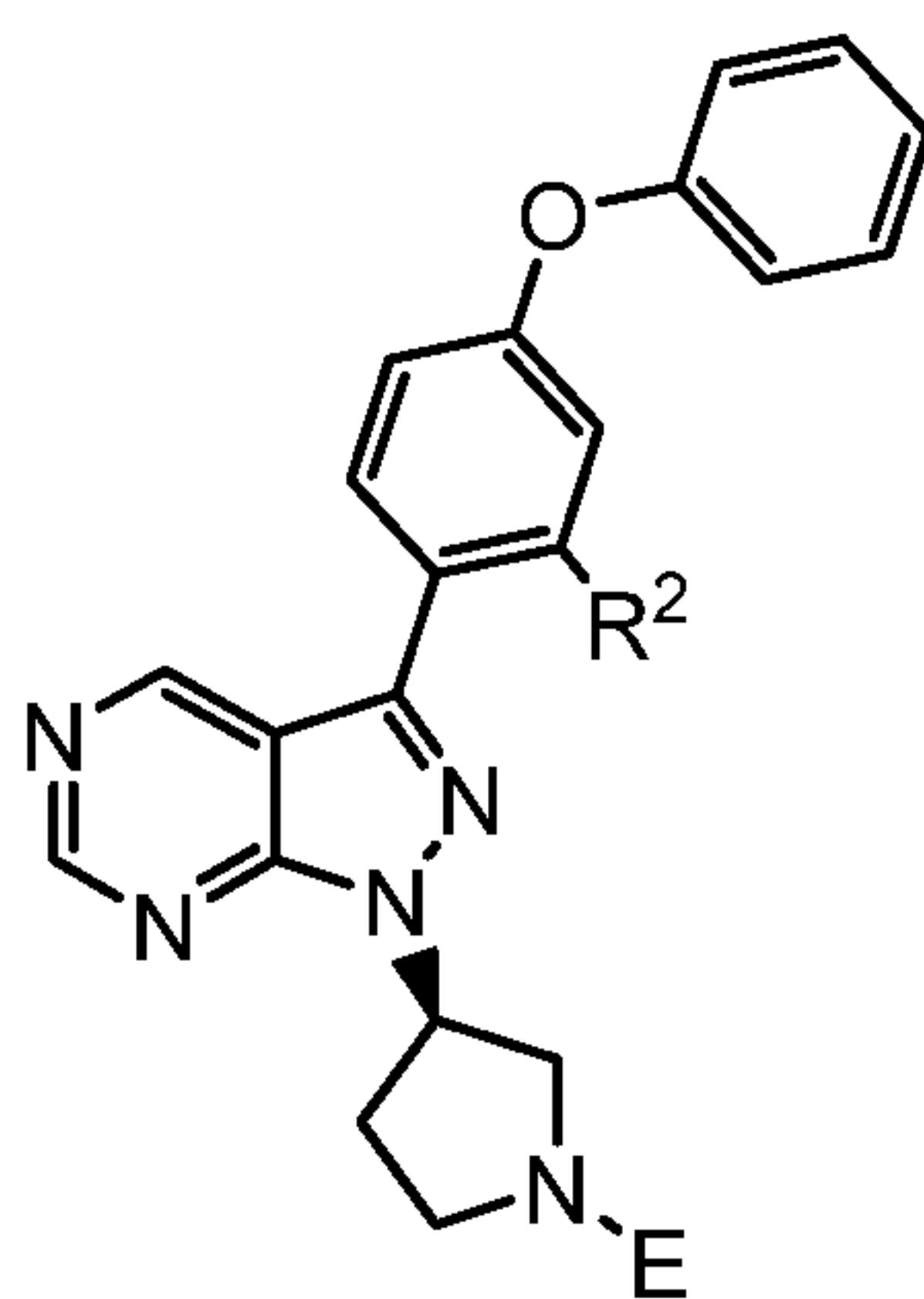
, wherein R^2 and E are as described herein. In embodiments, the



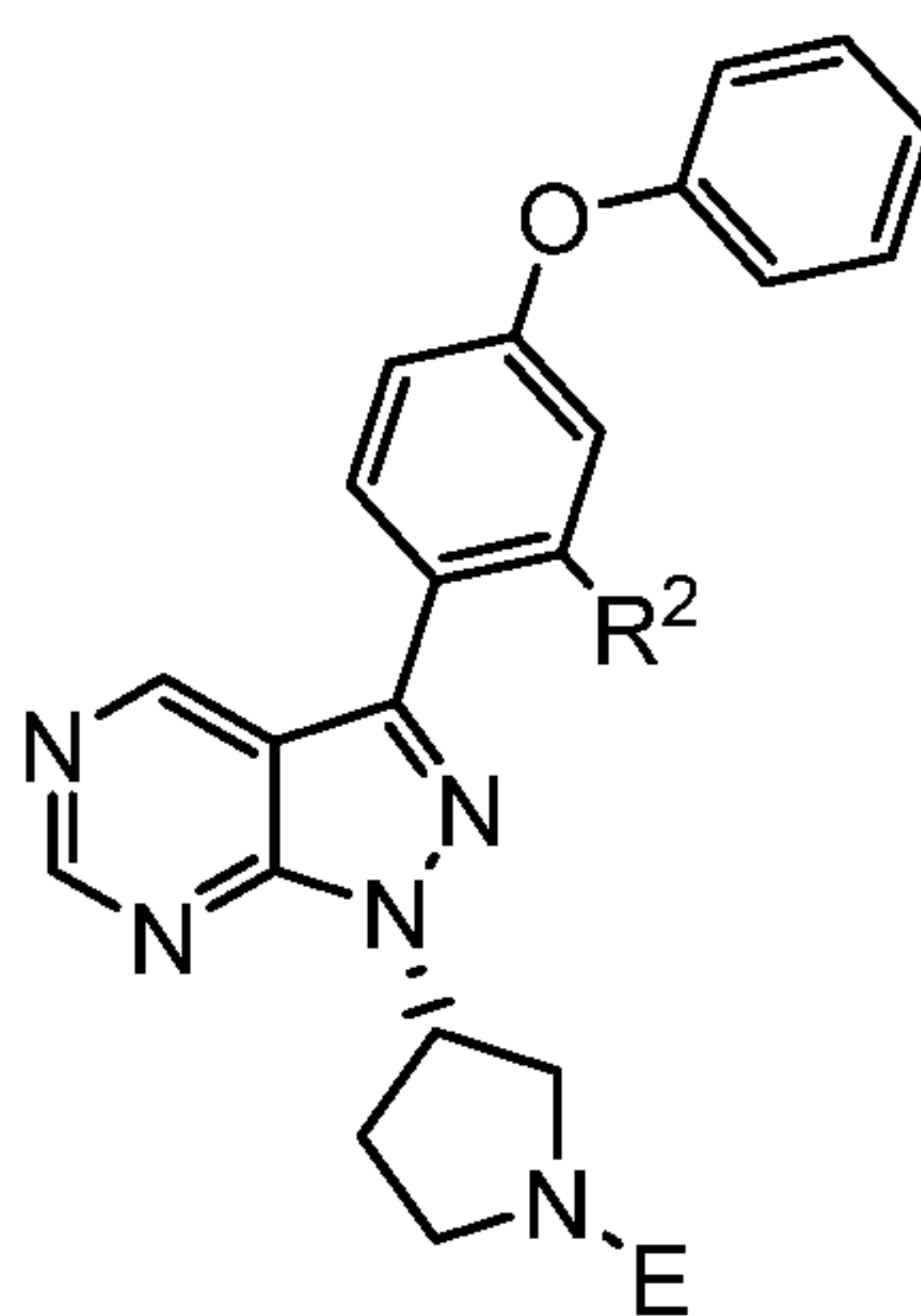
compound has the formula: , wherein R^2 and E are as described herein.

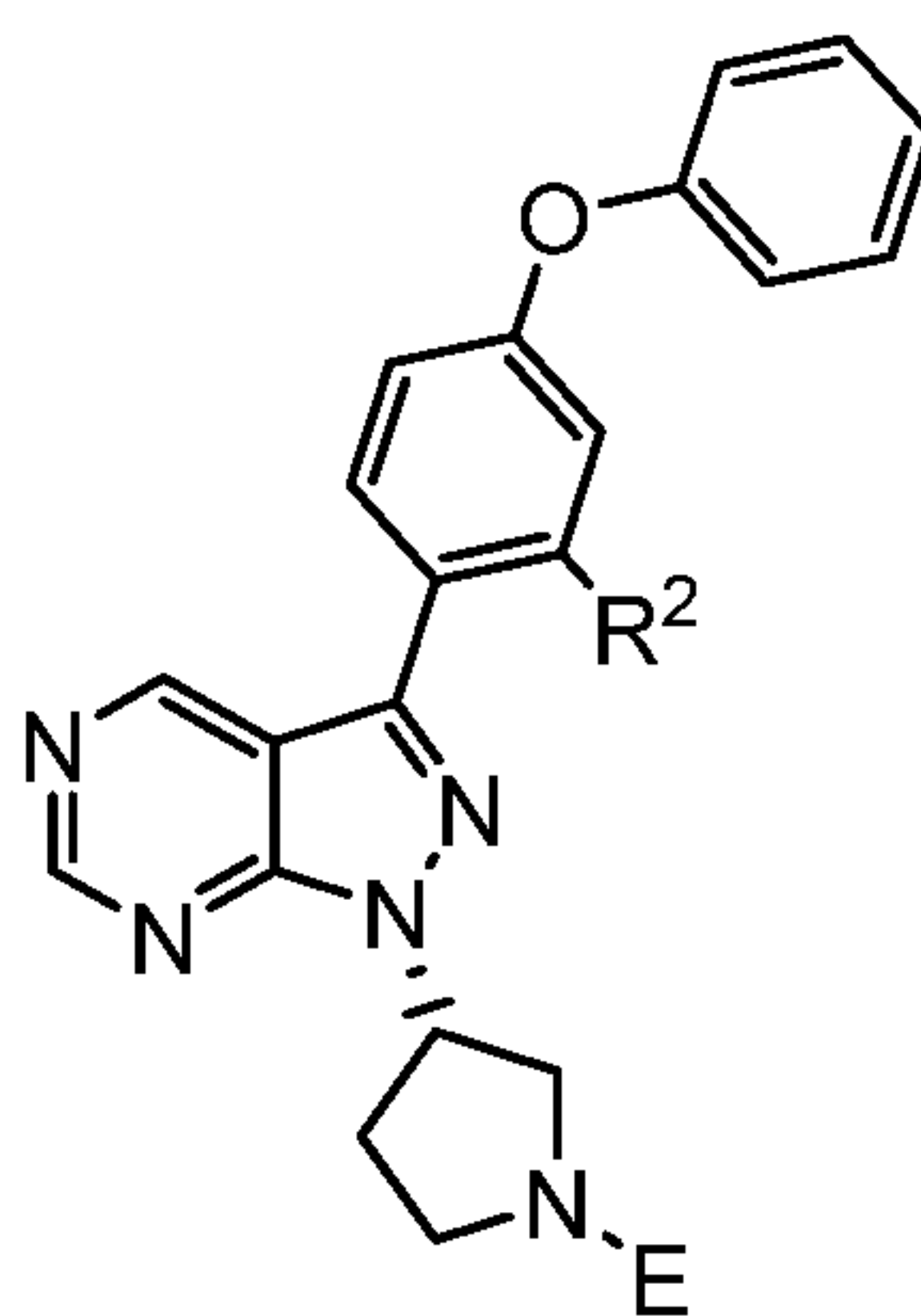


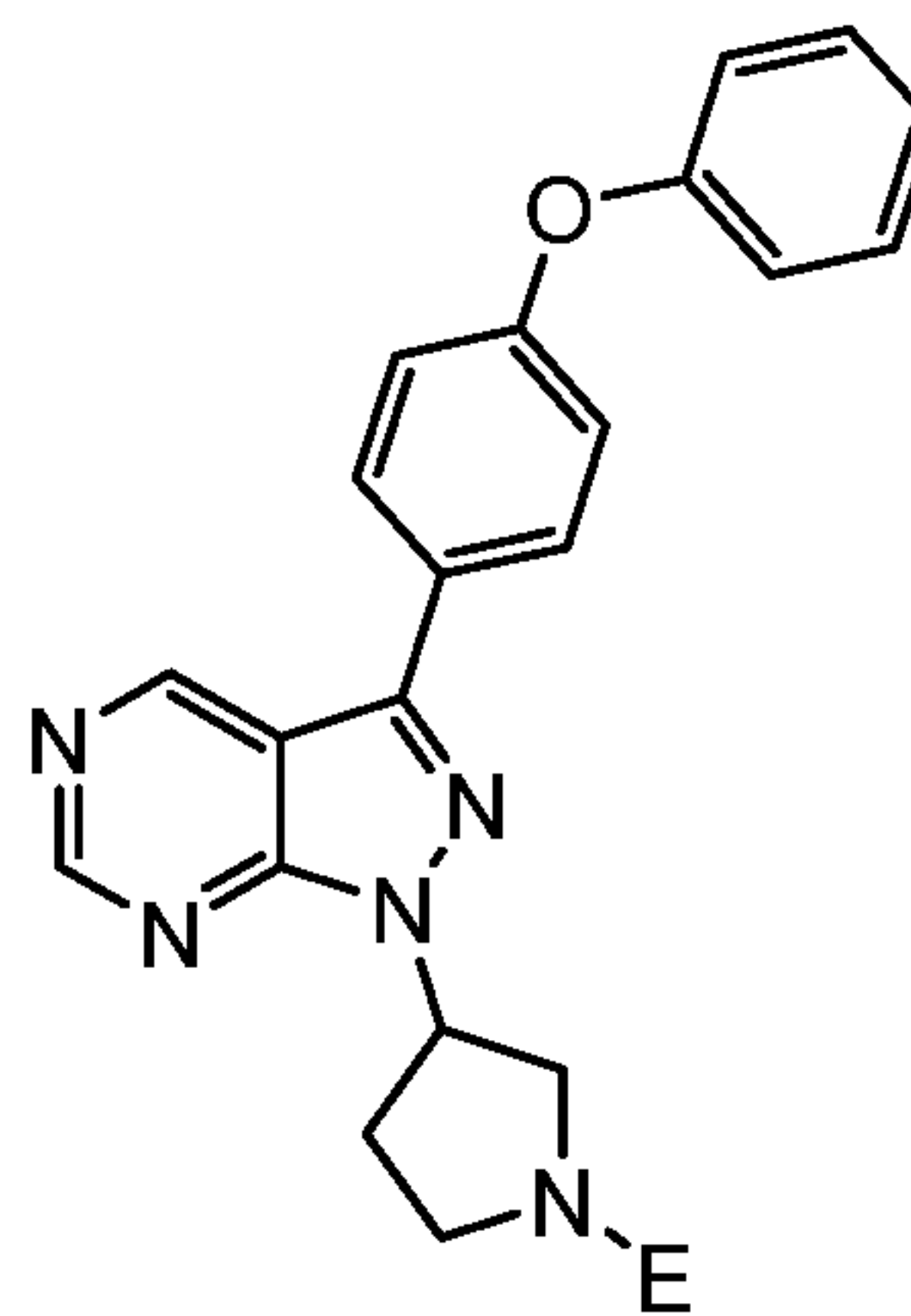
[0579] In embodiments, the compound has the formula: , wherein R² and E are as described herein. In embodiments, the compound has the formula:



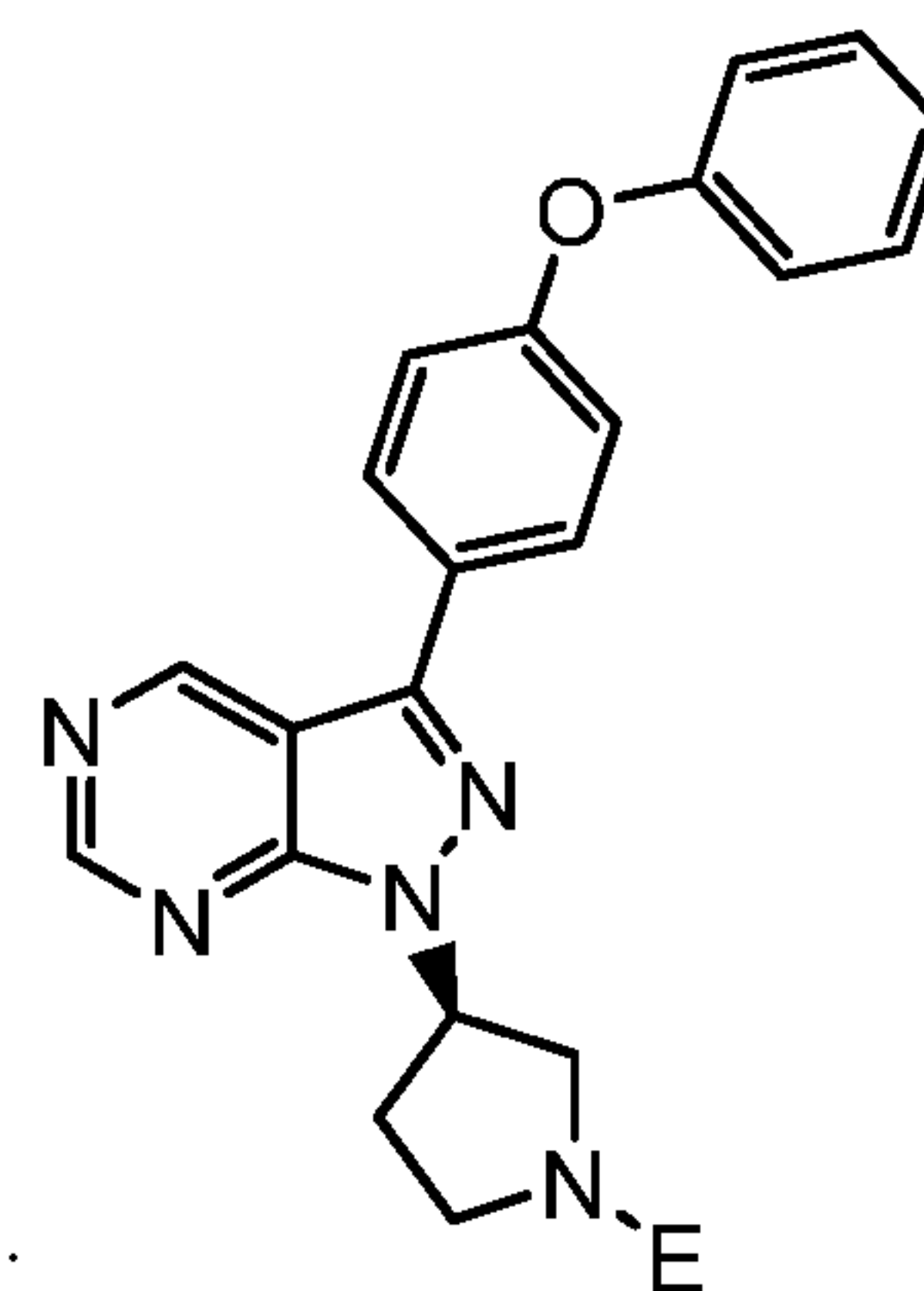
, wherein R² and E are as described herein. In embodiments, the



compound has the formula: , wherein R² and E are as described herein.

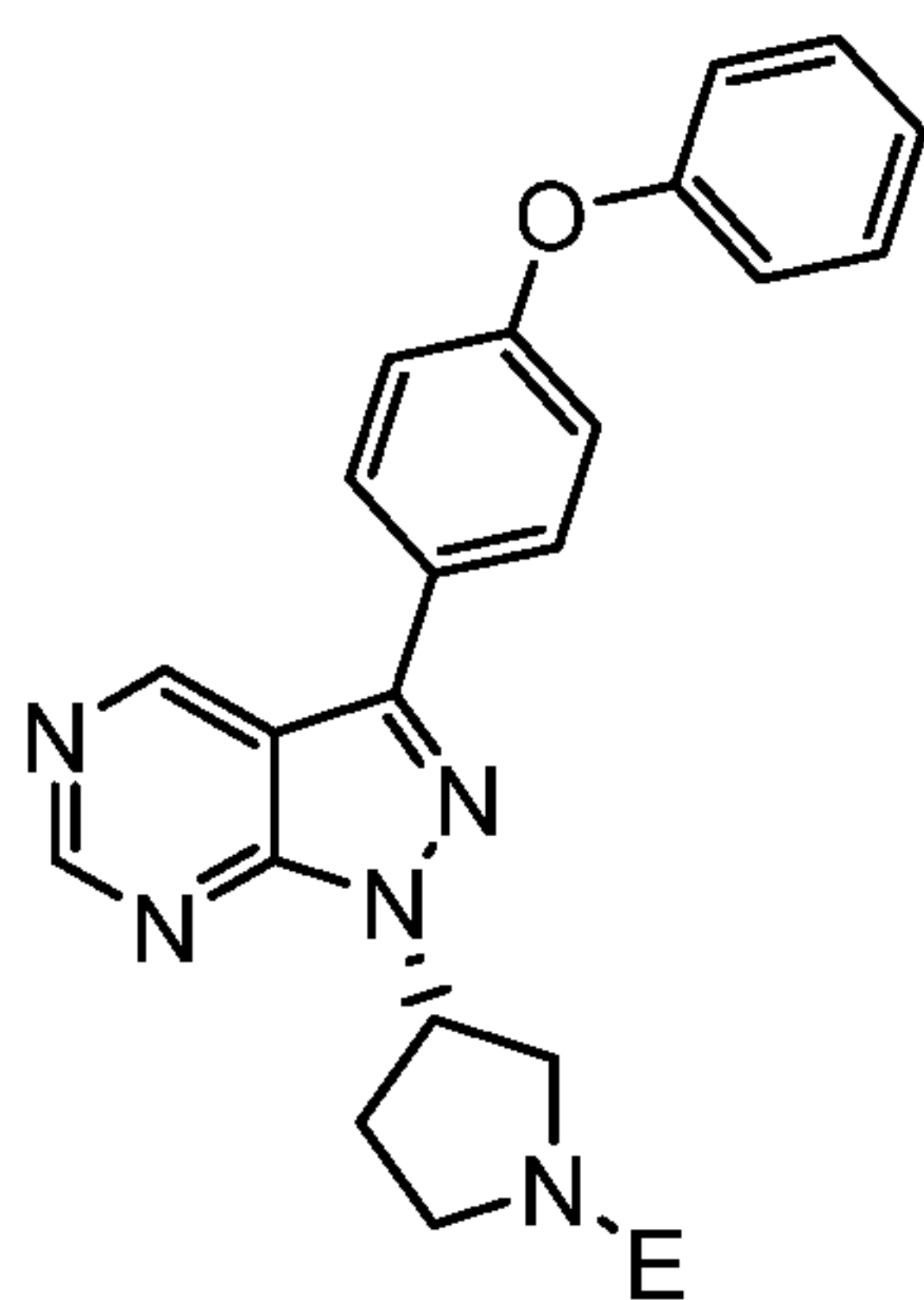


[0580] In embodiments, the compound has the formula: , wherein E

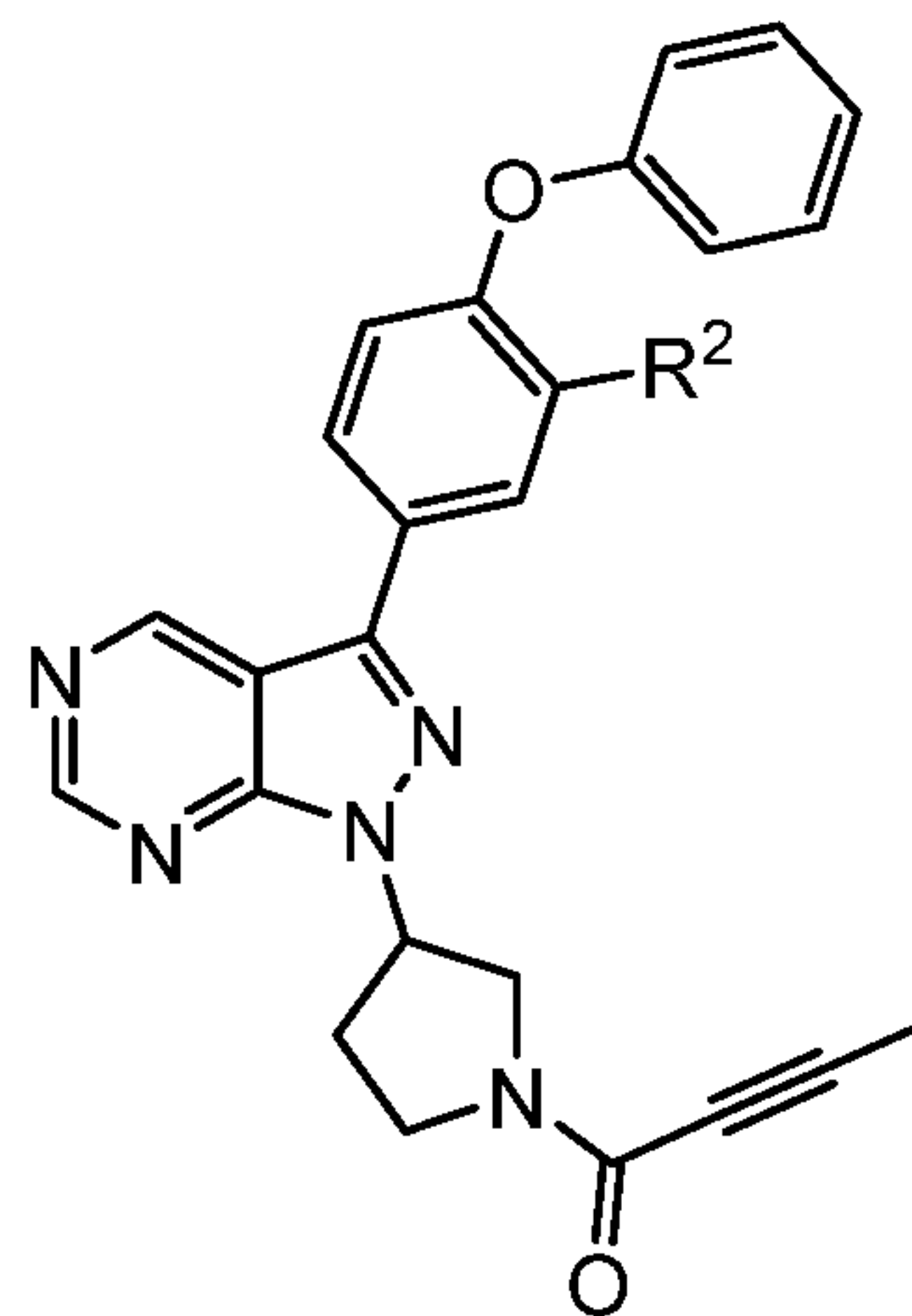


is as described herein. In embodiments, the compound has the formula:

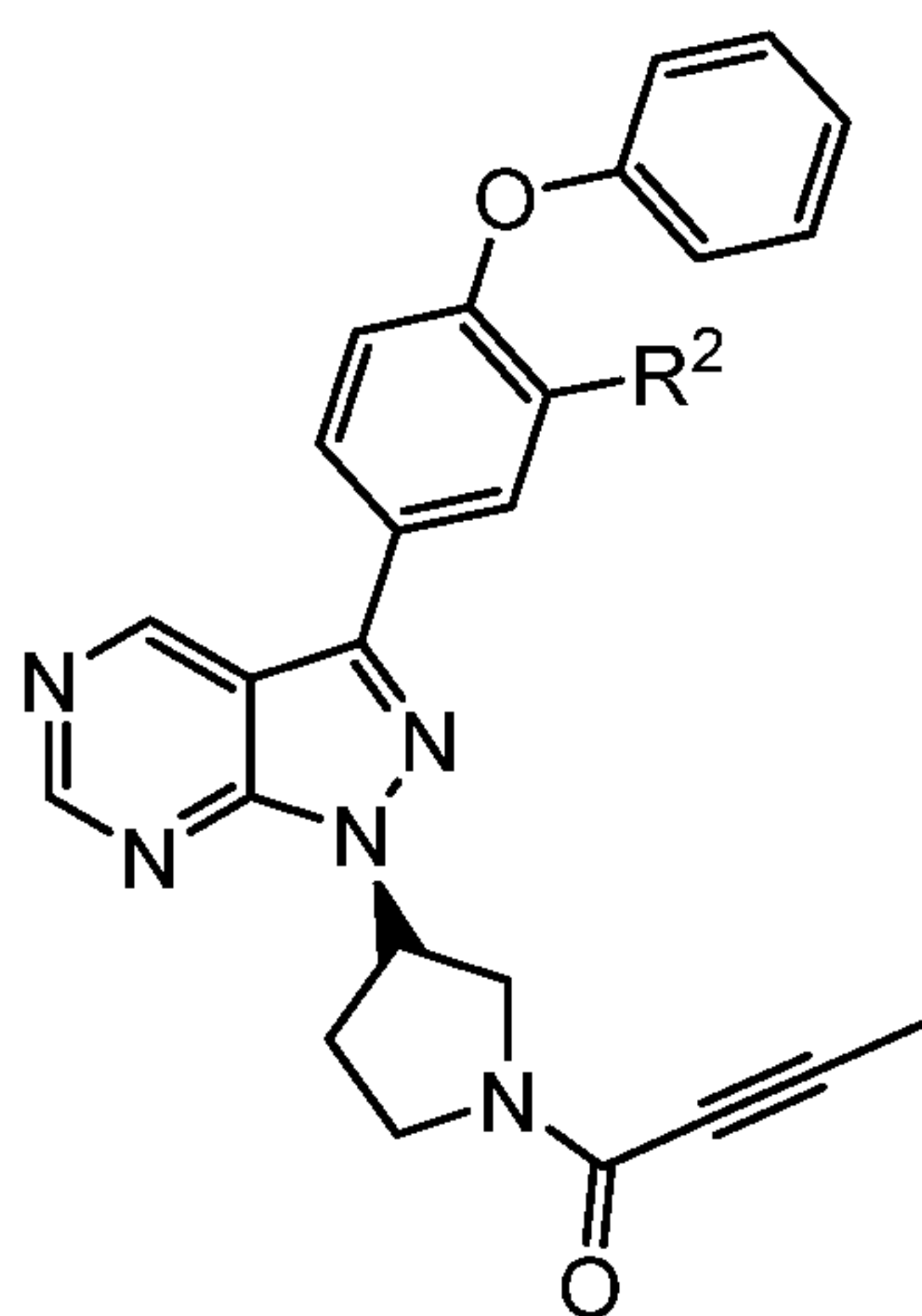
, wherein E is as described herein. In embodiments, the compound has the formula:



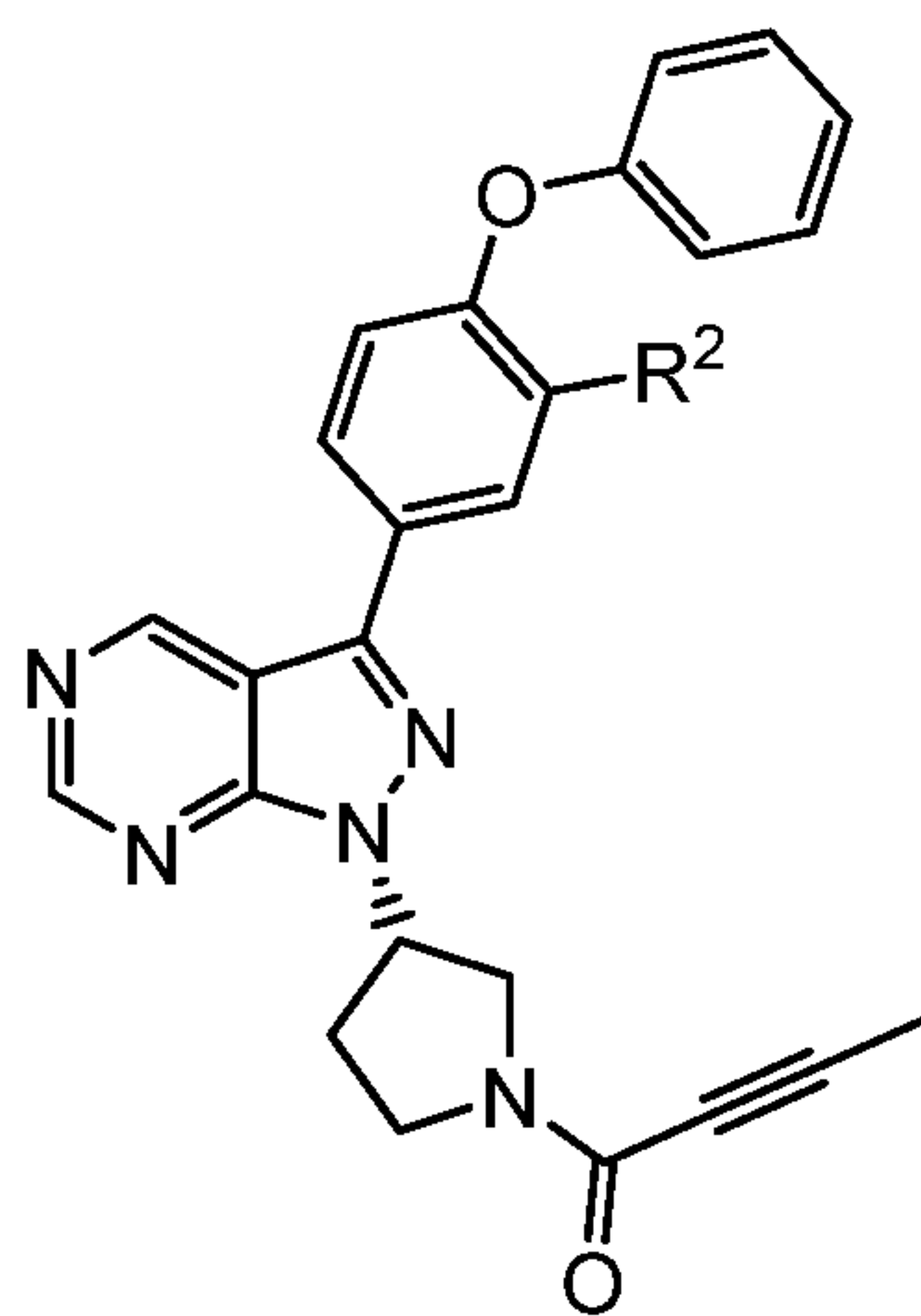
, wherein E is as described herein.



5 [0581] In embodiments, the compound has the formula: , wherein R^2 and E are as described herein. In embodiments, the compound has the formula:

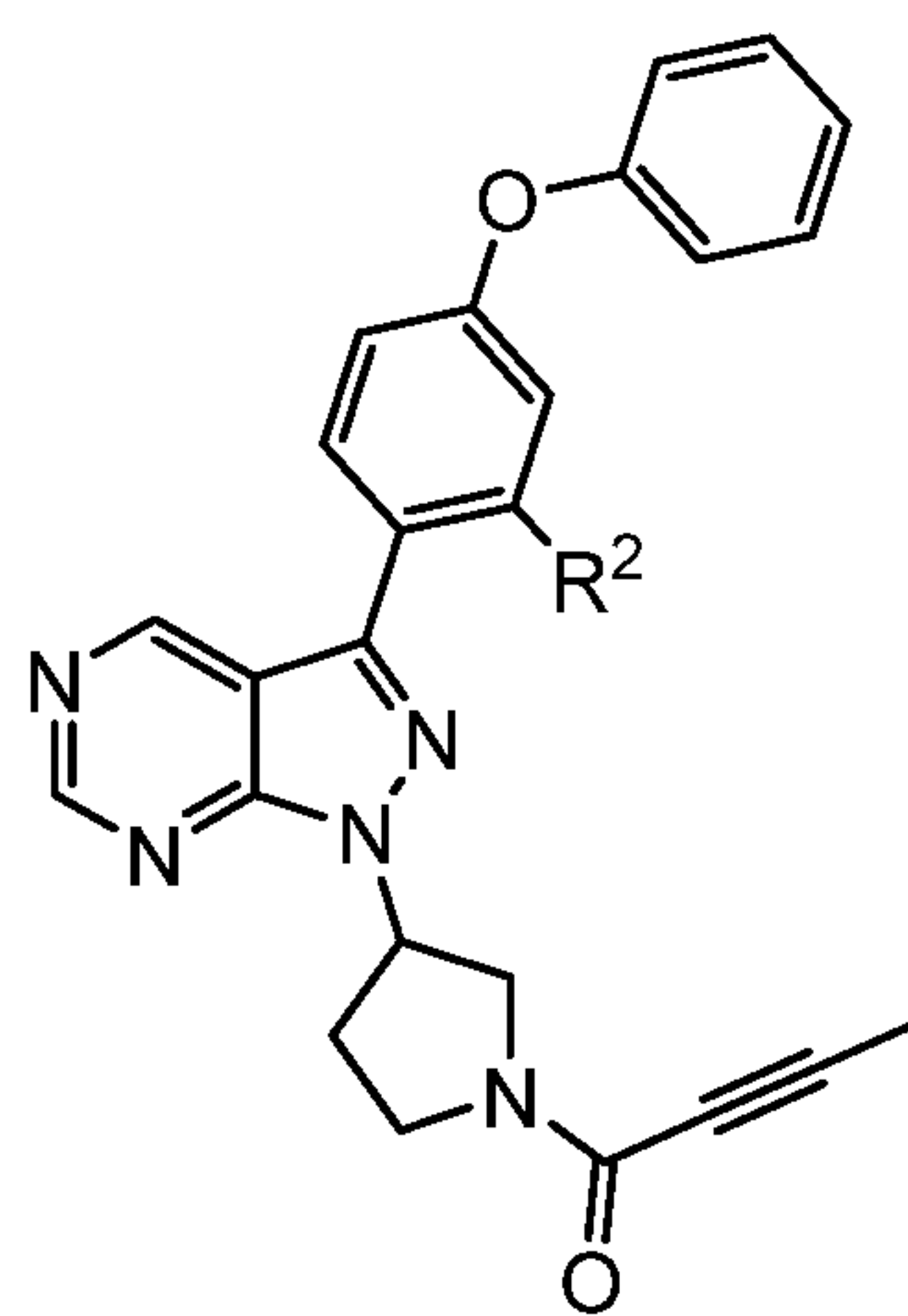


, wherein R^2 and E are as described herein. In embodiments, the



compound has the formula:
herein.

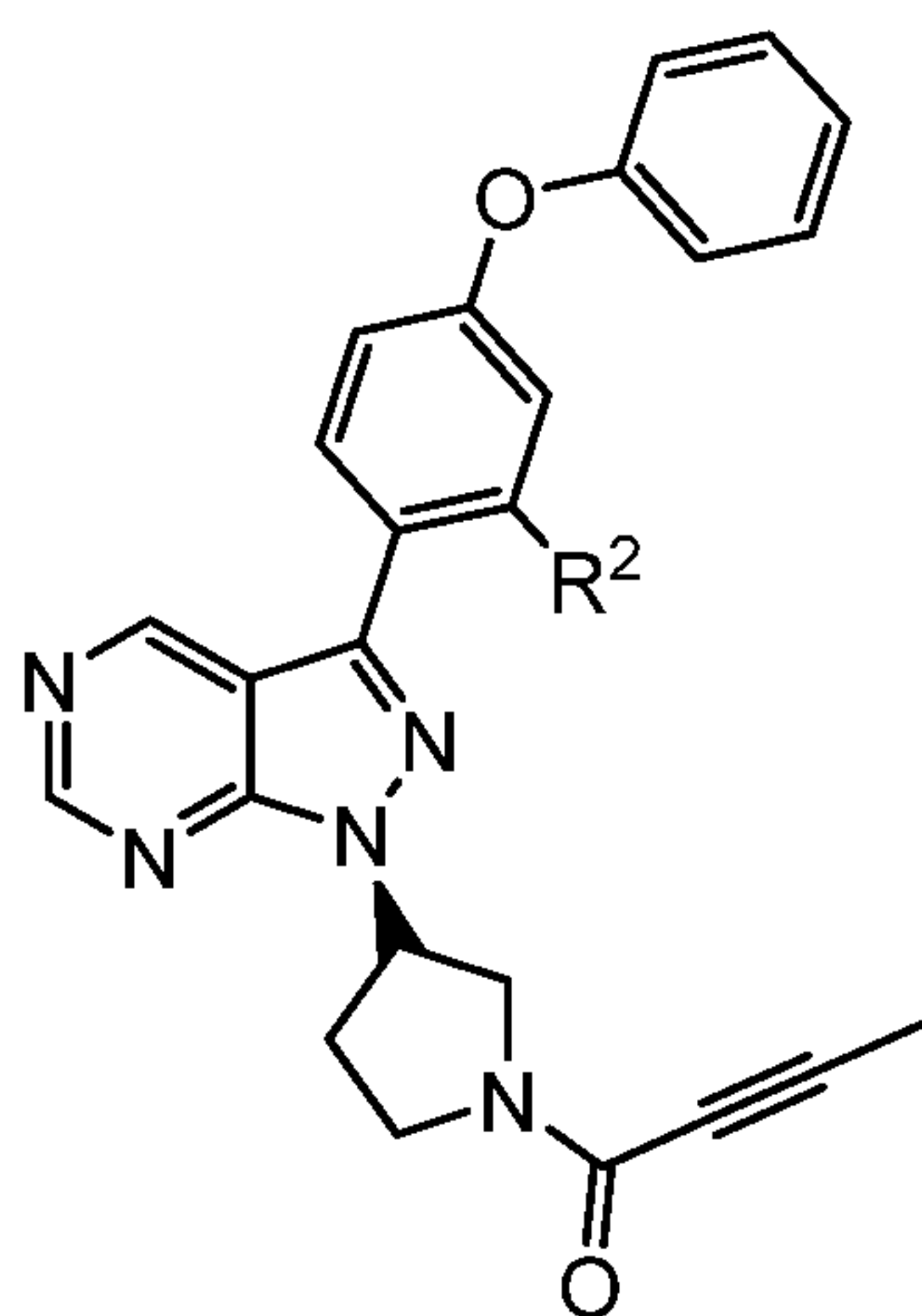
, wherein R^2 and E are as described



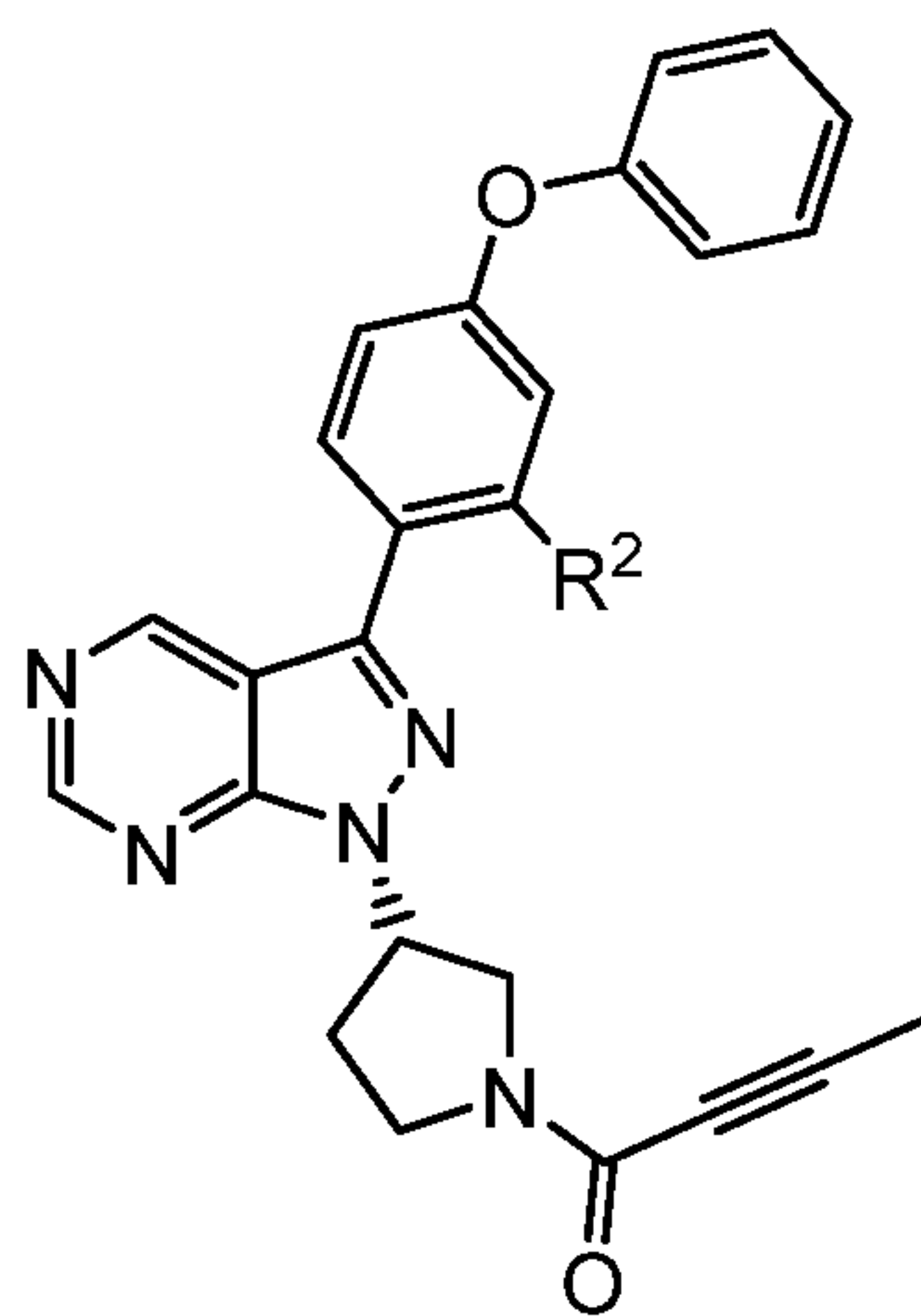
[0582] In embodiments, the compound has the formula:

, wherein

5 R^2 and E are as described herein. In embodiments, the compound has the formula:

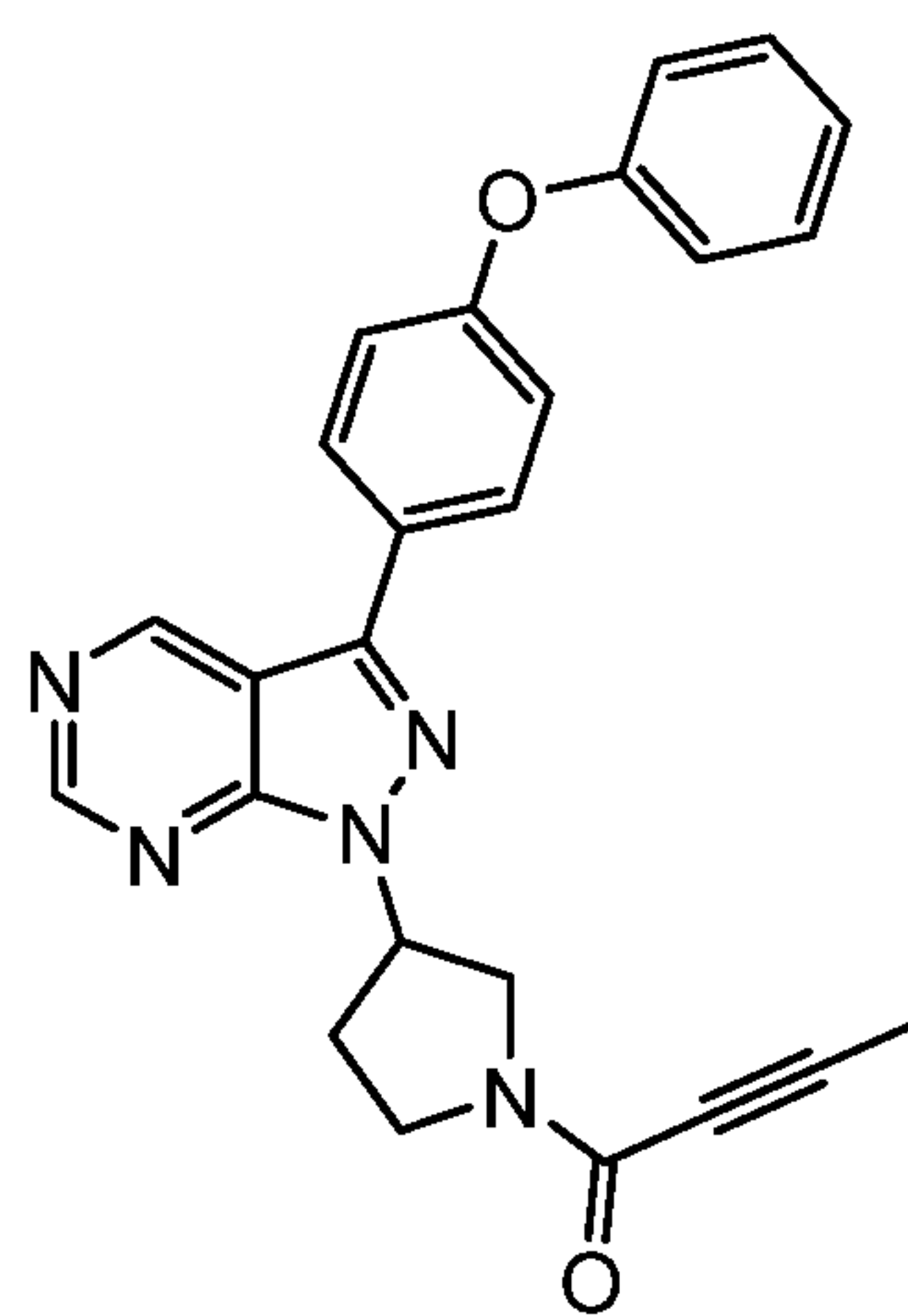


, wherein R² and E are as described herein. In embodiments, the



compound has the formula:
herein.

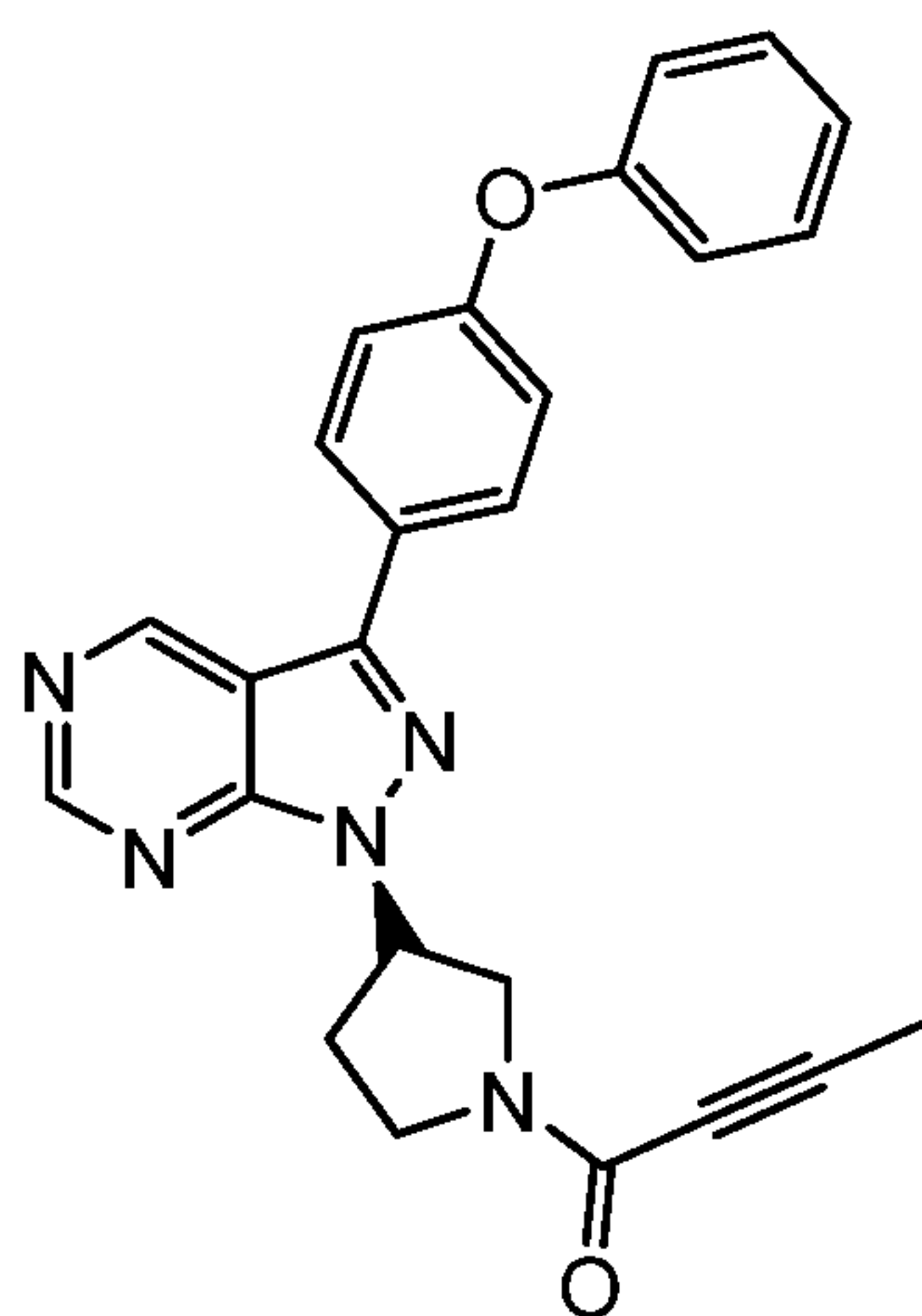
, wherein R² and E are as described



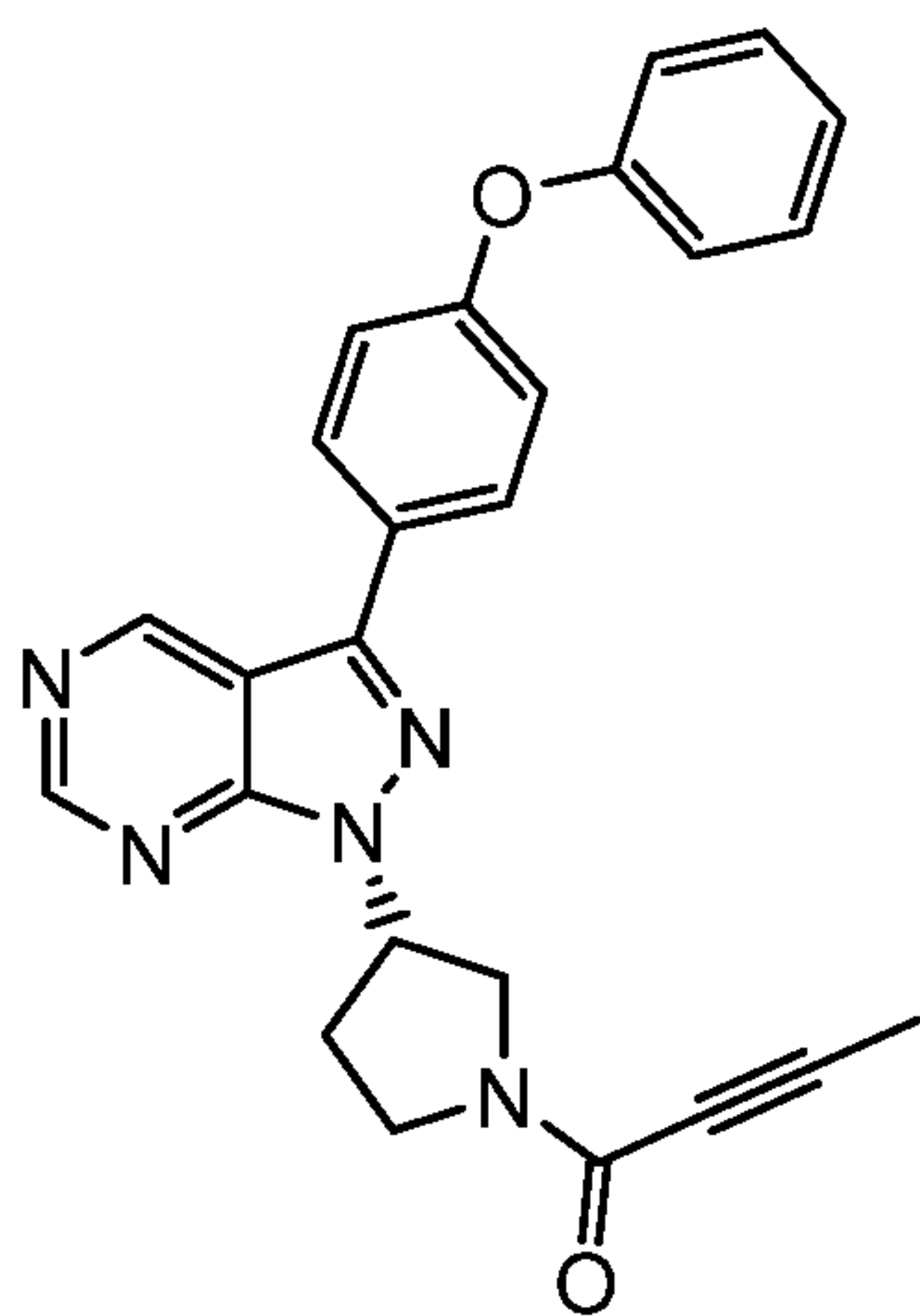
[0583] In embodiments, the compound has the formula:

, wherein

5 E is as described herein. In embodiments, the compound has the formula:

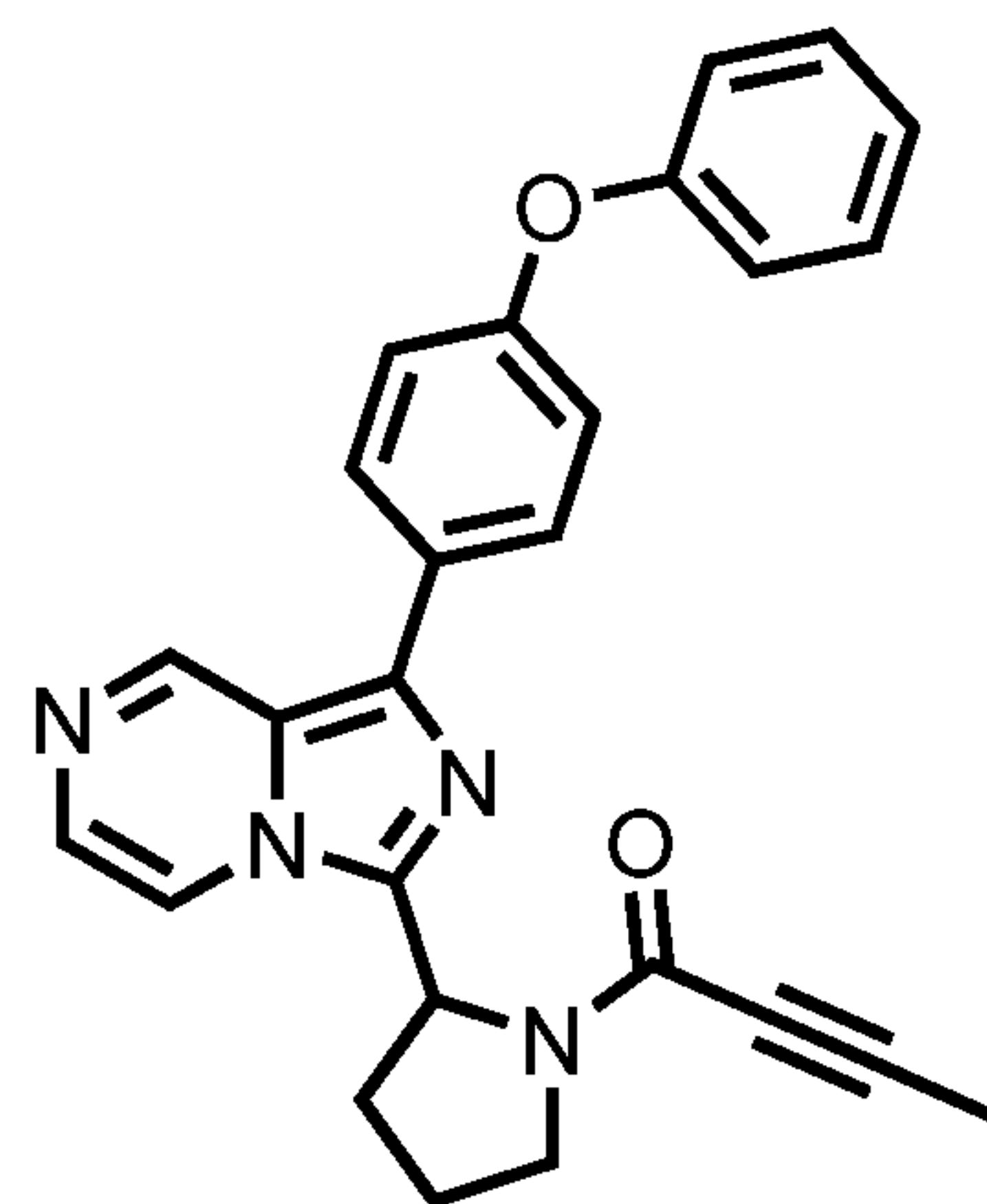


, wherein E is as described herein. In embodiments, the compound



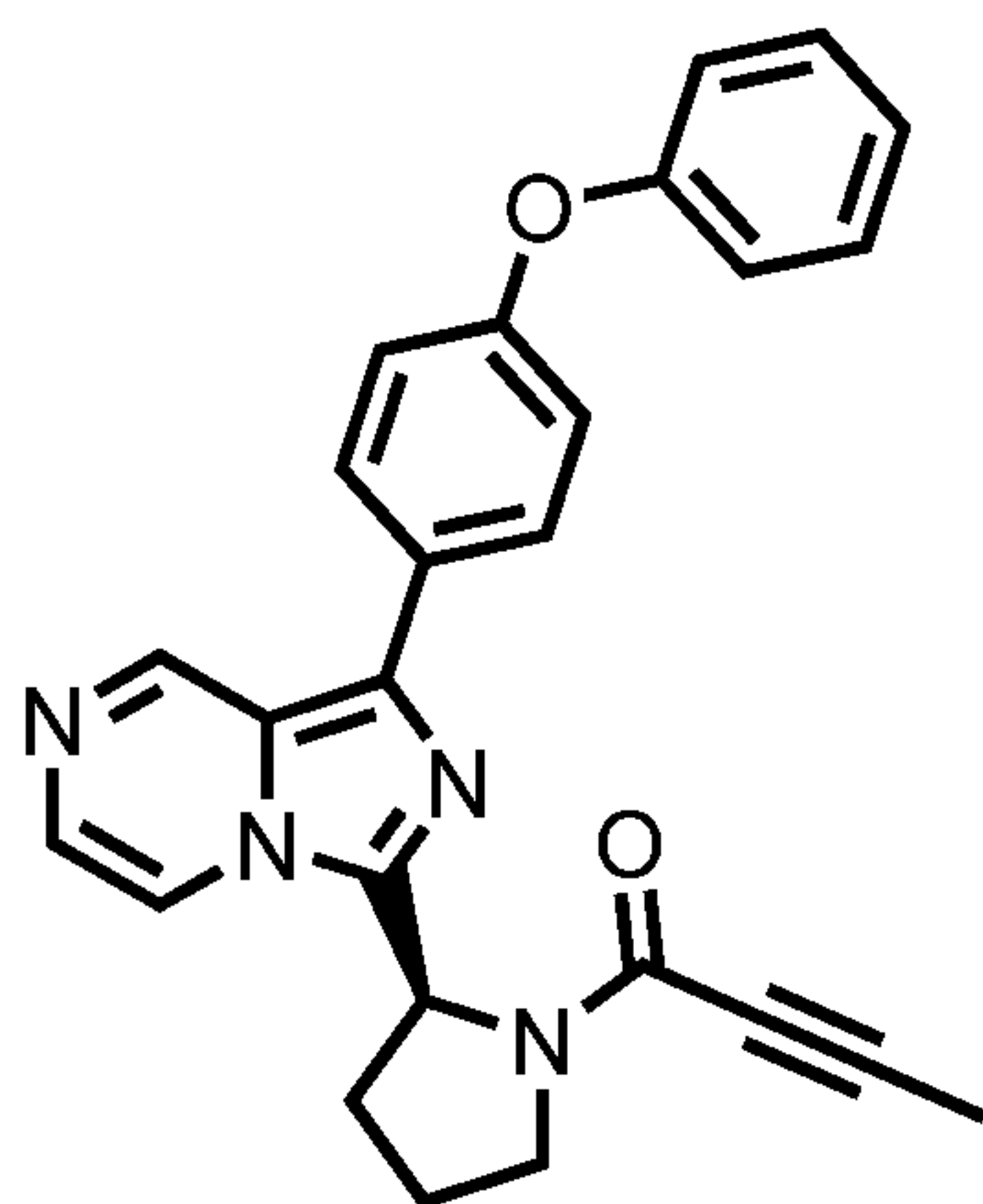
has the formula:

, wherein E is as described herein.

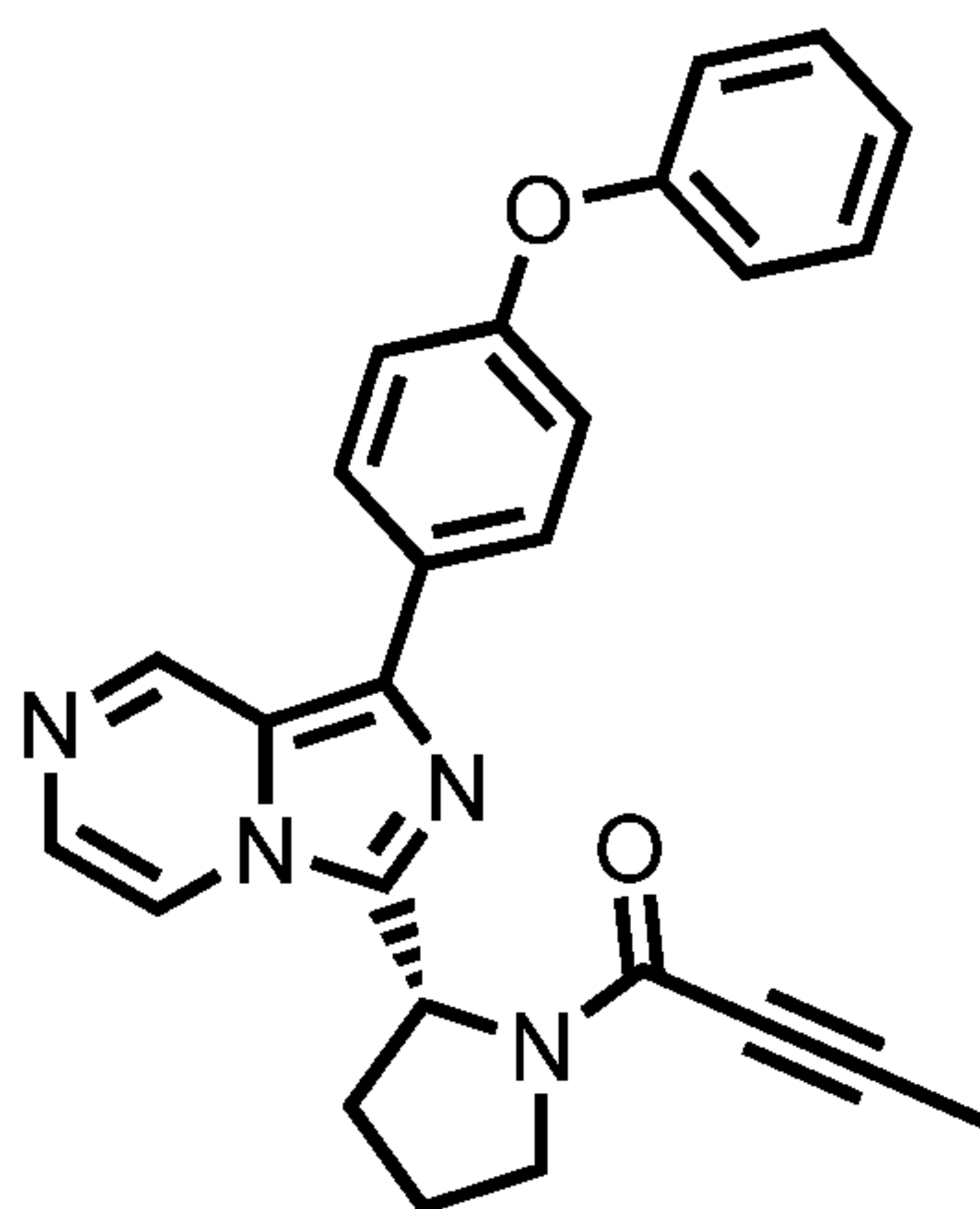


[0584] In embodiments, the compound has the formula:

5 wherein E is as described herein. In embodiments, the compound has the formula:

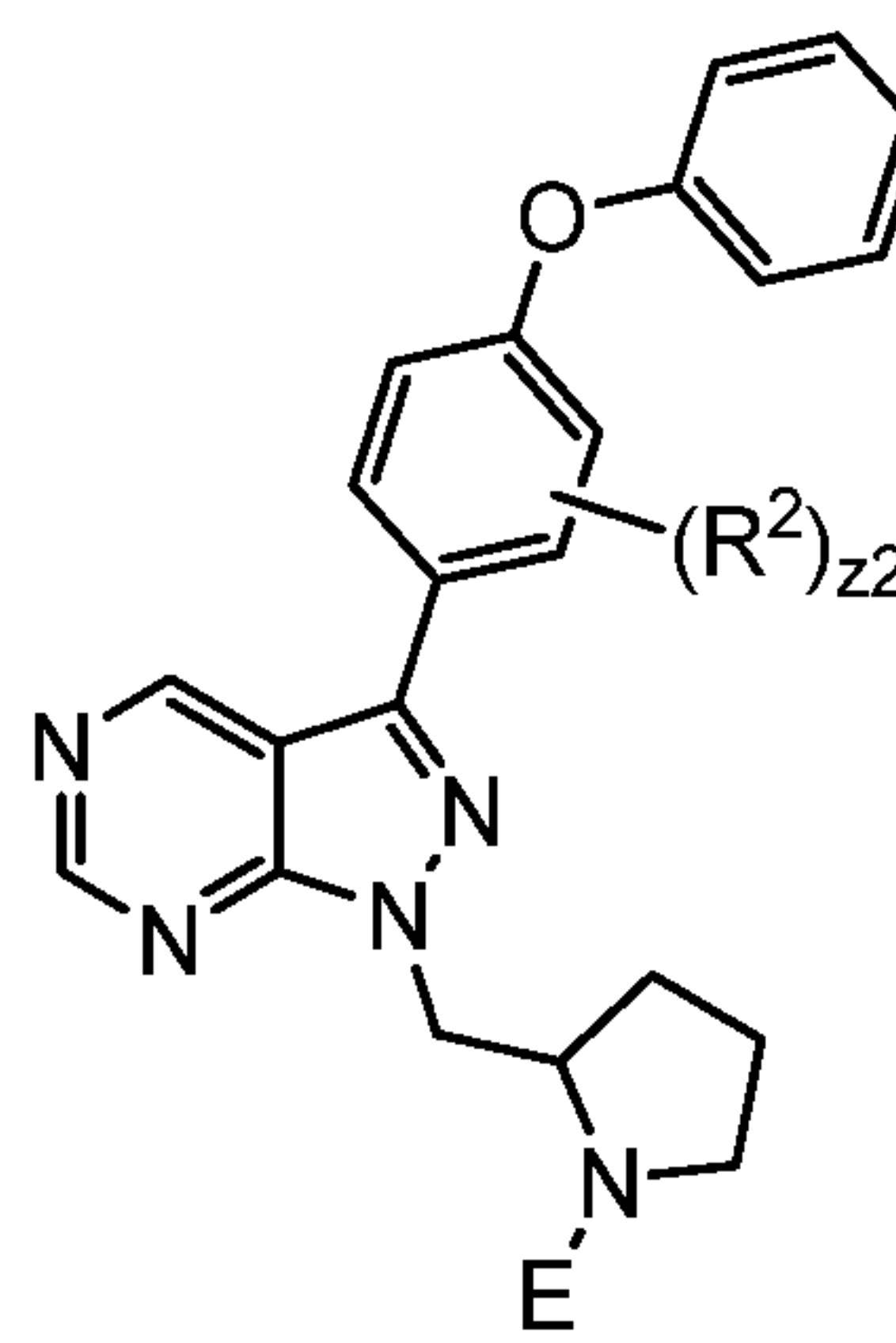


, wherein E is as described herein. In embodiments, the compound



has the formula:

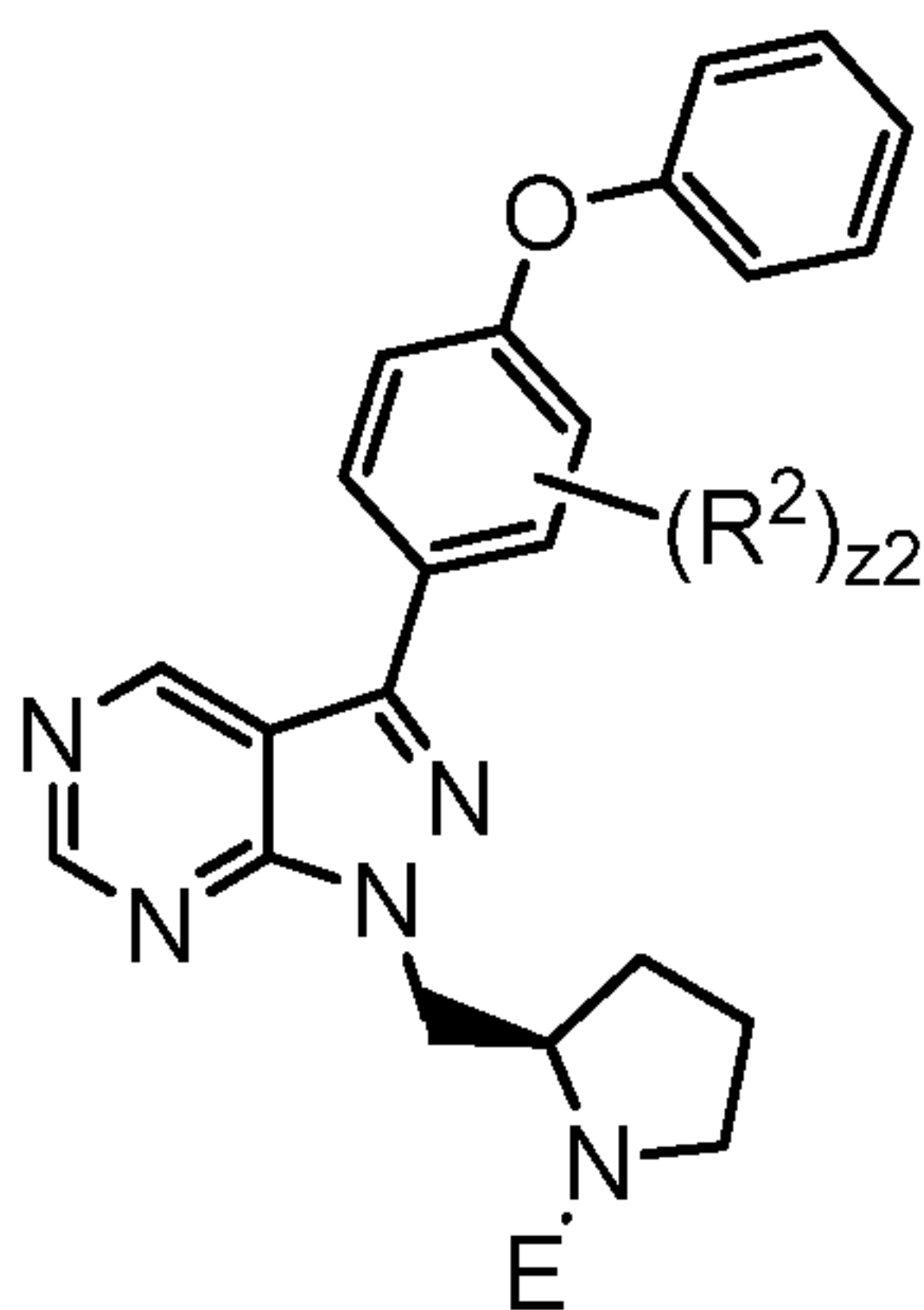
, wherein E is as described herein.



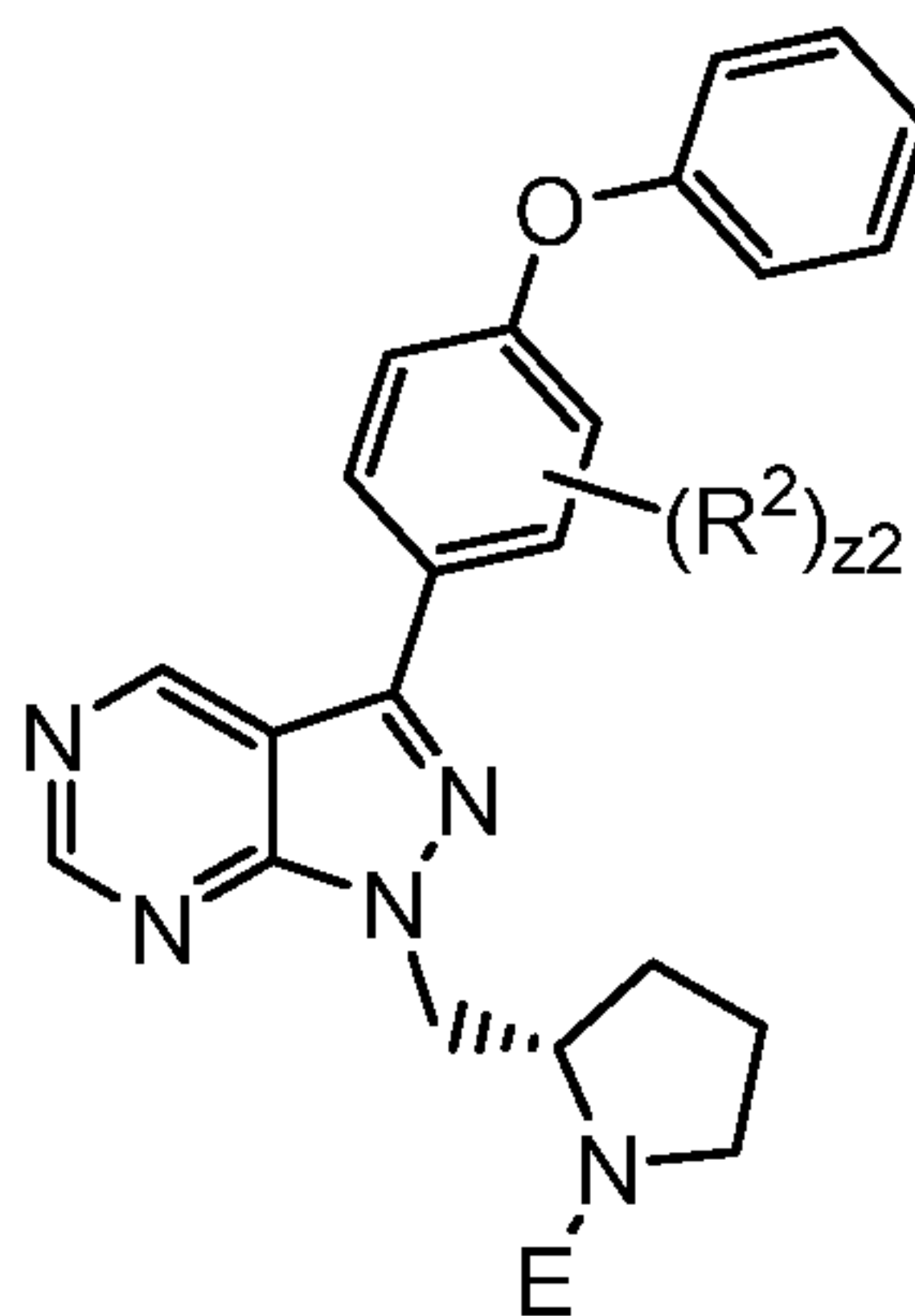
[0585] In embodiments, the compound has the formula:

, wherein R^2 ,

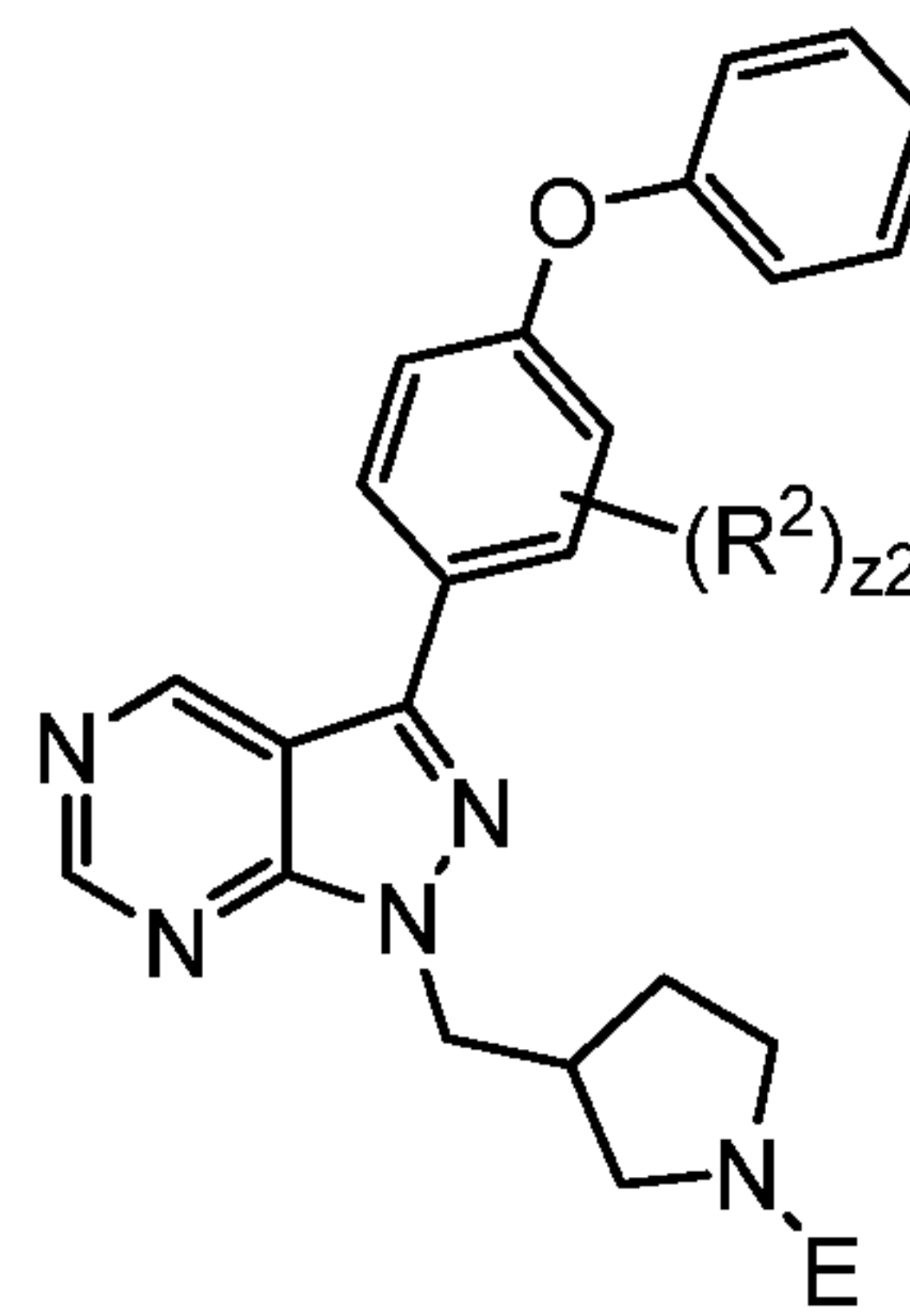
5 z_2 , and E are as described herein. In embodiments, the compound has the formula:



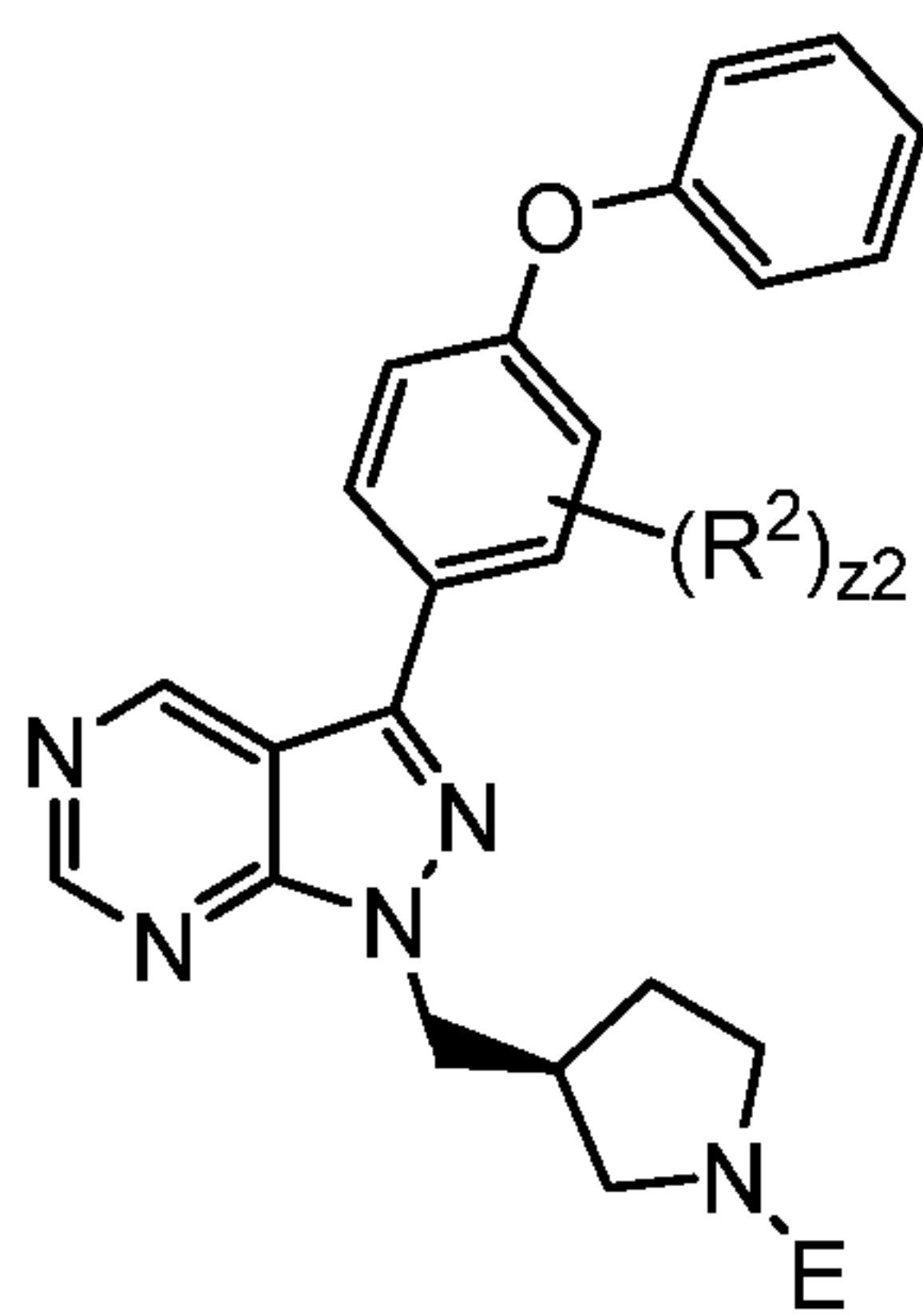
, wherein R^2 , z_2 , and E are as described herein. In embodiments, the



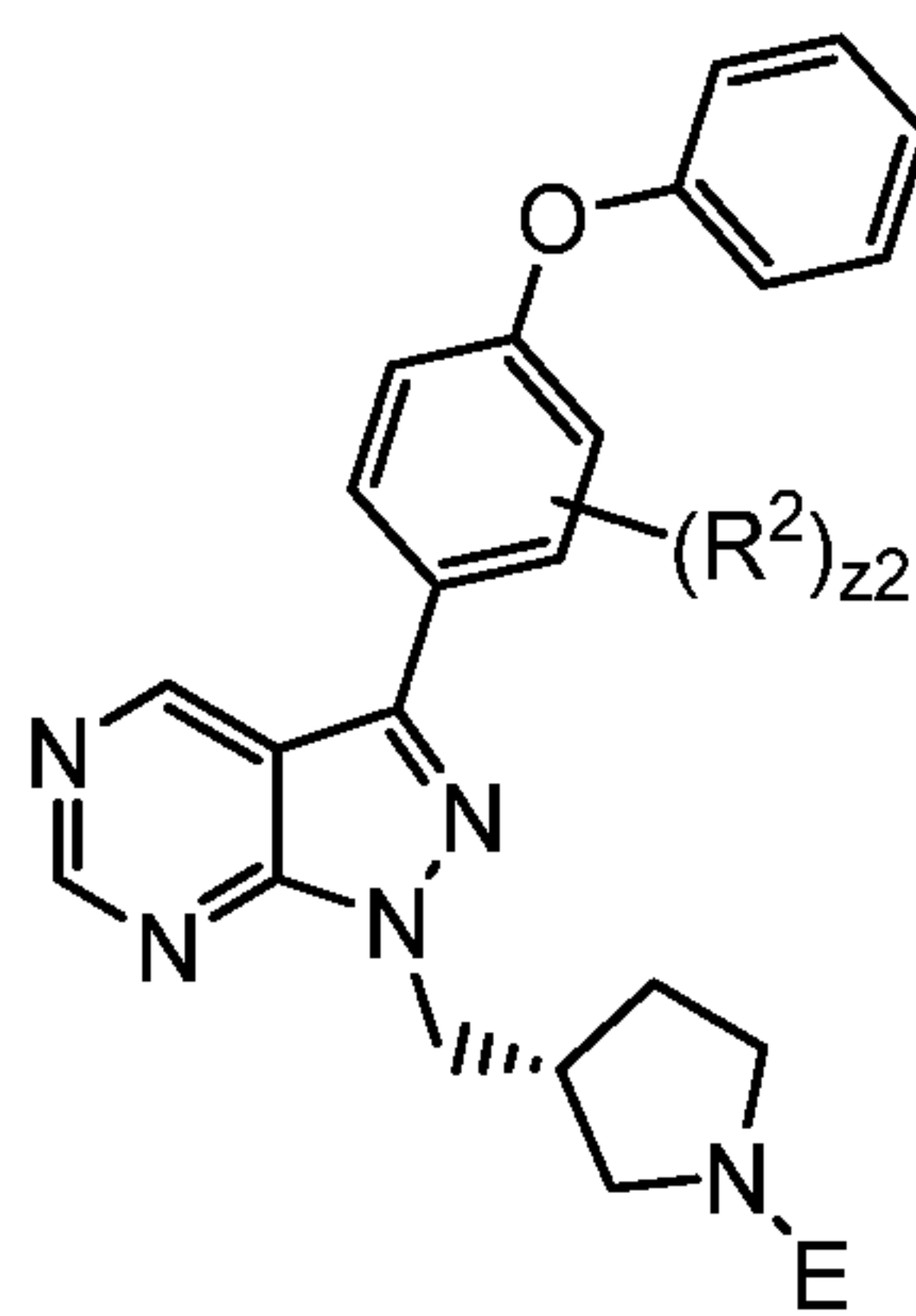
compound has the formula: , wherein R^2 , $z2$, and E are as described herein.



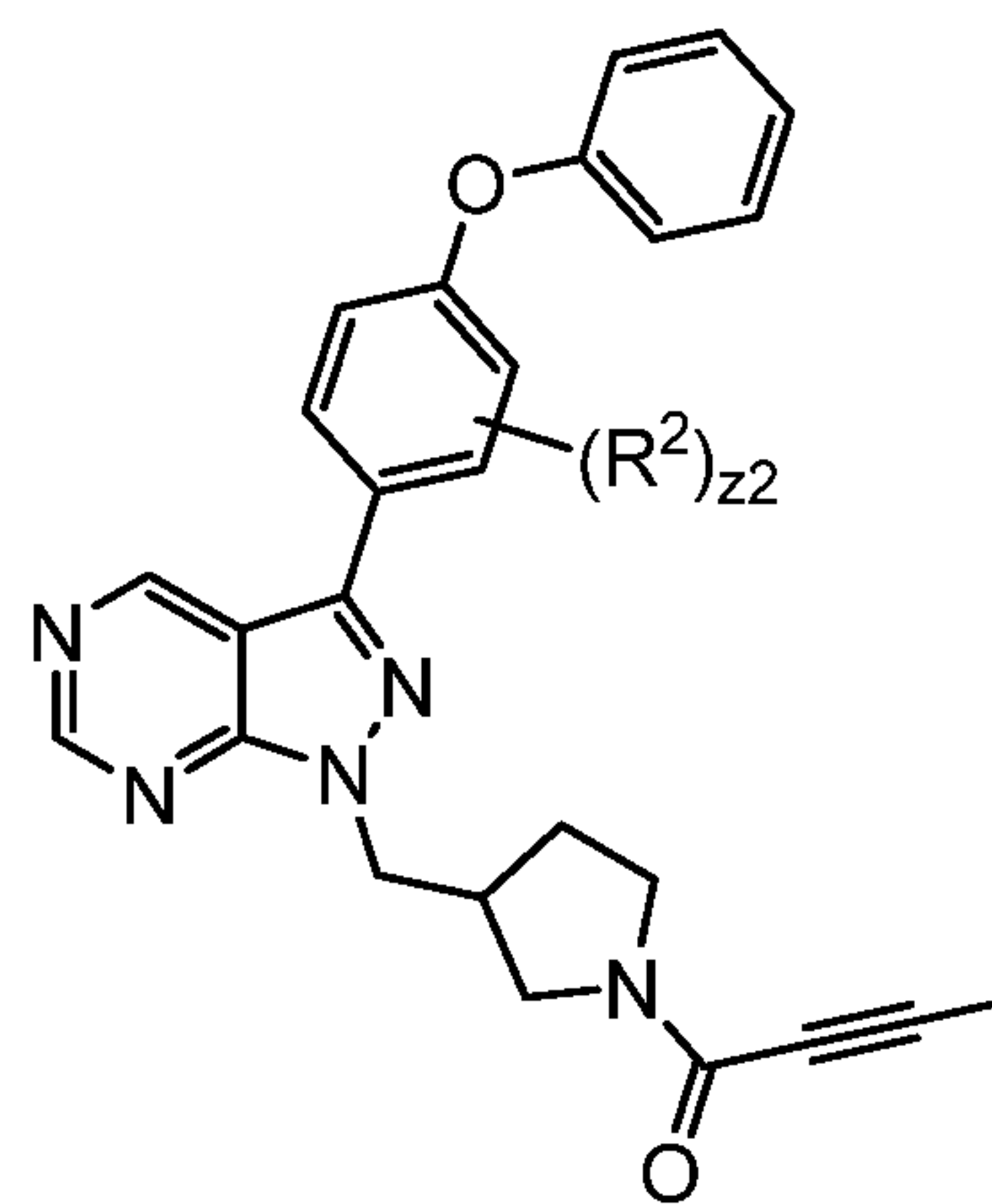
[0586] In embodiments, the compound has the formula: , wherein R^2 , $z2$, and E are as described herein. In embodiments, the compound has the formula:



5 , wherein R^2 , $z2$, and E are as described herein. In embodiments, the

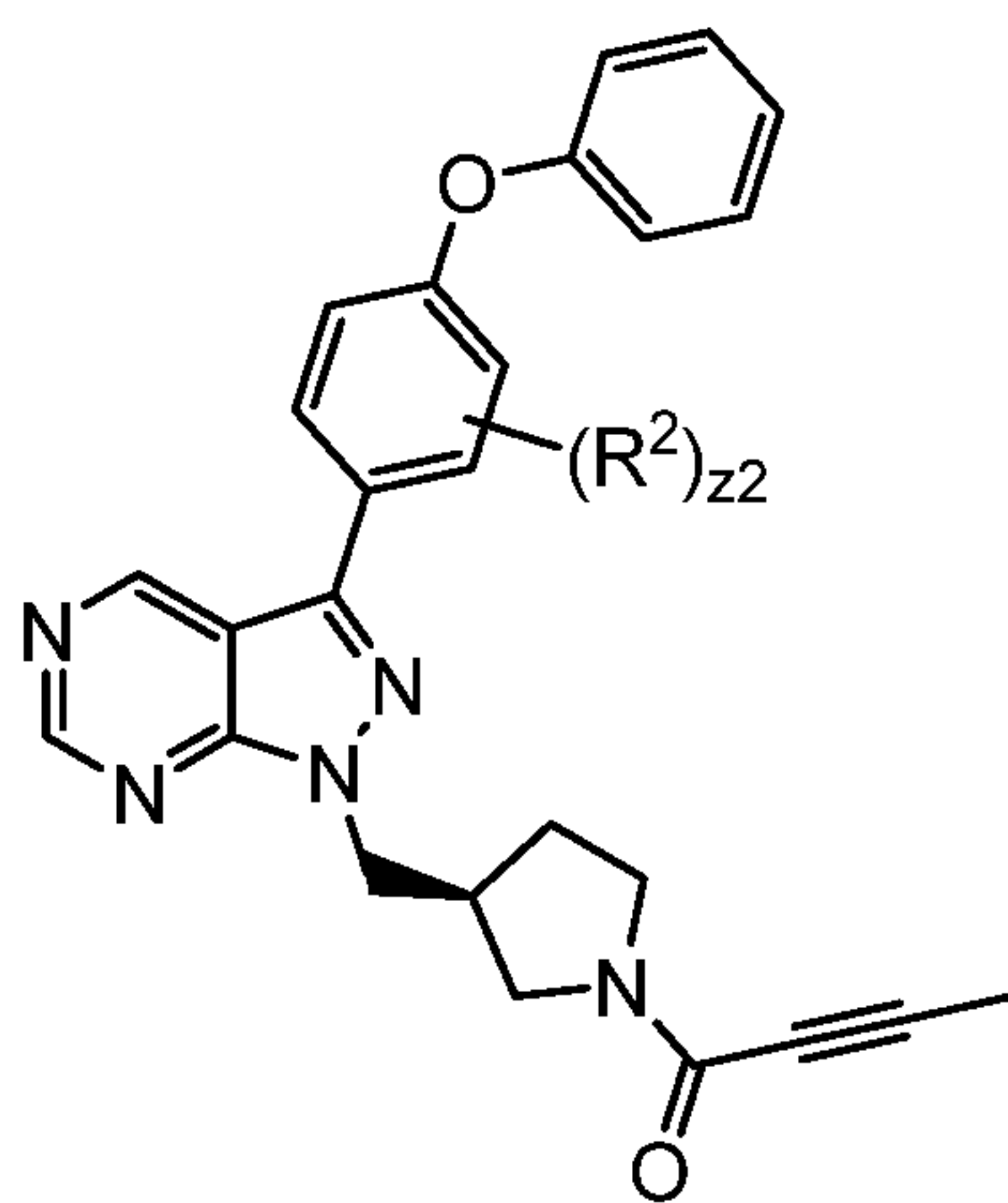


compound has the formula: , wherein R^2 , $z2$, and E are as described herein.

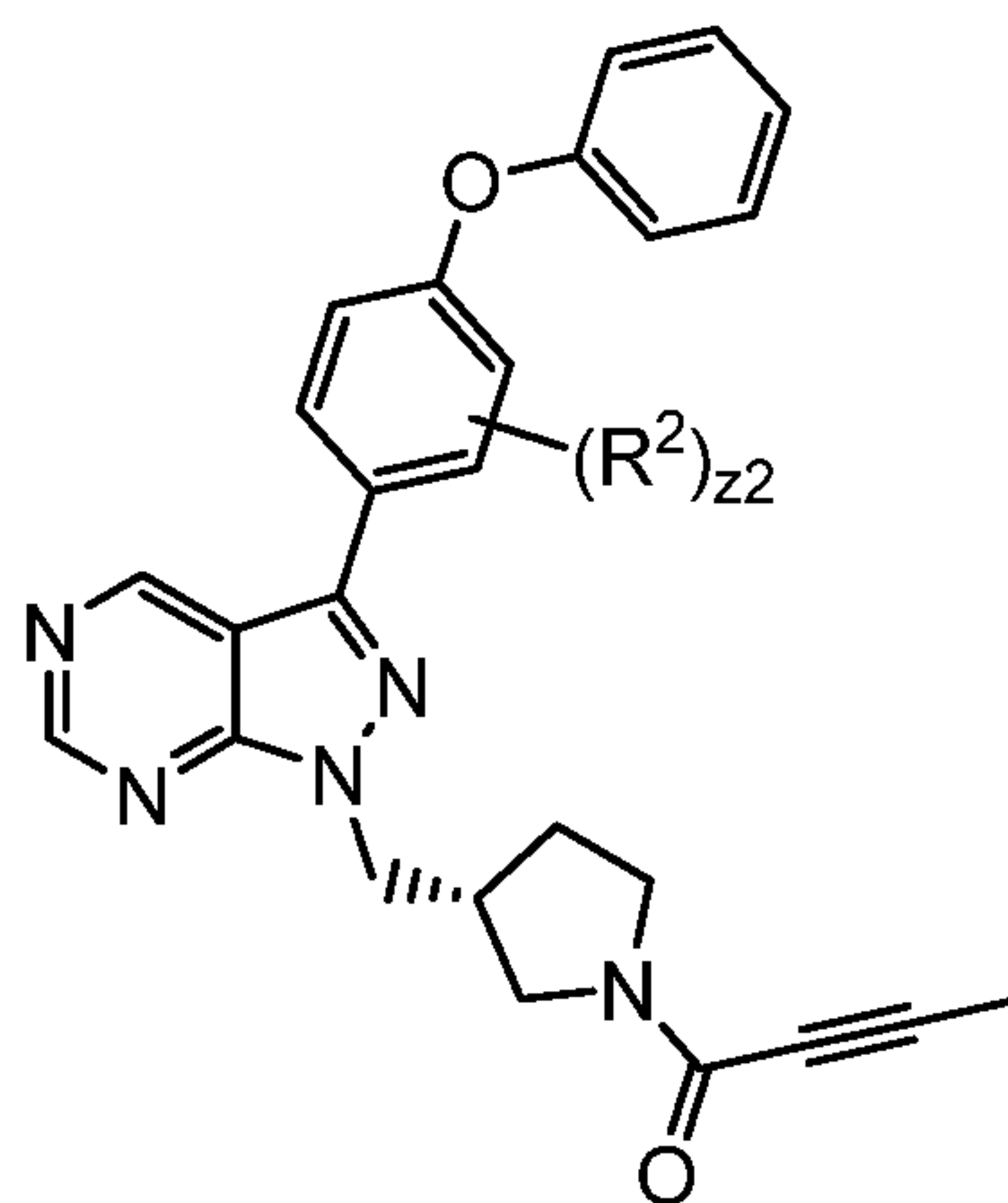


[0587] In embodiments, the compound has the formula:

wherein R^2 and $z2$ are as described herein. In embodiments, the compound has the formula:



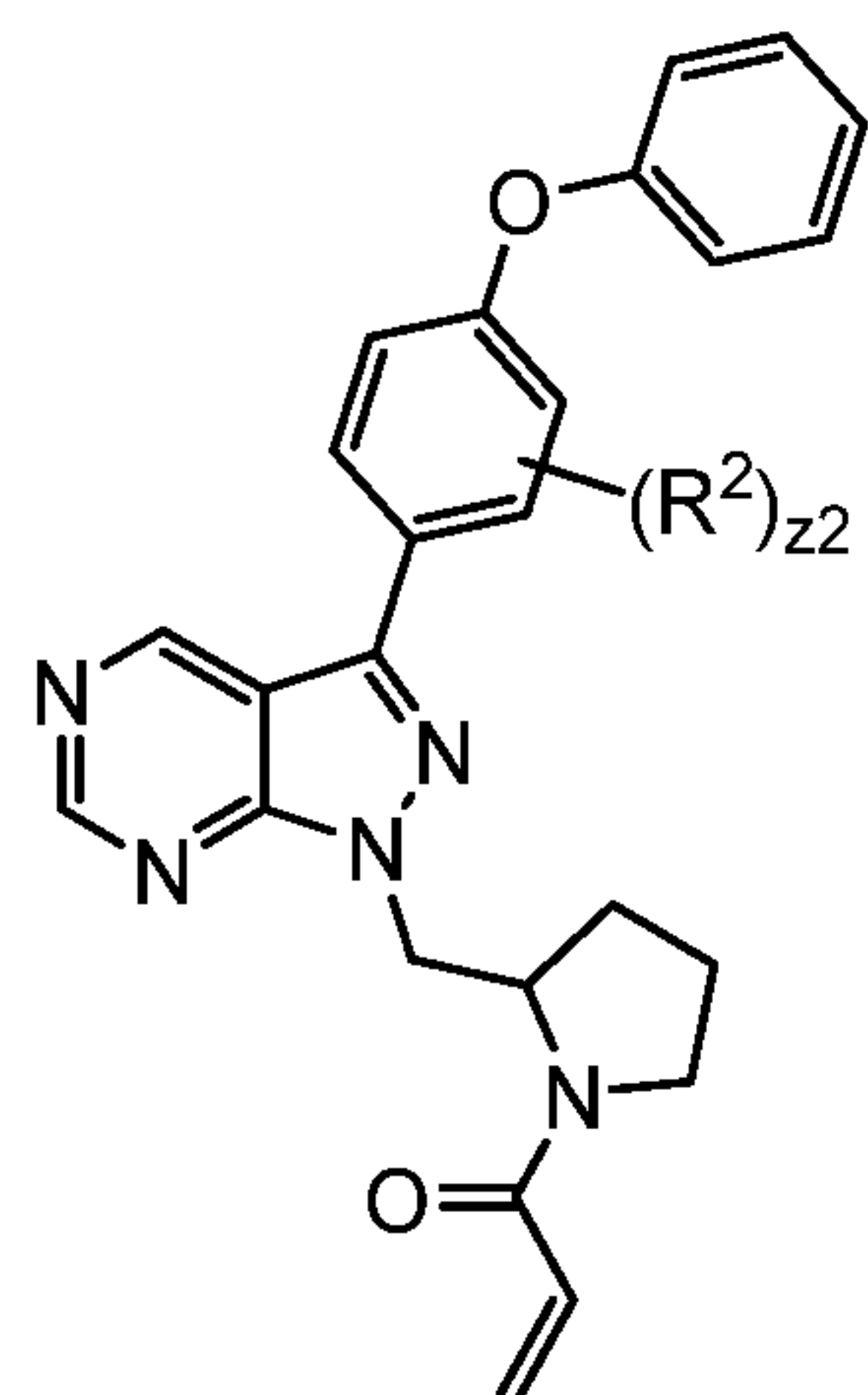
, wherein R^2 and $z2$ are as described herein. In embodiments, the

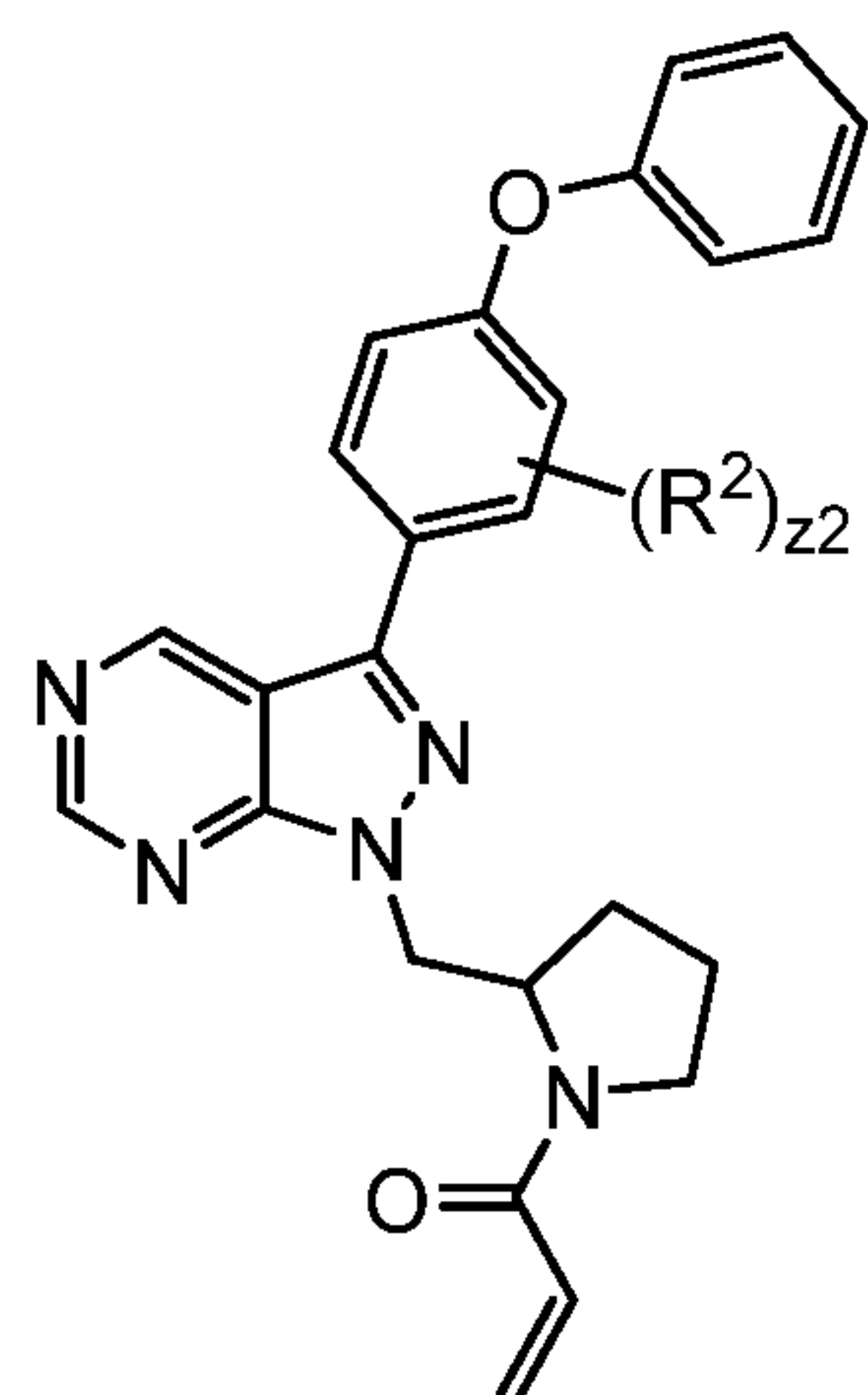


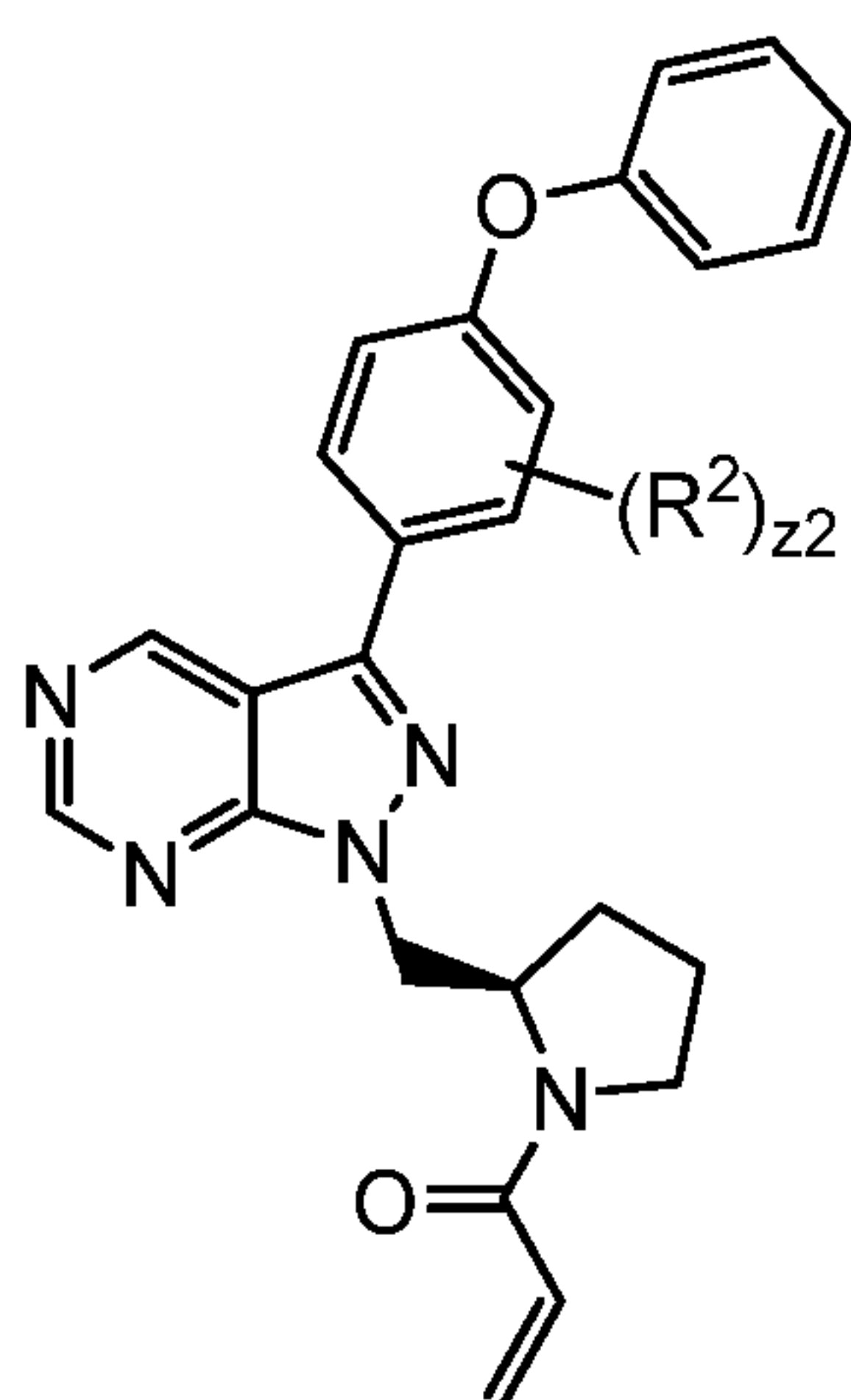
compound has the formula:

, wherein R^2 and $z2$ are as described

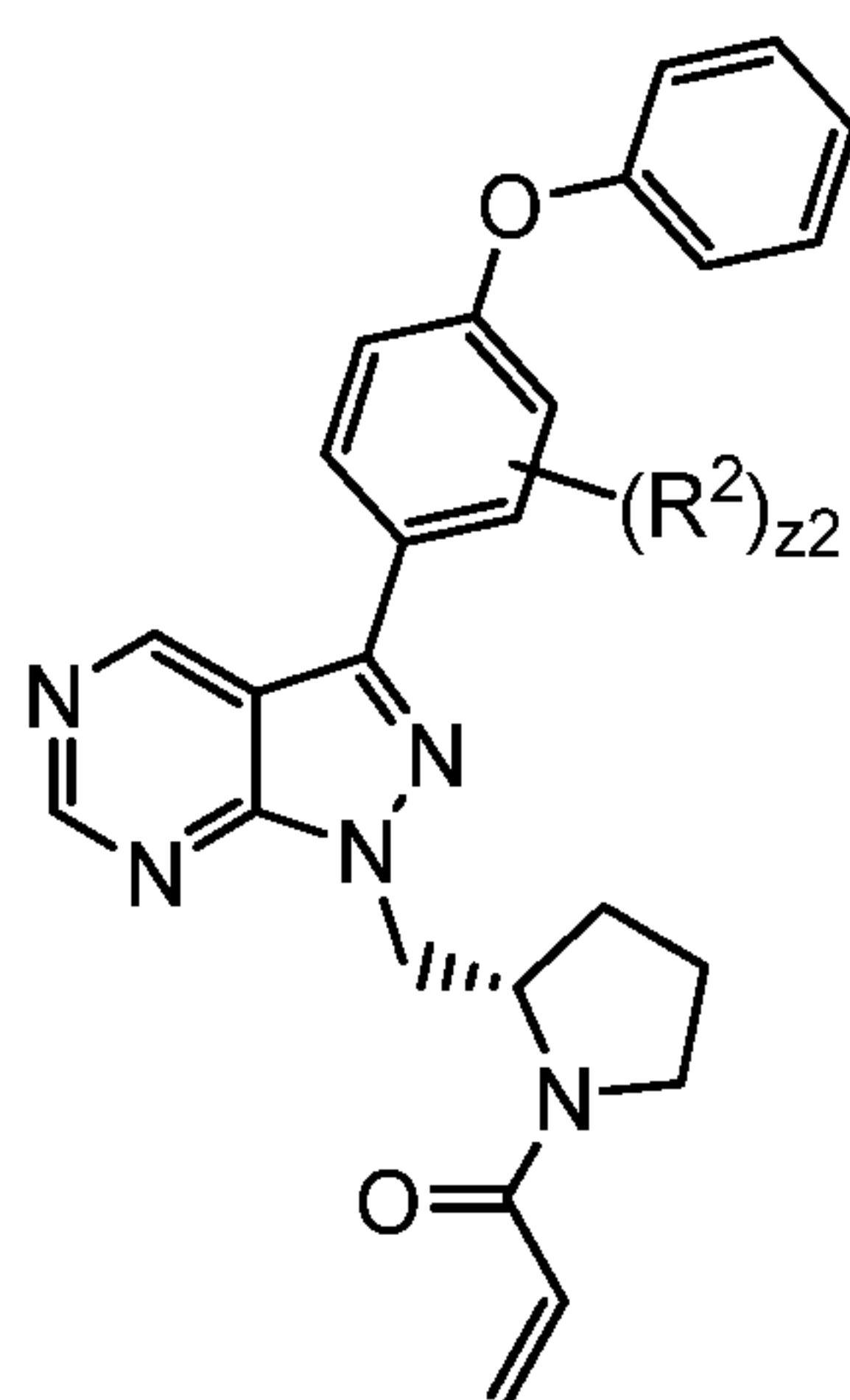
5 herein.

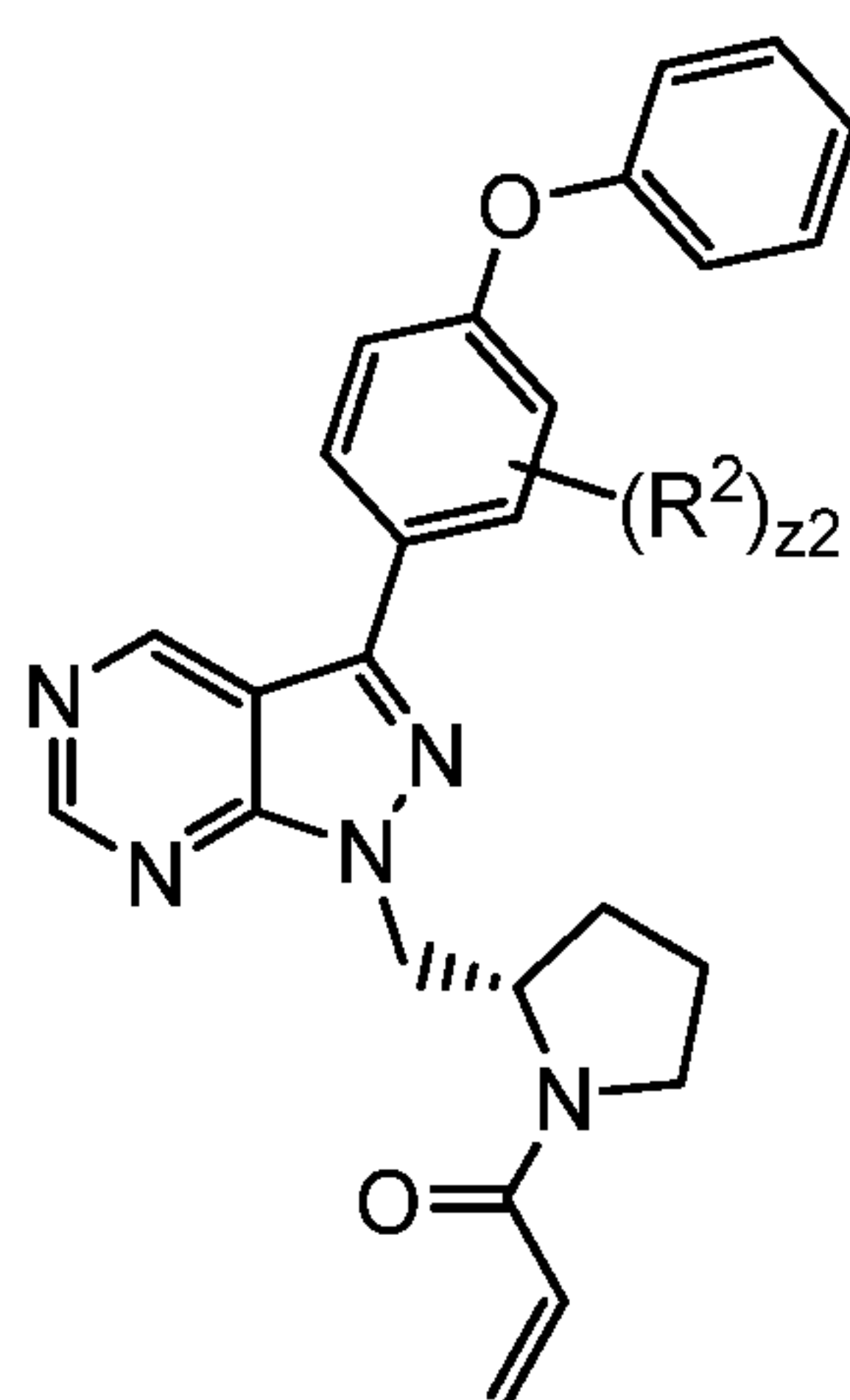


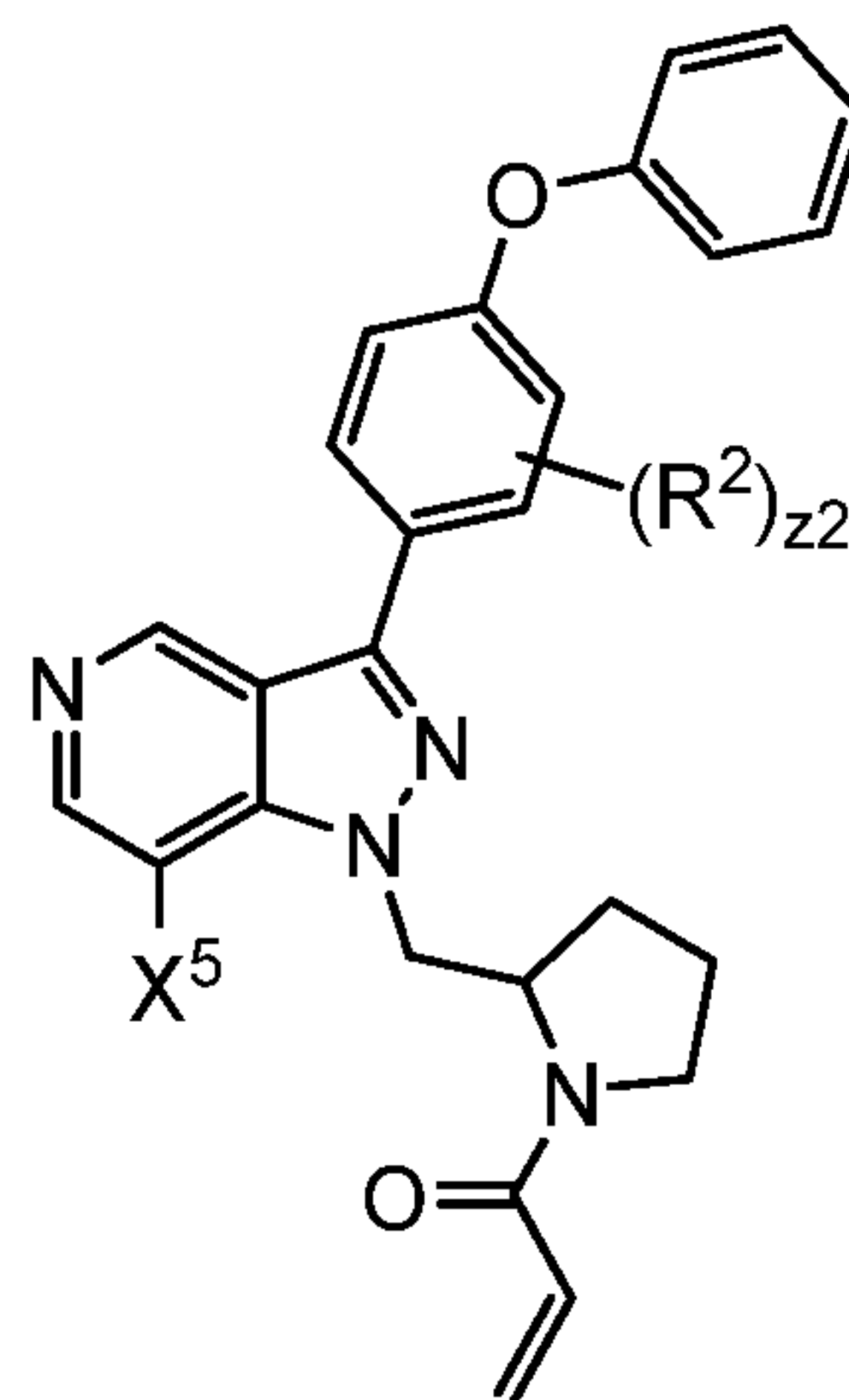
[0588] In embodiments, the compound has the formula: , wherein R^2 and z_2 are as described herein. In embodiments, the compound has the formula:

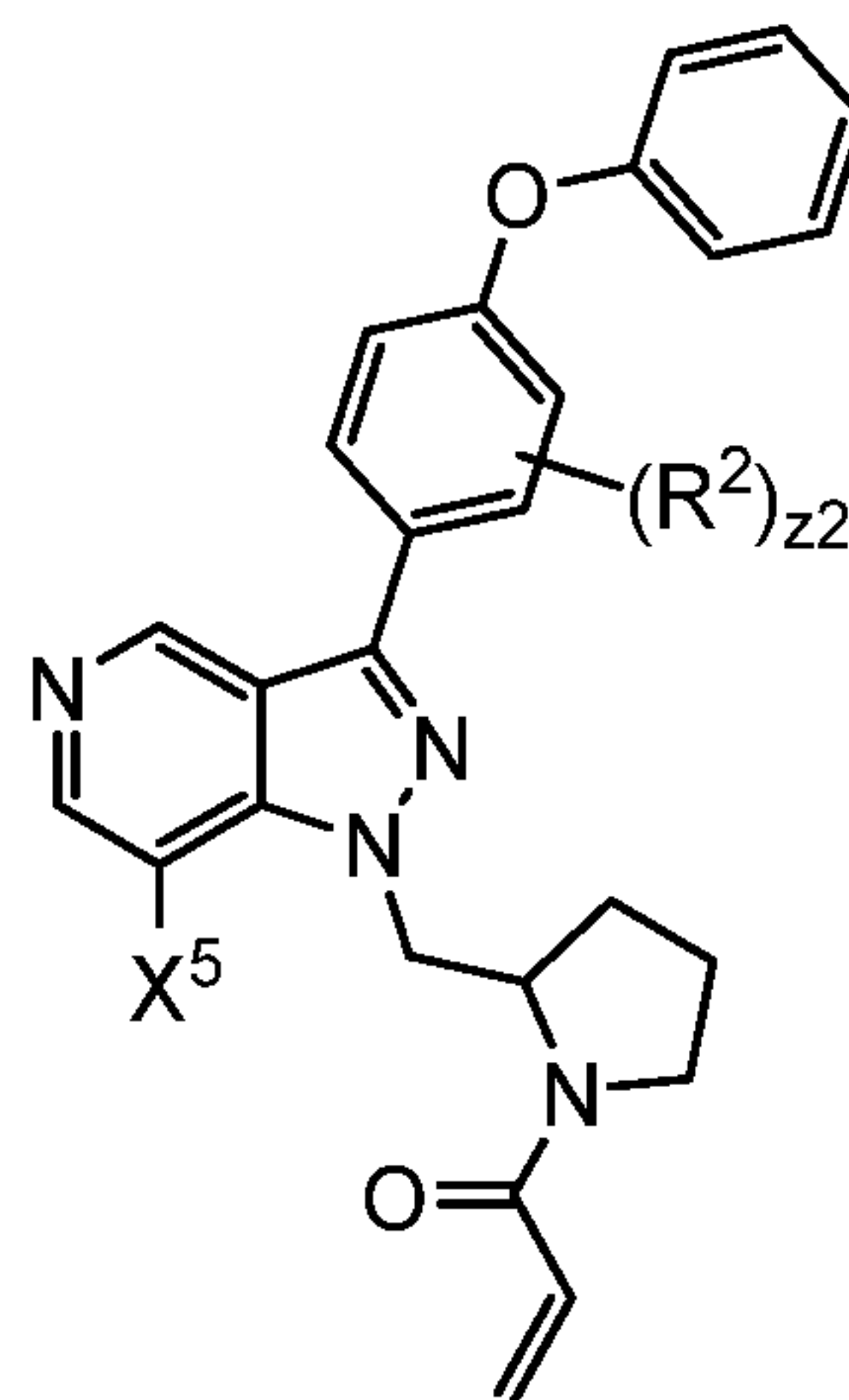


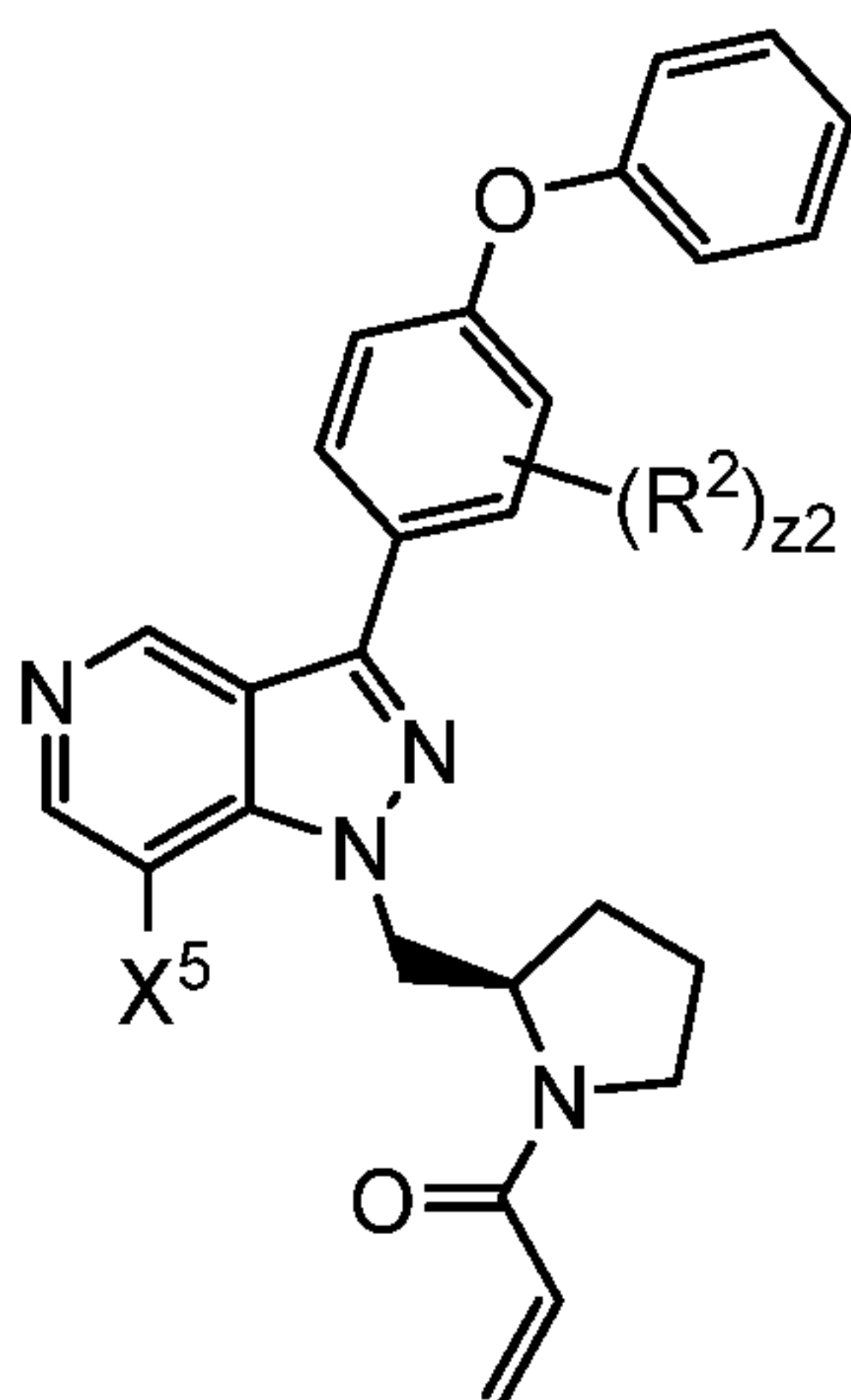
, wherein R^2 and z_2 are as described herein. In embodiments, the



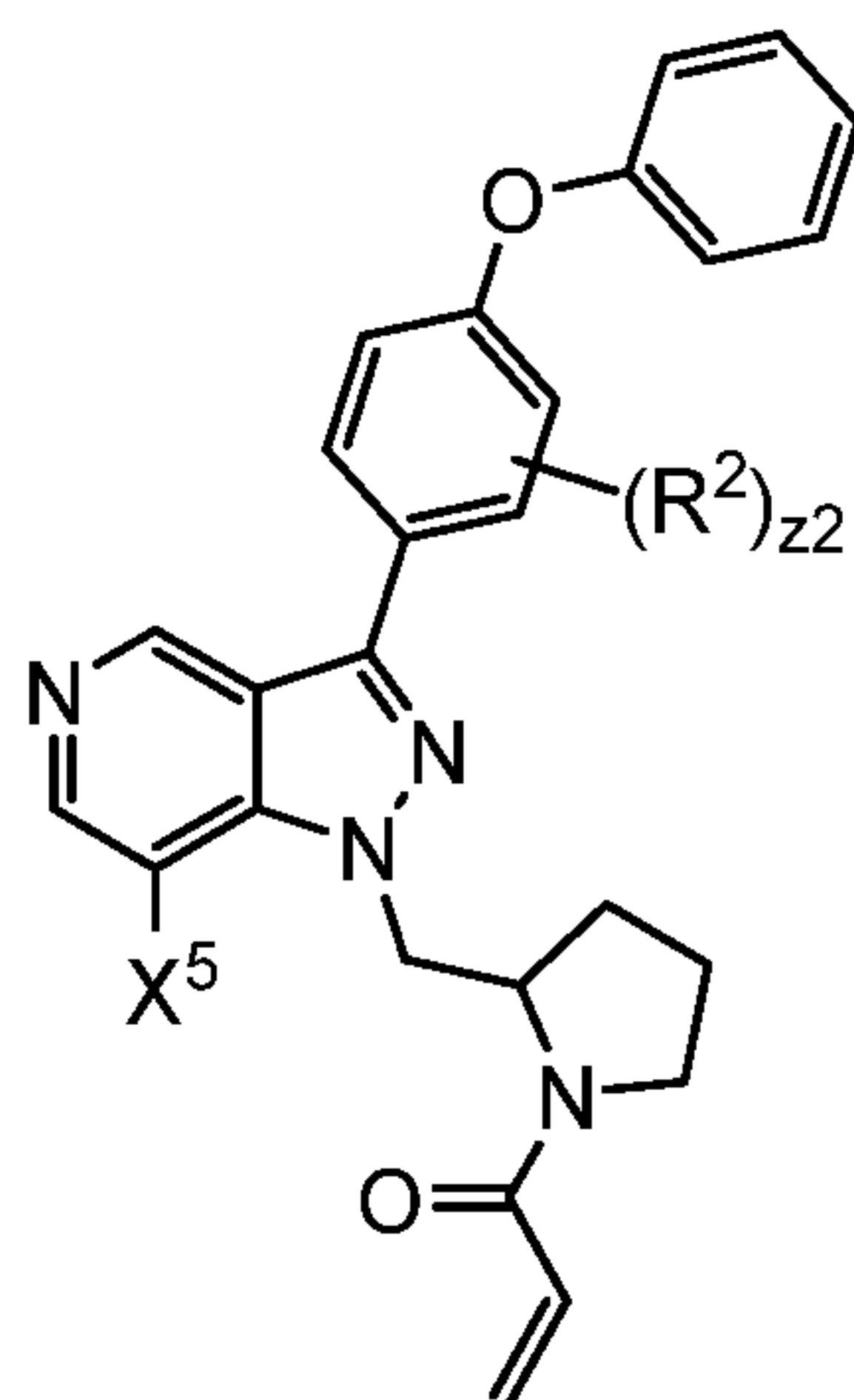
compound has the formula: , wherein R^2 and z_2 are as described herein.



[0589] In embodiments, the compound has the formula: , wherein X^5 , R^2 and $z2$ are as described herein. In embodiments, the compound has the formula:



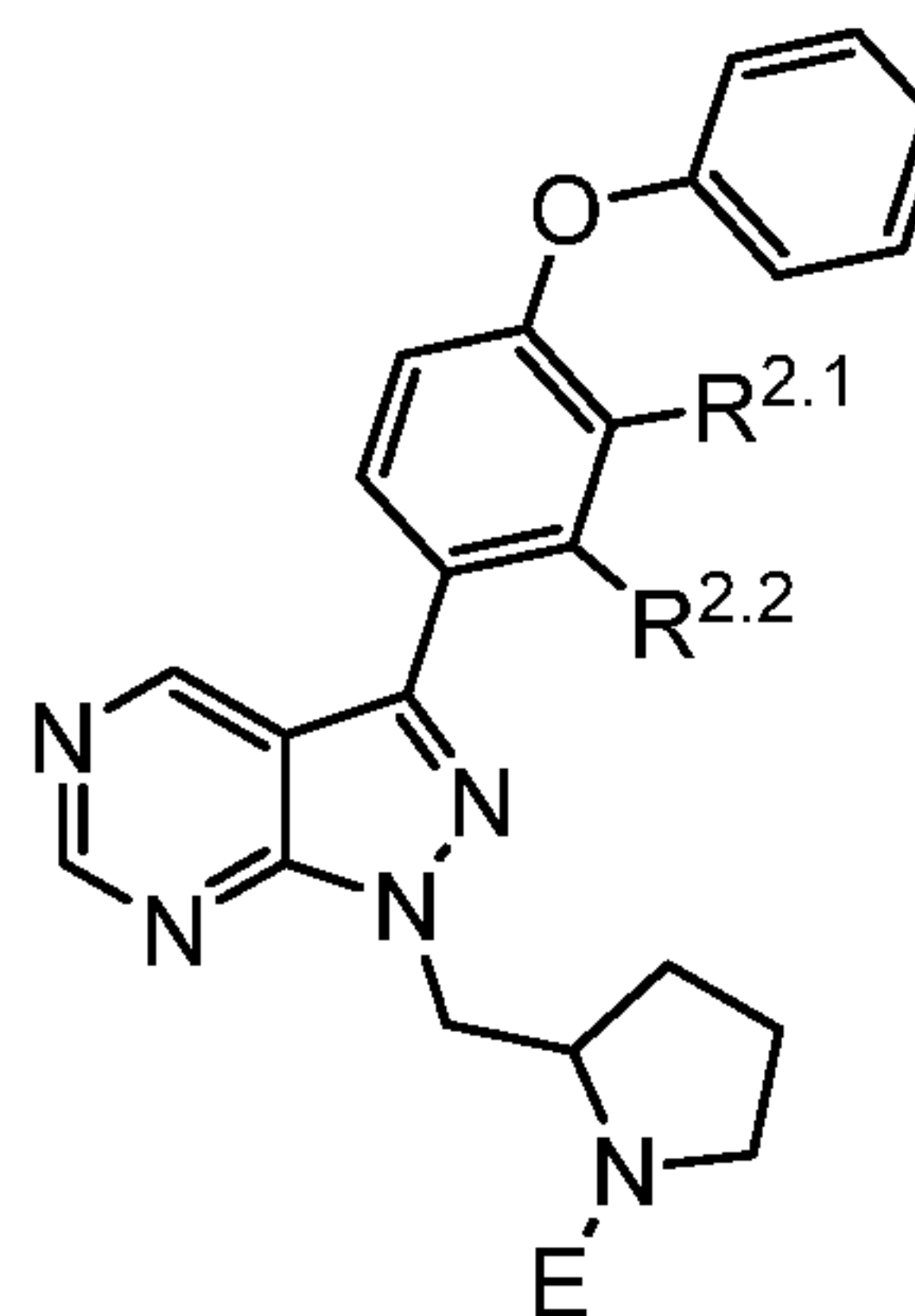
, wherein X^5 , R^2 and $z2$ are as described herein. In embodiments, the

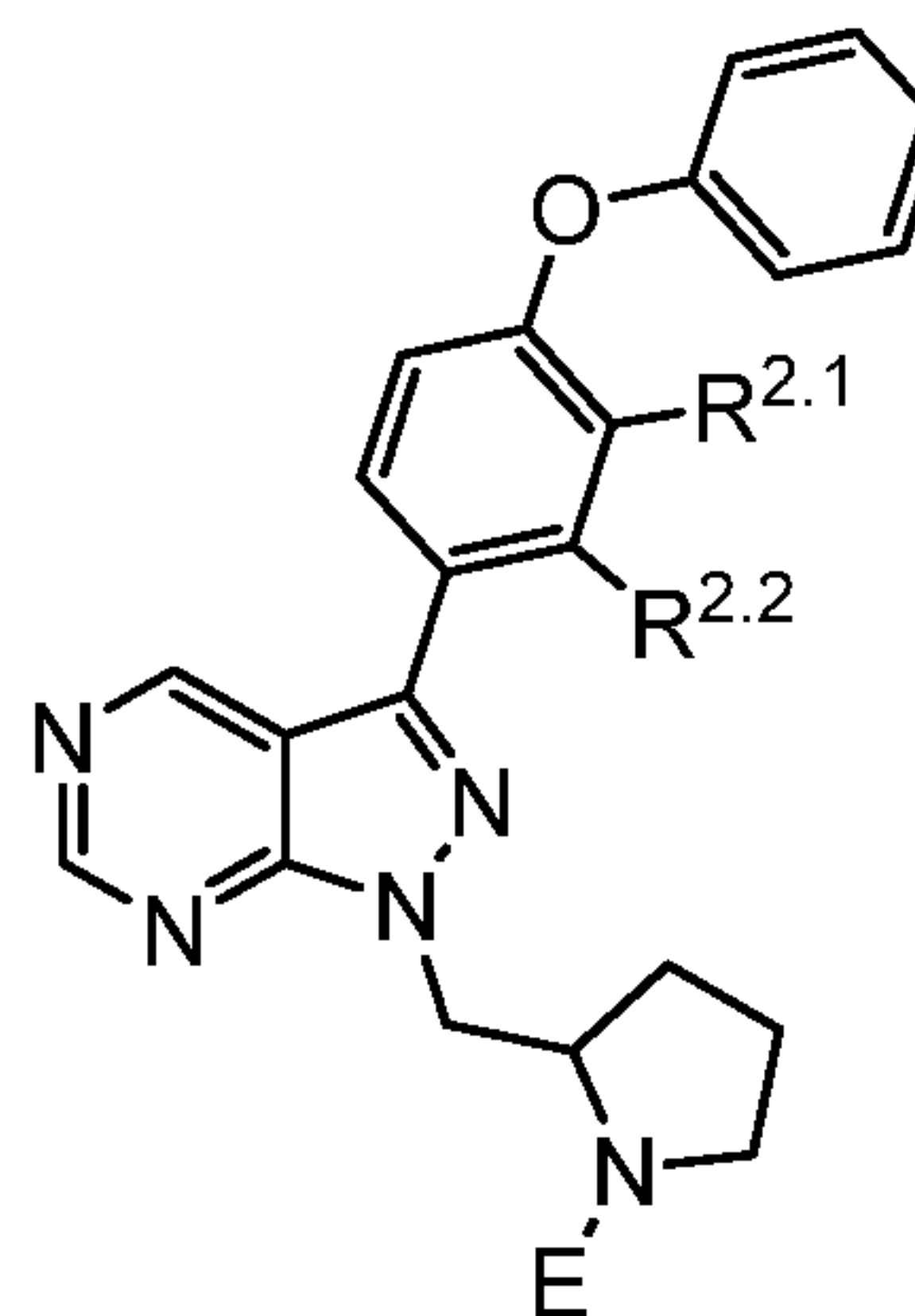


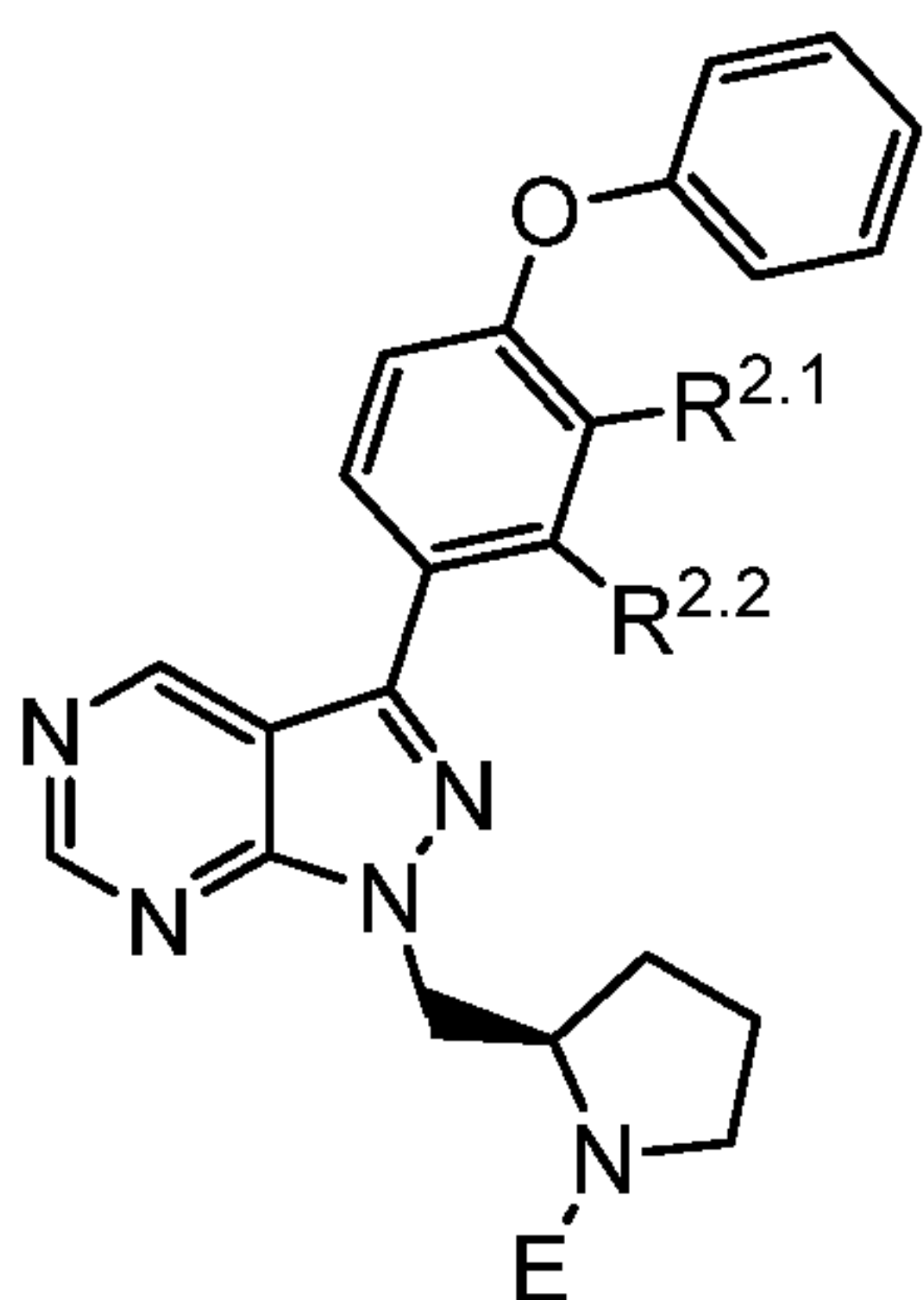
compound has the formula:

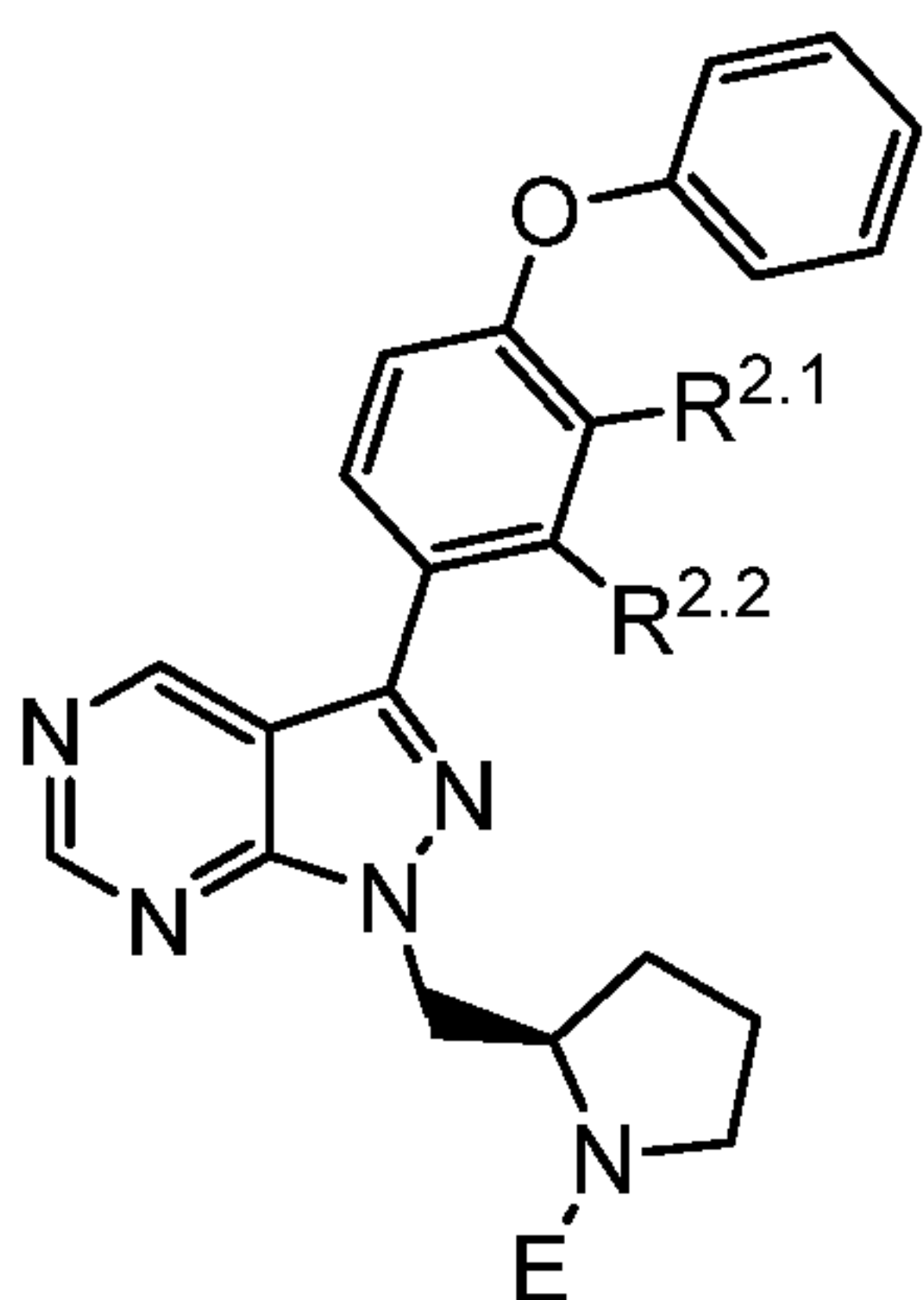
, wherein X^5 , R^2 and $z2$ are as described

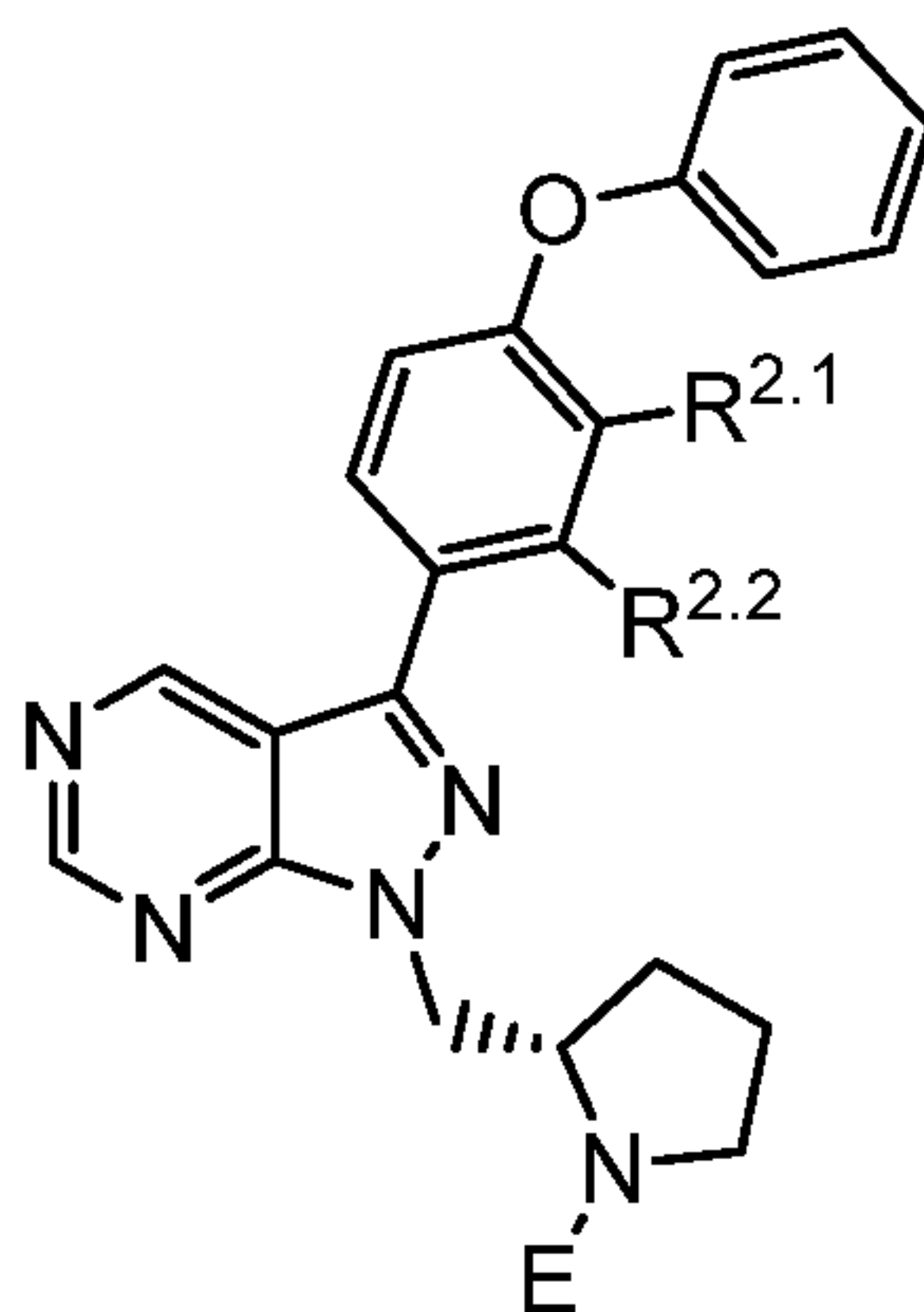
5 herein.

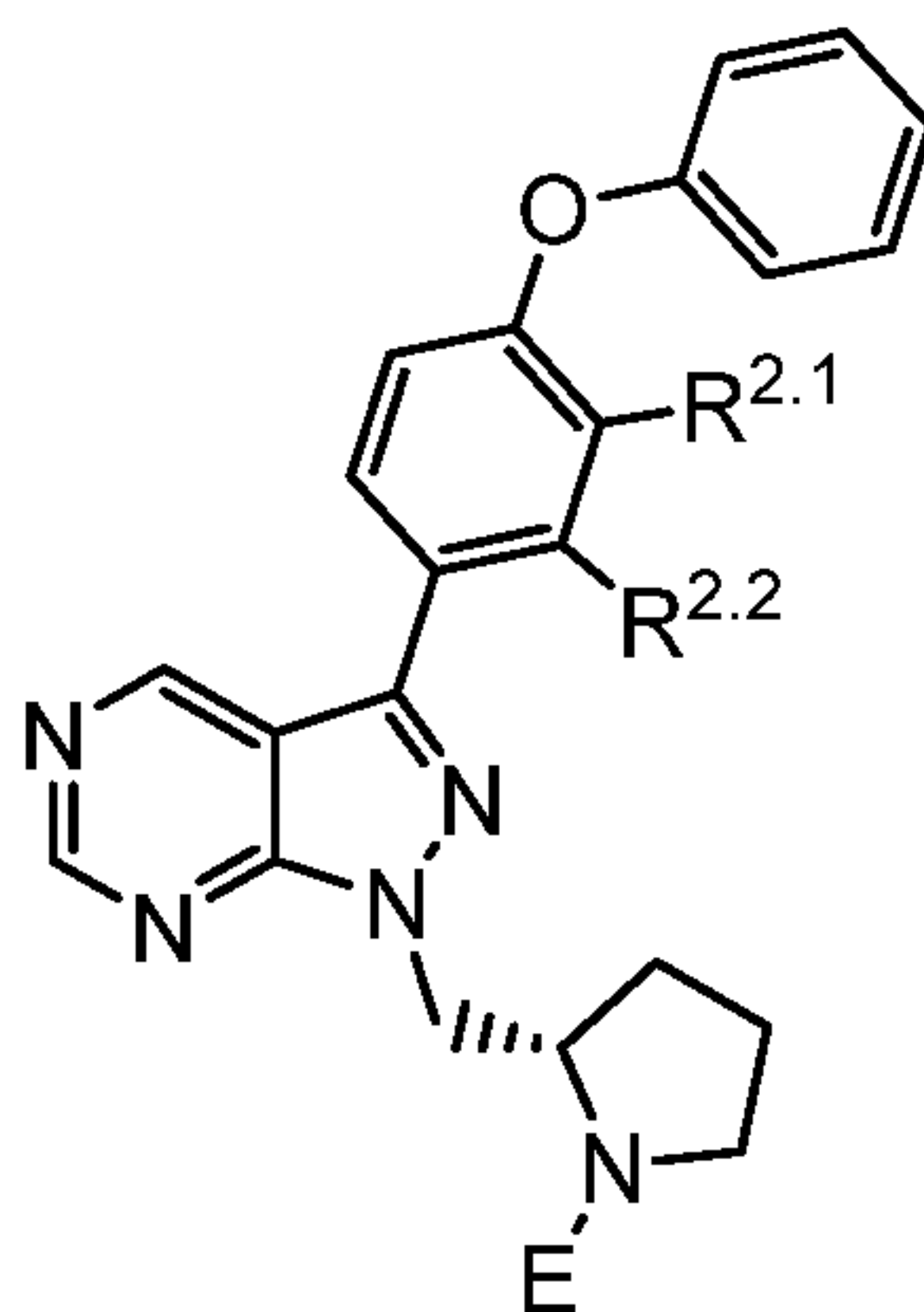


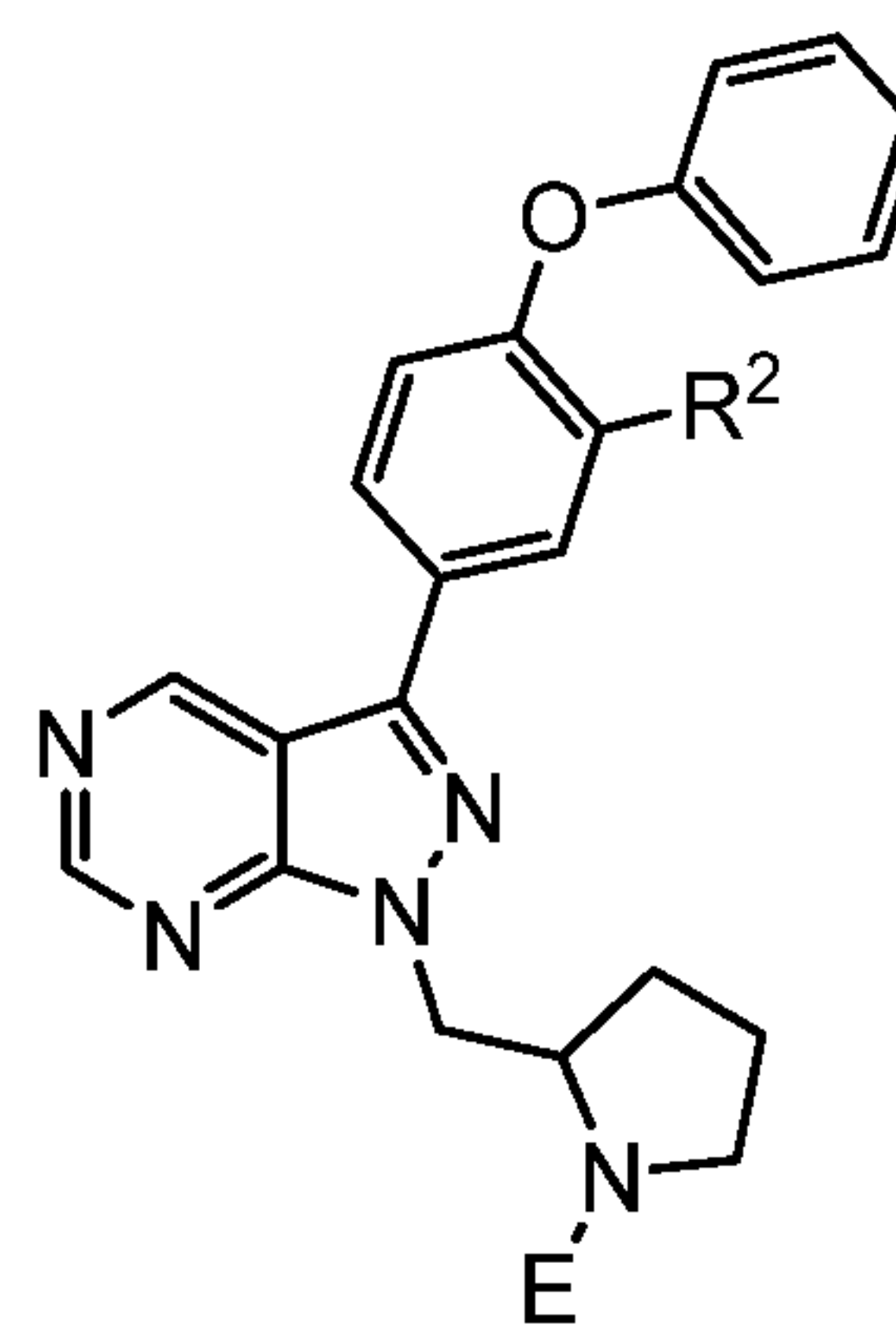
[0590] In embodiments, the compound has the formula: , wherein E is as described herein. $R^{2.1}$ and $R^{2.2}$ are each R^1 at a fixed position on the attached ring. $R^{2.1}$ and $R^{2.2}$ may be any substituent of R^2 described herein, including in any aspect, embodiment, example, figure, or claim. In embodiments, the compound has the formula:

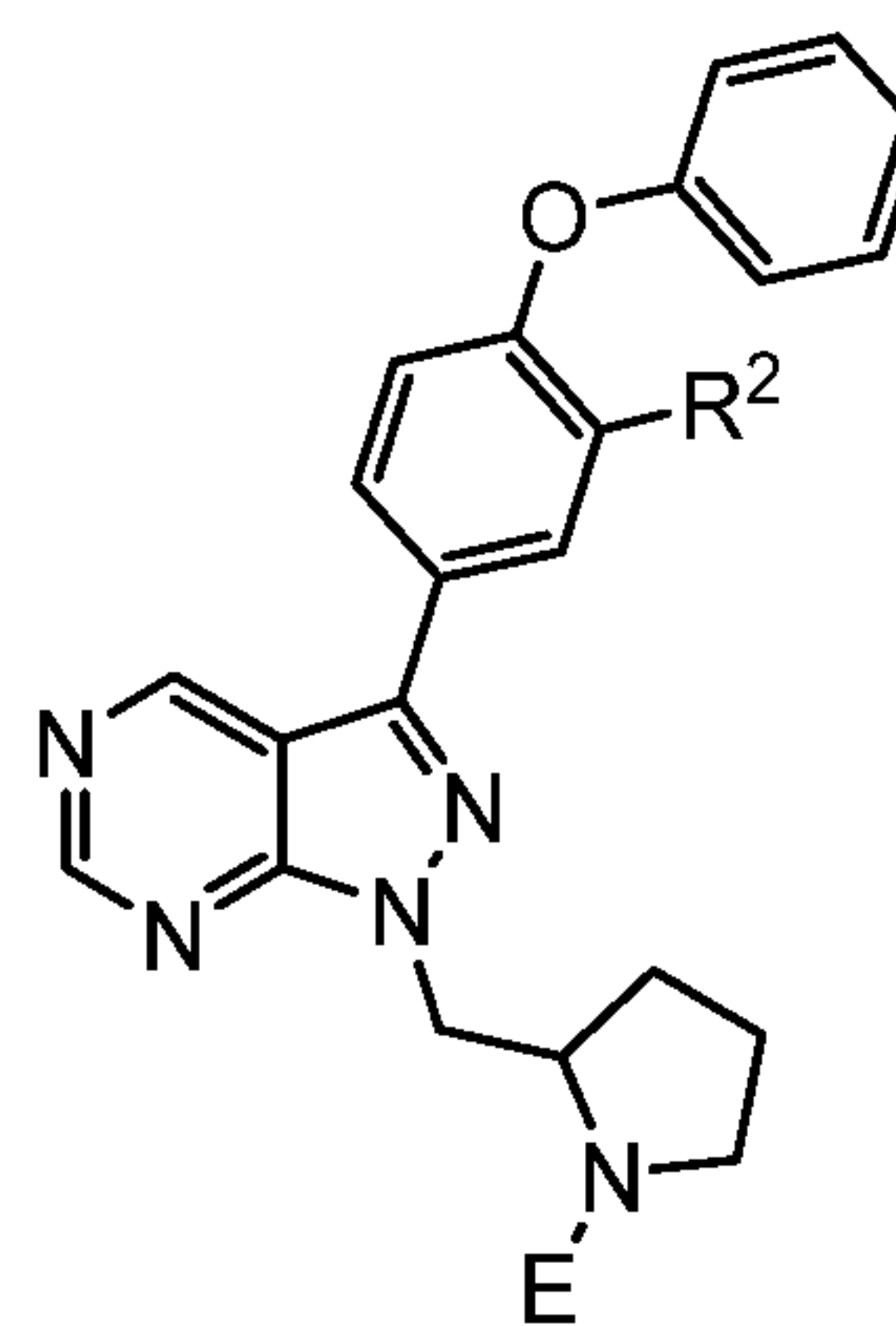


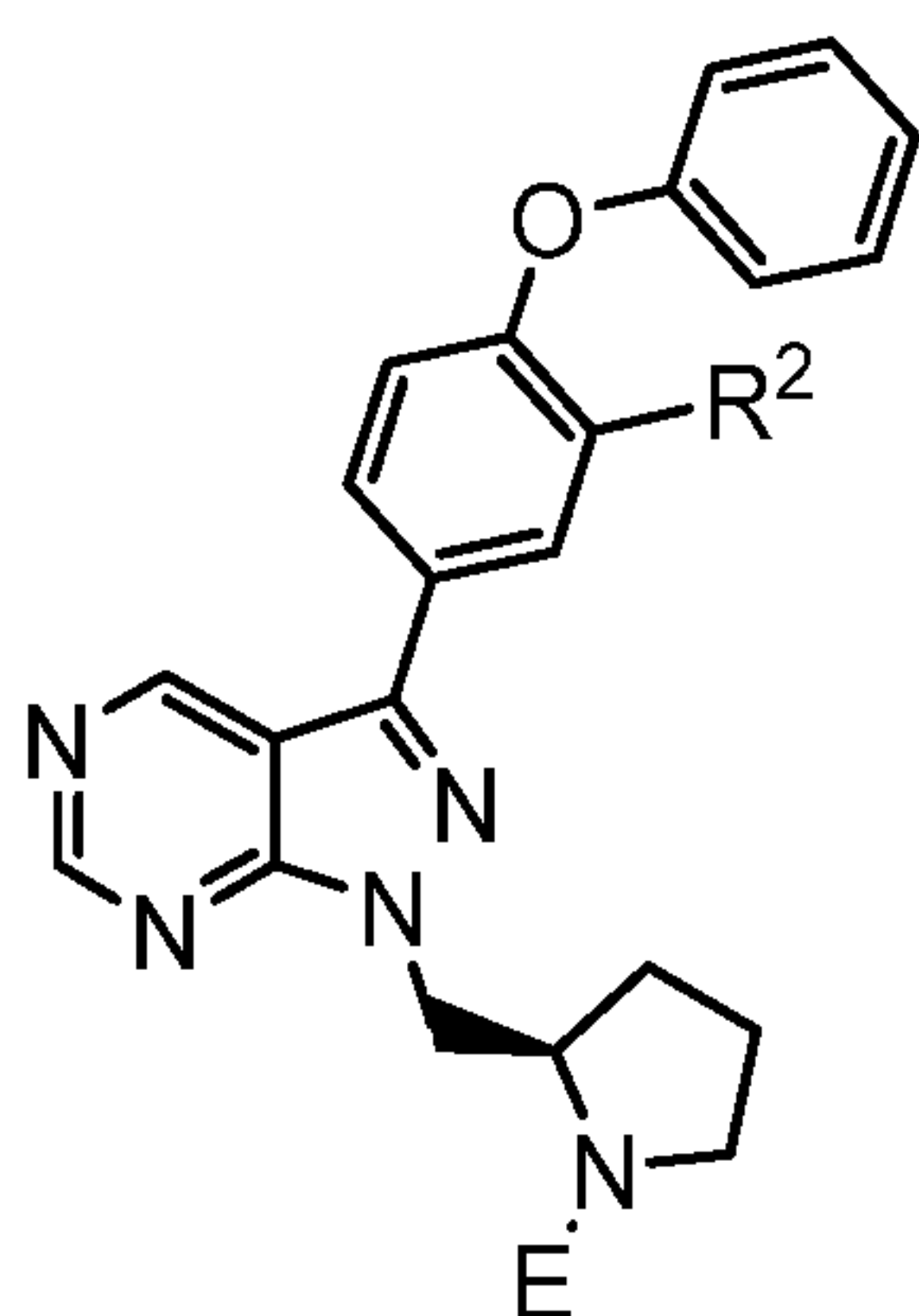
5 , wherein E is as described herein. $R^{2.1}$ and $R^{2.2}$ are each R^1 at a fixed position on the attached ring. $R^{2.1}$ and $R^{2.2}$ may be any substituent of R^2 described herein, including in any aspect, embodiment, example, figure, or claim. In embodiments, the



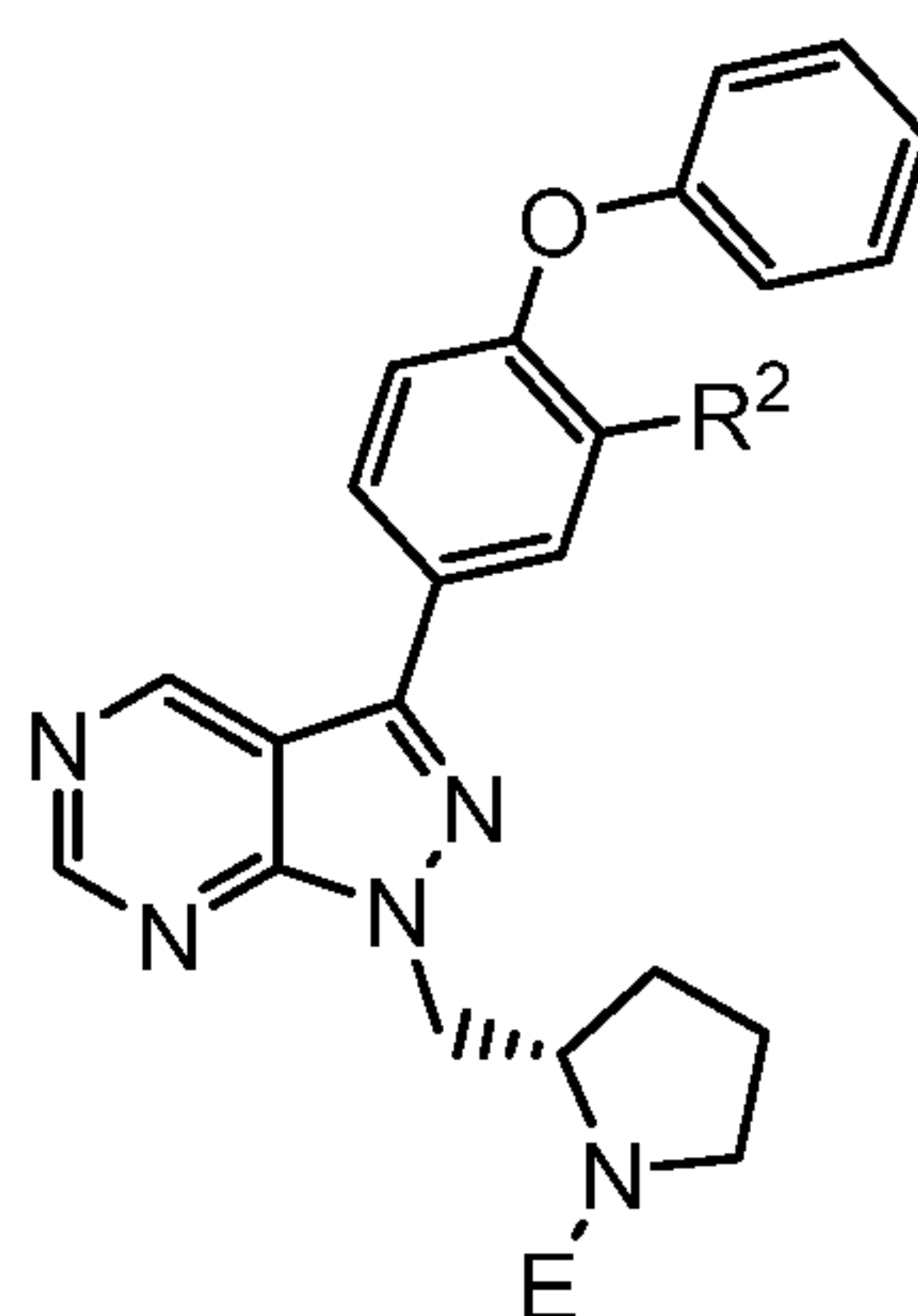
compound has the formula: , wherein E is as described herein. $R^{2.1}$ and $R^{2.2}$ are each R^1 at a fixed position on the attached ring. $R^{2.1}$ and $R^{2.2}$ may be any substituent of R^2 described herein, including in any aspect, embodiment, example, figure, or claim.

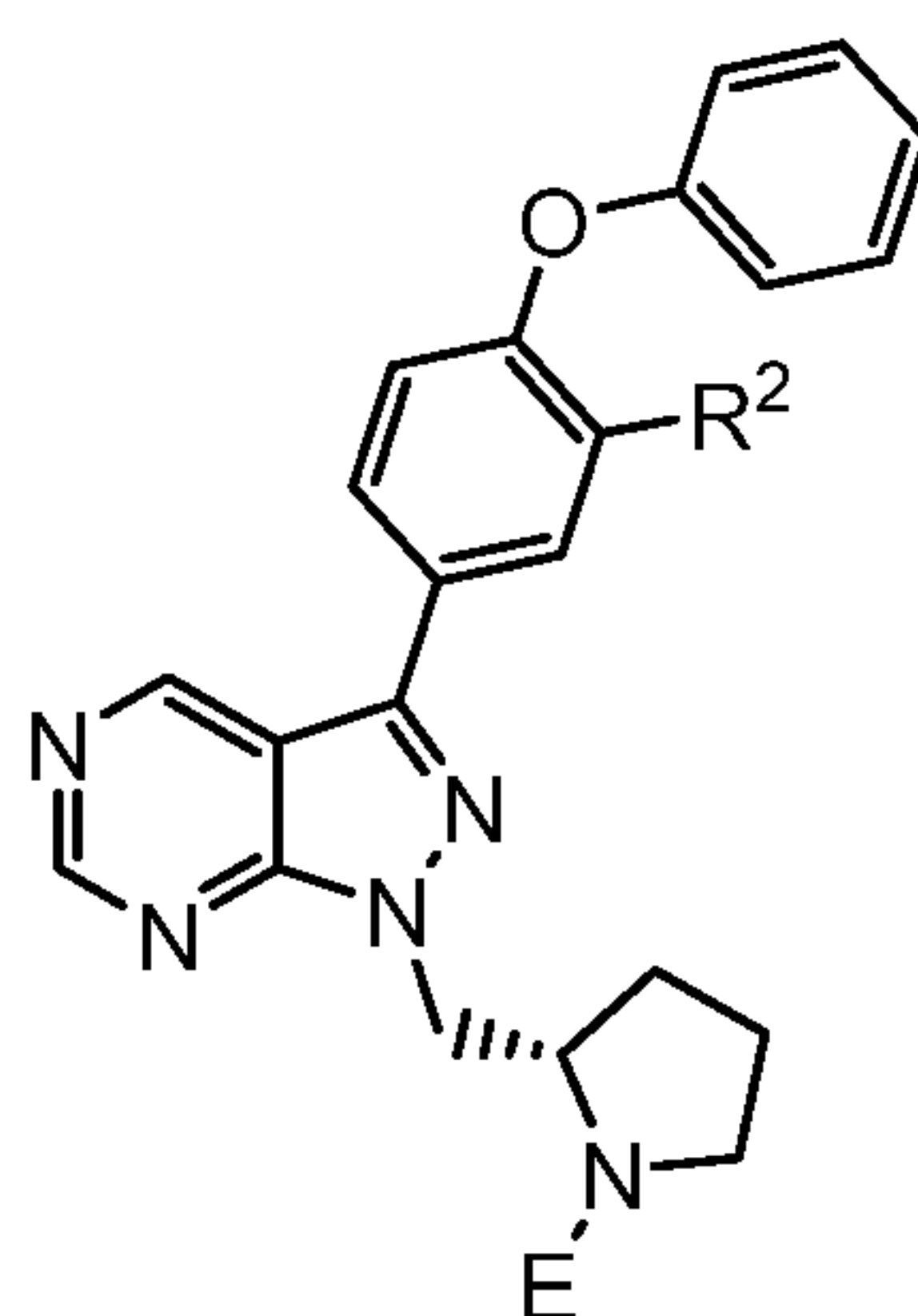


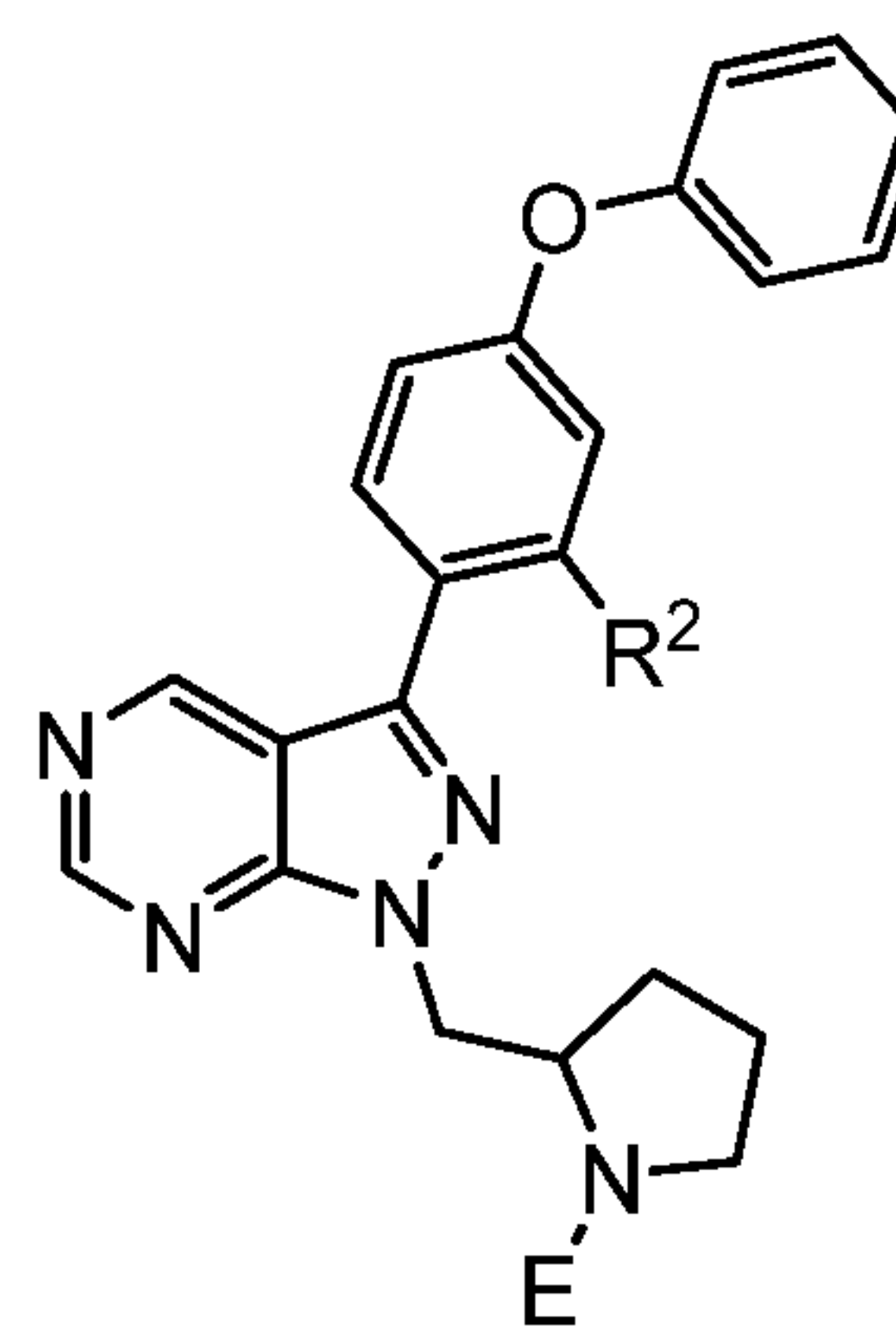
[0591] In embodiments, the compound has the formula: , wherein R² and E are as described herein. In embodiments, the compound has the formula:

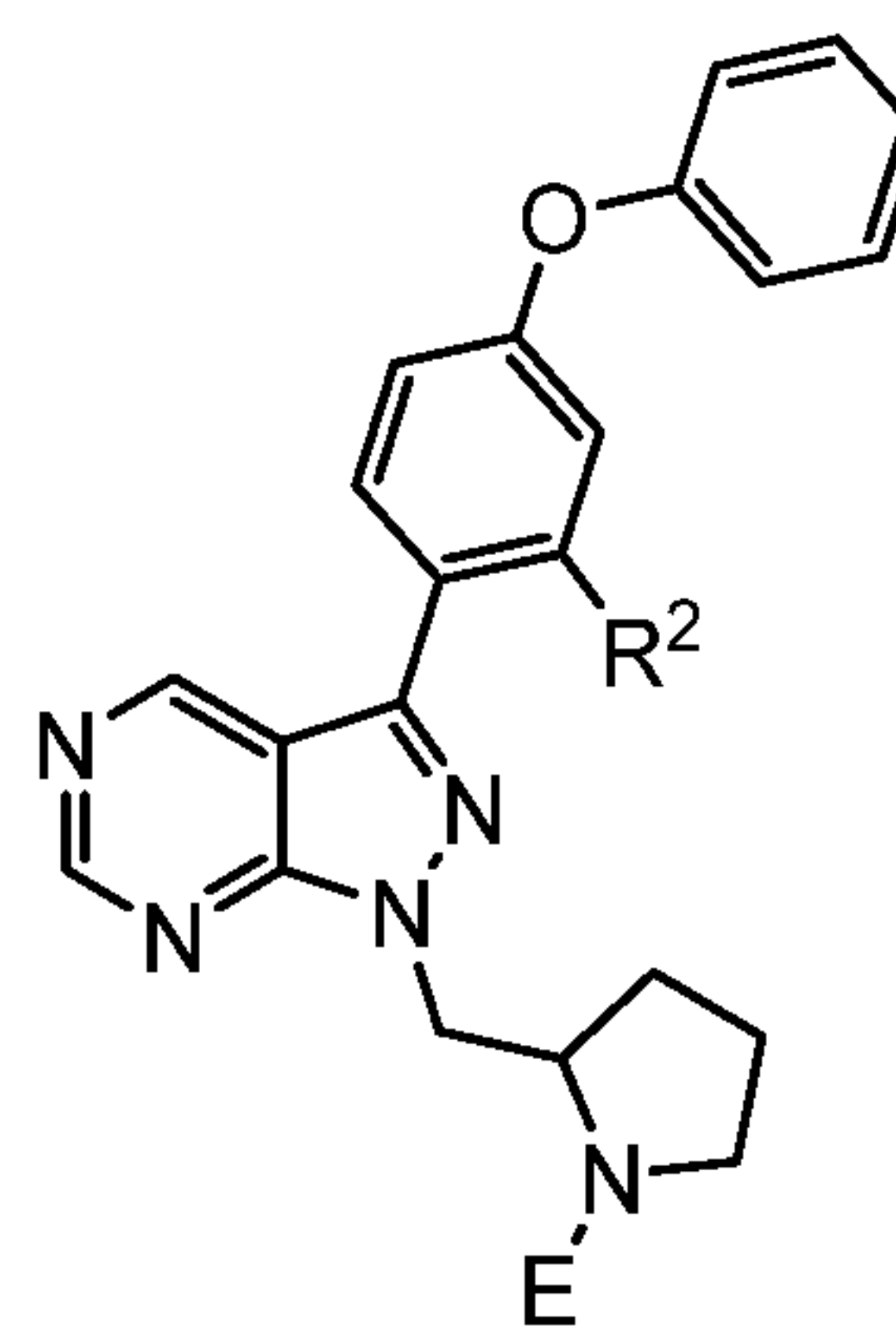


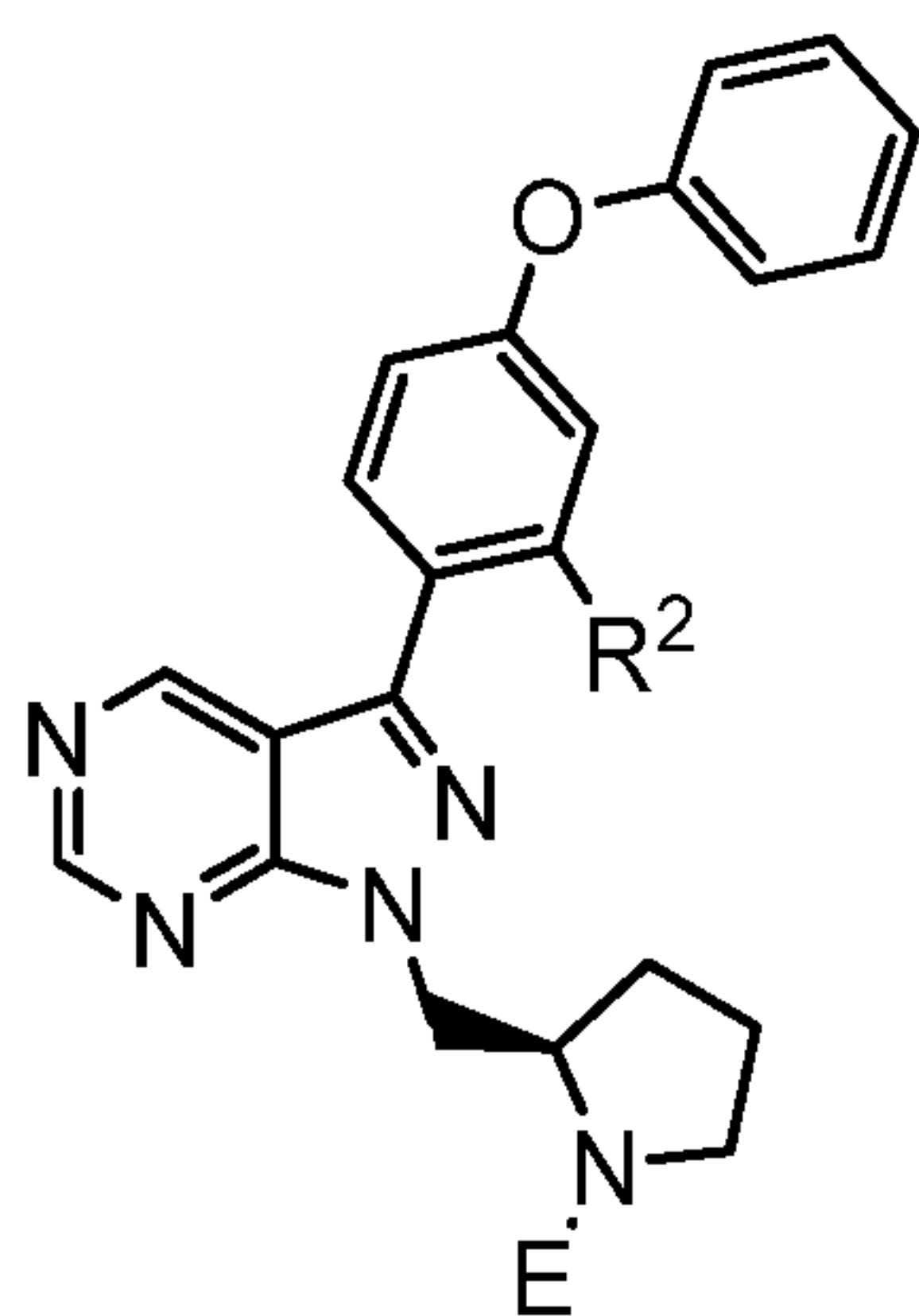
, wherein R² and E are as described herein. In embodiments, the



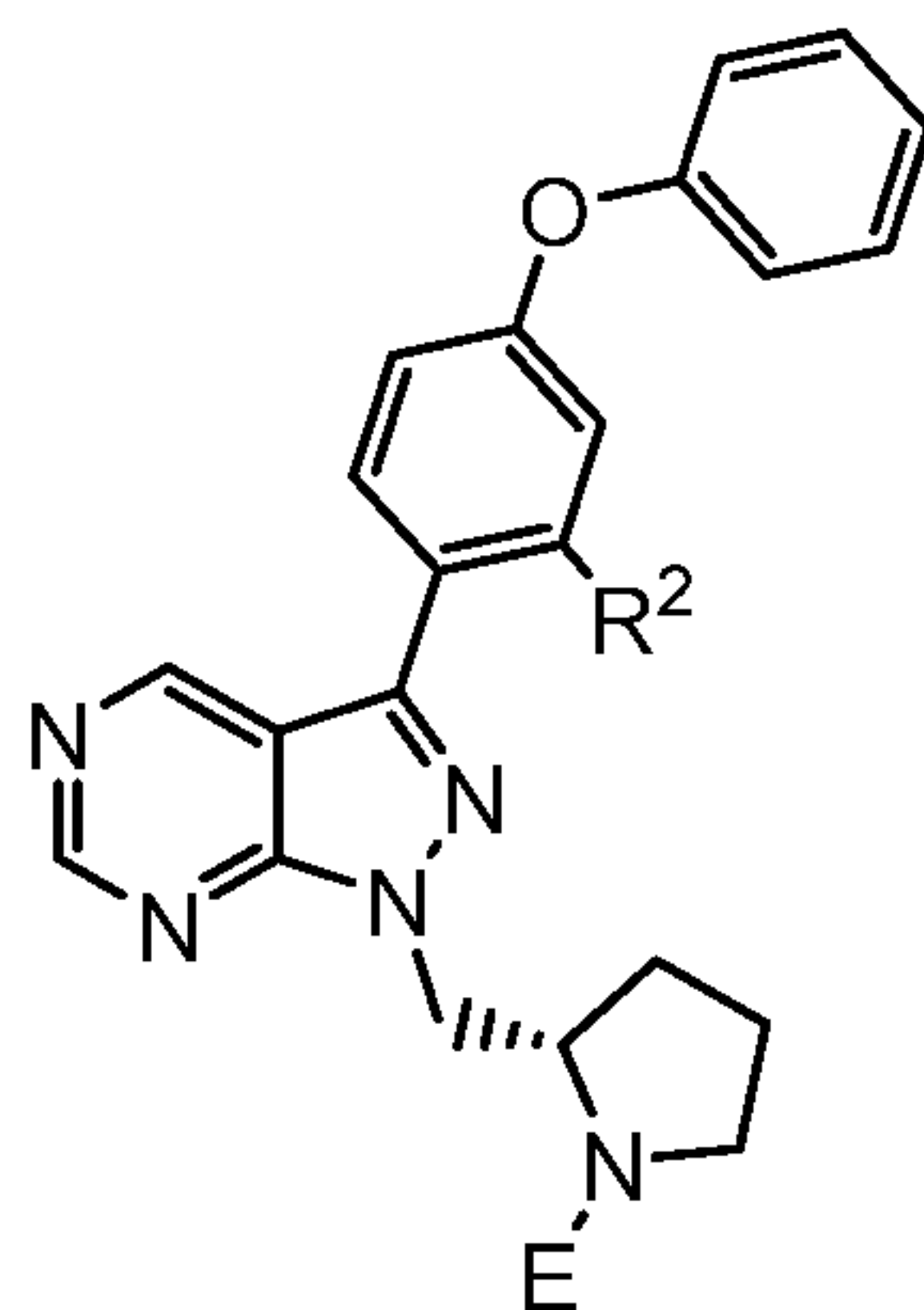
compound has the formula: , wherein R² and E are as described herein.



5 **[0592]** In embodiments, the compound has the formula: , wherein R² and E are as described herein. In embodiments, the compound has the formula:

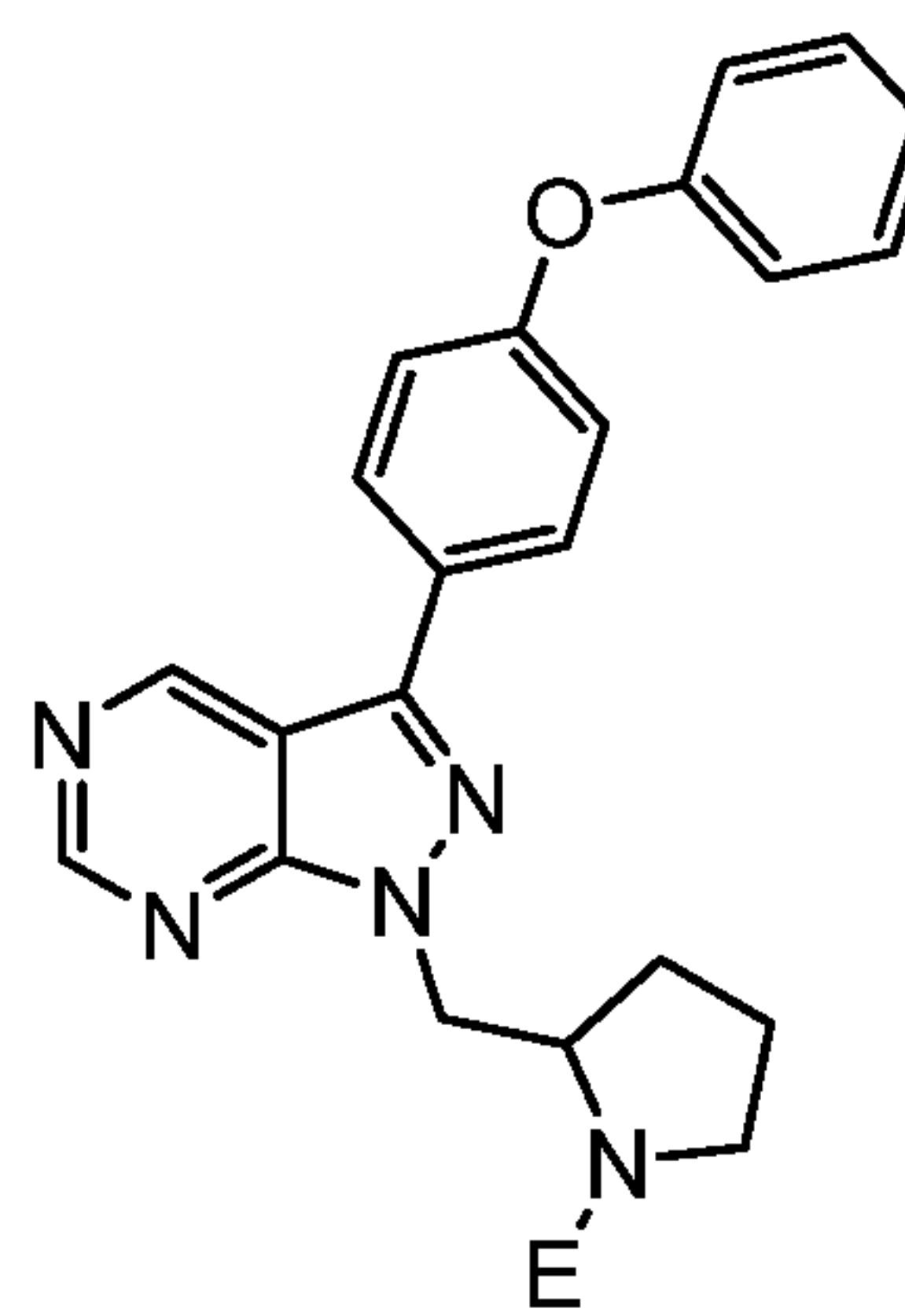


, wherein R² and E are as described herein. In embodiments, the



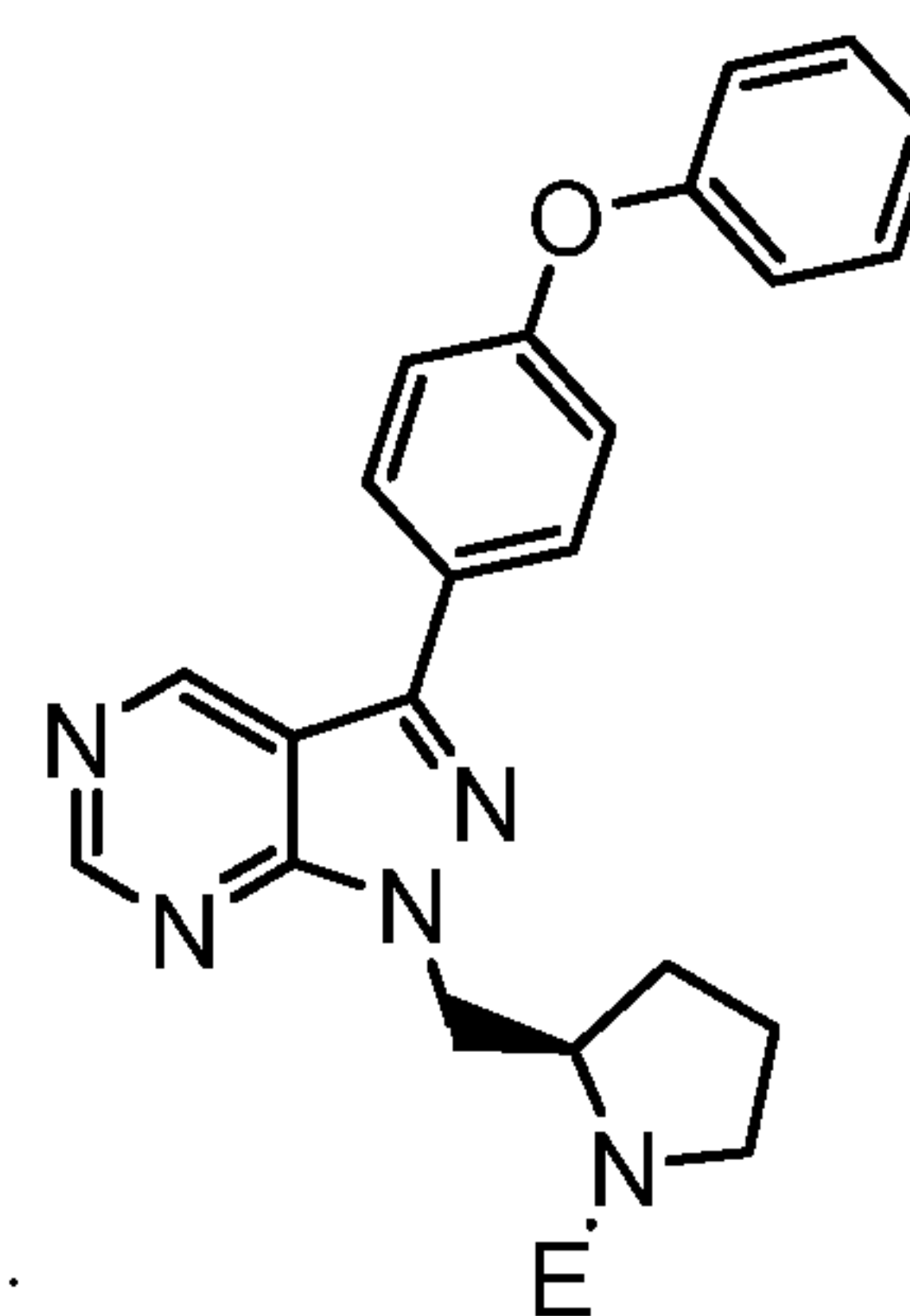
compound has the formula:

, wherein R² and E are as described herein.



[0593] In embodiments, the compound has the formula:

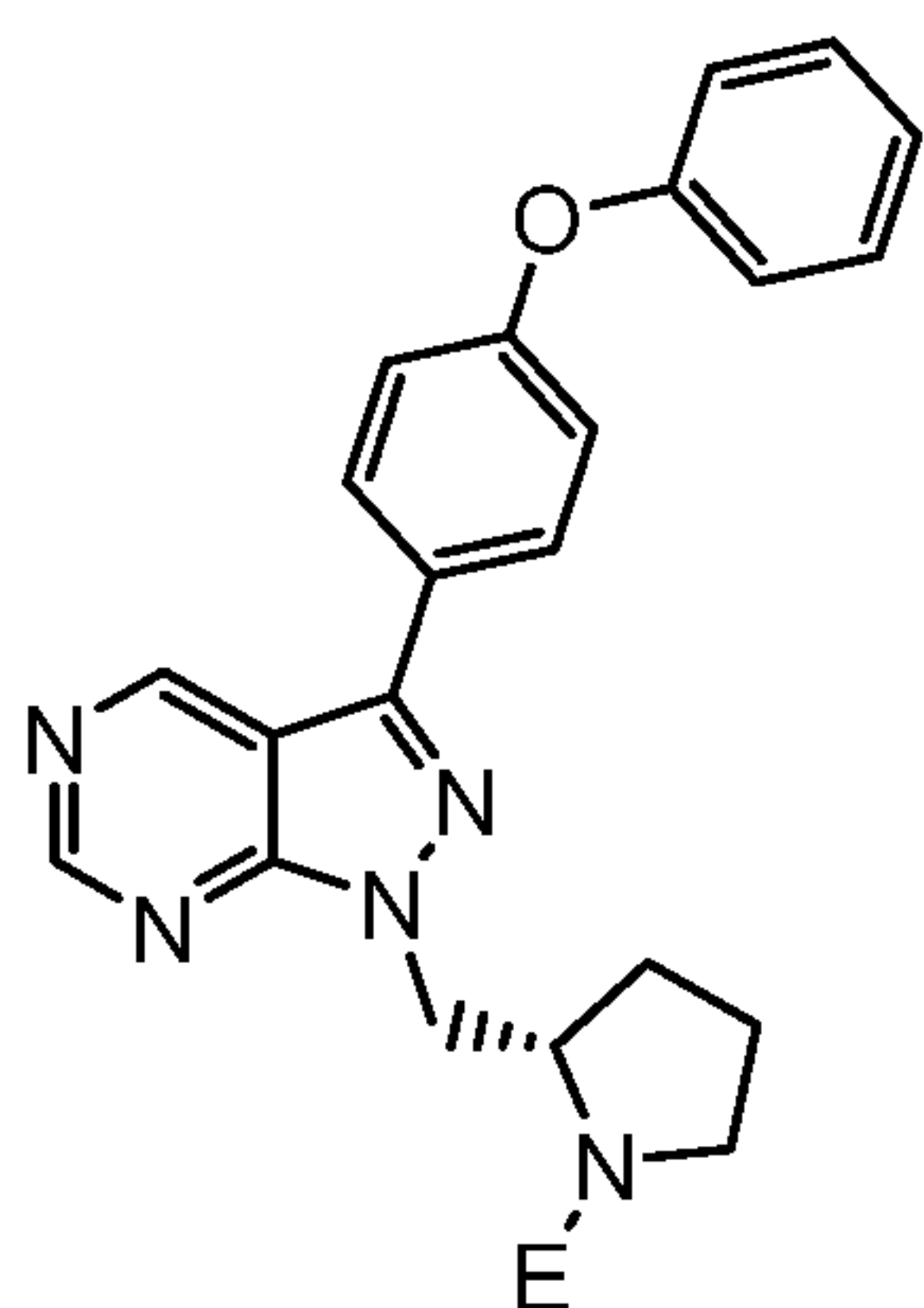
, wherein E



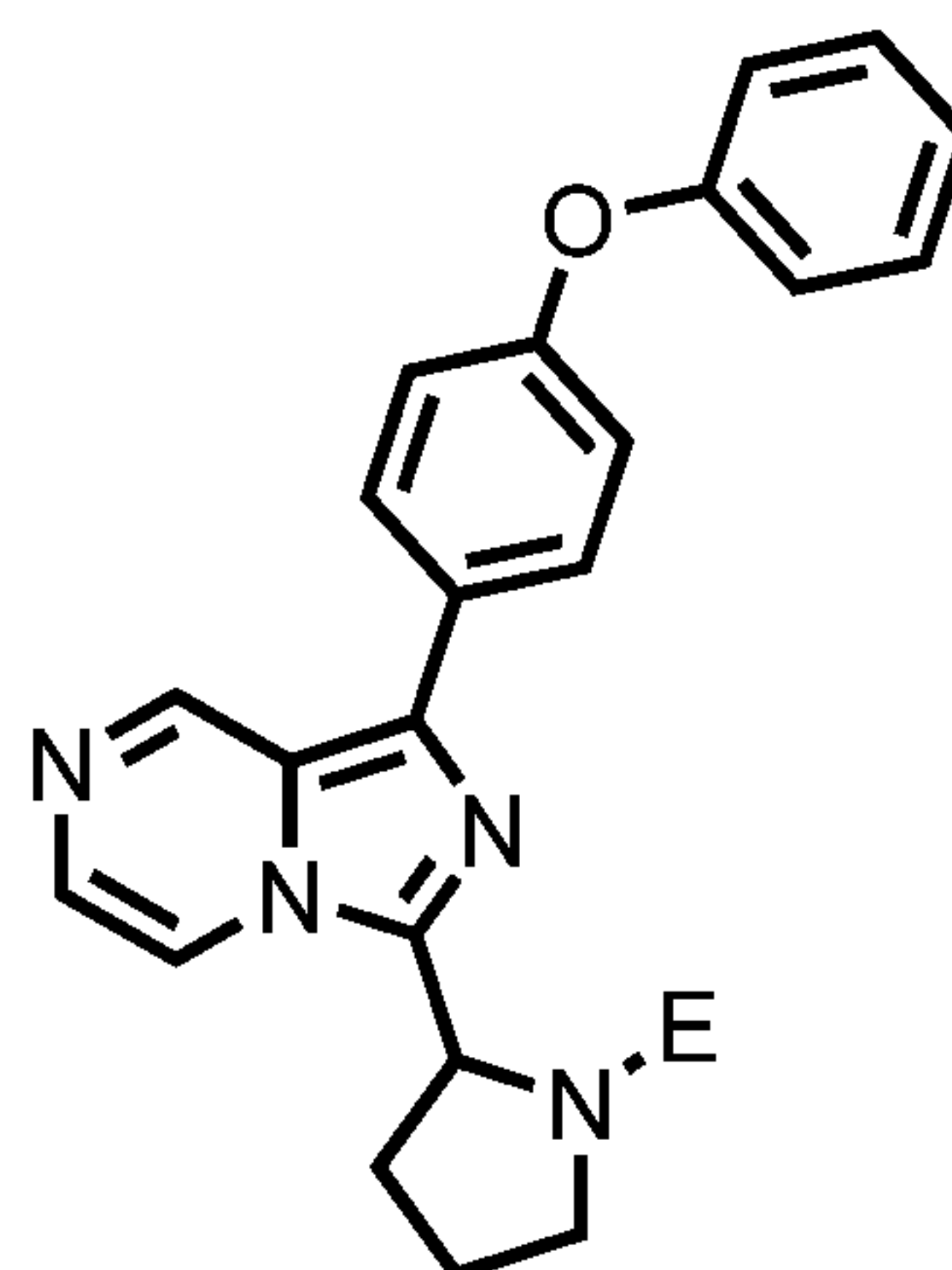
is as described herein. In embodiments, the compound has the formula:

,

wherein E is as described herein. In embodiments, the compound has the formula:



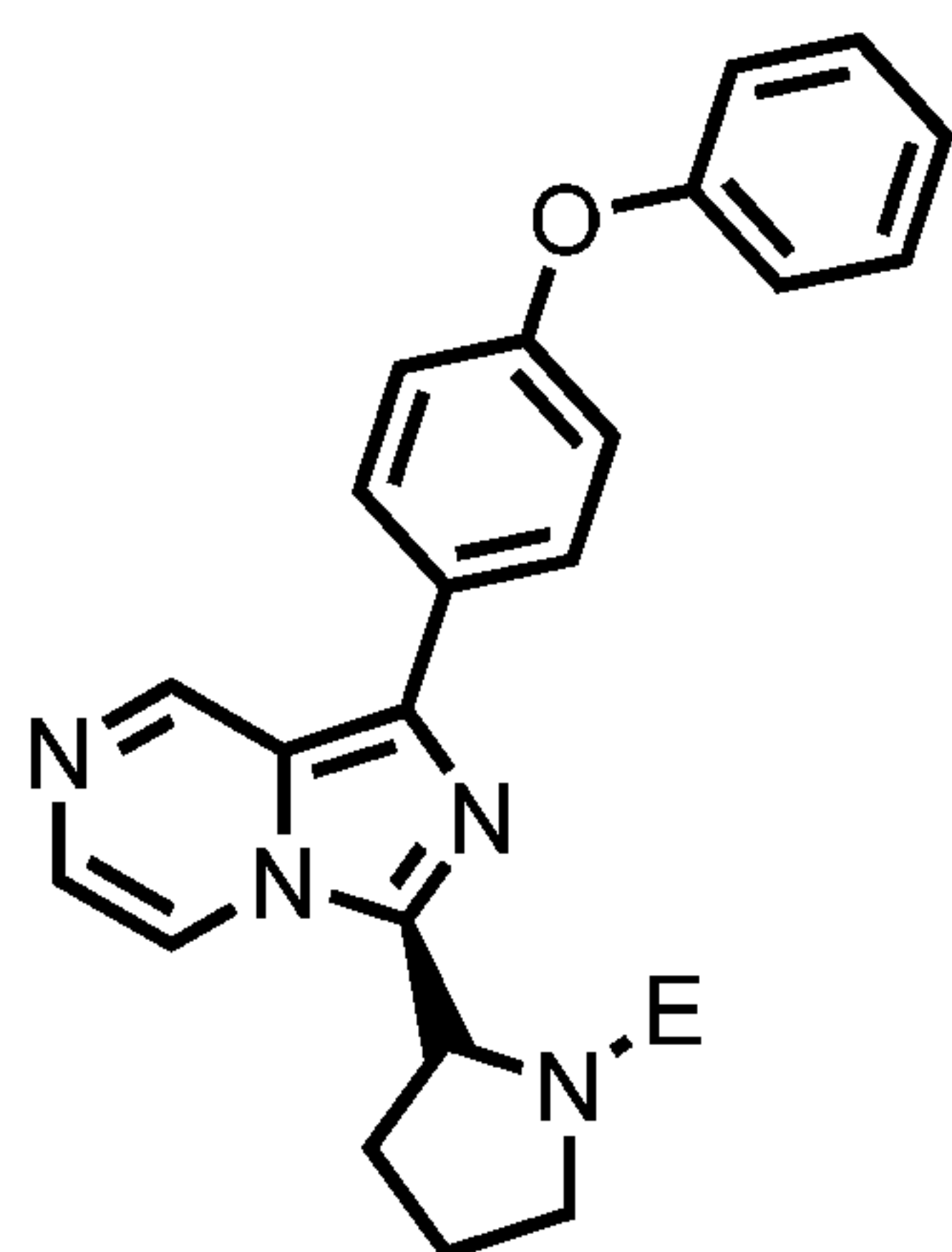
, wherein E is as described herein.



[0594] In embodiments, the compound has the formula:

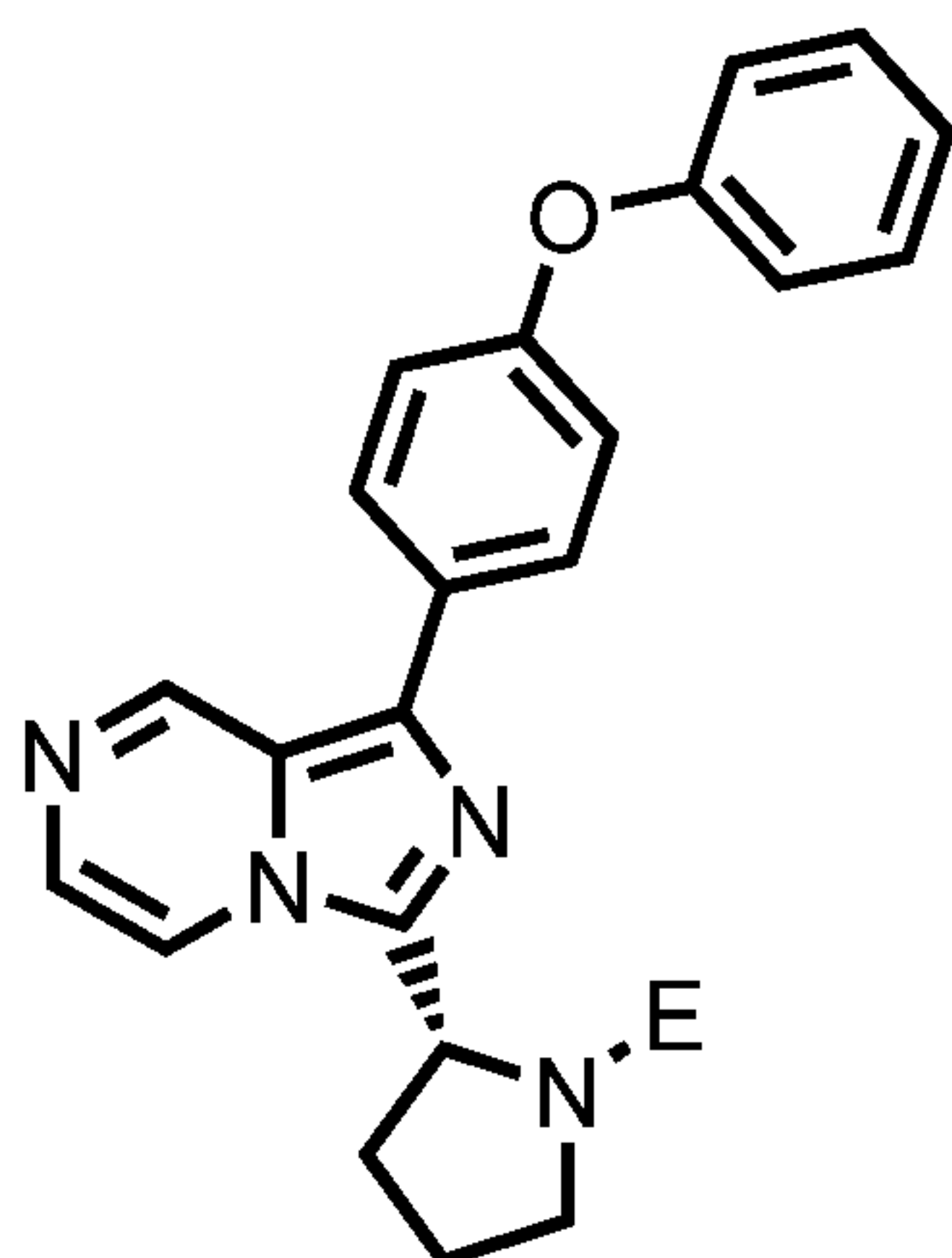
, wherein

E is as described herein. In embodiments, the compound has the formula:



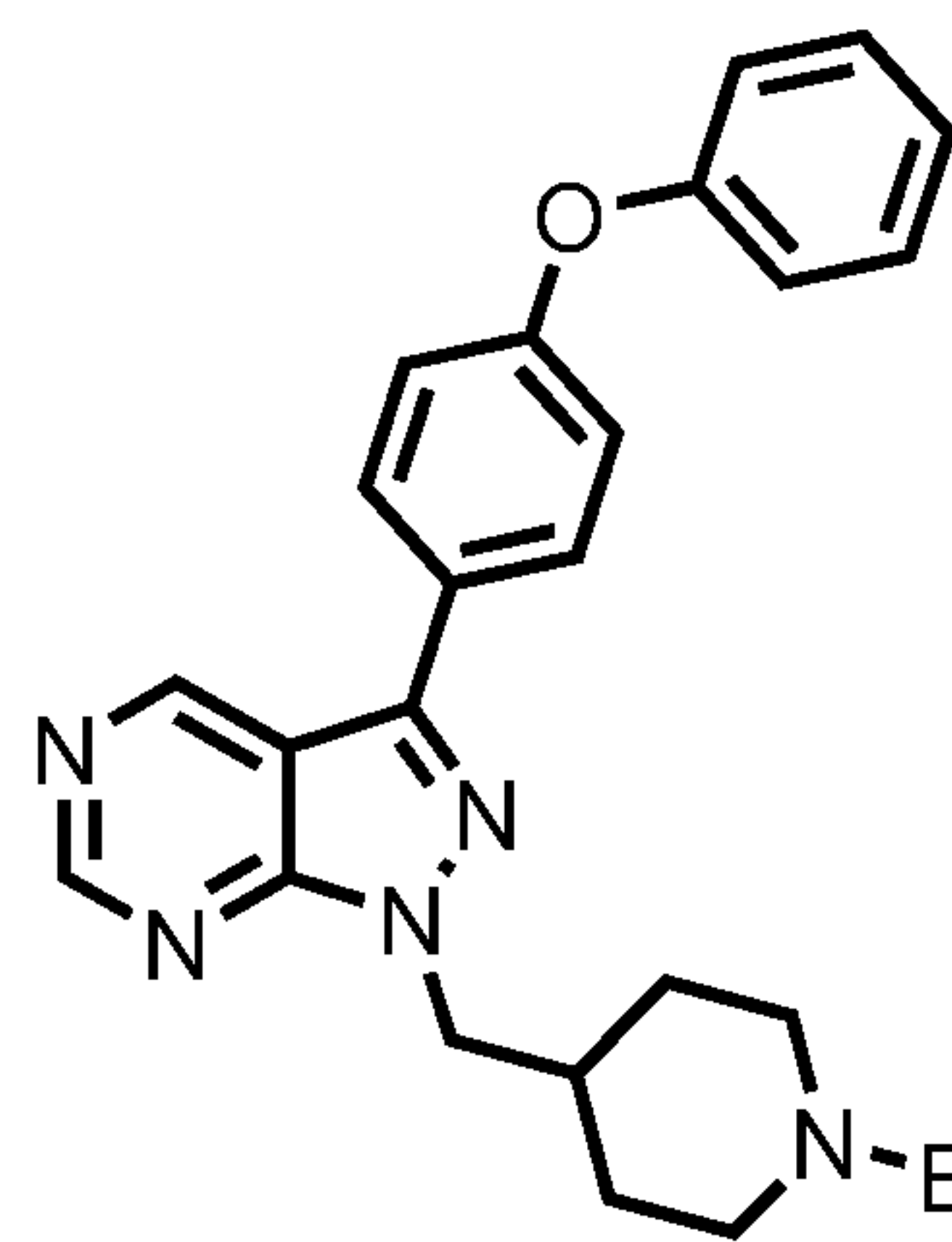
5

, wherein E is as described herein. In embodiments, the compound

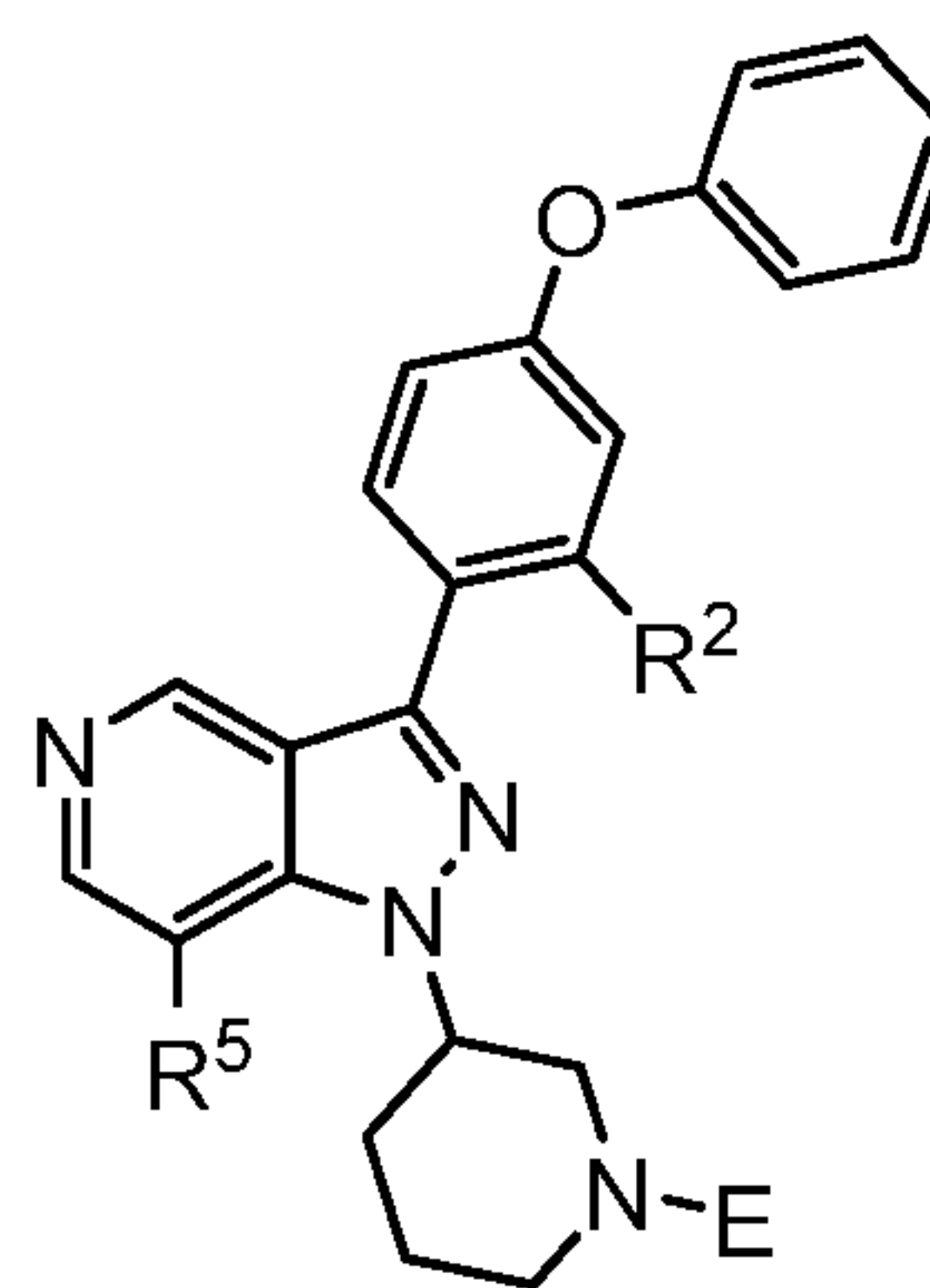


has the formula:

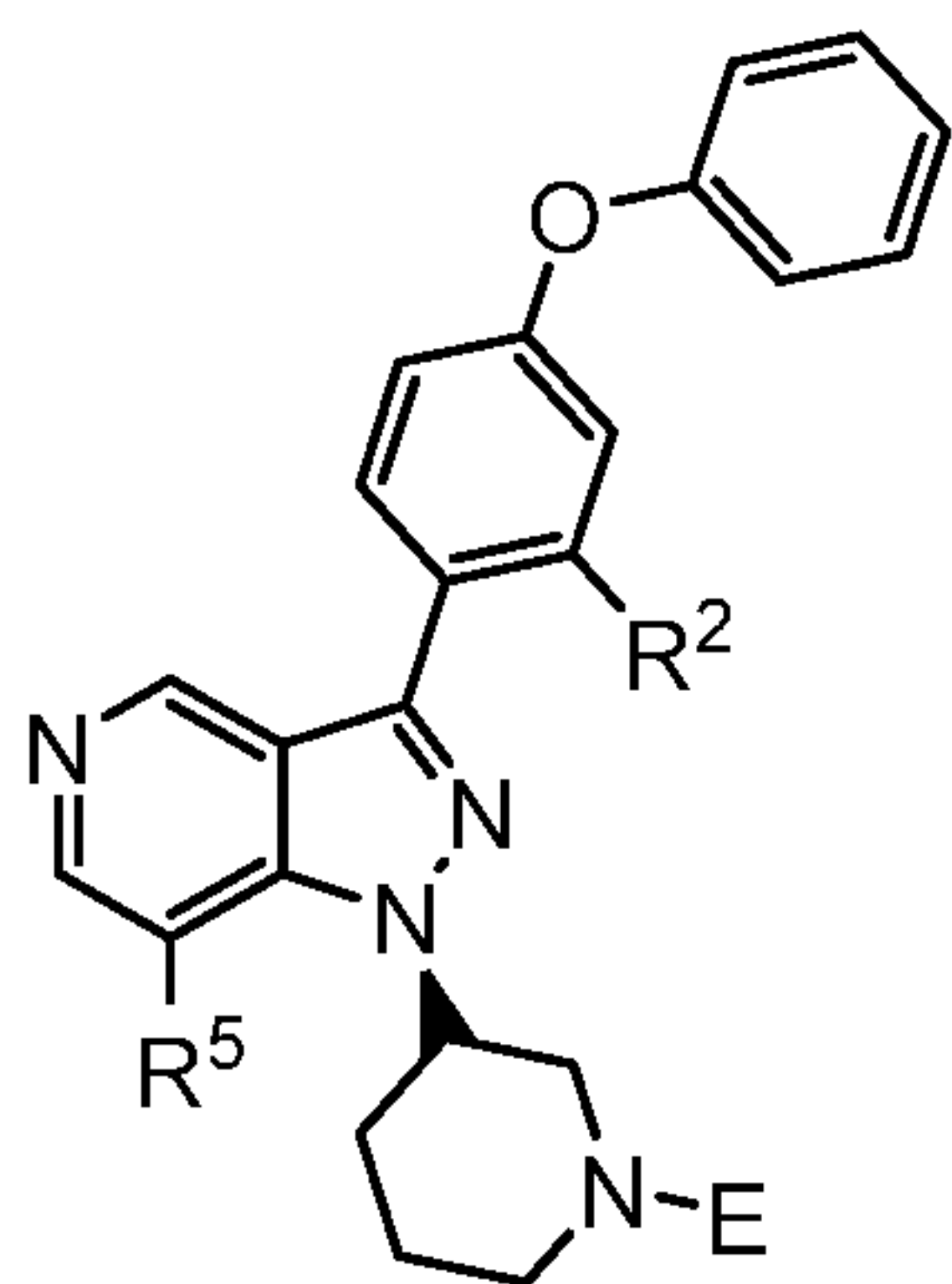
, wherein E is as described herein.



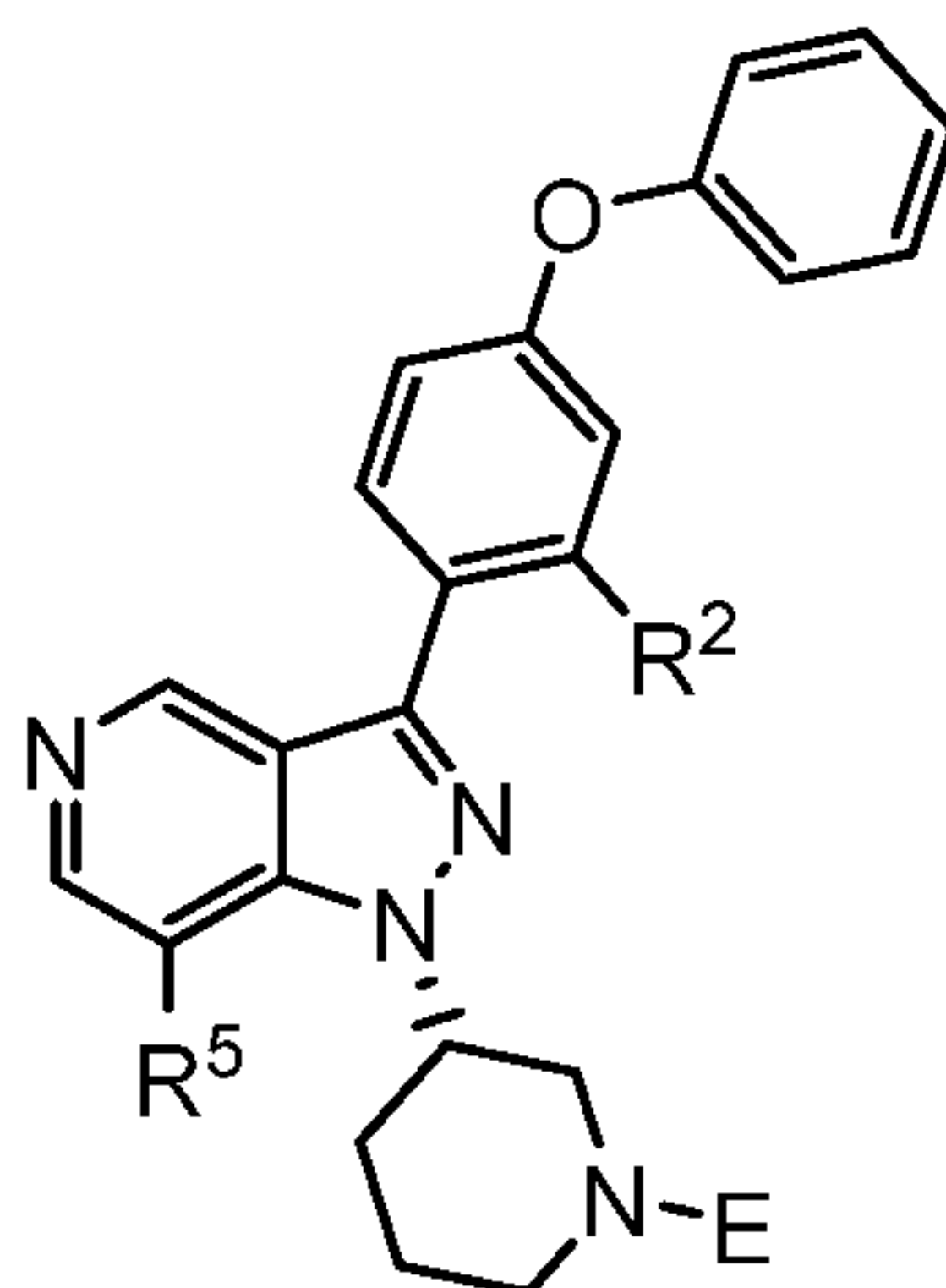
[0595] In embodiments, the compound has the formula:
E is as described herein.



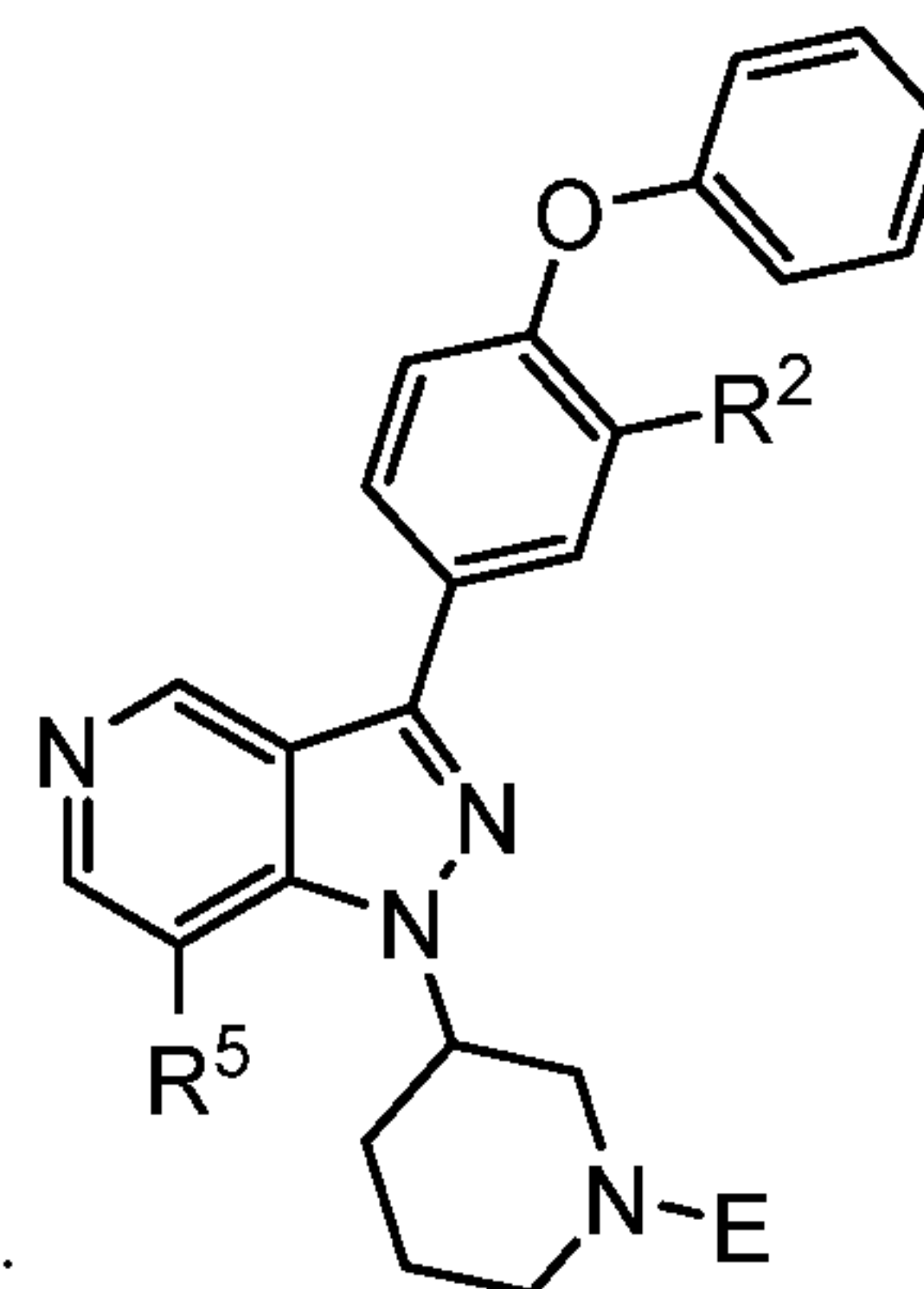
[0596] In embodiments, the compound has the formula:
R⁵, and E are as described herein. In embodiments, the compound has the formula:

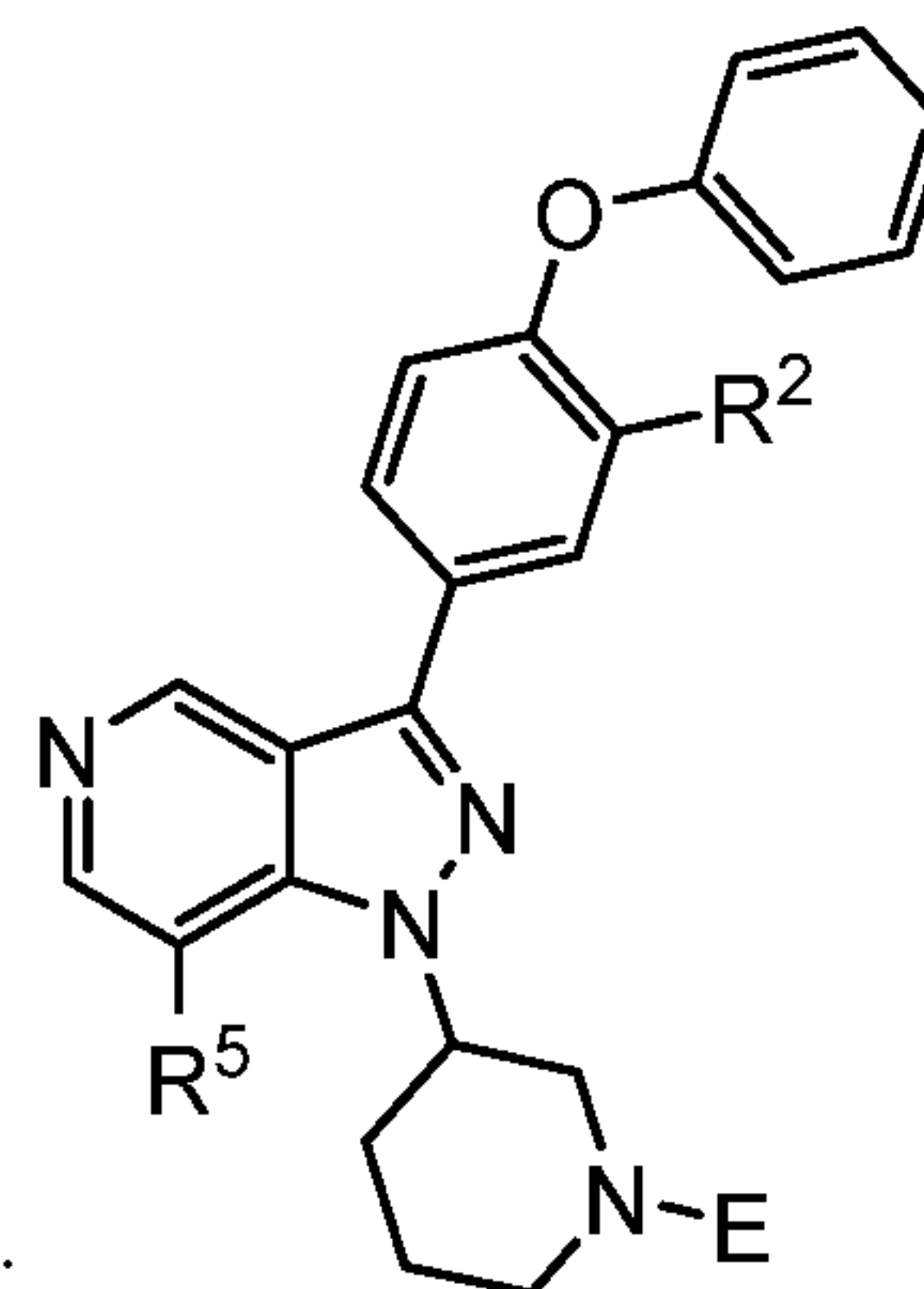


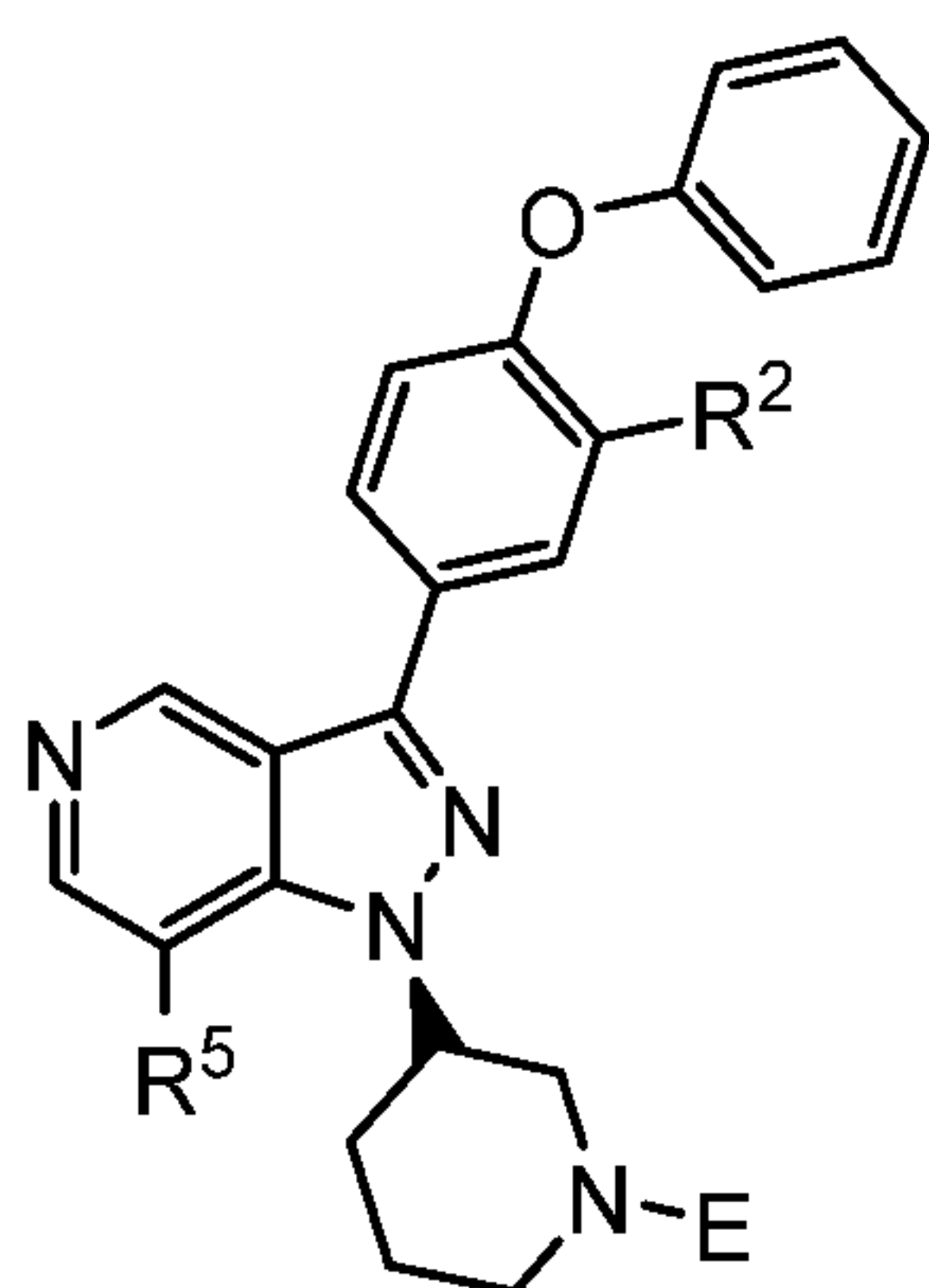
5 , wherein R², R⁵, and E are as described herein. In embodiments, the



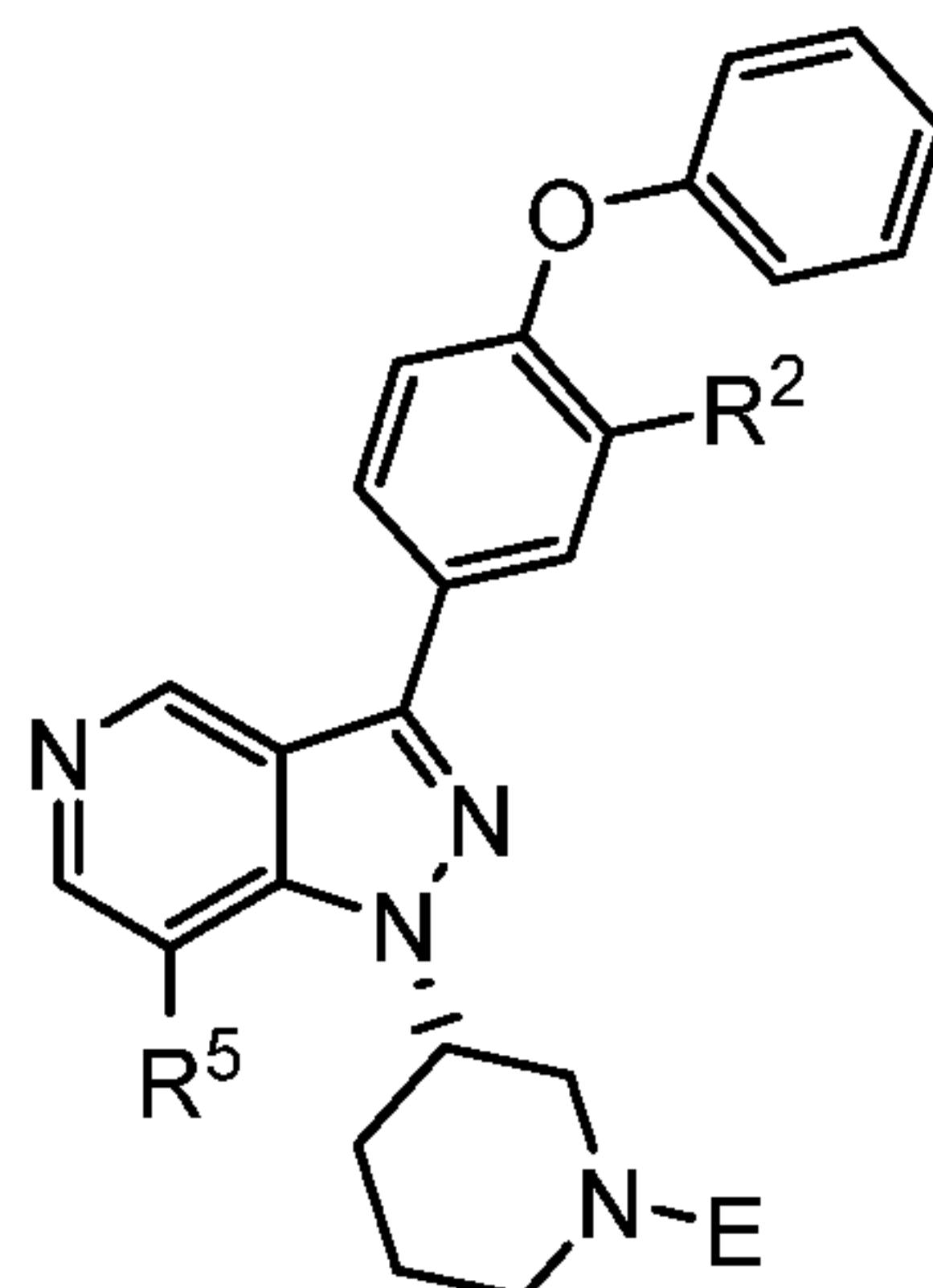
compound has the formula:
herein.

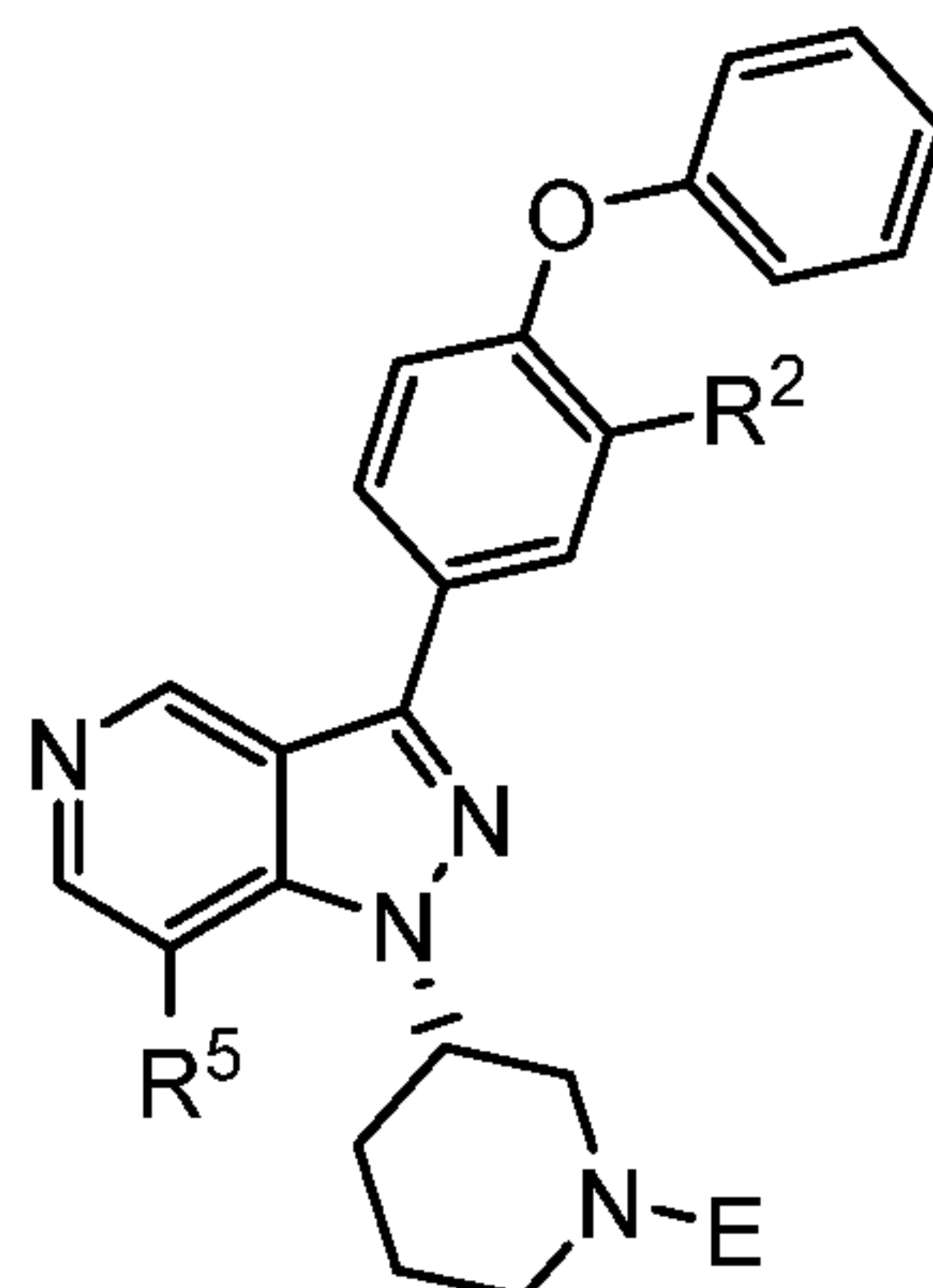


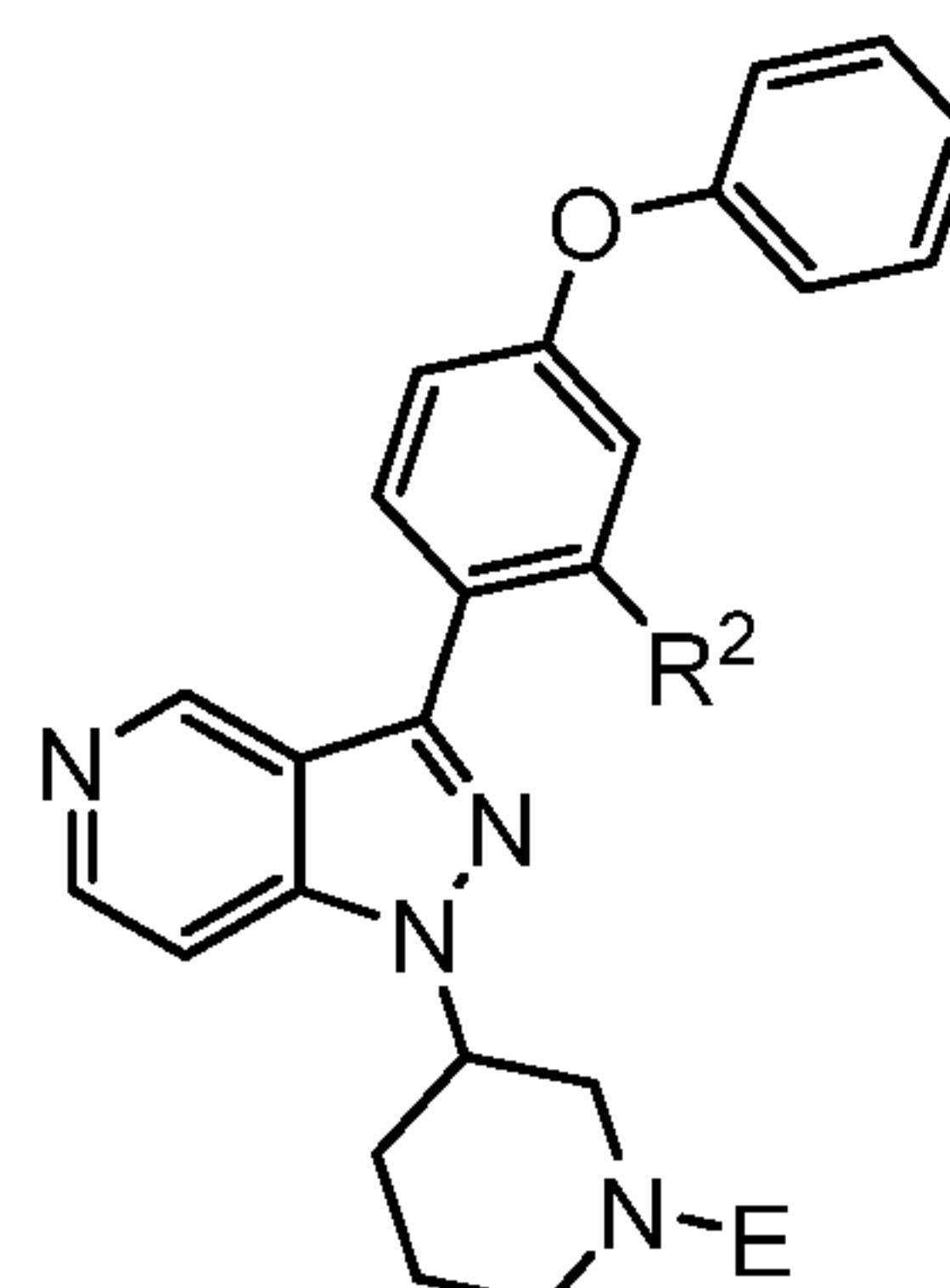
[0597] In embodiments, the compound has the formula: , wherein R^2 , R^5 , and E are as described herein. In embodiments, the compound has the formula:

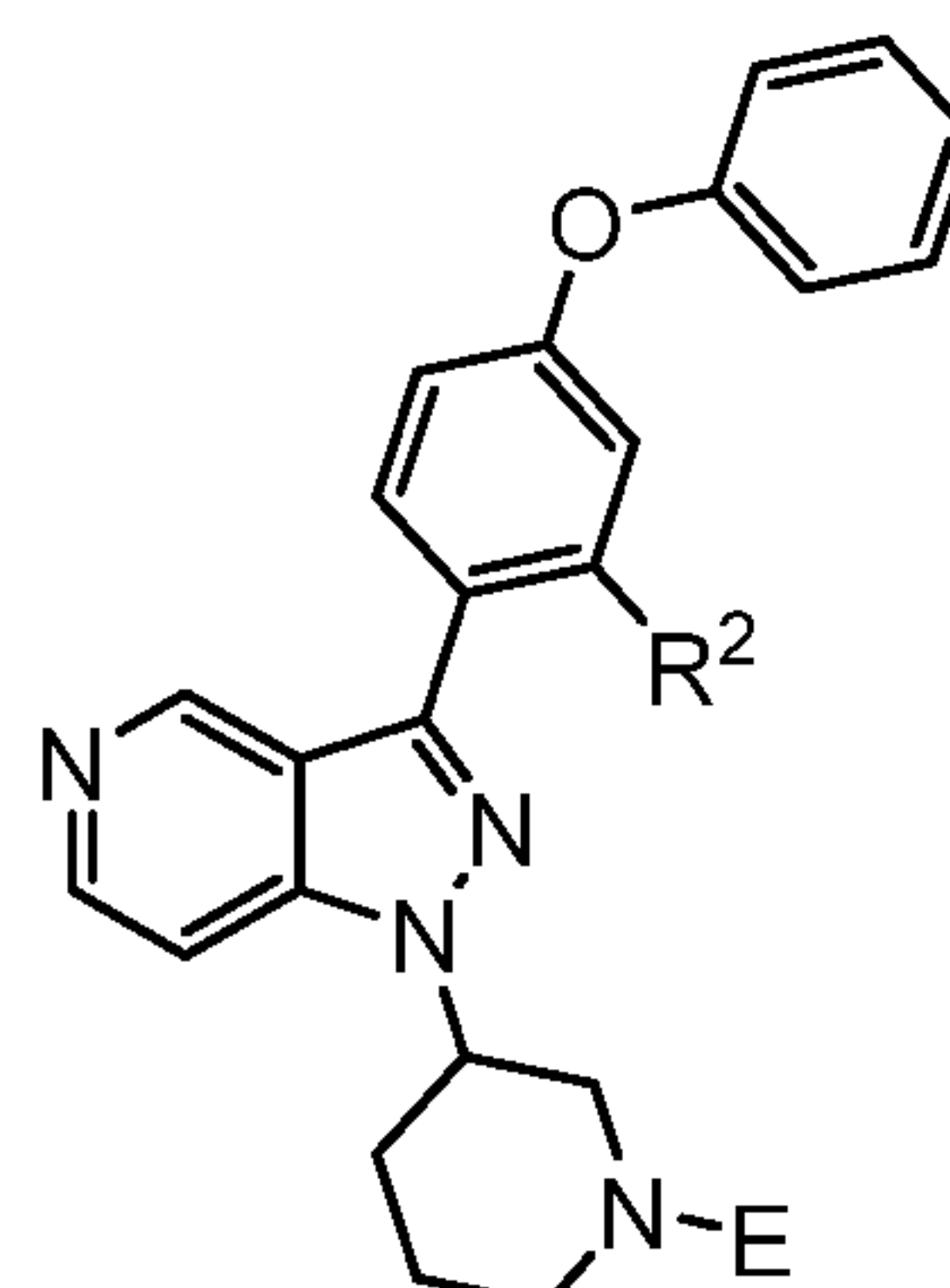


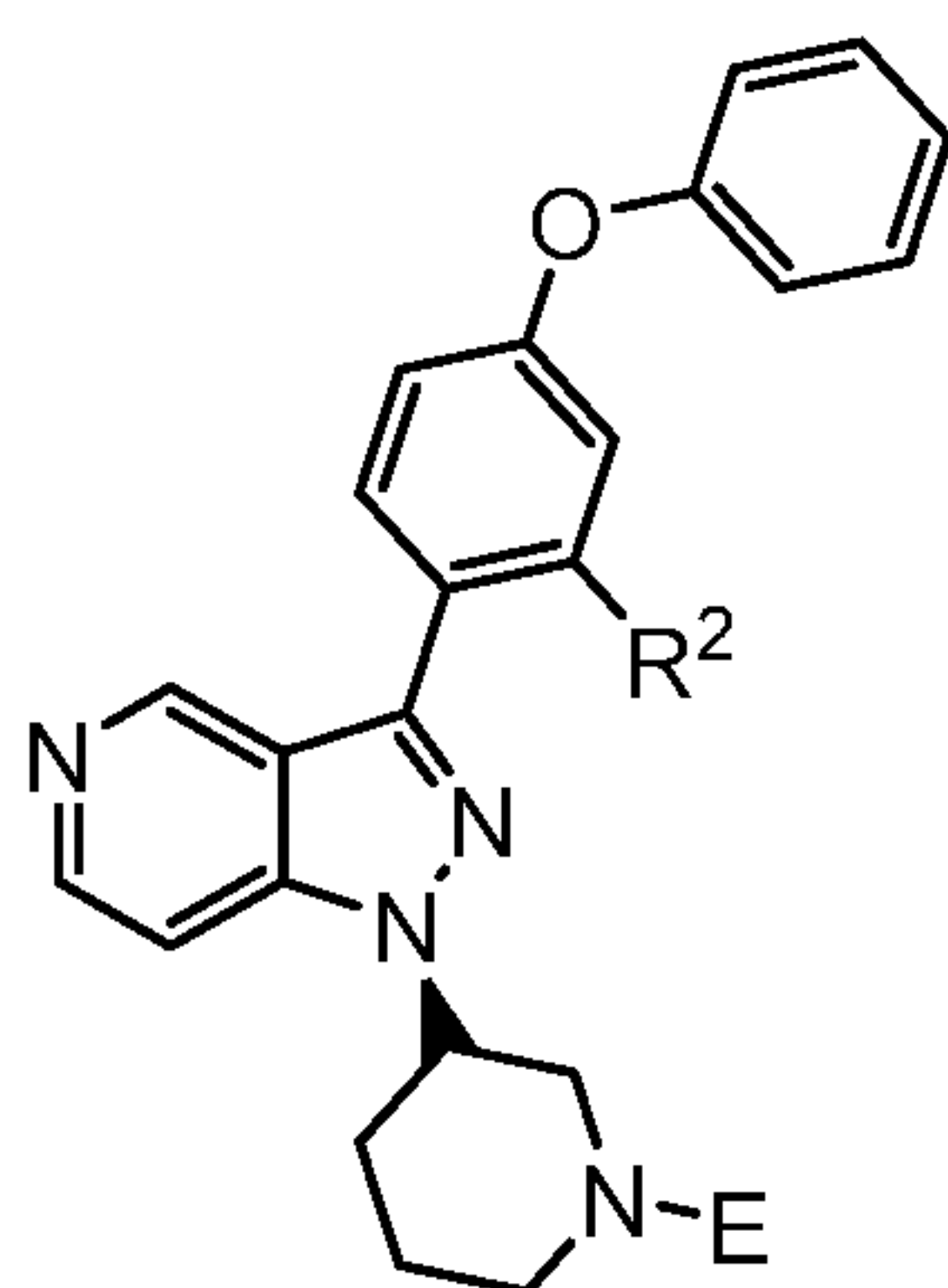
, wherein R^2 , R^5 , and E are as described herein. In embodiments, the



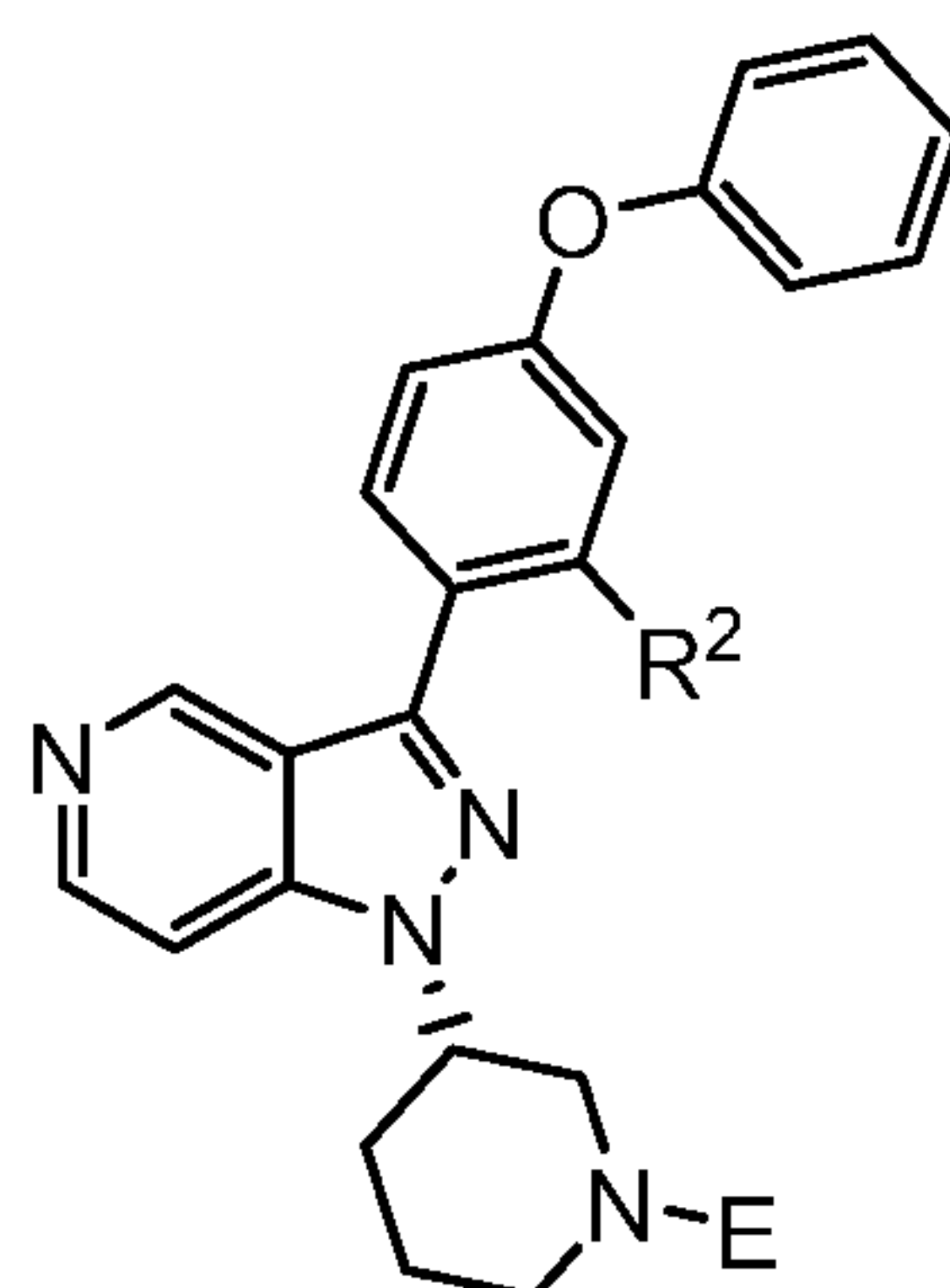
compound has the formula: , wherein R^2 , R^5 , and E are as described
5 herein.



[0598] In embodiments, the compound has the formula: , wherein R^2 and E are as described herein. In embodiments, the compound has the formula:

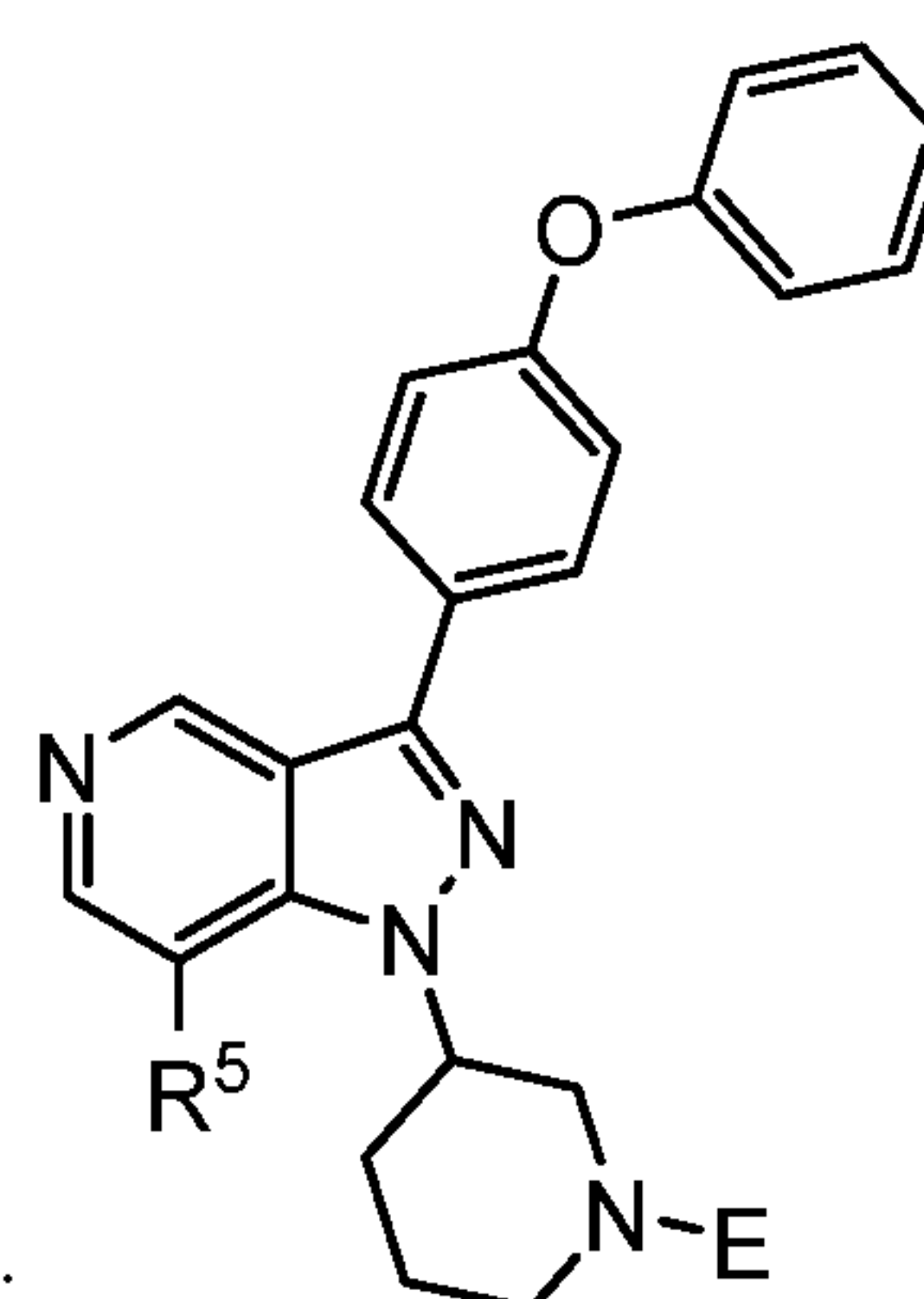


, wherein R^2 and E are as described herein. In embodiments, the



compound has the formula:

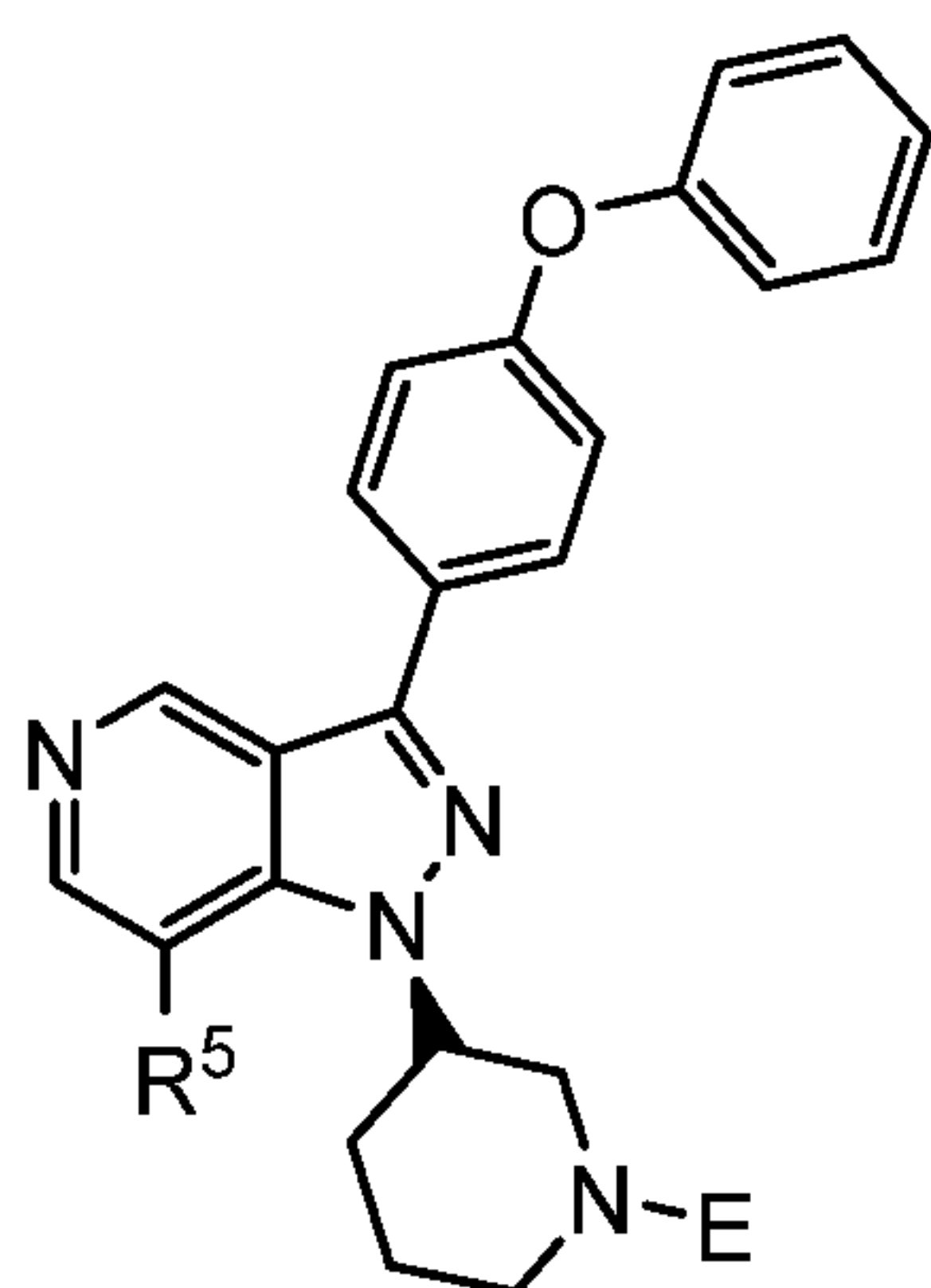
, wherein R^2 and E are as described herein.



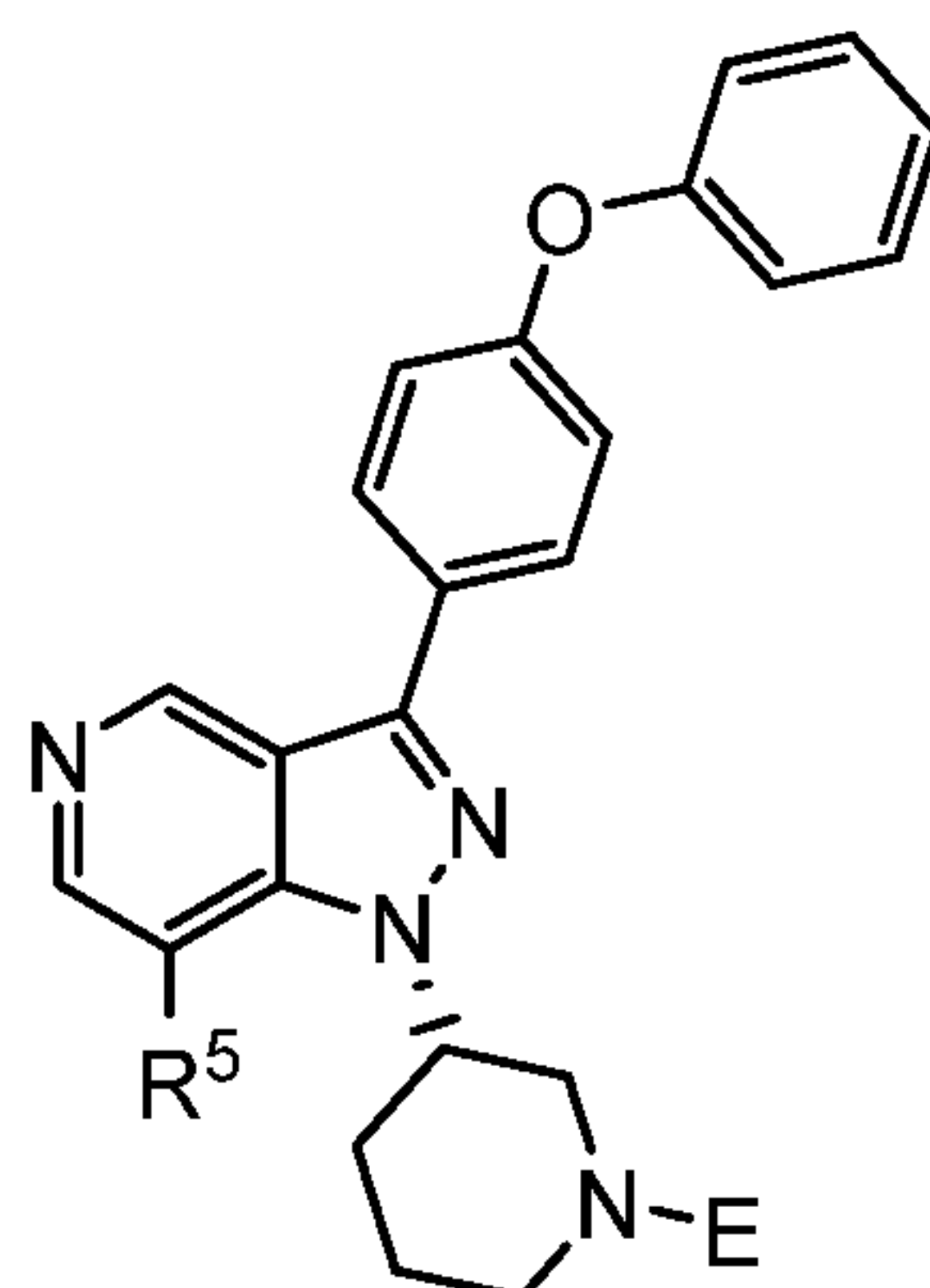
[0599] In embodiments, the compound has the formula:

, wherein R^5

and E are as described herein. In embodiments, the compound has the formula:

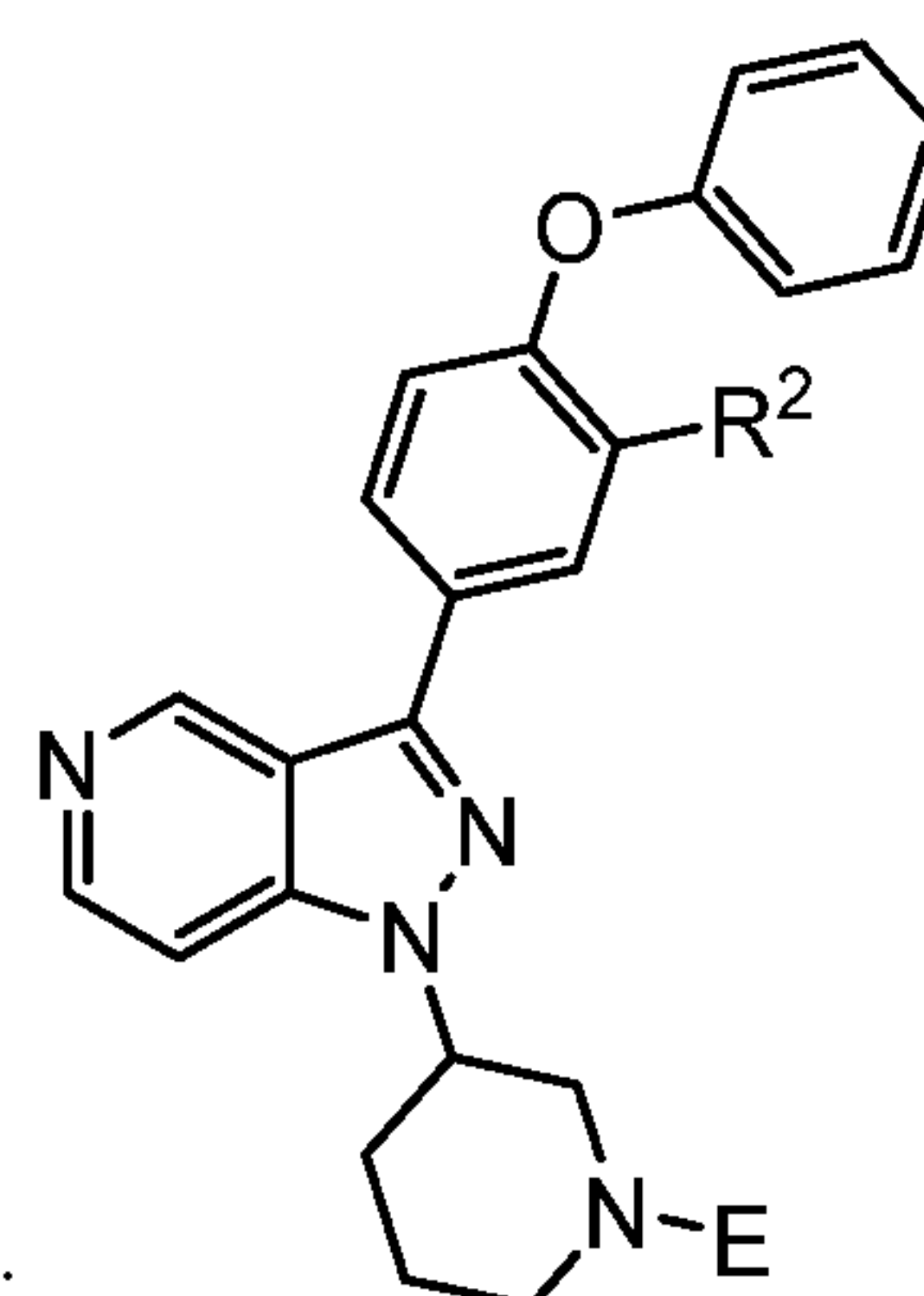


, wherein R^5 and E are as described herein. In embodiments, the



compound has the formula:

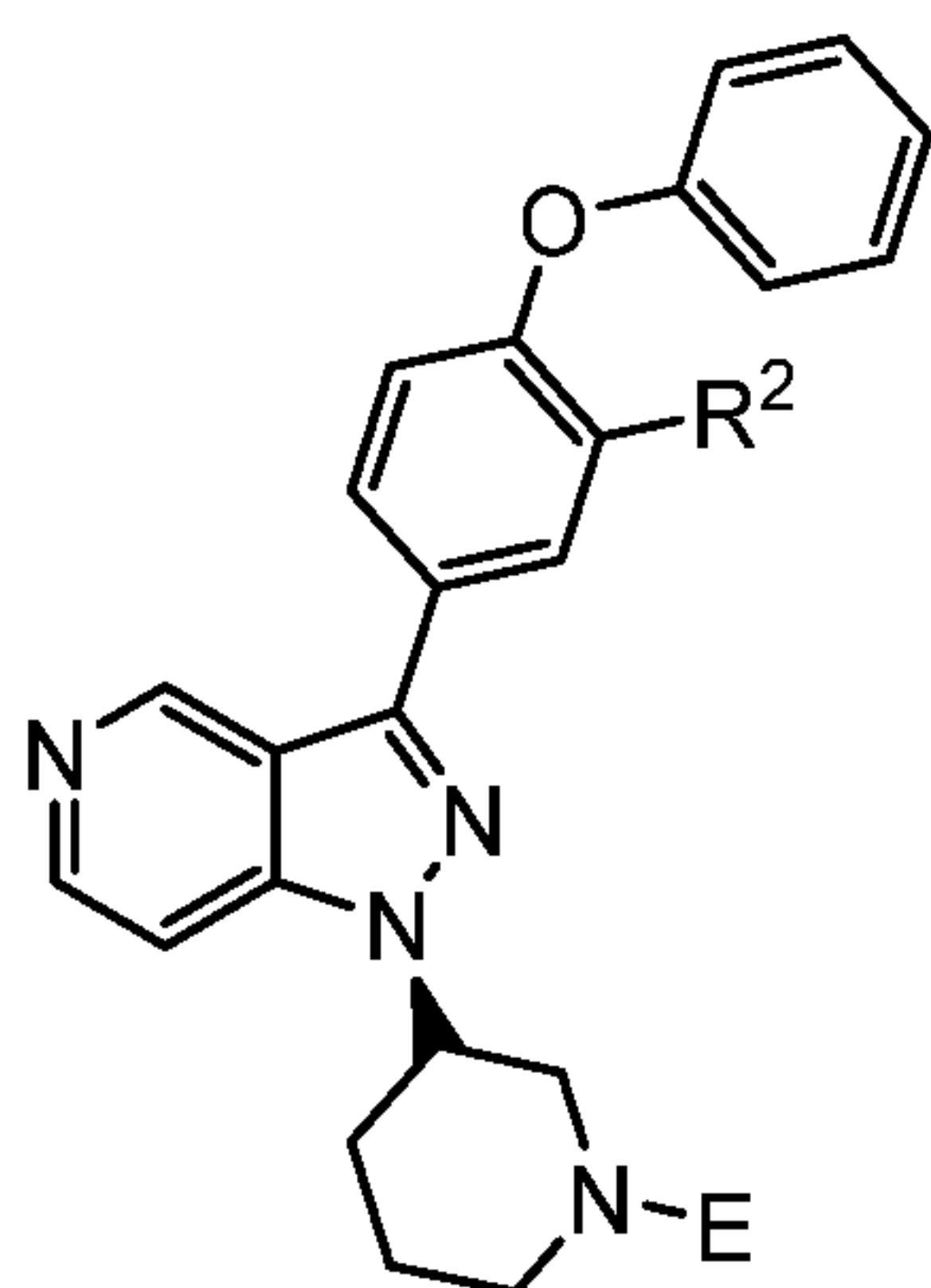
, wherein R^5 and E are as described herein.



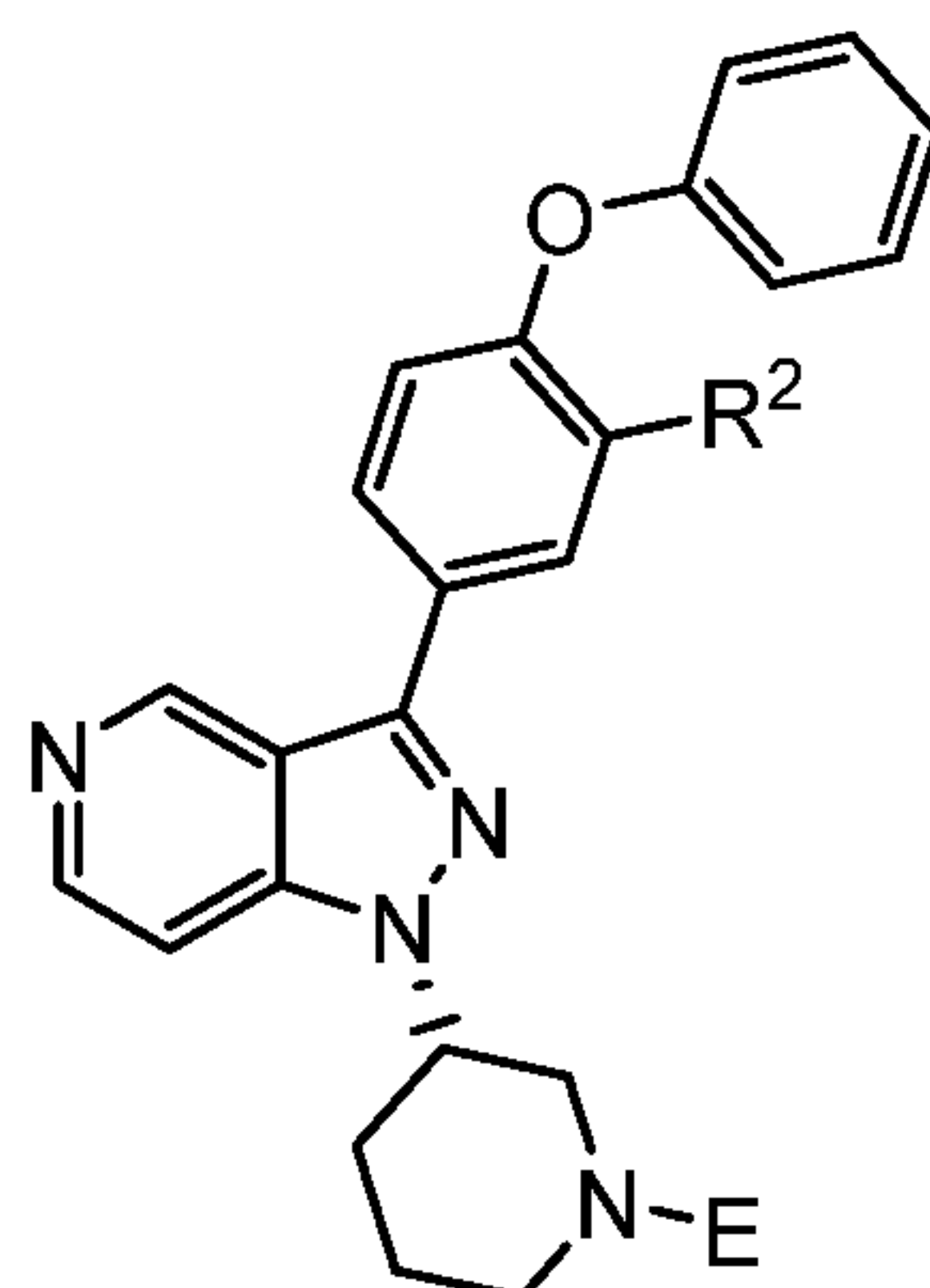
[0600] In embodiments, the compound has the formula:

, wherein R^2

5 and E are as described herein. In embodiments, the compound has the formula:

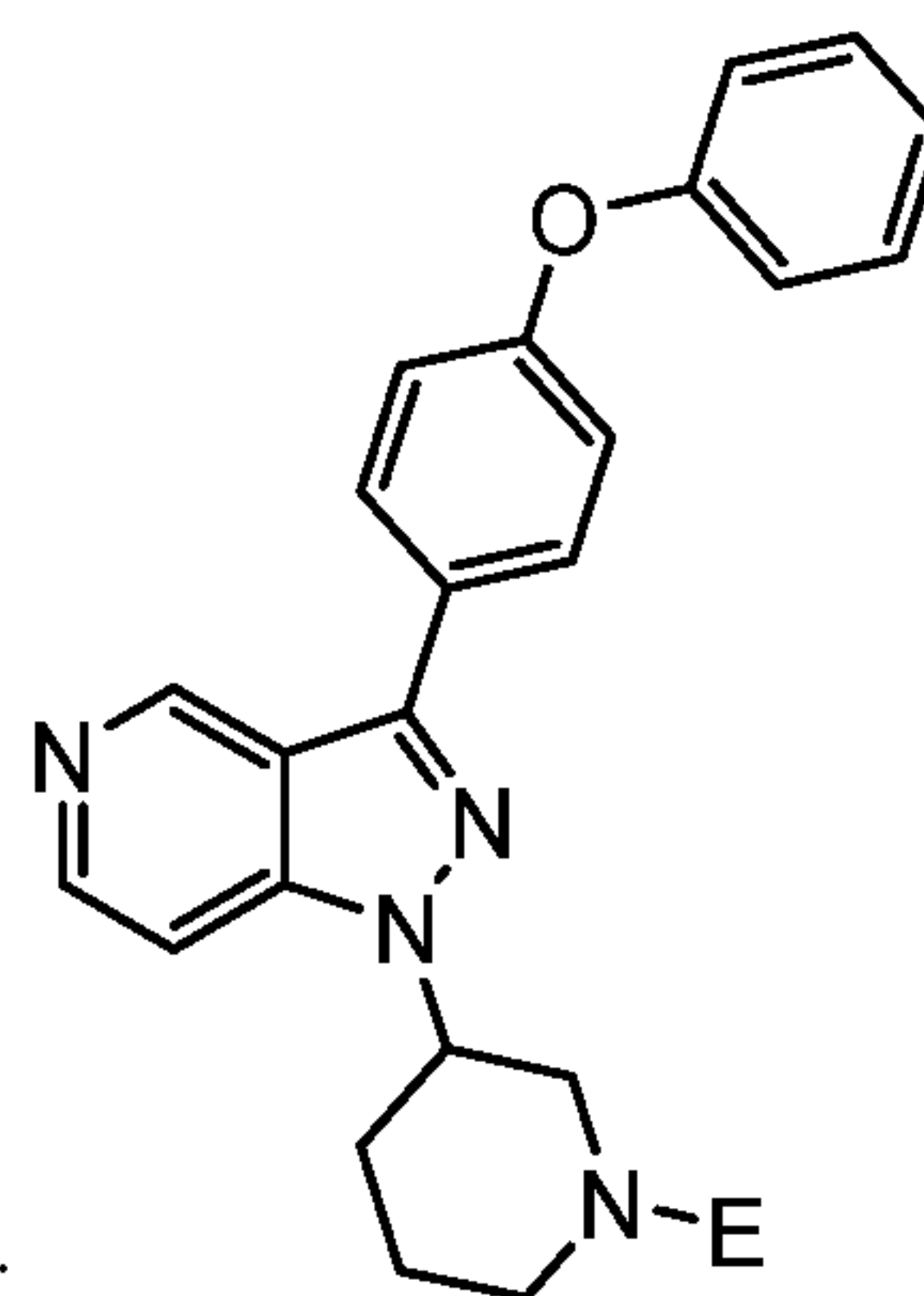


, wherein R^2 and E are as described herein. In embodiments, the



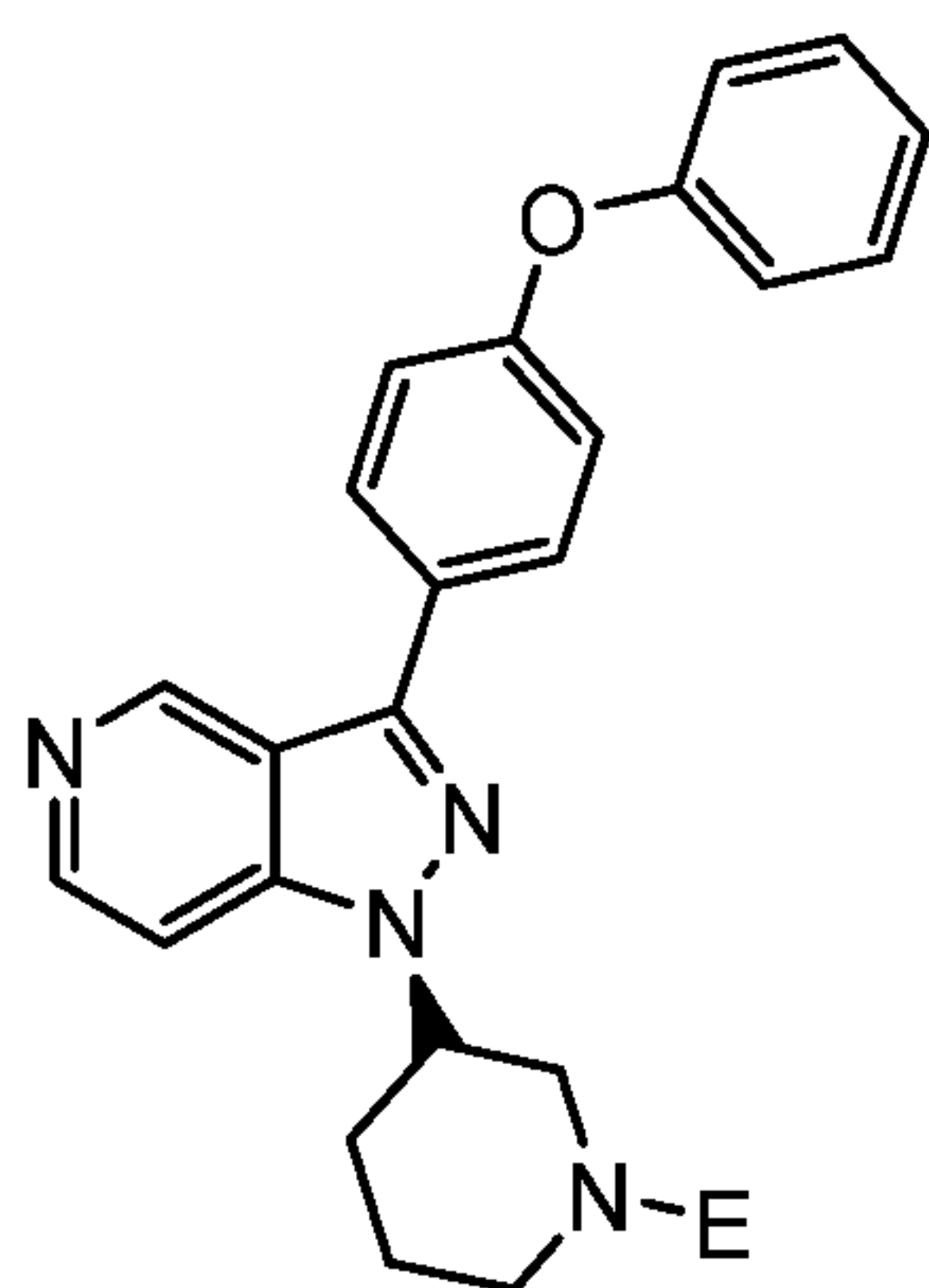
compound has the formula:

, wherein R^2 and E are as described herein.



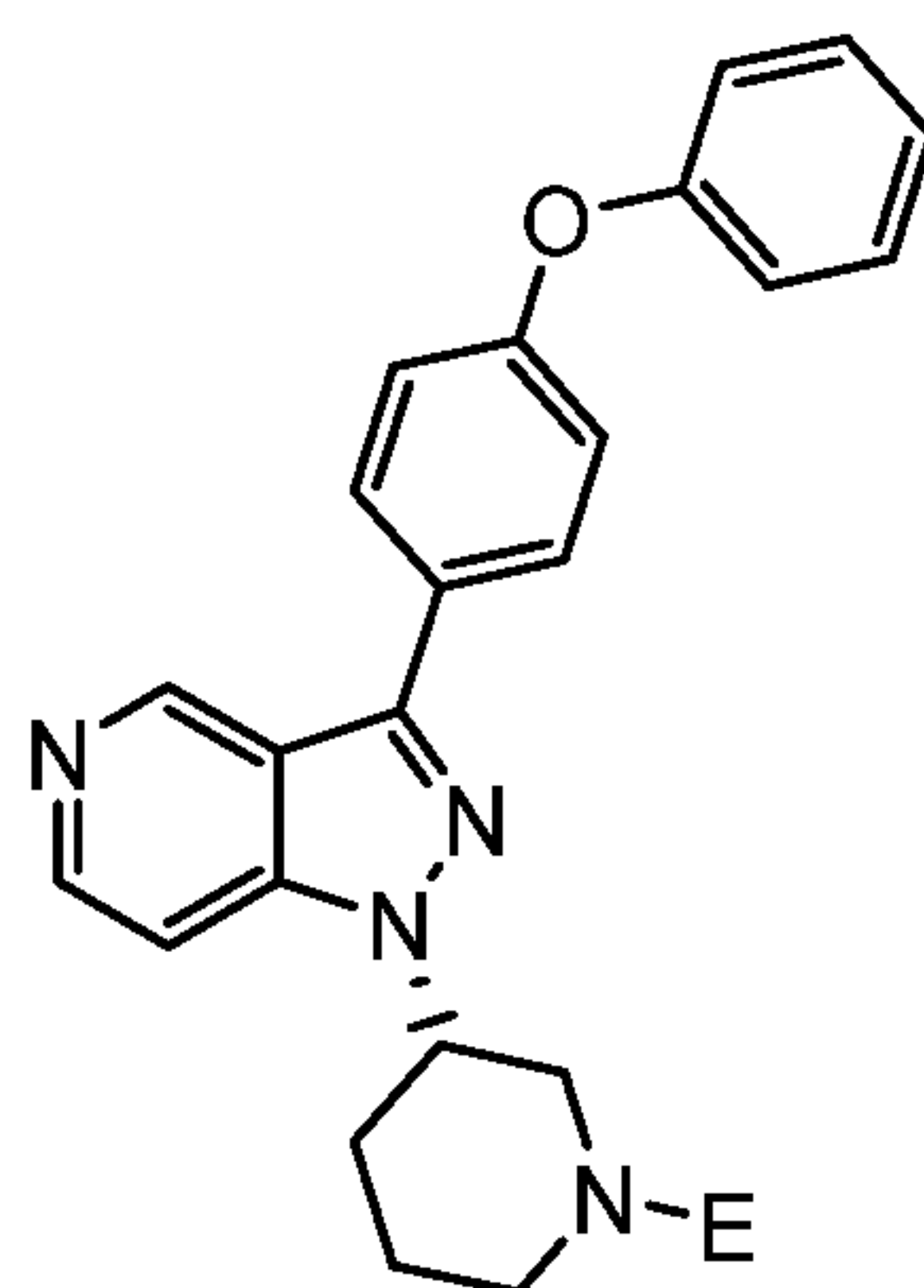
[0601] In embodiments, the compound has the formula:

, wherein R^2 , R^5 , and E are as described herein. In embodiments, the compound has the formula:



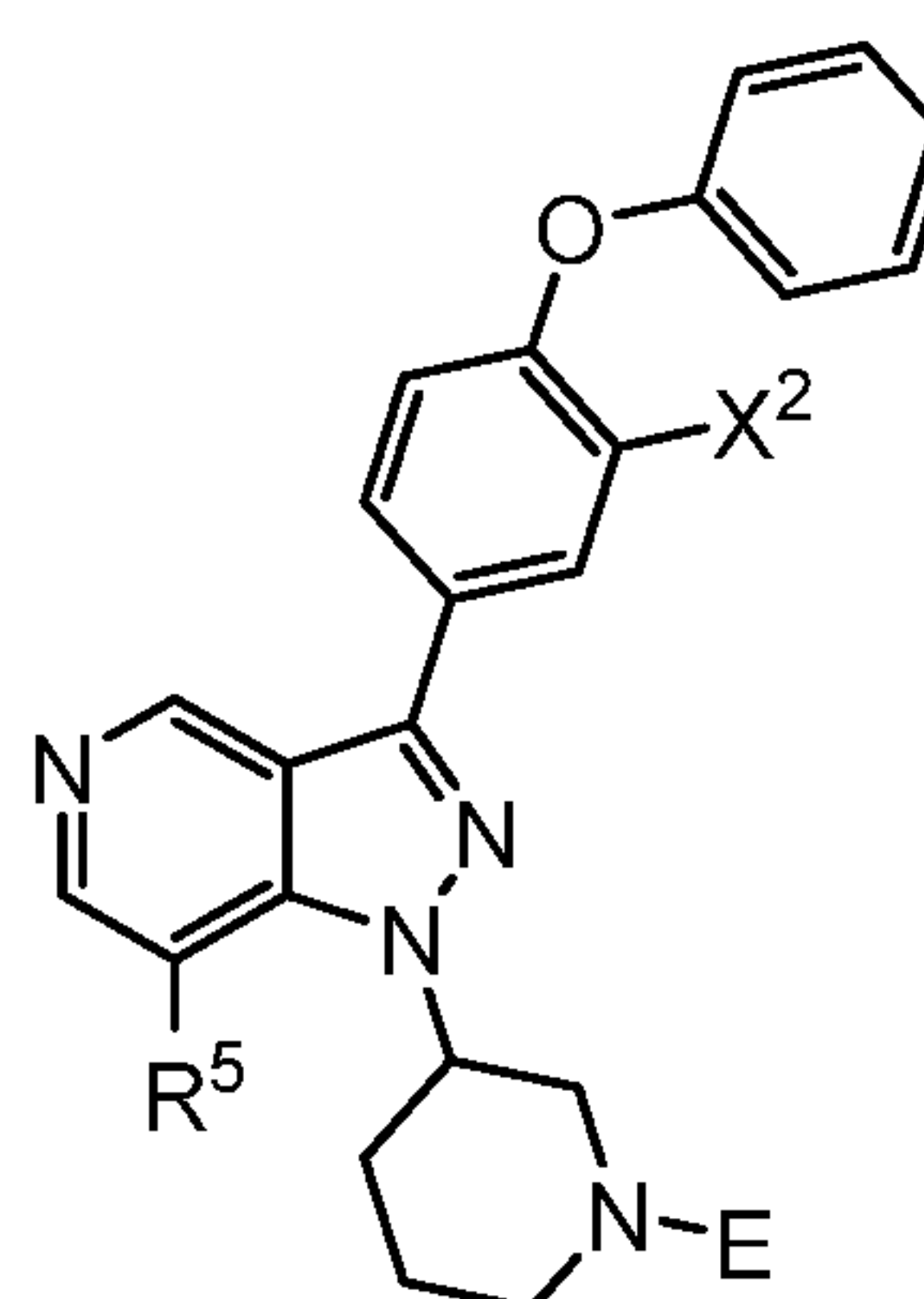
5

, wherein R^2 , R^5 , and E are as described herein. In embodiments, the



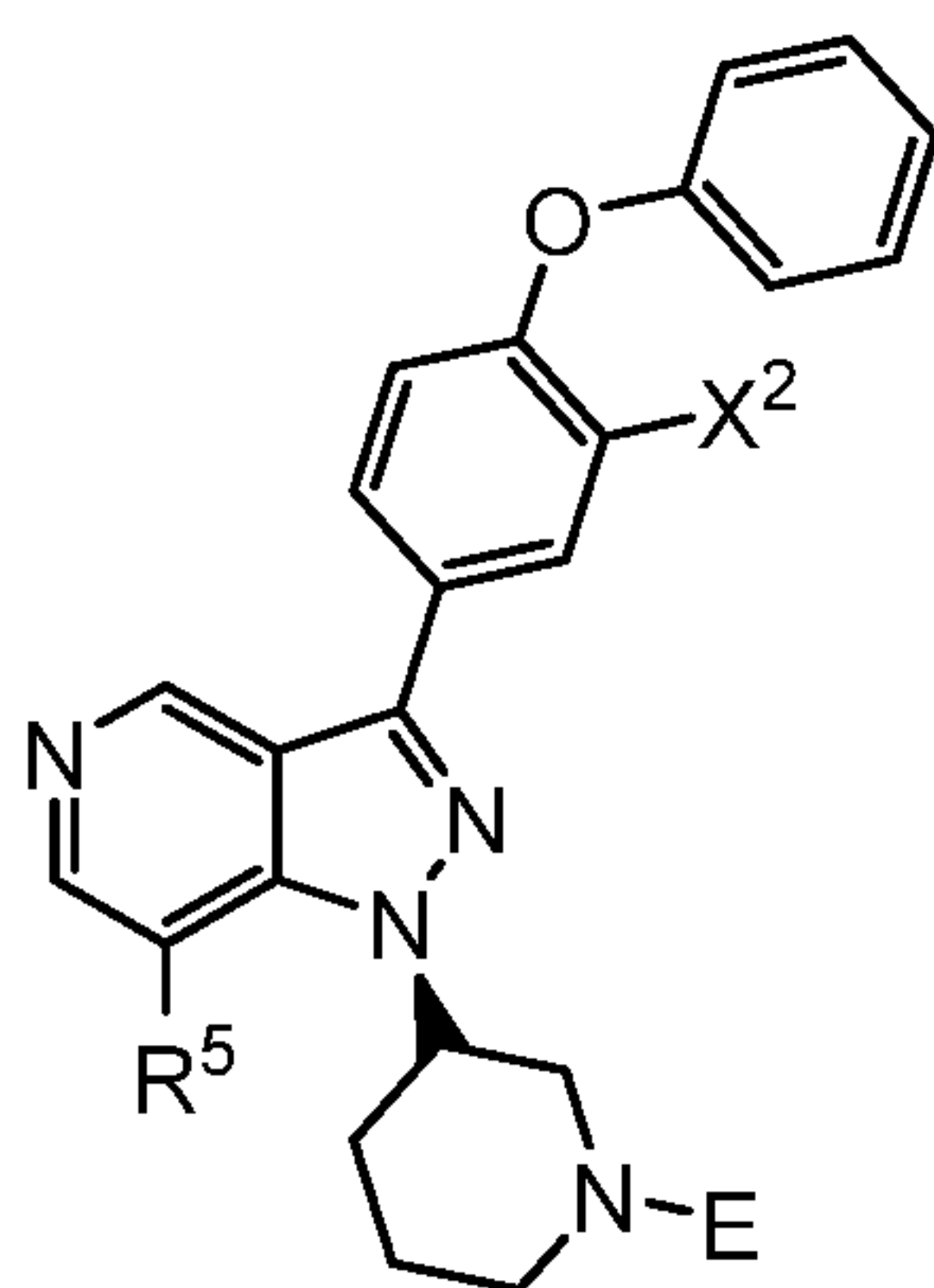
compound has the formula:
herein.

, wherein R^2 , R^5 , and E are as described



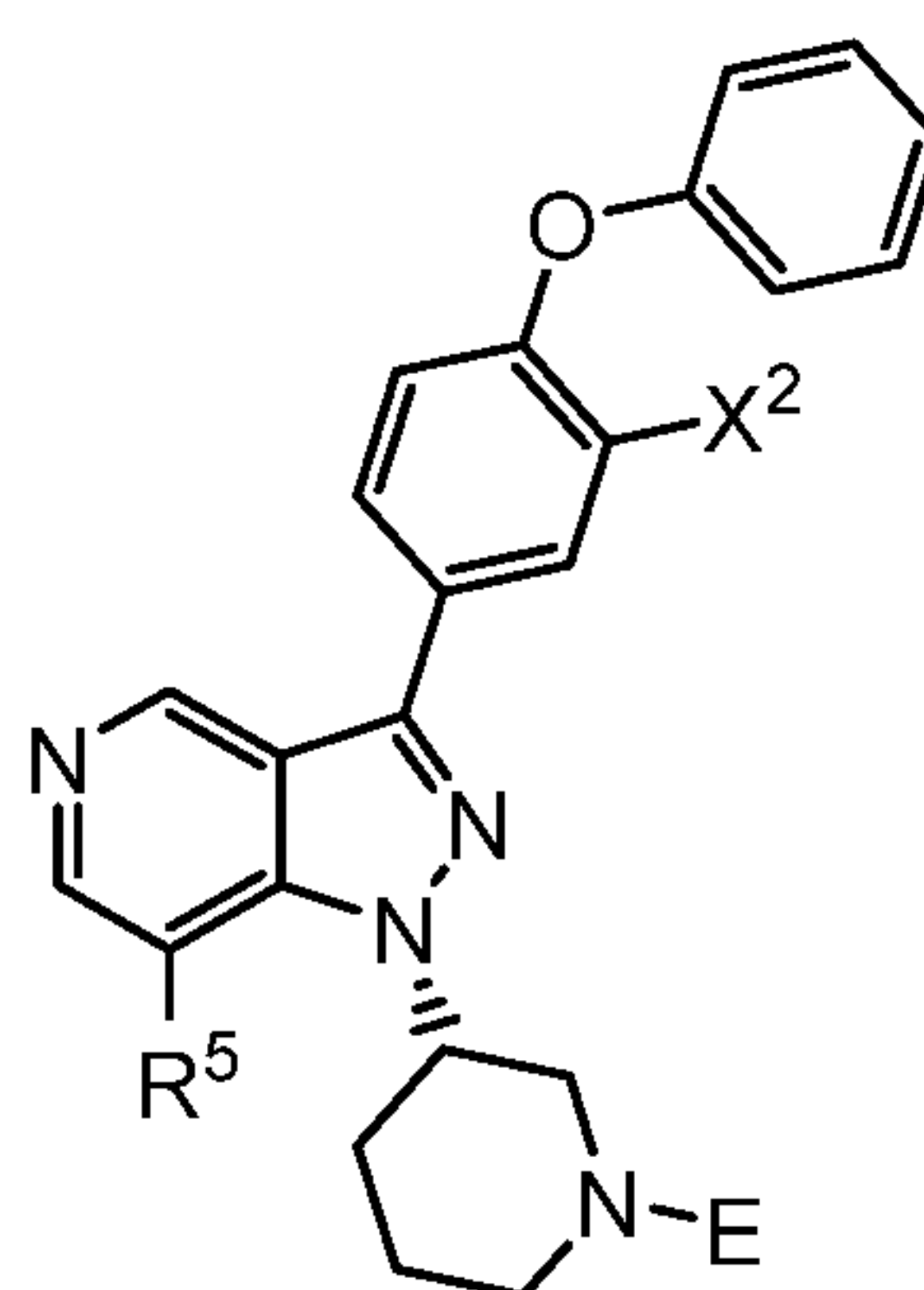
[0602] In embodiments, the compound has the formula:

R^5 , and E are as described herein. In embodiments, the compound has the formula:



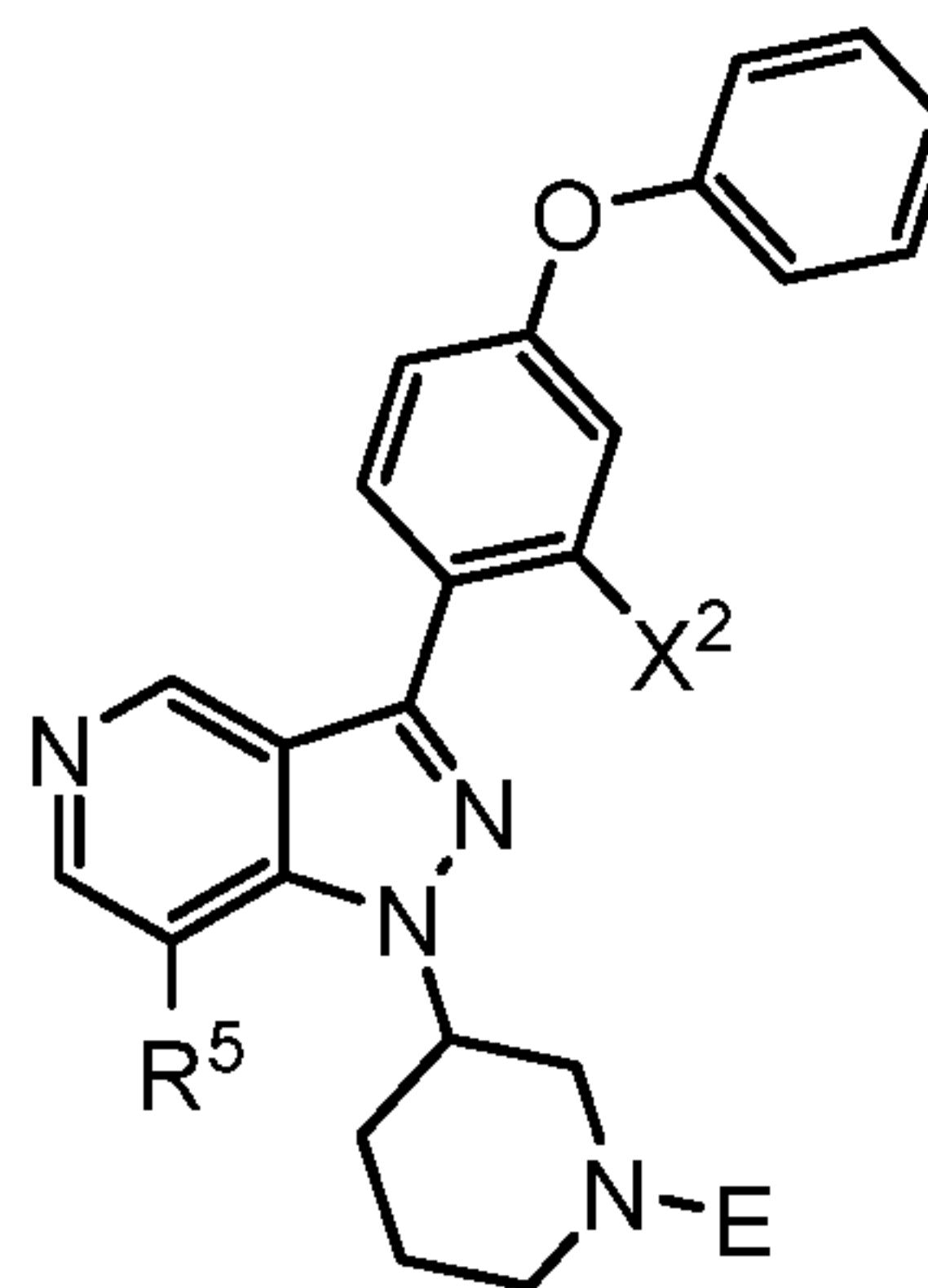
5

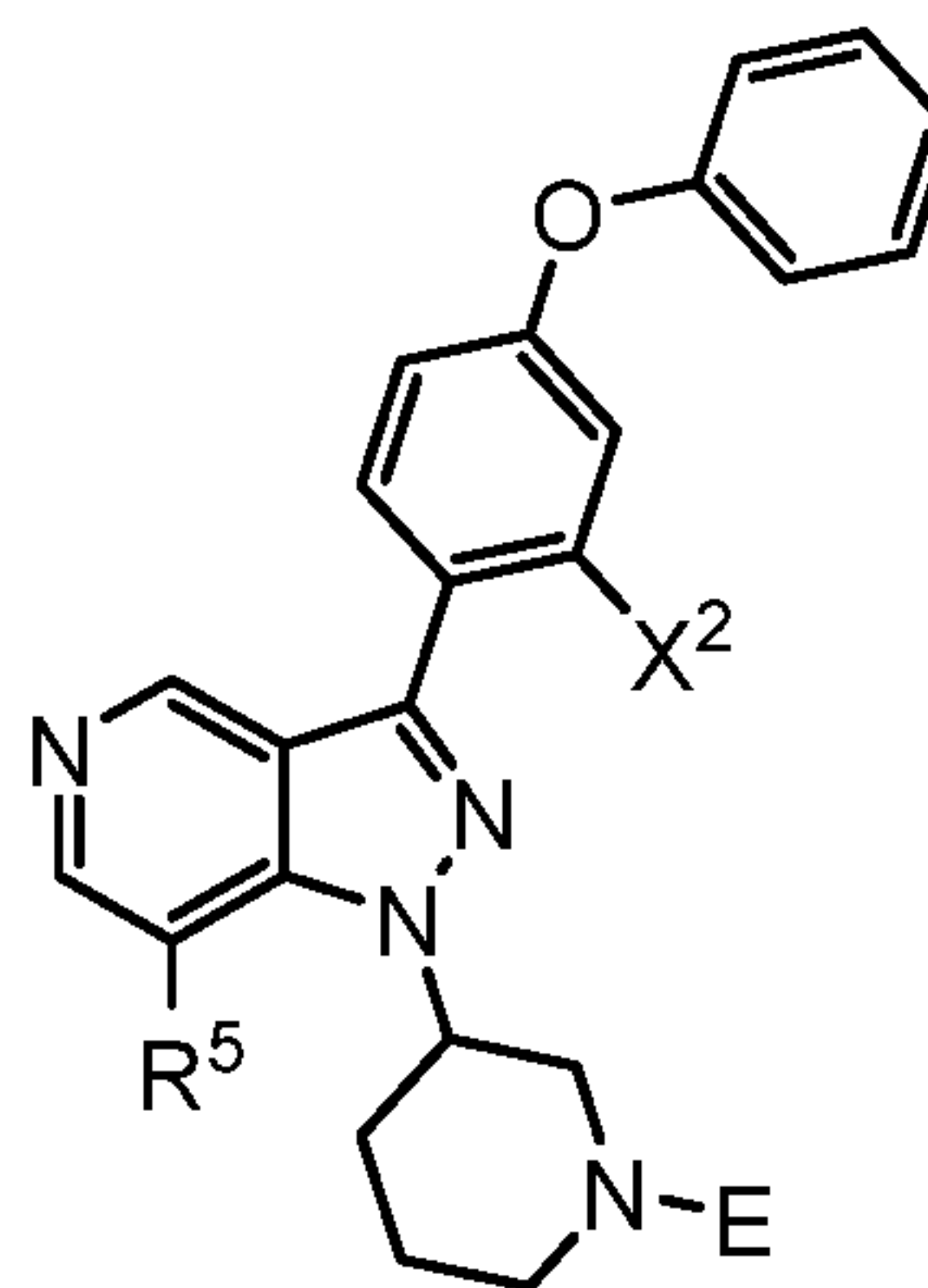
, wherein X^2 , R^5 , and E are as described herein. In embodiments, the

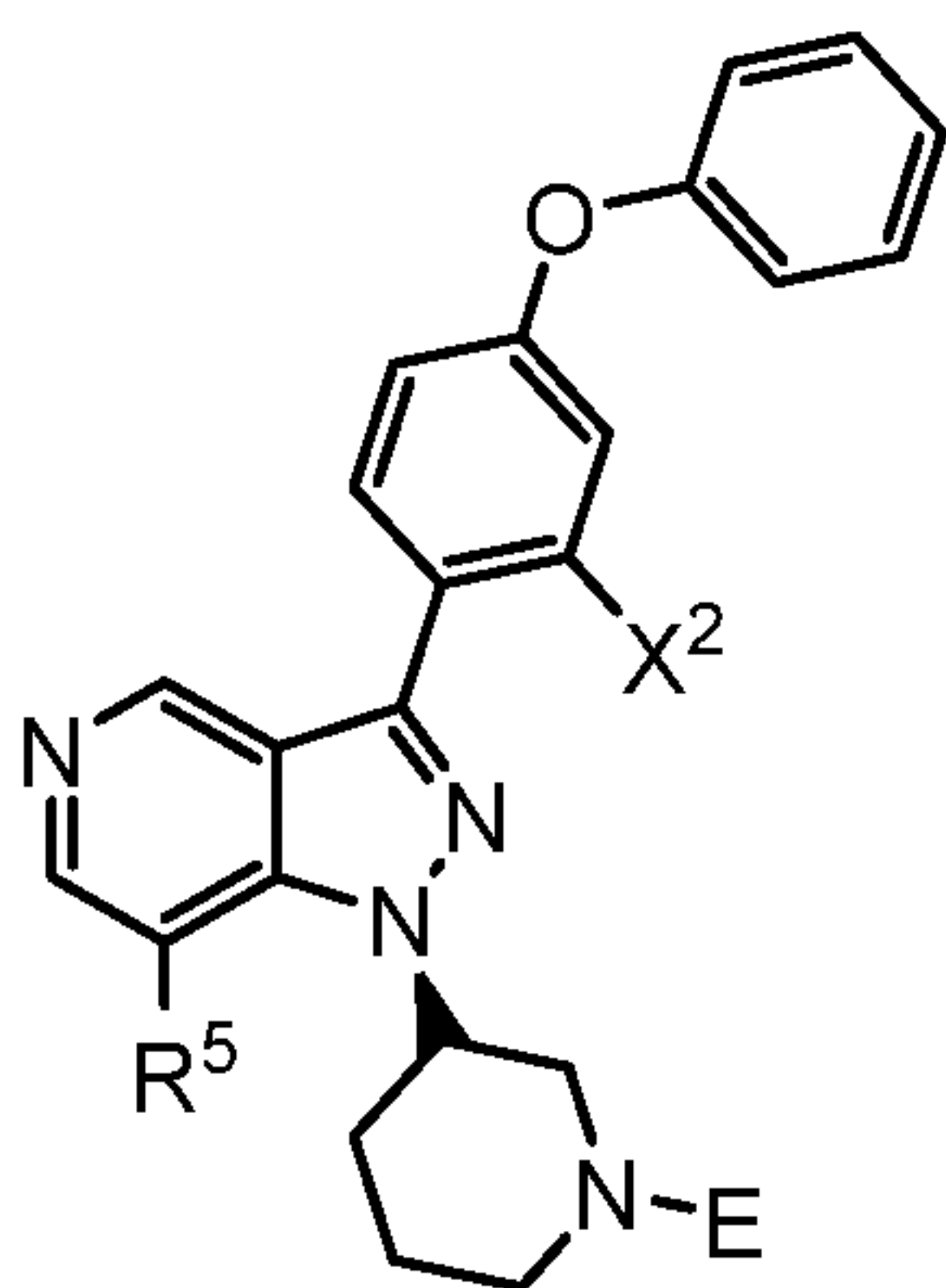


compound has the formula:
herein.

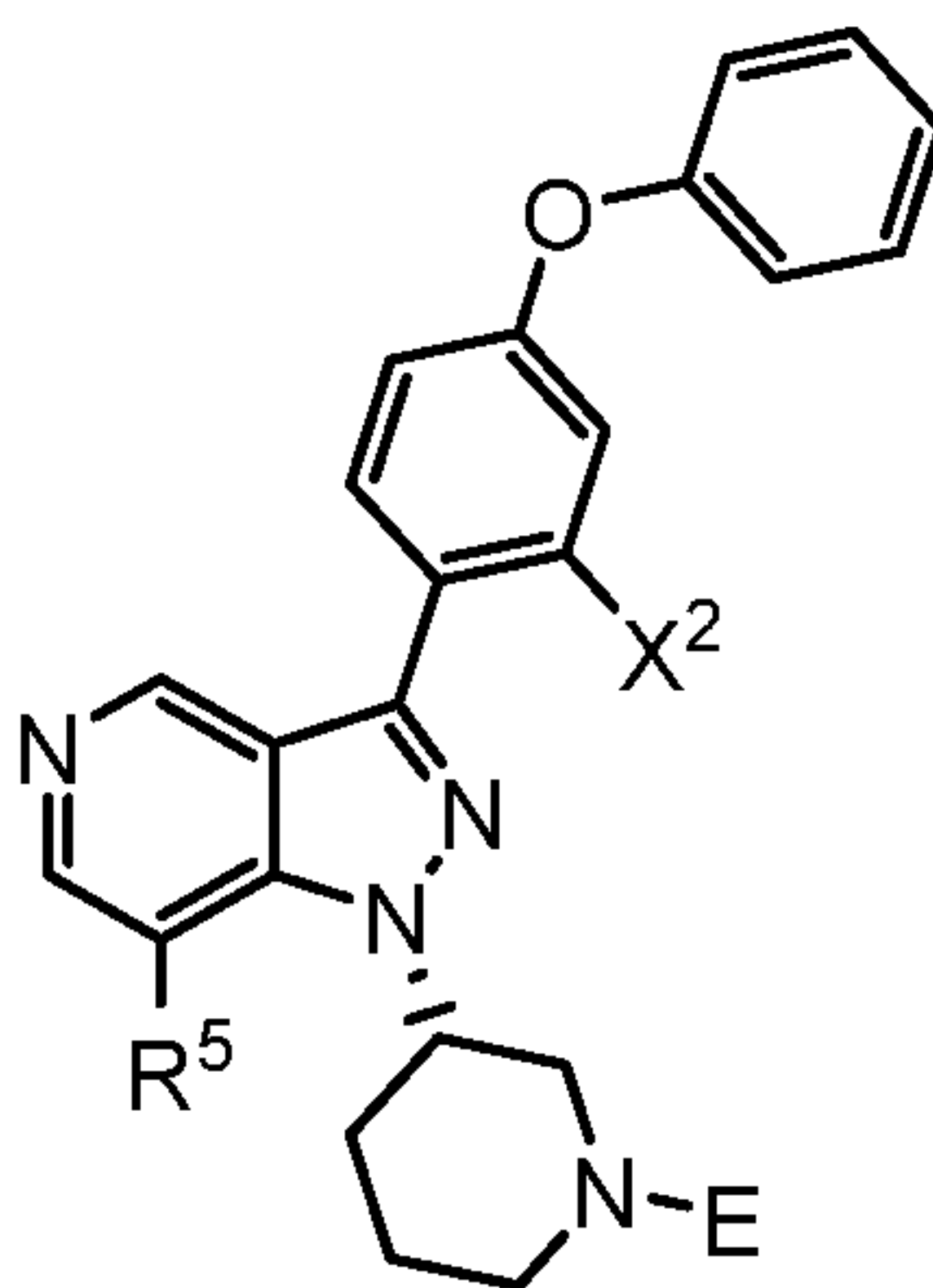
, wherein X^2 , R^5 , and E are as described



[0603] In embodiments, the compound has the formula: , wherein X^2 , R^5 , and E are as described herein. In embodiments, the compound has the formula:



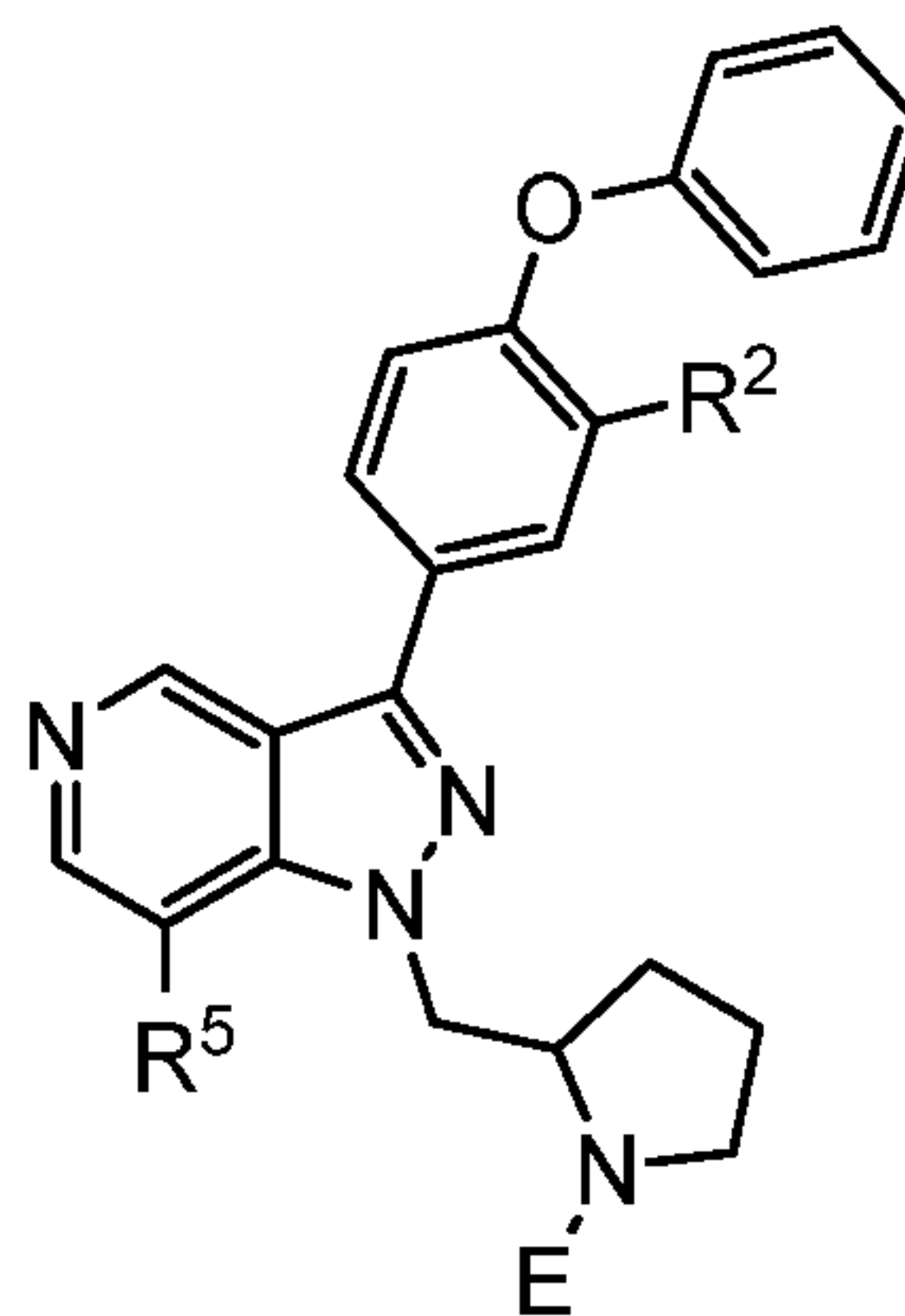
, wherein X^2 , R^5 , and E are as described herein. In embodiments, the

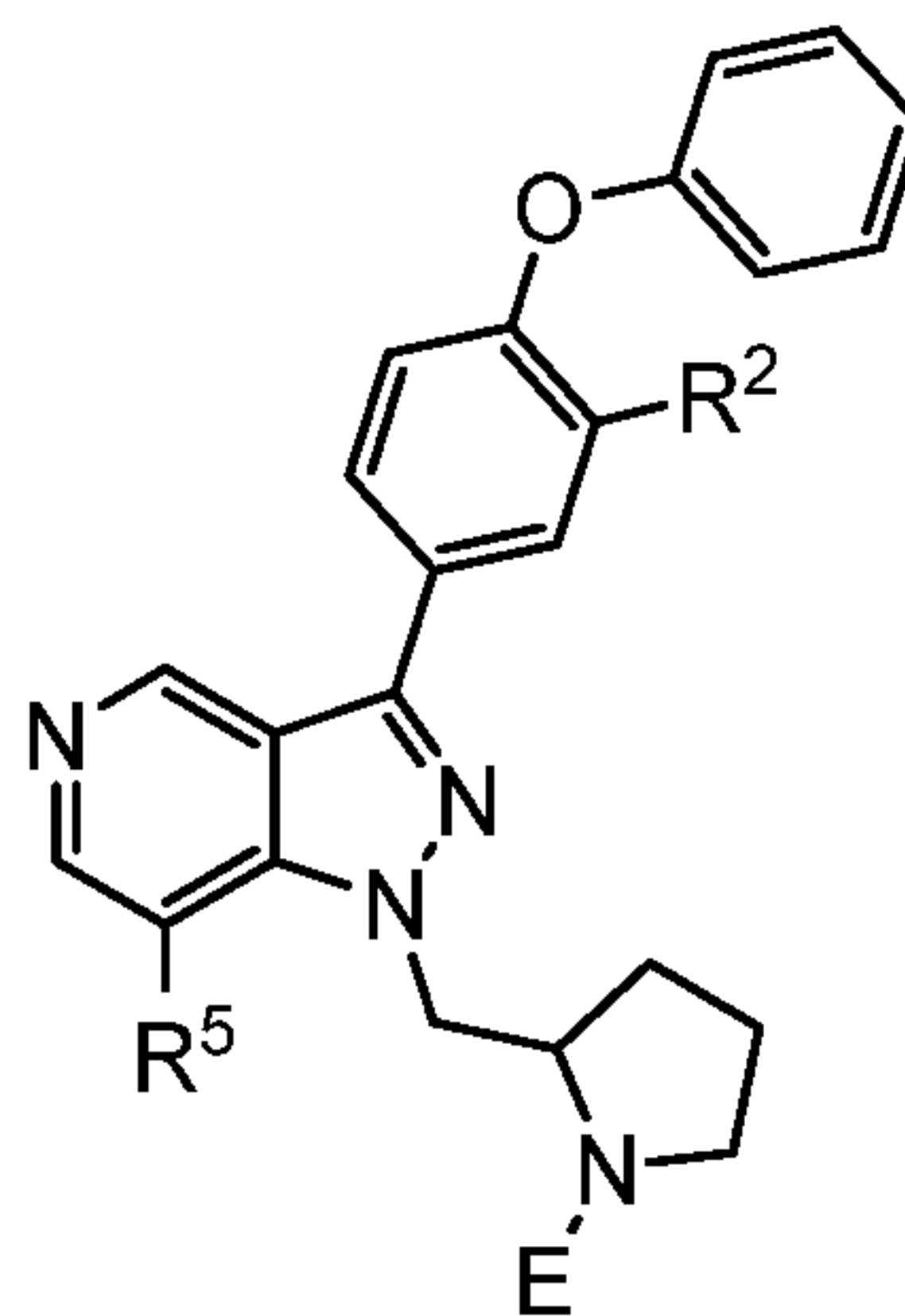


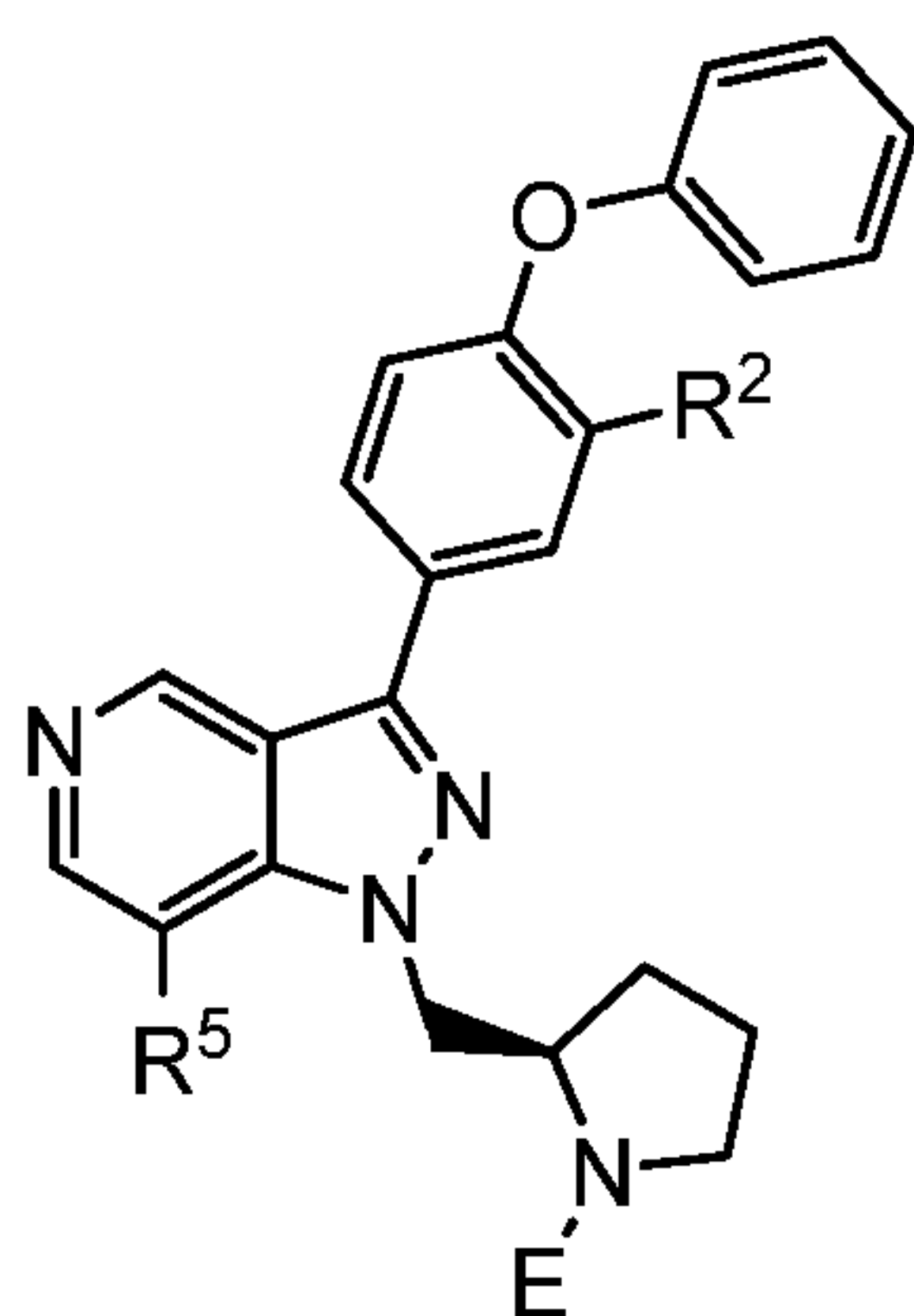
compound has the formula:

, wherein X^2 , R^5 , and E are as described

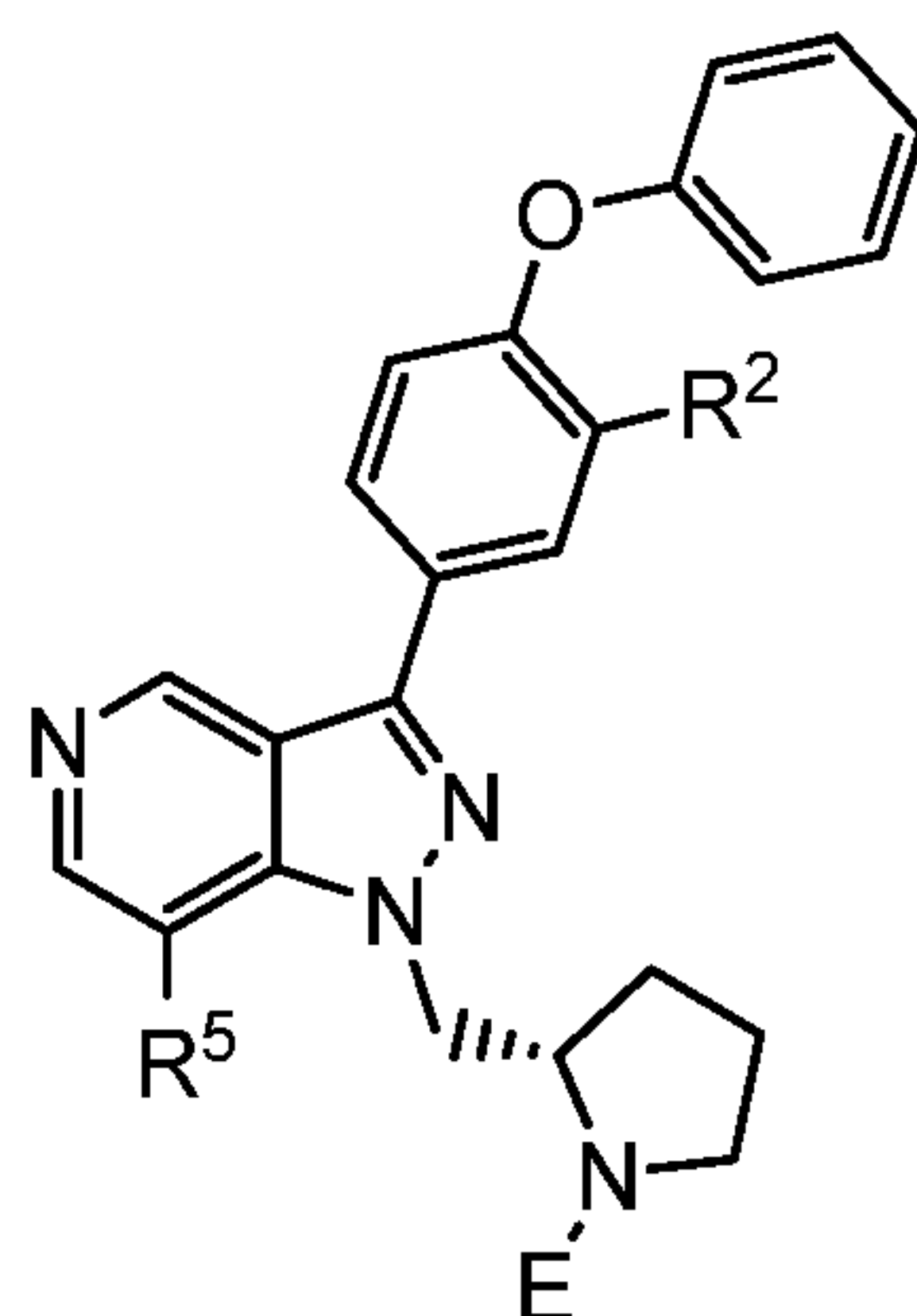
5 herein.



[0604] In embodiments, the compound has the formula: , wherein R^2 , R^5 , and E are as described herein. In embodiments, the compound has the formula:

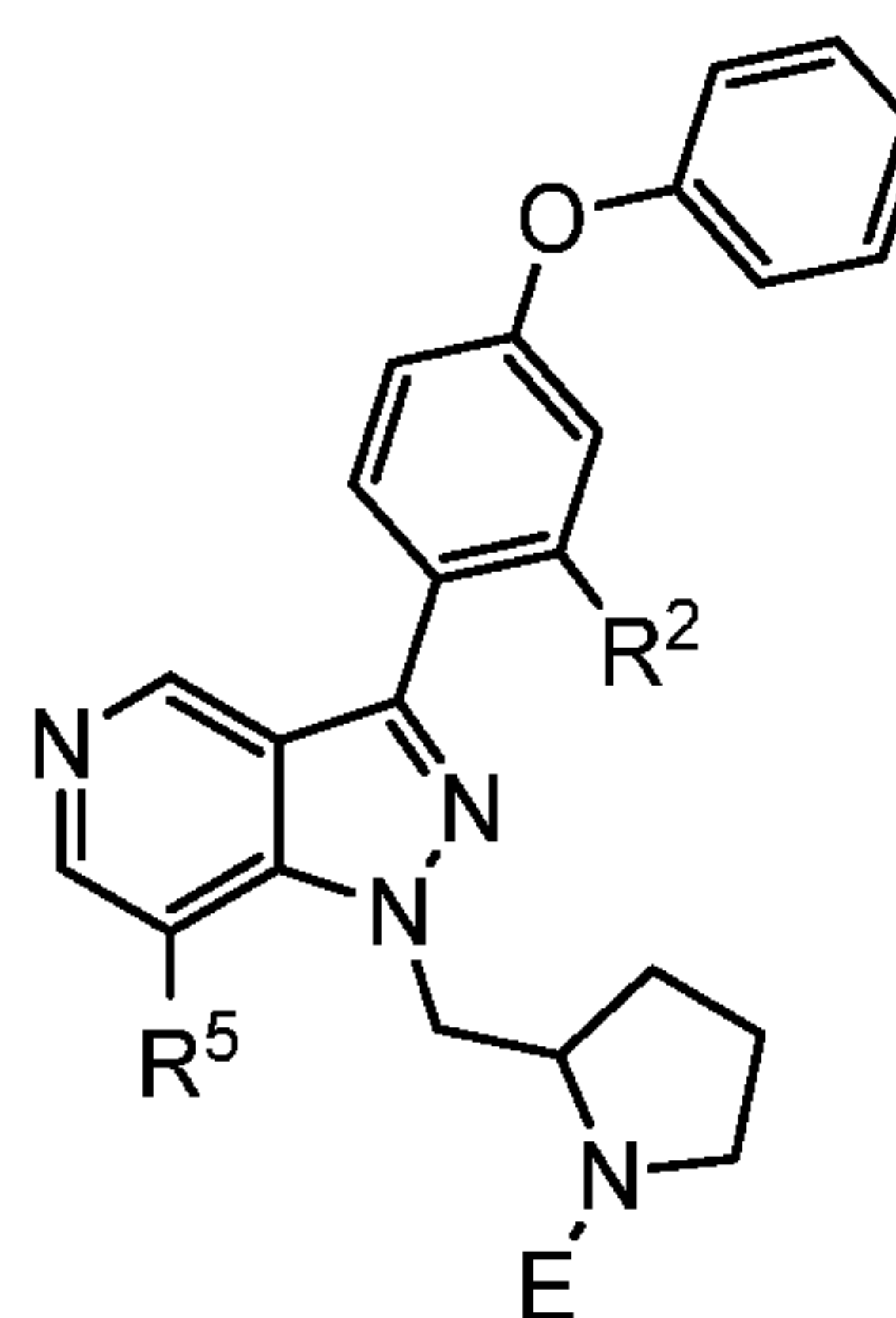


, wherein R^2 , R^5 , and E are as described herein. In embodiments, the



compound has the formula:
herein.

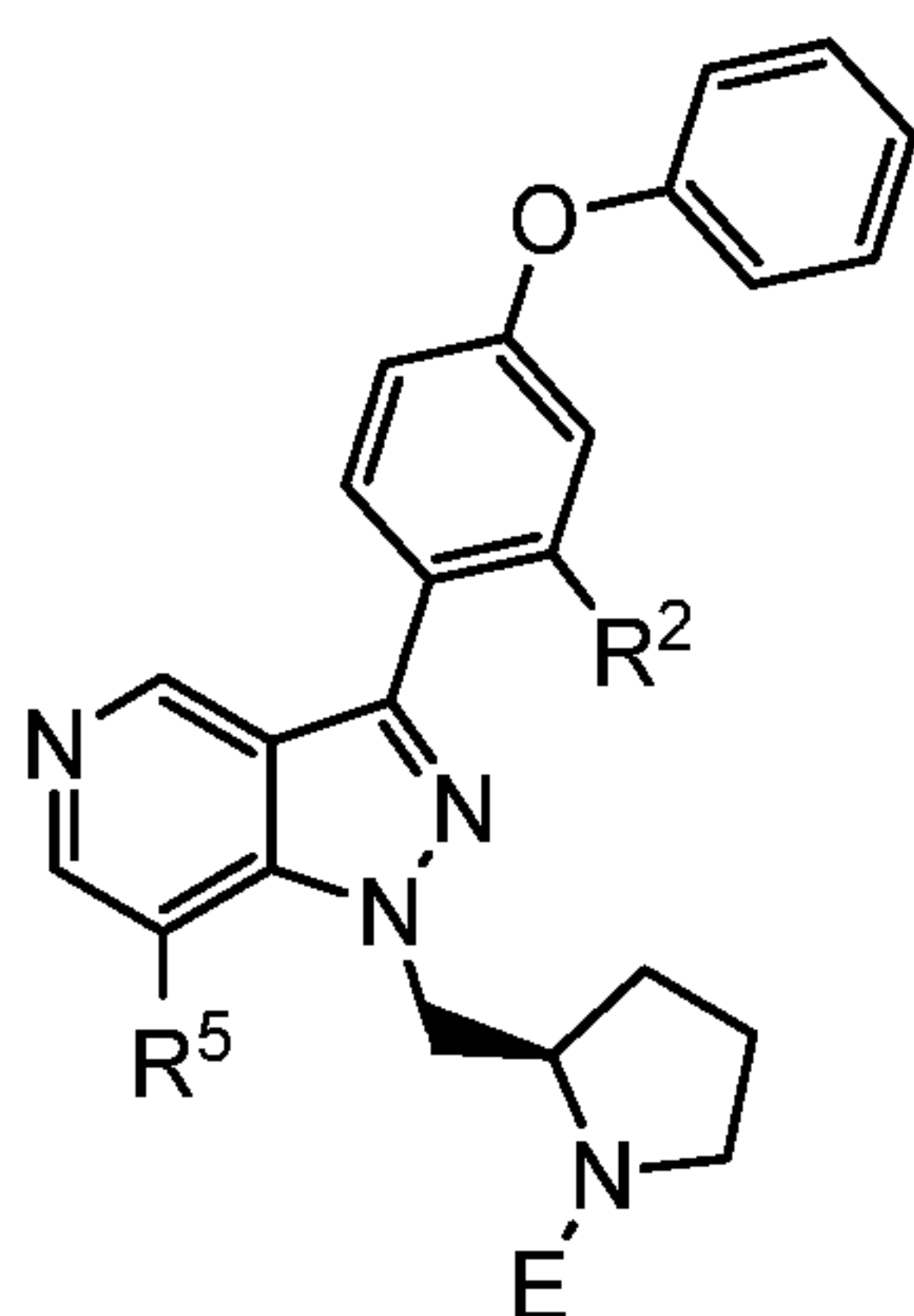
, wherein R^2 , R^5 , and E are as described



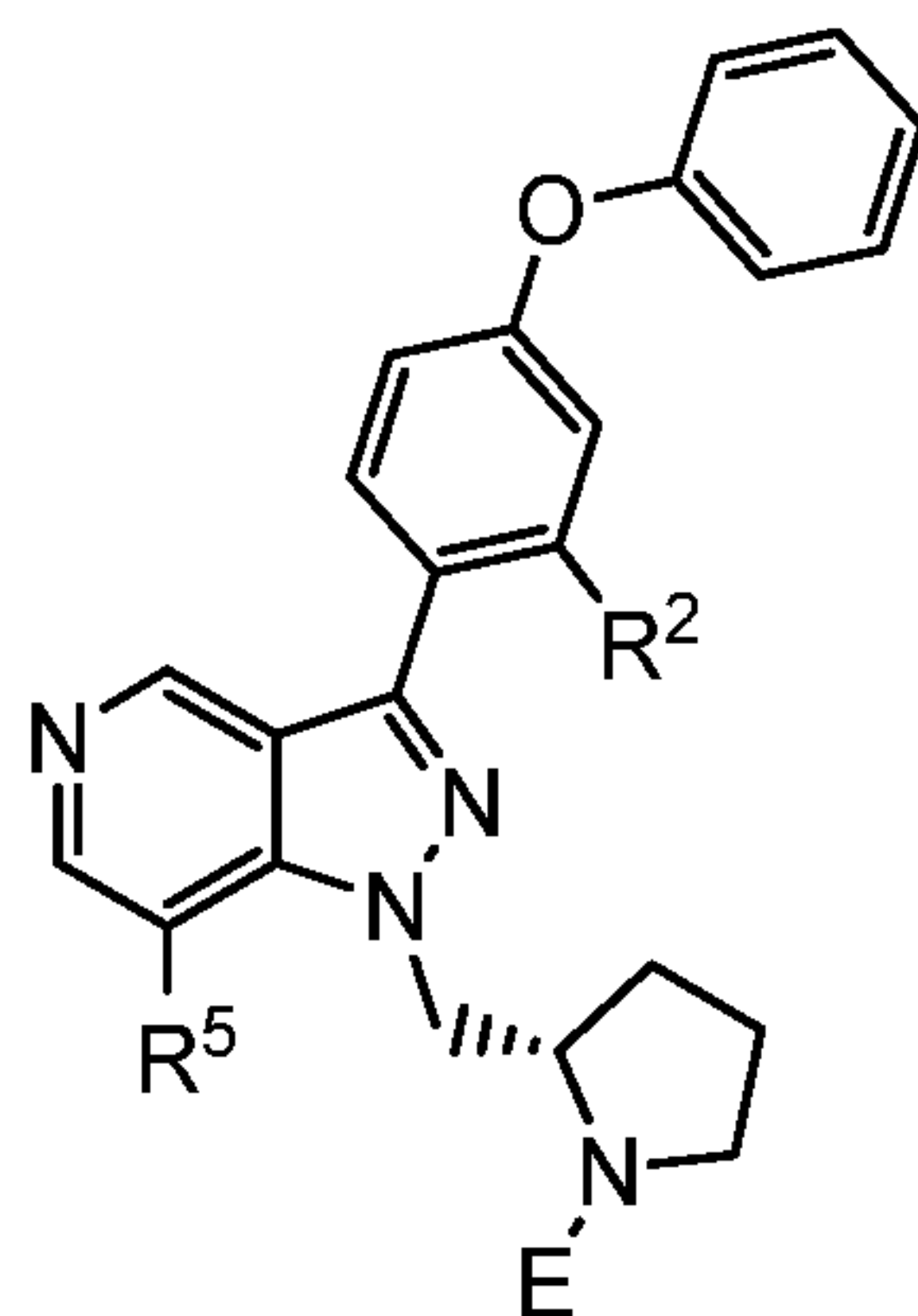
[0605] In embodiments, the compound has the formula:

, wherein R^2 ,

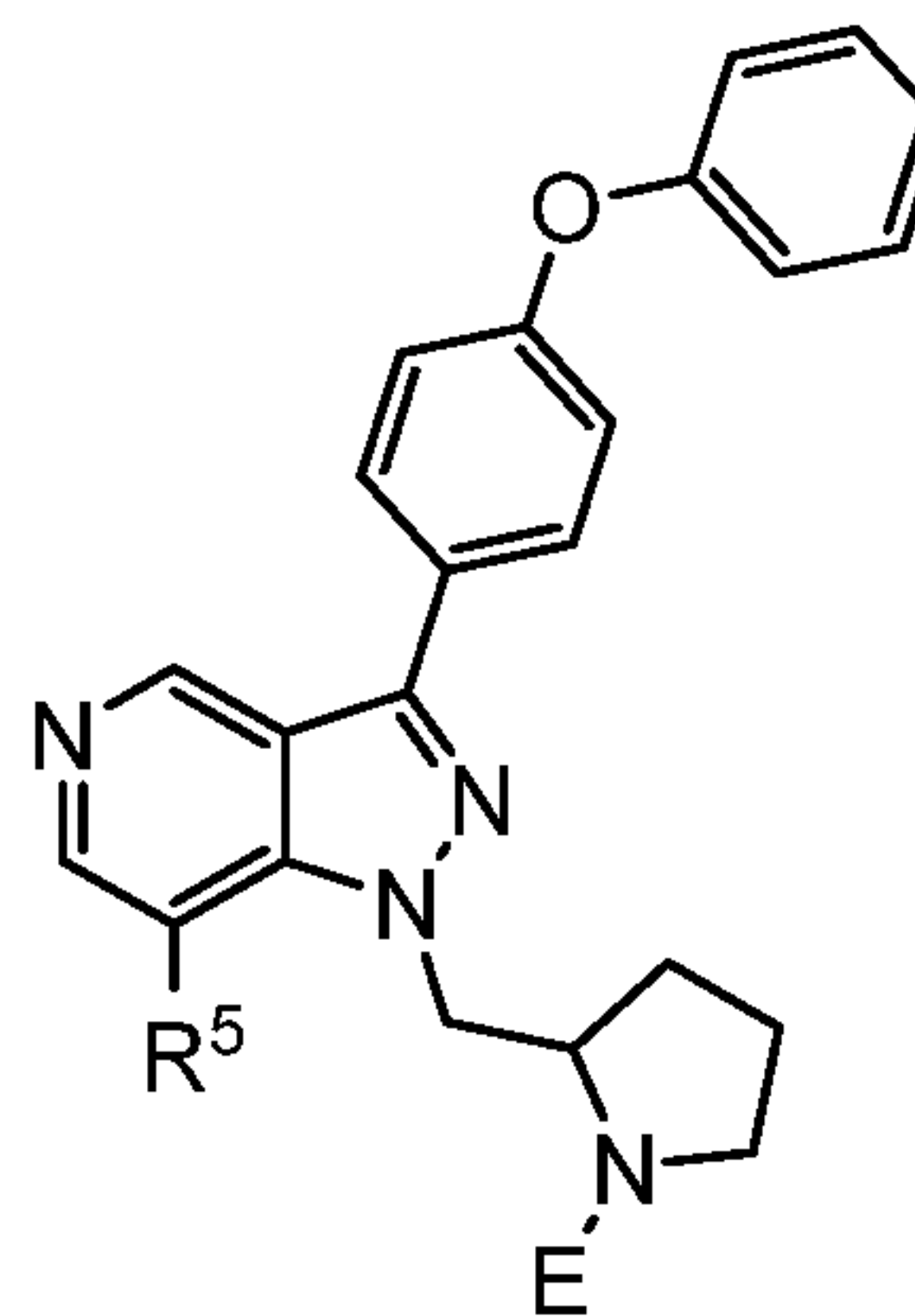
5 R^5 , and E are as described herein. In embodiments, the compound has the formula:



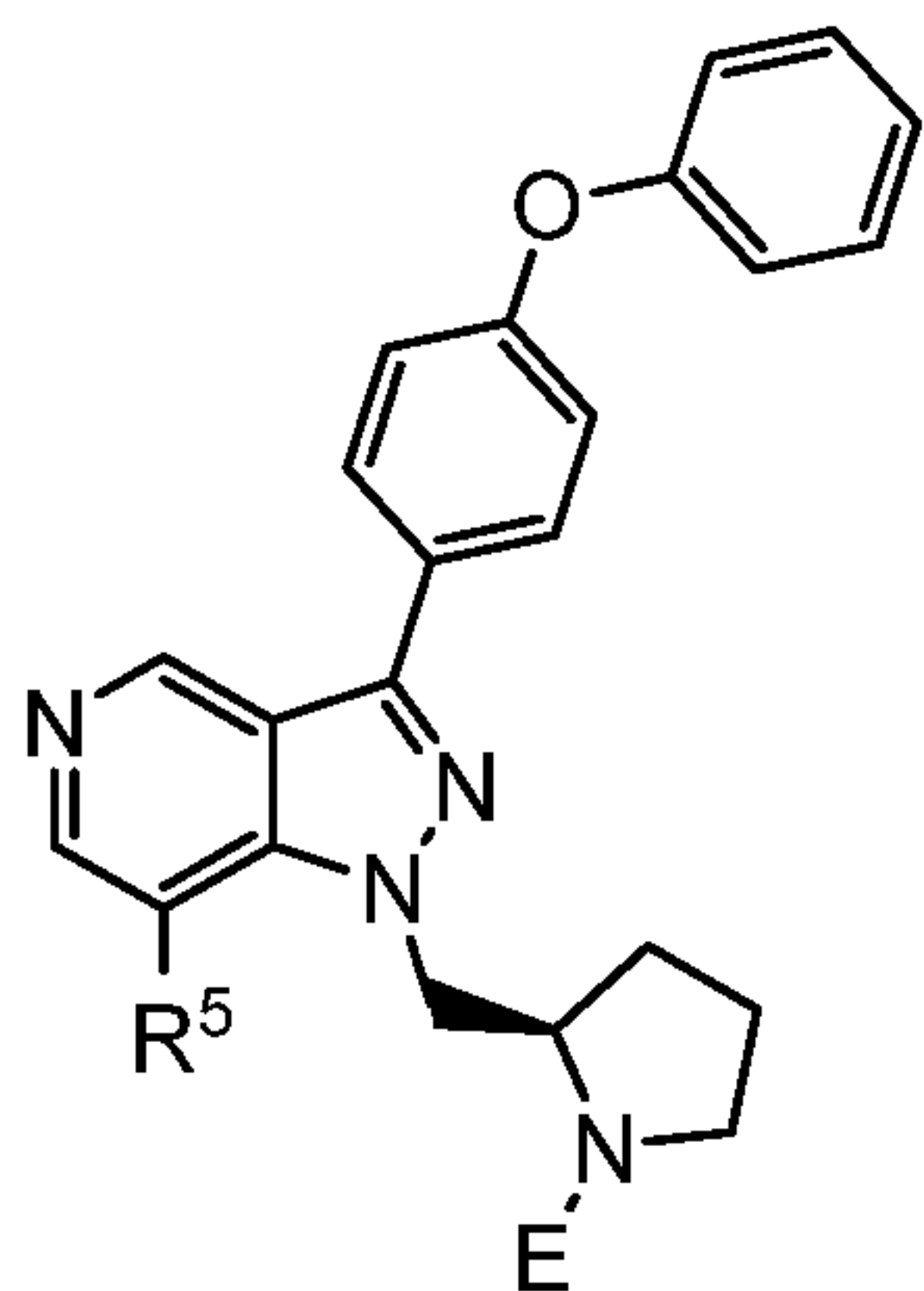
, wherein R^2 , R^5 , and E are as described herein. In embodiments, the



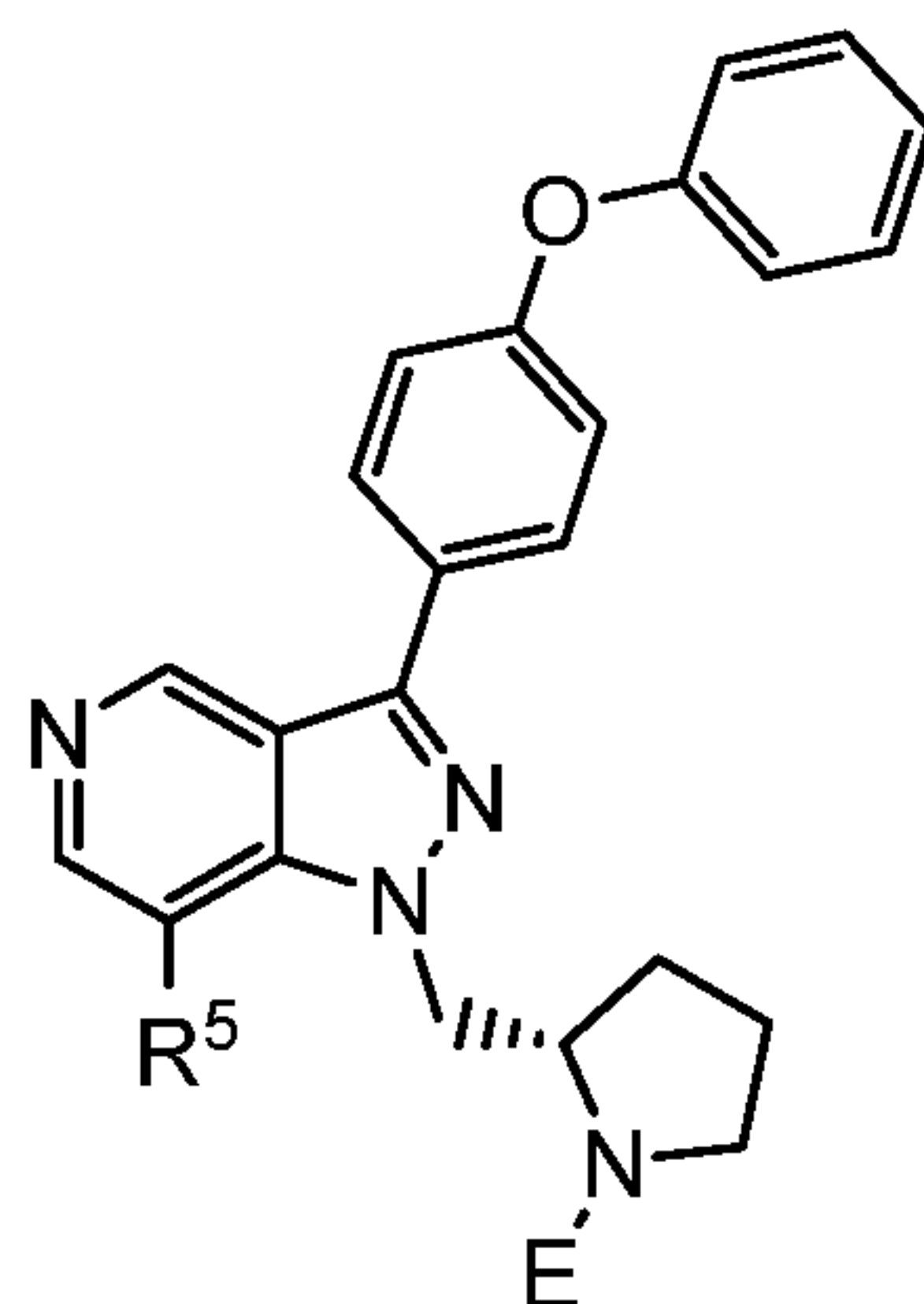
compound has the formula: , wherein R^2 , R^5 , and E are as described herein.



[0606] In embodiments, the compound has the formula: , wherein R^5 and E are as described herein. In embodiments, the compound has the formula:

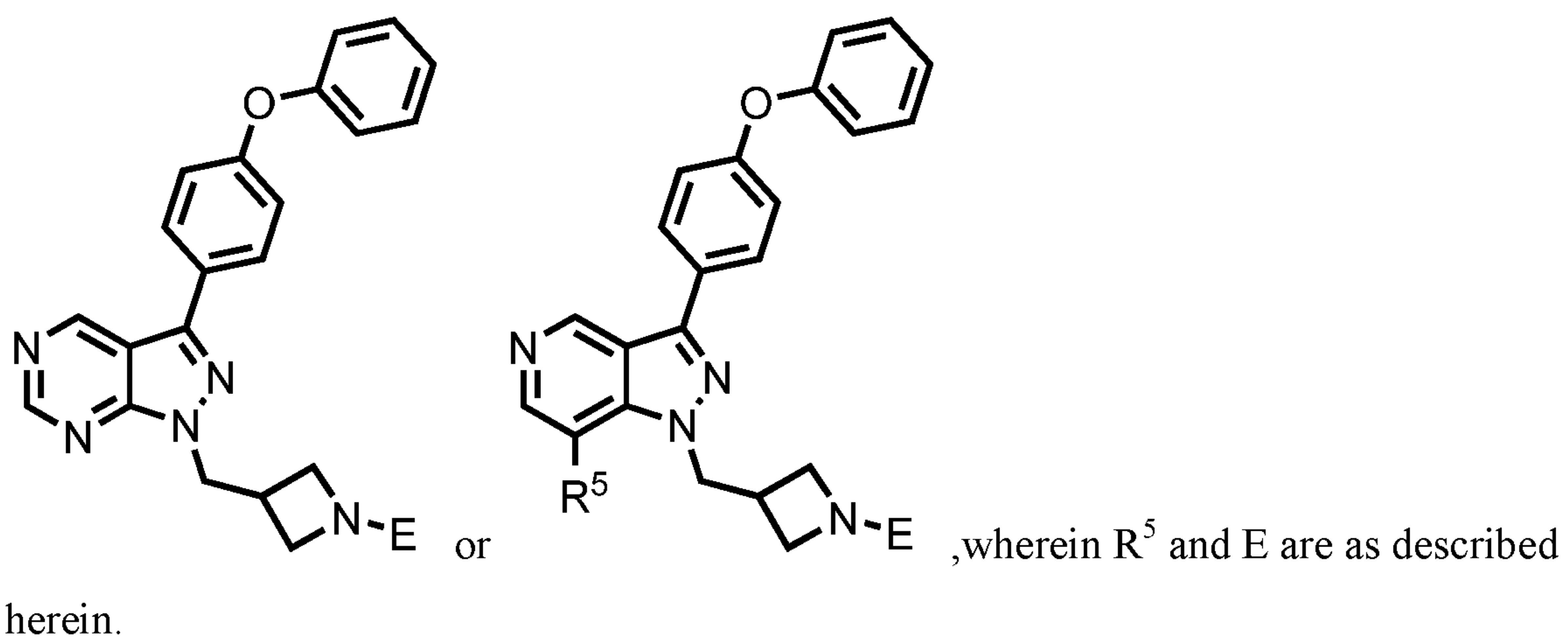


5 , wherein R^5 and E are as described herein. In embodiments, the

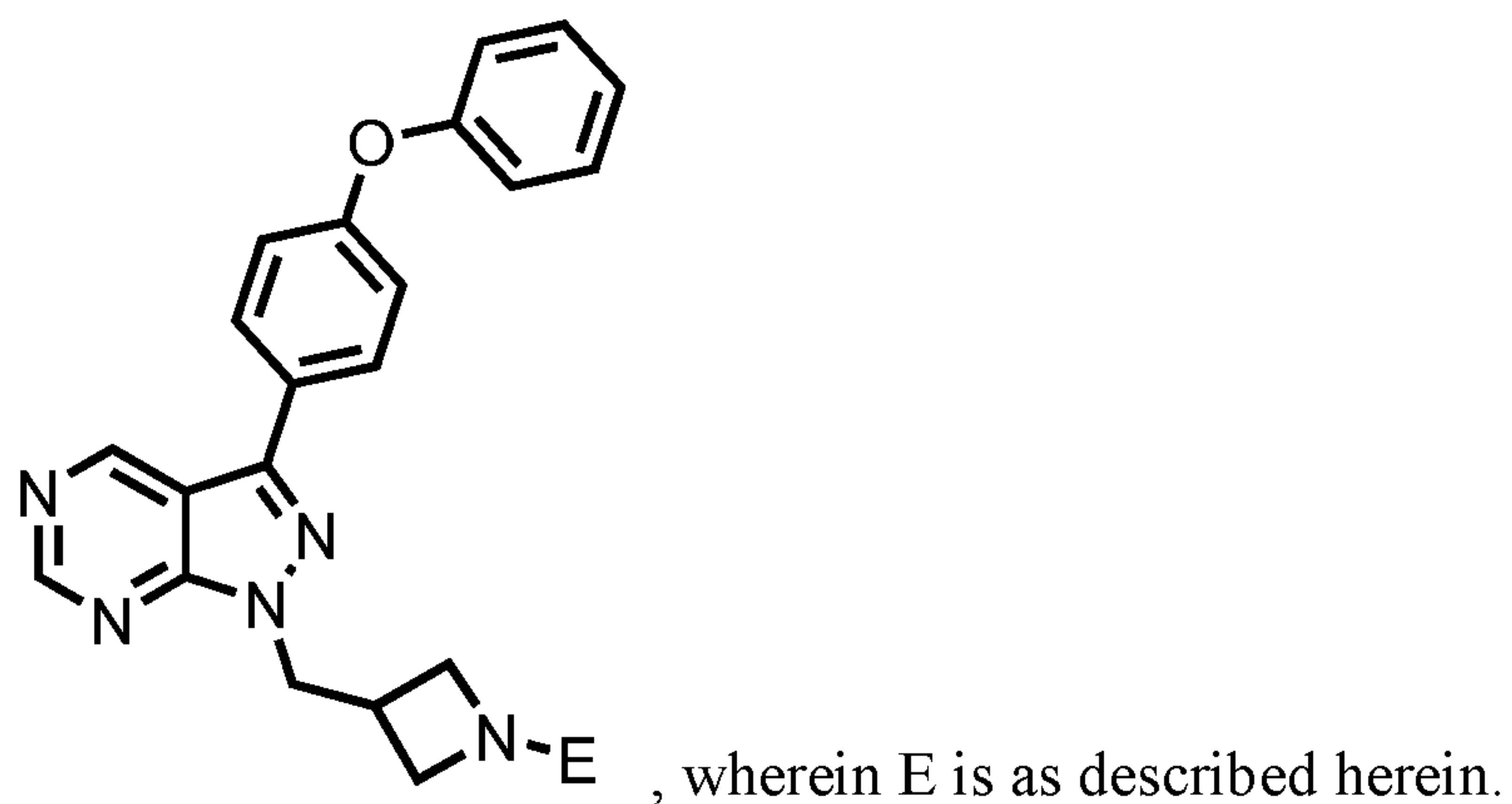


compound has the formula: , wherein R^5 and E are as described herein.

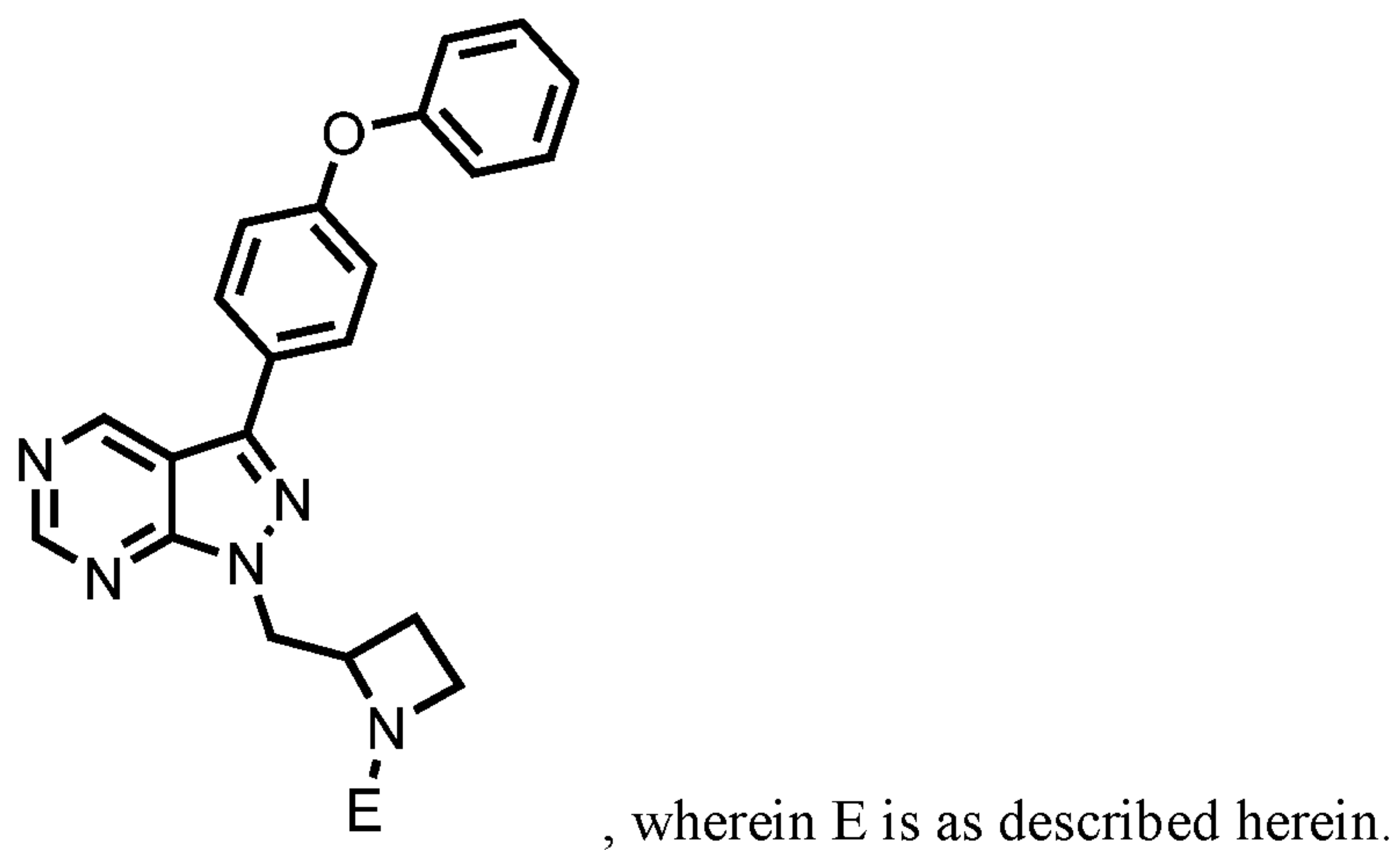
[0607] In embodiments, the compound has the formula:



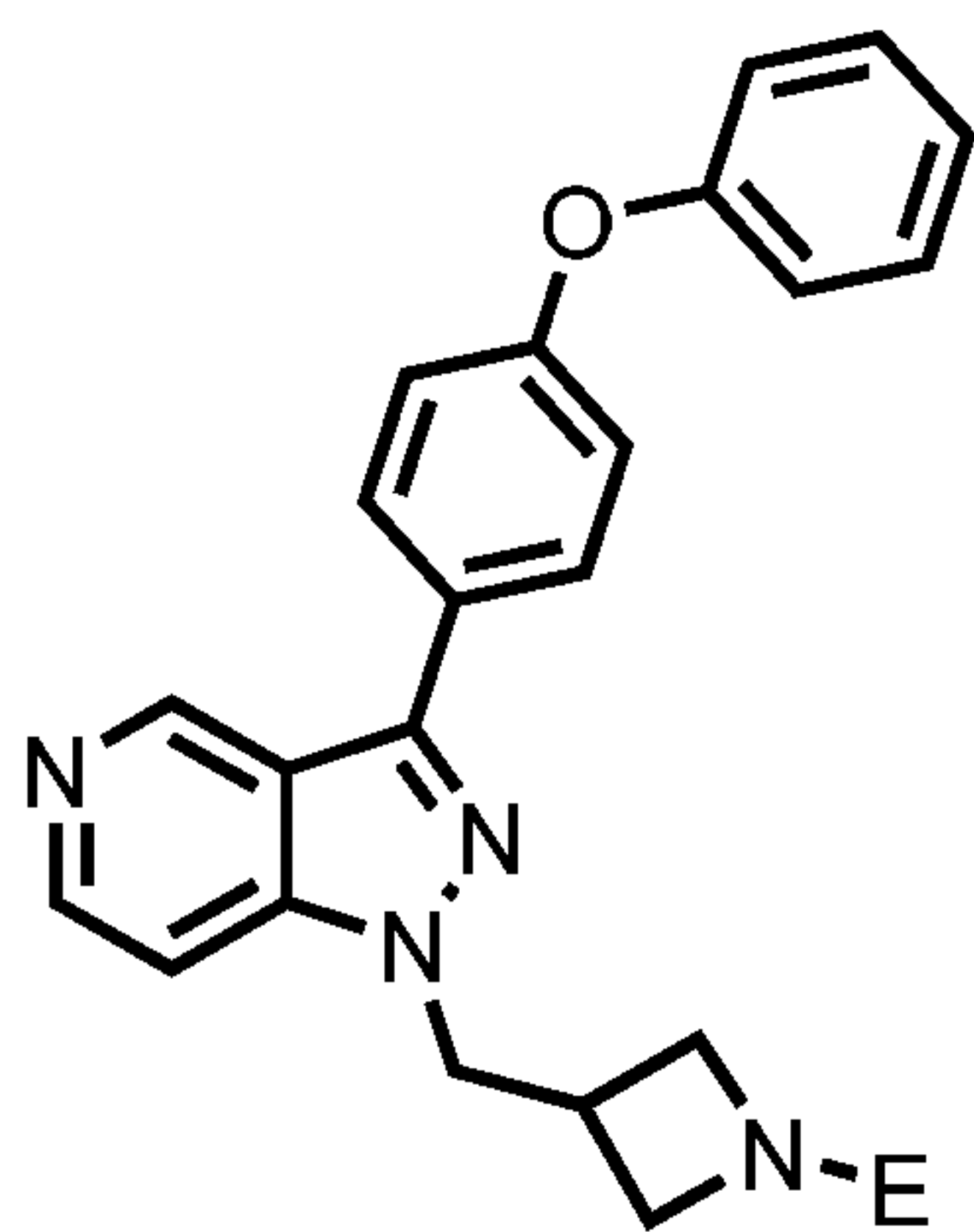
[0608] In embodiments, the compound has the formula:



5 **[0609]** In embodiments, the compound has the formula:

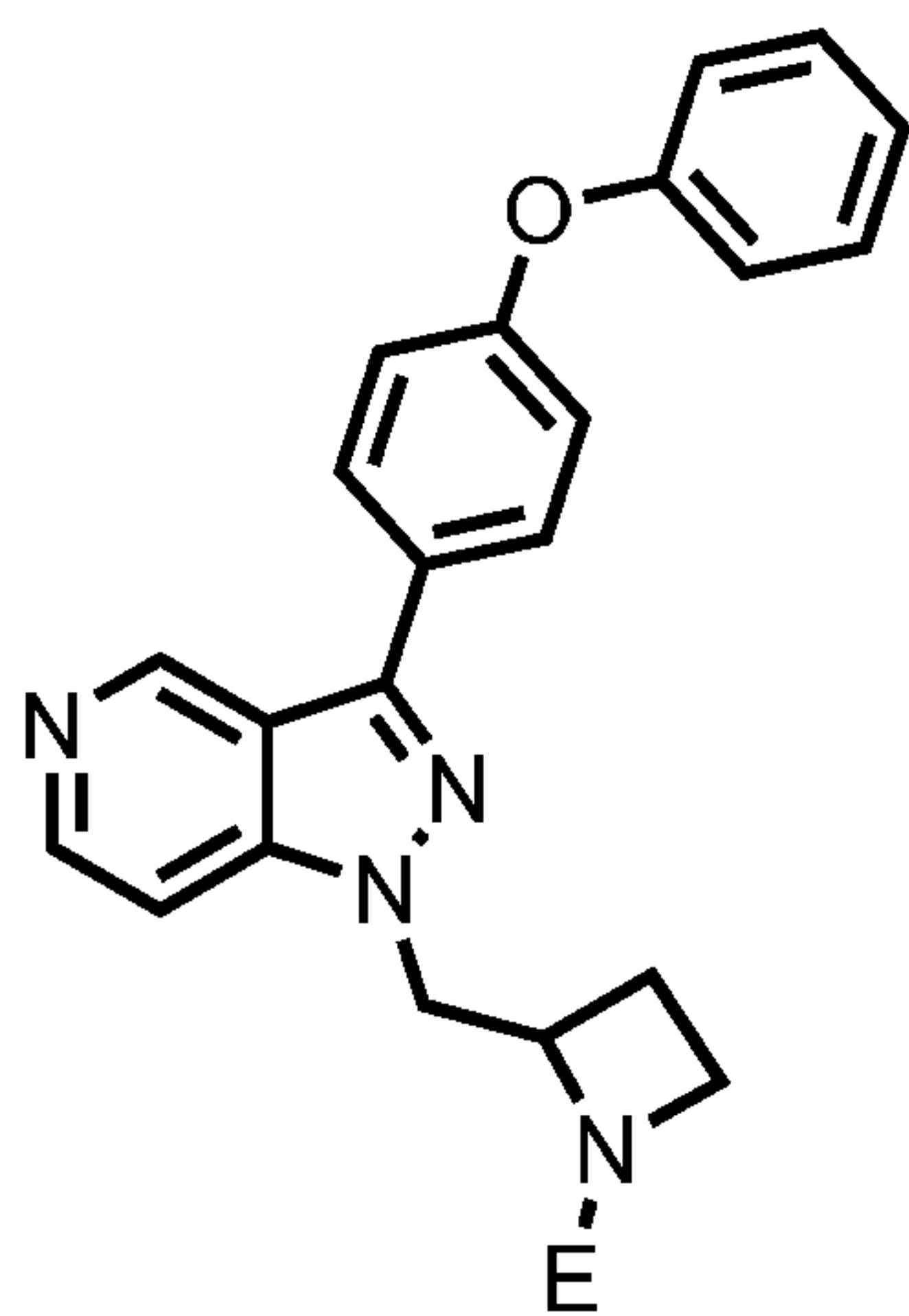


[0610] In embodiments, the compound has the formula:



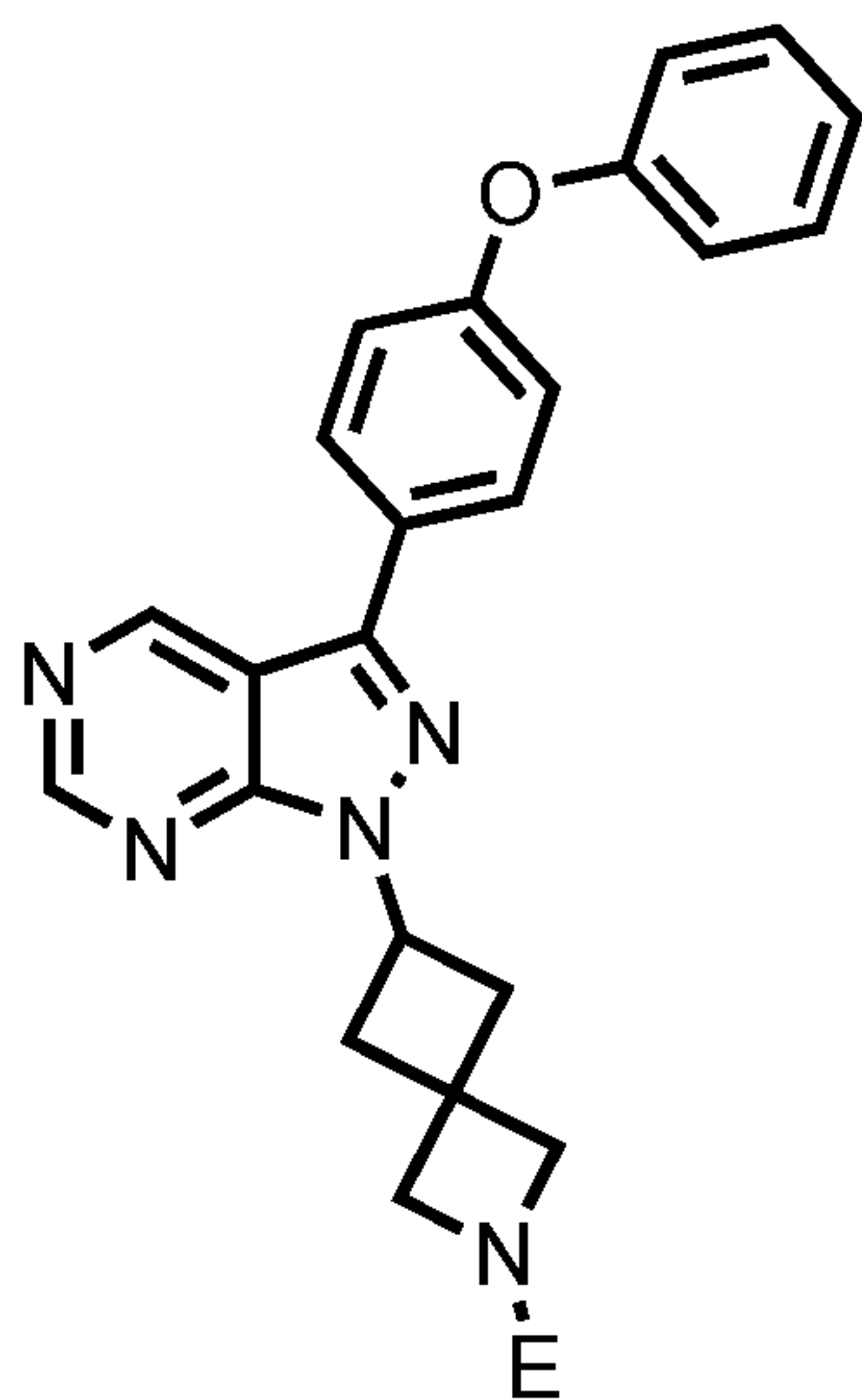
, wherein E is as described herein.

[0611] In embodiments, the compound has the formula:

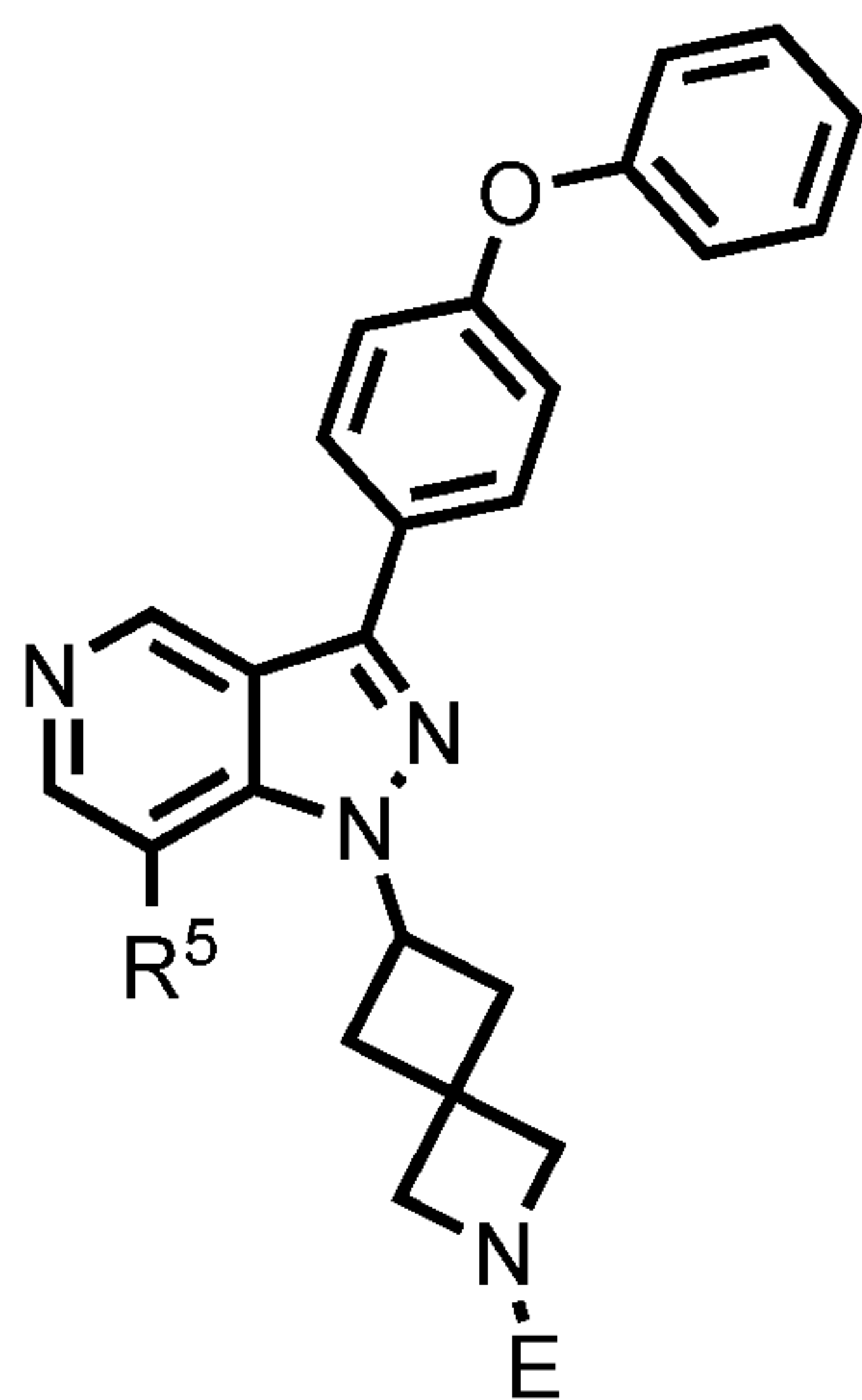


, wherein E is as described herein.

5 [0612] In embodiments, the compound has the formula:



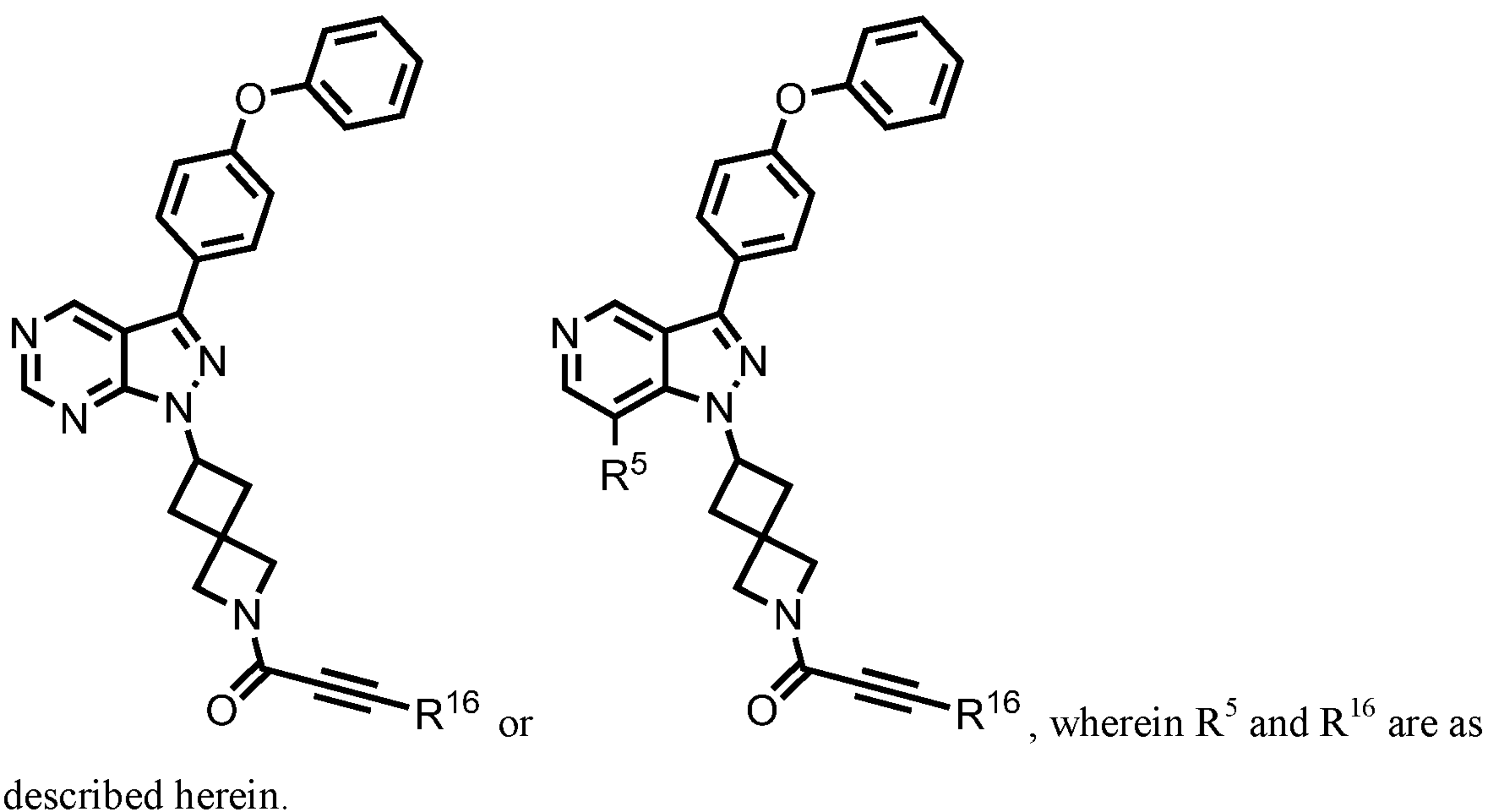
or



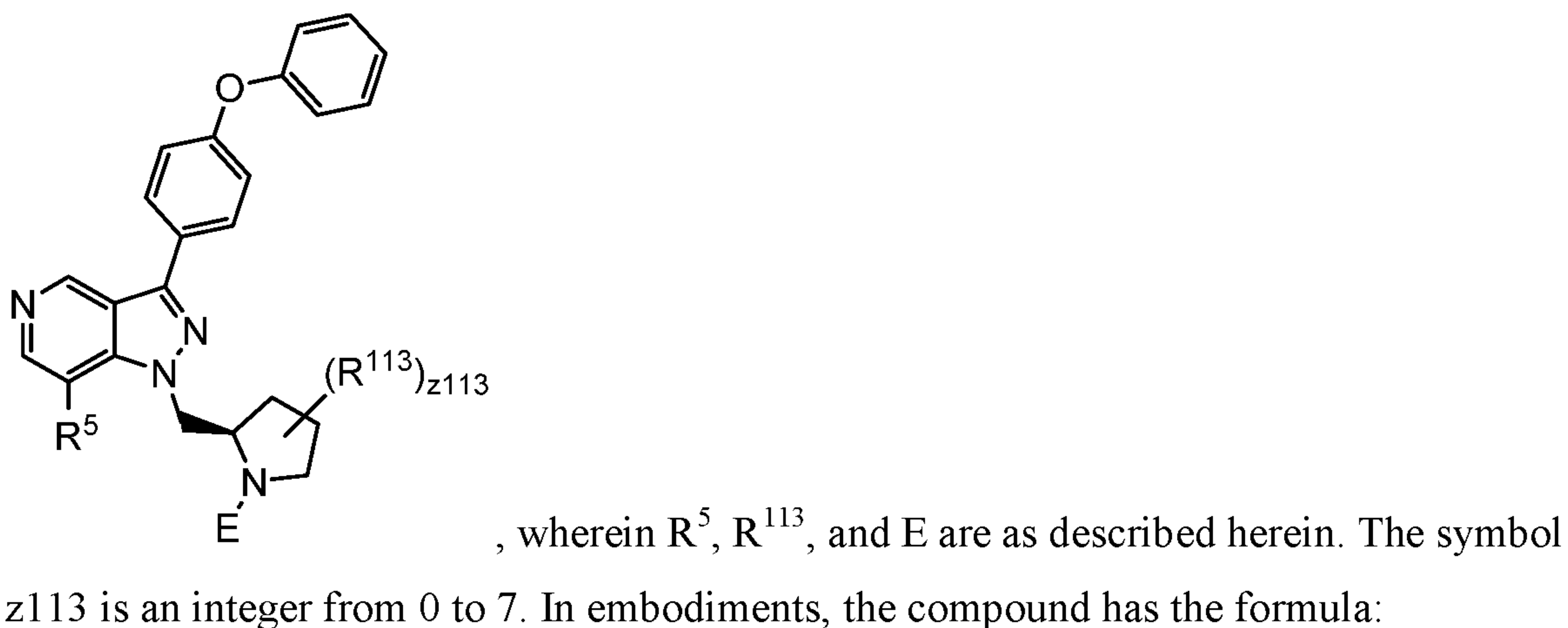
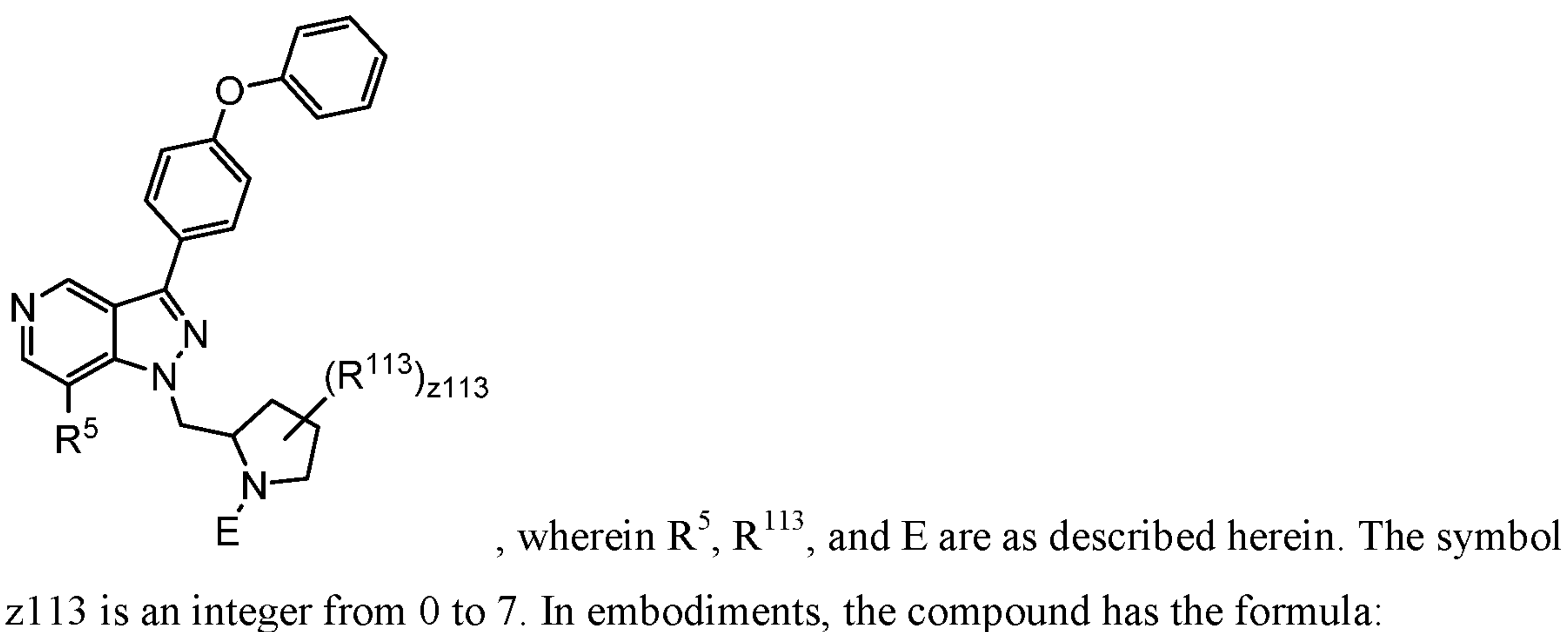
, wherein R⁵ and E are as described

herein.

[0613] In embodiments, the compound has the formula:



[0614] In embodiments, the compound has the formula:



DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 307

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 307

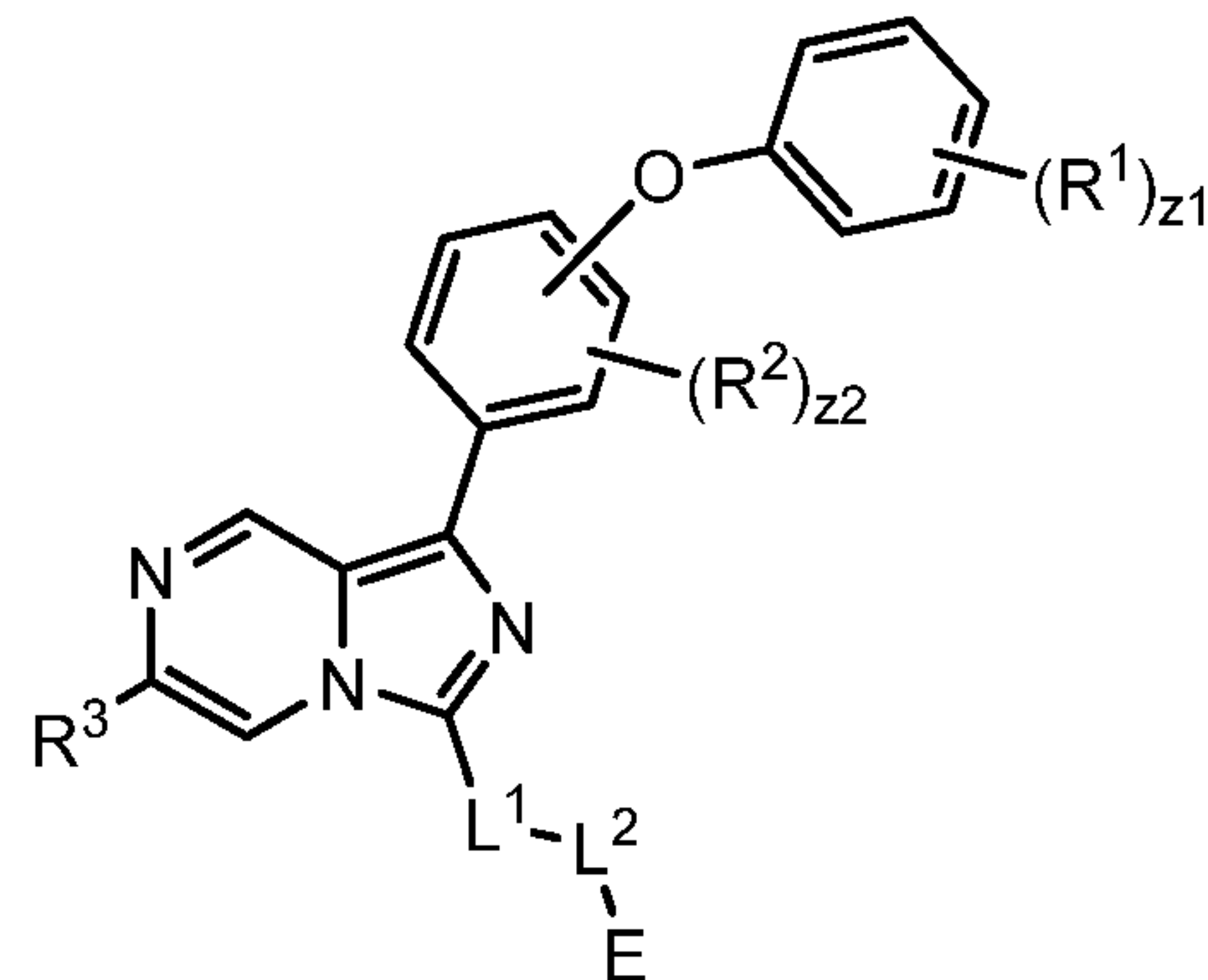
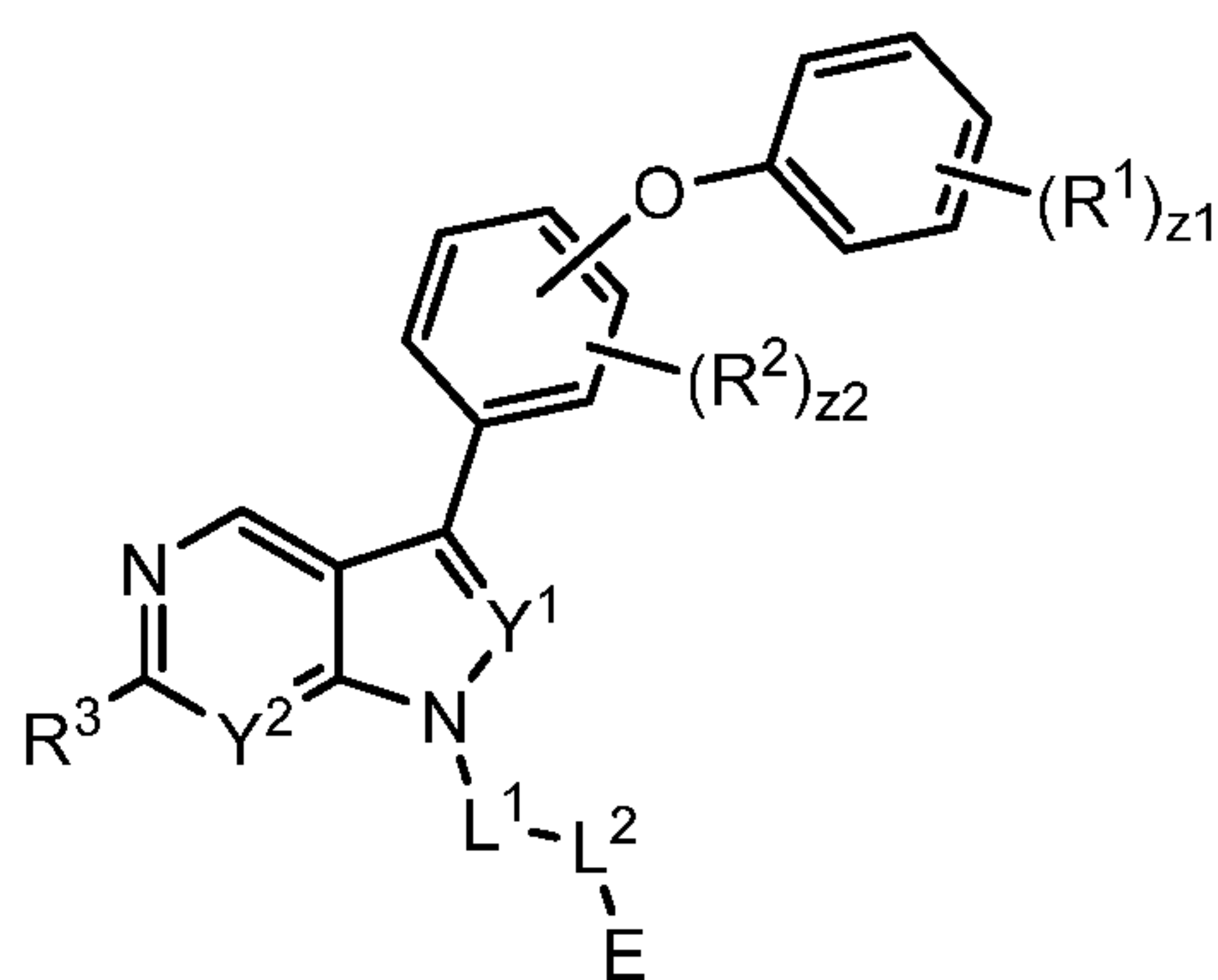
NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHER / FILE NAME :

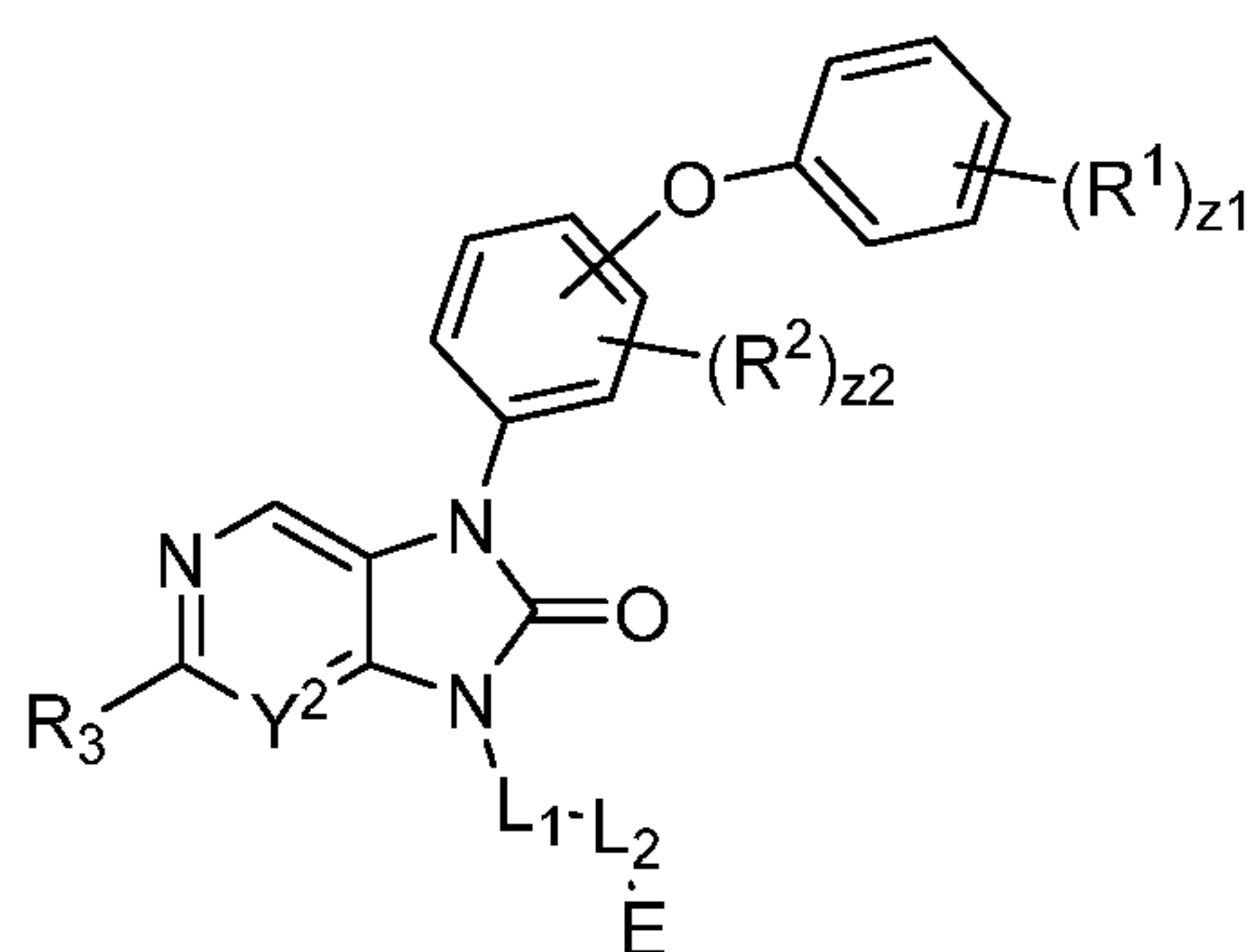
NOTE POUR LE TOME / VOLUME NOTE:

WHAT IS CLAIMED IS:

1. A compound having the formula:



(I), or



(II), or

(III);

wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, -

OCH_2X^1 , $-OCHX^1_2$, $-CN$, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$,

$-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)O$

R^{1C} , $-NR^{1A}OR^{1C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl,

substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl,

substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^1

substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl,

substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted

or unsubstituted heteroaryl;

$z1$ is an integer from 0 to 5;

R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, -

OCH_2X^2 , $-OCHX^2_2$, $-CN$, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$,

$-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)O$

R^{2C} , $-NR^{2A}OR^{2C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl,

substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl,

substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^2

substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z_2 is an integer from 0 to 4;

R^3 is hydrogen or $-NH_2$;

Y^1 is N or $C(R^4)$;

R^4 is hydrogen, halogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, $-CN$, $-SO_{n4}R^{4D}$, $-SO_{v4}NR^{4A}R^{4B}$, $-NHC(O)NR^{4A}R^{4B}$, $-N(O)_{m4}$, $-NR^{4A}R^{4B}$, $-C(O)R^{4C}$, $-C(O)-OR^{4C}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4D}$, $-NR^{4A}SO_2R^{4D}$, $-NR^{4A}C(O)R^{4C}$, $-NR^{4A}C(O)OR^{4C}$, $-NR^{4A}OR^{4C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

Y^2 is N or $C(R^5)$;

R^5 is hydrogen, halogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, $-CN$, $-SO_{n5}R^{5D}$, $-SO_{v5}NR^{5A}R^{5B}$, $-NHC(O)NR^{5A}R^{5B}$, $-N(O)_{m5}$, $-NR^{5A}R^{5B}$, $-C(O)R^{5C}$, $-C(O)-OR^{5C}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5D}$, $-NR^{5A}SO_2R^{5D}$, $-NR^{5A}C(O)R^{5C}$, $-NR^{5A}C(O)OR^{5C}$, $-NR^{5A}OR^{5C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^1 is a

bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^6-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^6-$, $-NR^6C(O)-$, $-NR^6C(O)NH-$, $-NHC(O)NR^6-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^6 is hydrogen, halogen, $-CX^6_3$, $-CHX^6_2$, $-CH_2X^6$, $-OCX^6_3$, $-OCH_2X^6$, $-OCHX^6_2$, $-CN$, $-SO_{n6}R^{6D}$, $-SO_{v6}NR^{6A}R^{6B}$, $-NHC(O)NR^{6A}R^{6B}$, $-N(O)_{m6}$, $-NR^{6A}R^{6B}$, $-C(O)R^{6C}$, $-C(O)-OR^{6C}$, $-C(O)NR^{6A}R^{6B}$, $-OR^{6D}$, $-NR^{6A}SO_2R^{6D}$, $-NR^{6A}C(O)R^{6C}$, $-NR^{6A}C(O)OR^{6C}$, $-NR^{6A}OR^{6C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^2 is a

bond, $-S(O)_2-$, $-S(O)_2-Ph-$, $-NR^7-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^7-$, $-NR^7C(O)-$, $-NR^7C(O)NH-$, $-NHC(O)NR^7-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or

unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^7 is hydrogen, halogen, $-CX^7_3$, $-CHX^7_2$, $-CH_2X^7$, $-OCX^7_3$, $-OCH_2X^7$, $-OCHX^7_2$, $-CN$, $-SO_{n7}R^{7D}$, $-SO_{v7}NR^{7A}R^{7B}$, $-NHC(O)NR^{7A}R^{7B}$, $-N(O)_{m7}$, $-NR^{7A}R^{7B}$, $-C(O)R^{7C}$, $-C(O)-OR^{7C}$, $-C(O)NR^{7A}R^{7B}$, $-OR^{7D}$, $-NR^{7A}SO_2R^{7D}$, $-NR^{7A}C(O)R^{7C}$, $-NR^{7A}C(O)OR^{7C}$, $-NR^{7A}OR^{7C}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

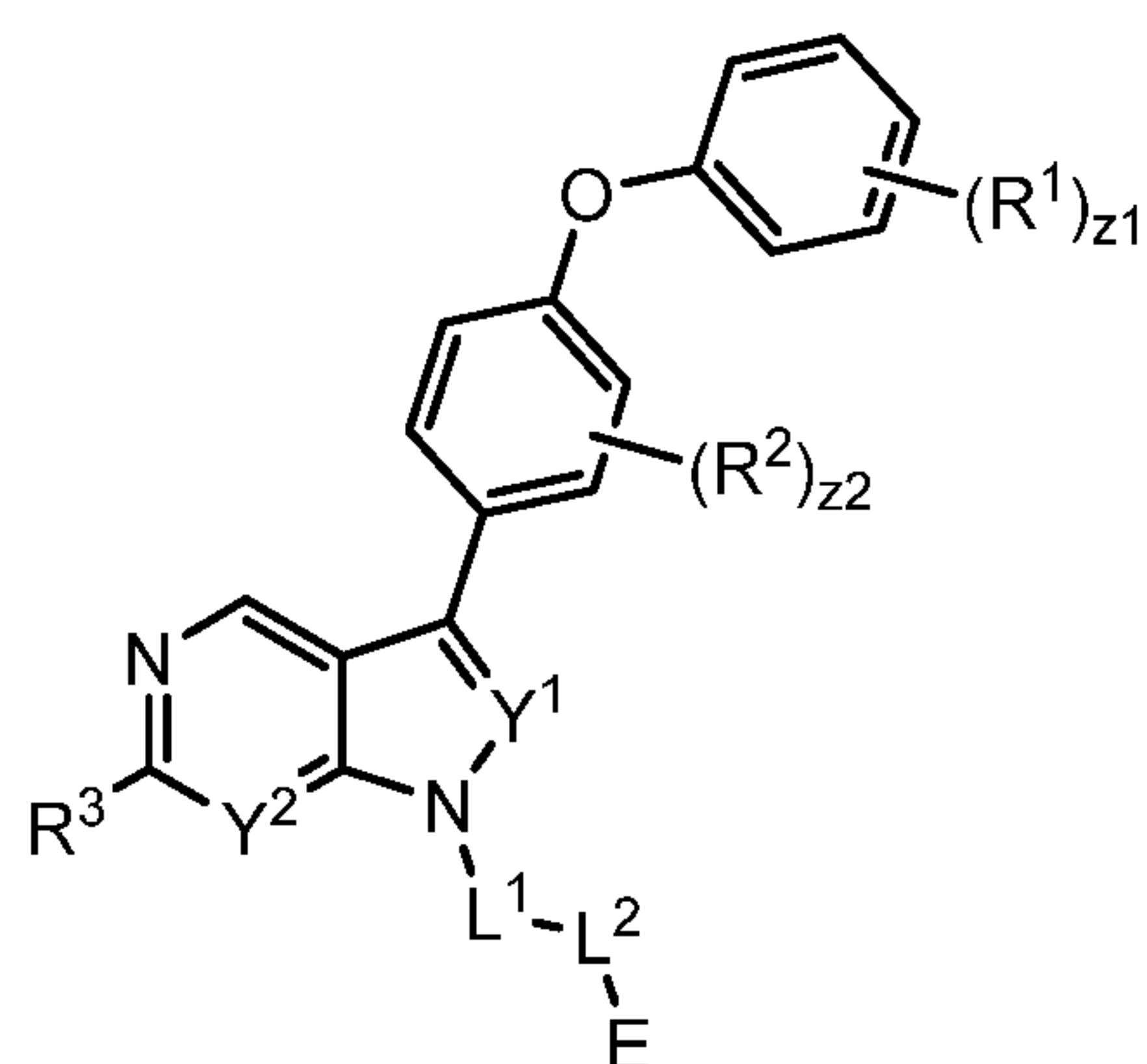
E is an electrophilic moiety;

Each R^{1A} , R^{1B} , R^{1C} , R^{1D} , R^{2A} , R^{2B} , R^{2C} , R^{2D} , R^{4A} , R^{4B} , R^{4C} , R^{4D} , R^{5A} , R^{5B} , R^{5C} , R^{5D} , R^{6A} , R^{6B} , R^{6C} , R^{6D} , R^{7A} , R^{7B} , R^{7C} , and R^{7D} is independently hydrogen, $-CX_3$, $-CN$, $-COOH$, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{6A} and R^{6B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{7A} and R^{7B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

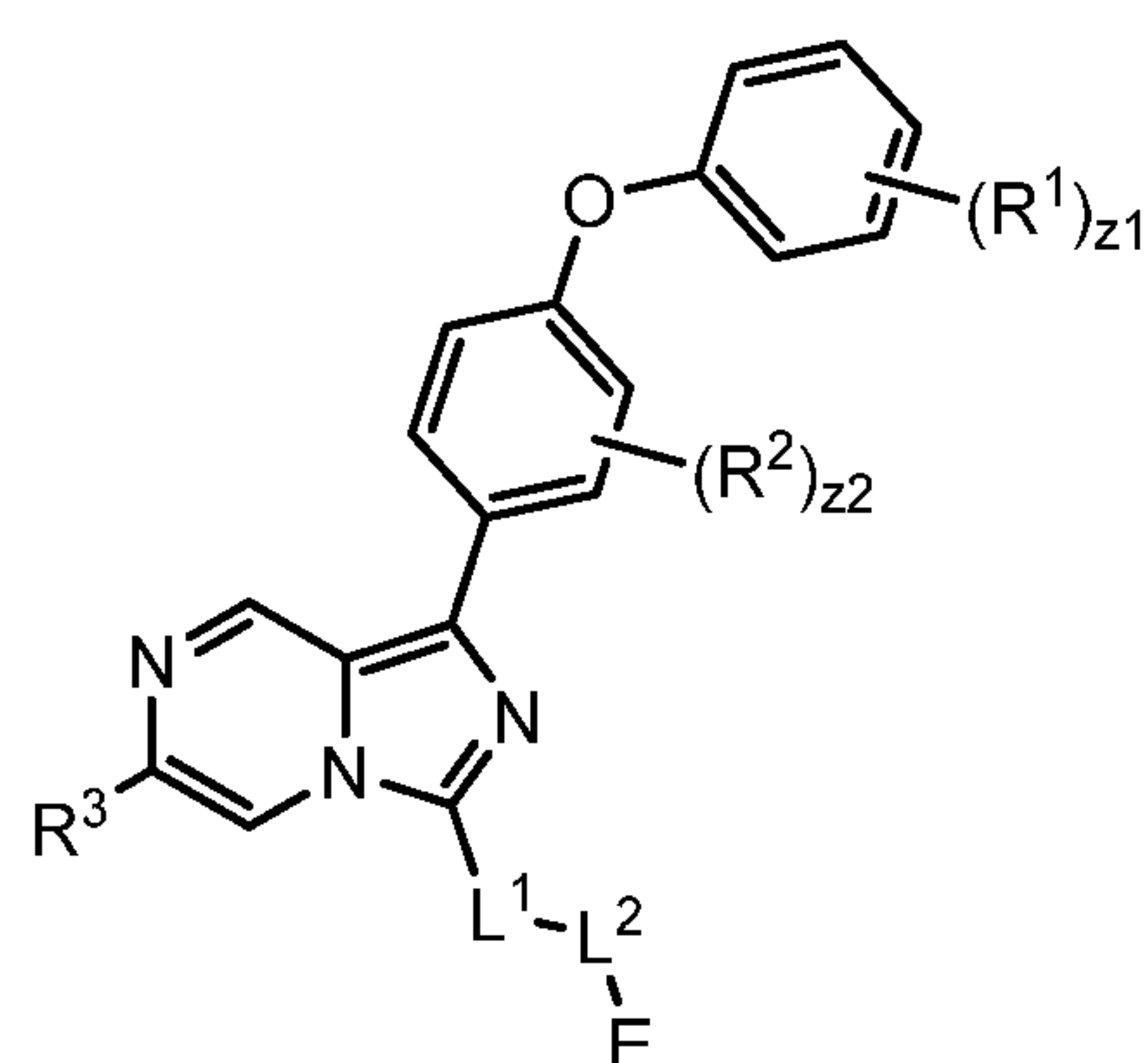
each X , X^1 , X^2 , X^4 , X^5 , X^6 , and X^7 is independently $-F$, $-Cl$, $-Br$, or $-I$;
 $n1$, $n2$, $n4$, $n5$, $n6$, and $n7$ are independently an integer from 0 to 4; and
 $m1$, $m2$, $m4$, $m5$, $m6$, $m7$, $v1$, $v2$, $v4$, $v5$, $v6$, and $v7$, are independently an integer from 1 to 2.

2. The compound of claim 1 having the formula:

2

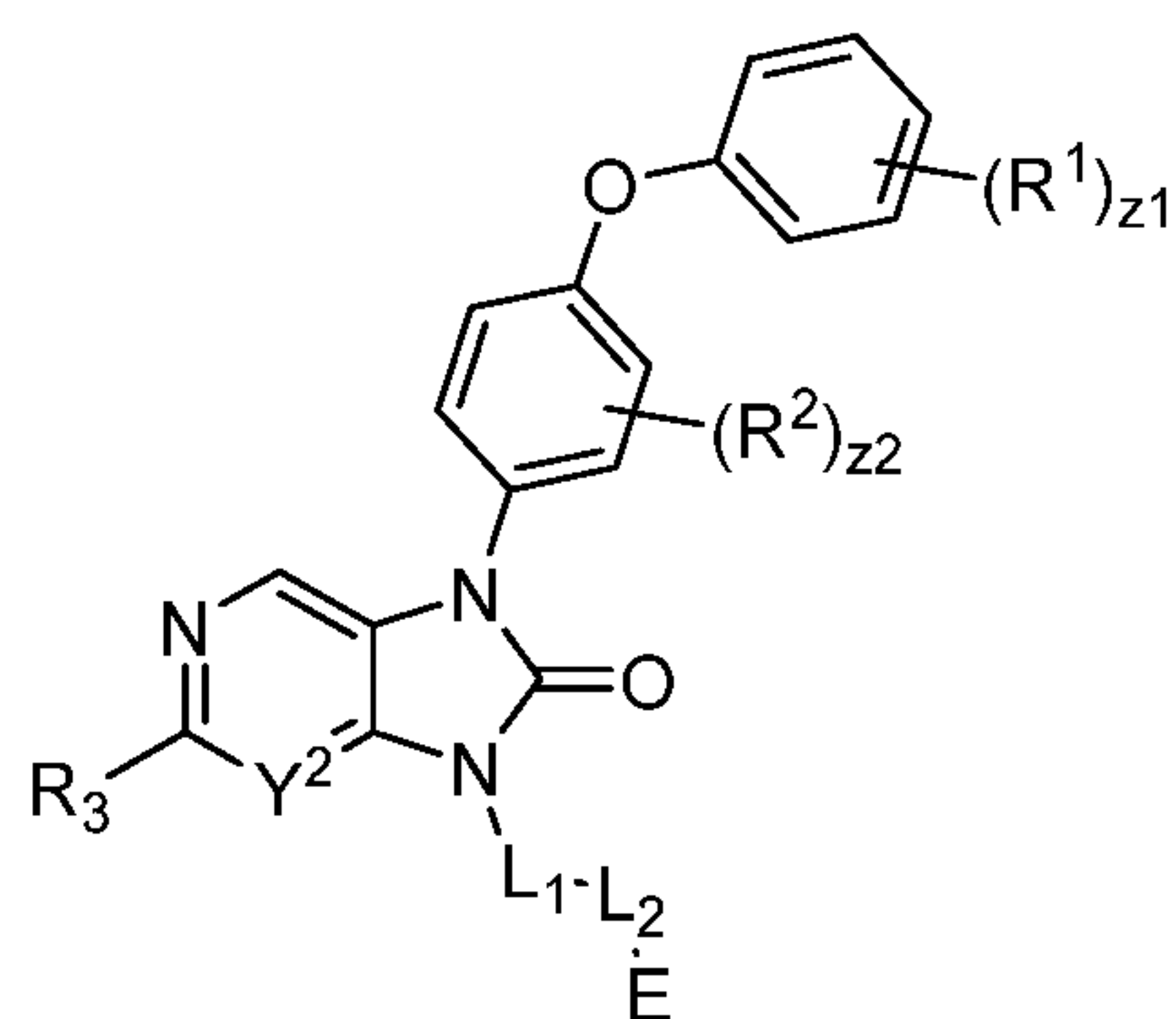


(IA) or

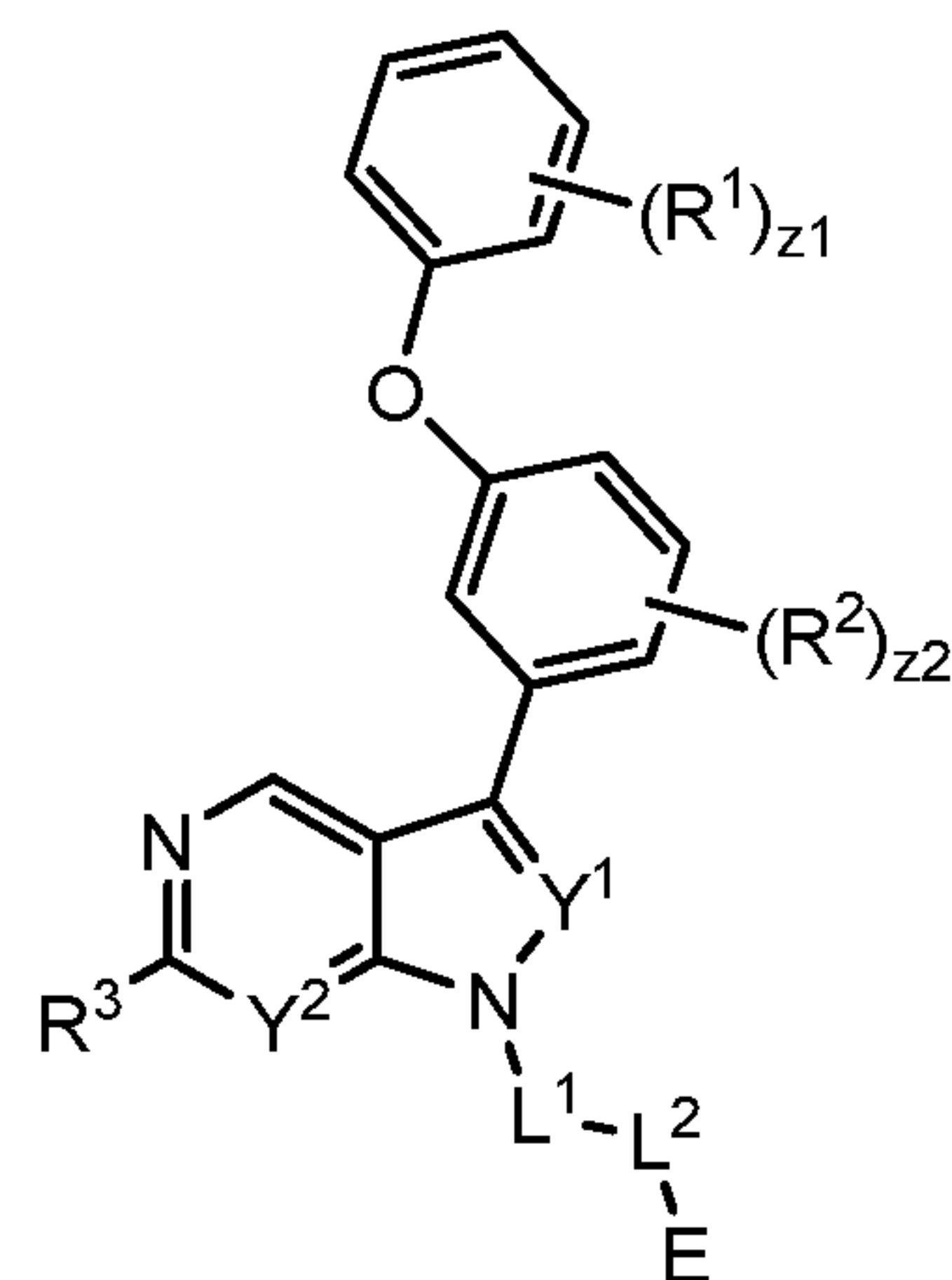


3

(IIA)

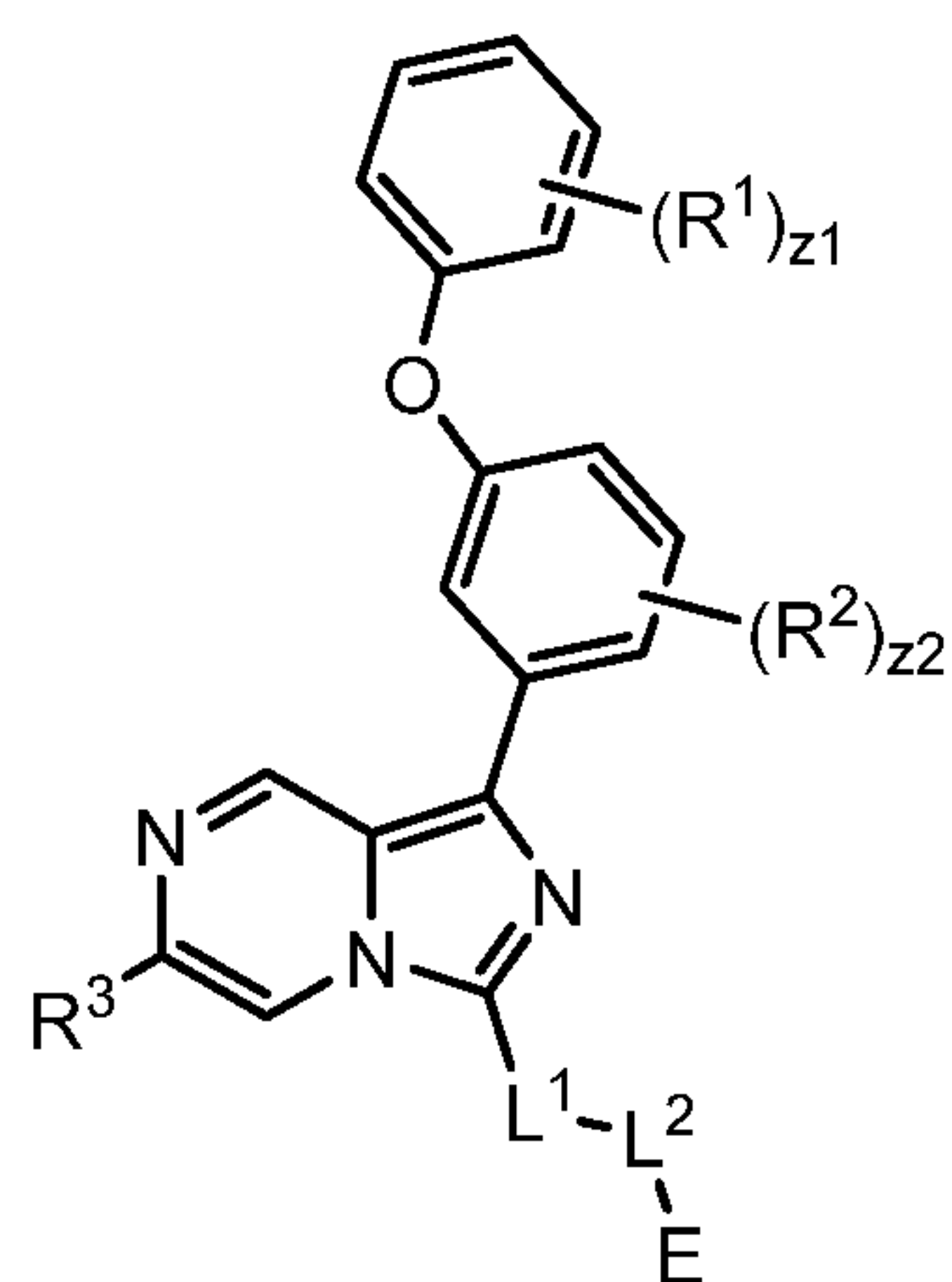


(IIIA),

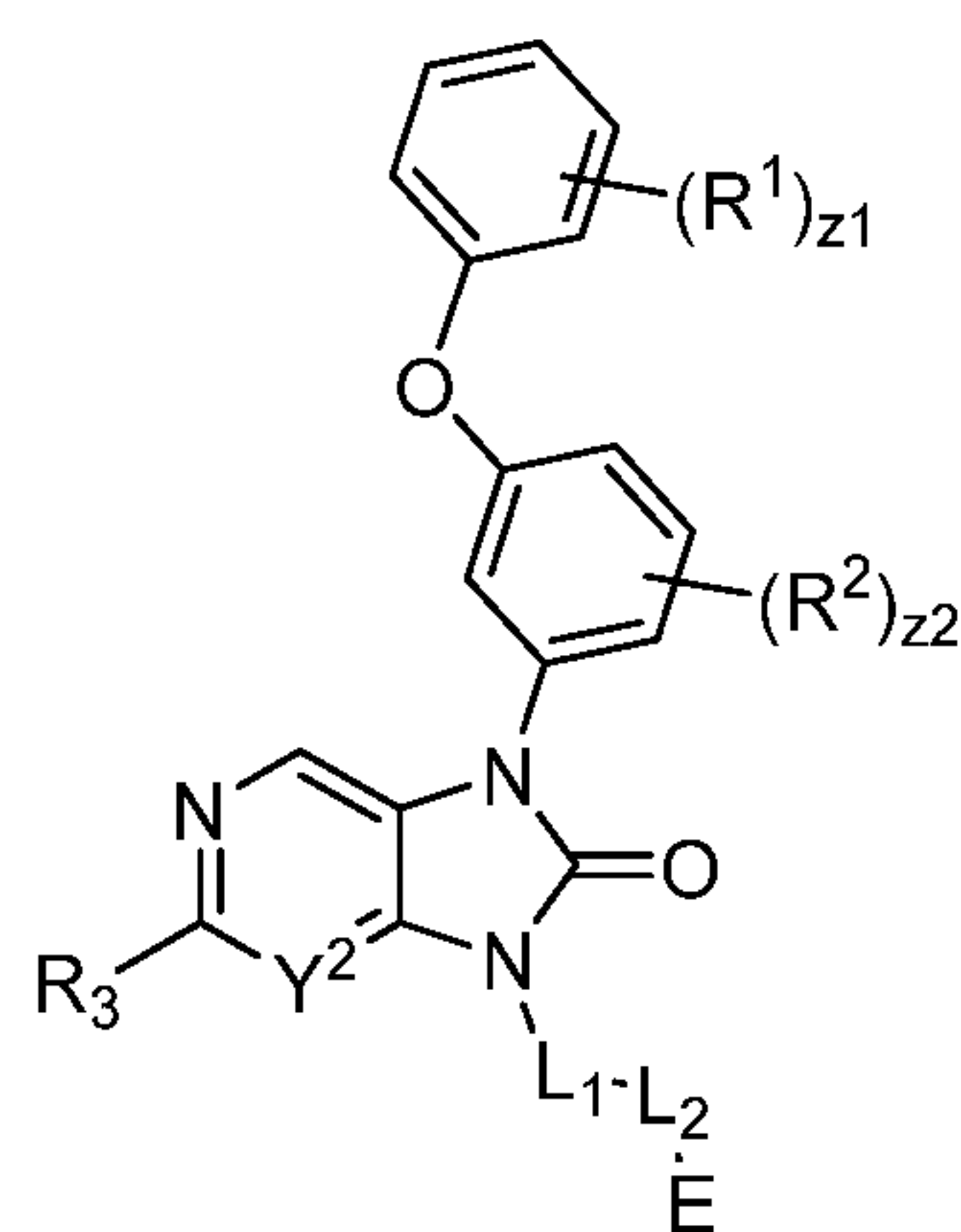


(IB) or

4



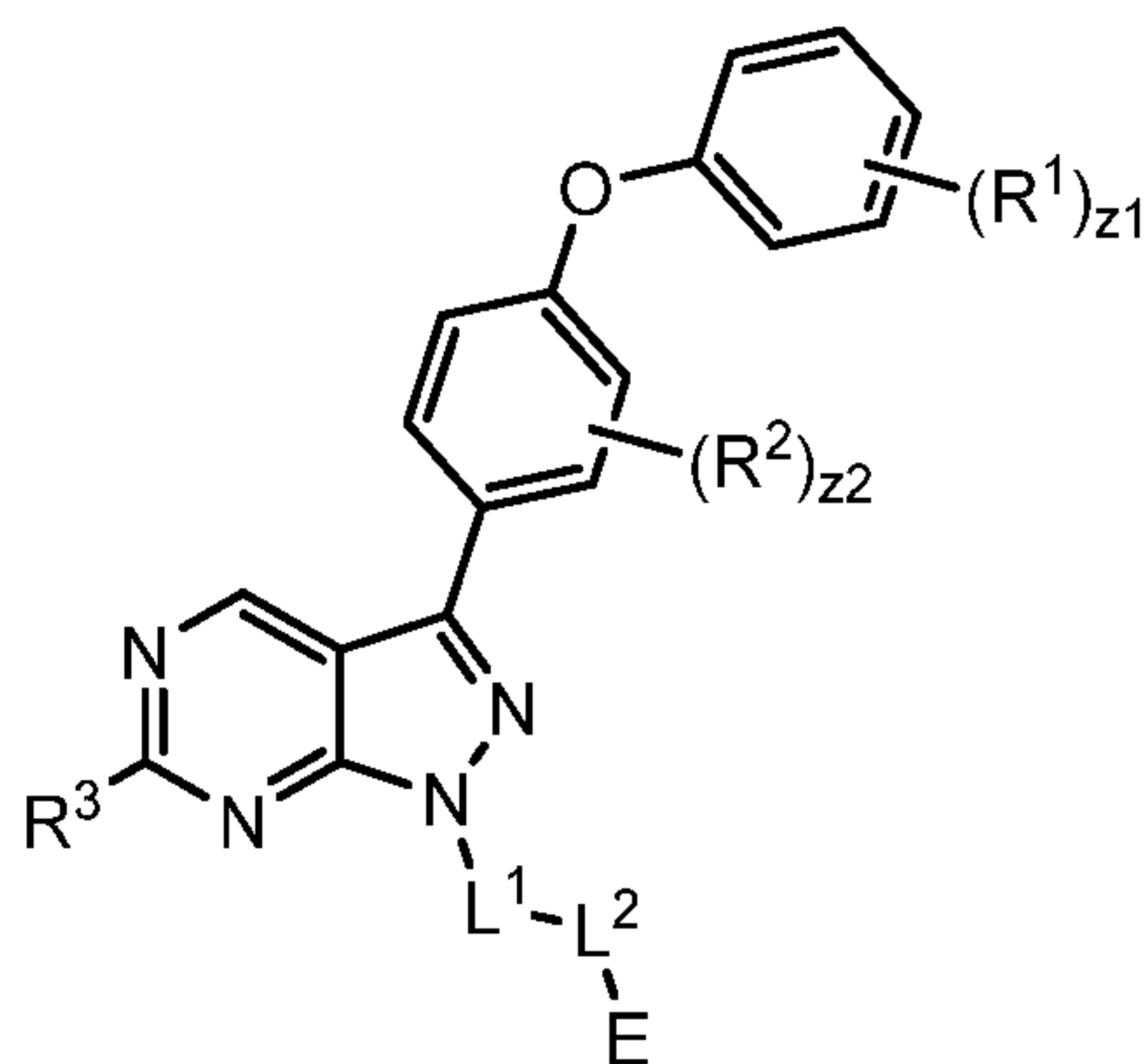
(IIB) or



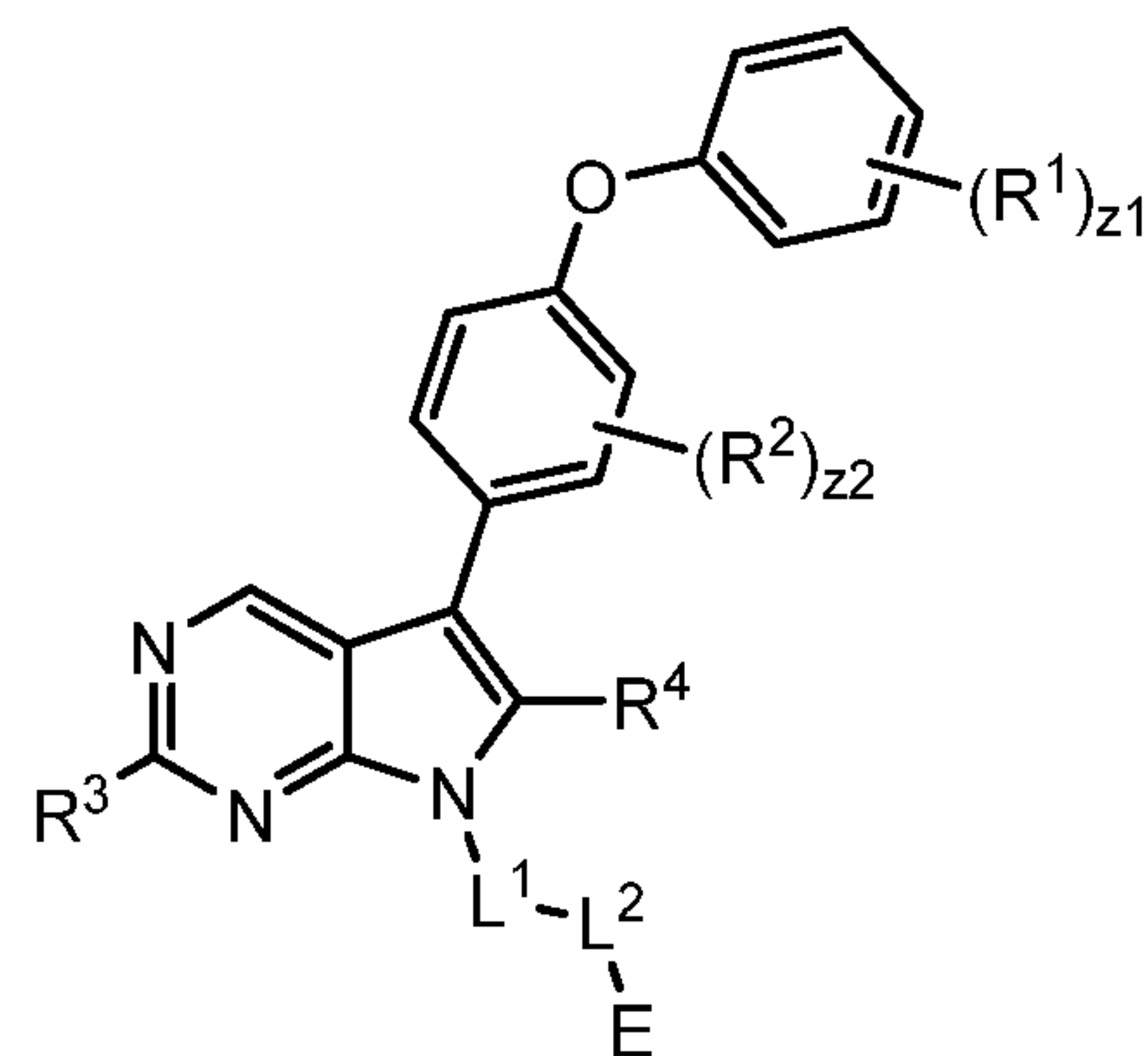
(IIIB).

1

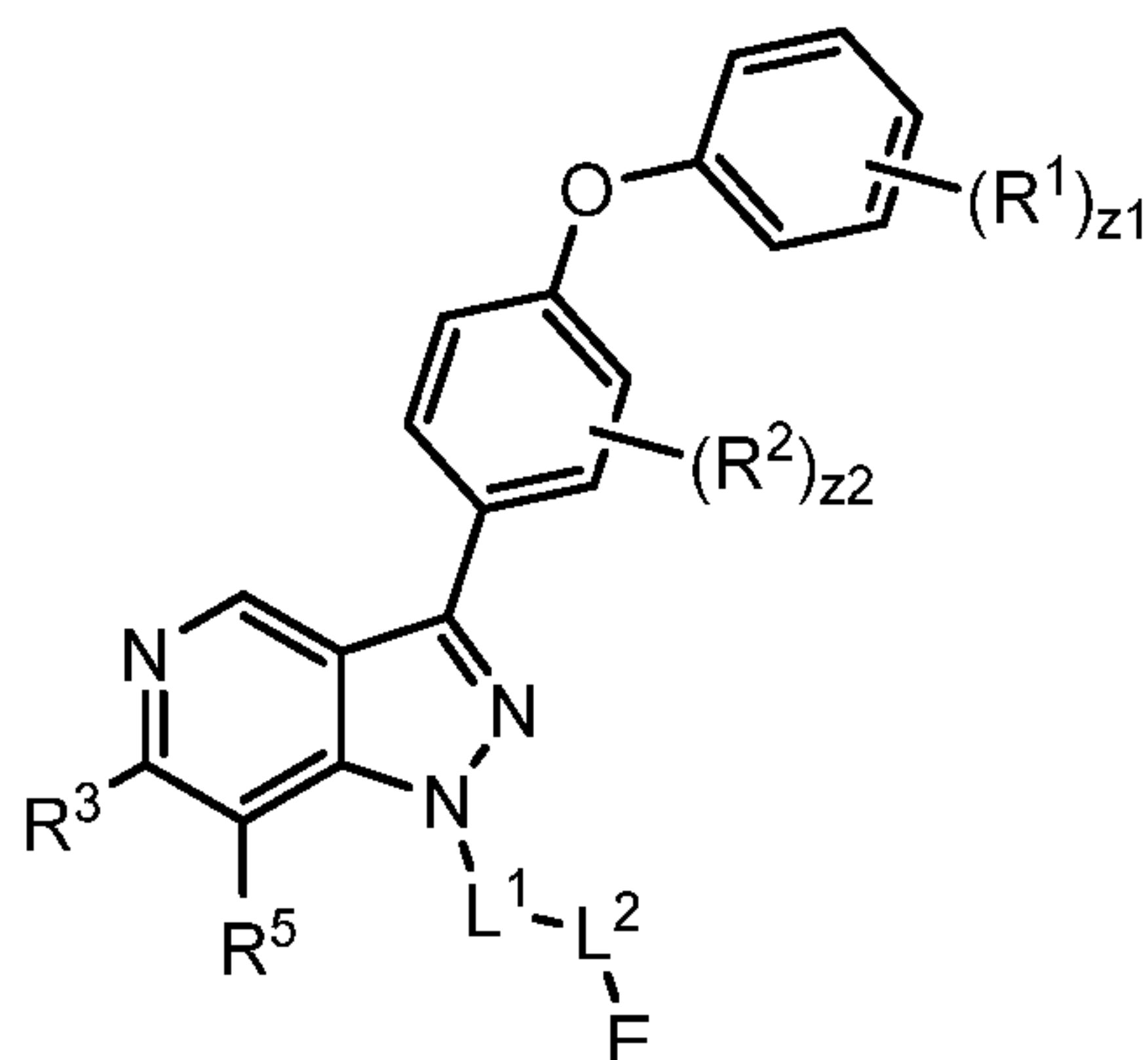
3. The compound of claim 1 having the formula:



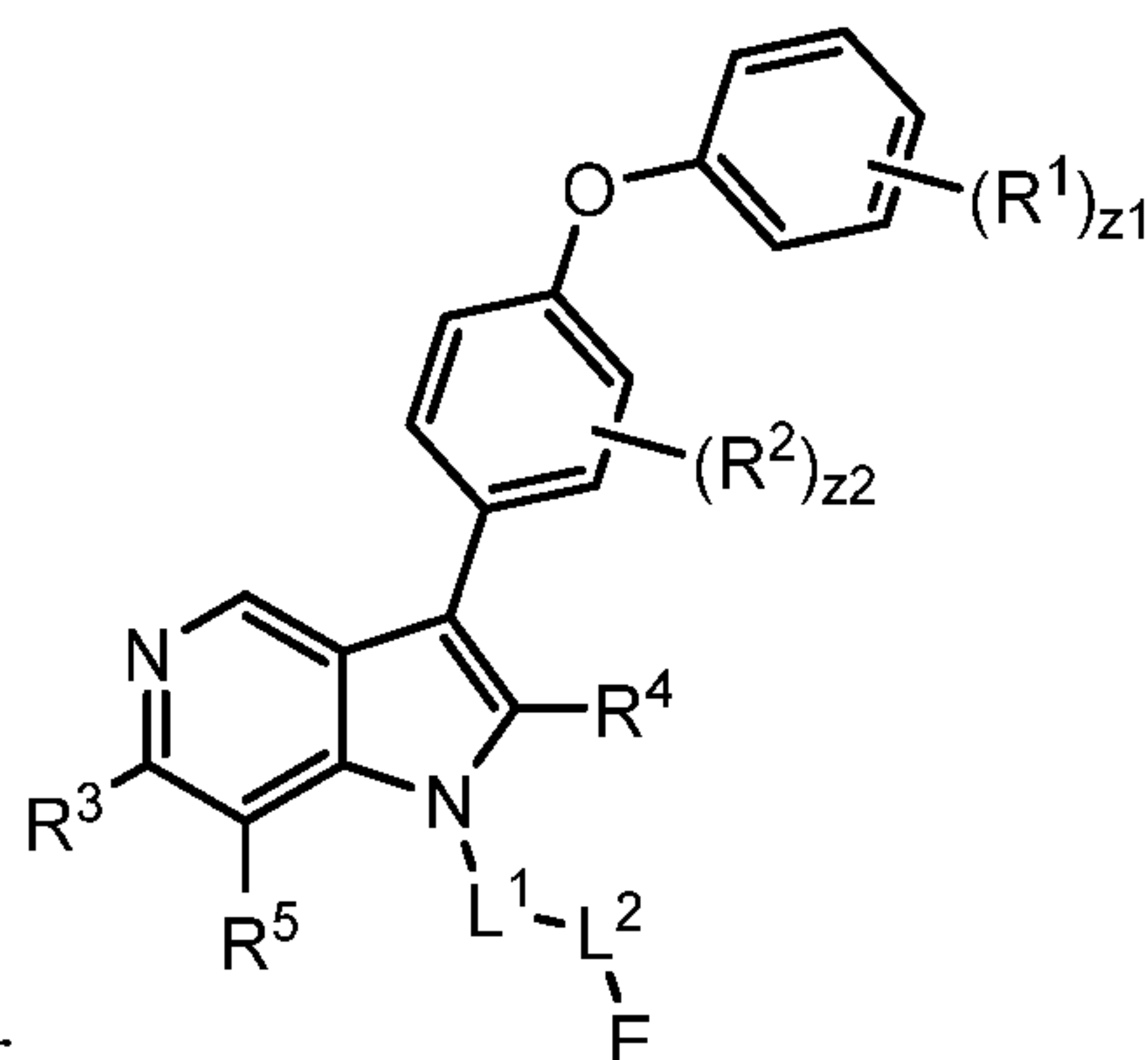
(IC),



(ID),

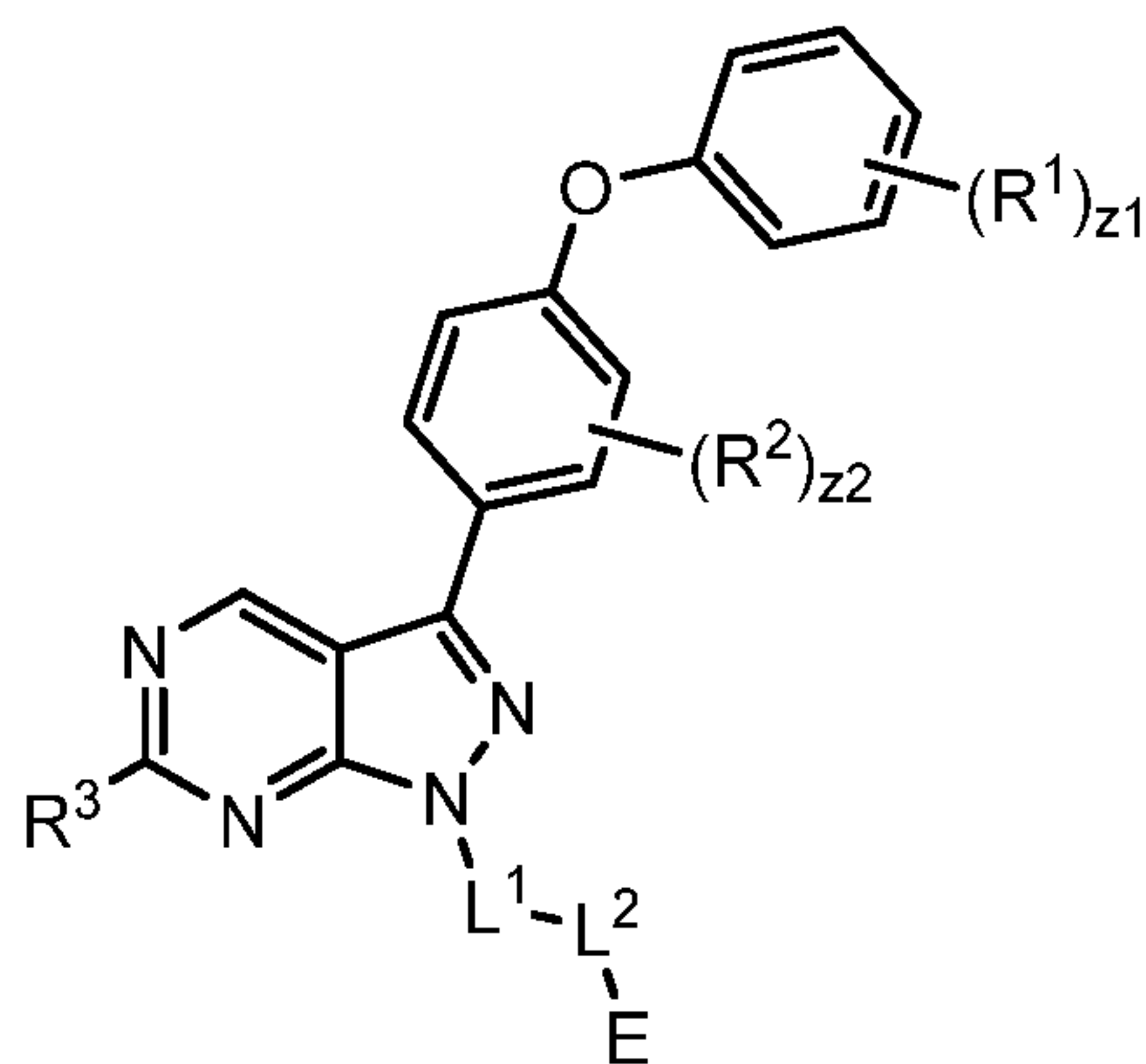


(IE), or



(IF).

4. The compound of claim 1 having the formula:



(IC).

5. The compound of claim 1, wherein R³ is hydrogen.

6. The compound of claim 1, wherein R³ is -NH₂.

7. The compound of claim 1, wherein R¹ is independently halogen, -CX¹₃, -CN, -OH, -NH₂, -COOH, -CONH₂, -NO₂, -SH, -OCX¹₃, -OCHX¹₂, -CHX¹₂, -CH₂X¹, substituted or unsubstituted C₁-C₈ alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl; two adjacent R¹ substituents may optionally be joined to form a substituted or unsubstituted C₃-C₈ cycloalkyl, substituted or unsubstituted 3 to 8 membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted 5 to 6 membered heteroaryl.

8. The compound of claim 1, wherein R^1 is independently halogen, $-CX^1_3$, $-CN$, unsubstituted C_1 - C_4 alkyl, or unsubstituted 2 to 4 membered heteroalkyl.

9. The compound of claim 1, wherein R^1 is independently halogen, $-CX^1_3$, $-CN$, unsubstituted methyl, unsubstituted ethyl, unsubstituted methoxy, or unsubstituted ethoxy.

10. The compound of claim 1, wherein z_1 is 0.

11. The compound of claim 1, wherein z_1 is 1.

12. The compound of claim 1, wherein R^2 is independently halogen, $-CX^2_3$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-OCX^2_3$, $-OCHX^2_2$, $-CHX^2_2$, $-CH_2X^2$, substituted or unsubstituted C_1 - C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted C_3 - C_8 cycloalkyl, substituted or unsubstituted 3 to 8 membered heterocycloalkyl, substituted or unsubstituted phenyl, or substituted or unsubstituted 5 to 6 membered heteroaryl.

13. The compound of claim 1, wherein R^2 is independently halogen, $-CX^2_3$, $-CN$, unsubstituted C_1 - C_4 alkyl, or unsubstituted 2 to 4 membered heteroalkyl.

14. The compound of claim 1, wherein R^2 is independently halogen, $-CX^2_3$, $-CN$, unsubstituted methyl, unsubstituted ethyl, unsubstituted methoxy, or unsubstituted ethoxy.

15. The compound of claim 1, wherein z_2 is 0.

16. The compound of claim 1, wherein z_2 is 1.

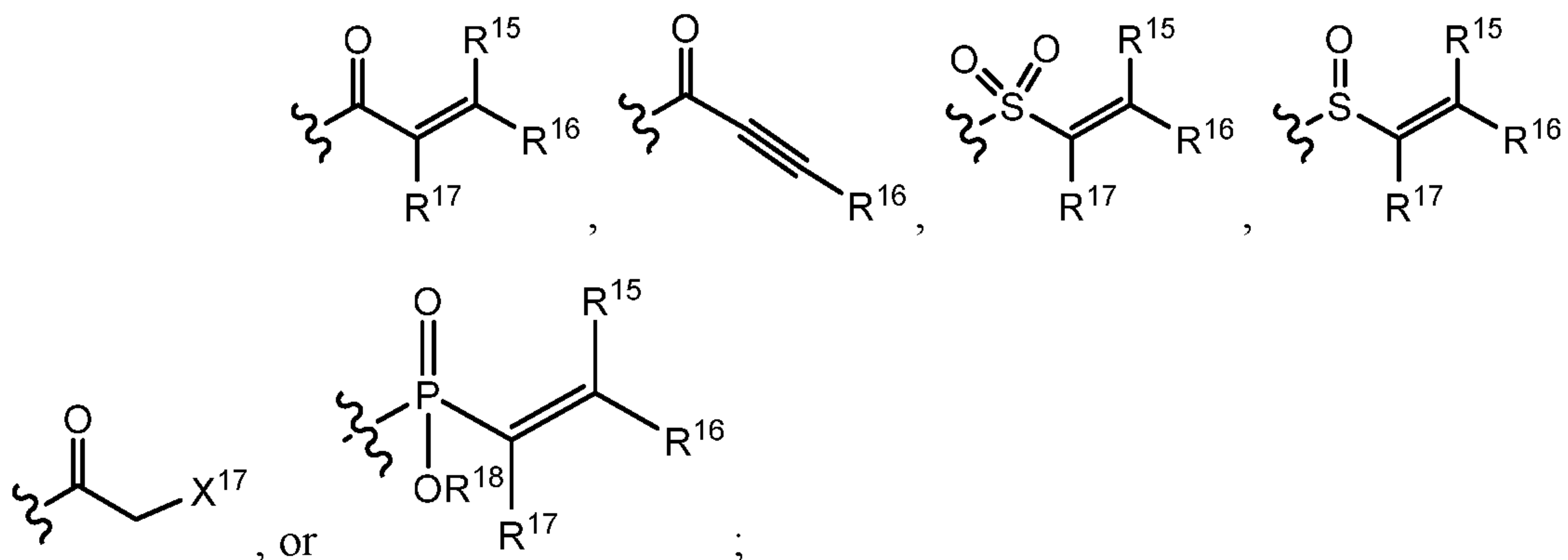
17. The compound of claim 1, wherein L^1 is a bond, $-S(O)_2-$, $-S(O)_2-Ph-$, substituted or unsubstituted C_1 - C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, substituted or unsubstituted C_3 - C_8 cycloalkylene, substituted or unsubstituted 3 to 8 membered heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5 to 6 membered heteroarylene.

- 1 18. The compound of claim 1, wherein L^1 is a bond.
- 1 19. The compound of claim 1, wherein L^1 is a substituted or unsubstituted
2 C_1 - C_6 alkylene, substituted or unsubstituted 2 to 6 membered heteroalkylene, substituted or
3 unsubstituted C_3 - C_6 cycloalkylene, substituted or unsubstituted 3 to 6 membered
4 heterocycloalkylene, substituted or unsubstituted phenylene, or substituted or unsubstituted 5
5 to 6 membered heteroarylene.
- 1 20. The compound of claim 1, wherein L^1 is an unsubstituted C_1 - C_6
2 alkylene, unsubstituted 2 to 6 membered heteroalkylene, or unsubstituted C_3 - C_6
3 cycloalkylene.
- 1 21. The compound of claim 1, wherein L^1 is an unsubstituted methylene.
- 1 22. The compound of one of claims 1 to 21, wherein L^2 is $-NR^7-$ or
2 substituted or unsubstituted heterocycloalkylene comprising a ring nitrogen bonded directly
3 to E.
- 1 23. The compound of claim 1, wherein L^2 is $-NR^7-$ or substituted or
2 unsubstituted spirocyclic heterocycloalkylene comprising a ring nitrogen bonded directly to
3 E.
- 1 24. The compound of claim 1, wherein L^2 is $-NR^7-$.
- 1 25. The compound of claim 24, wherein R^7 is hydrogen, substituted or
2 unsubstituted C_1 - C_6 alkyl, or substituted or unsubstituted 2 to 6 membered heteroalkyl.
- 1 26. The compound of claim 24, wherein R^7 is hydrogen or unsubstituted
2 C_1 - C_3 alkyl.
- 1 27. The compound of claim 24, wherein R^7 is hydrogen.
- 1 28. The compound of claim 1, wherein L^2 is substituted or unsubstituted
2 heterocycloalkylene.
- 1 29. The compound of claim 1, wherein L^2 is substituted or unsubstituted
2 piperidinylene or substituted or unsubstituted pyrrolindinylene.

30. The compound of claim 1, wherein L^2 is unsubstituted piperidinylene or unsubstituted pyrrolindinylene.

31. The compound of claim 1, wherein E is a covalent cysteine modifier moiety.

32. The compound of claim 1, wherein E is:



R^{15} is independently hydrogen, halogen, CX^{15}_3 , $-CHX^{15}_2$, $-CH_2X^{15}$, $-CN$, $-SO_{n15}R^{15D}$, $-SO_{v15}NR^{15A}R^{15B}$, $-NHN R^{15A}R^{15B}$, $-ONR^{15A}R^{15B}$, $-NHC(=O)NHN R^{15A}R^{15B}$, $-NHC(O)NR^{15A}R^{15B}$, $-N(O)_{m15}$, $-NR^{15A}R^{15B}$, $-C(O)R^{15C}$, $-C(O)-OR^{15C}$, $-C(O)NR^{15A}R^{15B}$, $-OR^{15D}$, $-NR^{15A}SO_2R^{15D}$, $-NR^{15A}C(O)R^{15C}$, $-NR^{15A}C(O)OR^{15C}$, $-NR^{15A}OR^{15C}$, $-OCX^{15}_3$, $-OCHX^{15}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

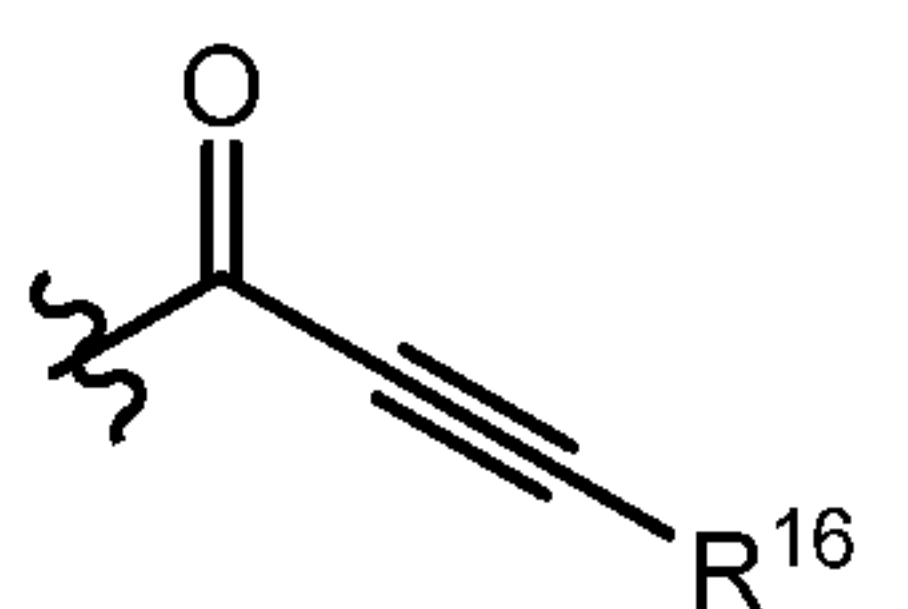
R^{16} is independently hydrogen, halogen, CX^{16}_3 , $-CHX^{16}_2$, $-CH_2X^{16}$, $-CN$, $-SO_{n16}R^{16D}$, $-SO_{v16}NR^{16A}R^{16B}$, $-NHN R^{16A}R^{16B}$, $-ONR^{16A}R^{16B}$, $-NHC(=O)NHN R^{16A}R^{16B}$, $-NHC(O)NR^{16A}R^{16B}$, $-N(O)_{m16}$, $-NR^{16A}R^{16B}$, $-C(O)R^{16C}$, $-C(O)-OR^{16C}$, $-C(O)NR^{16A}R^{16B}$, $-OR^{16D}$, $-NR^{16A}SO_2R^{16D}$, $-NR^{16A}C(O)R^{16C}$, $-NR^{16A}C(O)OR^{16C}$, $-NR^{16A}OR^{16C}$, $-OCX^{16}_3$, $-OCHX^{16}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{17} is independently hydrogen, halogen, CX^{17}_3 , $-CHX^{17}_2$, $-CH_2X^{17}$, $-CN$, $-SO_{n17}R^{17D}$, $-SO_{v17}NR^{17A}R^{17B}$, $-NHN R^{17A}R^{17B}$, $-ONR^{17A}R^{17B}$, $-NHC(=O)NHN R^{17A}R^{17B}$, $-NHC(O)NR^{17A}R^{17B}$, $-N(O)_{m17}$, $-NR^{17A}R^{17B}$, $-C(O)R^{17C}$, $-C(O)-OR^{17C}$, $-C(O)NR^{17A}R^{17B}$, $-OR^{17D}$, $-NR^{17A}SO_2R^{17D}$, $-NR^{17A}C(O)R^{17C}$, -

24 $\text{NR}^{17\text{A}}\text{C}(\text{O})\text{OR}^{17\text{C}}$, $-\text{NR}^{17\text{A}}\text{OR}^{17\text{C}}$, $-\text{OCX}^{17}_3$,
 25 $-\text{OCHX}^{17}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl,
 26 substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl,
 27 substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;
 28 R^{18} is independently hydrogen, $-\text{CX}^{18}_3$, $-\text{CHX}^{18}_2$, -
 29 CH_2X^{18} , $-\text{C}(\text{O})\text{R}^{18\text{C}}$, $-\text{C}(\text{O})\text{OR}^{18\text{C}}$, $-\text{C}(\text{O})\text{NR}^{18\text{A}}\text{R}^{18\text{B}}$, substituted or unsubstituted alkyl,
 30 substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or
 31 unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 32 heteroaryl;
 33 $\text{R}^{15\text{A}}$, $\text{R}^{15\text{B}}$, $\text{R}^{15\text{C}}$, $\text{R}^{15\text{D}}$, $\text{R}^{16\text{A}}$, $\text{R}^{16\text{B}}$, $\text{R}^{16\text{C}}$, $\text{R}^{16\text{D}}$, $\text{R}^{17\text{A}}$, $\text{R}^{17\text{B}}$, $\text{R}^{17\text{C}}$, $\text{R}^{17\text{D}}$, $\text{R}^{18\text{A}}$,
 34 $\text{R}^{18\text{B}}$, $\text{R}^{18\text{C}}$, $\text{R}^{18\text{D}}$, are independently hydrogen, $-\text{CX}_3$, $-\text{CN}$, $-\text{COOH}$, $-\text{CONH}_2$, $-\text{CHX}_2$, $-\text{CH}_2\text{X}$,
 35 substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or
 36 unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or
 37 unsubstituted aryl, or substituted or unsubstituted heteroaryl; $\text{R}^{15\text{A}}$ and $\text{R}^{15\text{B}}$ substituents
 38 bonded to the same nitrogen atom may optionally be joined to form a substituted or
 39 unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; $\text{R}^{16\text{A}}$ and $\text{R}^{16\text{B}}$
 40 substituents bonded to the same nitrogen atom may optionally be joined to form a substituted
 41 or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; $\text{R}^{17\text{A}}$ and $\text{R}^{17\text{B}}$
 42 substituents bonded to the same nitrogen atom may optionally be joined to form a substituted
 43 or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; $\text{R}^{18\text{A}}$ and $\text{R}^{18\text{B}}$
 44 substituents bonded to the same nitrogen atom may optionally be joined to form a substituted
 45 or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;
 46 each X, X^{15} , X^{16} , X^{17} and X^{18} is independently $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, or $-\text{I}$;
 47 n_{15} , n_{16} , n_{17} , v_{15} , v_{16} , and v_{17} , are independently an integer from 0 to 4;
 48 and
 49 m_{15} , m_{16} , and m_{17} are independently an integer from 1 to 2.

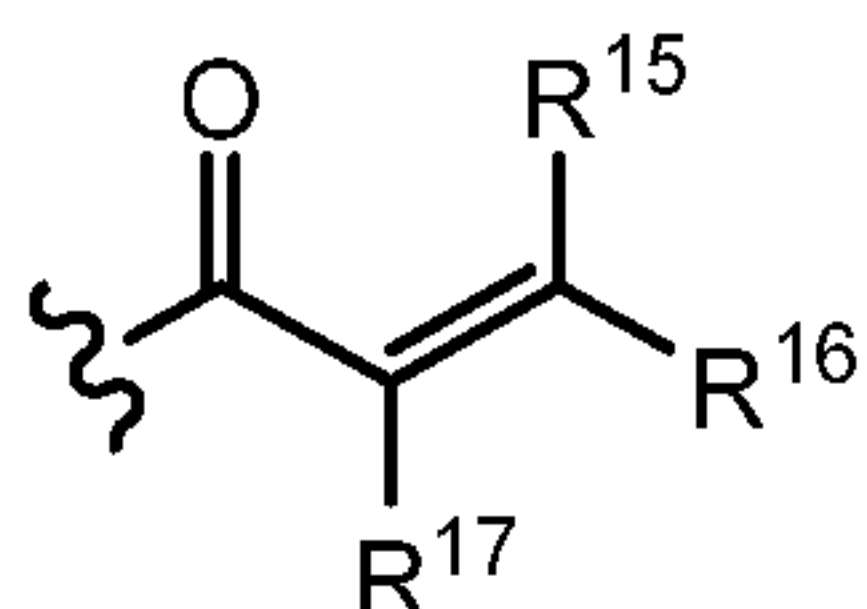
1 33. The compound of claim 32, wherein R^{15} , R^{16} , R^{17} , and R^{18} are
 2 hydrogen.

1 34. The compound of claim 32, wherein E is:

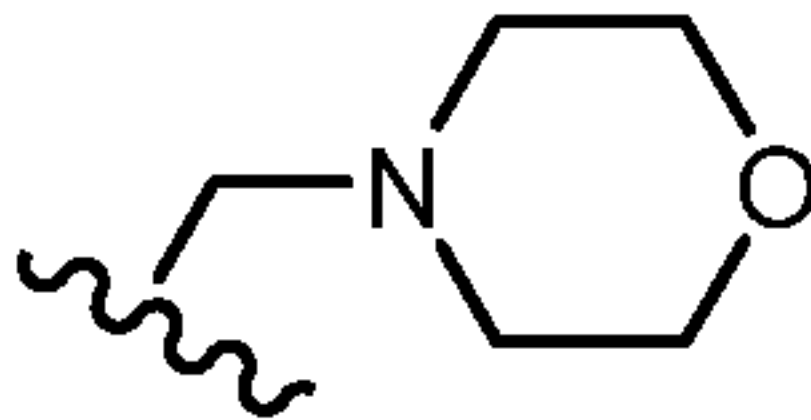


35. The compound of claim 34, wherein R^{16} is hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl.

36. The compound of claim 32, wherein E is:

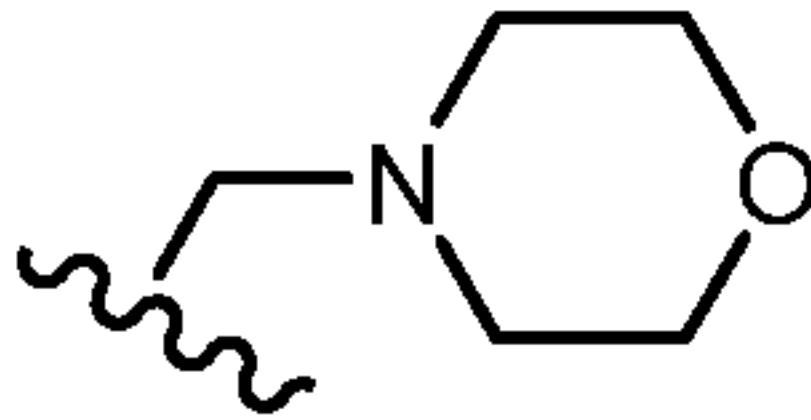


37. The compound of claim 36, wherein R^{15} is hydrogen;

R^{16} is hydrogen, $-CH_3$, $-CH_2NR^{16A}R^{16B}$, or  ;
 R^{17} is hydrogen; and
 R^{16A} and R^{16B} are independently hydrogen or unsubstituted alkyl.

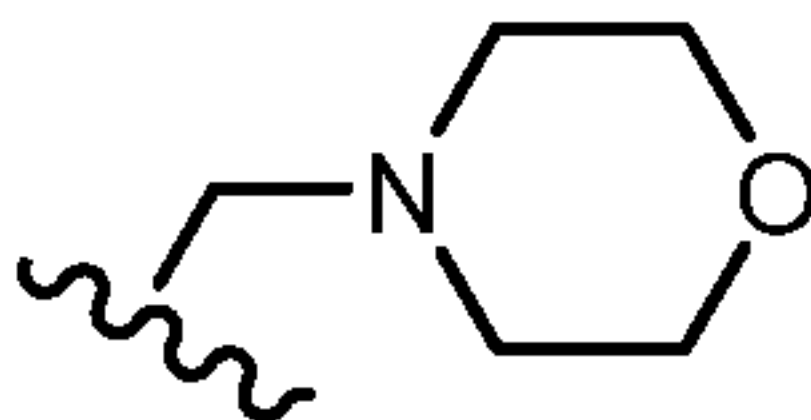
38. The compound of claim 37, wherein R^{16A} and R^{16B} are independently unsubstituted methyl.

39. The compound of claim 36, wherein R^{15} is hydrogen;
 R^{16} is hydrogen;

R^{17} is hydrogen, $-CH_3$, $-CH_2NR^{17A}R^{17B}$, or  ; and
 R^{17A} and R^{17B} are independently hydrogen or unsubstituted alkyl.

40. The compound of claim 39, wherein R^{17A} and R^{17B} are independently unsubstituted methyl.

41. The compound of claim 36, wherein

R^{15} is hydrogen, $-CH_3$, $-CH_2NR^{15A}R^{15B}$, or  ;
 R^{16} is hydrogen;
 R^{17} is hydrogen; and

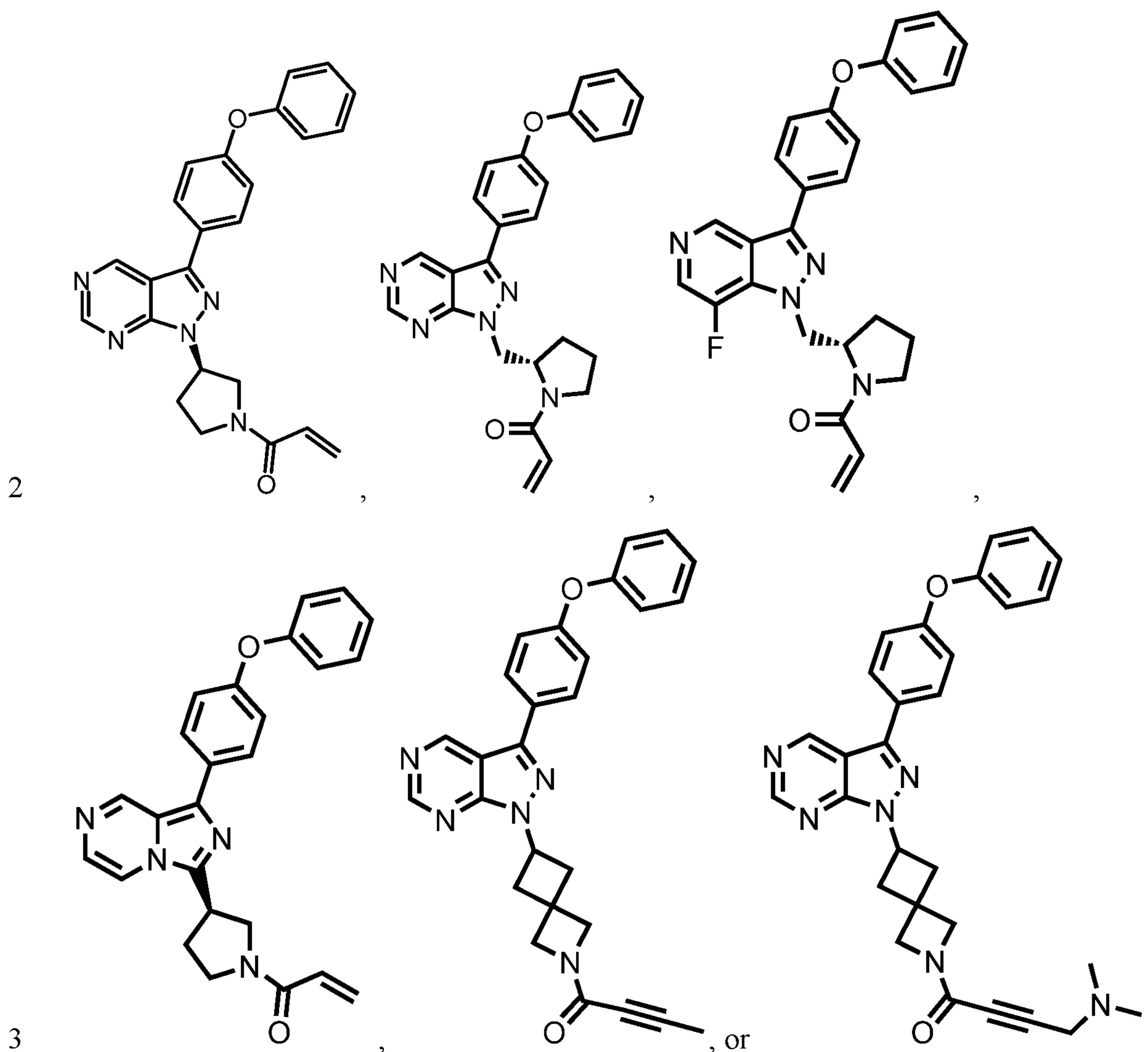
5 R^{15A} and R^{15B} are independently hydrogen or unsubstituted alkyl.

1 42. The compound of claim 41, wherein R^{15A} and R^{15B} are independently
2 unsubstituted methyl.

1 43. The compound of claim 1, wherein R^4 is hydrogen, substituted or
2 unsubstituted C_1 - C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl.

1 44. The compound of claim 1, wherein R^5 is hydrogen, substituted or
2 unsubstituted C_1 - C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl.

1 45. The compound of claim 1, wherein the compound has the formula:



1 46. The compound of one of claims 1 to 45, wherein the compound is
2 capable of entering the central nervous system of a patient following administration outside
3 of the central nervous system.

1 47. A pharmaceutical composition comprising the compound of any one of
2 claims 1 to 46 and a pharmaceutically acceptable excipient.

1 48. A method of inhibiting Bruton's tyrosine kinase activity, said method
2 comprising: contacting the Bruton's tyrosine kinase with an effective amount of a compound
3 of one of claims 1 to 46.

1 49. A method of treating cancer, said method comprising administering to
2 a subject in need thereof an effective amount of a compound of one of claims 1 to 46.

1 50. A Bruton's tyrosine kinase protein covalently bonded to a compound of
2 one of claims 1 to 46.

1 51. The Bruton's tyrosine kinase protein of claim 50, wherein the
2 compound is bonded to a cysteine residue of the protein.

1 52. The Bruton's tyrosine kinase protein of claim 50, covalently bonded to
2 a portion of a compound of one of claims 1 to 46.

1 53. The Bruton's tyrosine kinase protein of claim 50, irreversibly
2 covalently bonded to a portion of a compound of one of claims 1 to 46.

1 54. The Bruton's tyrosine kinase protein of claim 50, wherein the Bruton's
2 tyrosine kinase protein is in the central nervous system of a subject.

1 55. The Bruton's tyrosine kinase protein of claim 50, wherein the Bruton's
2 tyrosine kinase protein is in the brain of a subject.

1 56. A method of treating an inflammatory disease, said method comprising
2 administering to a subject in need thereof an effective amount of a compound of one of
3 claims 1 to 46.

1 57. A method of treating stroke including administering to a subject in
2 need thereof an effective amount of a compound of one of claims 1 to 46.

1 58. A method of treating an autoimmune disease, said method comprising
2 administering to a subject in need thereof an effective amount of a compound of one of
3 claims 1 to 46.

- 1 59. A method of treating a disease associated with aberrant Bruton's
2 Tyrosine Kinase activity including administering to a subject in need thereof an effective
3 amount of a compound of one of claims 1 to 46.