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(54) Title: ANTHELMINTIC COMPOUNDS COMPRISING A THIENOPYRIDINE STRUCTURE

(57) Abstract: The present invention relates to new anthelmintic compounds. These compounds can for example be used in the treatment of the kind of worm disease caused by helminths such as *Dirofilaria*, in particular *Dirofilaria immitis*.

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Anthelmintic compounds comprising a thienopyridine structure

The present invention relates to new anthelmintic compounds. These compounds can for example be used in the treatment of the kind of worm disease caused by helminths such as *Dirofilaria*, in particular *Dirofilaria immitis*.

5 Background

Several severe animal diseases are caused by helminths, wherein the helminths can be categorized in the following groups of a) cestodes: e.g. *Anaplocephala* spp.; *Dipylidium* spp.; *Diphyllobothrium* spp.; *Echinococcus* spp.; *Moniezia* spp.; *Taenia* spp.; b) trematodes e.g. *Dicrocoelium* spp.; *Fasciola* spp.; *Paramphistomum* spp.; *Schistosoma* spp.; or c) nematodes, e.g.
10 *Acanthocheilonema* spp.; *Ancylostoma* spp.; *Aneator* spp.; *Ascaridia* spp.; *Ascaris* spp.; *Brugia* spp.; *Bunostomum* spp.; *Capillaria* spp.; *Chabertia* spp.; *Cooperia* spp.; *Cyathostomum* spp.; *Cylicocyclus* spp.; *Cylicodontophorus* spp.; *Cylicostephanus* spp.; *Craterostomum* spp.; *Dictyocaulus* spp.; *Dipetalonema* spp.; *Dirofilaria* spp.; *Dracunculus* spp.; *Enterobius* spp.; *Filaroides* spp.; *Habronema* spp.; *Haemonchus* spp.; *Heterakis* spp.; *Hyostrongylus* spp.;
15 *Metastrongylus* spp.; *Meullerius* spp. *Necator* spp.; *Nematodirus* spp.; *Nippostrongylus* spp.; *Oesophagostomum* spp.; *Onchocerca* spp.; Onchocercidae spp.; *Ostertagia* spp.; *Oxyuris* spp.; *Parascaris* spp.; *Stephanurus* spp.; *Strongylus* spp.; *Syngamus* spp.; *Toxocara* spp.; *Strongyloides* spp.; *Teladorsagia* spp.; *Toxascaris* spp.; *Trichinella* spp.; *Trichuris* spp.; *Trichostrongylus* spp.; *Triodontophorous* spp.; *Uncinaria* spp., and/or *Wuchereria* spp.

20 The above helminths cause helminthiasis also known as worm infection. These helminths often live in the gastrointestinal tract of their host, but they may also burrow into other organs, where they induce physiological damage. For example, *Ascaridia* spp. are reported to cause from infections of the small intestine to partial or even total obstruction of the gastrointestinal tract of the affected animal, in particular feather animals such as birds. Further, another helminth,
25 *Haemonchus* spp. are known to affect animals like sheep and goats, wherein such infestation often results in the attachment in the abomasal mucosa for sucking blood from the host. Thus, the affected animal can get anaemic and short of breath. Even further, *Oesophagostomum* spp. are known to cause a nodule formation in the intestines of its infected hosts, which may result in dysentery.

30 Furthermore, heartworm disease, also known as cardiovascular dirofilariasis, is a serious and mostly fatal disease that may affect inner organs such as lung and heart in pets and certain mammals. The disease is caused by parasitic nematodes, *Dirofilaria immitis*, which in the adult

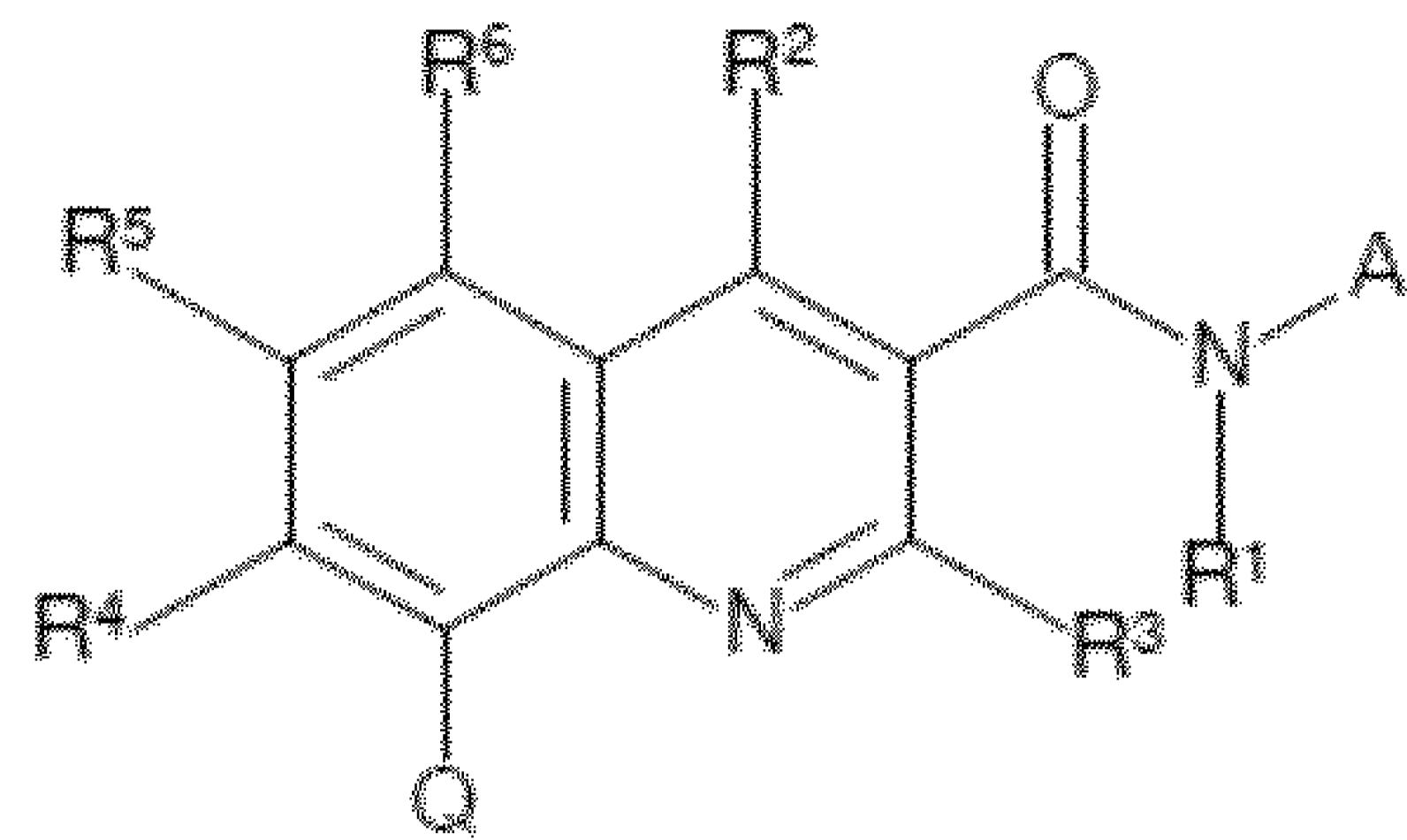
state can have a length up to about 30 centimetres and a thickness of about 1 millimetre. These nematodes live in the heart, the lung and associated blood vessels causing severe lung disease, heart failure and damage to other inner organs such as the liver and kidneys. Thus, heartworm infection may result in complication for the host, typically culminating in the host's death.

- 5 The heartworm disease is known to affect pets, in particular dogs, which are considered as the definitive host. However, also cats, ferrets, wolves, coyotes, jackals, foxes, bears, sea lions and in very rare cases even humans (zoonosis) may be affected by heartworms.

Heartworms have to go through different stages before they become adults residing in the host animal. The mosquito plays an essential role in the heartworm's life cycle since it is required as
10 an intermediate host. Adult female heartworms living in an infected host give birth to larvae called microfilaria, which can circulate in the bloodstream for as long as two years and are ingested by bloodsucking mosquitos. When a mosquito bites and takes up blood from such an infected host, it picks up said microfilaria, which start to develop in the mosquito such that the first and second larval stages (L₁) and (L₂) of the heartworm development occurs within the body of a mosquito.
15 Once said larvae have matured into the third larval stage (L₃), the infective larval stage, and the mosquito locates and bites a host, these infective larvae are deposited onto the surface of the host's skin and enter the new host through the mosquito's bite such that they are under the skin at the site of the bite wound. After a short period of about 2 weeks for further growth, they develop into the fourth larval stage (L₄) and migrate to the muscles of the chest and abdomen. 45 to 60 days after
20 infection the larvae become immature adults (fifth larval stage; L₅,) and between 75 and 120 days after infection (bite of the mosquito), these immature heartworms then enter the bloodstream and are carried to the heart and the pulmonary system, where they significantly increase in size over the next about three months. By seven months after the infection (bite of the mosquito) the adult worms have mated, and the females begin giving birth to the above-mentioned microfilaria. The
25 matured heartworms can live for up to about 7 years in dogs and up to about 3 years in cats. Due to the longevity of these worms, each mosquito season can lead to an increasing number of heartworms in an infected pet.

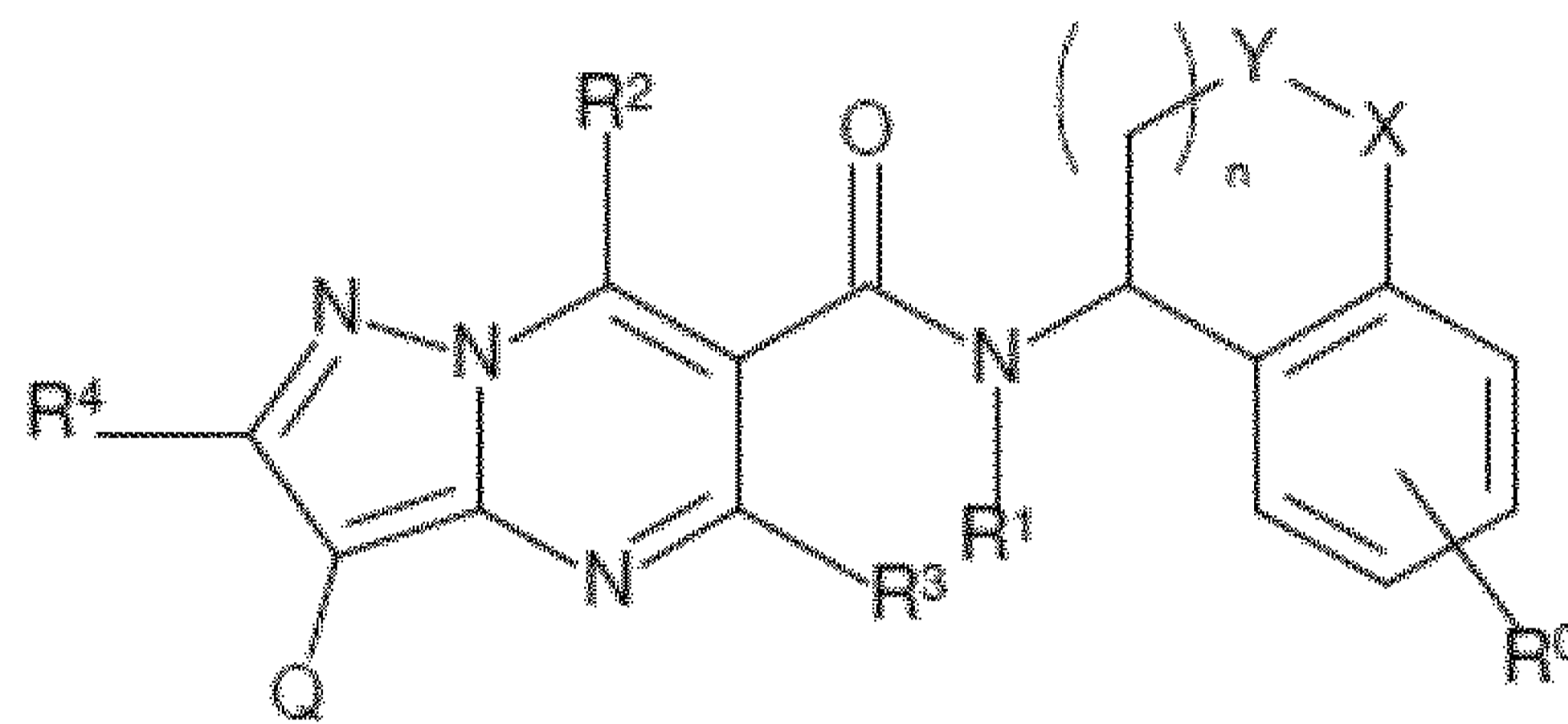
Due to the extensive use of anthelmintic compounds, a highly resistant worm population is reported to have occurred. The occurrence of this resistance against known anthelmintics is
30 considered to cause growing problems for a successful treatment of the above-mentioned disease(s).

WO 2018/087036 A1 and WO 2019/025341 A1 both disclose a compound considered as anthelmintic, namely a quinoline 3-carboxamide derivative of the following structure



wherein residues R¹, R², R³, R⁴, R⁵, R⁶, A and Q are defined correspondingly.

Further, WO 2017/178416 discloses a compound considered as anthelmintic, namely a pyrazolopyrimidine derivative of the following structure



5 wherein residues R⁰, R¹, R², R³, R⁴, Q, X and Y as well as variable n are defined correspondingly.

The molecules are considered as modulators of the calcium-activated potassium channel slo-1 of nematodes, wherein slo-1 can be regarded as the helminth's ortholog of the human KCa1.1 channel (potassium calcium-activated channel subfamily M alpha 1), which is encoded by the KCNMA1 gene (KCa1.1 and KCNMA1 are often used synonymously). Slo-1 exhibits calcium-activated potassium channel activity and voltage-gated potassium channel activity. Slo-1 channels play an important role in the neuromuscular system as well as in secretory cells among others. Thus, slo-1 modulators are reported to be involved in several processes including behavioural response to ethanol, locomotion and pharyngeal pumping. More particularly they disrupt neuromuscular transmission causing a flaccid paralysis and also affect feeding and egg-laying. Further, they slow the development of the larvae and the adults of the corresponding helminth.

Nevertheless, especially in view of the occurrence of resistance to known anthelmintic compounds there is still an urgent need for new active pharmaceutical ingredients that are able to address infections by helminths.

20 Hence, it is an object of the present invention to overcome one or more of the drawbacks of the prior art.

It is an object to provide new anthelmintic compounds which can be used to address infections in mammals, in particular in pets such as cats and dogs, especially in dogs. In particular, it is an object to provide new anthelmintic compounds which can be used to address infections in mammals by

parasitic helminths such *Ostertagia ostertagi*, *Cooperia oncophora*, *Cooperia punctata*, *Trichostrongylus axei*, *Haemonchus placei*, *Haemonchus contortus*, *Nematodirus helvetianus*, *Nematodirus spathiger*, *Trichostrongylus colubriformis*, *Trichostrongylus circumcincta*, *Oesophagostomum venulosum*, *Chabertia ovina*, *Dictyocaulus viviparous*, *Dictyocaulus filaria*,
 5 *Dirofilaria immitis*, *Dirofilaria repens*; b) Trematodes: *Fasciola hepatica*, *Fascioloides magna*, *Dicrocoelium dentriticum*, *Paramphistomum cervi*, c) Cestodes: *Monezia expansa*, in particular infections by *Dirofilaria immitis* (heartworm).

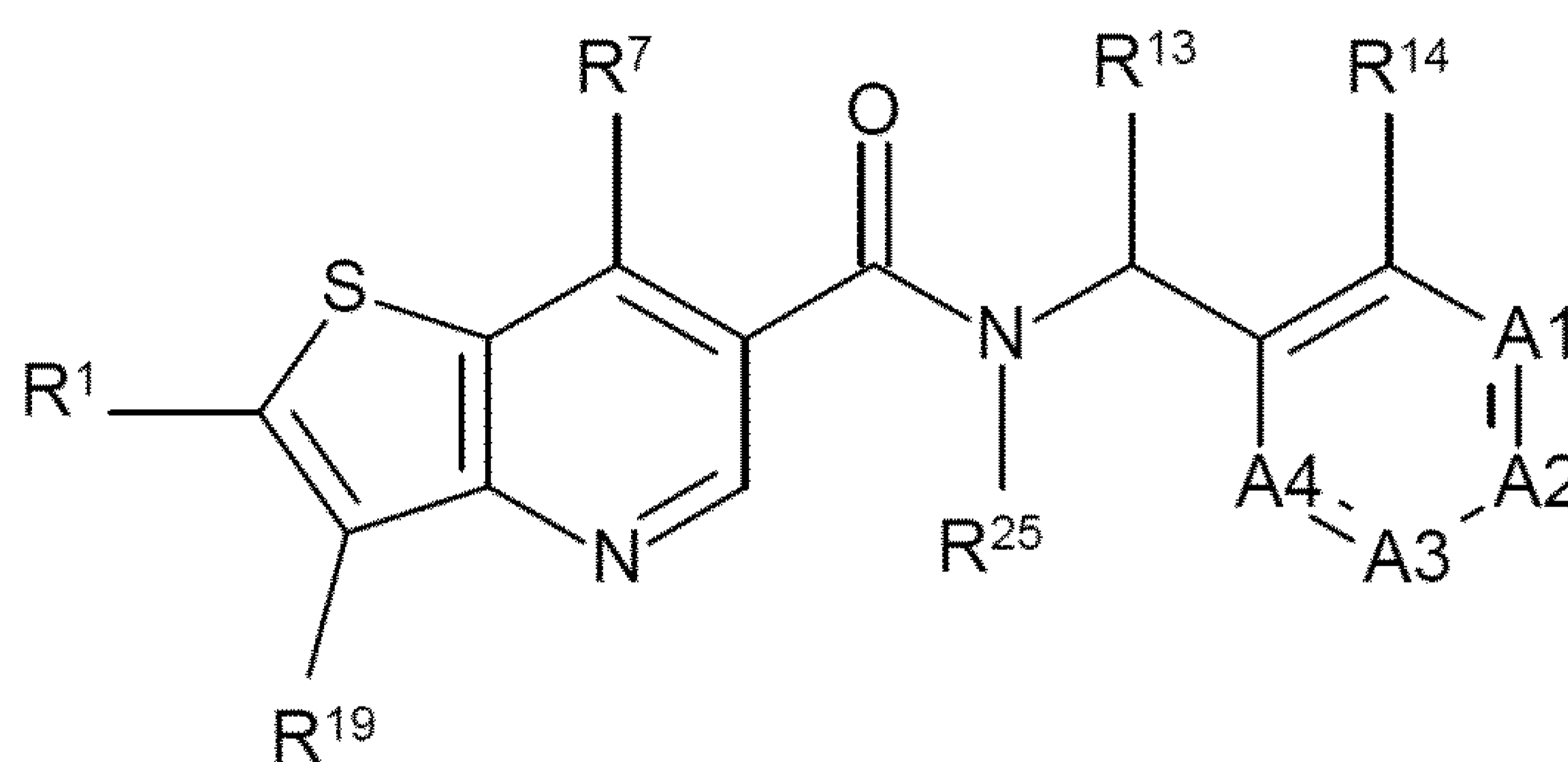
Another object is to provide new anthelmintic compounds which can be used to address infections in mammals, wherein these compounds are compatible with standard antiparasitic treatments in
 10 pets, in particular in cats and dogs, especially in dogs. In particular, it is an object to provide new anthelmintic compounds which can be used to address infections in pets such as cats and dogs and which can be administered orally or topically.

More specifically, it is an object to provide new anthelmintic compounds which can be used to address infections in mammals by parasitic helminths, in particular infections by *Dirofilaria immitis* (heartworm), but does not negatively affect the host by undesired side-effects.
 15

Moreover, it is an object that said new anthelmintic compounds can be used in different treatment schedules, in particular in monthly or longer treatment schedules.

Summary of the invention

Surprisingly it was found that at least one of the objects can be met by providing a compound
 20 according to Formula (I)



Formula (I)

wherein

R¹ is independently selected from the group consisting of

25 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto,

halogen, cyano, nitro, hydroxy, mercapto, NR^2R^3 , COOH , C(=O)OR^4 , SR^4 , SOR^4 , SO_2R^4 , $\text{SO}_2\text{NR}^5\text{R}^6$ and $\text{C(=O)NR}^5\text{R}^6$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy or C_{1-6} -alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, C_{1-6} -alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, $\text{NR}^{2'}\text{R}^{3'}$, $\text{C(=O)OR}^{4'}$, $\text{SR}^{4'}$, $\text{SOR}^{4'}$, $\text{SO}_2\text{R}^{4'}$, $\text{SO}_2\text{NR}^{5'}\text{R}^{6'}$ and $\text{C(=O)NR}^{5'}\text{R}^{6'}$,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy- C_{1-6} -alkyl, C_{1-6} -alkyl substituted with C_{3-10} -cycloalkyl, C_{1-6} -alkyl substituted with 5- to 10- membered heterocyclyl, C_{1-6} -alkyl substituted with C_{6-10} -aryl and C_{1-6} -alkyl substituted with 5- to 10- membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10-membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy- C_{1-6} -alkyl, C_{1-6} -alkyl substituted with C_{3-10} -cycloalkyl, C_{1-6} -alkyl substituted with 5- to 10- membered heterocyclyl, C_{1-6} -alkyl substituted with C_{6-10} -aryl or C_{1-6} -alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, $\text{NR}^{2''}\text{R}^{3''}$, $\text{C(=O)OR}^{4''}$, $\text{SR}^{4''}$, $\text{SOR}^{4''}$, $\text{SO}_2\text{R}^{4''}$, $\text{SO}_2\text{NR}^{5''}\text{R}^{6''}$ and $\text{C(=O)NR}^{5''}\text{R}^{6''}$,

R^4 , R^5 and R^6 are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{2'}$, $R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{6'}$ are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{2''}$, $R^{3''}$, $R^{4''}$, $R^{5''}$ and $R^{6''}$ are independently selected from hydrogen and C₁₋₆-alkyl,

R^7 is independently selected from the group consisting of

- 5 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 4- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR⁸R⁹, COOH, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰, SO₂NR¹¹R¹² and C(=O)NR¹¹R¹²,

10 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 4- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'}, SR^{10'}, SOR^{10'}, SO₂R^{10'}, SO₂NR^{11'}R^{12'} and C(=O)NR^{11'}R^{12'},

R^8 and R^9 are independently selected from the group consisting of

20 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl and C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

25 R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

30 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl or C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by

R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{8''}R^{9''}, C(=O)OR^{10''}, SR^{10''}, SOR^{10''}, SO₂R^{10''}, SO₂NR^{11''}R^{12''} and C(=O)NR^{11''}R^{12''},

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

10 R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

R¹³ is hydrogen or C₁₋₃ alkyl,

R¹⁴ is hydrogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, NR^{14'}R^{14''}, wherein R^{14'} and R^{14''} are independently C₁₋₃-alkyl or

15 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

20 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

25 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

R¹⁹ is independently selected from the group consisting of C₆₋₁₀-aryl and 5- to 10- membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR²⁰R²¹, C(=O)OR²², SR²², SOR²², SO₂R²², SO₂NR²³R²⁴ and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl, C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{20'}R^{21'}, C(=O)OR^{22'}, SR^{22'}, SOR^{22'}, SO₂R^{22'}, SO₂NR^{23'}R^{24'}, and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl,

R²⁵ is independently selected from hydrogen and C₁₋₆-alkyl,

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof.

In one embodiment of the invention and/or embodiments thereof, R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

5 wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

10 R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O,

15 wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{1-6} -alkoxy,

R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-6} -alkyl.

20 In one embodiment of the invention and/or embodiments thereof, R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy and halogen,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy and $NR^{2'}R^{3'}$,

wherein $R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-3} -alkyl.

In one embodiment of the invention and/or embodiments thereof, R^1 is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride, in particular hydrogen and methyl.

In one embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

5 hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4- to 10 membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

10 wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4- to 10 membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5- to 10 membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, NR^8R^9 , $C(=O)OR^{10}$, and $C(=O)NR^{11}R^{12}$,

R^8 and R^9 are independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5- to 10 membered heterocyclyl and 5- to 10 membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

20 wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5- to 10 membered heterocyclyl, and 5- to 10 membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, $NR^{8''}R^{9''}$, $C(=O)-OR^{10''}$ and $C(=O)NR^{11''}R^{12''}$;

R^{10} , R^{11} and R^{12} are independently selected from hydrogen and C_{1-6} -alkyl,

R^8 , R^9 , R^{10} , R^{11} and R^{12} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{8''}$, $R^{9''}$, $R^{10''}$, $R^{11''}$ and $R^{12''}$ are independently selected from hydrogen and C_{1-6} -alkyl.

In one embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

5 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, 5- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, and 5- to 10 membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, and 5- to 10 membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''},

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen or C₁₋₆-alkyl,

20 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₆-alkyl.

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₆-alkyl.

In one embodiment of the invention and/or embodiments thereof, R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

In one embodiment of the invention and/or embodiments thereof, R⁷ is independently selected from the group consisting of

10 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, hydroxyethylamino, 2-hydroxyethylmethylamino, methoxyethylamino, cyclopropylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl.

15 In one embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

20 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

25 A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl.

In one embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms
5 containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

10 A1 is CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is CR¹⁷, wherein R¹⁷ is hydrogen,

15 A4 is CR¹⁸, wherein R¹⁸ is hydrogen.

In one embodiment of the invention and/or embodiments thereof, none, one or two of residues A1, A2, A3 and A4 is N.

In one embodiment of the invention and/or embodiments thereof, R¹⁹ is independently selected from the group consisting of

20 C₆₋₁₀-aryl and 5- to 10- membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, C₃₋₁₀-cycloalkyl or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

10 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'}

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

In one embodiment of the invention and/or embodiments thereof, R¹⁹ is independently selected from the group consisting of

15 C₆₋₁₀-aryl and 5- to 10- membered heteroaryl

wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In one embodiment of the invention and/or embodiments thereof, R¹⁹ is C₆₋₁₀-aryl,

25 wherein the C₆₋₁₀-aryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, halogen, cyano and nitro, wherein each C₁₋₆-alkyl, is optionally substituted with one or more halogen.

In one embodiment of the invention and/or embodiments thereof, R¹⁹ is C₆₋₁₀-aryl,

wherein the C₆₋₁₀-aryl is phenyl substituted with one, two or three substituents independently selected from the group consisting of

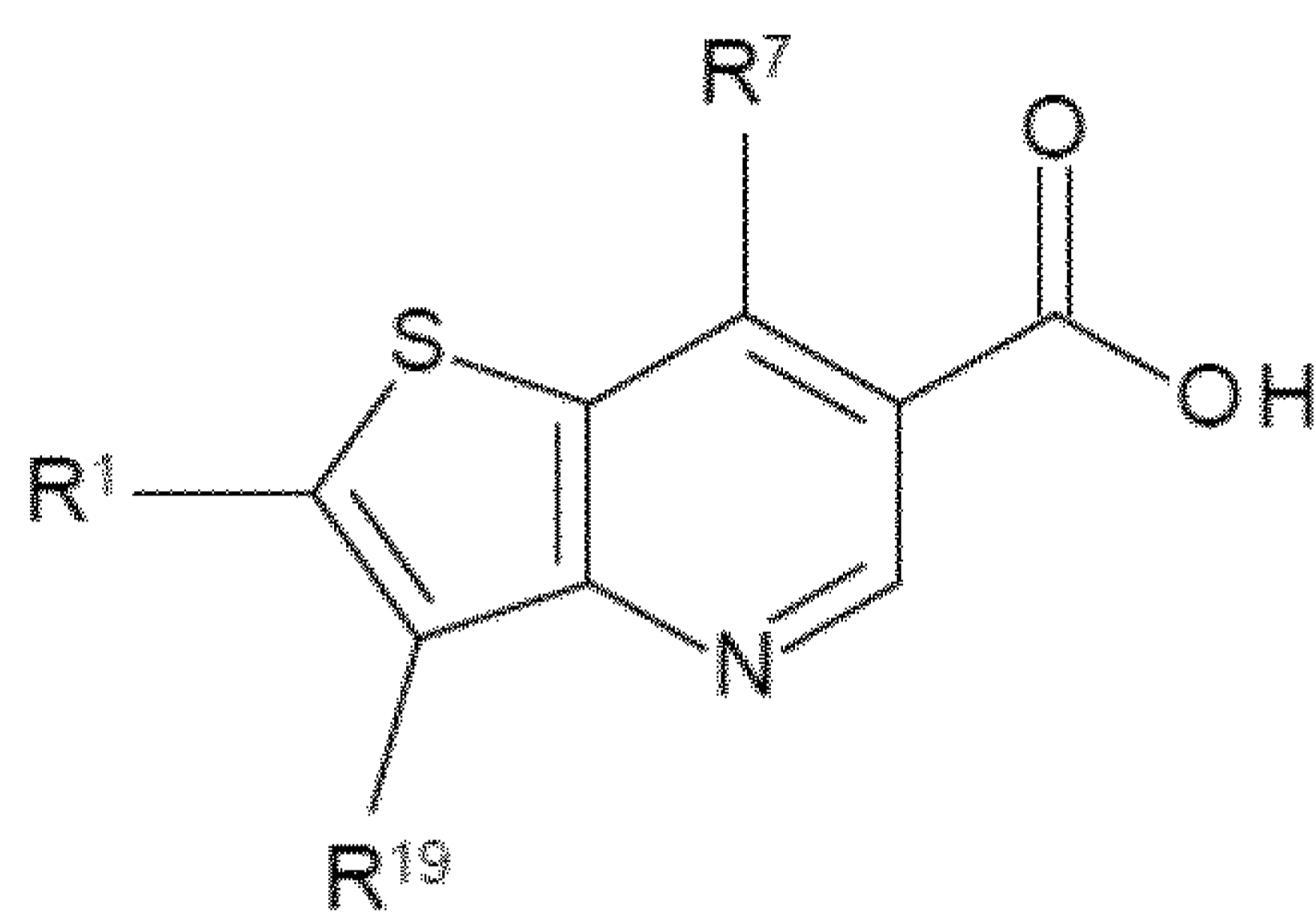
fluoride, chloride bromide, trifluoromethoxy and trifluoromethyl.

In one embodiment of the invention and/or embodiments thereof, R²⁵ is hydrogen.

- 5 In one embodiment of the invention and/or embodiments thereof the compound according to Formula (I) is present in form of the (*S*)-enantiomer.

Further, the present invention provides a process for preparing the compound according to Formula (I) comprising the step of

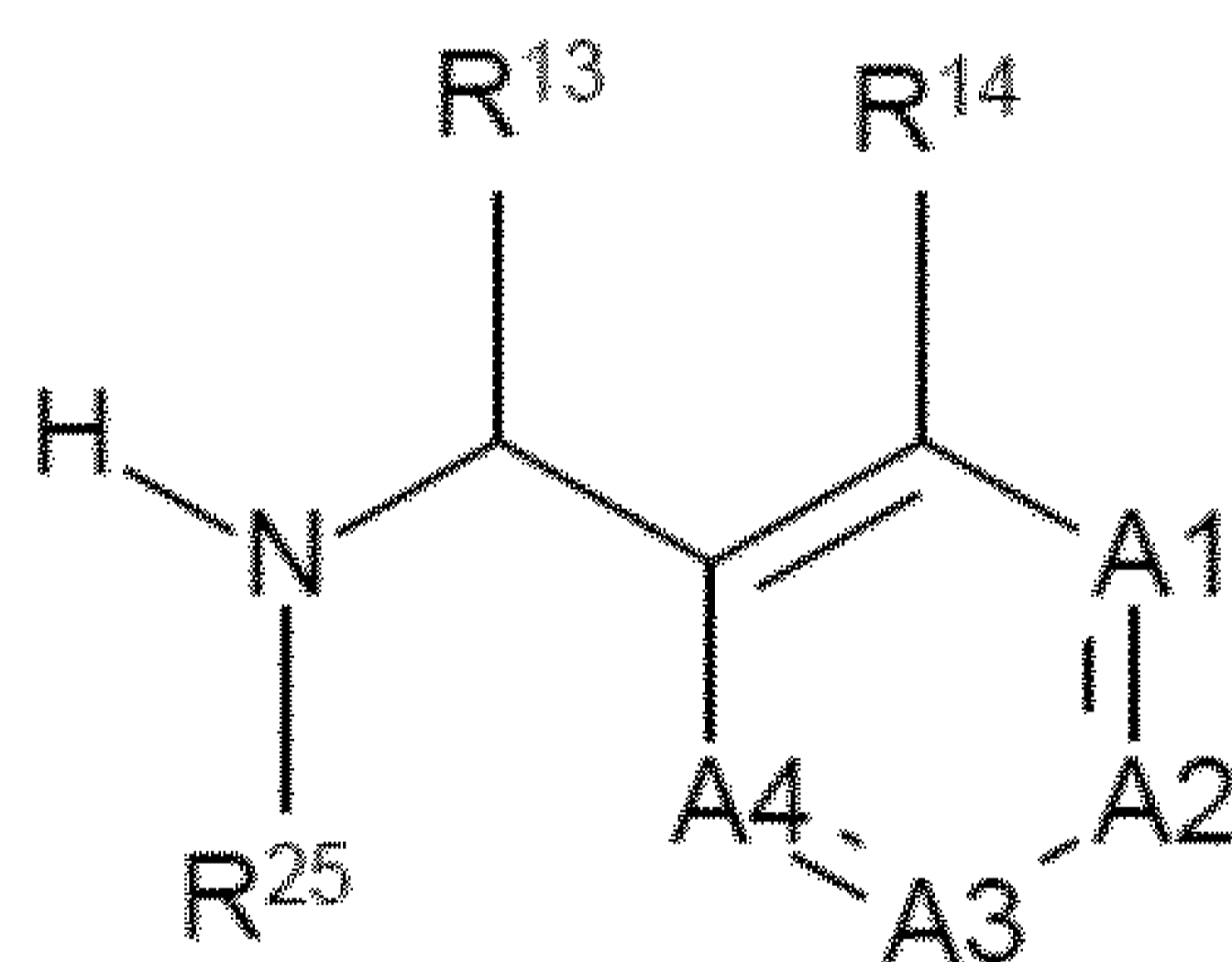
reacting a compound of Formula (A)



10

Formula (A)

with a compound of Formula (B)



Formula (B)

- 15 wherein R¹, R⁷, R¹³, R¹⁴, A1, A2, A3, A4, R¹⁹ and R²⁵ are defined as in any one of the embodiments as described herein,

to obtain the compound according to Formula (I).

Further, the present invention provides a veterinary composition comprising

- compound according to Formula (I) as defined as in any one of the embodiments as described herein, and

20

-one or more physiologically acceptable excipient(s).

In one embodiment of the invention and/or embodiments thereof, the one or more physiologically acceptable excipient(s) are selected from carriers, fillers, flavours, binders, antioxidants, buffers, sugar components, lubricants, surfactants, stabilizers, flow agents, disintegration agents and
5 preservatives and mixtures thereof.

Further, the present invention provides compounds according to Formula (I) as defined as in any one of the embodiments as described herein or the veterinary composition according to the invention for use as a medicament.

Further, the present invention provides compounds according to Formula (I) or the veterinary
10 composition according to the invention for use in the treatment of disorders/diseases caused by helminths.

In one embodiment of the invention and/or embodiments thereof, the disease is the heartworm disease.

In one embodiment of the invention and/or embodiments thereof, the helminths are *Dirofilaria*
15 *immitis*.

Detailed description

It was found that compounds according to Formula (I) or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof are useful in the treatment of helminthiasis such as disorders/diseases caused by helminths such as *Ascaridia galli*,
5 *Haemonchus contortus*, *Oesophagostomum dentatum* and by *Dirofilaria immitis*. In particular, the compounds according to the invention and/or any embodiments thereof are useful in the treatment of the heartworm disease. Optionally, the compounds according to the invention and/or any
embodiments thereof are useful in the treatment of the disorders/diseases caused by nematodes, in particular *Dirofilaria immitis*, wherein the disorder/disease caused by *Dirofilaria immitis* is the
10 heartworm disease.

Advantageously the compounds according to the invention and/or any embodiments thereof are effective against helminth such as *Dirofilaria immitis*, but not effective against bacteria that are especially relevant in the mammal's, in particular the dog's, health, such as *Acinetobacter baumannii* or *Staphylococcus* spp. or *Streptococcus* spp.

15 The inventors found that the compounds of the invention meet such needs and are therefore very useful in the treatment (and prevention) of diseases caused by helminths such as the heartworm disease.

The following abbreviations and definitions are used throughout this application:

Generally, reference to a certain element is meant to include all isotopes of that element. For
20 example, if a group is defined to include hydrogen or a residue is hydrogen, it also includes deuterium and tritium.

The term "C₁₋₆-alkyl" refers to alkyl groups having 1 to 6 carbon atoms that do not contain heteroatoms. Thus, the term includes straight chain alkyl groups such as methyl, ethyl, propyl, butyl, pentyl and hexyl. The term also includes branched chain isomers of straight chain alkyl
25 groups, including but not limited to, the following that are provided by way of example: -CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -CH(CH₂CH₃)₂, -C(CH₃)₃, -CH₂CH(CH₃)₂, -CH₂CH(CH₂CH₃)₂, -CH₂C(CH₃)₃, -CH(CH₃)CH(CH₃)(CH₂CH₃), -CH₂CH₂CH(CH₃)₂, -CH₂CH₂CH(CH₃)(CH₂CH₃), -CH₂CH₂C(CH₃)₃ and others. Thus, the term "C₁₋₆-alkyl" includes primary alkyl groups having 1 to 6 carbon atoms, secondary alkyl groups having 3 to 6 carbon atoms and tertiary
30 alkyl groups having 4 to 6 carbon atoms.

Correspondingly, the term "C₁₋₃-alkyl" refers to alkyl groups having 1 to 3 carbon atoms that do not contain heteroatoms. Thus, the term includes straight chain alkyl groups such as methyl, ethyl,

and propyl. The term also includes branched chain isomers of straight chain alkyl groups, namely $\text{CH}(\text{CH}_3)_2$. Thus, the term "C₁₋₃-alkyl" includes primary alkyl groups having 1 to 3 carbon atoms, and a secondary alkyl groups having 3 carbon atoms.

The term "C₂₋₆-alkenyl" refers to straight and branched chain alkenyl groups such as those
 5 described with respect to the "C₂₋₆-alkyl" defined above, except that at least one double bond exists between two carbon atoms. Examples include, but are not limited to $-\text{CH}=\text{CH}_2$, $-\text{C}(\text{CH}_3)=\text{CH}_2$, $-\text{CH}=\text{CH}(\text{CH}_3)$, $-\text{CH}=\text{C}(\text{CH}_3)_2$, $-\text{CH}=\text{CH}(\text{CH}_3)$, $-\text{C}(\text{CH}_3)=\text{CH}(\text{CH}_3)$, $-\text{C}(\text{CH}_2\text{CH}_3)\text{H}=\text{CH}_2$, $-\text{CH}_2=\text{CH}(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}_2-\text{CH}=\text{CH}_2$, $\text{CH}_2\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}_2$, $\text{CH}_2\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)\text{H}$, $-\text{CH}=\text{CH}-(\text{CH}_2)_2\text{CH}_3$, $-\text{CH}=\text{C}(\text{CH}_3)-\text{CH}_2\text{CH}_3$, $-(\text{CH}_2)_3-\text{CH}=\text{CH}_2$, $-(\text{CH}_2)_4-$
 10 $\text{CH}=\text{CH}_2$, $-(\text{CH}_2)_2-\text{CH}=\text{C}(\text{CH}_3)_2$, butadienyl, pentadienyl, and hexadienyl among others.

The term "C₂₋₆-alkynyl" refers to straight and branched chain alkynyl groups such as those described with respect to the "C₂₋₆-alkyl" defined above, except that at least one triple bond exists between two carbon atoms. Examples include, but are not limited to, $-\text{C}\equiv\text{CH}$, $-\text{C}\equiv\text{CCH}_3$, $-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_3$, $-\text{CH}_2-\text{C}\equiv\text{CH}$, $-\text{CH}(\text{CH}_3)-\text{C}\equiv\text{CH}$, $-\text{C}(\text{CH}_3)_2-\text{C}\equiv\text{CH}$, $-\text{CH}_2-\text{C}\equiv\text{CCH}_3$, $-\text{CH}(\text{CH}_3)-\text{C}\equiv\text{CCH}_3$,
 15 $-\text{C}(\text{CH}_3)_2-\text{C}\equiv\text{CCH}_3$, $-\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_3$, $-\text{CH}(\text{CH}_3)-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_3$, $-\text{C}(\text{CH}_3)_2-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_3$, $-(\text{CH}_2)_2-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_3$, $-(\text{CH}_2)_3-\text{C}\equiv\text{C}-\text{CH}_3$ among others.

The term "C₃₋₁₀-cycloalkyl" refers to non-aromatic monocyclic alkyl groups having 3 to 10 carbon atoms or non-aromatic polycyclic alkyl groups having 3 to 10 carbons atoms, wherein said groups consist solely of carbon and hydrogen atoms. Cycloalkyl may include fused or bridged ring
 20 systems having 3 to 10 carbon atoms. Non-aromatic monocyclic alkyl groups having 3 to 10 carbon atoms include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl and the like. Non-aromatic polycyclic alkyl groups having 3 to 10 carbon atoms include, but are not limited to, adamantane, norbornane, decalinyl, 7,7-dimethyl-bicyclo[2.2.1]heptanyl and the like.

The term "5 to 10-membered heterocyclyl" refers to cyclic groups wherein 5 to 10 members (atoms) form the skeleton, wherein the skeleton of said cyclic compounds comprises at least one carbon atom and at least one heteroatom. Examples of heteroatoms include, but are not limited to, N, O and S. Unless specifically stated otherwise in the specification, the "5 to 10-membered heterocyclyl" may be a monocyclic, bicyclic or polycyclic group which may include fused or
 30 bridged ring systems, wherein a part of the fused ring system may be aromatic; the nitrogen, carbon or sulphur atoms in the "5 to 10-membered heterocyclyl" may be optionally oxidized; the nitrogen atom may be optionally quaternized, and the heterocyclyl residue radical may be partially saturated.

Examples of heterocyclyl groups include, but are not limited, to pyrrolinyl, 3H-pyrazolyl, 4H-pyrazolyl dihydropyridyl, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, homopiperazinyl, indolinyl, quinuclidinyl, morpholinyl, thiomorpholinyl thiazolodinyl, dihydrodithiinyl, dihydrodithionyl, tetrahydrothiophene, tetrahydrothiopyran, benzothiazinyl such as 2H-1,4-
5 benzothiazinyl, dihydrobenzothiazinyl such a 2H-3,4-dihydrobenzothiazinyl, benzodioxolyl such as 1, 3-benzodioxoyl, dihydrooxathiinyl, 1,4-oxathianyl. Further examples of heterocyclyl groups include, but are not limited to, those described above in which one or more S atoms in the ring is double-bonded to one or two oxygen atoms (sulfoxides and sulfones) such as tetrahydrothiophene, tetrahydrothiophene oxide and tetrahydrothiophene-1,1-dioxid as well as thiomorpholine,
10 thiomorpholine oxide and thiomorpholine -1,1 dioxide.

The term " C_{6-10} aryl" refers to a group with an aromatic skeletal structure, wherein the ring atoms of the aromatic skeletal structure are carbon atoms. In other words, the " C_{6-10} aryl" does not contain heteroatoms such as N, S, O in the aromatic skeletal structure.

Examples for aryl groups include, but are not limited, to phenyl, biphenyl and naphthyl.

15 The term "5 to 10-membered heteroaryl" refers to an aromatic group wherein 5 to 10 members (atoms) form the skeleton, wherein the skeleton of said cyclic compound comprises at least one carbon atom and at least one heteroatom. Examples of heteroatoms include, but are not limited to, N, O and S. Unless specifically stated otherwise in the specification, the "5 to 10-membered heterocyclyl" may be a monocyclic or bicyclic or polycyclic group, which may include fused ring
20 systems.

Examples of 5 to 10-membered heteroaryl groups include, but are not limited to, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl such as 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, 1H-1,2,4-triazolyl and 4H-1,2,4-triazlyl, tetrazolyl such as 1H-tetrazolyl, 2H tetrazolyl and 5H-tetrazoyl, indolyl, isoindolyl, indolinyl, indolizinyl,
25 benzimidazolyl, quinolyl, isoquinolyl, indazolyl, naphthyridinyl, benzotriazolyl, oxazolyl, isoxazolyl, oxadiazolyl such as 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, benzoxazolyl, benzoxadiazolyl, benzoxazinyl such as 2H-1,4-benzoxazinyl thiazolyl, isothiazolyl, thiadiazolyl such 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, thienyl, benzothiazolyl, benzothiadiazolyl, benzothiazinyl, benzofuranyl, quinolinyl,
30 isoquinolin, cinnolinyl, quinaxolinyl quinoxalinyl, triazinyl, tetrazinyl, purinyl, pteridinyl, furyl, benzodioxolyl such as 1, 3-benzodioxoyl, benzothienyl, benzodithiinyl and benzoxathiinyl.

The term "C₁₋₆-alkoxy" refers to a group which based on an alkyl group having 1 to 6 carbon atoms bound to an oxygen. The alkyl group having 1 to 6 carbon atoms refers to straight and branched chains such as those described with respect to the "C₁₋₆-alkyl" defined above.

Correspondingly, the term "C₁₋₃-alkoxy" refers to a group which is based on an alkyl group having 1 to 3 carbon atoms bound to an oxygen. The alkyl group having 1 to 3 carbon atoms refers to straight and branched chains such as those described with respect to the "C₁₋₃-alkyl" defined above.

The term "C₁₋₆-alkylmercapto" refers to a group which is based on an alkyl group having 1 to 6 carbon atoms bound to a sulfur. The alkyl group having 1 to 6 carbon atoms refers to straight and branched chains such as those described with respect to the "C₁₋₆-alkyl" defined above.

"Optionally substituted" refers to the optional replacement of one or more hydrogen(s) of the group to be substituted with one or more of the defined substituent(s).

Further amines, hydroxyl and mercapto groups may be protected. The term "protected" with regard to these groups refers to forms of these functionalities with a protecting group to prevent said groups from undesirable reaction. Such protecting groups are known to those skilled in the art for example from *Protective Groups in Organic Synthesis*; Wuts, P. G. M. John Wiley & Sons, New York, NY, (53th Edition, 2014). The protecting groups can be added or removed using the procedures set forth therein.

Examples of protected hydroxyl groups include, but are not limited to, silyl ethers such as those obtained by reaction of a hydroxyl group with a reagent such as, but not limited to, t-butyl dimethylchlorosilane, trimethylchlorosilane, triisopropylchlorosilane, triethylchlorosilane; substituted methyl and ethyl ethers such as, but not limited to, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, t-butoxymethyl ether, 2-methoxyethoxymethyl ether, tetrahydropyranyl ethers, 1-ethoxyethyl ether, allyl ether, benzyl ether; esters such as, but not limited to, benzoylformate, formate, acetate, trichloroacetate and trifluoroacetate.

Examples of protected amine groups include, but are not limited to, amides such as formamide, acetamide, trifluoroacetamide and benzamide; imides, such as phthalimide and dithiosuccinimide; carbamate such as tert-butyloxycarbonyl (Boc) and others.

Examples of protected mercapto groups include, but are not limited to, thioether such as S-benzyl thioether, and S-4-picolyl thioether; substituted S-methyl derivatives such as hemithio, dithio and aminothio acetals and others.

Stereoisomers include compounds which are made of the same atoms connected in the same sequence, but the atoms are positioned differently in space. Stereoisomers include diastereoisomers and enantiomers.

A "physiologically acceptable salt" is referred to as salt with an inorganic base, organic base,
5 inorganic acid, organic acid or basic or acidic amino acid.

Examples of suitable inorganic acids for making (physiologically acceptable) salts include, but are not limited to, hydrochloric, hydrobromic, hydroiodic, nitric, carbonic, sulfuric and phosphoric acid.

Examples of suitable organic acids for making (pharmaceutically acceptable) salts include, but are
10 not limited to, cholic acid, sorbic acid, lauric acid, acetic acid, trifluoroacetic acid, formic acid, propionic acid, succinic acid, glycolic acid, gluconic acid, digluconic acid, lactic acid, malic acid, tartaric acid, citric acid, ascorbic acid, glucuronic acid, maleic acid, fumaric acid, pyruvic acid, aspartic acid, glutamic acid, benzoic acid, anthranilic acid, mesylic acid, stearic acid, salicylic acid, p-hydroxybenzoic acid, phenylacetic acid, mandelic acid, embonic acid, ethanesulfonic acid,
15 benzenesulfonic acid, toluene sulfonic acid, pantothenic acid, 2-hydroxyethanesulfonic acid, sulfanilic acid, cyclohexylaminosulfonic acid, β -hydroxybutyric acid, galactaric acid, galacturonic acid, adipic acid, alginic acid, butyric acid, camphoric acid, camphorsulfonic acid, cyclopentanepropionic acid, dodecylsulfonic acid, glycoheptanoic acid, glycerophosphic acid, heptanoic acid, hexanoic acid, nicotinic acid, 2-naphthalesulfonic acid, oxalic acid, palmoic acid,
20 pectinic acid, 3-phenylpropionic acid, picric acid, pivalic acid, thiocyanic acid, tosylic acid, undecanoic acid and acidic amino acids such as aspartic acid and glutamic acid.

Examples of base addition salts may include, for example, metallic salts and organic salts.

Metallic salts include, but are not limited to, alkali metal (group Ia) salts, alkaline earth metal (group IIa) salts and other physiologically acceptable metal salts. Examples of such salts may be
25 made from aluminium, calcium, lithium, magnesium, potassium, sodium, and zinc. For example, a free acid compound may be mixed with sodium hydroxide to form such a base addition salt.

Organic salts may be made from amines, such as trimethylamine, diethylamine, N,N'-dibenzyl-ethylenediamine, chlorprocaine, ethanolamine, diethanolamine, ethylenediamine, N-methyl-glucamine, procaine and basic amino acids such as arginine, lysine and ornithine.

30 As used herein, the term "pharmaceutically acceptable ester" refers to esters that hydrolyze in vivo and include those that break down readily in the human body to leave the parent compound or a salt thereof. Suitable ester groups include, for example, those derived from pharmaceutically

acceptable aliphatic carboxylic acids, particularly alkanoic, alkenoic, cycloalkanoic and alkanedioic acids in which each alkyl or alkenyl moiety advantageously has not more than 6 carbon atoms. Representative examples of particular esters include, but are not limited to, formates, acetates, propionates, butyrates, acrylates and ethylsuccinates.

5 A solvate of a compound can be regarded as a compound in which an organic solvent or water adheres to said compound. Organic solvents refer to the ones which are known by the skilled person. In case that water is adhered to the compound the corresponding compound is known as a hydrate.

The term "polymorph" as used herein and as generally understood by the skilled person refers to
10 different crystalline forms of the same molecular entity. Therefore, due to their different chemical compositions, solvates and hydrates as discussed above are not included in the definition of polymorphism but are rather designated "pseudopolymorphs" instead.

The term "prodrug" refers to compounds that are rapidly transformed *in vivo* to yield the parent compound of the above Formula ((I), for example by hydrolysis in blood. A thorough discussion
15 is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A. C. S. Symposium Series, and in Edward B. Roche, Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987.

The term "pharmaceutically acceptable prodrugs" as used herein refers to those prodrugs of the compounds of the present invention that are, within the scope of sound medical judgment, suitable
20 for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, commensurate with a reasonable benefit/risk ratio and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the invention.

The invention provides a compound according to the invention and/or embodiments thereof,
25 wherein R¹ is defined as below.

In an embodiment of the invention and/or embodiments thereof, R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²R³, C(=O)OR⁴ and C(=O)NR⁵R⁶,

30 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R² and R³ together with the N atom to which they are attached form a saturated or unsaturated
 5 heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3
 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or
 the heterocyclic ring formed by R² and R³ together with the N atom to which they are
 attached is optionally substituted with one or more substituent(s) independently selected
 10 from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen
 and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen
 15 and C₁₋₃-alkyl.

Optionally, in an embodiment of the invention and/or embodiments thereof, R¹ is independently
 selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more
 20 substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl.

Optionally, in an embodiment of the invention and/or embodiments thereof, R¹ is independently
 25 selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy and halogen,

wherein C₁₋₆-alkyl and C₁₋₆-alkoxy is optionally substituted with one or more
 substituent(s) independently selected from the group consisting of

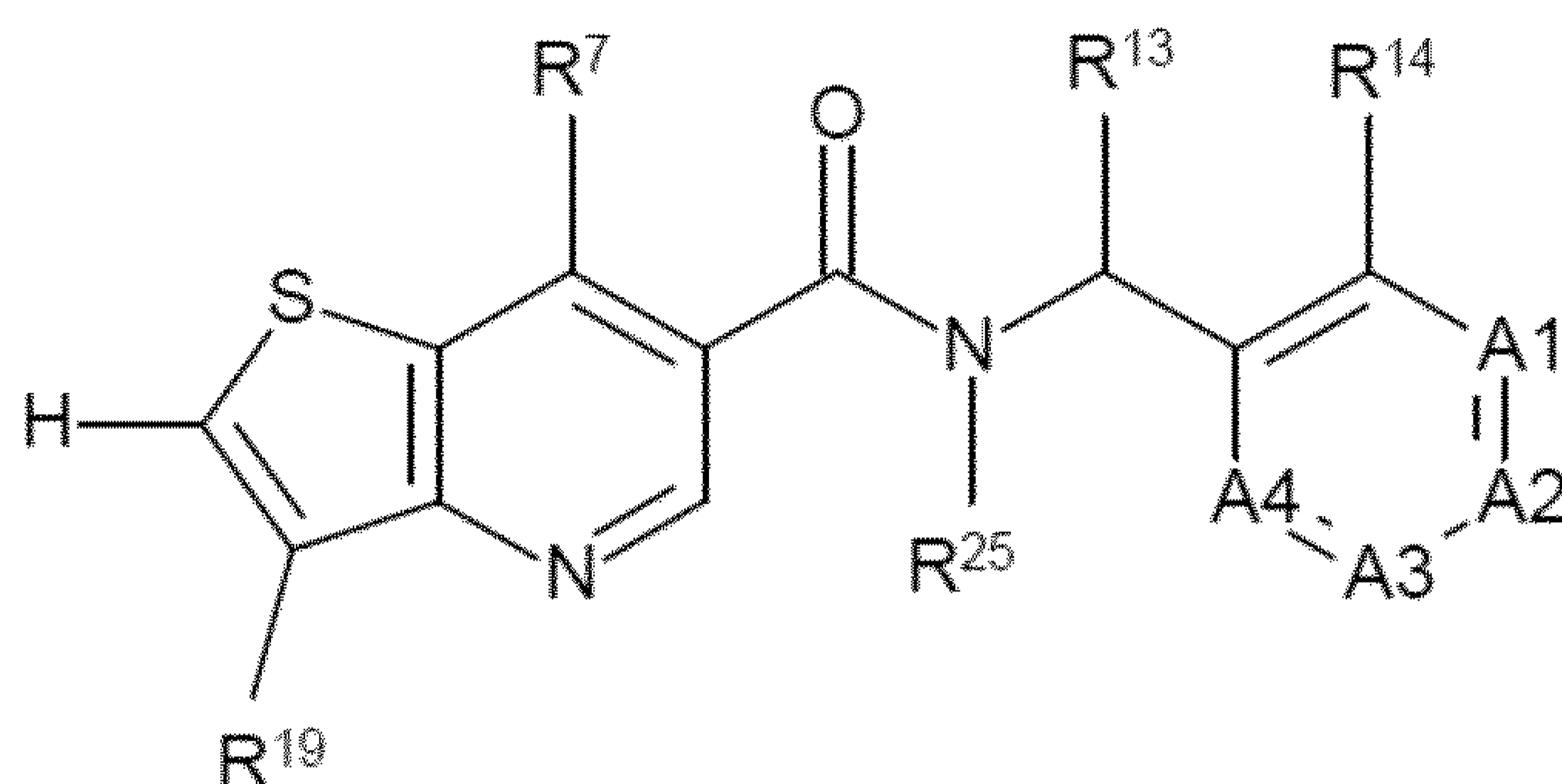
C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy and NR^{2'}R^{3'},

wherein R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl, more preferably from hydrogen and methyl.

In one embodiment of the invention and/or embodiments thereof, R¹ is independently selected
5 from the group consisting of

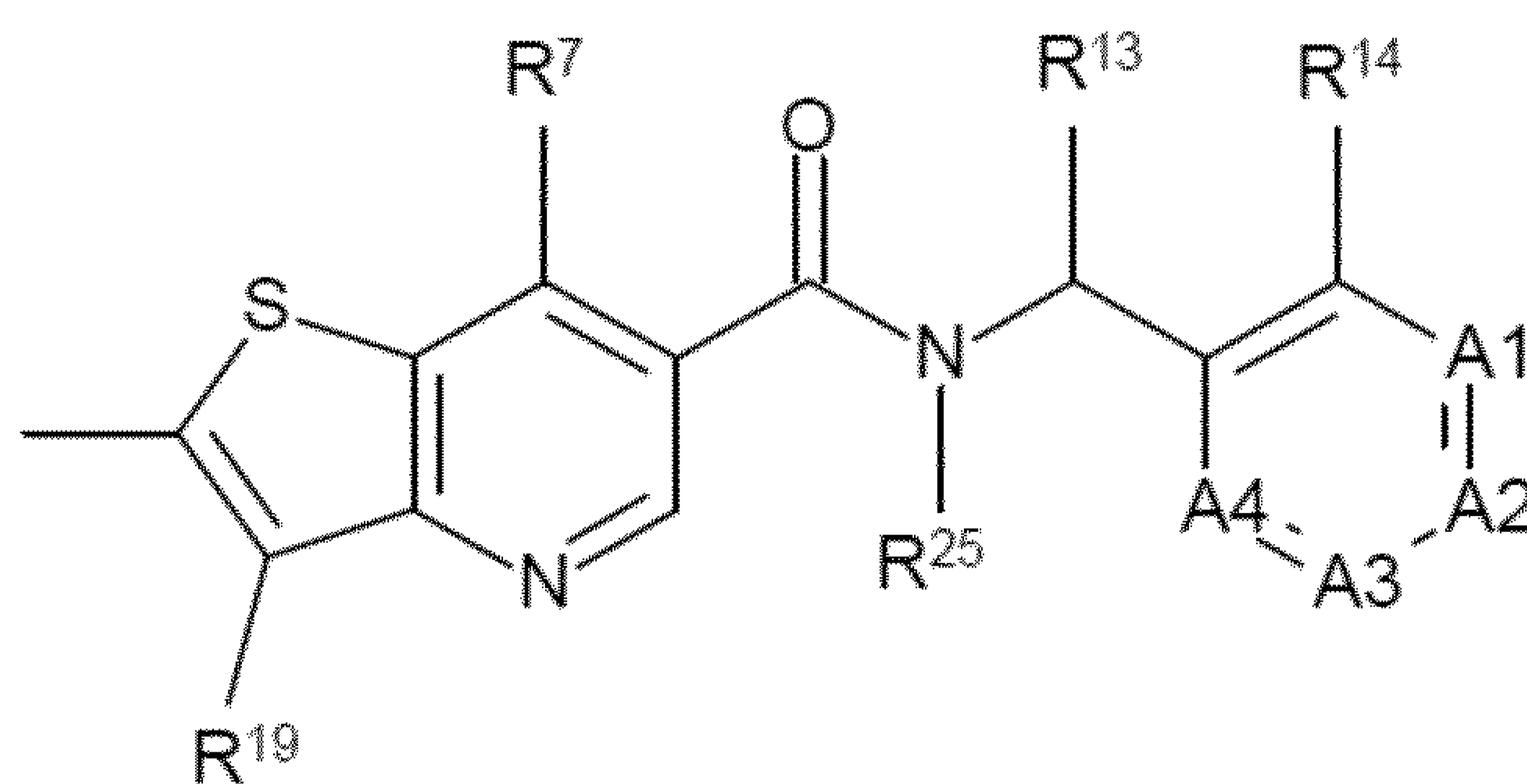
hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride, in particular hydrogen and methyl.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iai), (Iaii), (Iaiii) or (Iaiv)

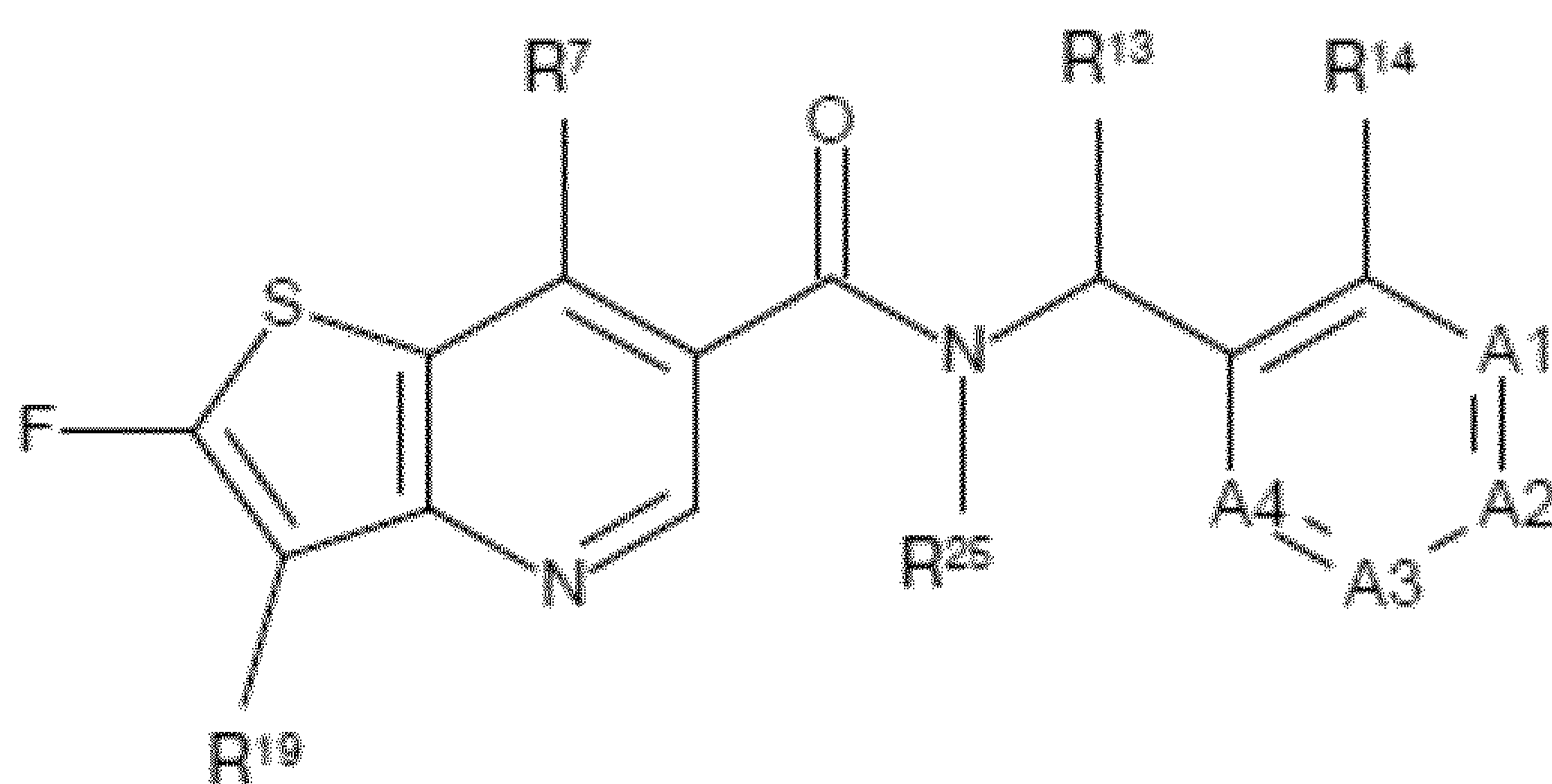


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Formula (Iai)

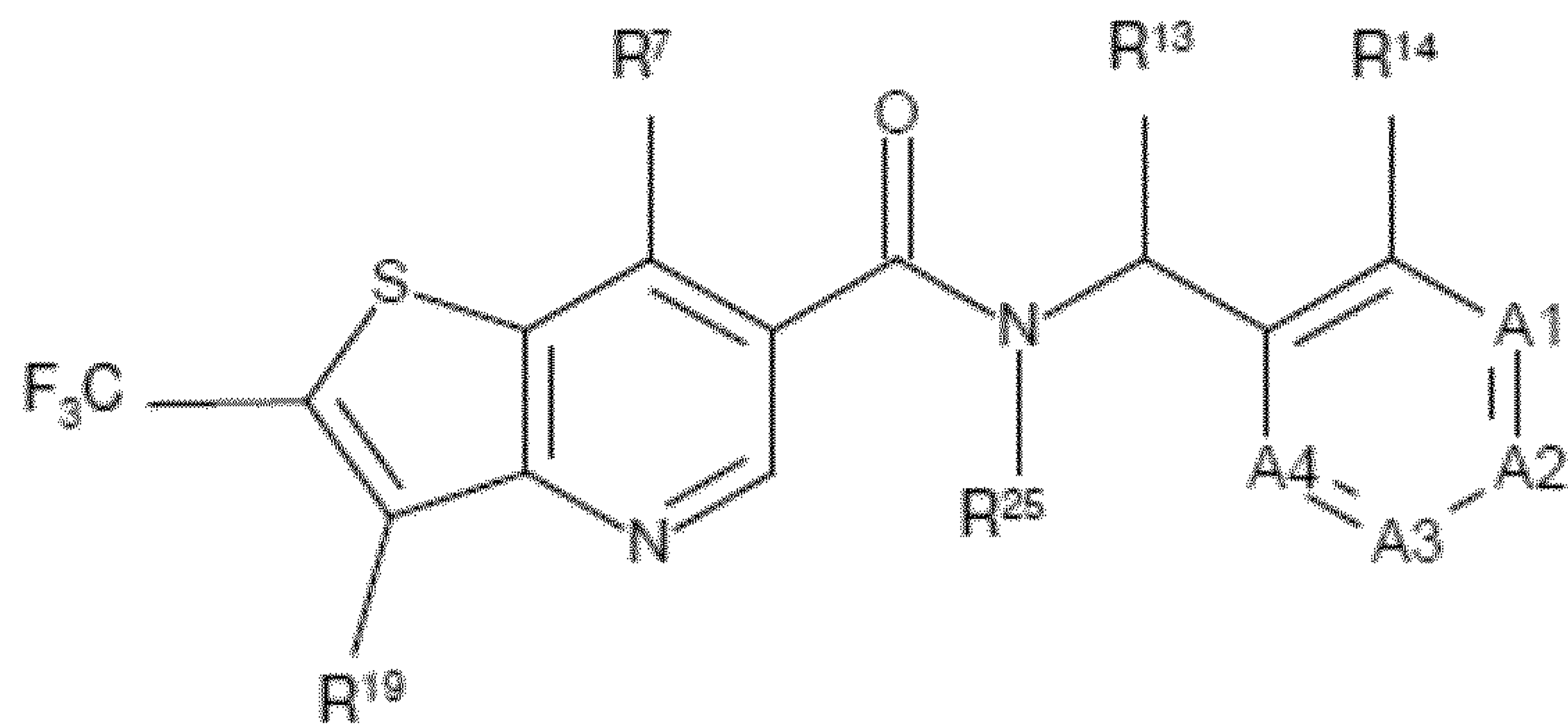


Formula (Iaii)



15

Formula (Iaiii)



Formula (Iaiv)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 , R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are defined as in any of the
5 embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iai), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
embodiments thereof, the compounds are according to Formula (Iaii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds
10 are according to Formula (Iaiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iaiv), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^7 is defined as below.

15 In an embodiment of the invention and/or embodiments thereof, R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

20 wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, NR^8R^9 , $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

25 R^8 and R^9 are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl.

In an embodiment of the invention and/or embodiments thereof, wherein R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen or C₁₋₆-alkyl, preferably from hydrogen or C₁₋₃-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₆-alkyl, preferably from hydrogen or C₁₋₃-alkyl,

10 R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₆-alkyl, preferably from hydrogen or C₁₋₃-alkyl.

In an embodiment of the invention and/or embodiments thereof, R⁷ is independently selected from the group consisting of

15 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

25 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

5 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl.

In an embodiment of the invention and/or embodiments thereof, R⁷ is independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

15 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

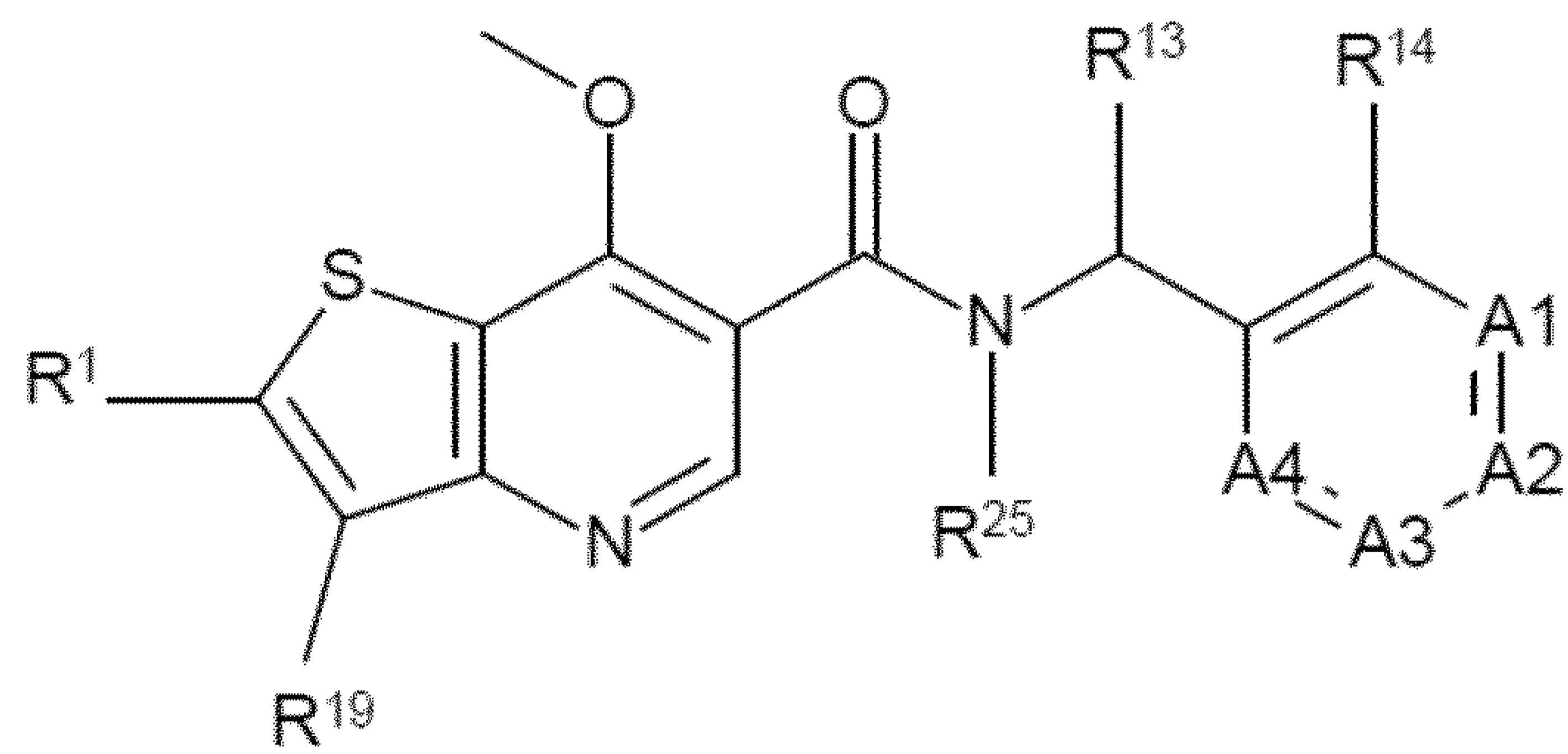
wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

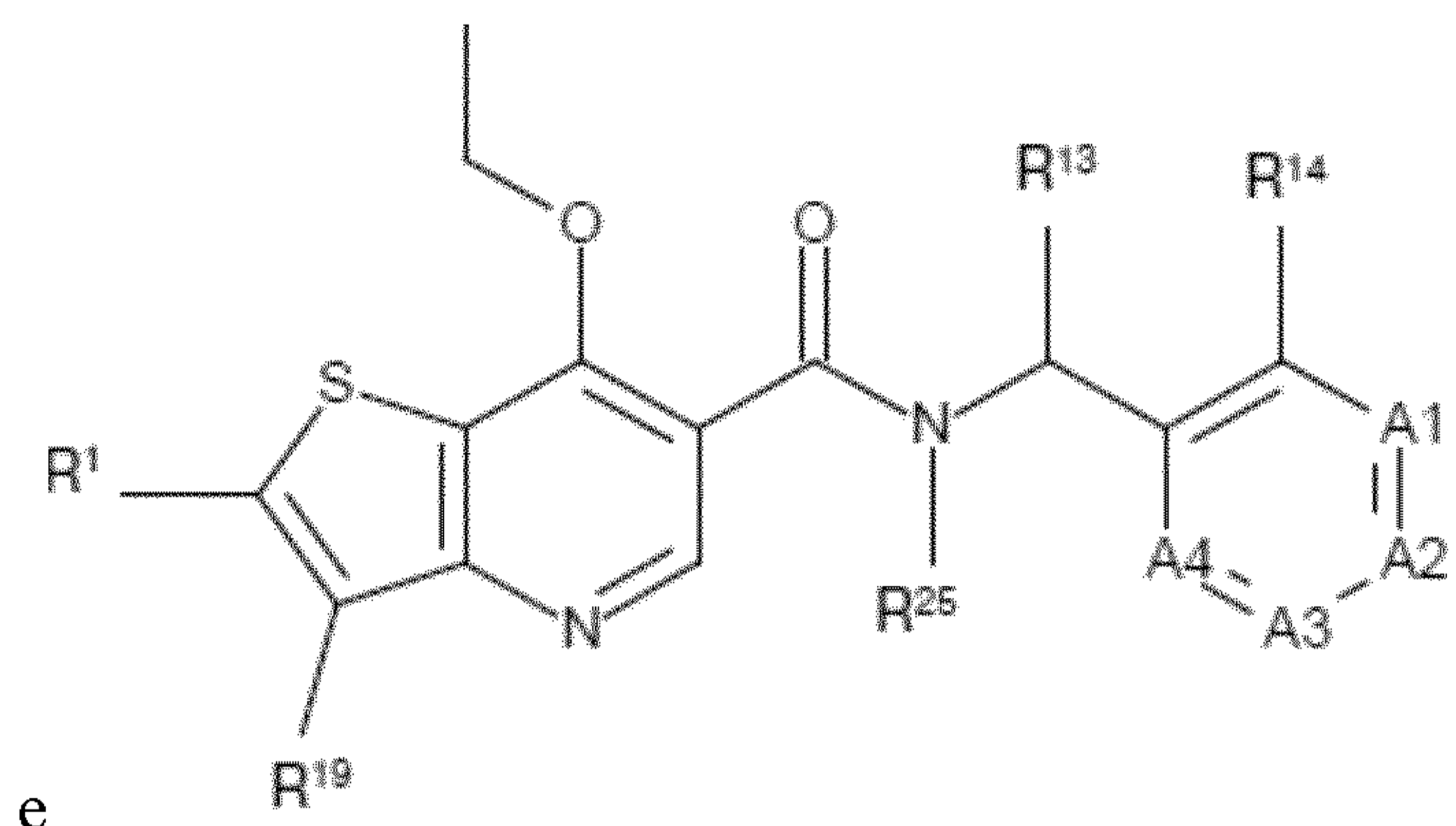
20 In an embodiment of the invention and/or embodiments thereof, R⁷ is independently selected from the group consisting of

25 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, hydroxyethylamino, 2-hydroxyethylmethylamino, methoxyethylamino, cyclopropylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl, in particular dimethylamino and morpholin-4-yl.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ibi), (Ibii), (Ibiii), (Ibiv), (Ibv) or (Ibvi)

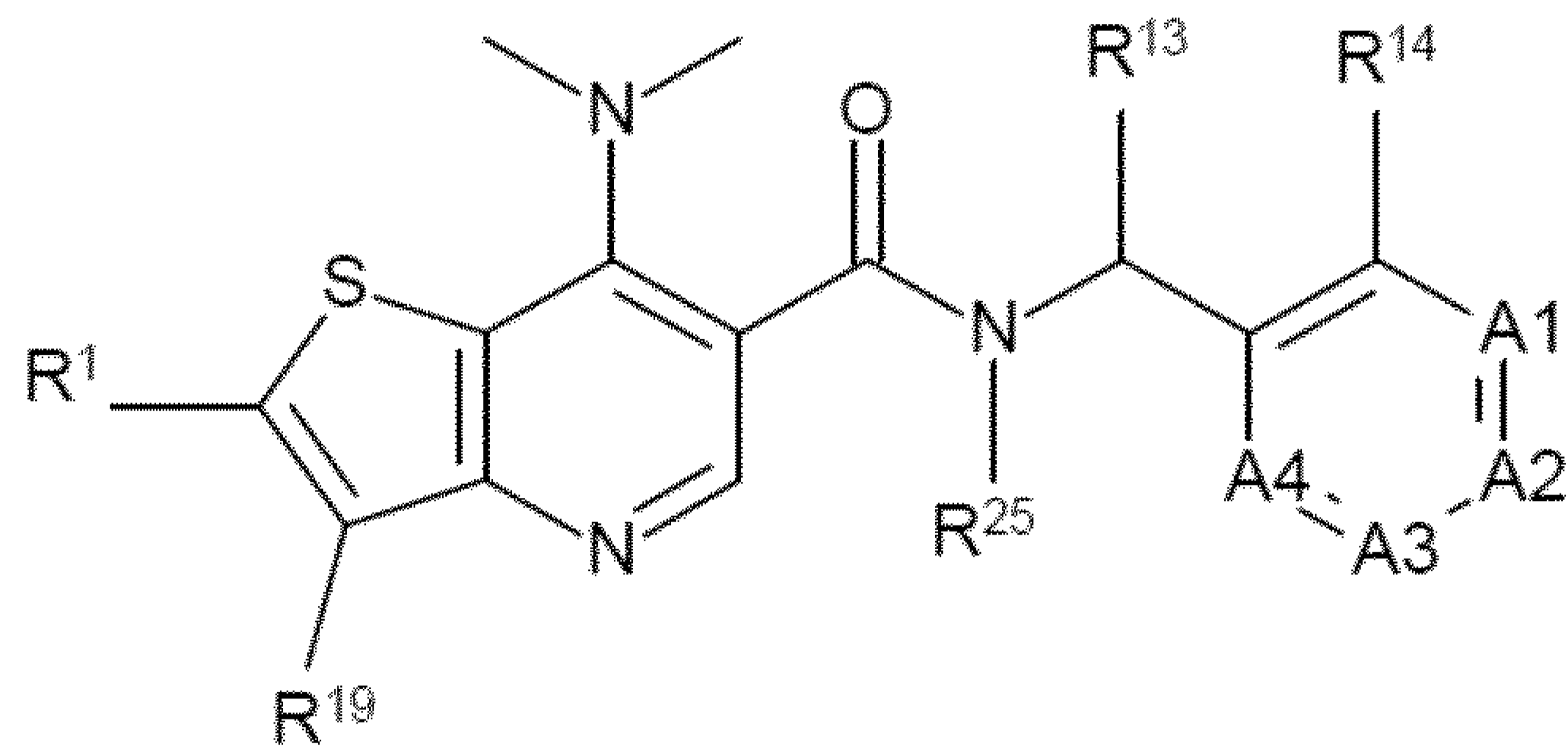


Formula (Ibi)

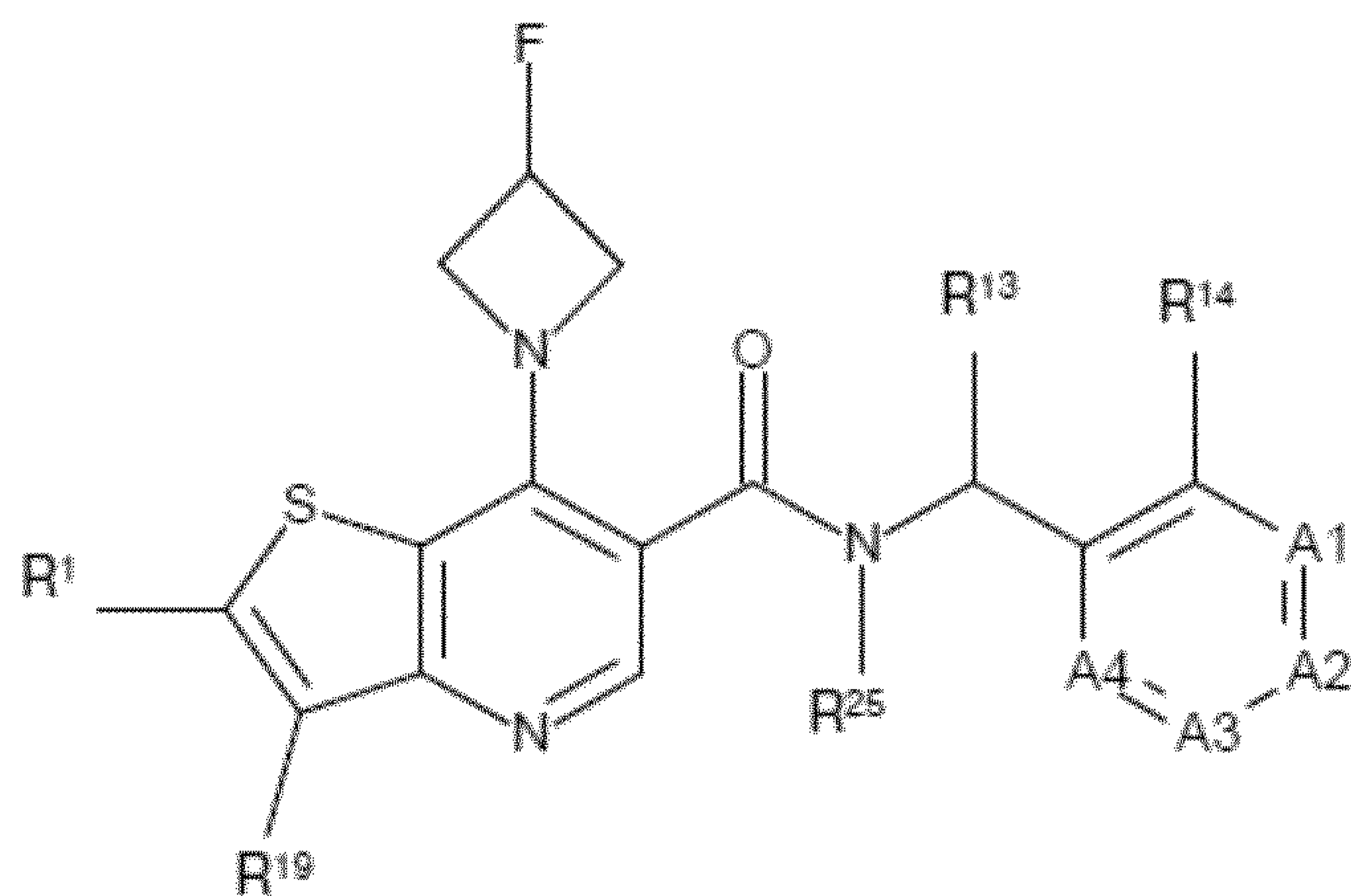


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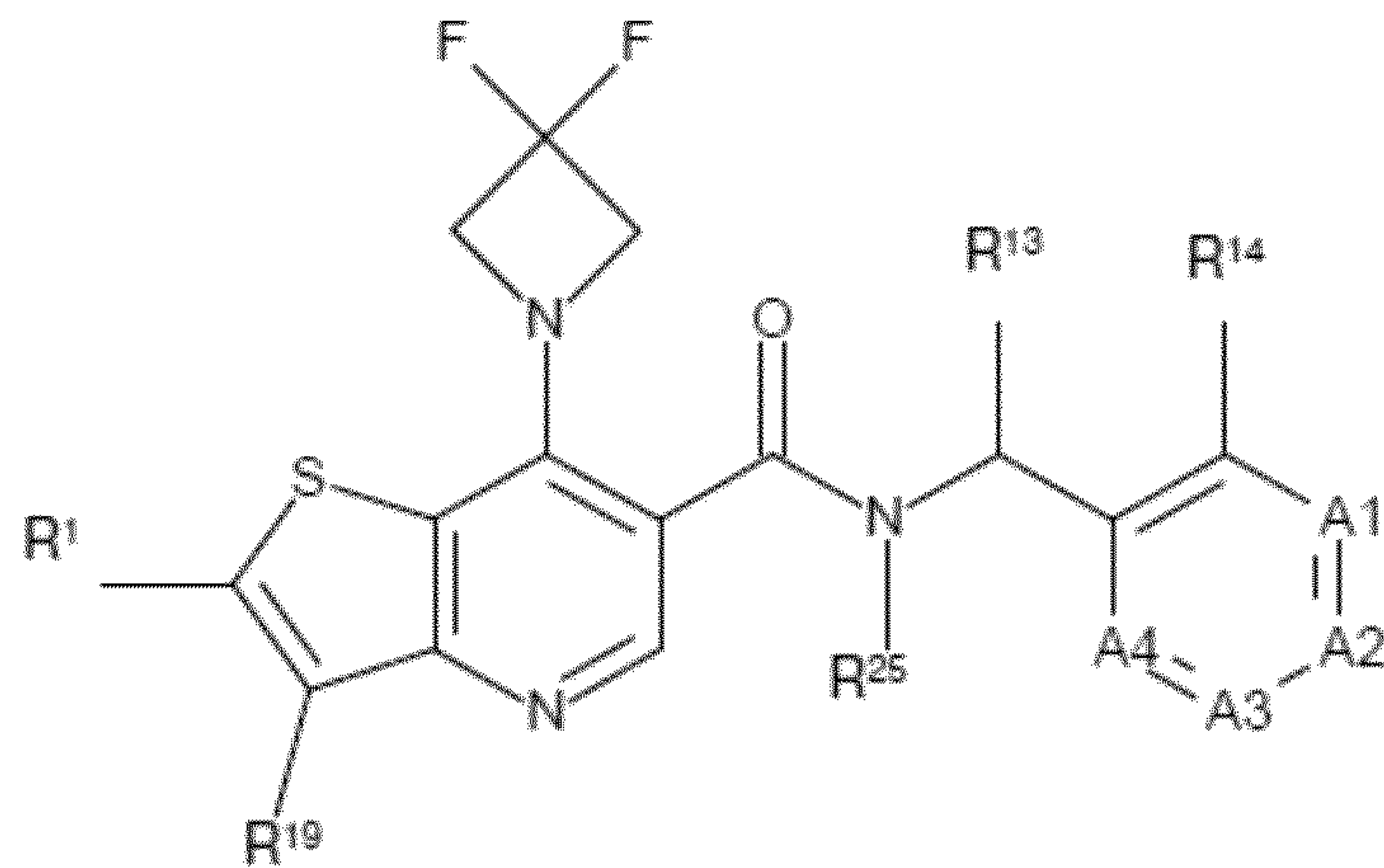
Formula (Ibii)



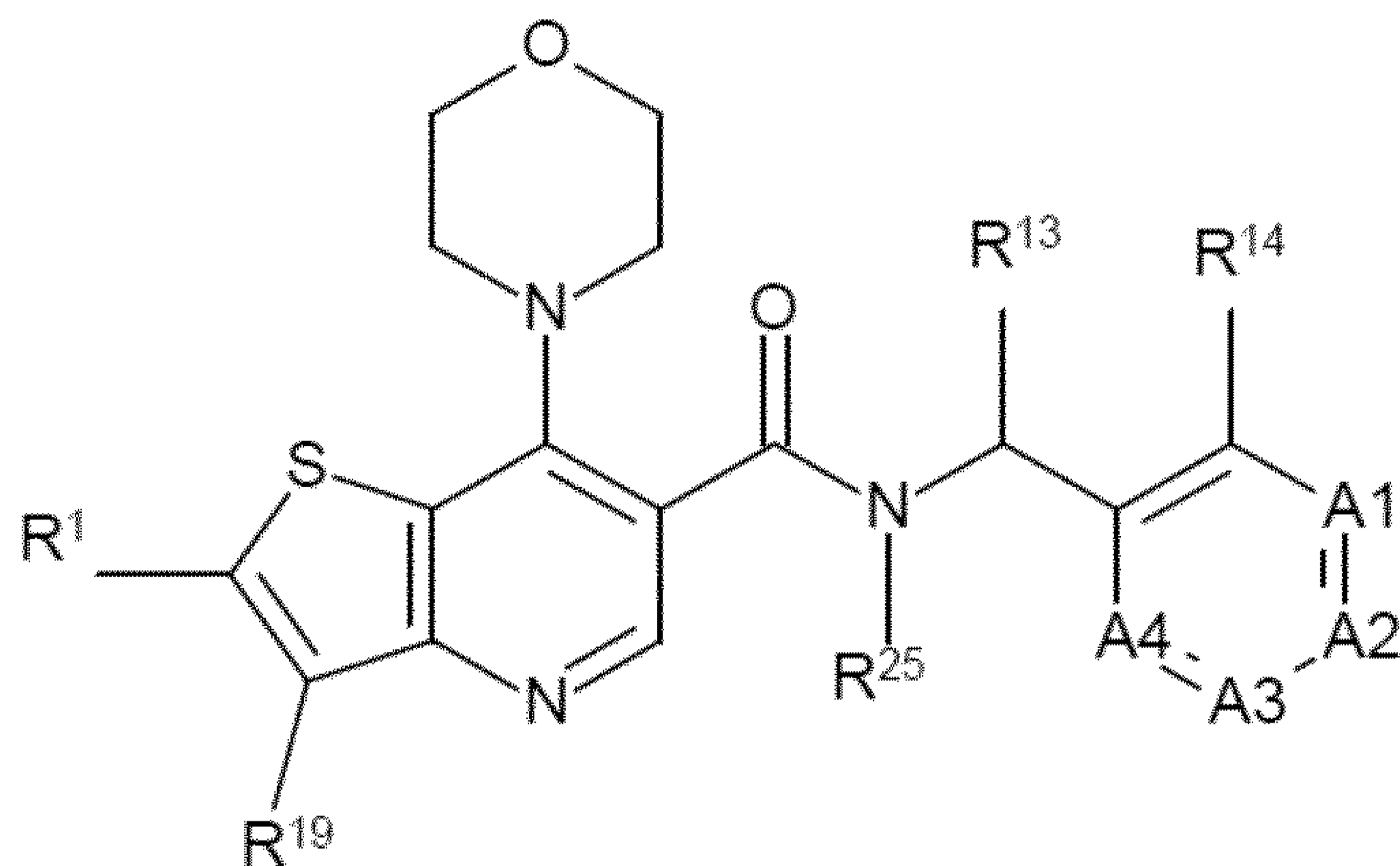
Formula (Ibiii)



Formula (Ibiv)



Formula (Ibv)



5

Formula (Ibvi)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ibi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Ibii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ibiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ibiv),
 15 preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ibv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ibvi), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^{13} and R^{14} as well as A1, A2, A3 and A4 are defined as below.

In an embodiment of the invention and/or embodiments thereof,

R^{13} is hydrogen or C_{1-3} alkyl and

5 R^{14} is hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

10 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl.

More suitably, in an embodiment of the invention and/or embodiments thereof,

15 R^{13} is hydrogen or C_{1-3} alkyl and

R^{14} is hydrogen or C_{1-3} alkyl

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl, C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, C_{1-3} alkyl, C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, C_{1-3} alkyl, C_{1-3} alkoxy,

20 A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, C_{1-3} alkyl, C_{1-3} alkoxy,

wherein none, one or two of residues A1, A2, A3 and A4 is N.

More suitably, in an embodiment of the invention and/or embodiments thereof,

R^{13} is hydrogen, methyl or ethyl, preferably hydrogen or methyl and

R^{14} is hydrogen or methyl, preferably hydrogen

25 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen or C_{1-3} alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen or C_{1-3} alkyl,

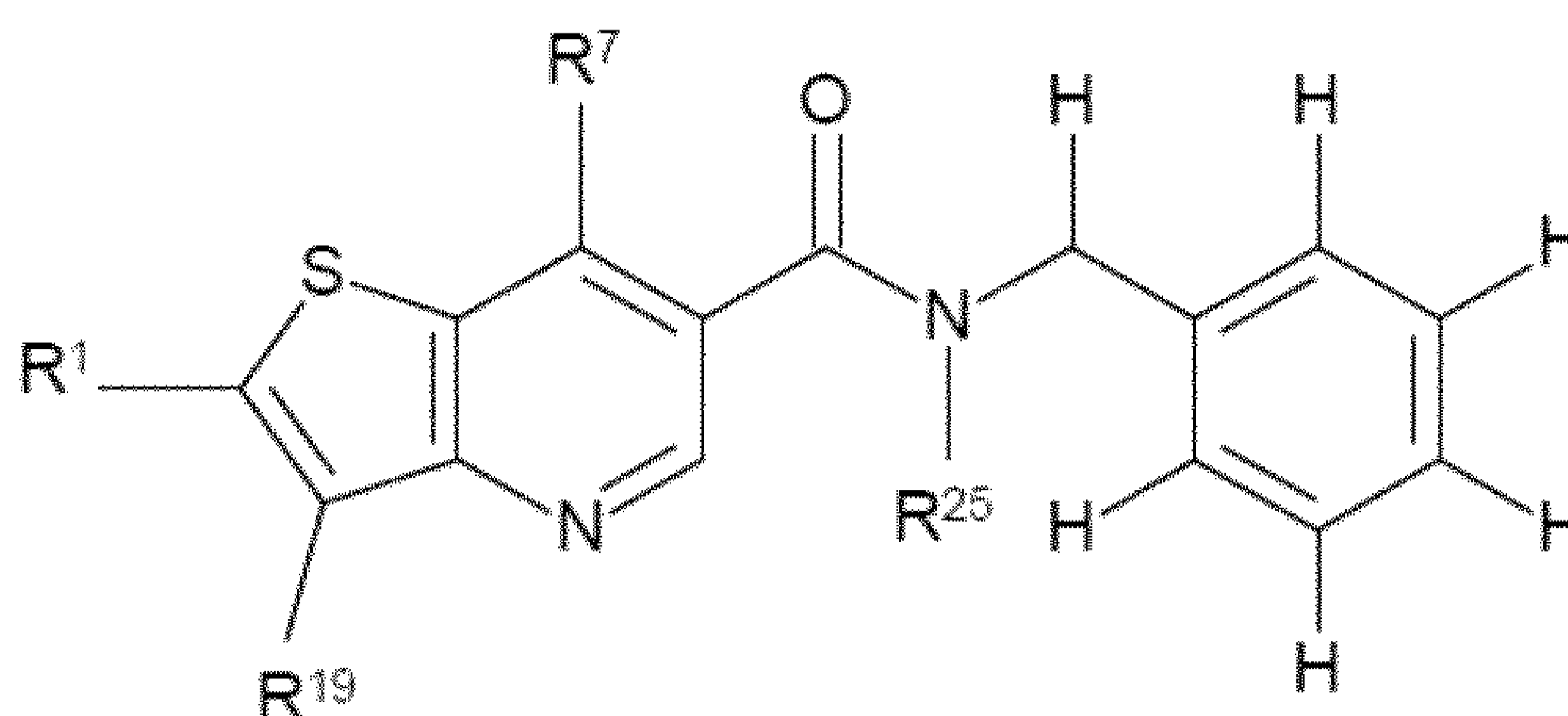
A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkyl,

wherein none, one or two of residues A1, A2, A3 and A4 is N.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to

5 Formula (Ici).



Formula (Ici)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹, R⁷, R¹⁹ and R²⁵ are defined as in any of the embodiments described herein.

10 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ici), preferably in form of the (*S*)-enantiomer.

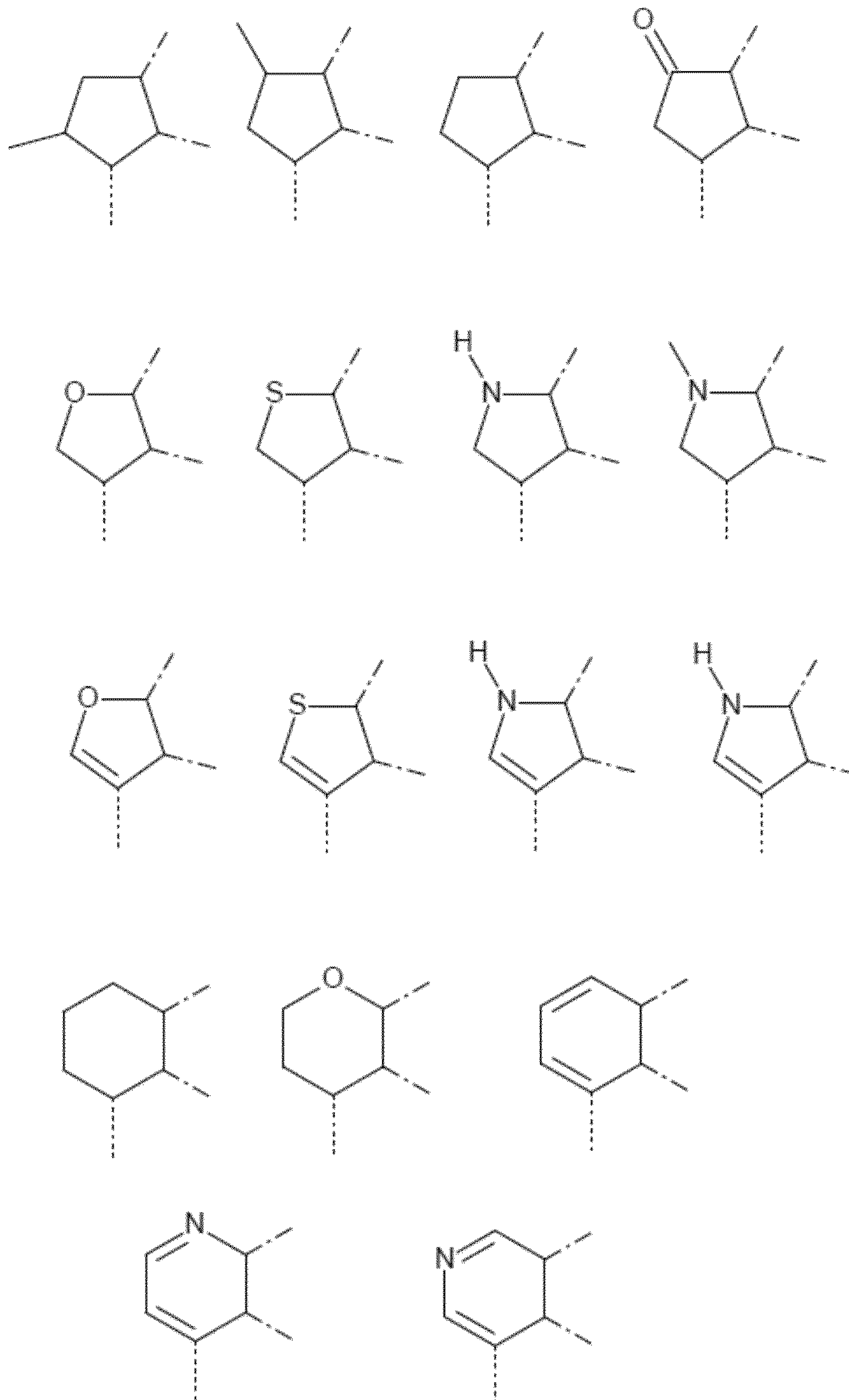
In one embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
15 by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
20 by -NH-, -N=, =N-, -O- or -S-.

Examples of the 5 or 6 carbon atoms containing saturated or unsaturated rings, wherein the 5 or 6- carbon atoms containing saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and wherein one or more of the saturated ring forming carbon atoms are optionally replaced by -NH-, -N=, N-, -O-, -S(O)-, -S(O)₂- or -S-, and examples of the 5 or 6- carbon atoms containing
25 unsaturated or unsaturated rings, wherein the 5 or 6- carbon atoms containing saturated ring is optionally substituted with one or more C₁₋₃-alkyl, and wherein one or more of the unsaturated

ring forming carbon atoms are optionally replaced by -NH-, -N=, N-, -O-, - or -S-, include, but are not limited to, the residues which are represented by the below structures



wherein

- 5 ----- denotes the bond to the amide group; and
- - — denotes the bond with which the above ring system is fused with the aromatic ring inter alia comprising A1, A2, A3 and A4.

In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

5 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

10 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl.

In one embodiment of the invention and/or embodiments thereof,

15 R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

20 A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

In one embodiment of the invention and/or embodiments thereof,

25 R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH- or -O-,

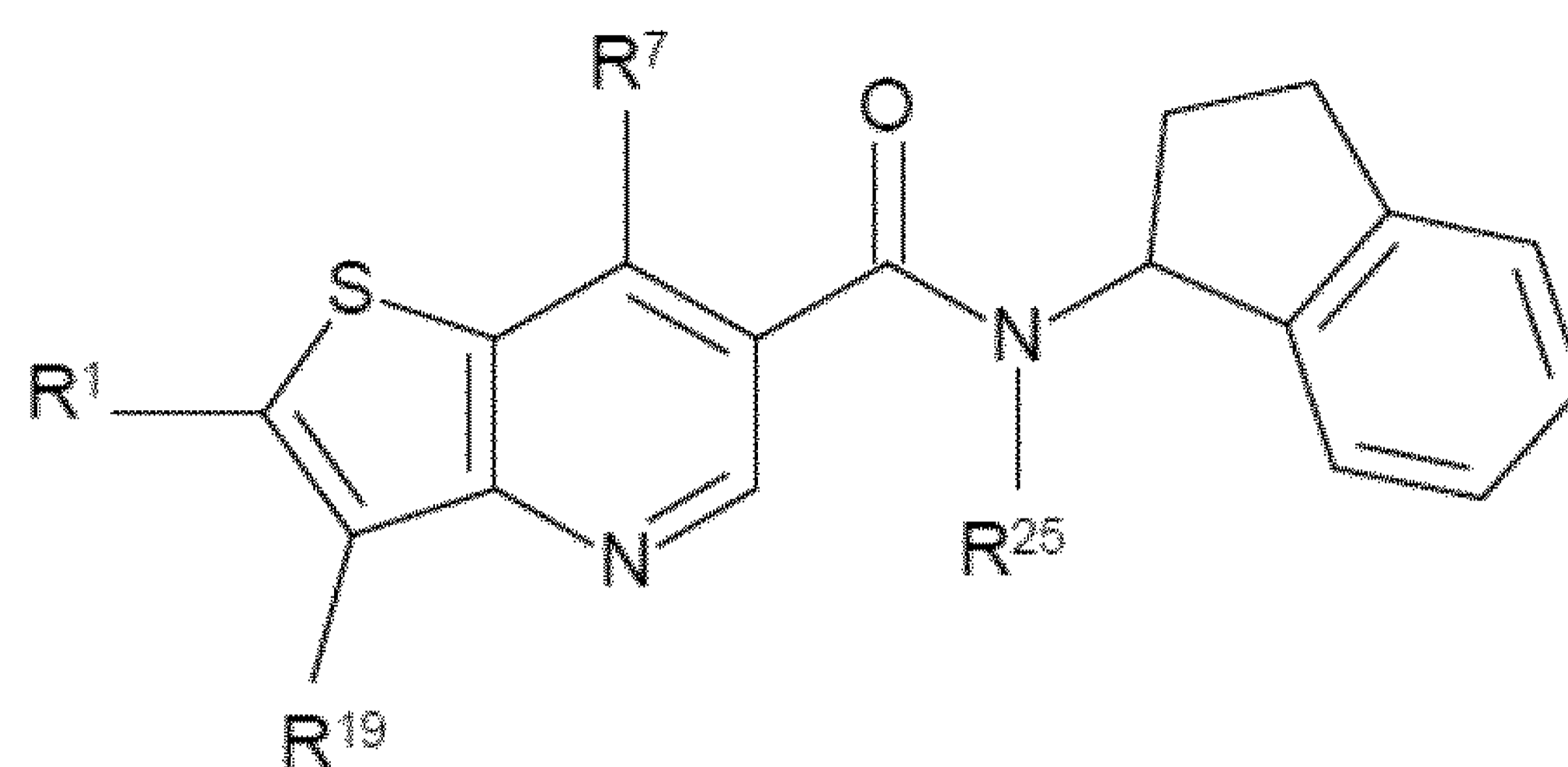
A1 is N or CR^{15} , wherein R^{15} is independently hydrogen or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen or C_{1-3} alkoxy,

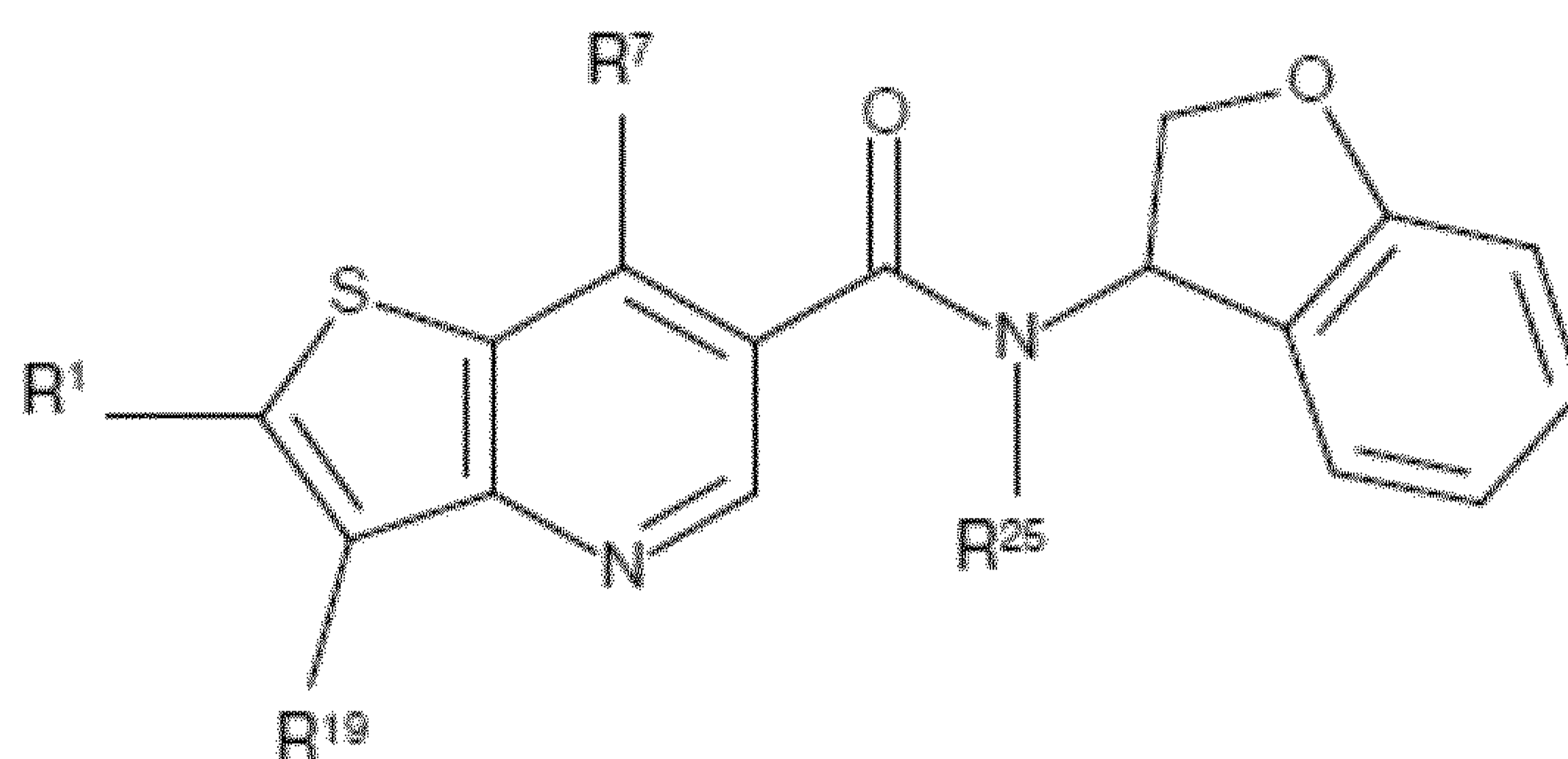
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,
wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to
Formula (Icii), (Iciii), (Iciv) or (Icv)

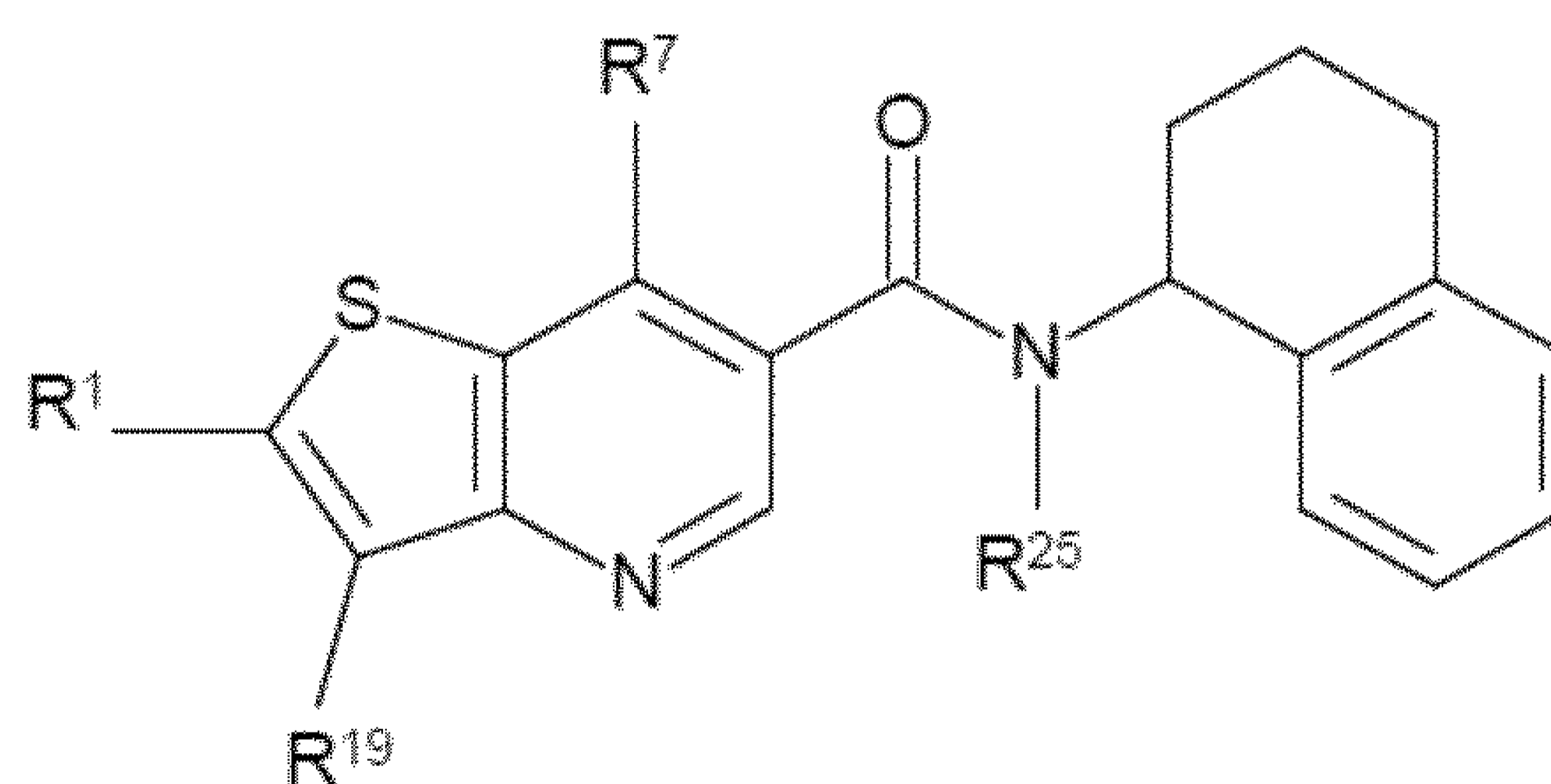


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Formula (Icii)

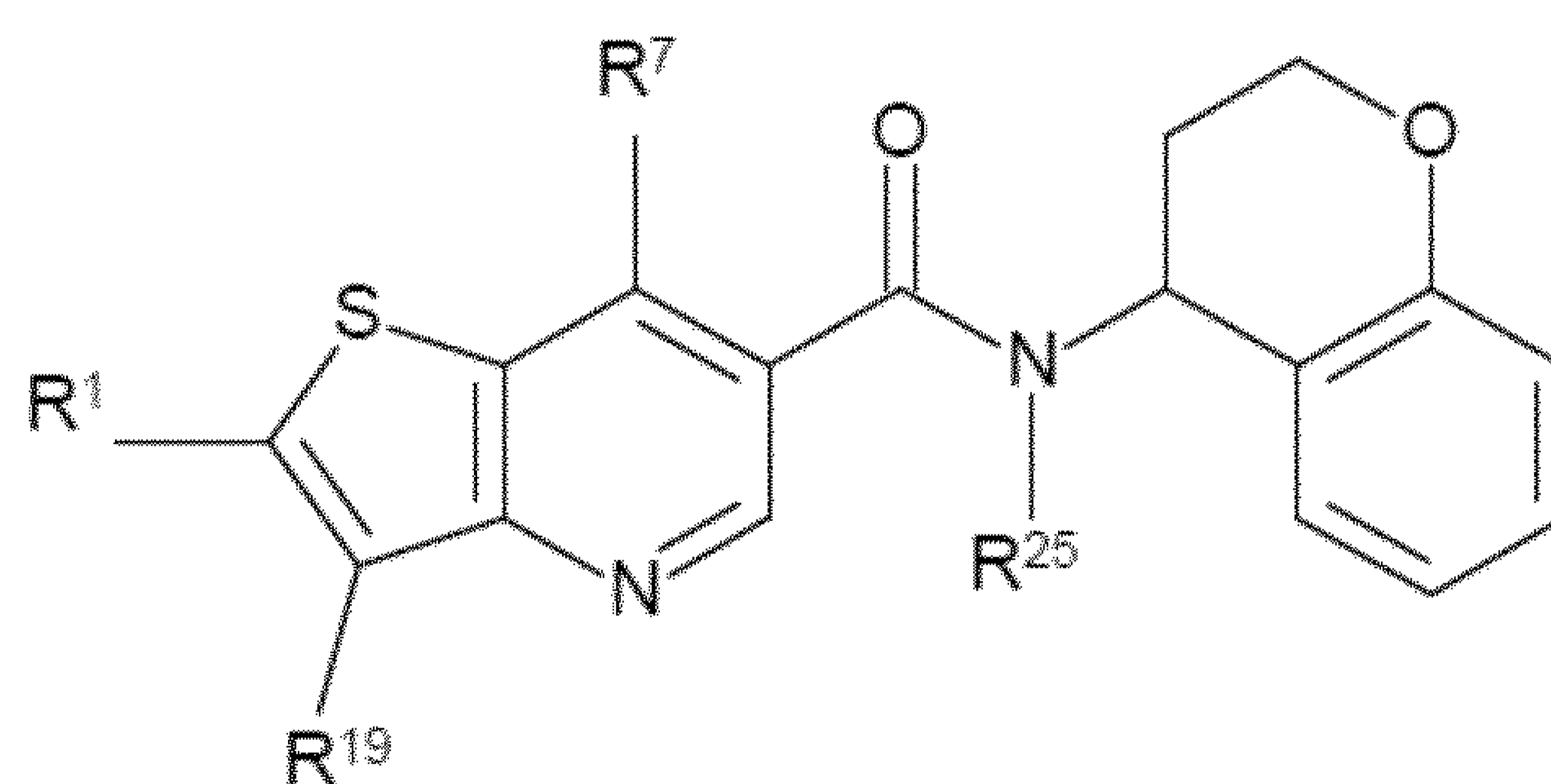


Formula (Iciii)



10

Formula (Iciv)



Formula (Icv)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 , R^{19} and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Icii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 5 embodiments thereof, the compounds are according to Formula (Iciii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iciv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Icv), preferably in form of the (*S*)-enantiomer.

10 In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C_{1-3} -alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

15 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

20 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl.

In an embodiment of the invention and/or embodiments thereof

25 R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,
 wherein none, one or two of A1, A2, A3 and A4 are N.

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms
 containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally
 5 replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

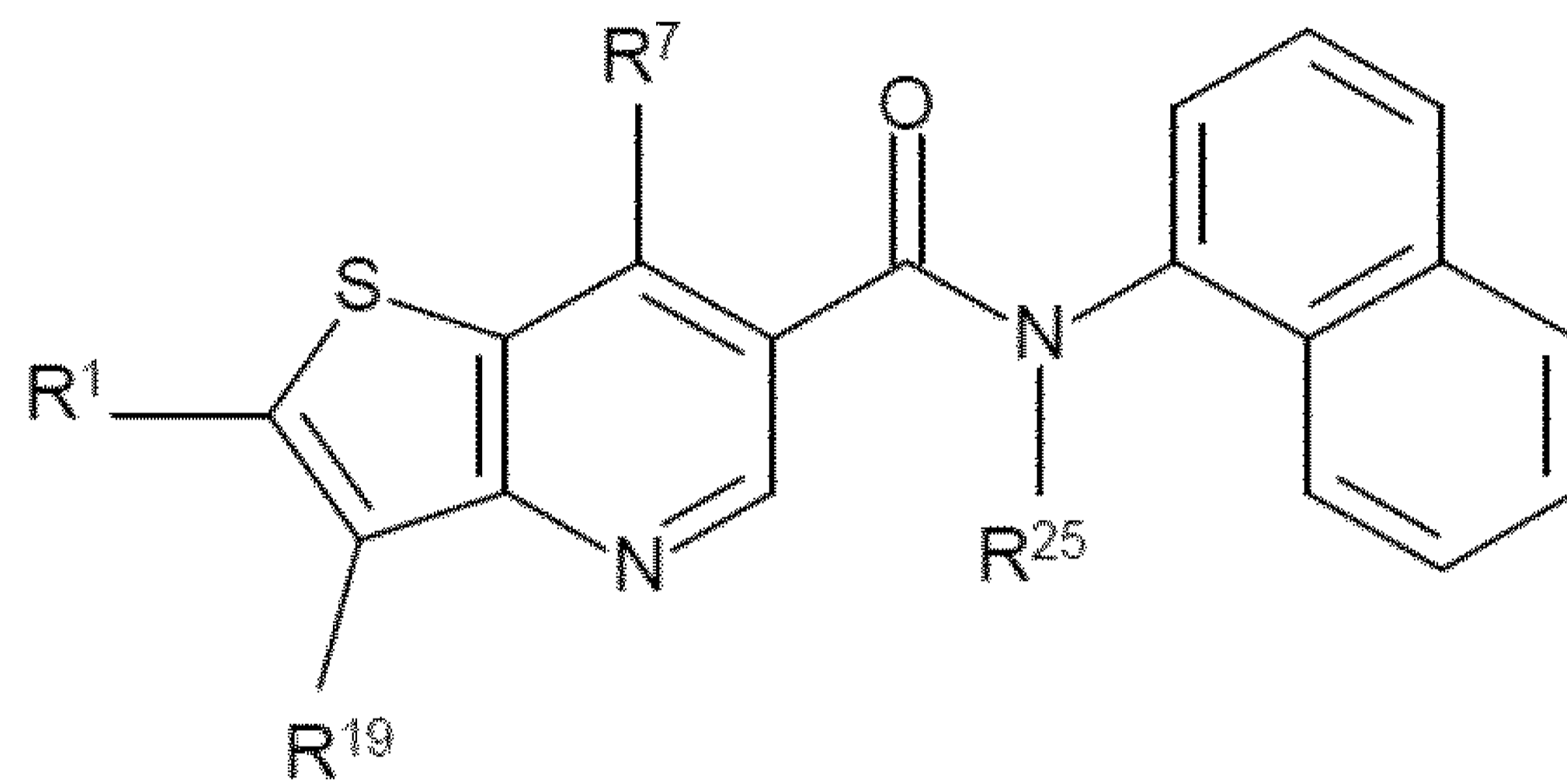
A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

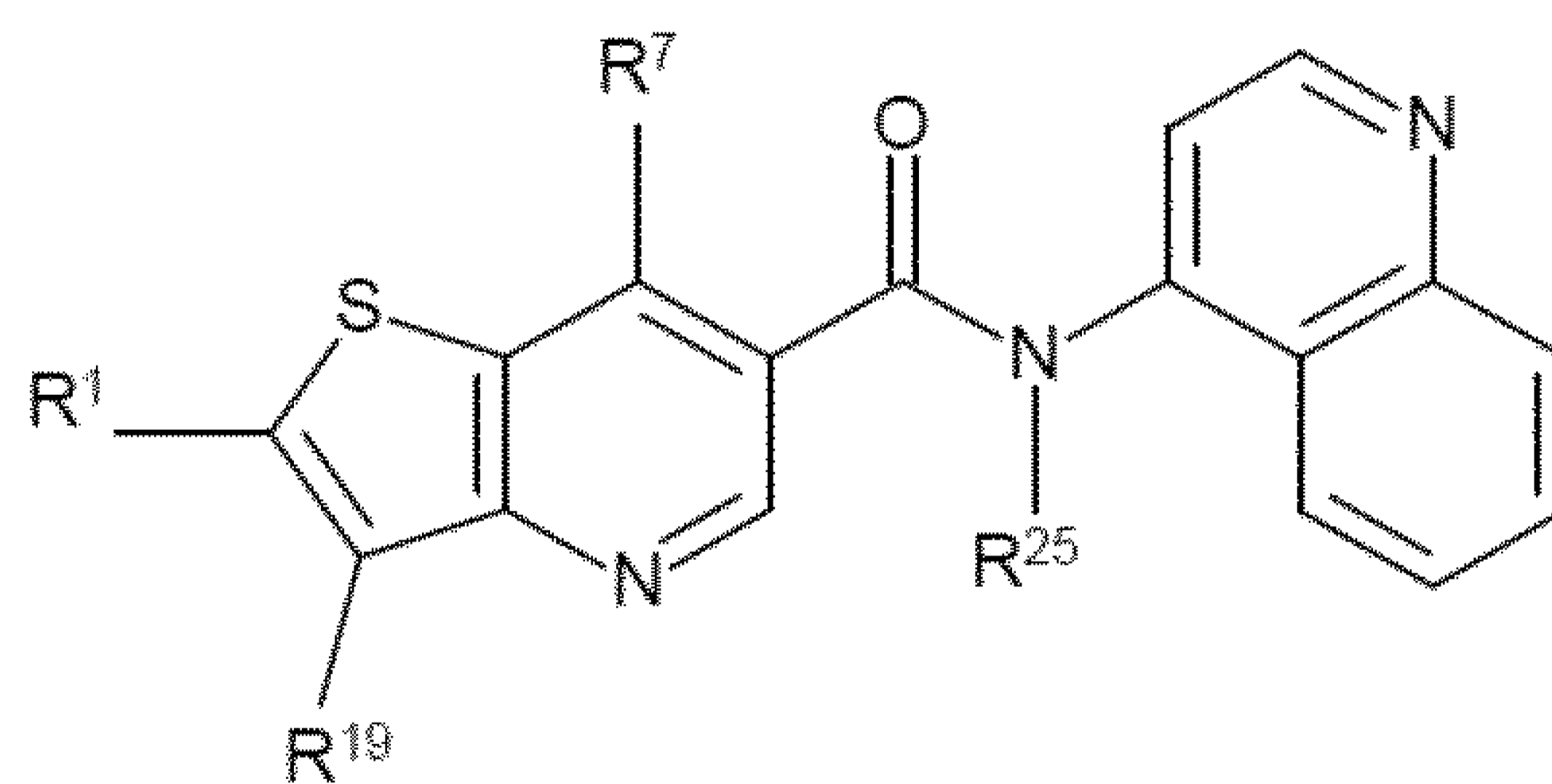
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

10 wherein none, one or two of A1, A2, A3 and A4 are N.

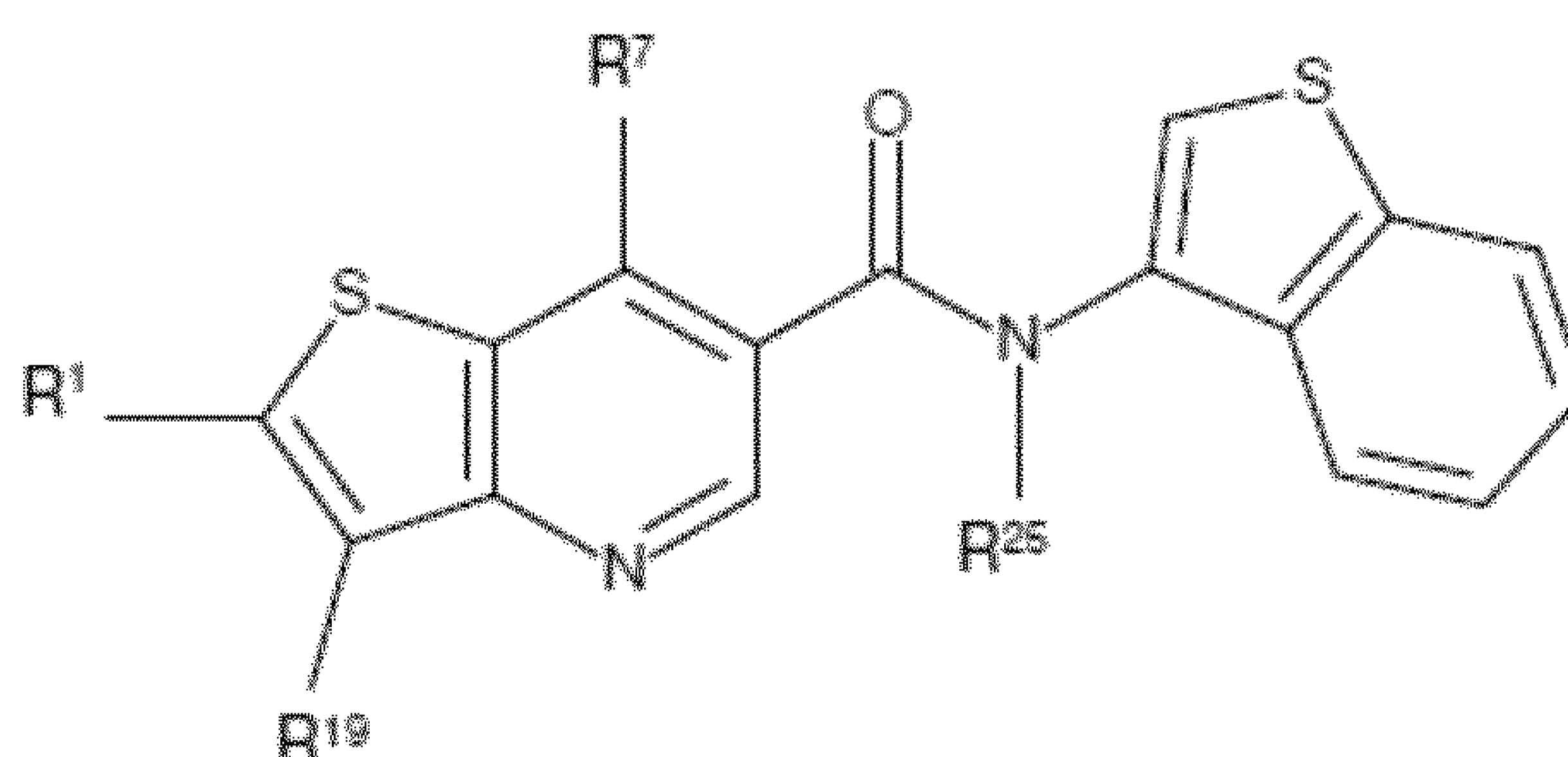
In an embodiment of the invention and/or embodiments thereof, the compounds are according to
 Formula (Icvi), (Icvii) or (Icviii)



Formula (Icvi)



Formula (Icvii)



15

Formula (Icviii)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 , R^{19} and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Icvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
5
embodiments thereof, the compounds are according to Formula (Icvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Icviii), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof,
10
wherein R^{19} is defined as below.

In one embodiment of the invention and/or embodiments thereof,

R^{19} is independently selected from the group consisting of

C_{6-10} -aryl and 5 to 10-membered heteroaryl,

wherein each C_{6-10} -aryl or 5 to 10-membered heteroaryl is optionally substituted with one
15
or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl,
5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, $NR^{20}R^{21}$, $C(=O)OR^{22}$
and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

20
hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{6-10} -aryl or

R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl C_{1-6} -alkoxy, or C_{6-10} -aryl or the heterocyclic ring
25
formed by R^{20} and R^{21} together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl,
5 to 10-membered heteroaryl, halogen, cyano, hydroxy, $NR^{20'}R^{21'}$, $C(=O)OR^{22'}$ and
30
 $C(=O)NR^{23'}R^{24'}$,

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20} , R^{21} , R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C₁₋₆-alkyl.

In an embodiment of the invention and/or embodiments thereof,

R^{19} is independently selected from the group consisting of

5 C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, C(=O)OR²², SO₂R²², SO₂NR²³R²⁴ and C(=O)NR²³R²⁴, wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen,

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C₁₋₆-alkyl.

In an embodiment of the invention and/or embodiments thereof,

15 R^{19} is independently selected from the group consisting of C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, C(=O)OR²² and C(=O)NR²³R²⁴, wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen

25 R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl.

In an embodiment of the invention and/or embodiments thereof,

R^{19} is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy, wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In an embodiment of the invention and/or embodiments thereof, R¹⁹ is a 5 to 10-membered heteroaryl

10 wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano and nitro and hydroxy, wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

15 In an embodiment of the invention and/or embodiments thereof, R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl optionally substituted with one or more halogen and halogen, preferably halogen.

Examples of 5 to 10-membered heteroaryl groups include, but are not limited to, pyrrolyl, imidazolyl, pyrazolyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-3-yl, pyrimidin-4-yl, pyrazinyl, pyridazinyl, triazolyl such as 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, 1H-1,2,4-triazolyl and 4H-1,2,4-triazolyl, tetrazolyl such as 1H-tetrazolyl, 2H tetrazolyl and 5H-
25 tetrazolyl, indolyl, isoindolyl, indolinyl, indoliziny, benzimidazolyl, quinoline 4-yl, quinoline-8-yl, isoquinolyl, indazolyl, naphthyridinyl, benzotriazolyl, oxazolyl, isoxazolyl, oxadiazolyl such as 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl and 1,2,5-oxadiazolyl, benzoxazolyl, benzoxadiazolyl, benzoxazinyl such as 2H-1,4-benzoxazinyl, thiazolyl, isothiazolyl, thiadiazolyl such 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl and 1,2,5-thiadiazolyl, thien-2-yl, thien-3-yl
30 benzothiazolyl, benzothiadiazolyl, benzothiazinyl, benzofuranyl, quinolinyl, isoquinolinyl, cinnolinyl, quinaxolinyl, quinoxalinyl, triazinyl, tetrazinyl, purinyl, pteridinyl, furyl,

benzodioxolyl such as 1, 3-benzodioxoyl, benzothienyl, benzodithiynyl and benzoxathiynyl. Preferred are pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-3-yl, pyrimidin-4-yl, quinoline-8-yl, thien-2-yl and thien-3-yl.

In an embodiment of the invention and/or embodiments thereof, R¹⁹ is a 5 to 10-membered
5 heteroaryl,

wherein the 5 to 10-membered heteroaryl is substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl optionally substituted with one or more halogen and halogen, preferably halogen.

10 In an embodiment of the invention and/or embodiments thereof, R¹⁹ is selected from the group consisting of

2,5-dichloropyridin-4-yl, 2,6-dichloropyridin-4-yl, 5-chlorothien-2-yl, 5-chlorothien-3-yl and 2,6-difluoropyridin-yl.

In an embodiment of the invention and/or embodiments thereof, R¹⁹ is selected from the group
15 consisting of

3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-
20 chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl.

In an embodiment of the invention and/or embodiments thereof, wherein R¹⁹ is C₆₋₁₀-aryl,

wherein the C₆₋₁₀ aryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano and nitro wherein each C₁₋₆-alkyl, C₁₋₆-
25 alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In an embodiment of the invention and/or embodiments thereof, wherein R¹⁹ is C₆₋₁₀-aryl,

wherein C₆₋₁₀ aryl is phenyl substituted with one, two or three substituents independently selected
30 from the group consisting of

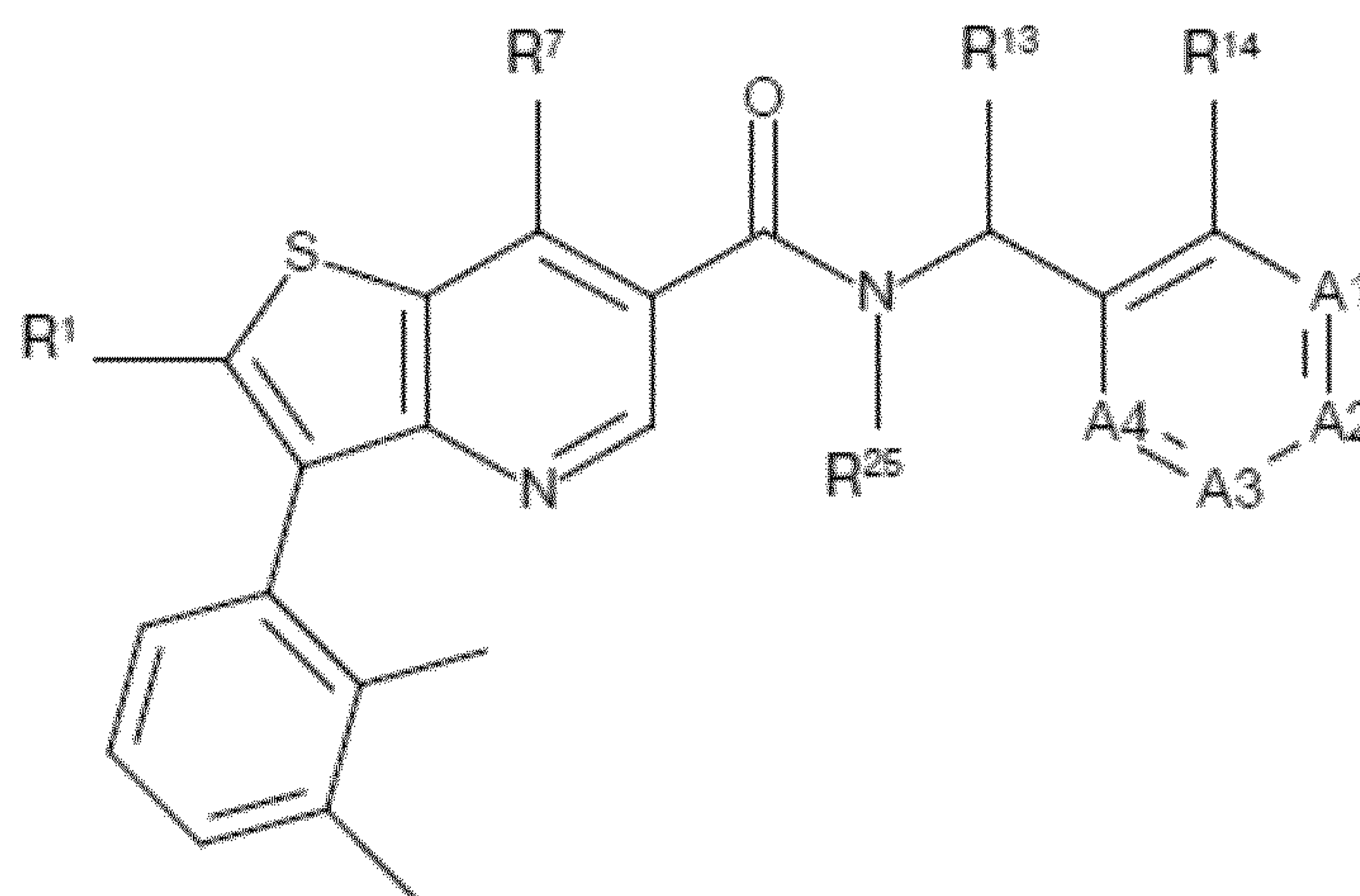
fluoride, chloride bromide, trifluoromethyl and trifluoromethoxy.

Examples of phenyl substituted with one, two or three substituents independently selected from the group consisting of

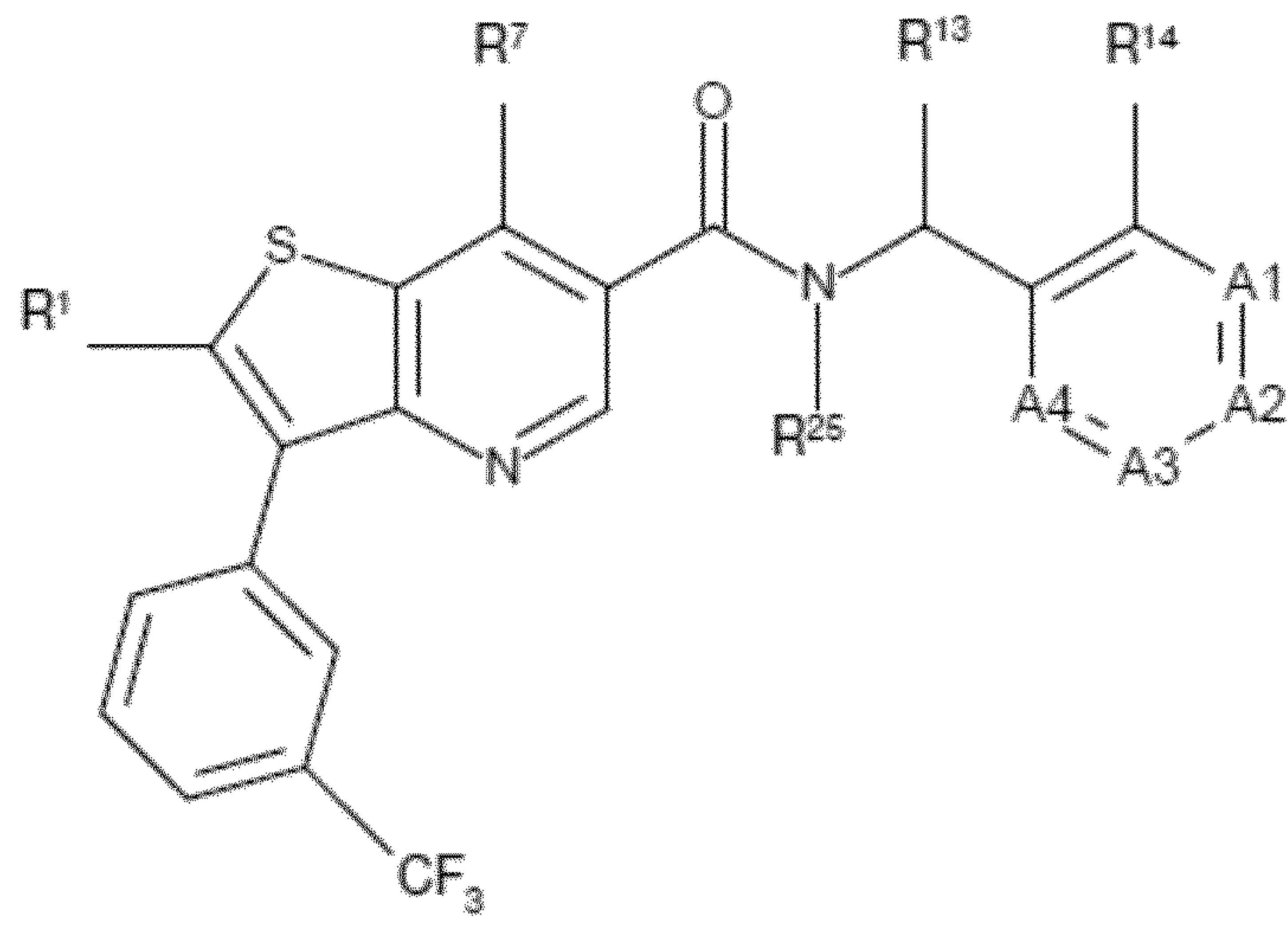
fluoride, chloride, bromide, methyl, methoxy, dimethylamine, trifluoromethyl and
5 trifluoromethoxy include, but are not limited to, 2-fluorophenyl, 3-fluorophenyl, 4-
fluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-bromophenyl, 3-
bromophenyl, 4-bromophenyl, 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl,
3,4-difluorophenyl, 3,5-difluorophenyl, 2,6-difluorophenyl, 2,3-dichlorophenyl, 2,4-
dichlorophenyl, 2,5-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2,3-
10 dibromophenyl, 2,4-dibromophenyl, 2,5-dibromophenyl, 3,4-dibromophenyl, 3,5-
dibromophenyl, 2,3,4-trifluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 2,3,4-
trichlorophenyl, 2,3,5-trichlorophenyl, 3,4,5-trichlorophenyl, 2,3,4-tribromophenyl, 2,3,5-
tribromophenyl, 3,4,5-tribromophenyl, 2-chloro-3-fluorophenyl, 2-chloro-4-fluorophenyl,
2-chloro-5-fluorophenyl, 3-chloro-2-fluorophenyl, 3-chloro-4-fluorophenyl, 3-chloro-5-
15 fluorophenyl, 3-chloro-6-fluorophenyl, 4-chloro-2-fluorophenyl, 4-chloro-3-fluorophenyl,
4-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-4-
fluorophenyl, 3-bromo-2-fluorophenyl, 3-bromo-5-fluorophenyl, 3-bromo-6-fluorophenyl,
4-bromo-2-chlorophenyl, 4-bromo-3-chlorophenyl, 3,4-dichloro-2-fluorophenyl, 3,5-
dichloro-2-fluorophenyl, 3,5-dichloro-4-fluorophenyl, 4,5-dichloro-3-fluorophenyl, 3,4-
20 dibromo-2-fluorophenyl, 3,5-dibromo-2-fluorophenyl, 4,5-dibromo-3-fluorophenyl, 2-
chloro-3,4-difluorophenyl, 2-chloro-3,5-difluorophenyl, 3-chloro-4,5-difluorophenyl, 3-
chloro-5,6-difluorophenyl, 3,4-dibromo-2-chlorophenyl, 3,5-dibromo-2-chlorophenyl, 4,5-
dibromo-3-chlorophenyl, 2-bromo-3,4-difluorophenyl, 2-bromo-3,5-difluorophenyl, 3-
bromo-4,5-difluorophenyl, 2-bromo-3,4-dichlorophenyl, 2-bromo-3,5-dichlorophenyl, 3-
25 bromo-4,5-dichlorophenyl, 4-bromo-3-chloro-2-fluorophenyl, 4-bromo-2-chloro-3-
fluorophenyl, 2-bromo-3-chloro-4-fluorophenyl, 5-bromo-3-chloro-2-fluorophenyl, 5-
bromo-2-chloro-3-fluorophenyl, 2-bromo-3-chloro-5-fluorophenyl, 5-bromo-4-chloro-3-
fluorophenyl, 5-bromo-3-chloro-4-fluorophenyl, 3-bromo-4-chloro-5-fluorophenyl, 2-
fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, 2-trifluoromethylphenyl, 3-
30 trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 2-fluoro-5-chlorophenyl, 2-
trifluoromethoxyphenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3-fluoro-5-
trifluoromethylphenyl, 2-chloro-5-trifluoromethylphenyl, 2-chloro-3-
trifluoromethylphenyl, 3-chloro-5-trifluoromethylphenyl, 3-fluoro-5-
trifluoromethylphenyl,

In an embodiment of the invention and/or embodiments thereof, R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,6-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 3-chloro-5-fluorophenyl, 3-chloro-6-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl, 2-fluoro-3-chlorophenyl, and 2,3,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,6-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 3-chloro-5-fluorophenyl, 2-fluoro-3-chlorophenyl, 2,3,5-trichlorophenyl, and 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

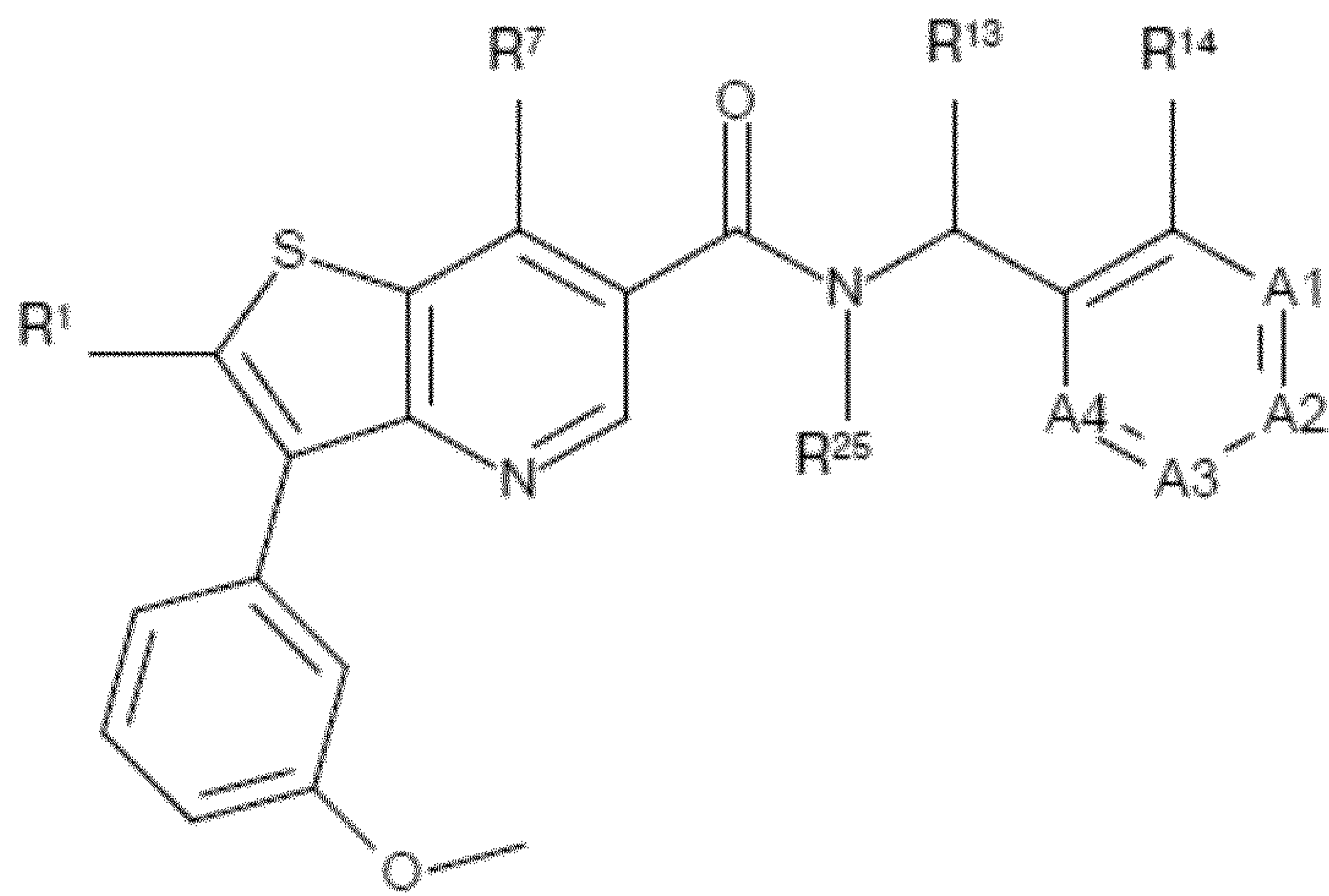
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Idi), (Idii), (Idiii), (Idiv), (Idv), (Idvi), (Idvii) or (Idviii)



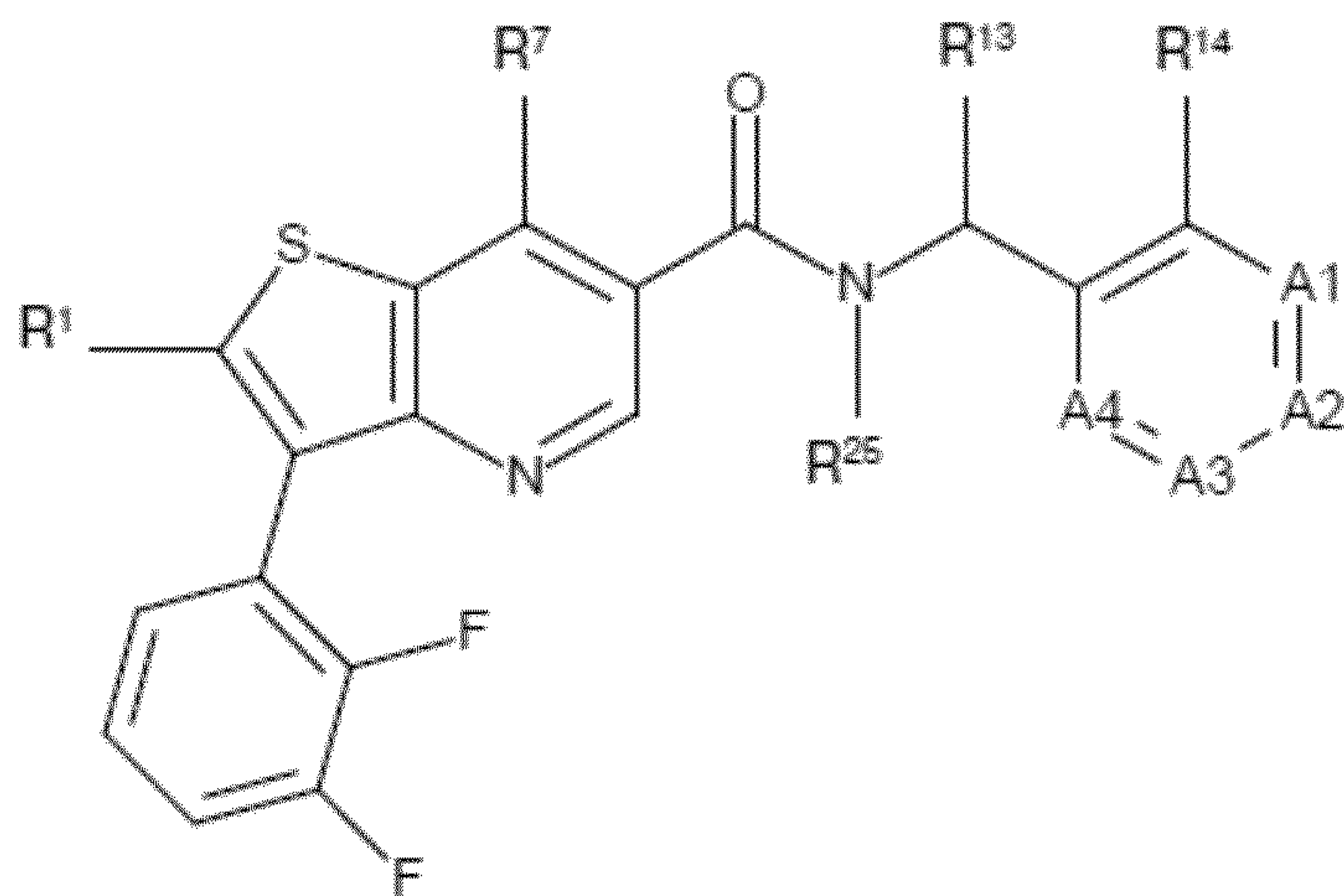
Formula (Idi)



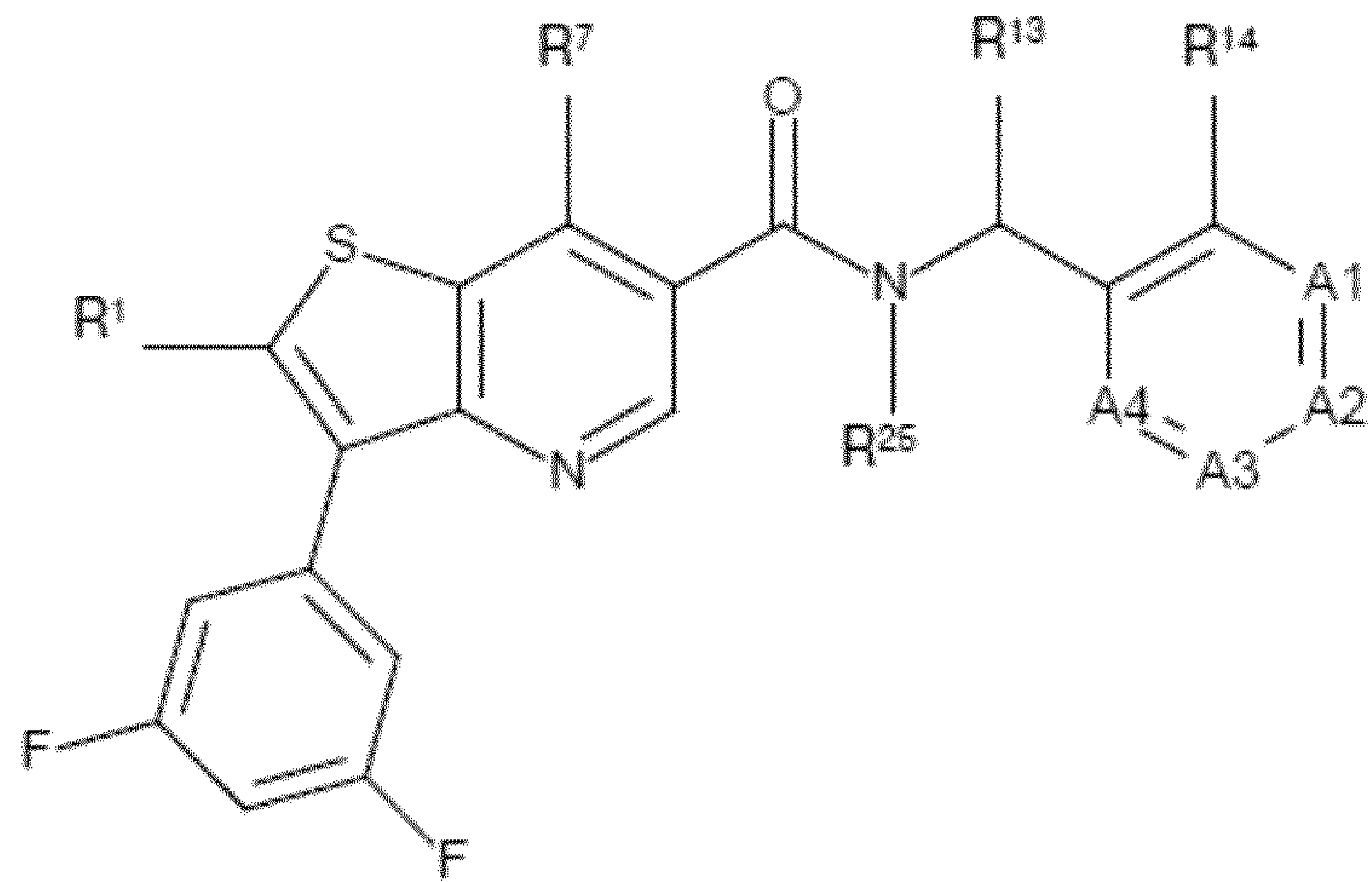
Formula (Idii)



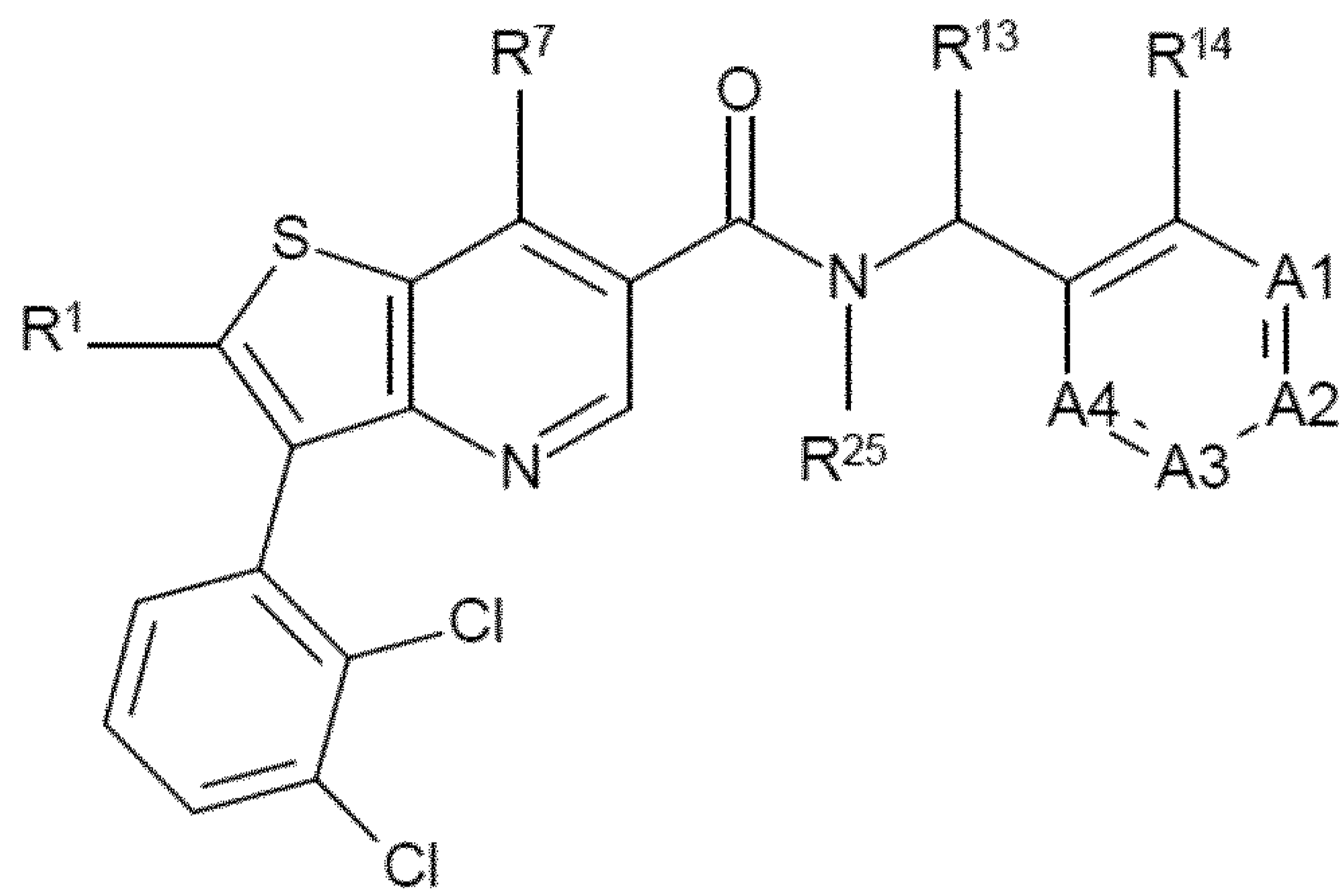
Formula (Idiii)



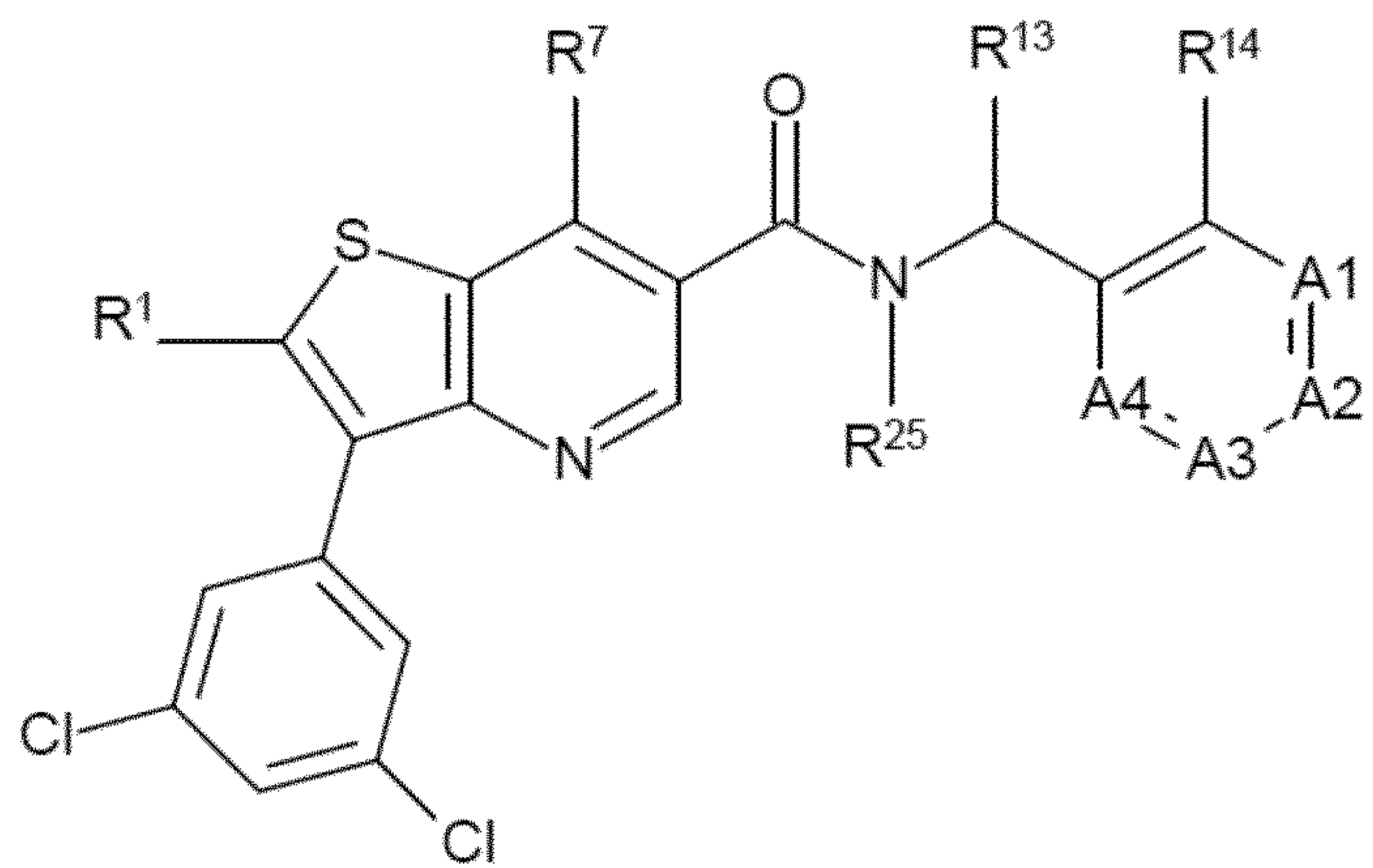
Formula (Idiv)



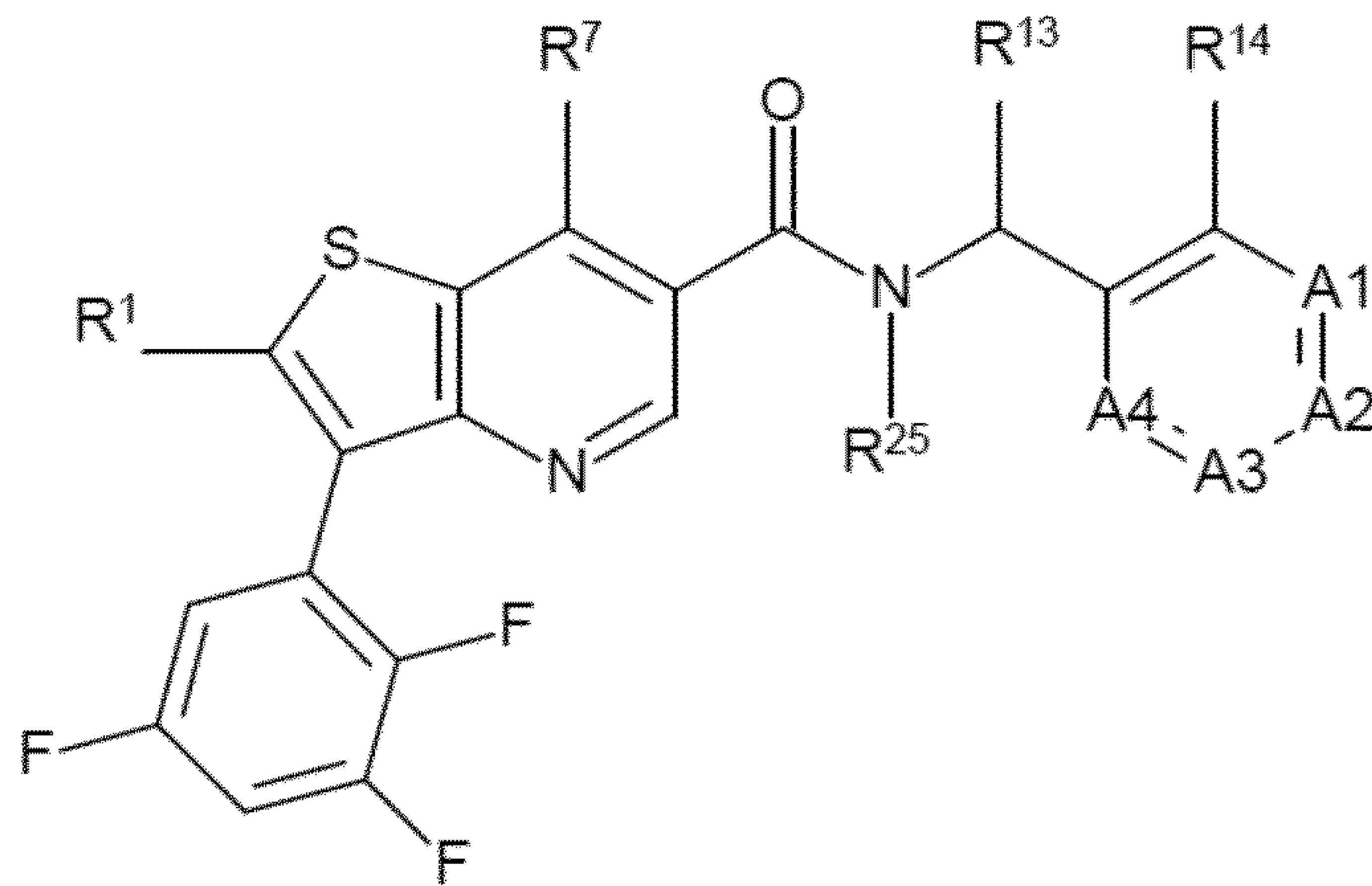
Formula (Idv)



Formula (dvi)



Formula (Idvii)



Formula (Idviii)

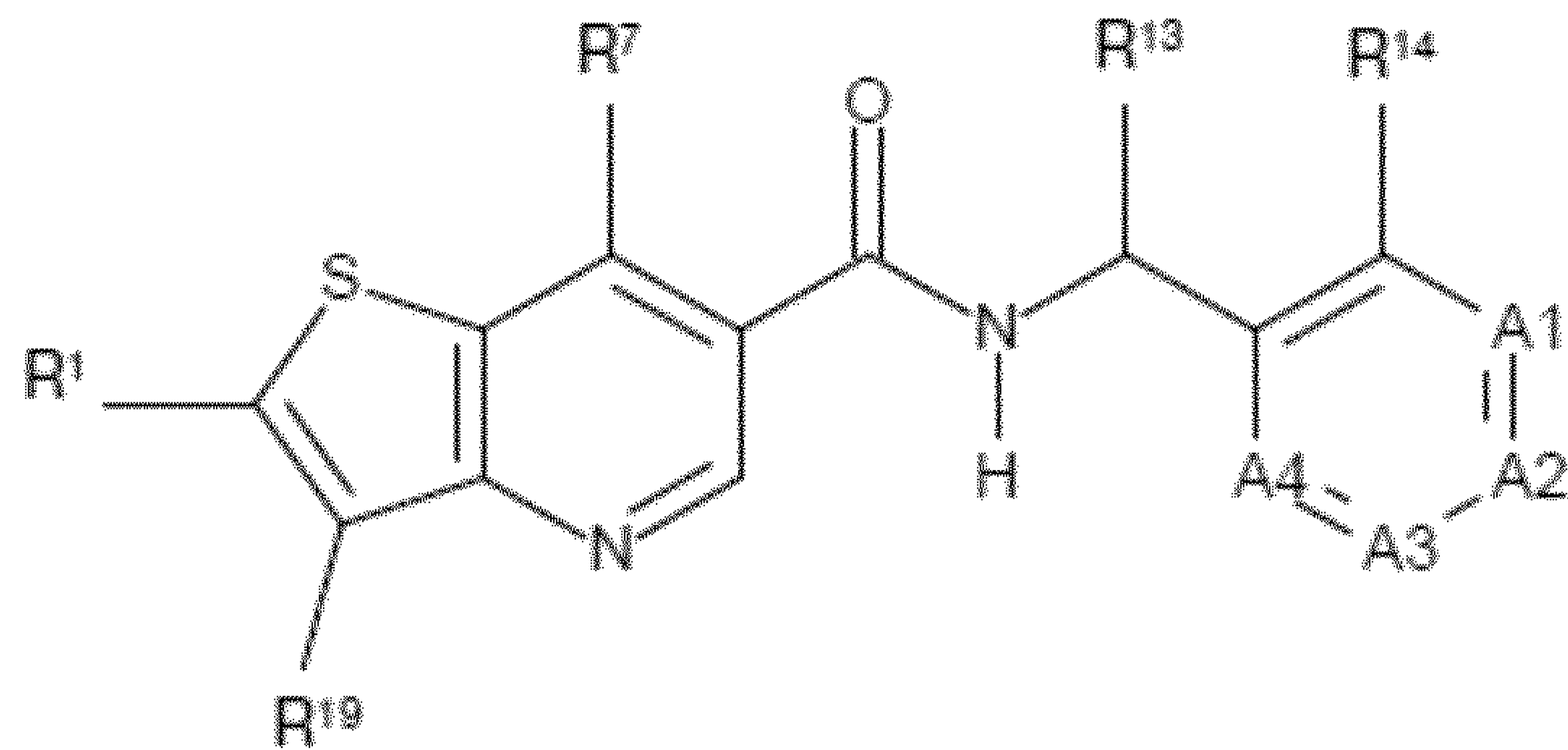
or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 , R^{13} , R^{14} , A1, A2, A3, A4 and R^{25} are defined as in any of the embodiments
5 described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Idi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
embodiments thereof, the compounds are according to Formula (Idii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds
10 are according to Formula (Idiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Idiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Idv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to
15 Formula (Idvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Idvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Idviii), preferably in form of the (*S*)-enantiomer.

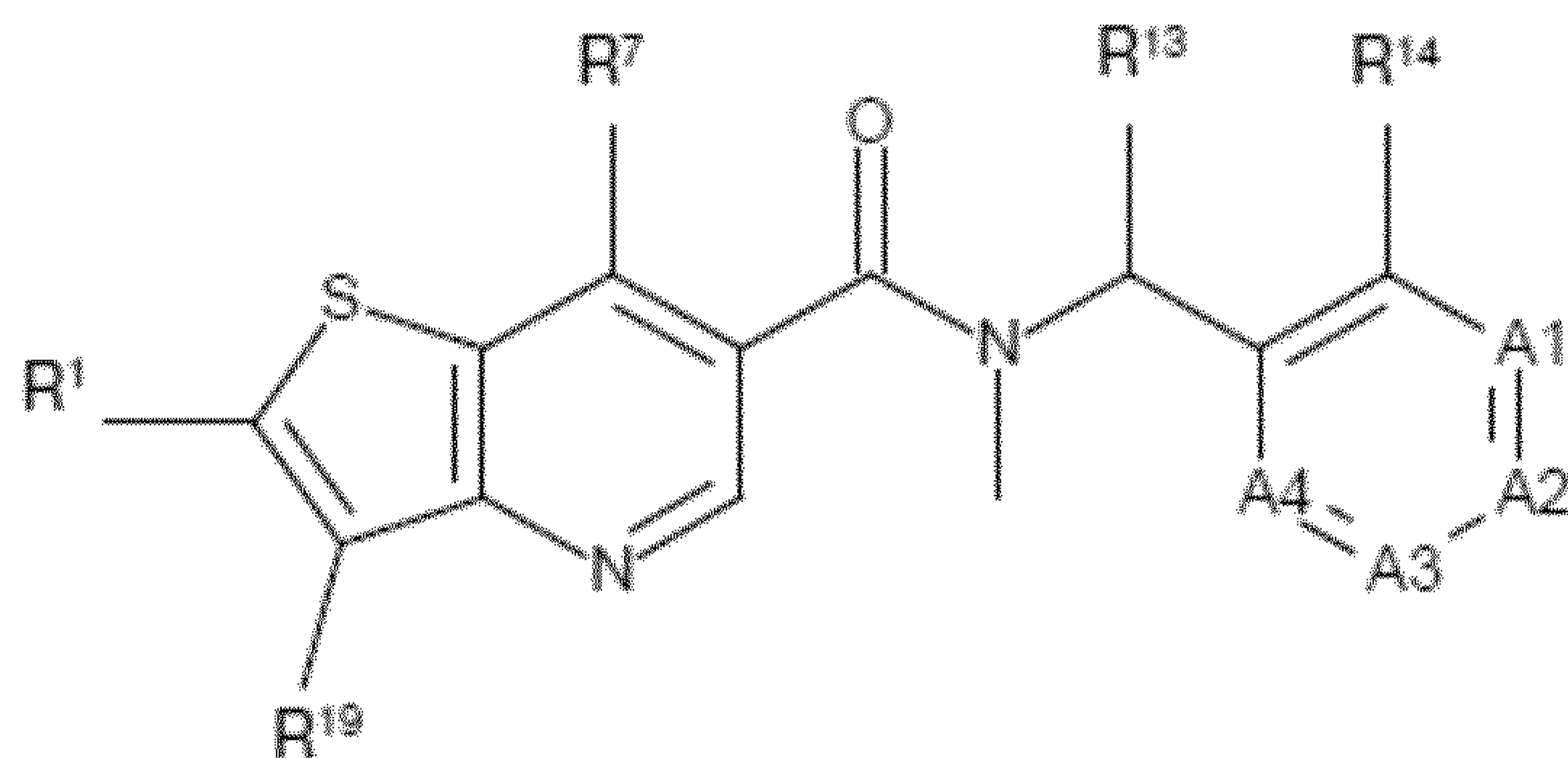
The invention provides a compound according to the invention and/or embodiments thereof,
20 wherein R^{25} is defined as below.

In an embodiment of the invention and/or embodiments thereof, R^{25} is hydrogen or methyl, more preferably hydrogen.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iei) or (Ieii)



Formula (Iei)



Formula (Ieii)

- 5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 , R^{13} , R^{14} , A1, A2, A3, A4 and R^{19} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iei), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Ieii), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 and R^7 are defined as below.

In an embodiment of the invention and/or embodiments thereof,

- 15 R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

- 20 C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and NR^2R^3 ,

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

and

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

10 R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,
R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,
R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl.

In an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

15 hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

20 R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl.

and

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

5 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

10 wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

15 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl.

In one embodiment of the invention and/or embodiments thereof,

20 R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride.

and

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

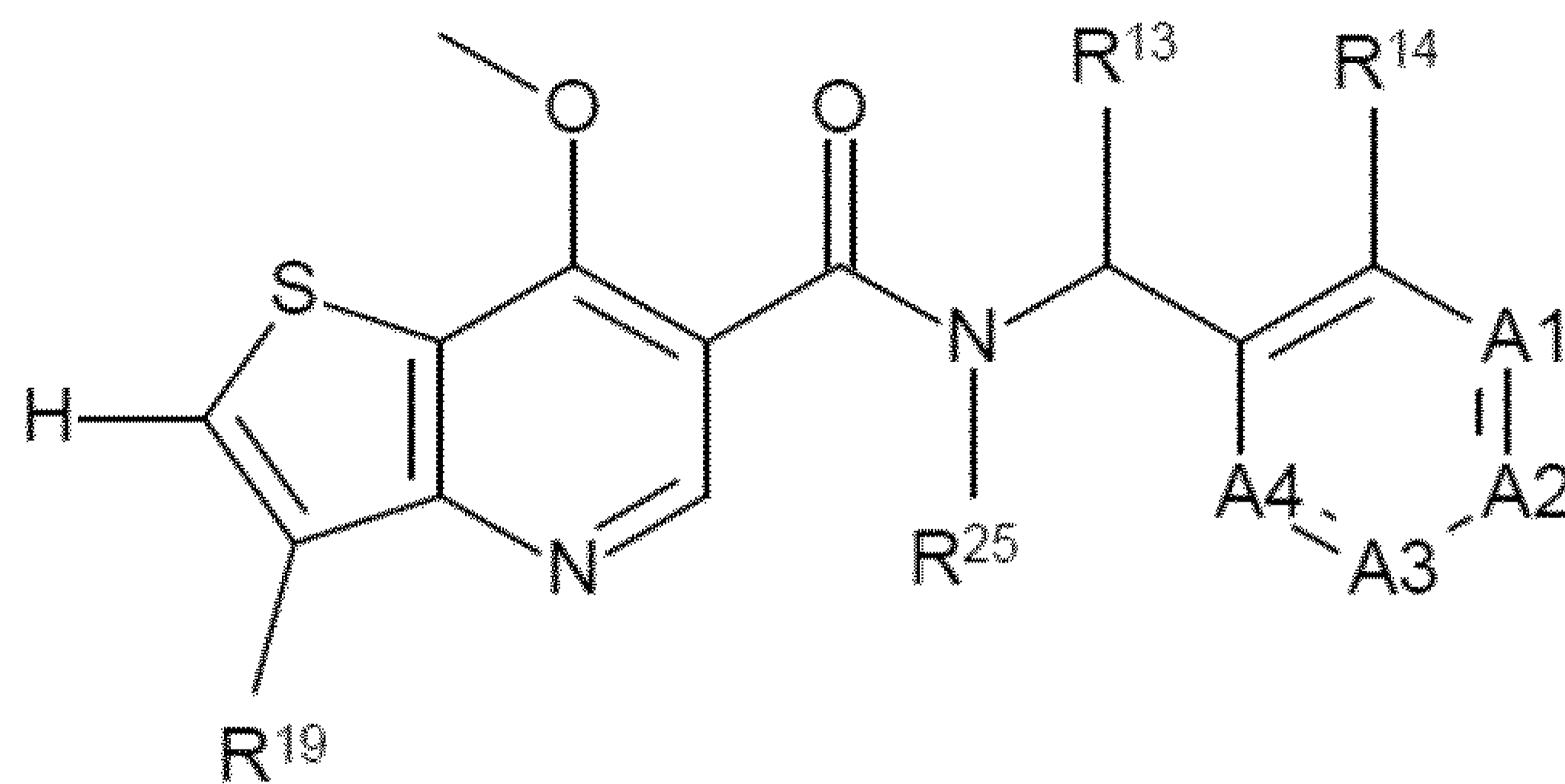
wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

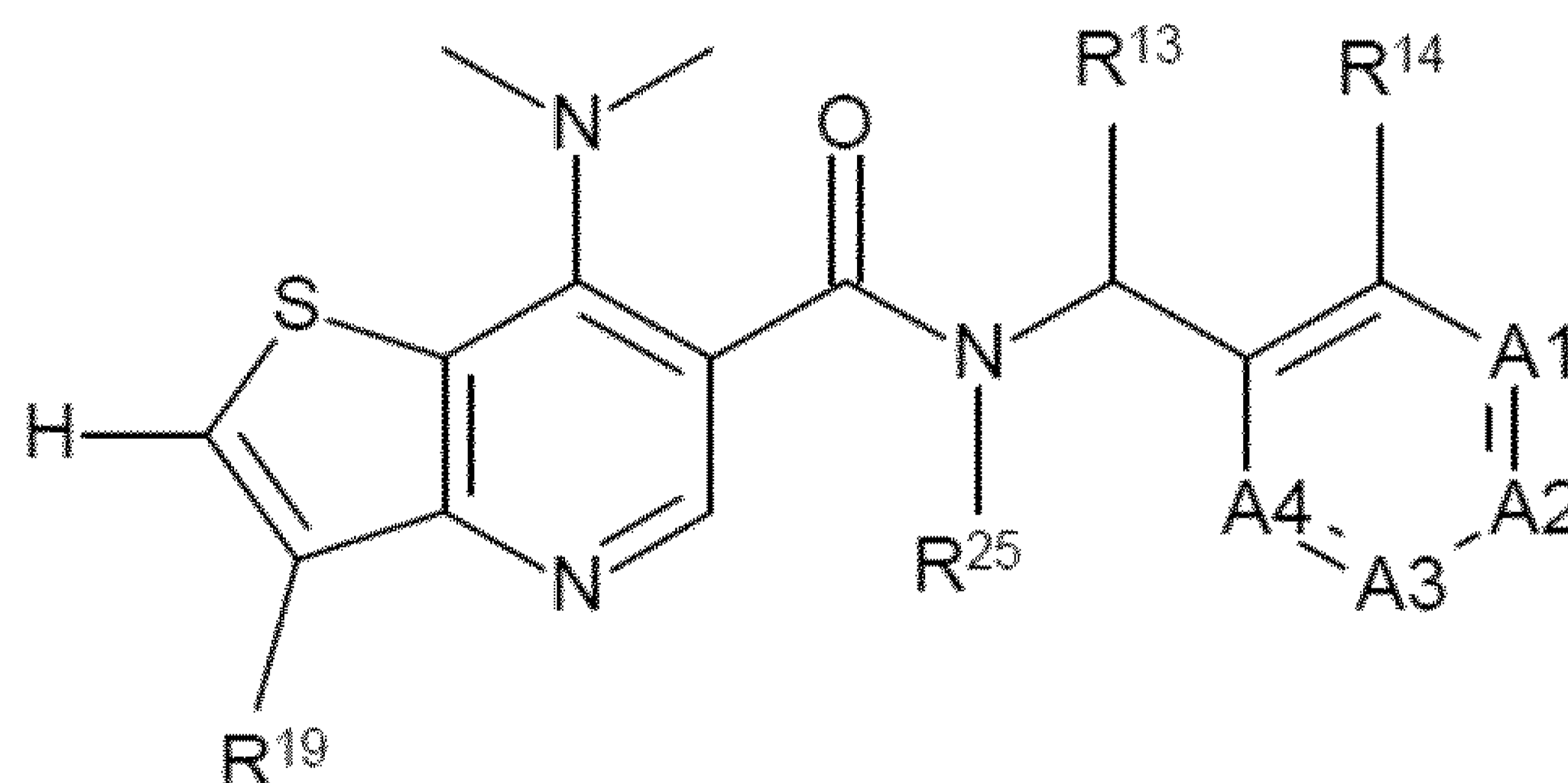
Suitably R⁷ is independently selected from the group consisting of

10 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, hydroxyethylamino, 2-hydroxyethylmethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl.

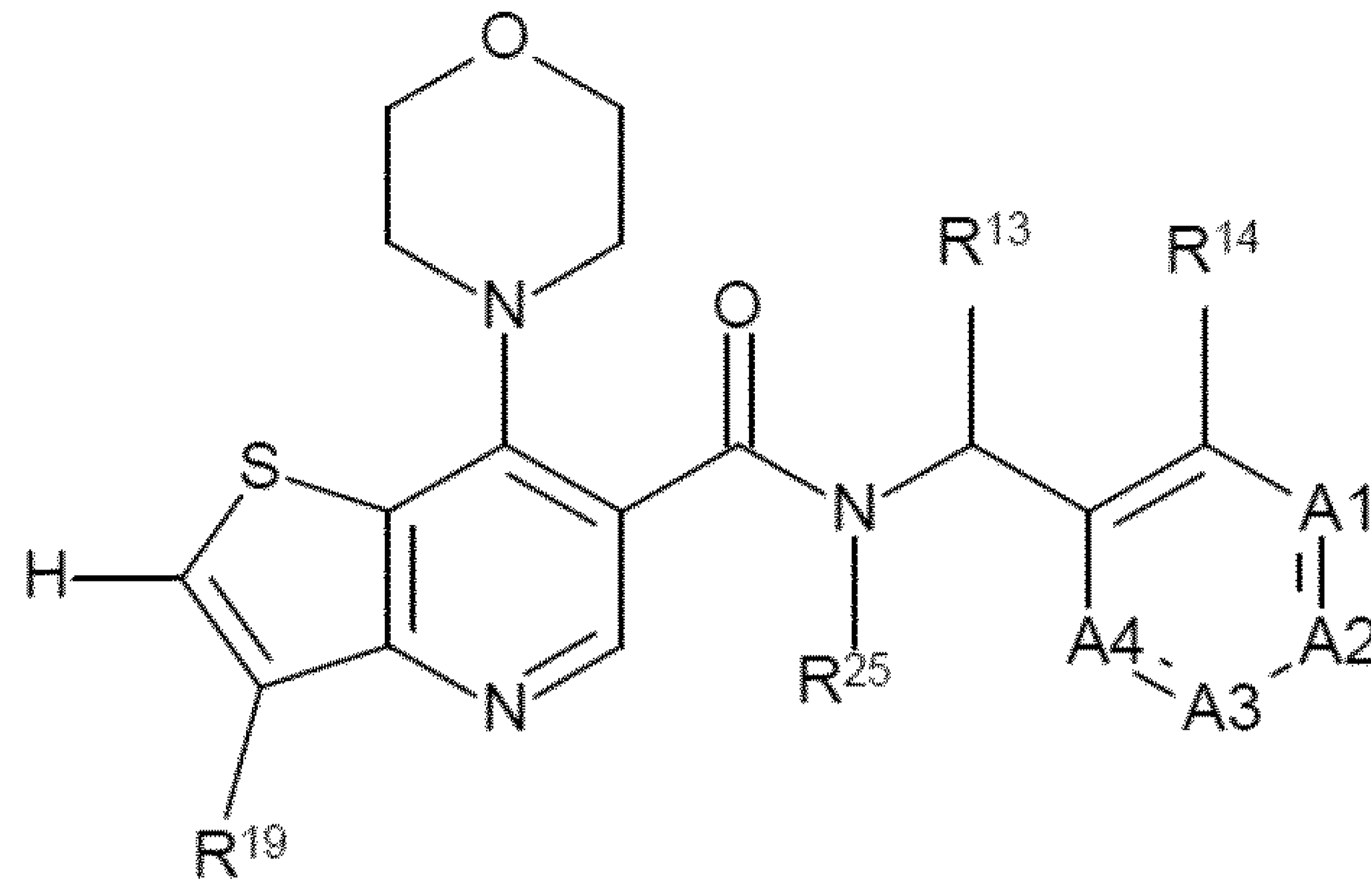
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ifi), (Ifii), (Ifiii), (Ifiv), (Ifv) or (Ifvi)



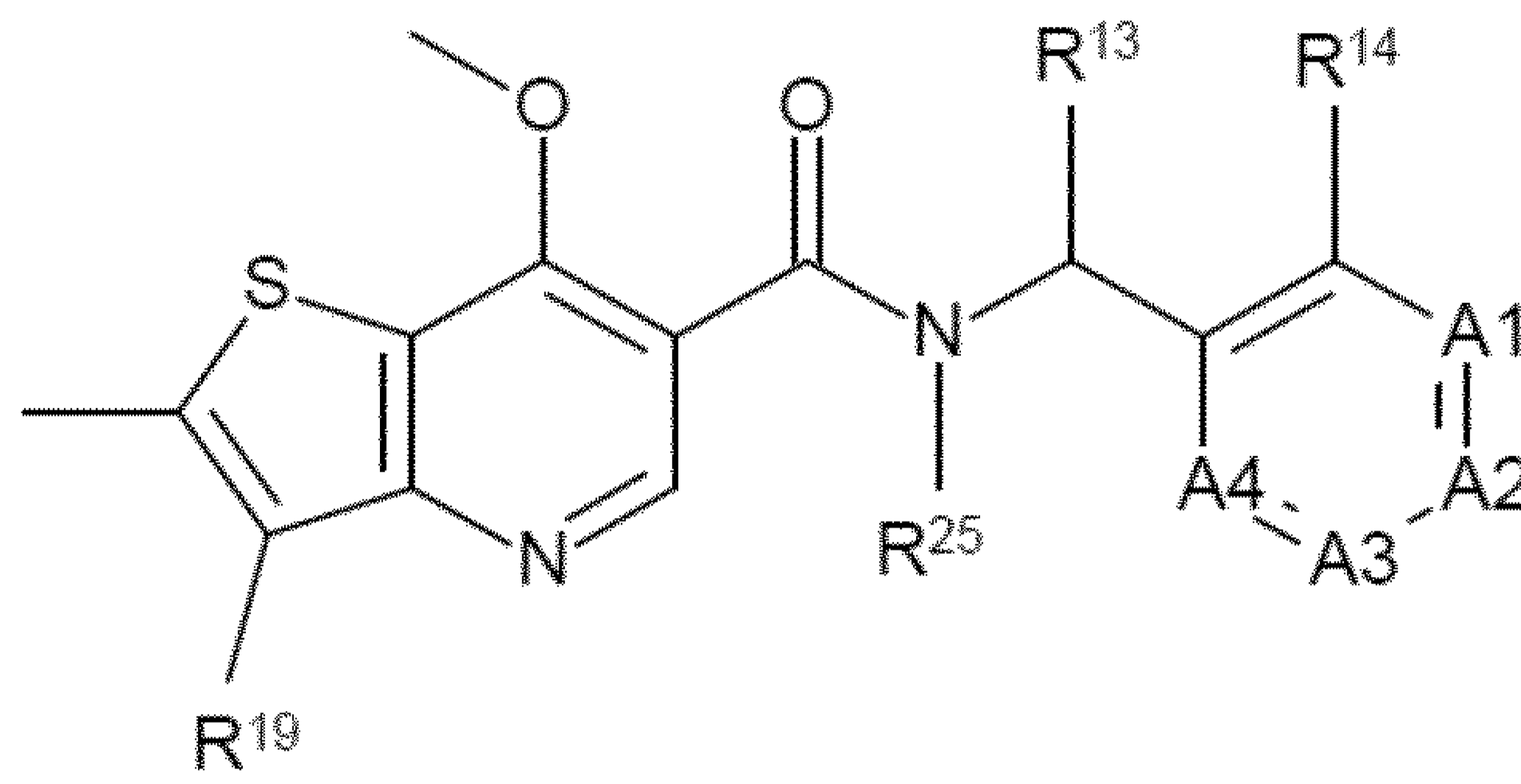
Formula (Ifi)



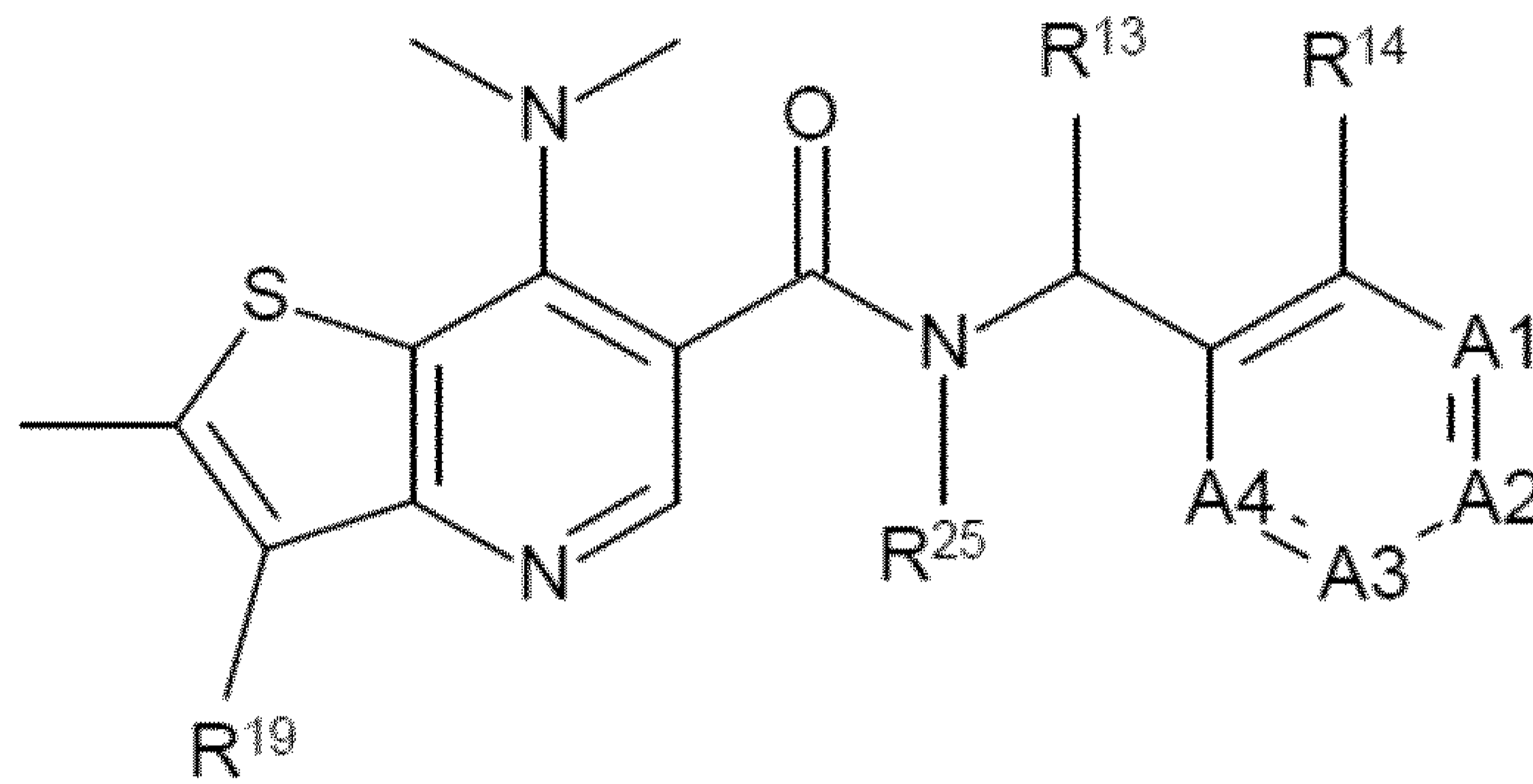
Formula (Ifii)



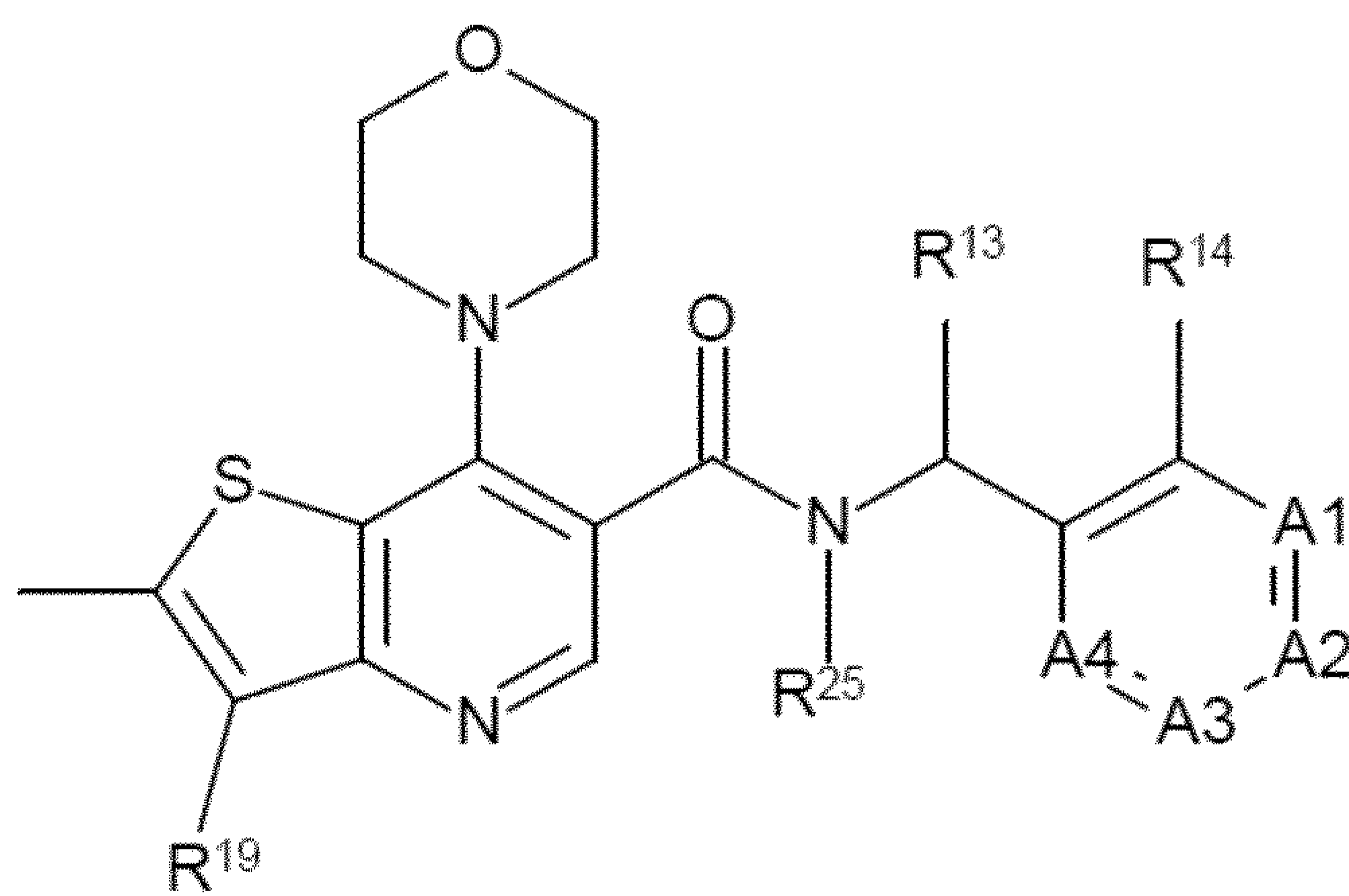
Formula (Ifiii)



Formula (Ifiv)



Formula (Ifv)



Formula (Ifvi)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ifi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 5 embodiments thereof, the compounds are according to Formula (Ifii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ifiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ifiv), preferably
 10 in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ifv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ifvi), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof,
 15 wherein R^1 as well as R^{13} , R^{14} , A1, A2, A3, A4 are defined as below.

In an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

20 wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and NR^2R^3 ,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

25 R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are

attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl.

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A₁ is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A₂ is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A₃ is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A₄ is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl.

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

- 5 A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,
A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,
A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,
wherein none, one or two of A1, A2, A3 and A4 are N.

- 10 In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

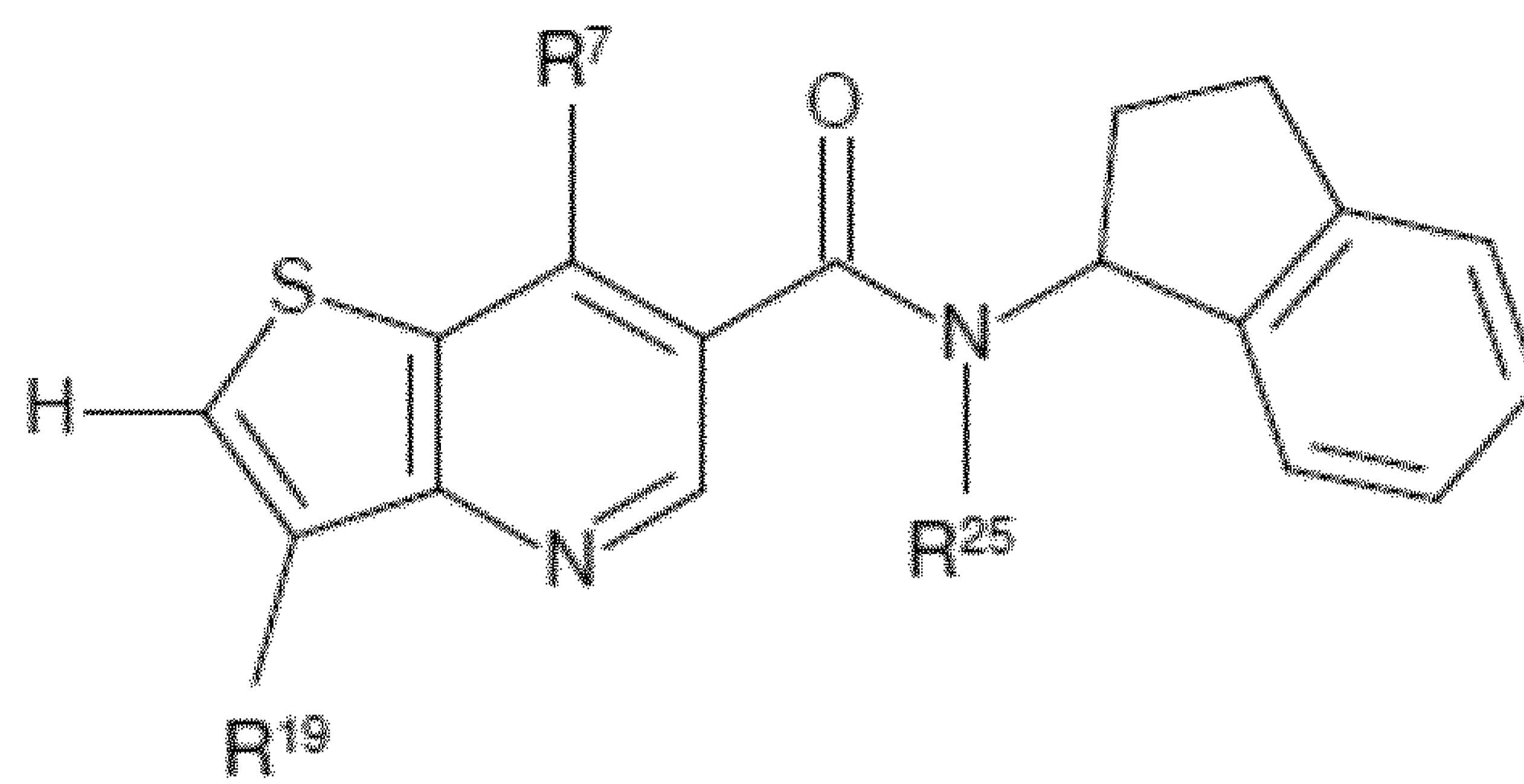
hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride.

and

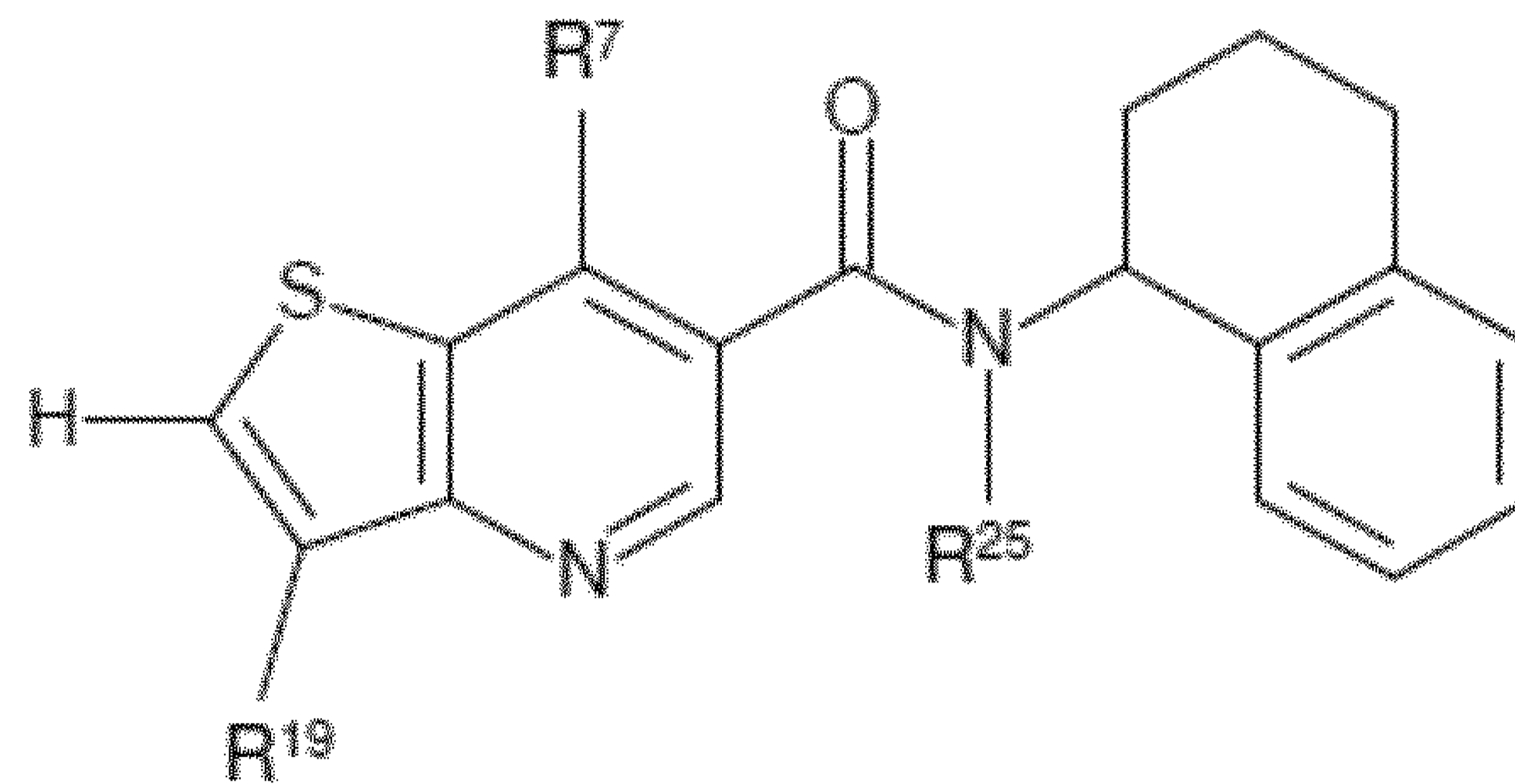
- 15 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH- or -O-,

- A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,
A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,
A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,
20 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,
wherein none, one or two of A1, A2, A3 and A4 are N.

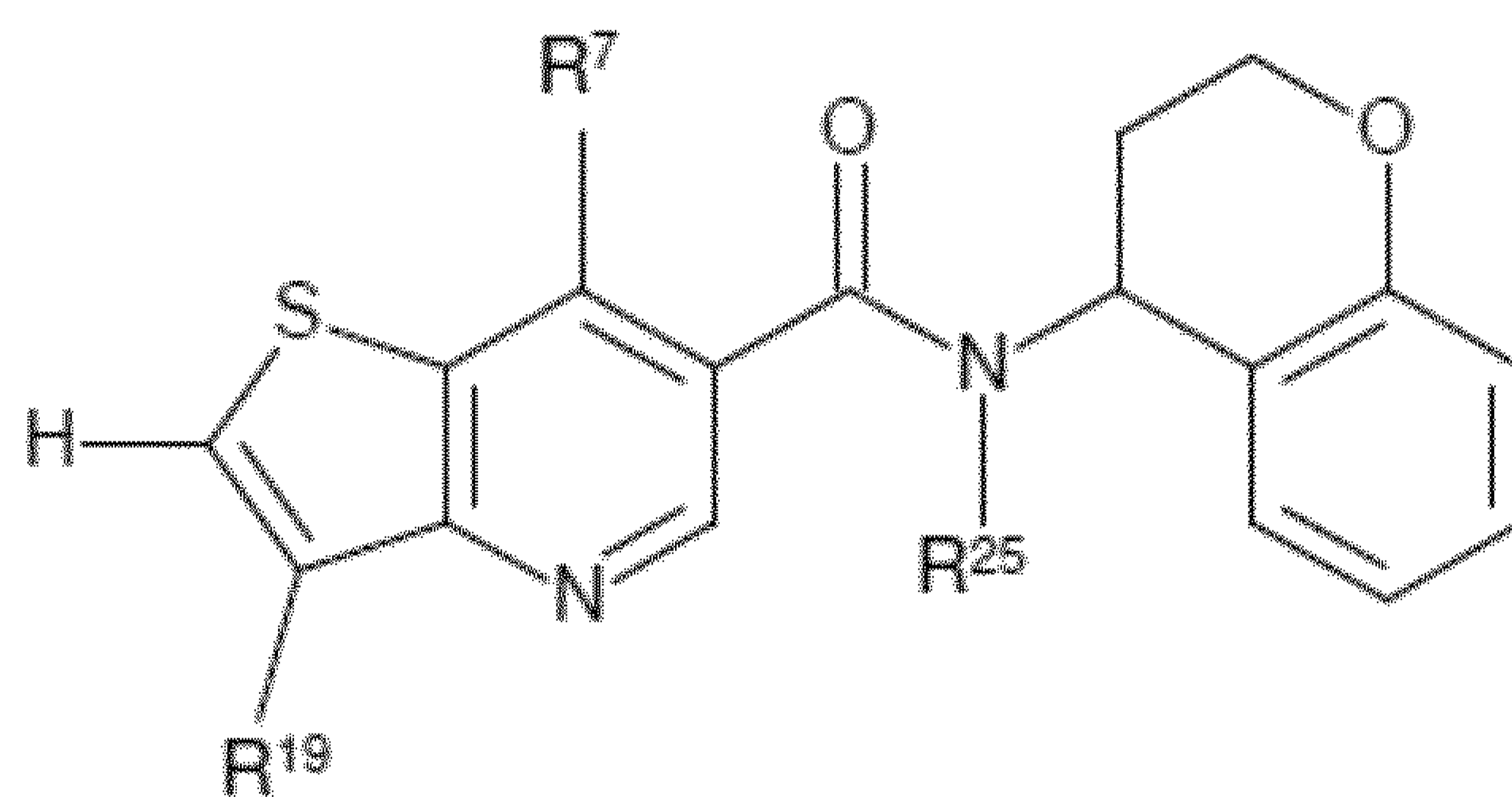
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igi), (Igii) (Igiii), (Igiv), (Igv) or (Igvi)



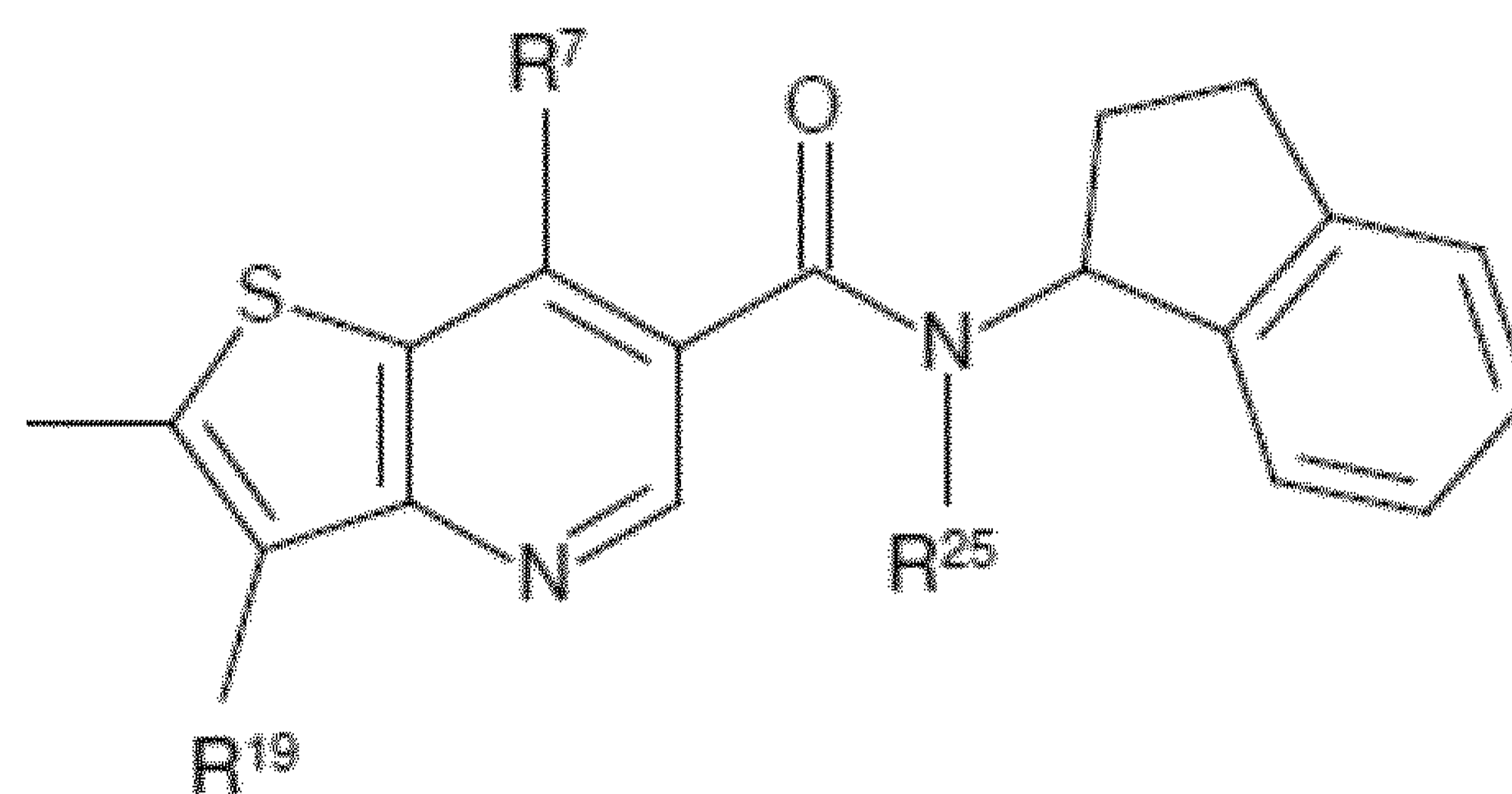
Formula (Igi)



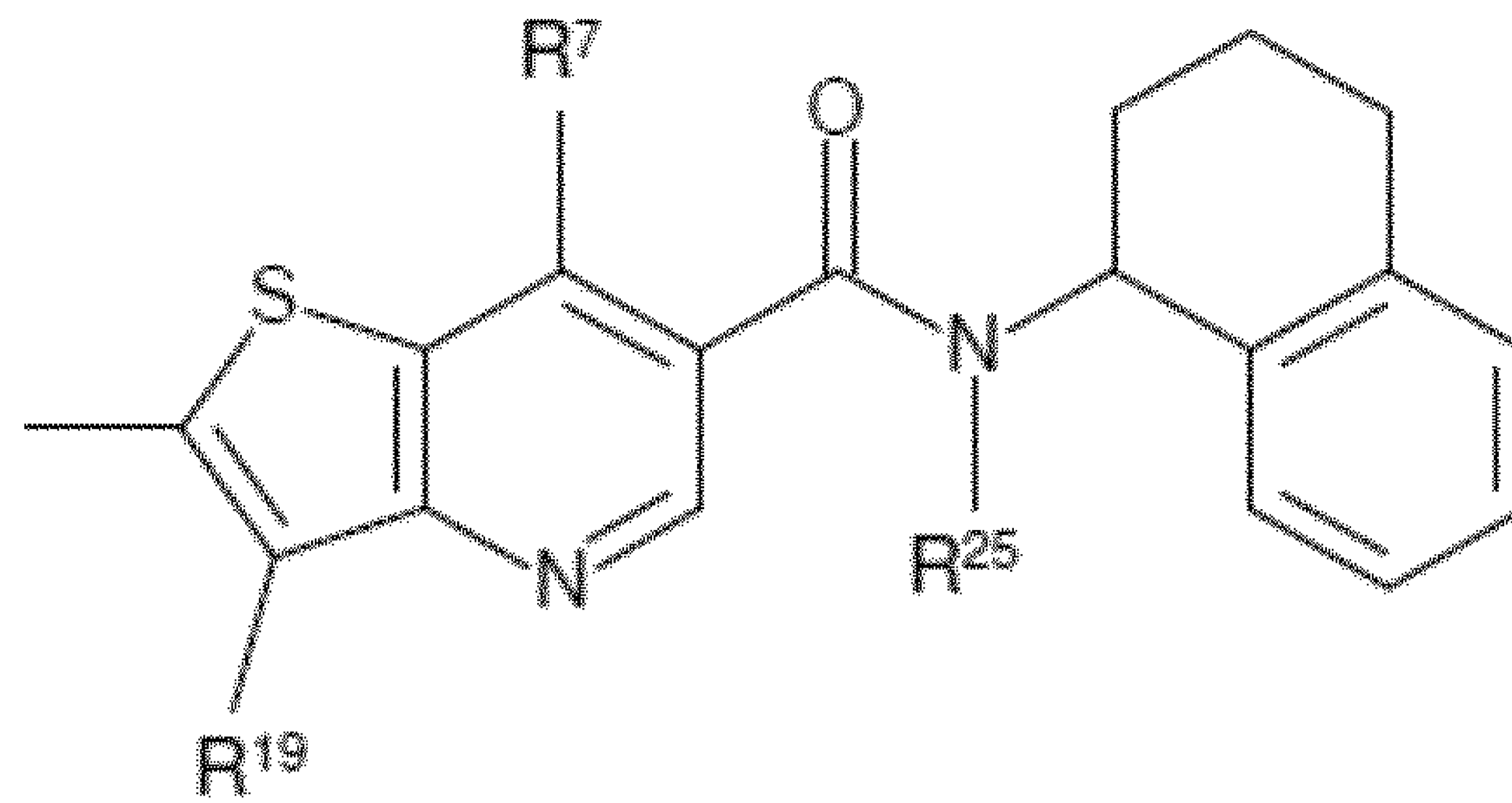
Formula (Igii)



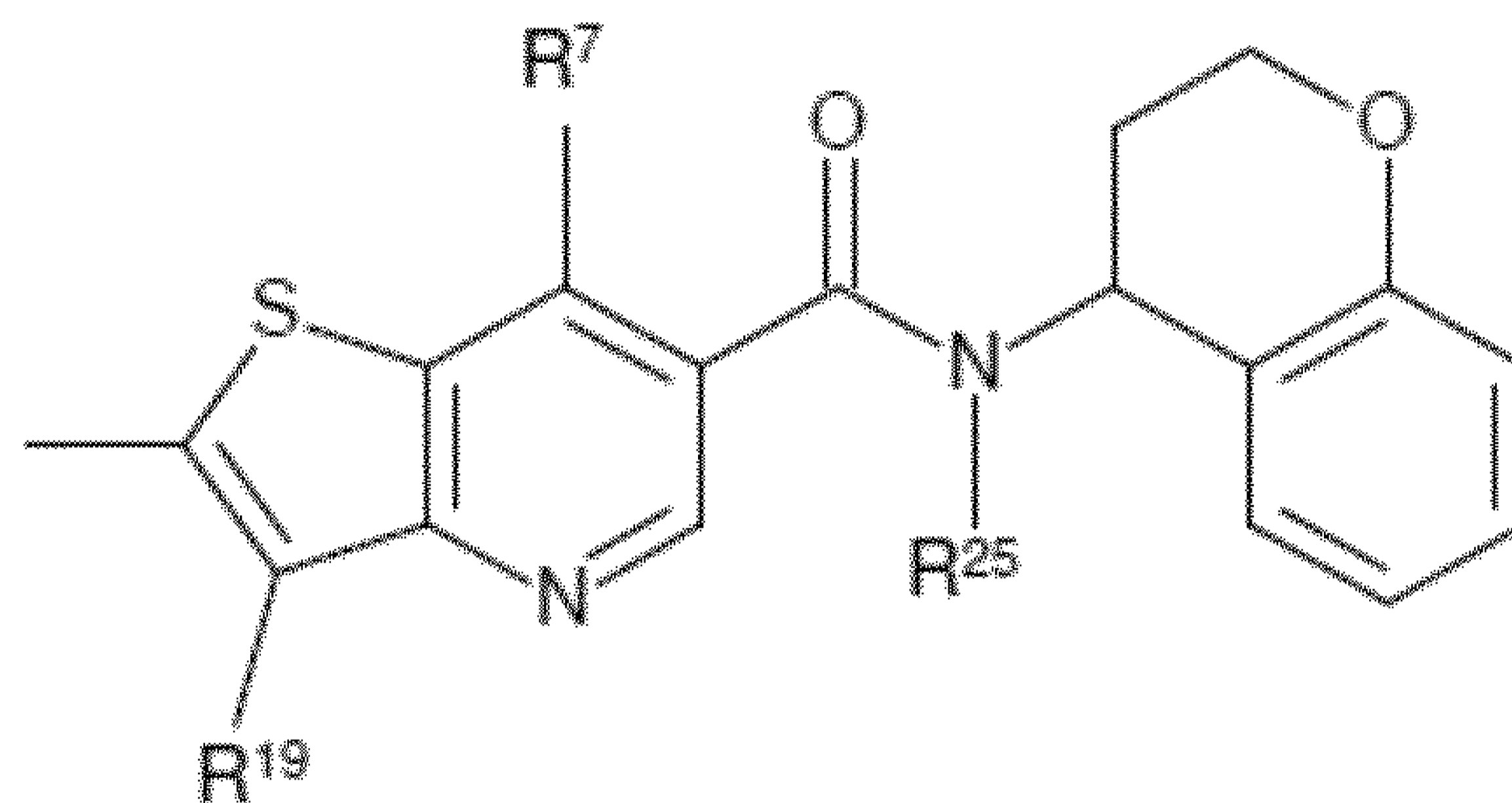
Formula (Igiii)



Formula (Igiv)



Formula (Igv)



Formula (Igi)

- 5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 , R^{19} and R^{25} are defined as in any of the embodiments described herein.

- In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Igi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igv), preferably in form of the (*S*)-enantiomer.
 15 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igi), preferably in form of the (*S*)-enantiomer.

In an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

- hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and
 20 $C(=O)NR^5R^6$,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R² and R³ are independently selected from the group consisting of

5 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

10 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

15 R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl.

and

20 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

25 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

5 hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

10 R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl.

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

15 A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

20 In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride.

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

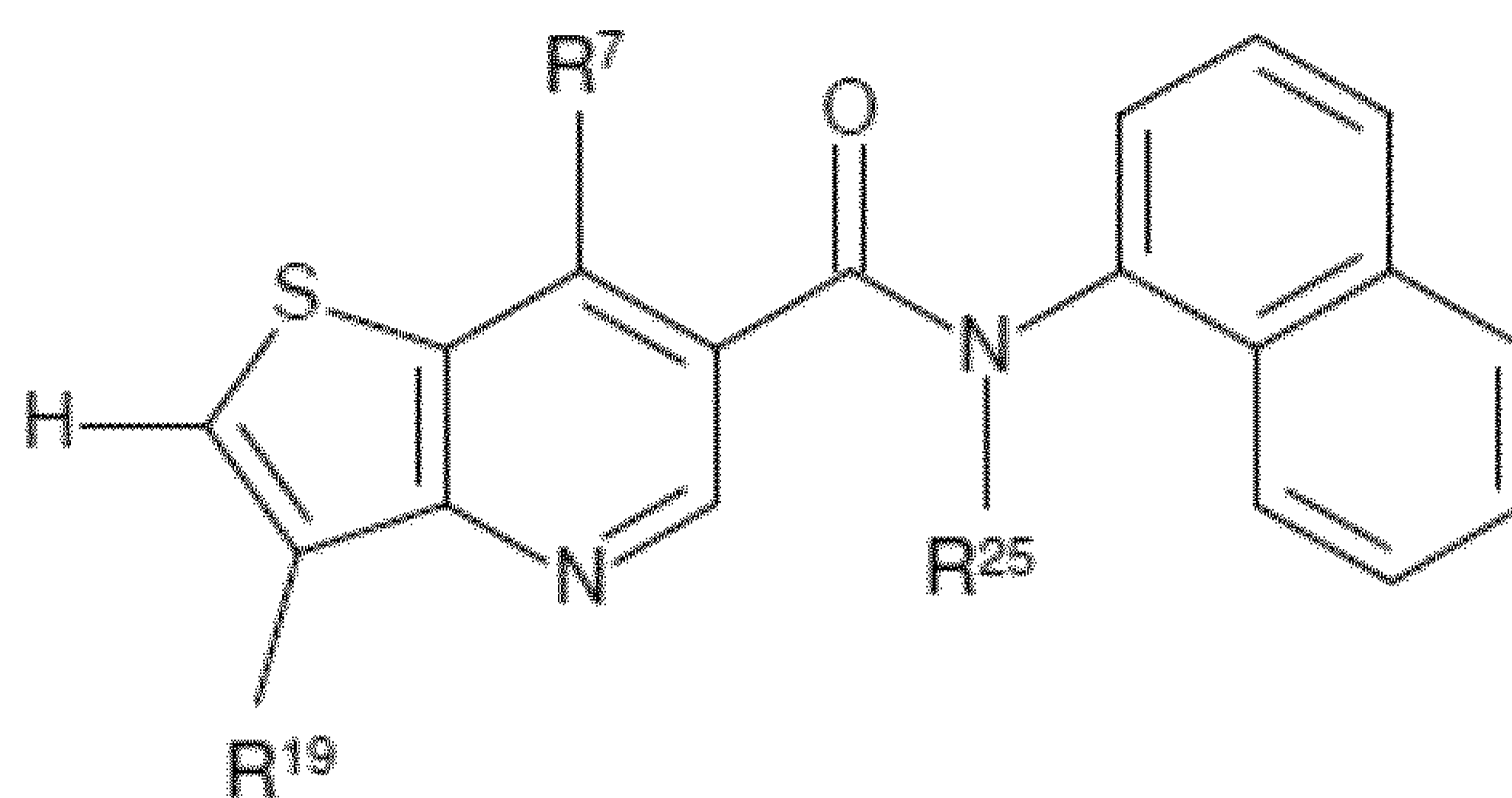
A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

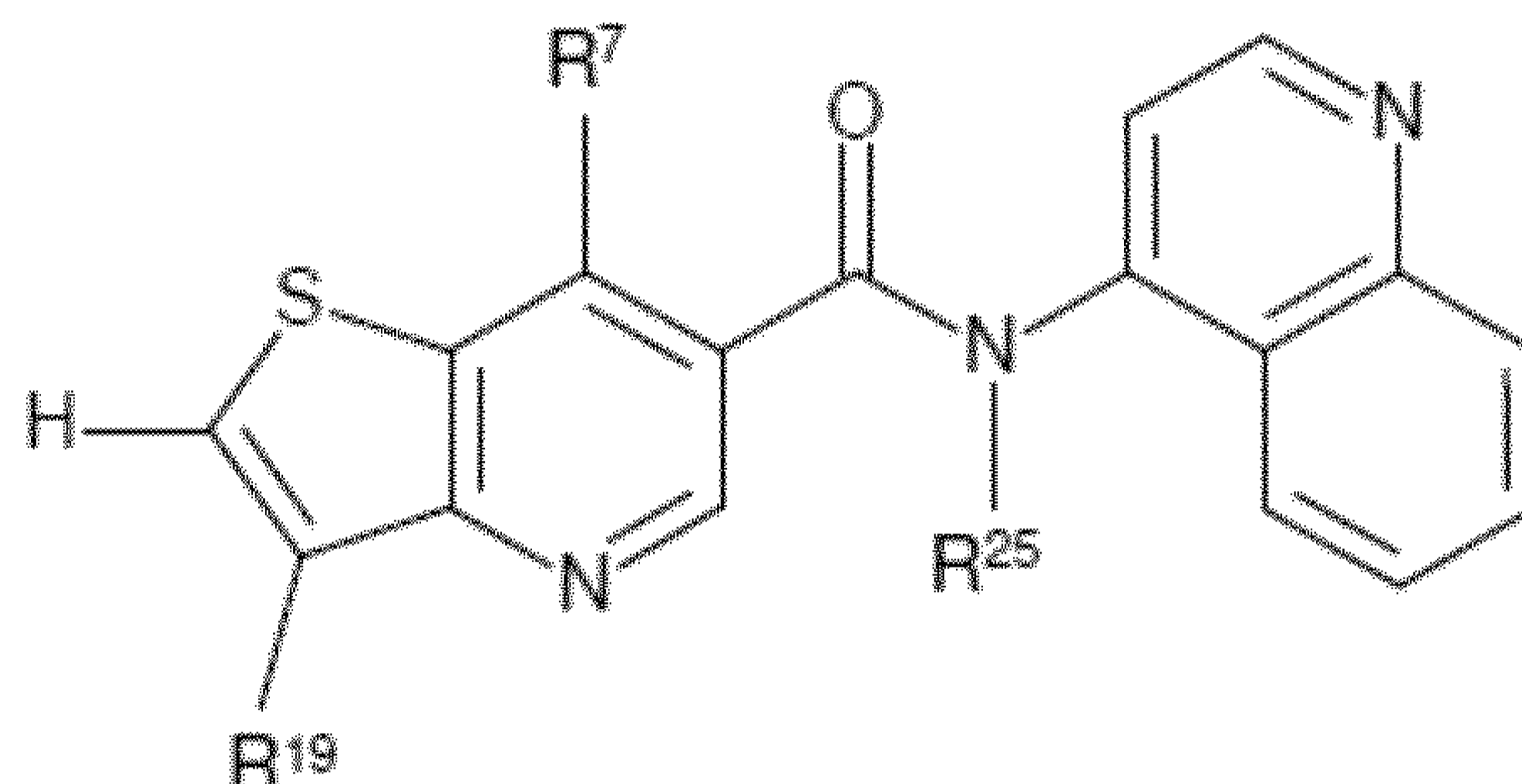
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

- 5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igvii), (Igviii) (Igx) or (Igx)

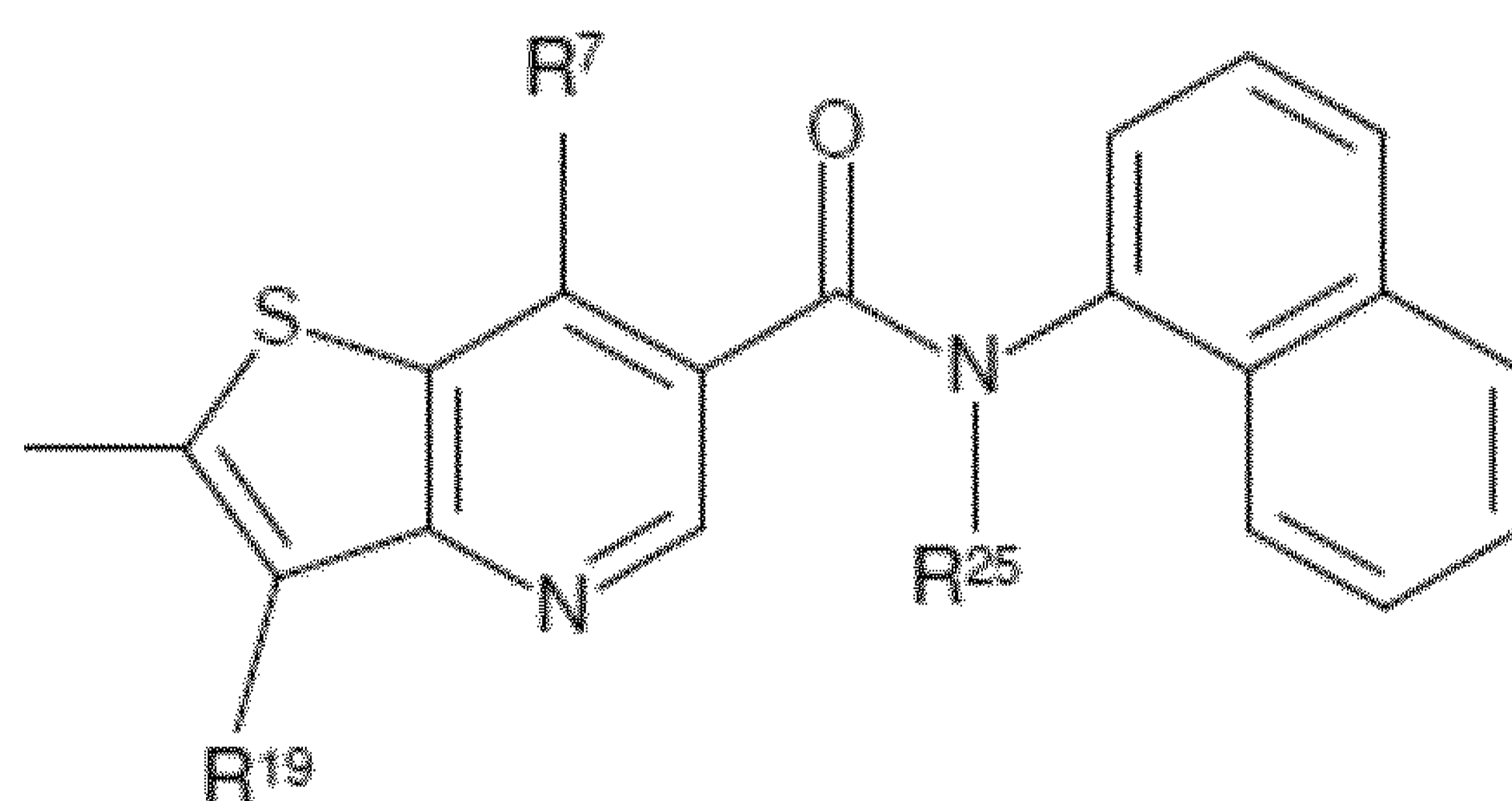


Formula (Igvii)

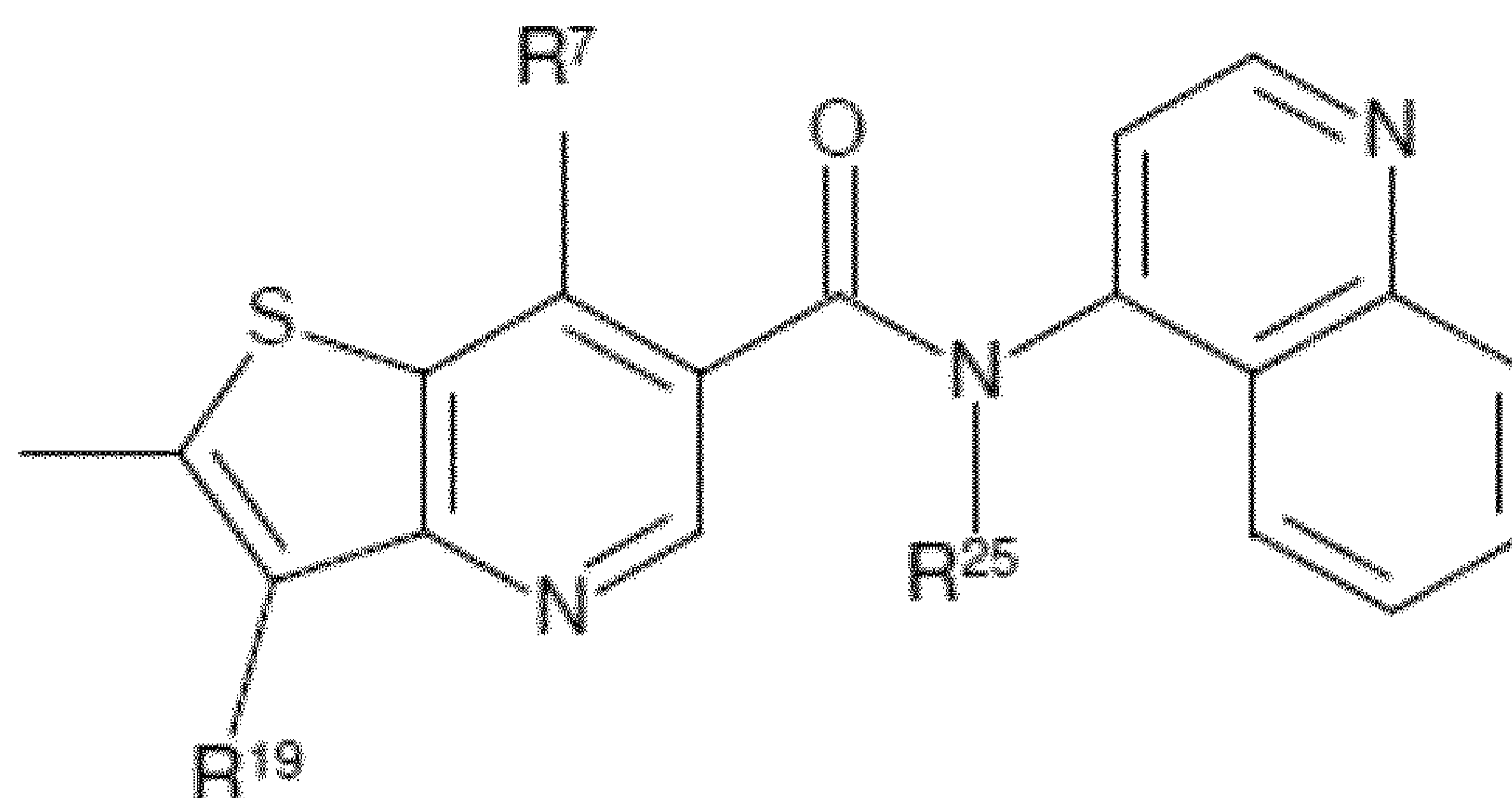


Formula (Igviii)

10



Formula (Igx)



Formula (Igx)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 , R^{19} and R^{25} are defined as in any of the embodiments described herein.

- 5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igviii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igx), preferably in form of the (*S*)-enantiomer. In an
- 10 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Igx), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 and R^{19} are defined as below.

In an embodiment of the invention and/or embodiments thereof,

- 15 R^1 is independently selected from the group consisting of
- hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

- 20 C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

- R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3
- 25 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

10 and

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

20 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

25 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20} , R^{21} , R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C₁₋₆-alkyl.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

5 hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R^5 and R^6 are independently selected from hydrogen and C₁₋₃-alkyl,

10 $R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C₁₋₃-alkyl,

and

R^{19} is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy, wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In one embodiment of the invention and/or embodiments thereof,

20 R^1 is independently selected from the group consisting of

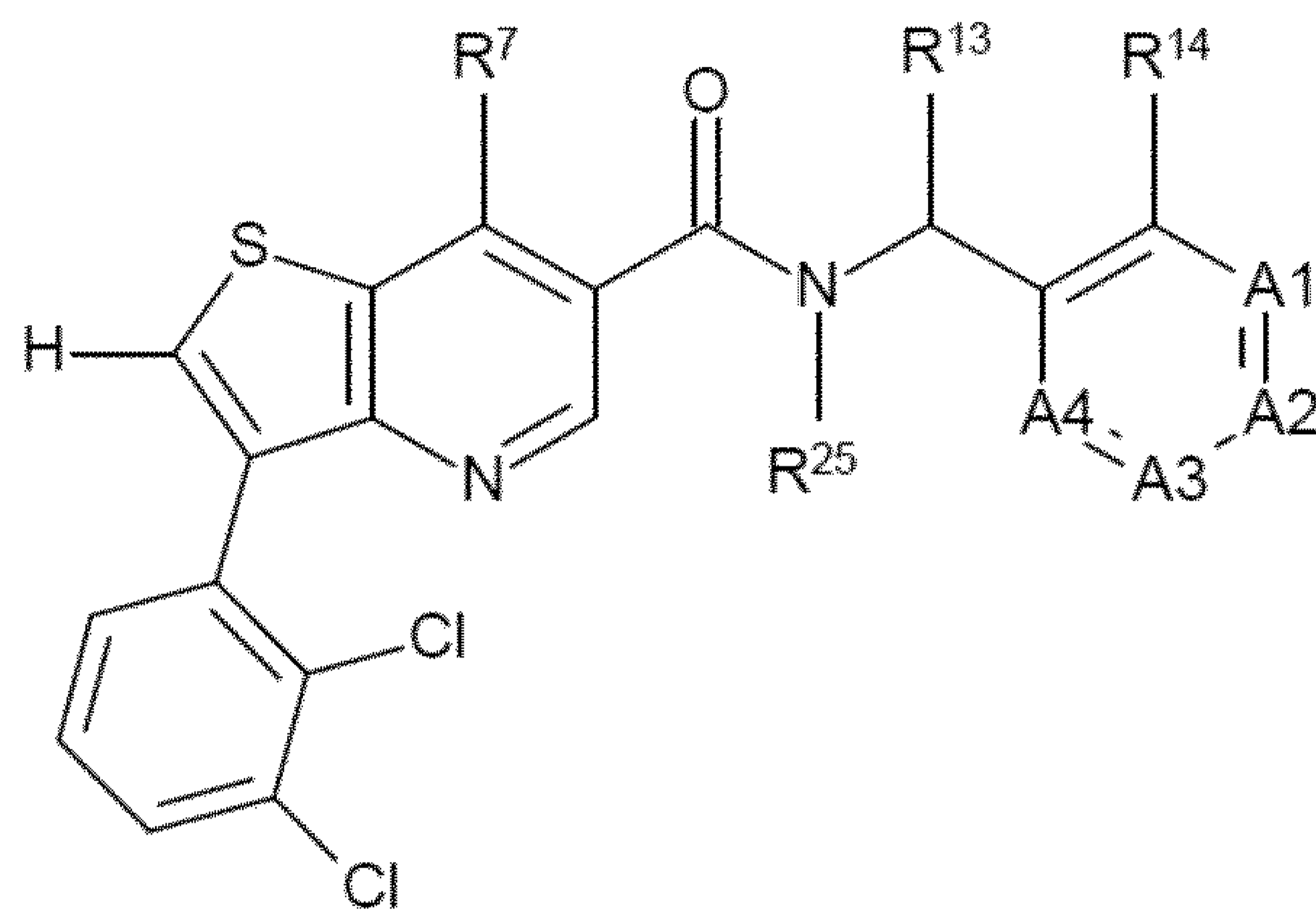
hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

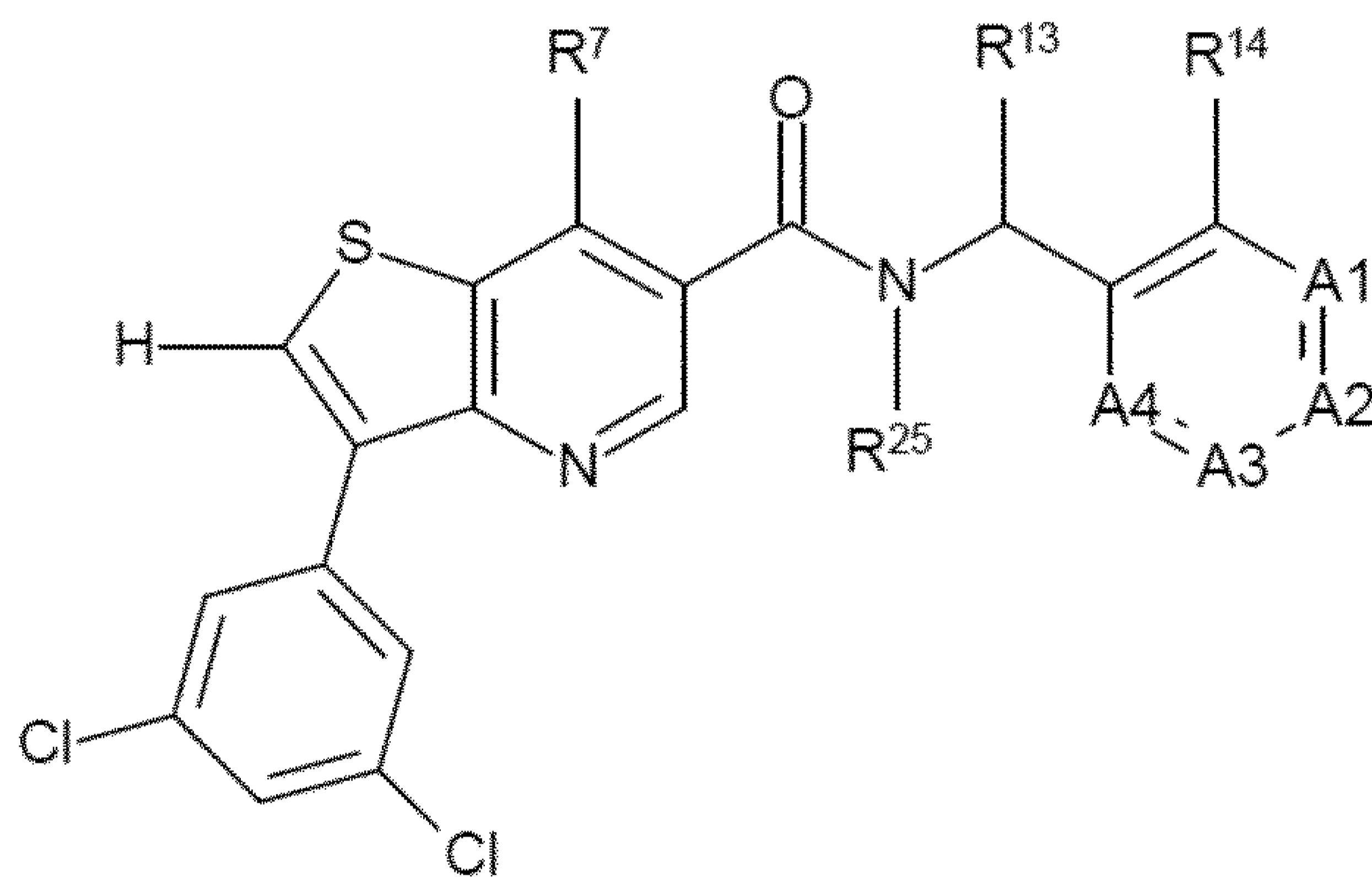
R^{19} is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-
25 trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably, 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl,

3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

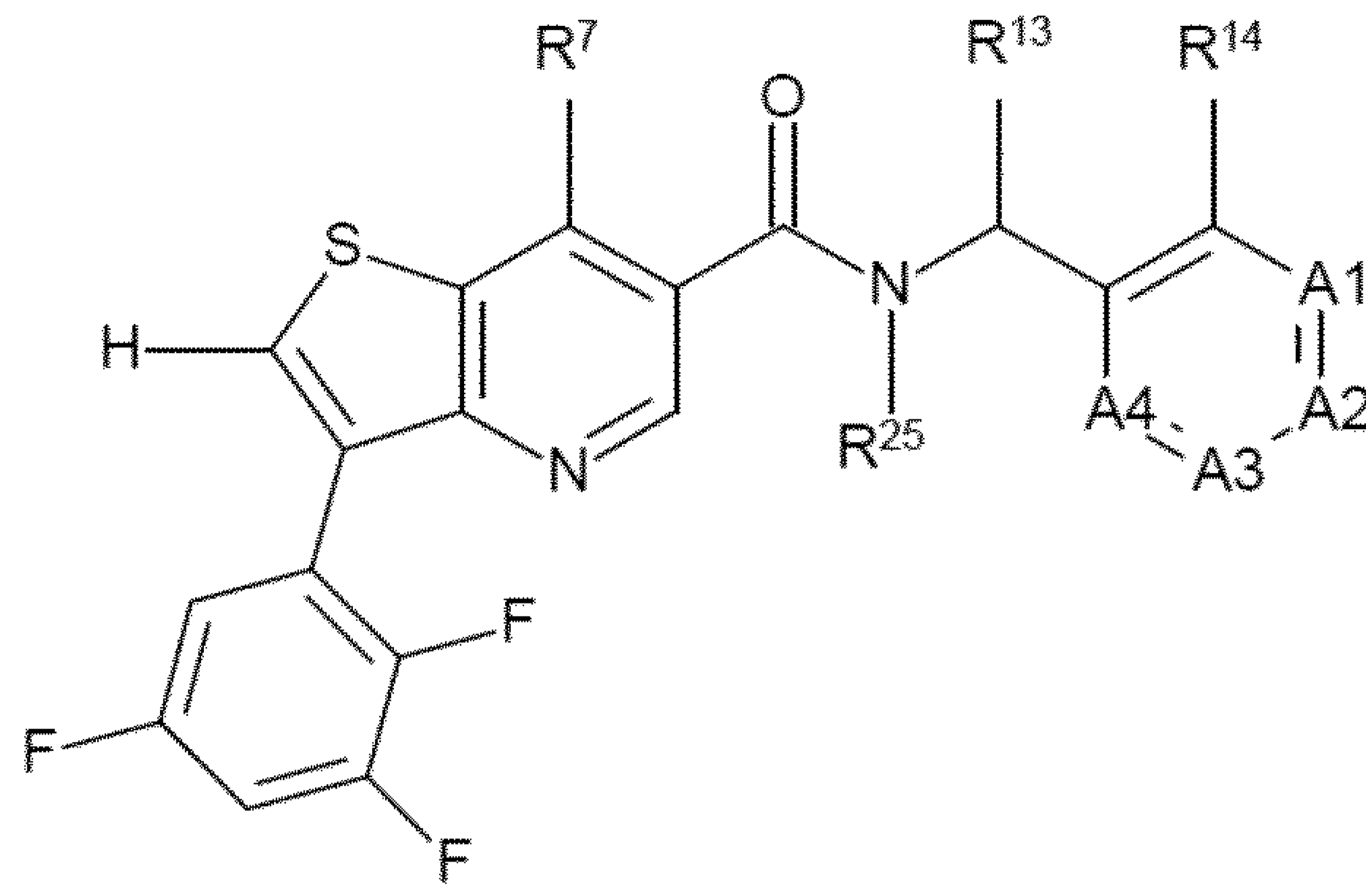
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ihi), (Ihii), (Ihiii), (Ihiv), (Ihvi) or (Ihvi)



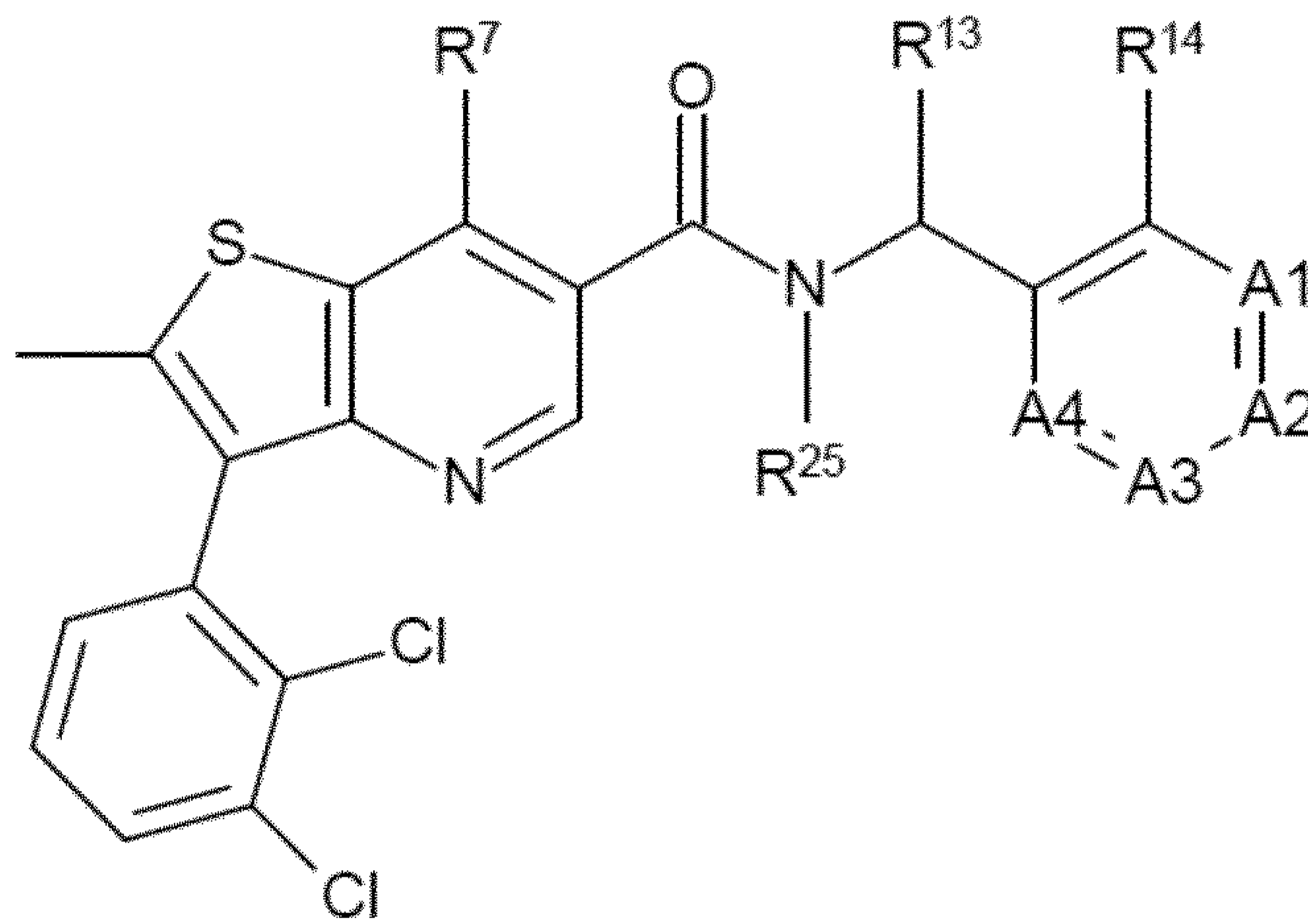
Formula (Ihi)



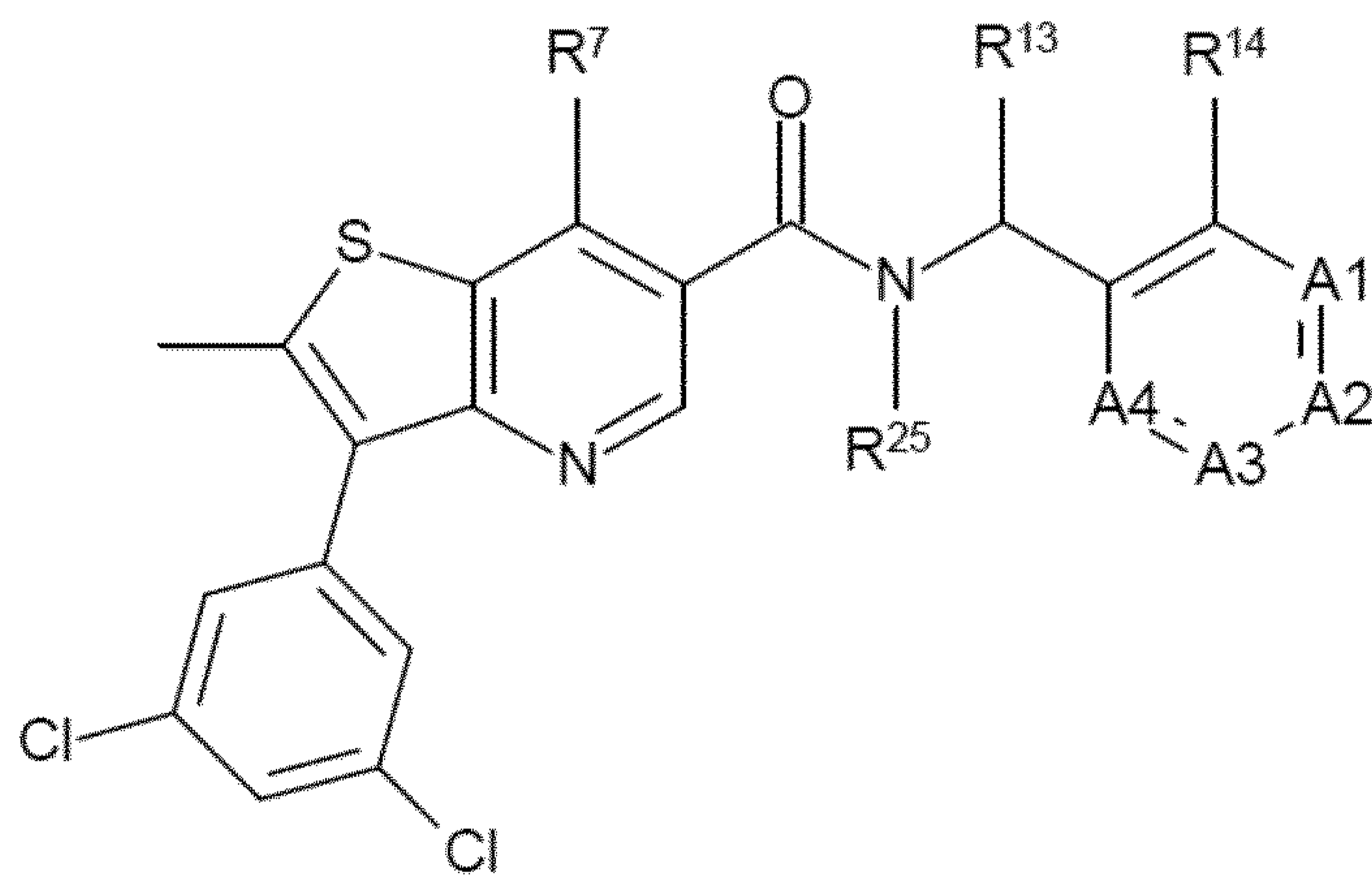
Formula (Ihii)



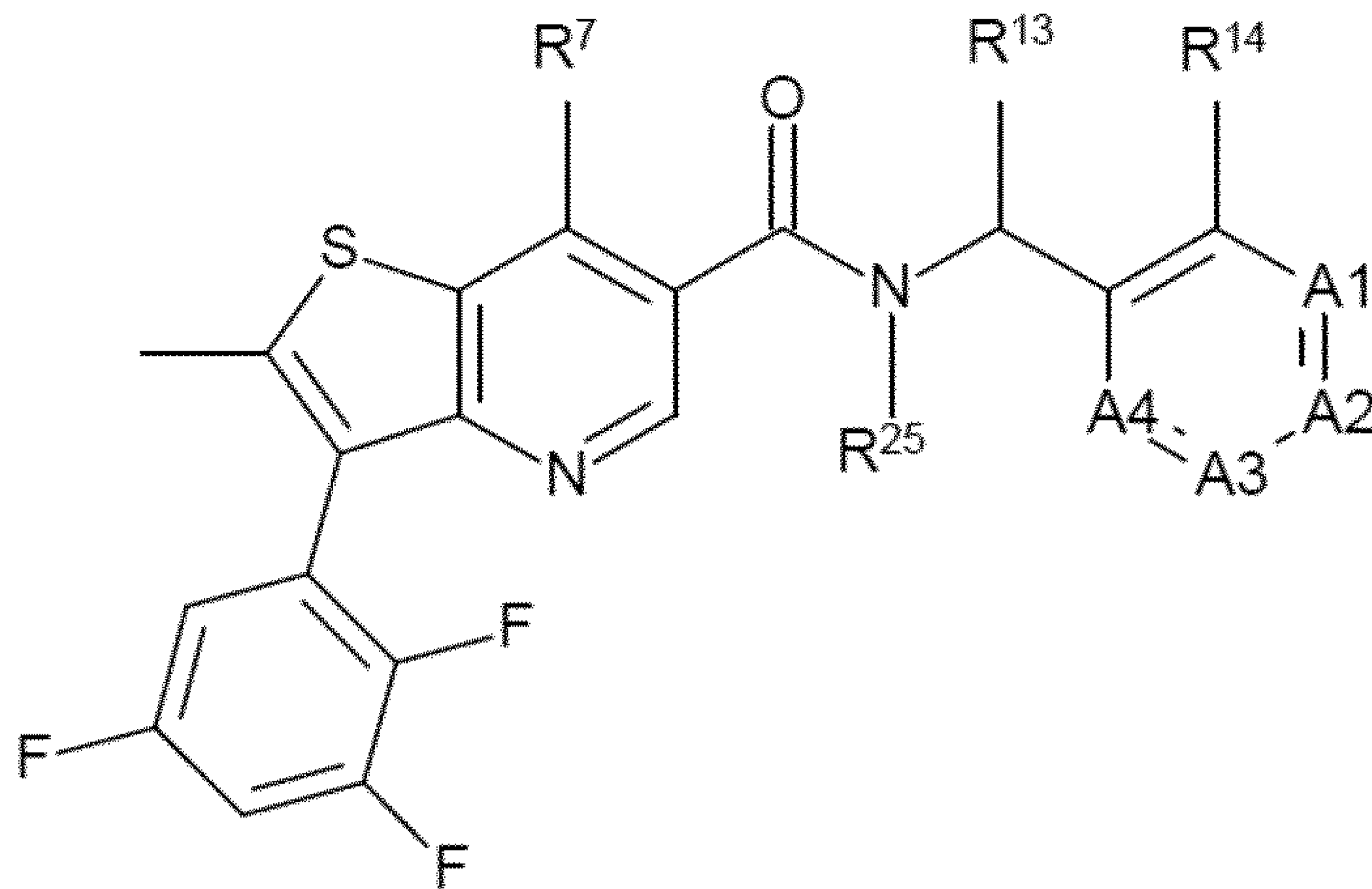
Formula (Ihiii)



Formula (Ihiv)



Formula (Ihv)



Formula (Ihvi)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 , R^{13} , R^{14} , A1, A2, A3, A4 and R^{25} are defined as in any of the embodiments
5 described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ihi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
embodiments thereof, the compounds are according to Formula (Ihii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds
10 are according to Formula (Ihiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ihiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ihvi), preferably in form of the (*S*)-enantiomer.
15 Formula (Ihvi), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 and R^{25} are defined as below.

In an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

20 hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and NR^2R^3 ,

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3

5 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

15 and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

20 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl,

25 and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

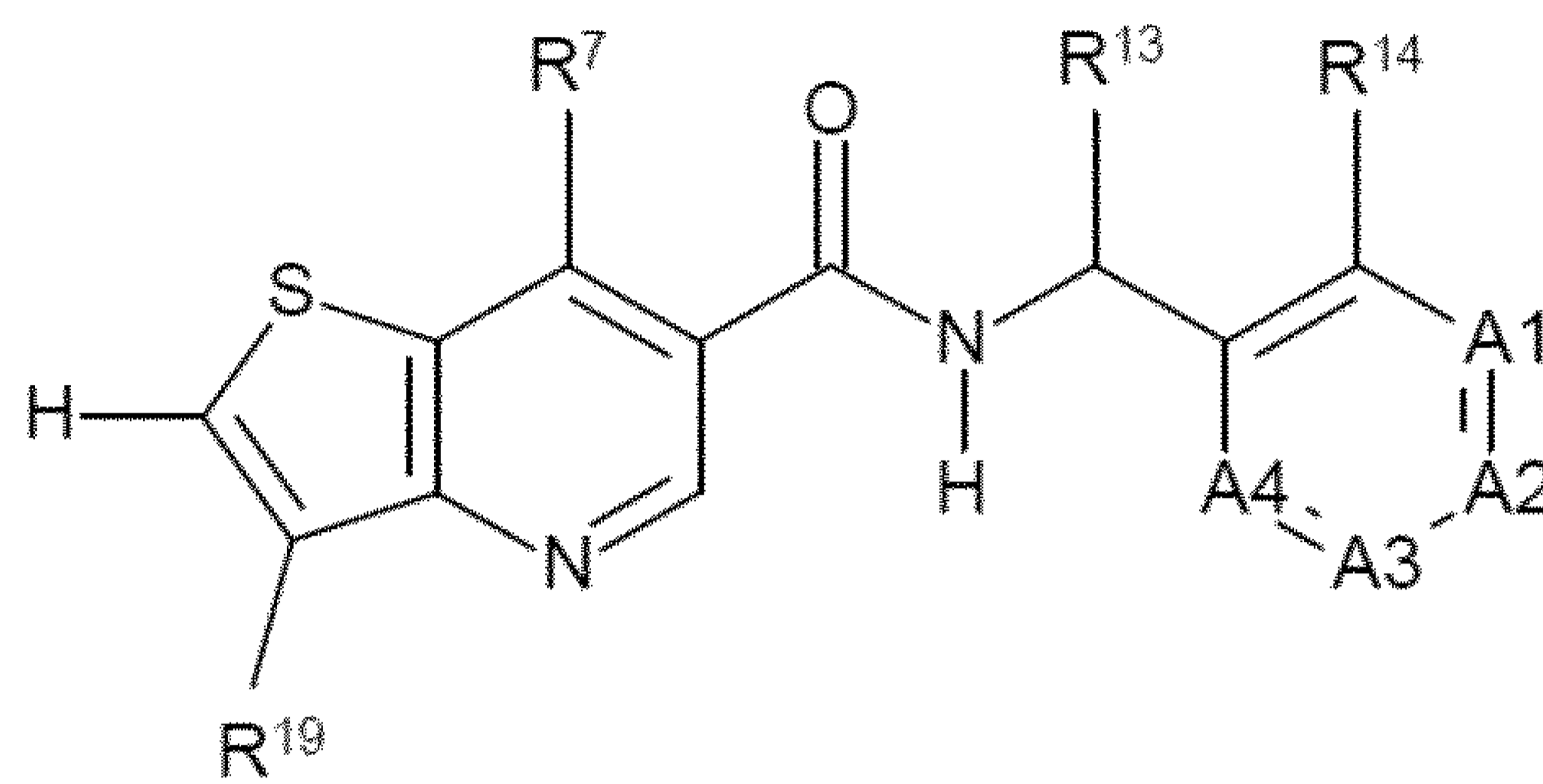
R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

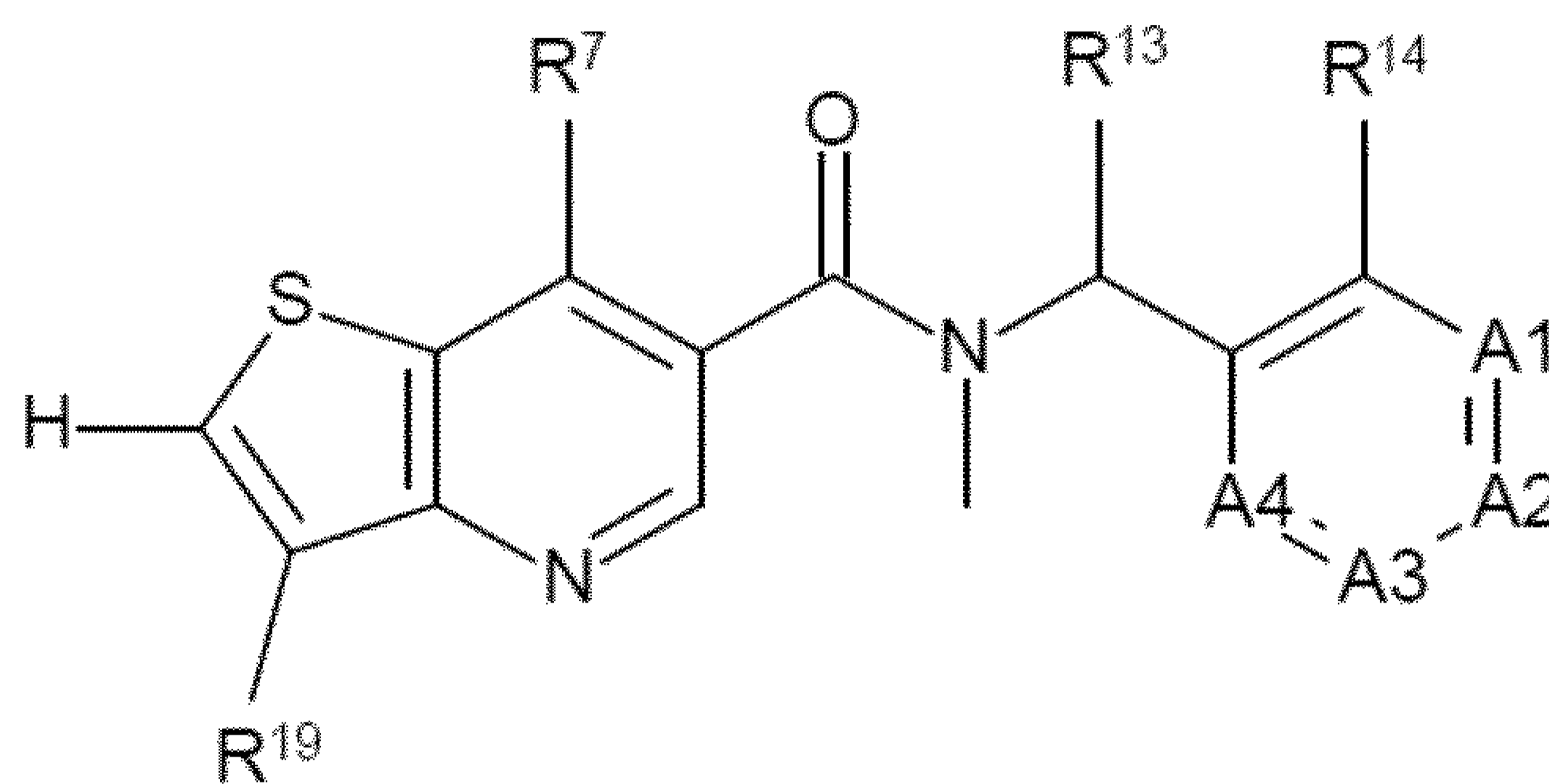
and

R²⁵ is hydrogen or methyl, more preferably hydrogen.

- 5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iii), (Iiii), (Iiiii) or (Iiiv)

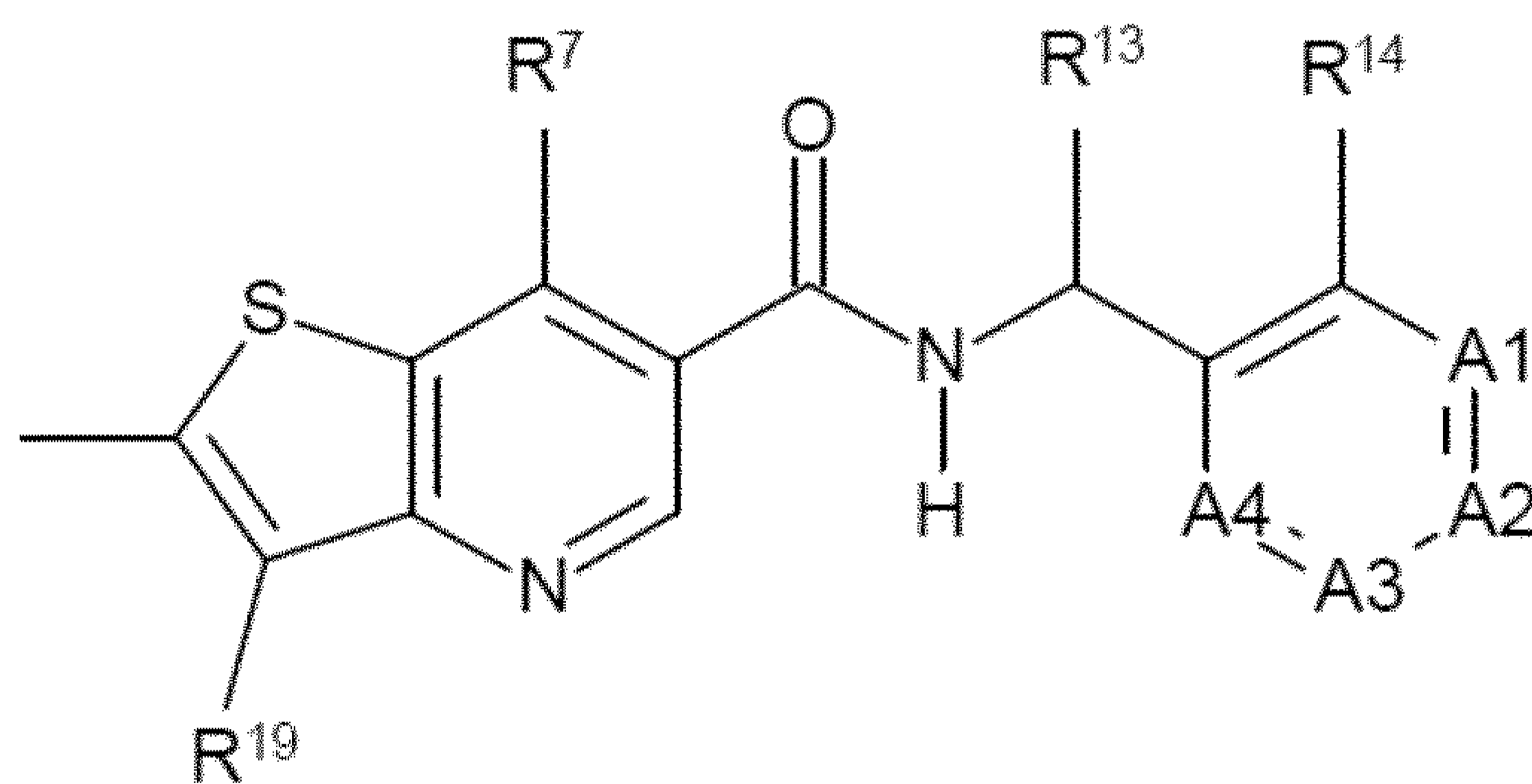


Formula (Iii)

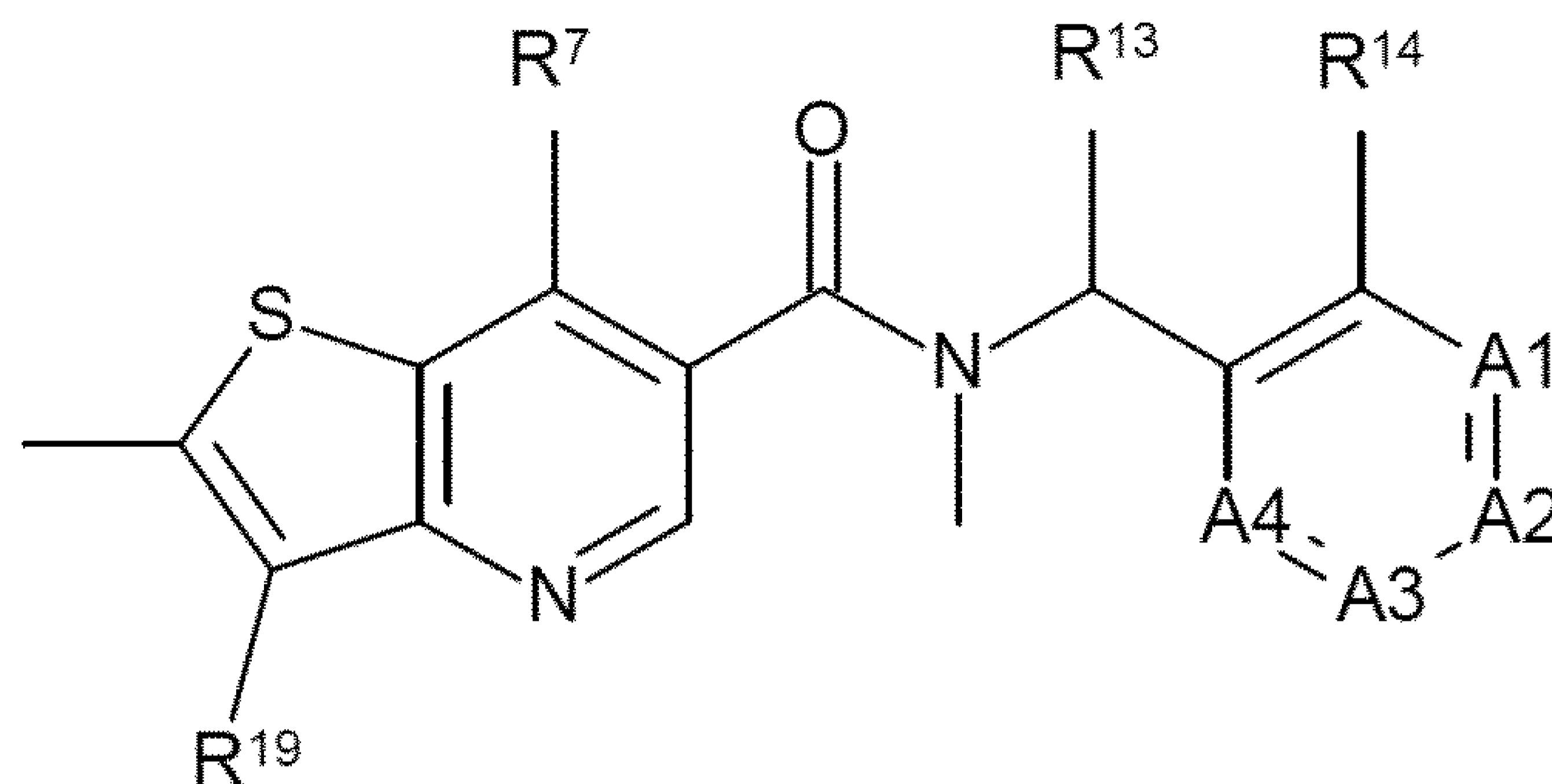


Formula (Iiii)

10



Formula (Iiiii)



Formula (Ijiv)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 , R^{13} , R^{14} , A1, A2, A3, A4 and R^{19} are defined as in any of the embodiments
5 described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
embodiments thereof, the compounds are according to Formula (Iiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds
10 are according to Formula (Iiiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iiiv), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 is hydrogen.

15 The invention provides a compound according to the invention and/or embodiments thereof, wherein R^7 as well as R^{13} , R^{14} , A1, A2, A3 and A4 are defined as below.

In an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -
20 alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

- 5 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

- 10 C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

- R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated
15 heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

- wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group
20 consisting of C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

- 25 R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

5 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof,

10 R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, 25 hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH- or -O-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen or C_{1-3} alkoxy,

5 A2 is N or CR^{16} , wherein R^{16} is independently hydrogen or C_{1-3} alkoxy,

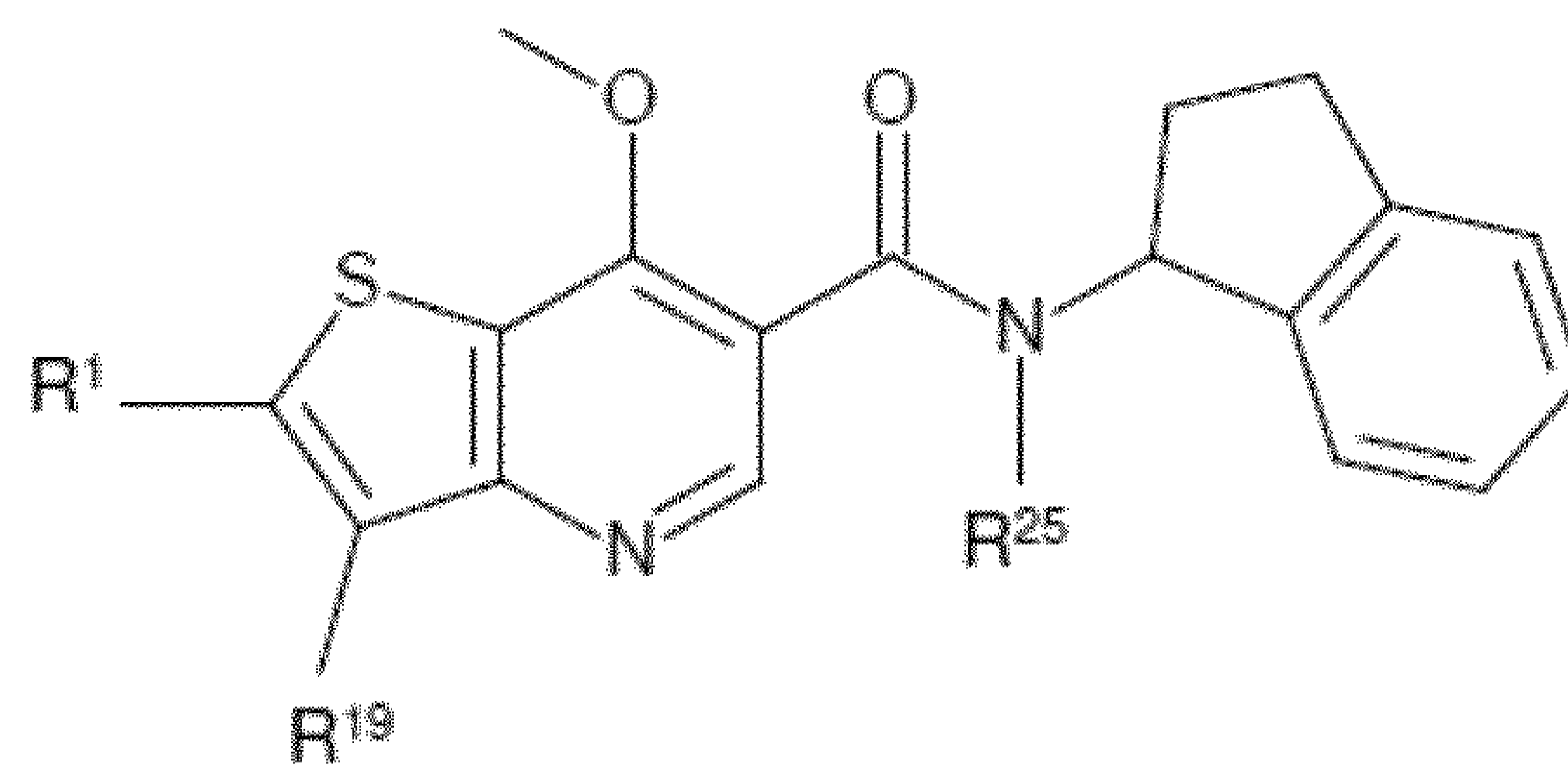
A3 is N or CR^{17} , wherein R^{17} is independently hydrogen or C_{1-3} alkoxy,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen or C_{1-3} alkoxy,

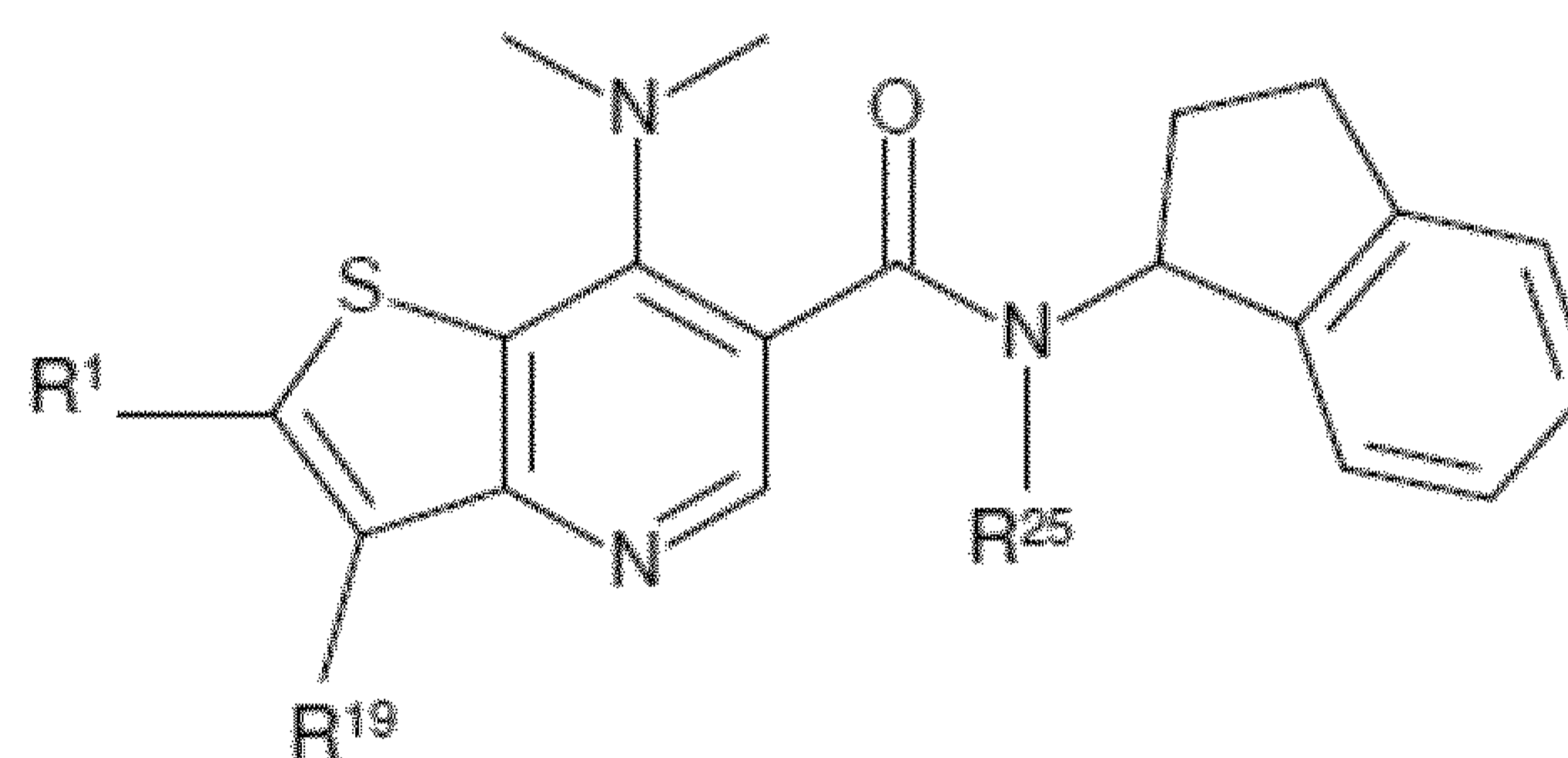
wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to

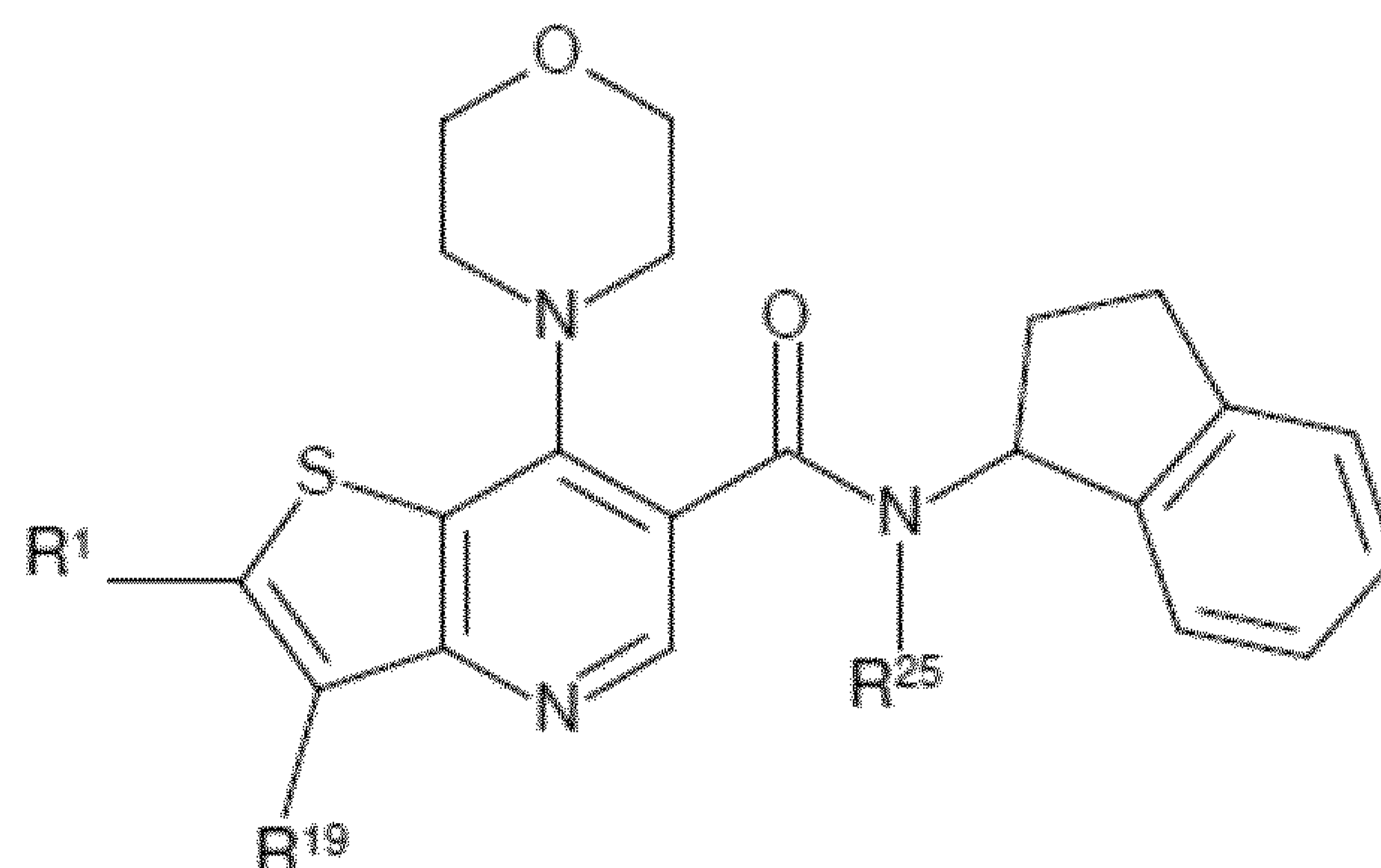
10 Formula (Iji), (Ijii), (Ijiii), (Ijiv), (Ijv), (Ijvi), (Ijvii), (Ijviii) or (Ijix)



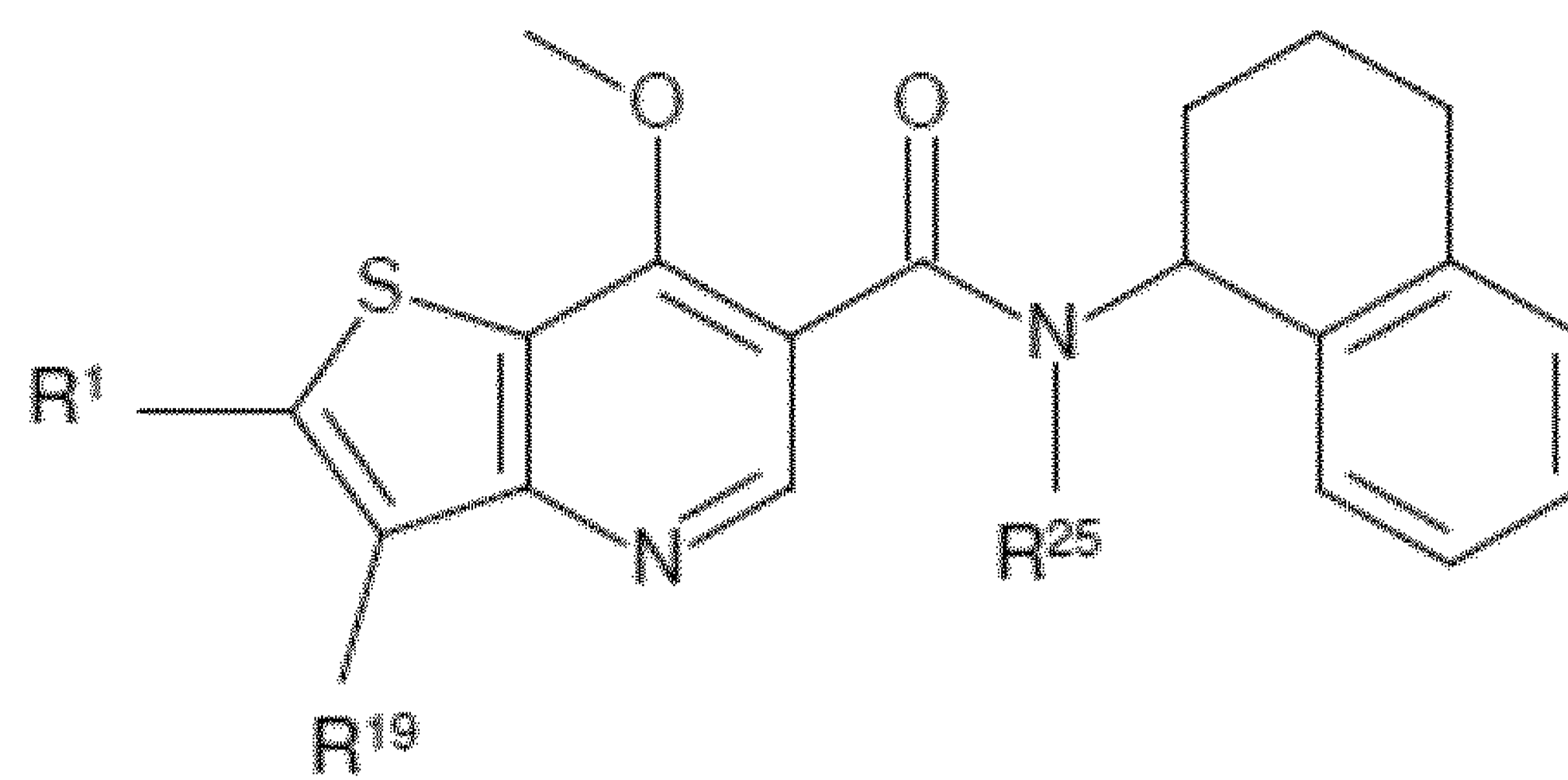
Formula (Iji)



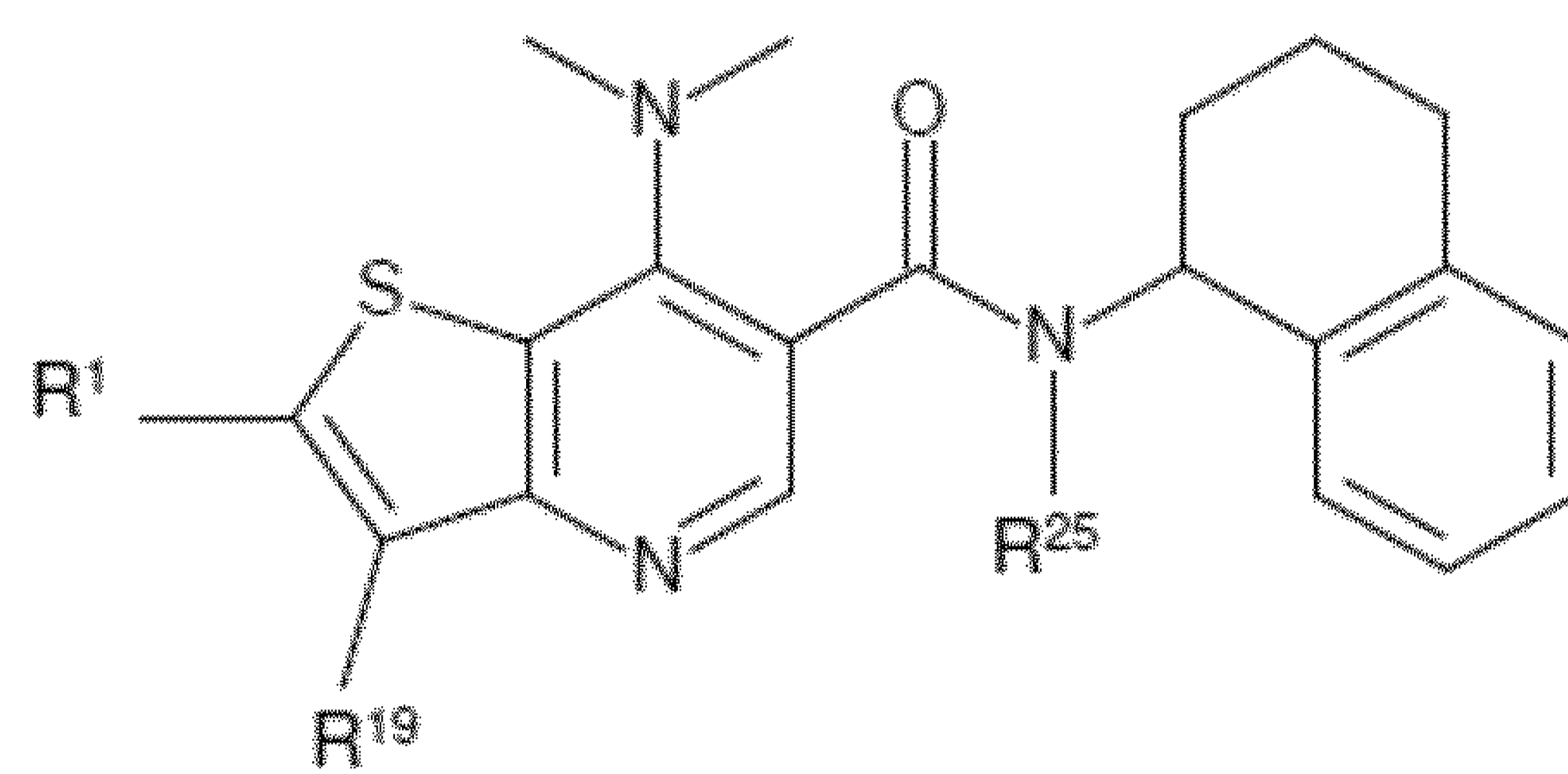
Formula (Ijii)



Formula (Ijiii)

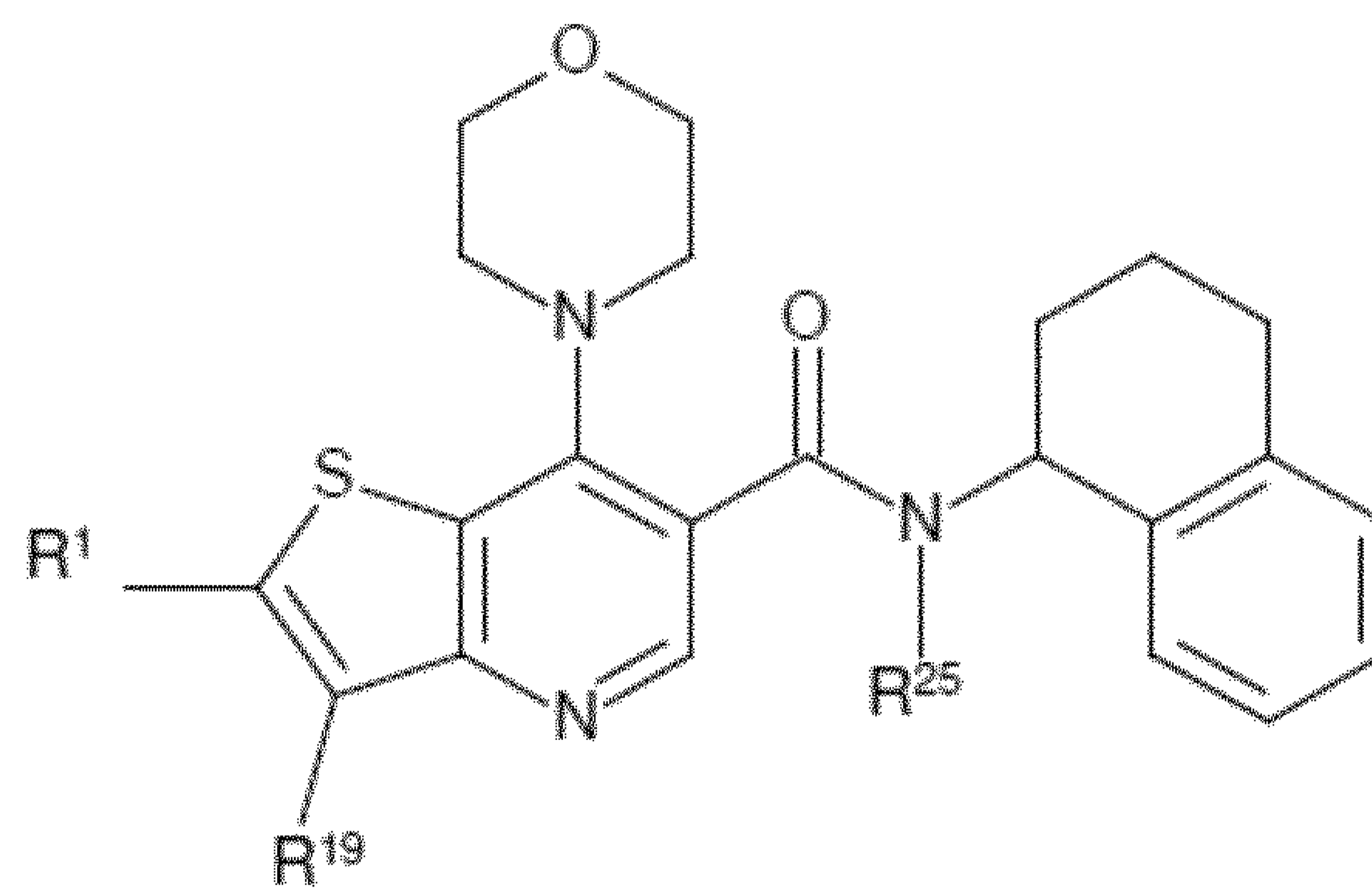


Formula (Ijiv)

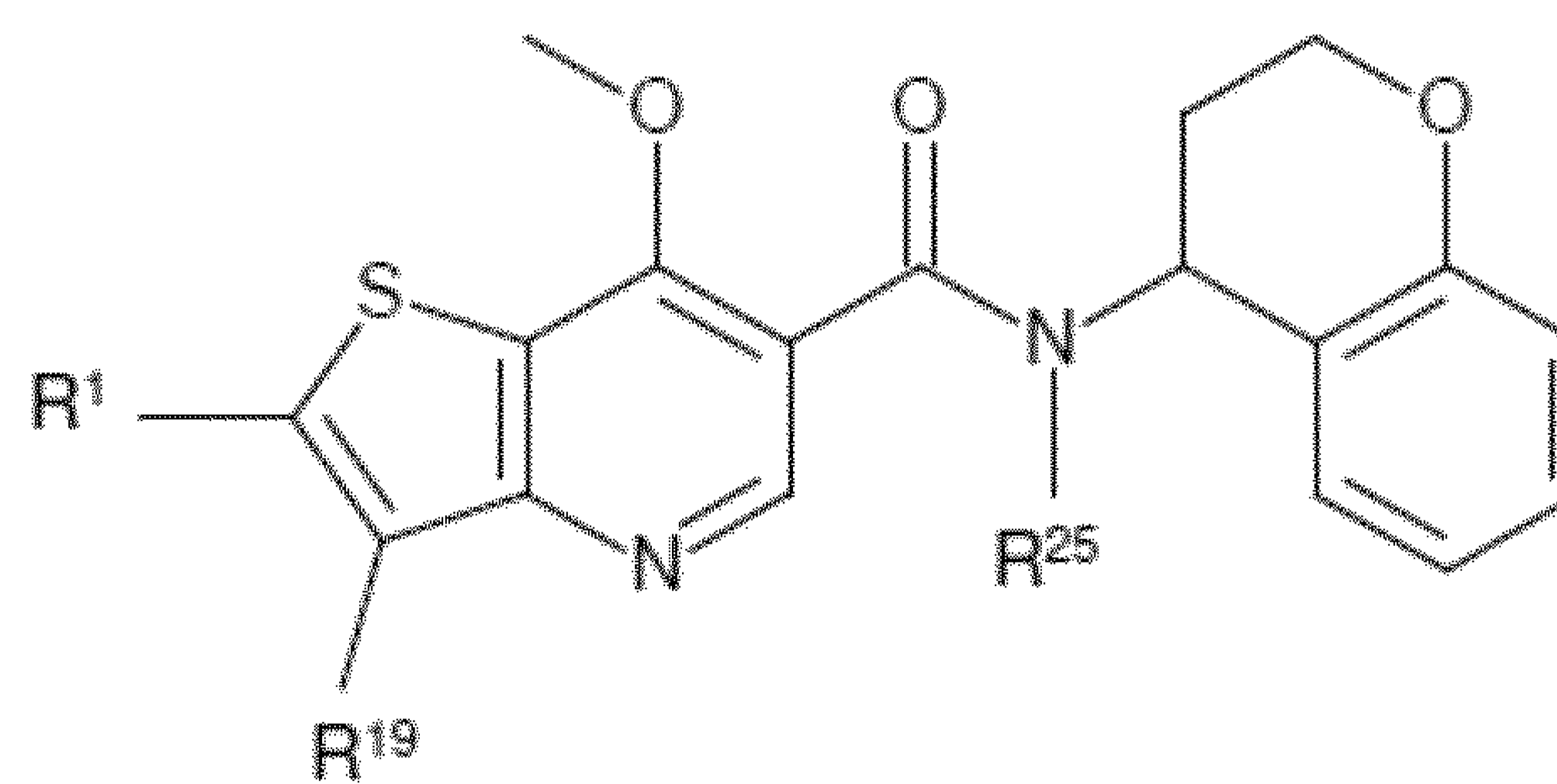


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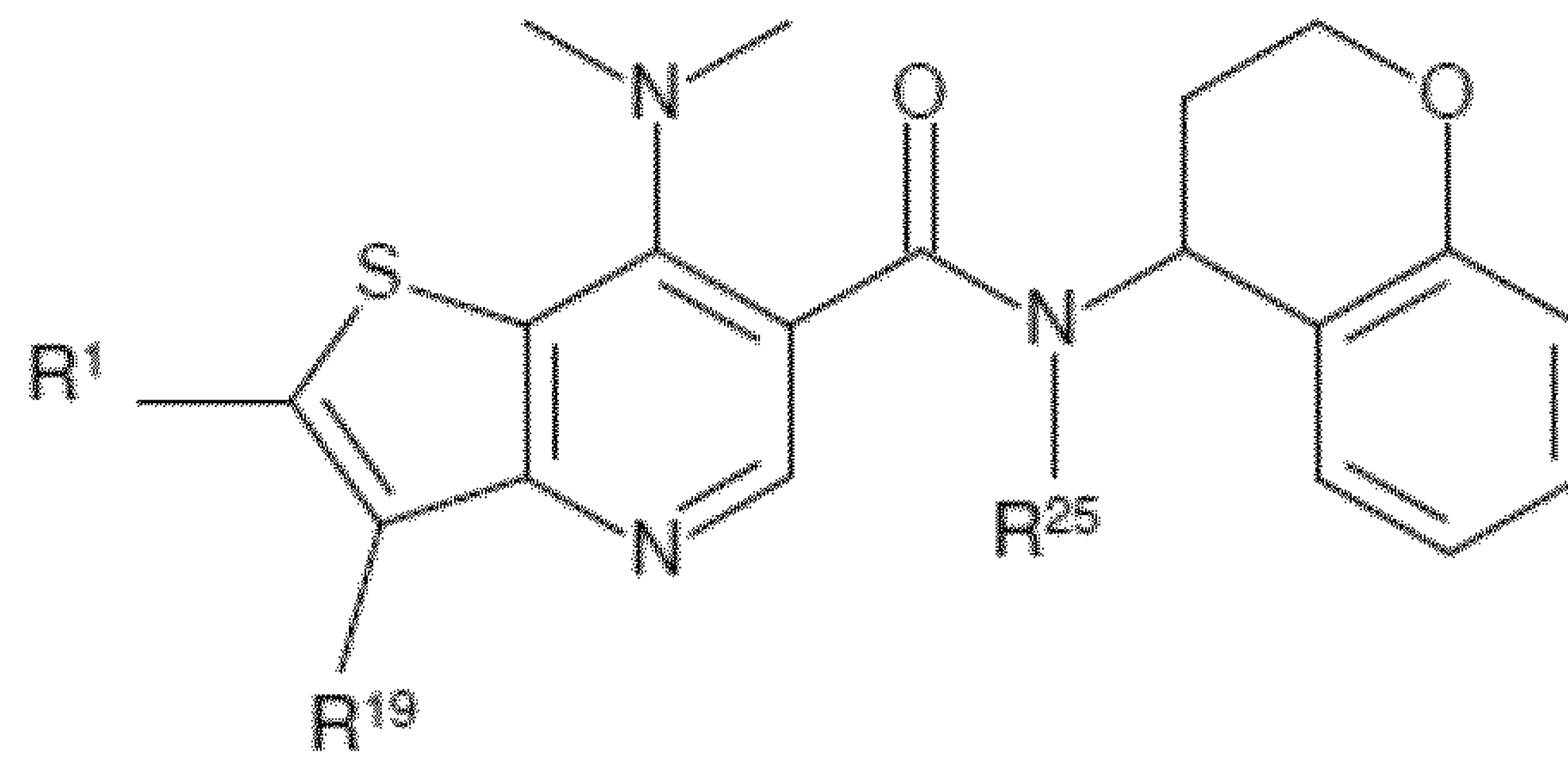
Formula (Ijv)



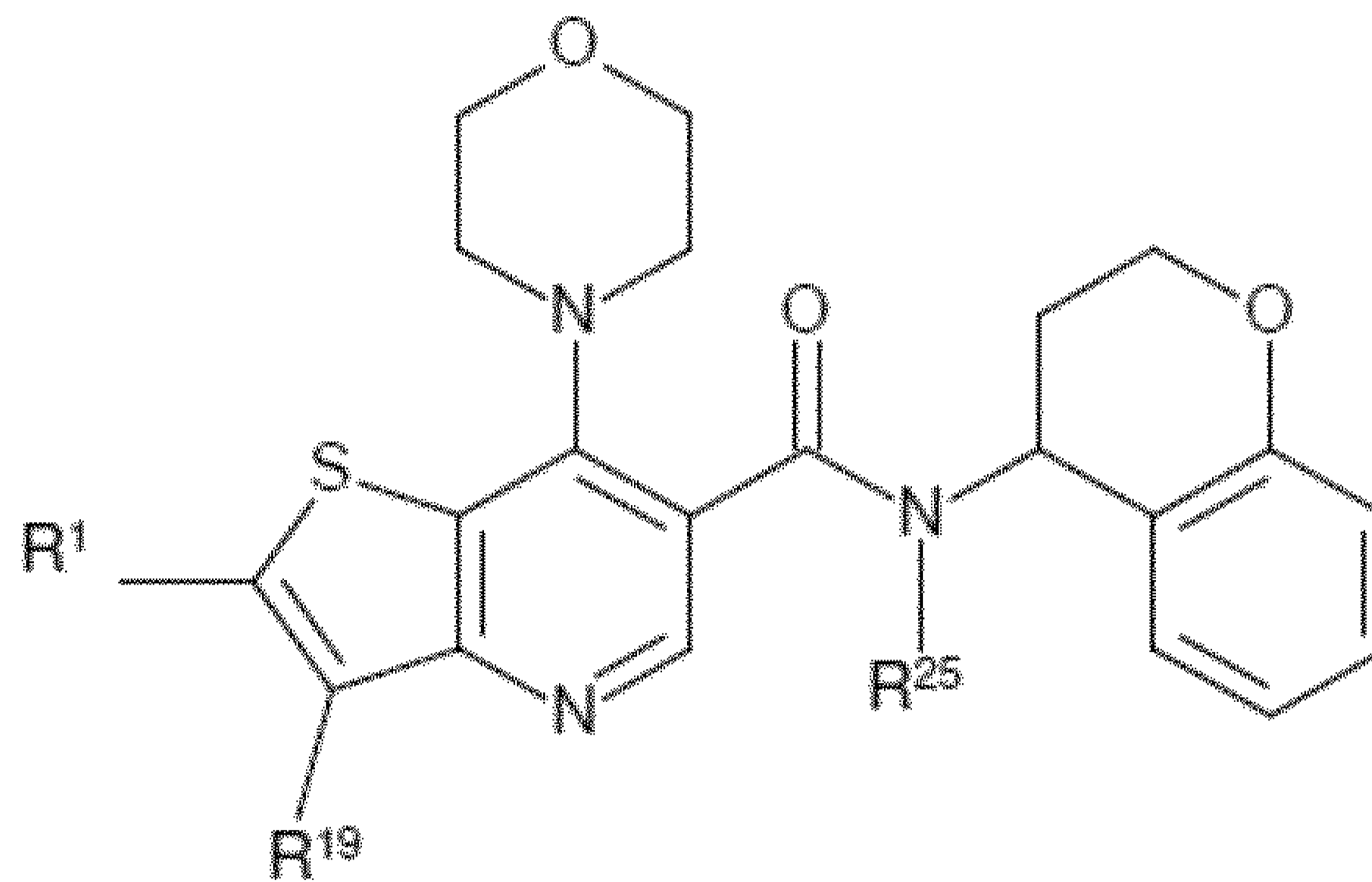
Formula (Ijvi)



Formula (Ijvii)



Formula (Ijviii)



Formula (Ijix)

5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^{19} and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iji), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Ijii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijkiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijv), preferably in form of the (*S*)-enantiomer.
 15 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijviii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 20 embodiments thereof, the compounds are according to Formula (Ijix), preferably in form of the (*S*)-enantiomer.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

5 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

10 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3
15 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

25 and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

5 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl.

In an embodiment of the invention and/or embodiments thereof,

10 R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

20 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

25

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

$R^{8''}$ and $R^{9''}$ are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

5 and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

10 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof,

15 R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R^7 is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-
 5 hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally
 10 replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen or C_{1-3} alkoxy,

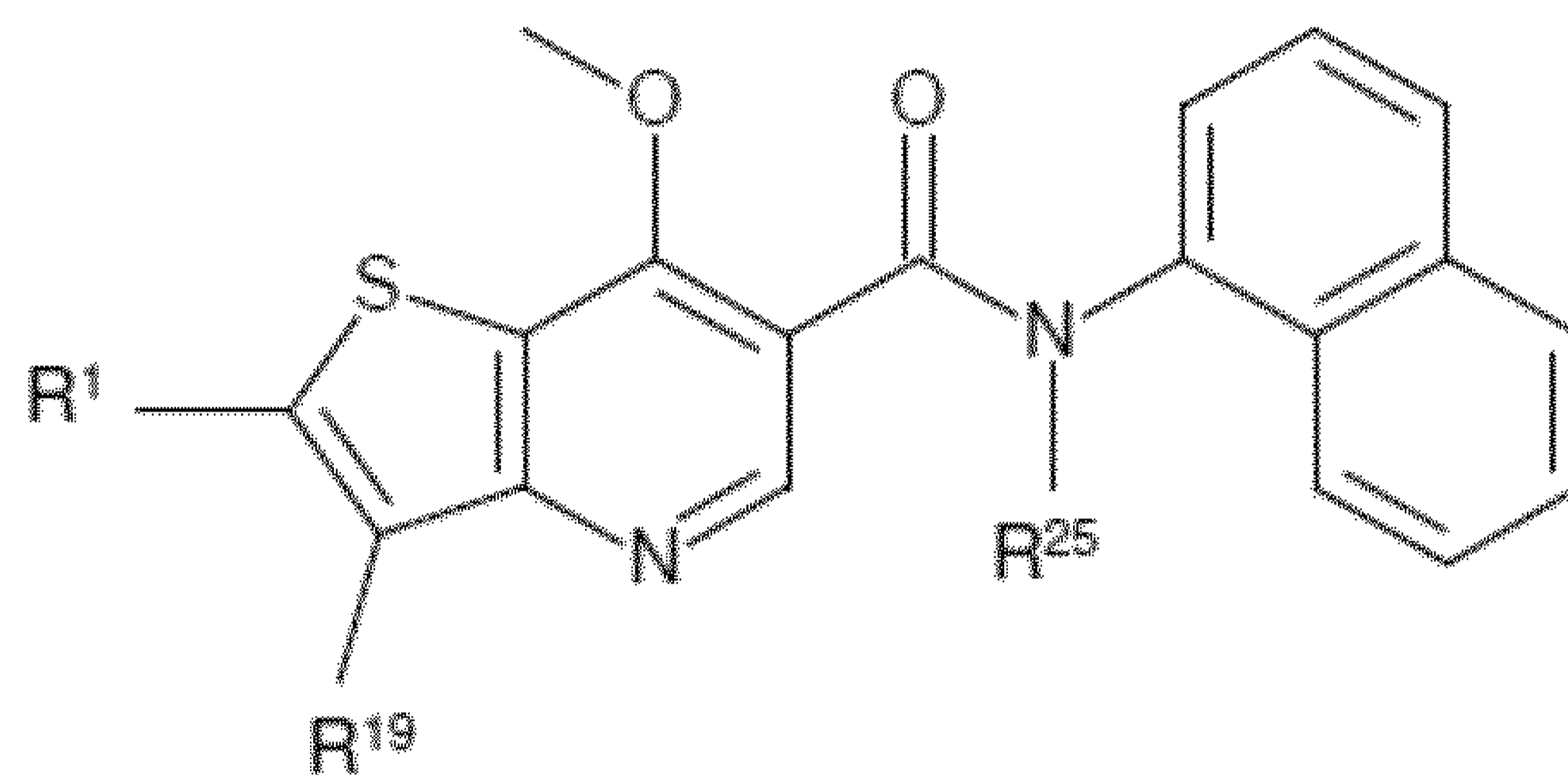
A2 is N or CR^{16} , wherein R^{16} is independently hydrogen or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen or C_{1-3} alkoxy,

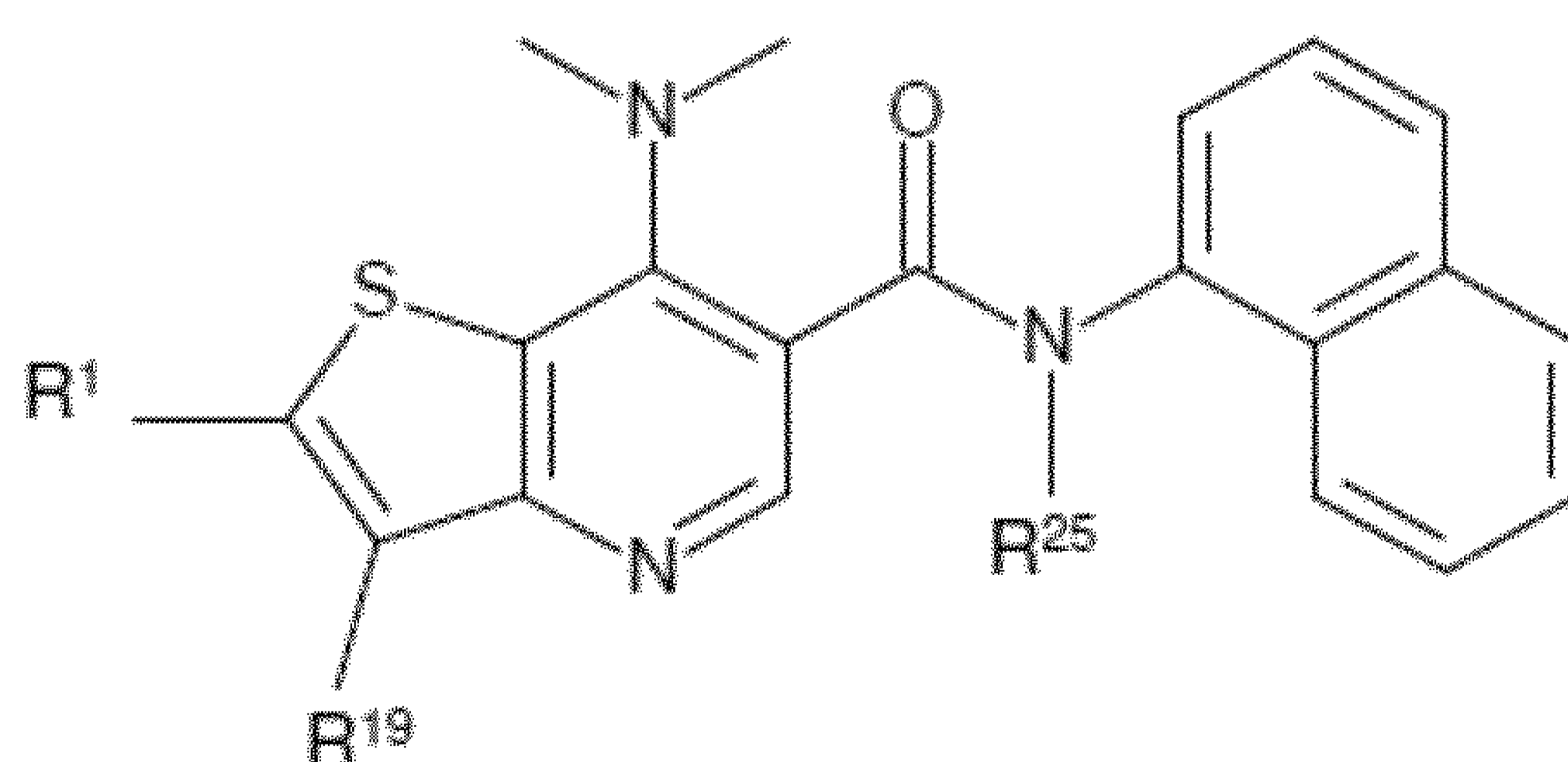
A4 is N or CR^{18} , wherein R^{18} is independently hydrogen or C_{1-3} alkoxy,

15 wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijx), (Ijxi), (Ijxii), (Ijxiii), (Ijxiv) or (Ijxv)

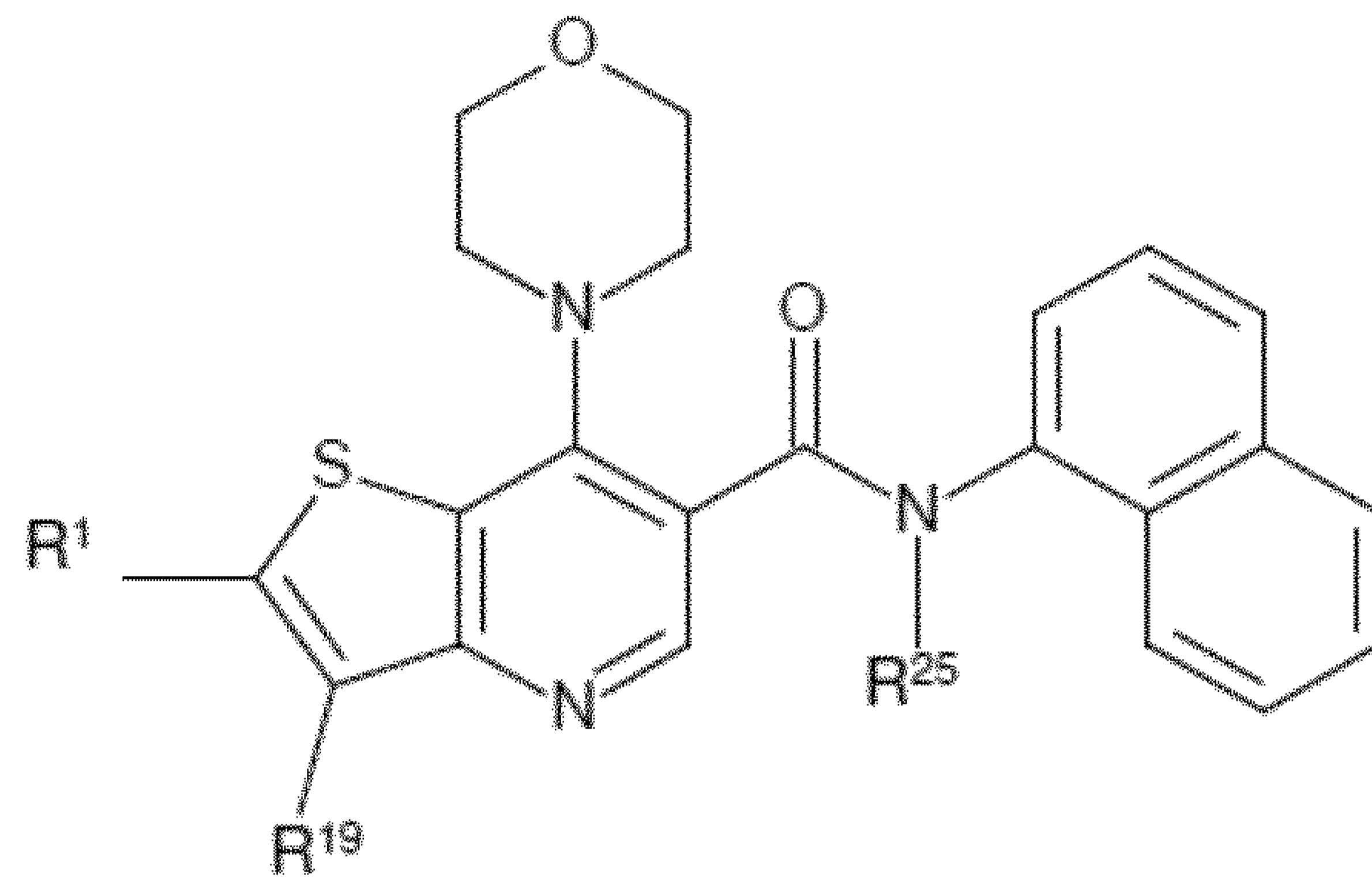


Formula (Ijx)

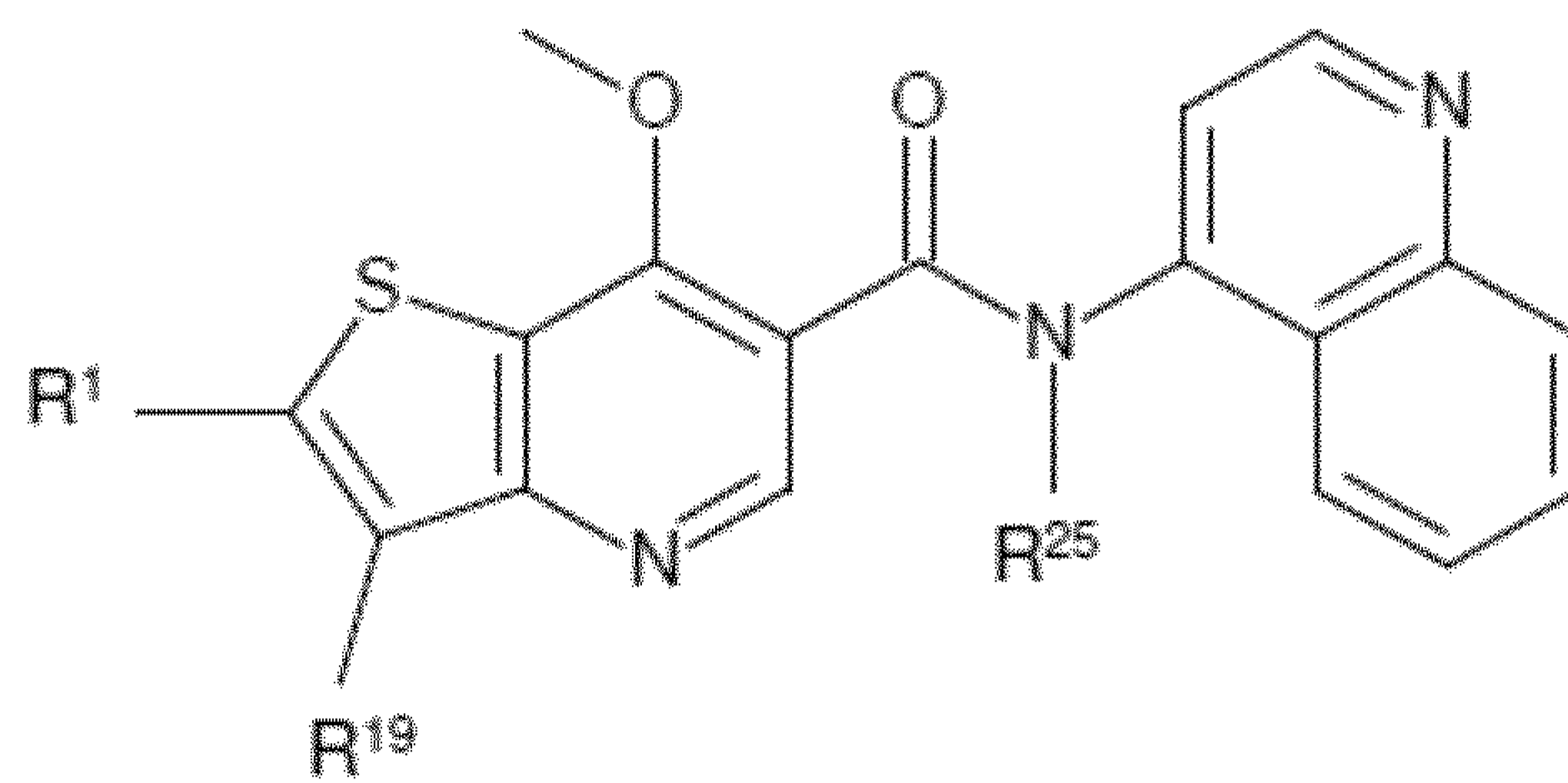


Formula (Ijxi)

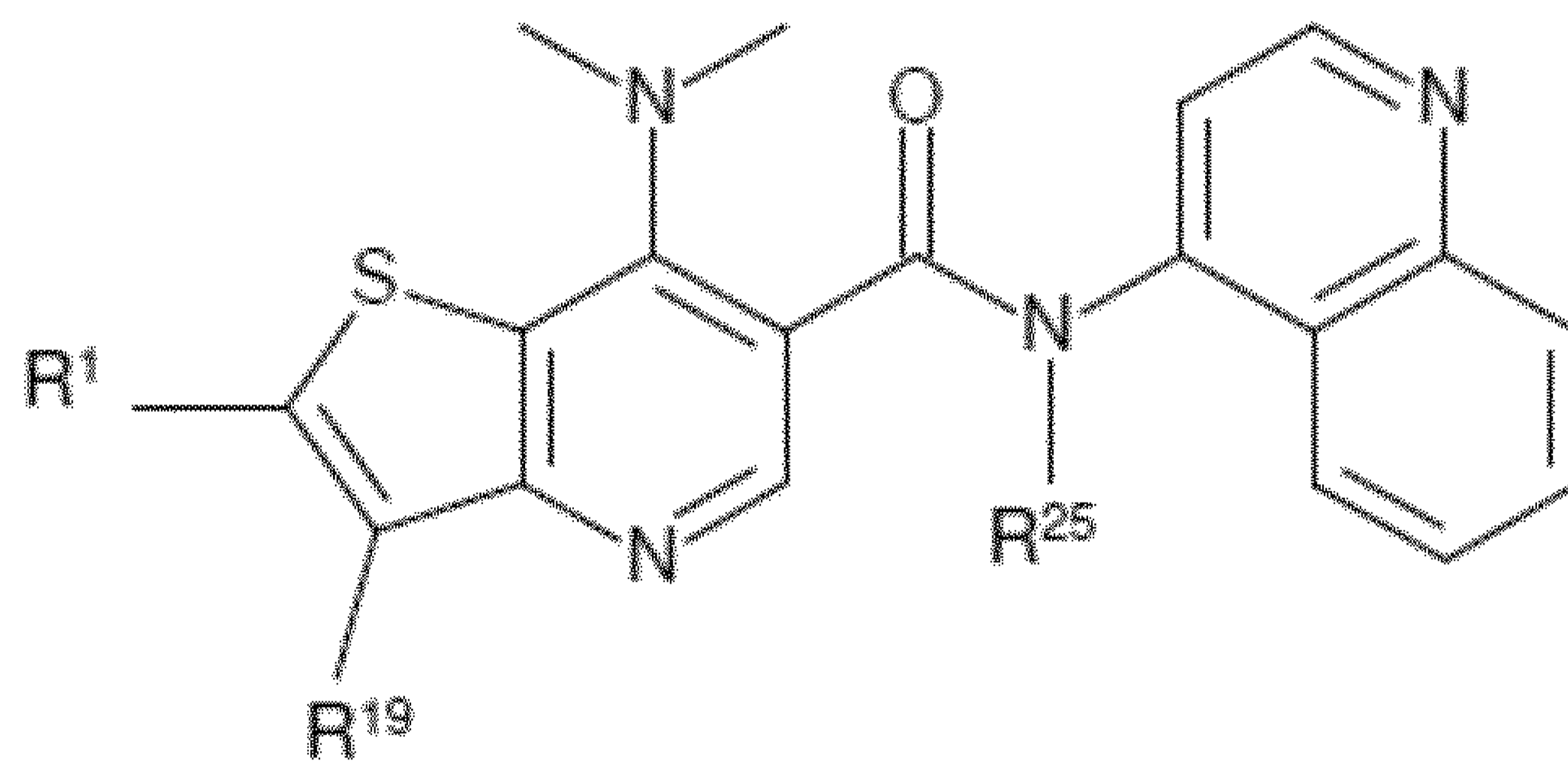
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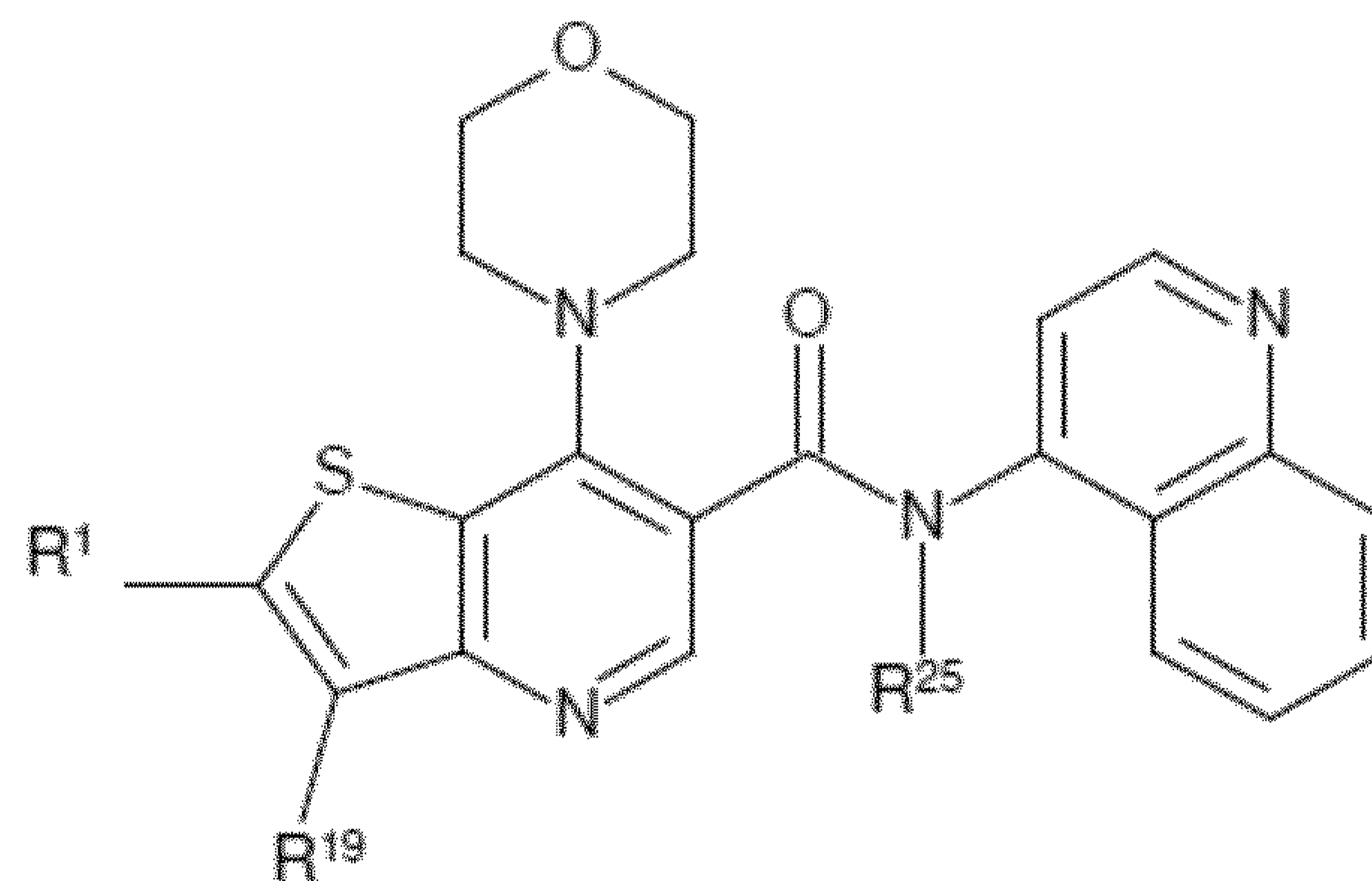
Formula (Ijxii)



Formula (Ijxiii)



Formula (Ijxiv)



Formula (Ijxv)

5

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures
 10 thereof, wherein R¹, R¹⁹ and R²⁵ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijx), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijxi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijxii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijxiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijxiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ijxv), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^7 and R^{19} are defined as below.

In an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, $NR^{8'}R^{9'}$, $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the

N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

- 5 R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,
 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,
 R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,
 and

R¹⁹ is independently selected from the group consisting of

- 10 C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

- 15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl,
 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²²
 and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

- 20 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

- 25 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl,
 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and
 C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{20'}$, $R^{21'}$, $R^{22'}$, $R^{23'}$ and $R^{24'}$ are independently selected from hydrogen and C₁₋₆-alkyl.

In an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy,
 5 NR^8R^9 , SR^{10} , SOR^{10} and SO_2R^{10} ,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy,
 10 oxo, NR^8R^9 , $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3
 15 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and $NR^{8''}R^{9''}$;

R^{10} is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^8 , R^9 , $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

25 $R^{8''}$ and $R^{9''}$ are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

R^{19} is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

5 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

15 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

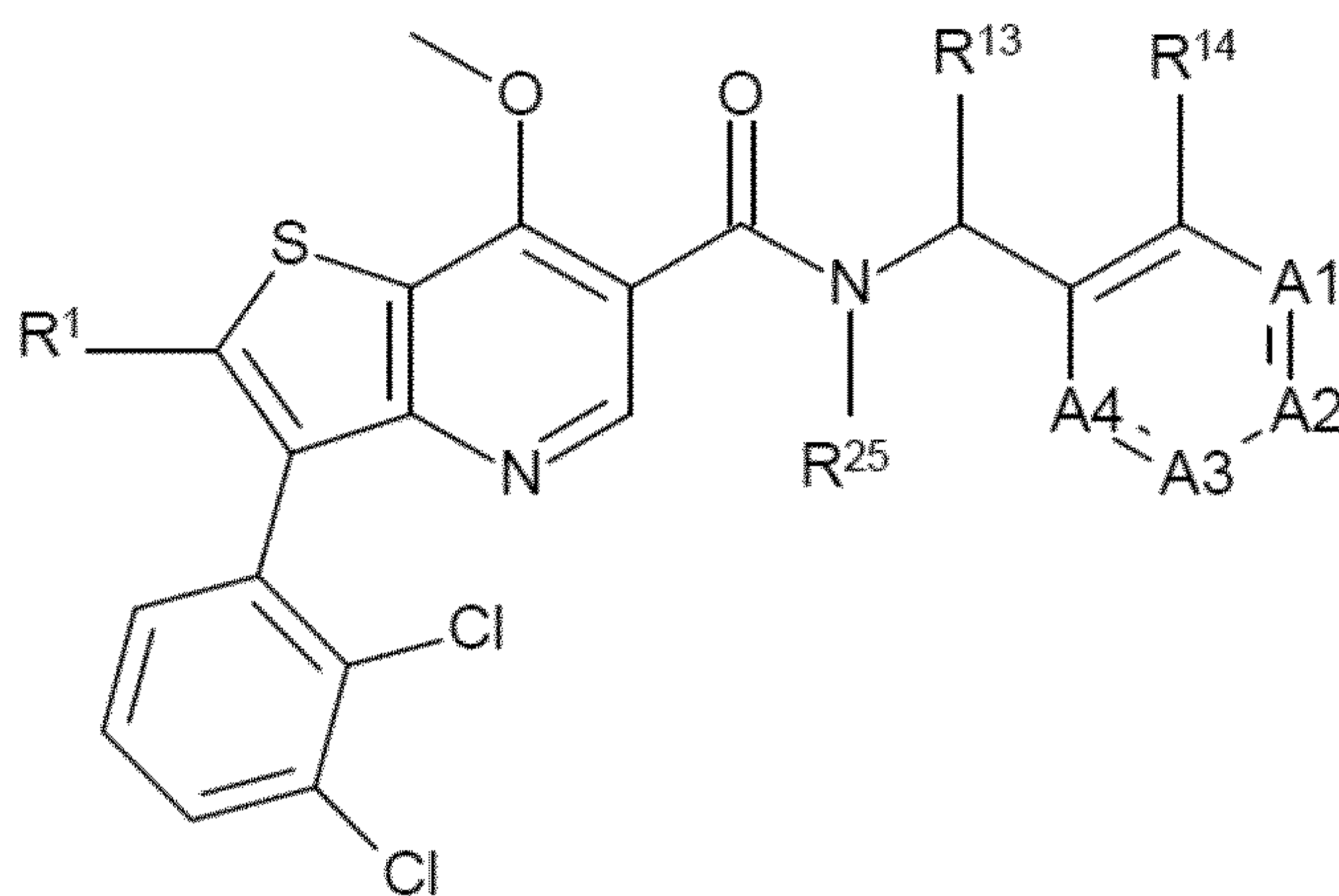
20 Suitably R⁷ is independently selected from the group consisting of

25 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl,

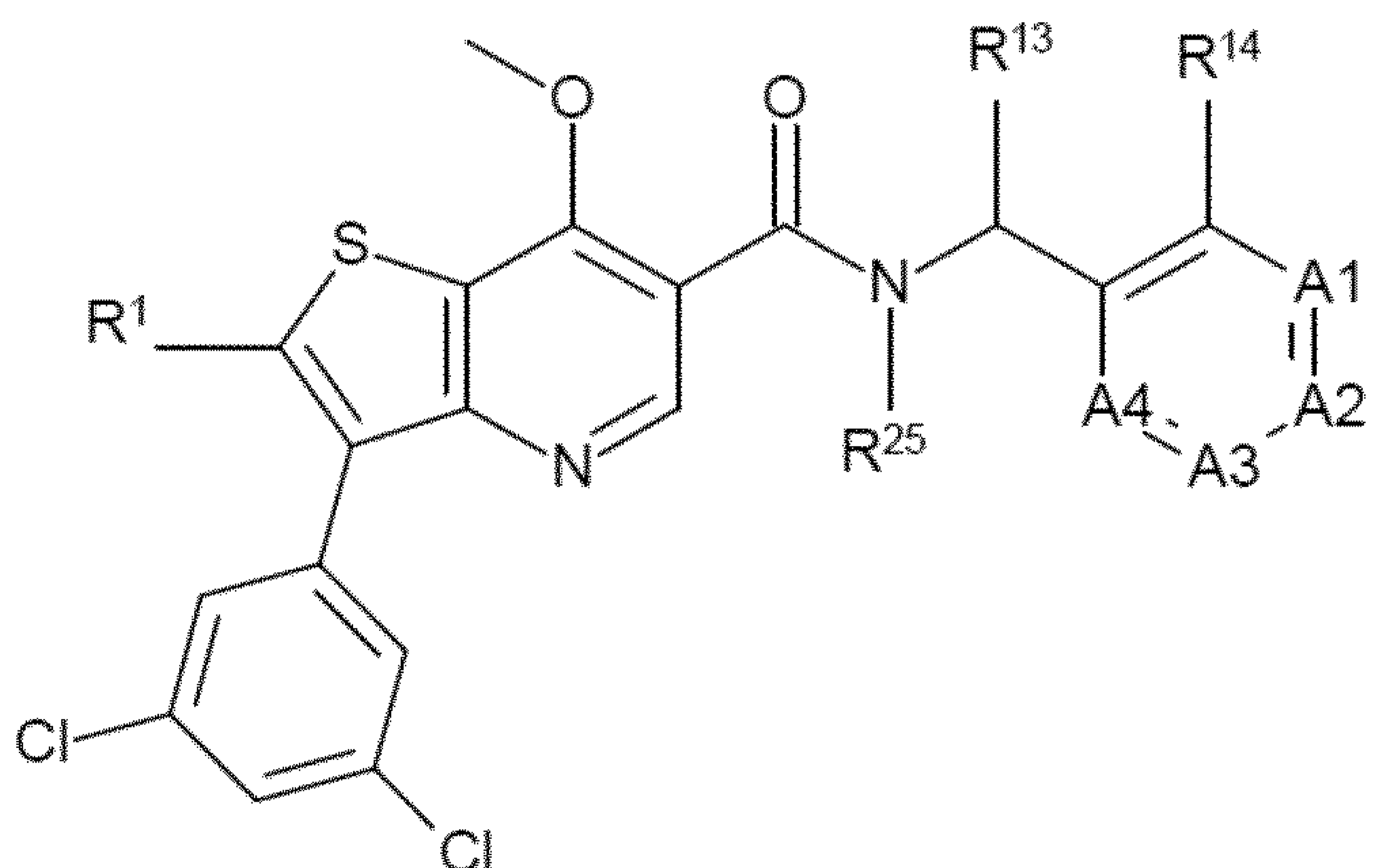
and

R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

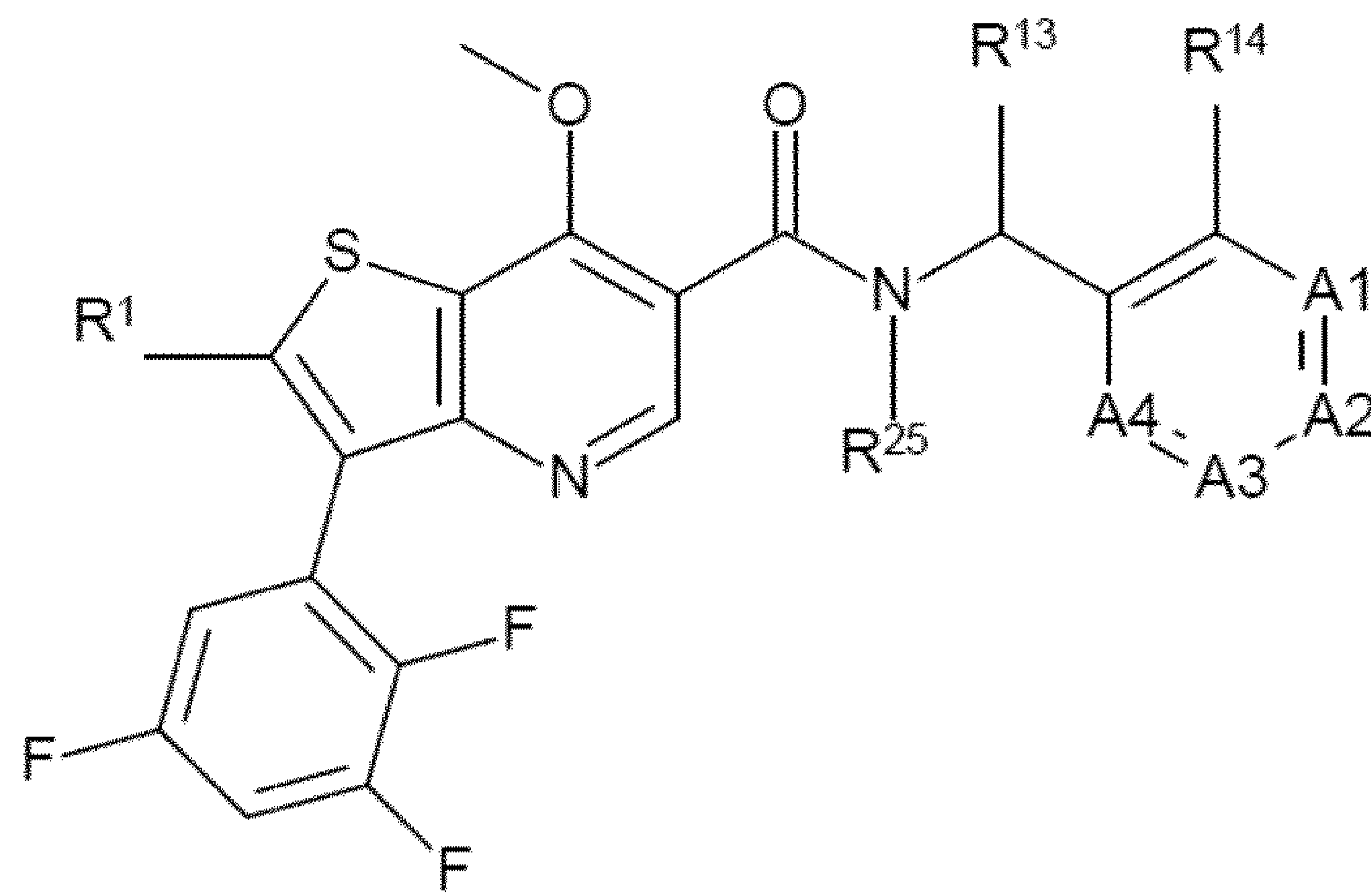
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iki), (Ikii), (Ikiii), (Ikiv), (Ikv), (Ikvi), (Ikvii), (Ikviii) or (Ikix)



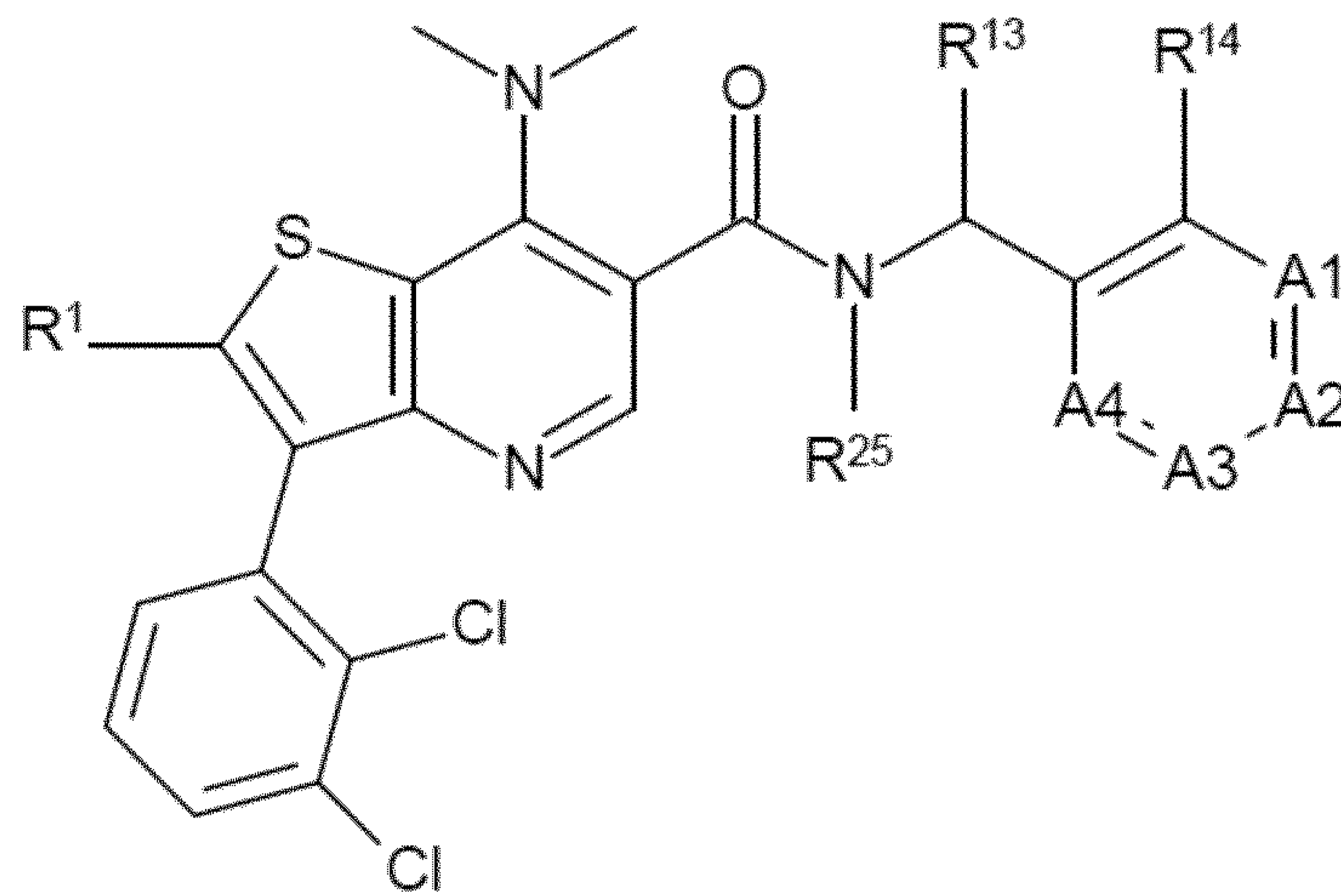
Formula (Iki)



Formula (Ikii)

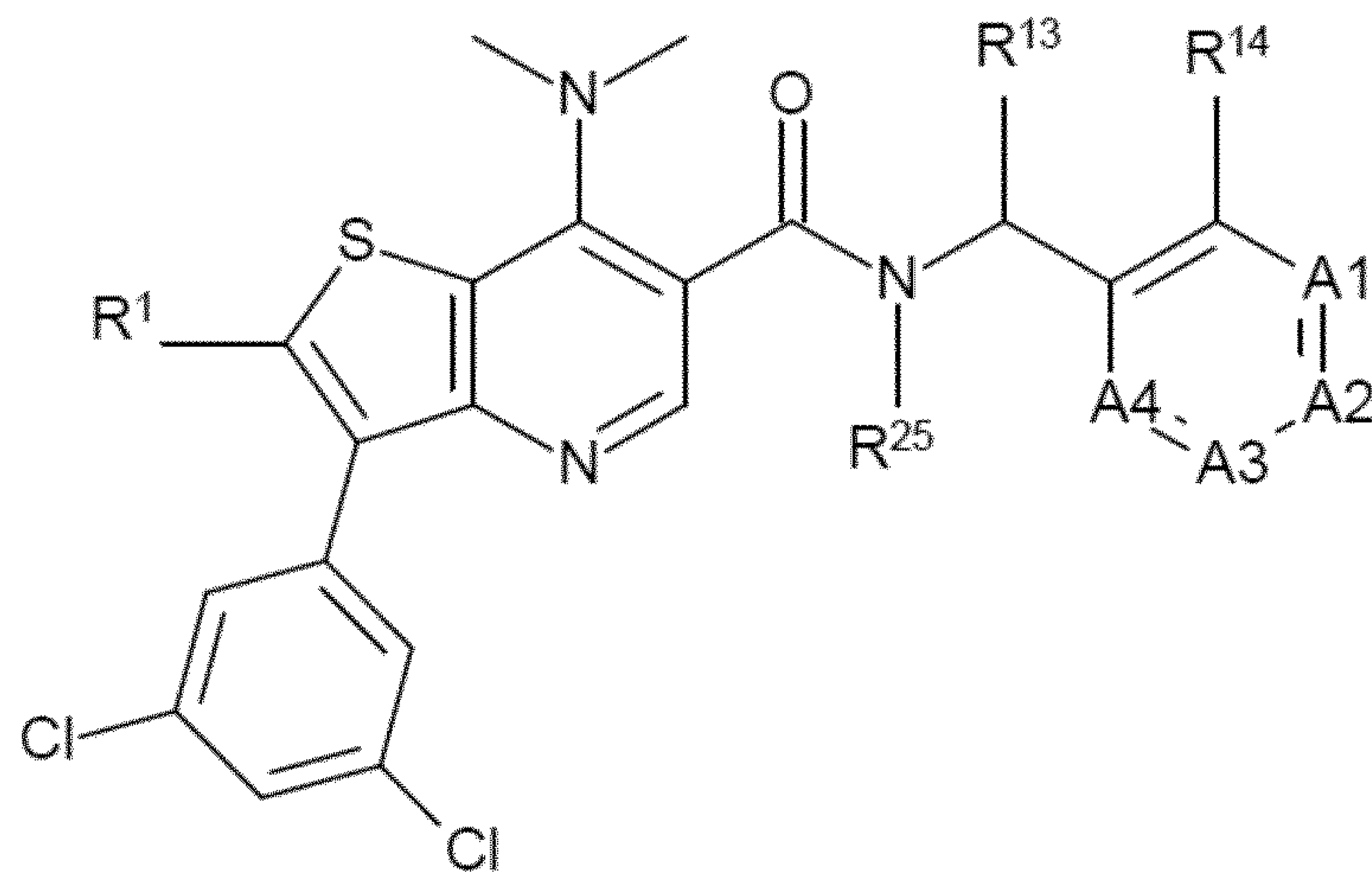


Formula (Ikiii)

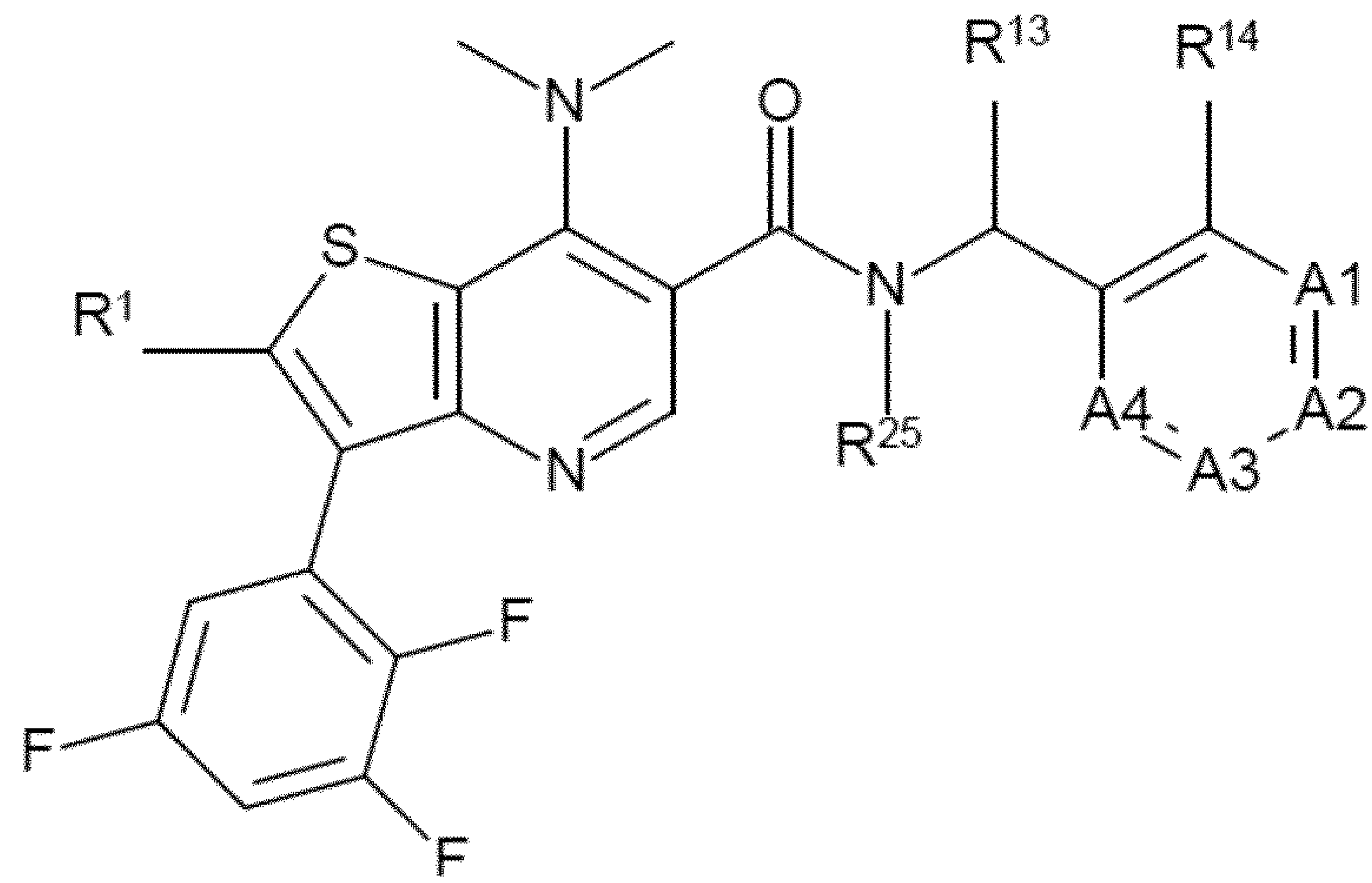


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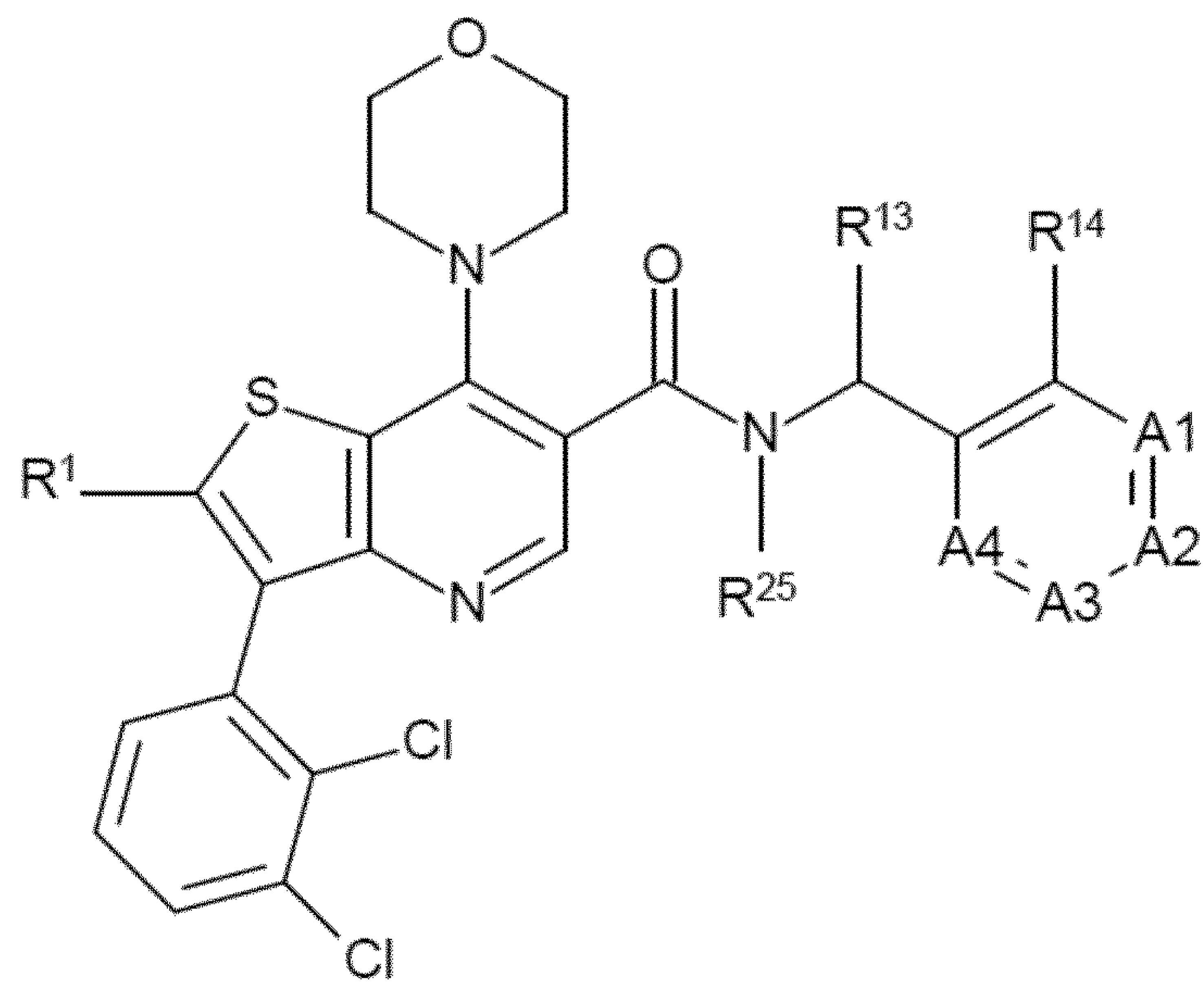
Formula (Ikiv)



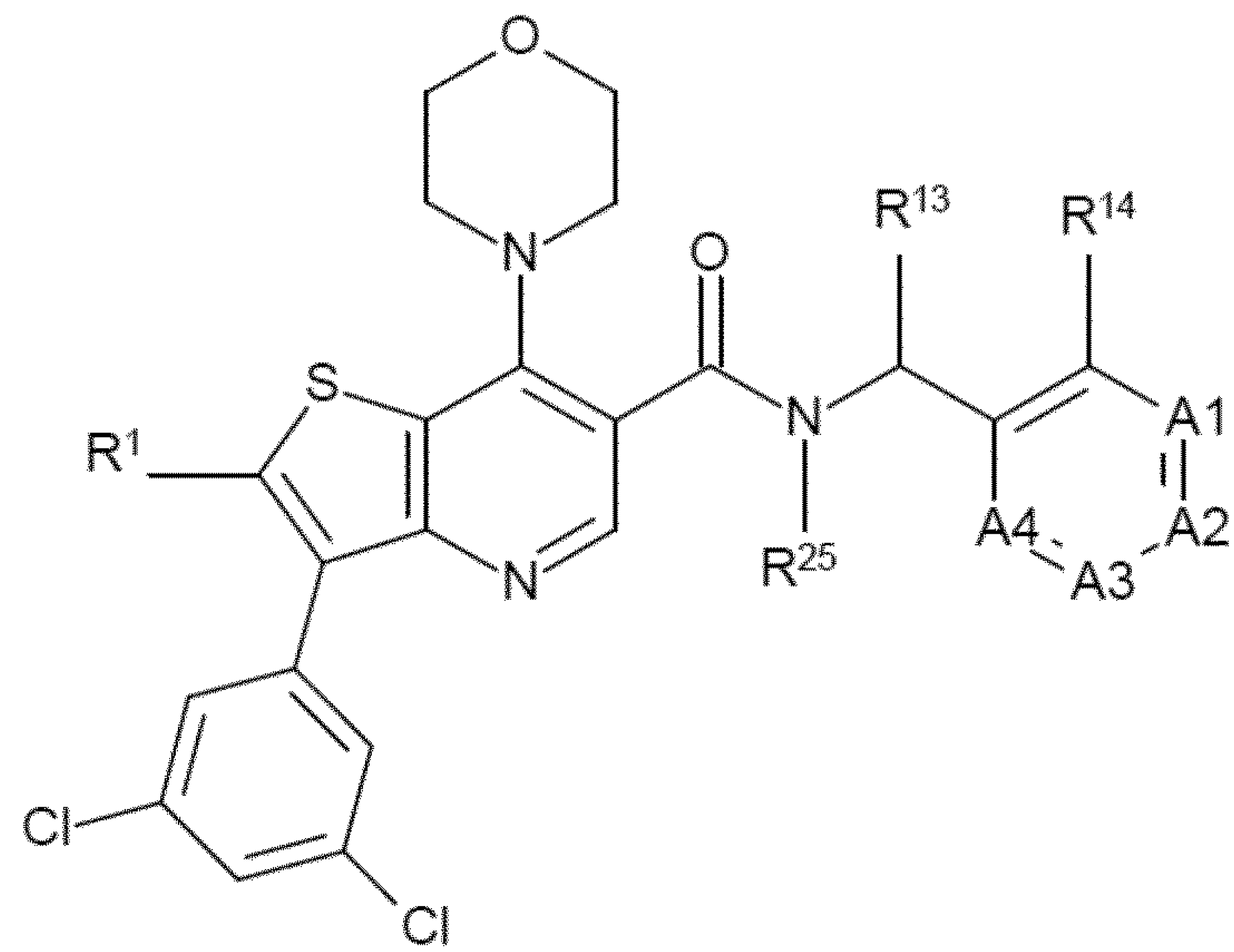
Formula (Ikiv)



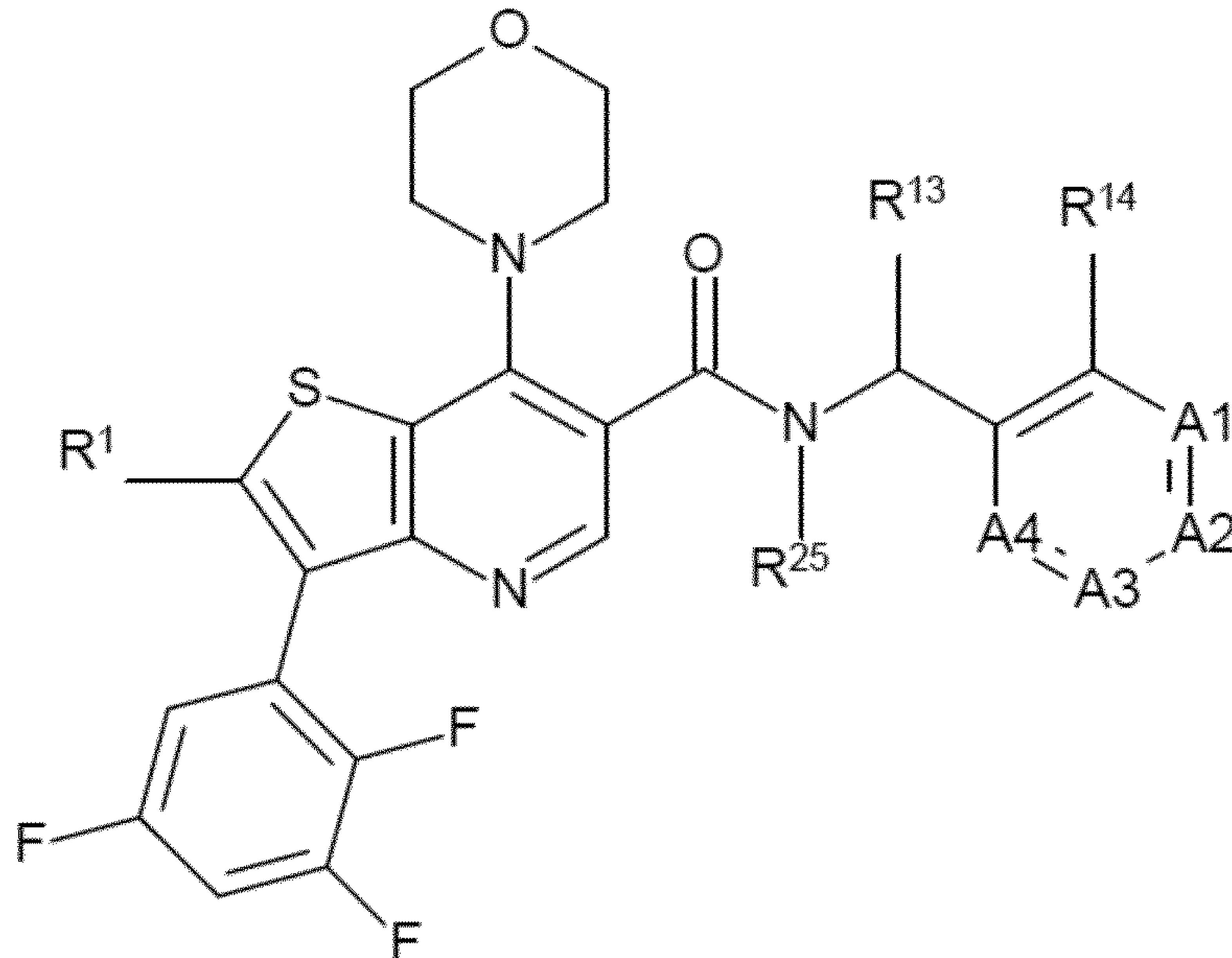
Formula (Ikvii)



Formula (Ikviii)



Formula (Ikviiii)



Formula (Ikix)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^{13} , R^{14} , A1, A2, A3; A4 and R^{25} are defined as in any of the embodiments
5 described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iki), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
embodiments thereof, the compounds are according to Formula (Ikii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds
10 are according to Formula (Ikiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ikiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ikv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
15 embodiments thereof, the compounds are according to Formula (Ikvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ikvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ikviii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
20 embodiments thereof, the compounds are according to Formula (Ikix), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^7 and R^{25} are defined as below.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

5 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

10 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3
15 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

25 and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

5 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

10 Suitably R⁷ is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino,

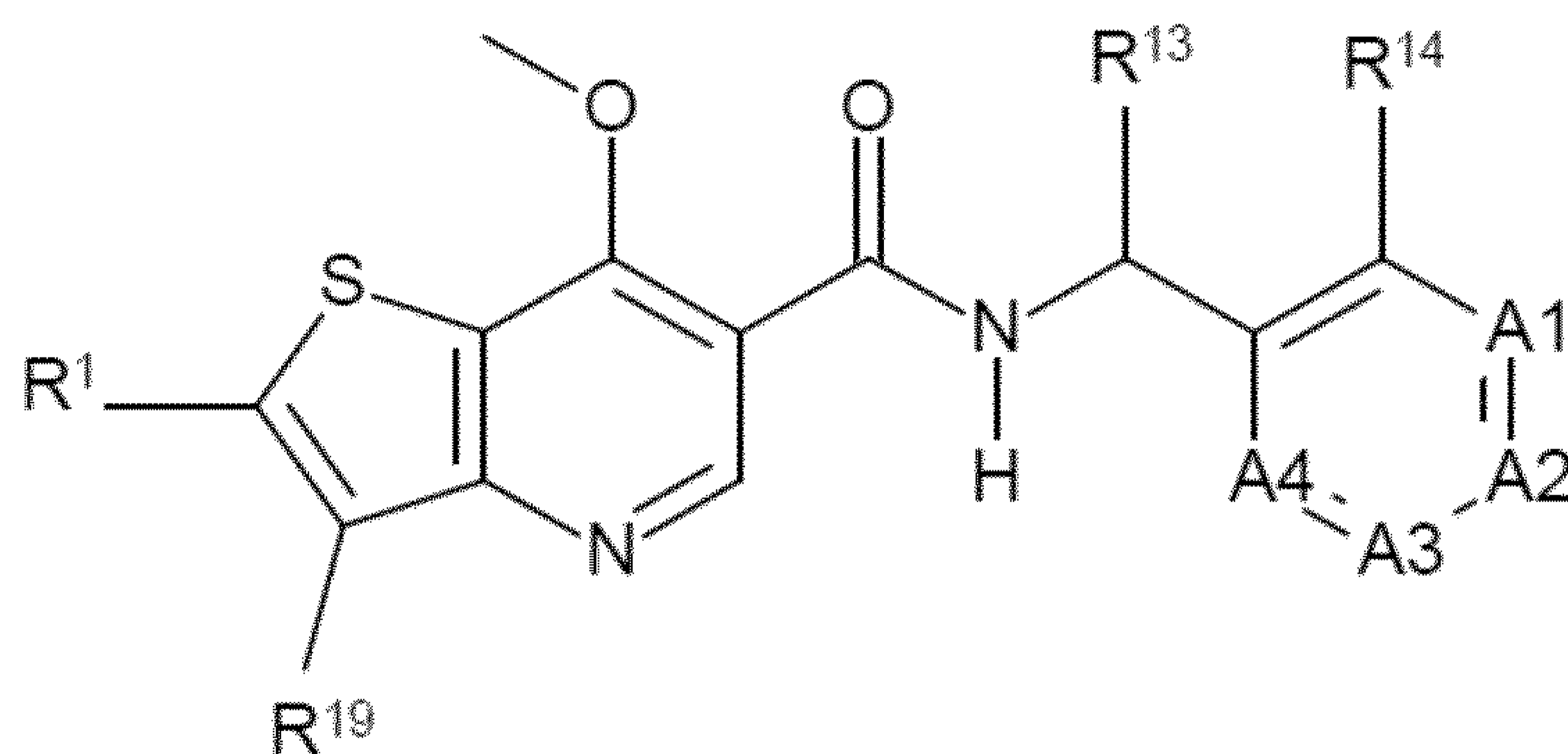
15 hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl,

and

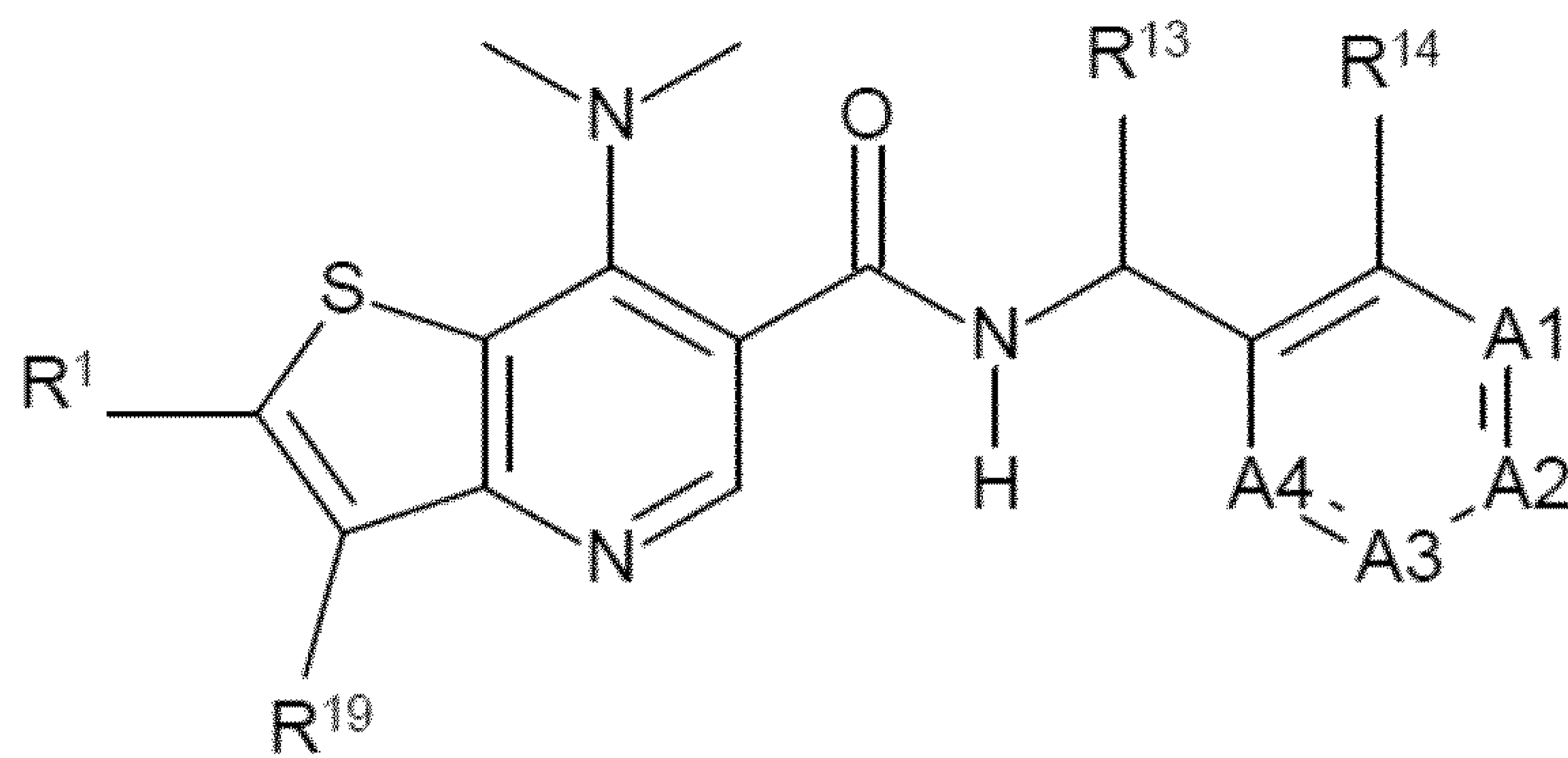
R²⁵ is hydrogen or methyl, more preferably hydrogen.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to

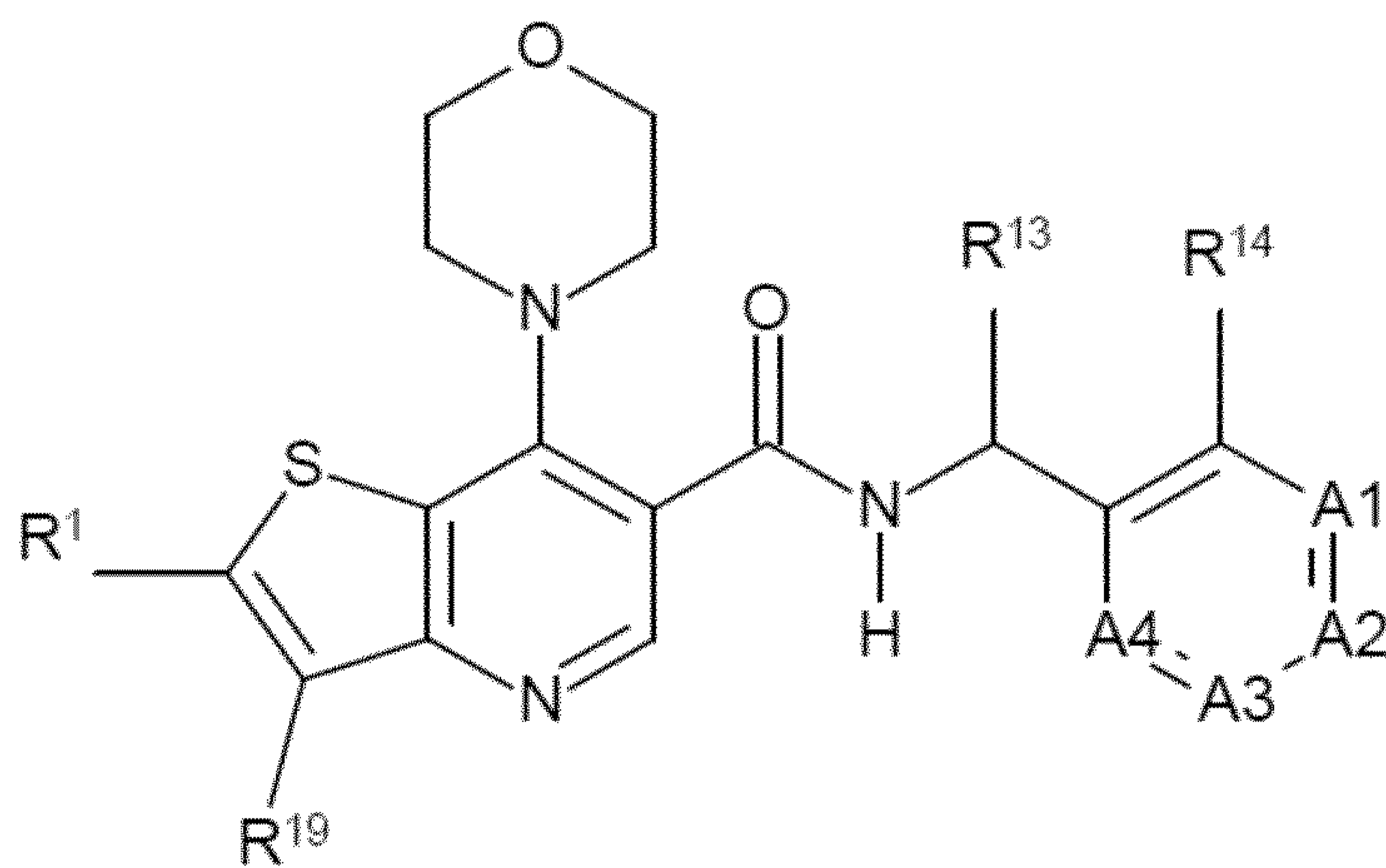
20 Formula (Ii), (Iii), (Iiii), (Iiv), (Iv) or (Ivi)



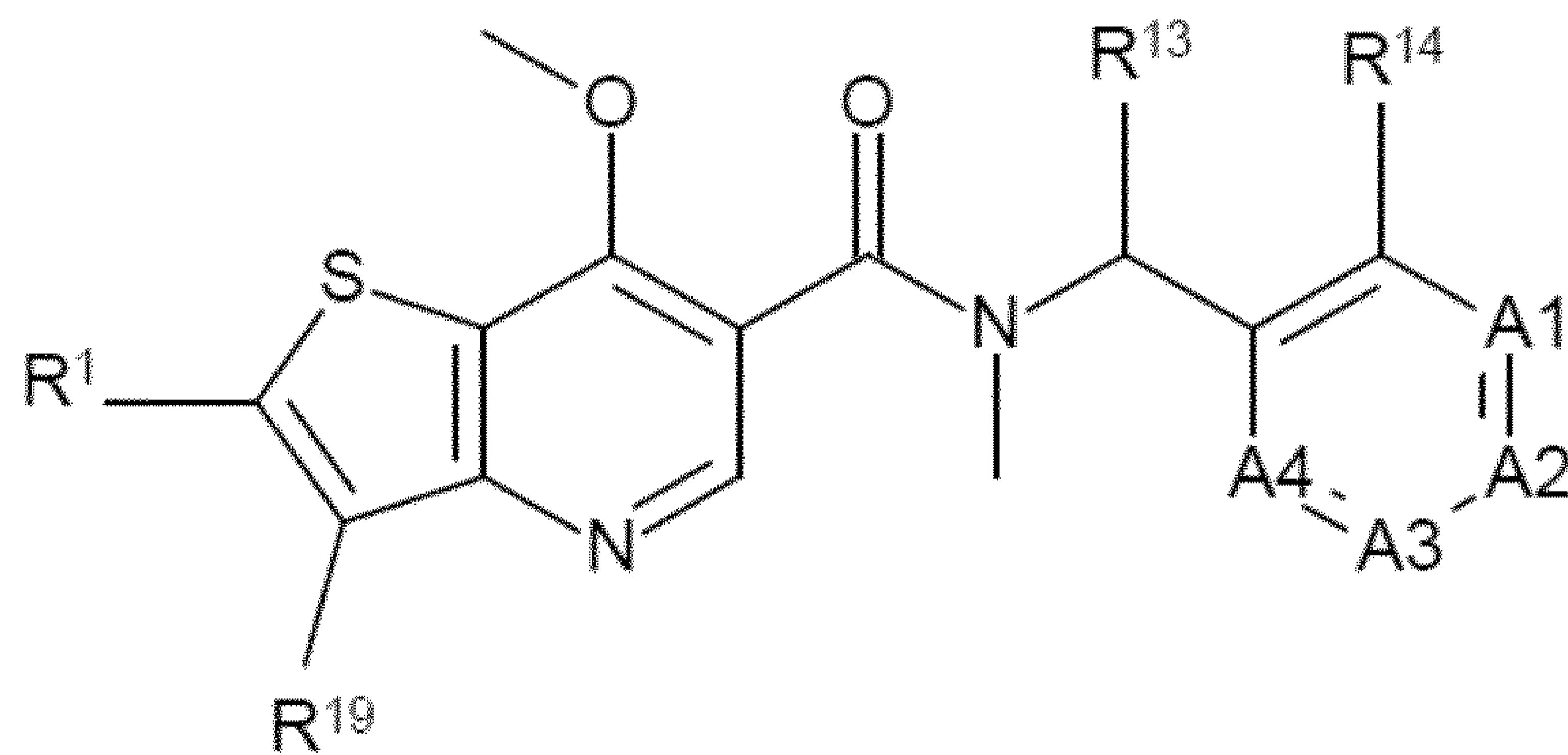
Formula (Ii)



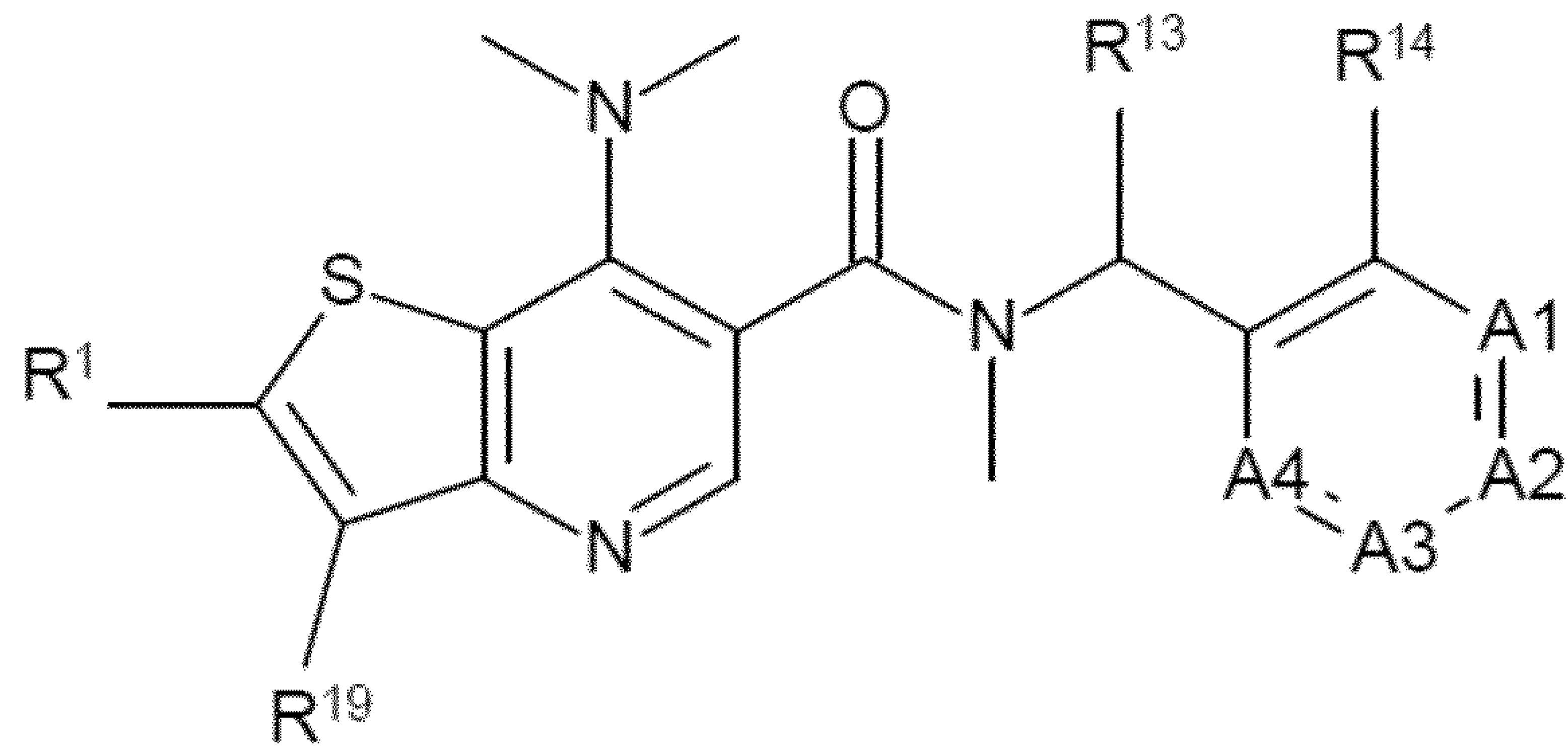
Formula (Iii)



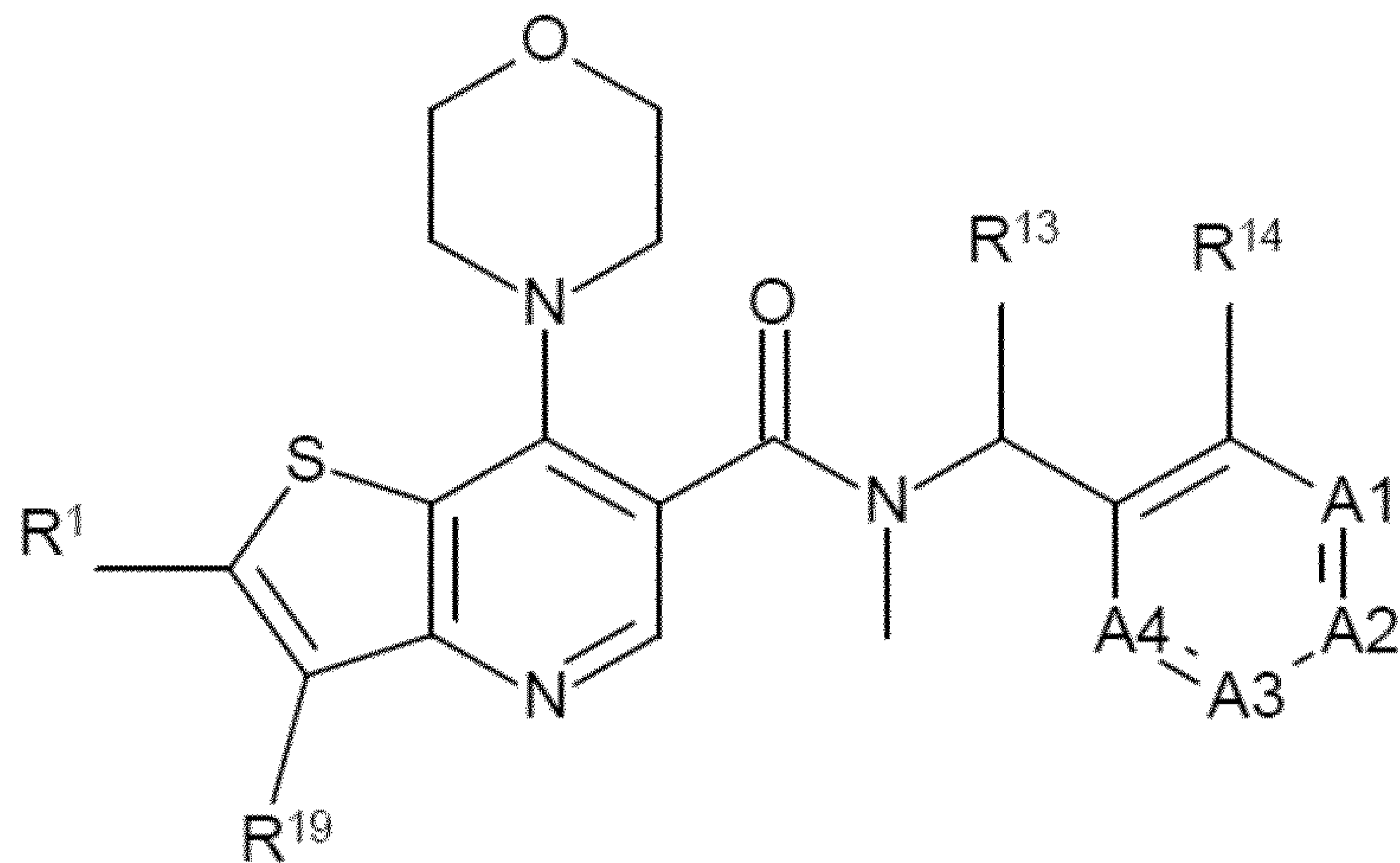
Formula (Iiii)



Formula (Iiv)



Formula (Iiv)



Formula (Iivi)

5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹, R¹³, R¹⁴, A₁, A₂, A₃, A₄ and R¹⁹ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Iiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the
 15 compounds are according to Formula (Iv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivi), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R¹³, R¹⁴, A₁, A₂, A₃ and A₄ as well as R¹⁹ are defined as below.

In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
5 by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

10 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

15 R^{19} is independently selected from the group consisting of

C_{6-10} -aryl and 5 to 10-membered heteroaryl,

wherein each C_{6-10} -aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, $NR^{20}R^{21}$, $C(=O)OR^{22}$ and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{6-10} -aryl or

25 R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, or C_{6-10} -aryl or the heterocyclic ring formed by R^{20} and R^{21} together with the N atom to which they are attached is optionally

substituted with one or more substituents independently selected from the group consisting of

5 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

In one embodiment of the invention and/or embodiments thereof,

10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

15 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R¹⁹ is a 5 to 10-membered heteroaryl

20 wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

25 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In an embodiment of the invention and/or embodiments thereof

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring forming carbon atoms are optionally replaced by -NH- or -O-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

5 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

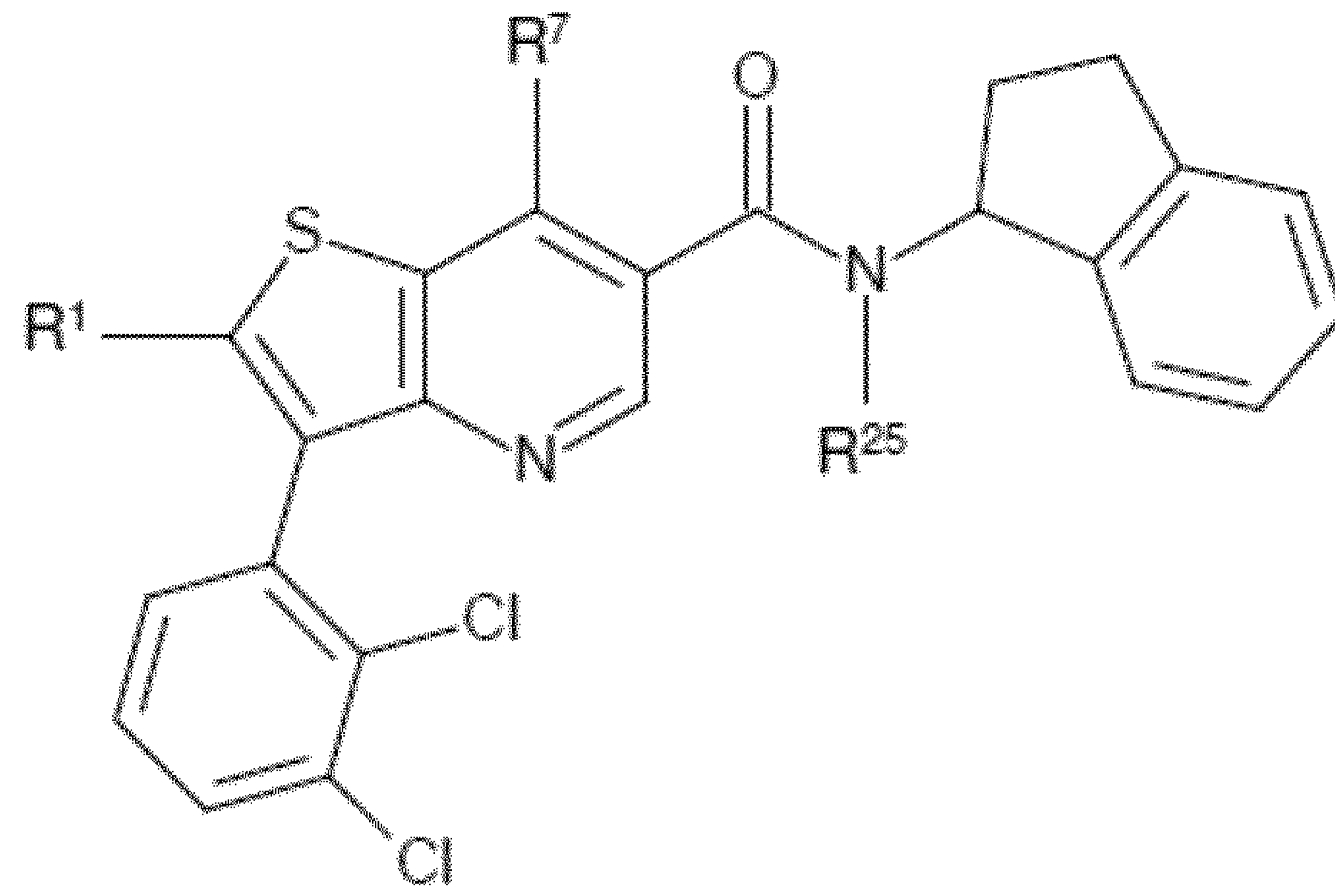
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

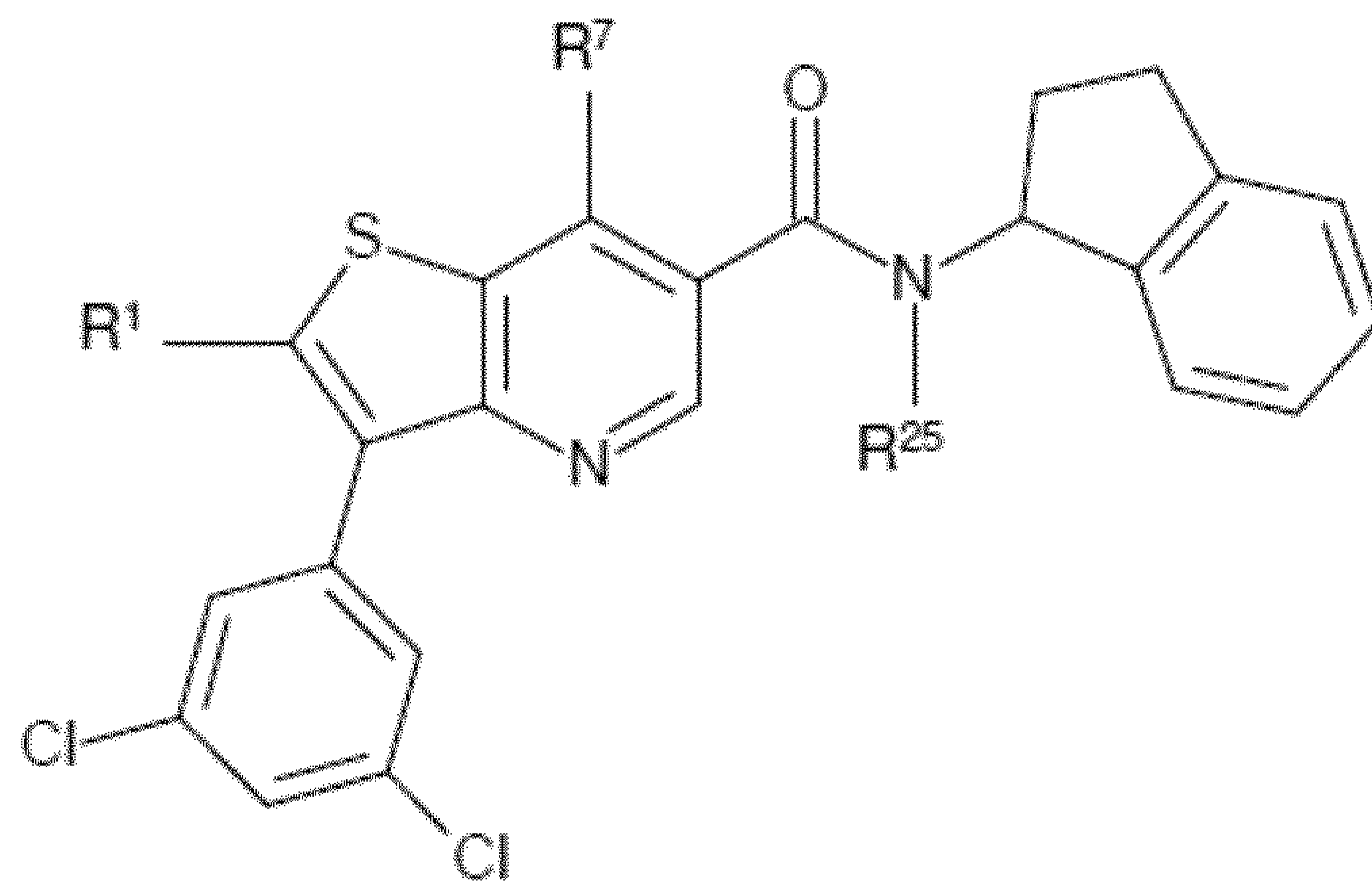
and

10 R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-
15 flurorophenyl, 3-chlorophenyl, 2,3-difluorophenyl 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorphenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.
20

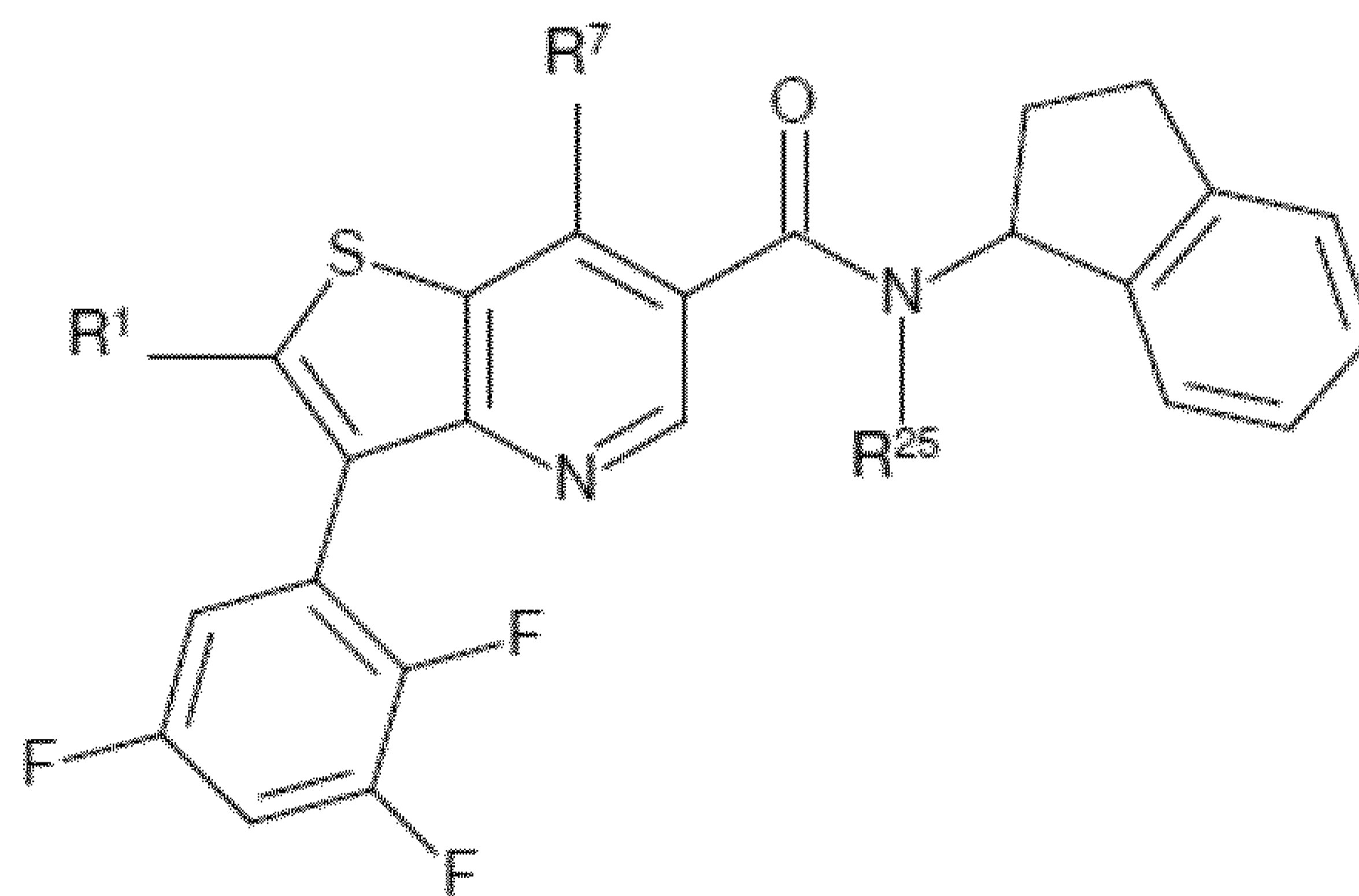
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imi), (Imii), (Imiii), (Imiv), (Imv), (Imvi), (Imvii), (Imviii) or (Imix)



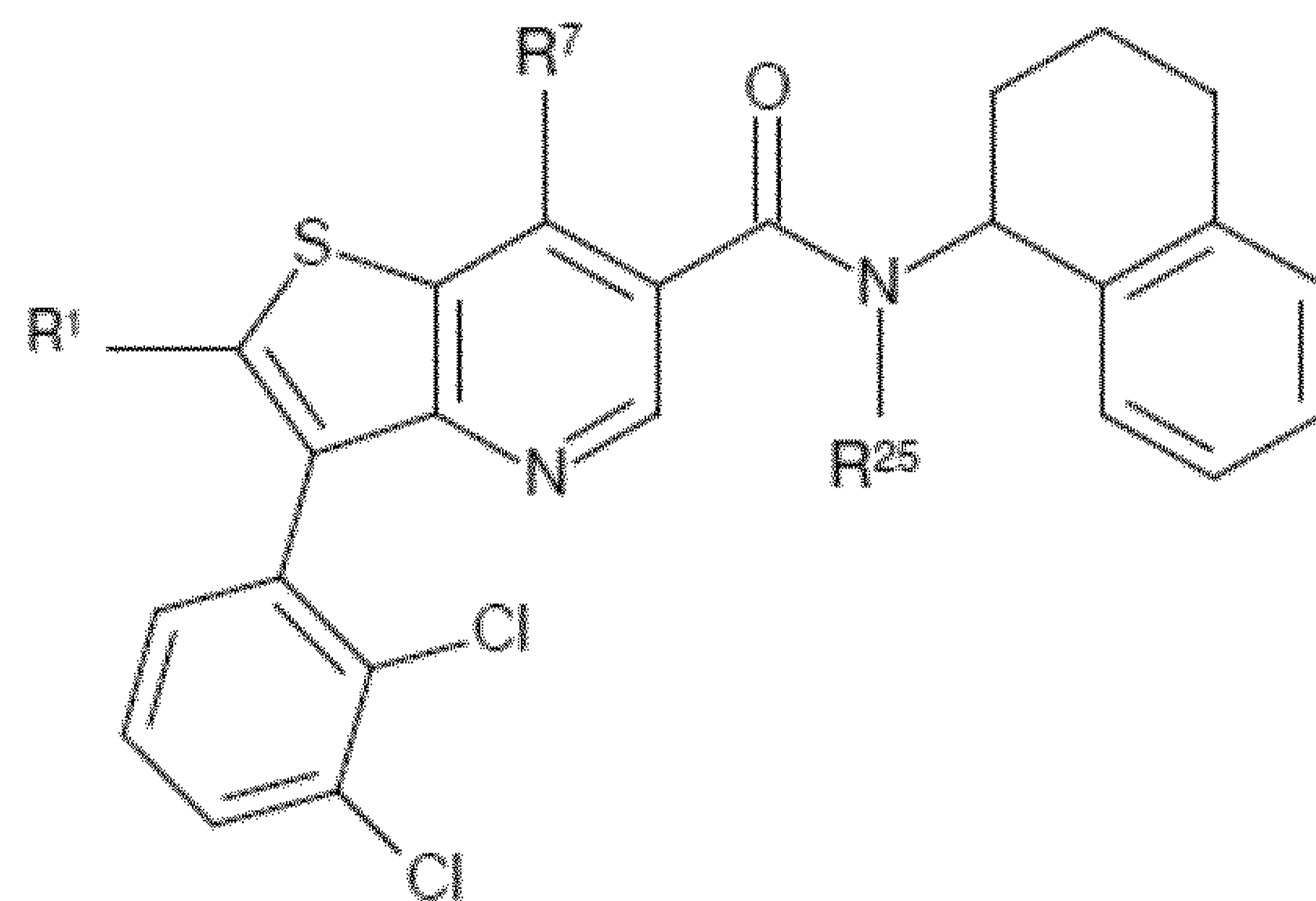
Formula (Imi)



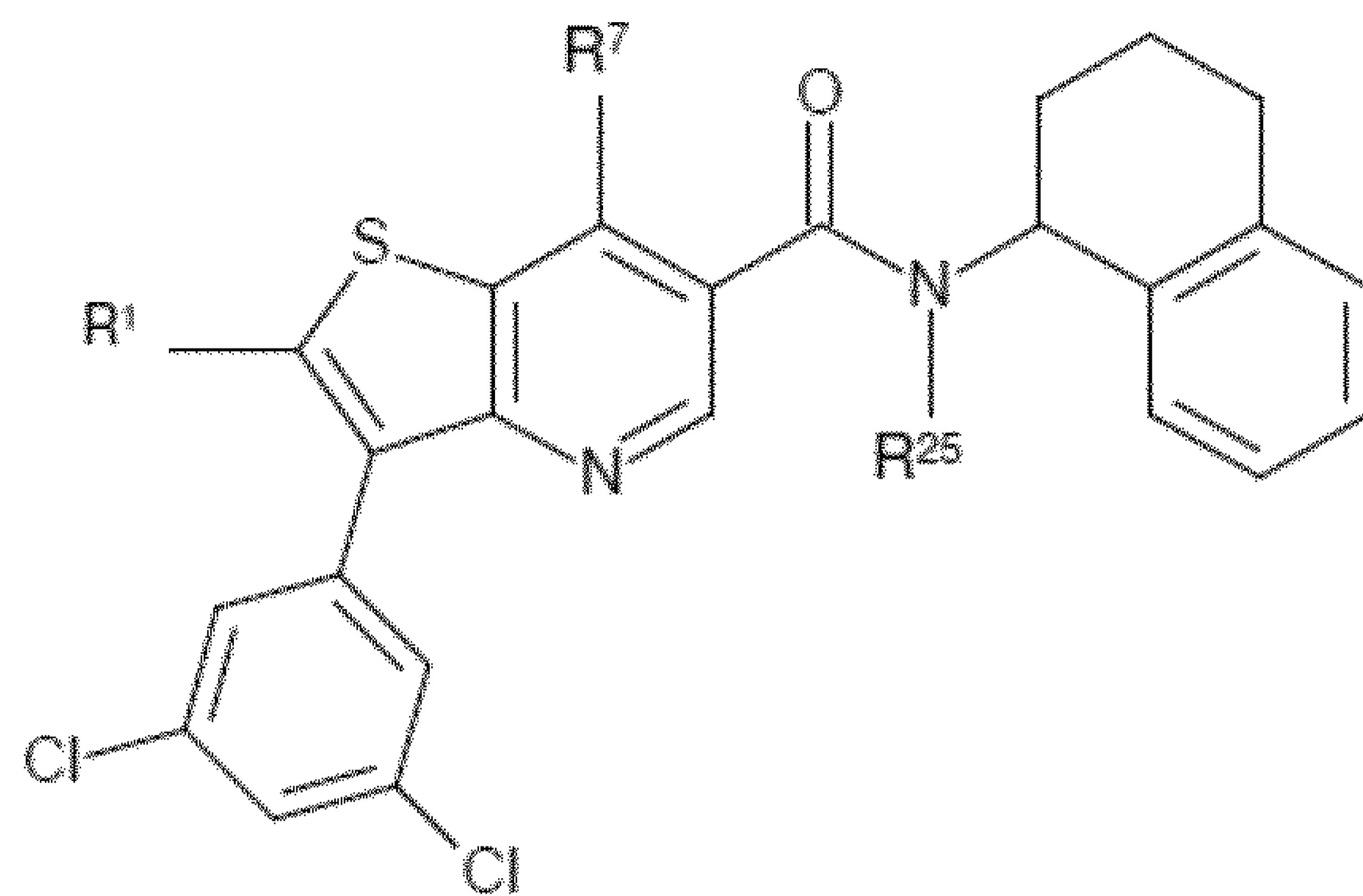
Formula (Imii)



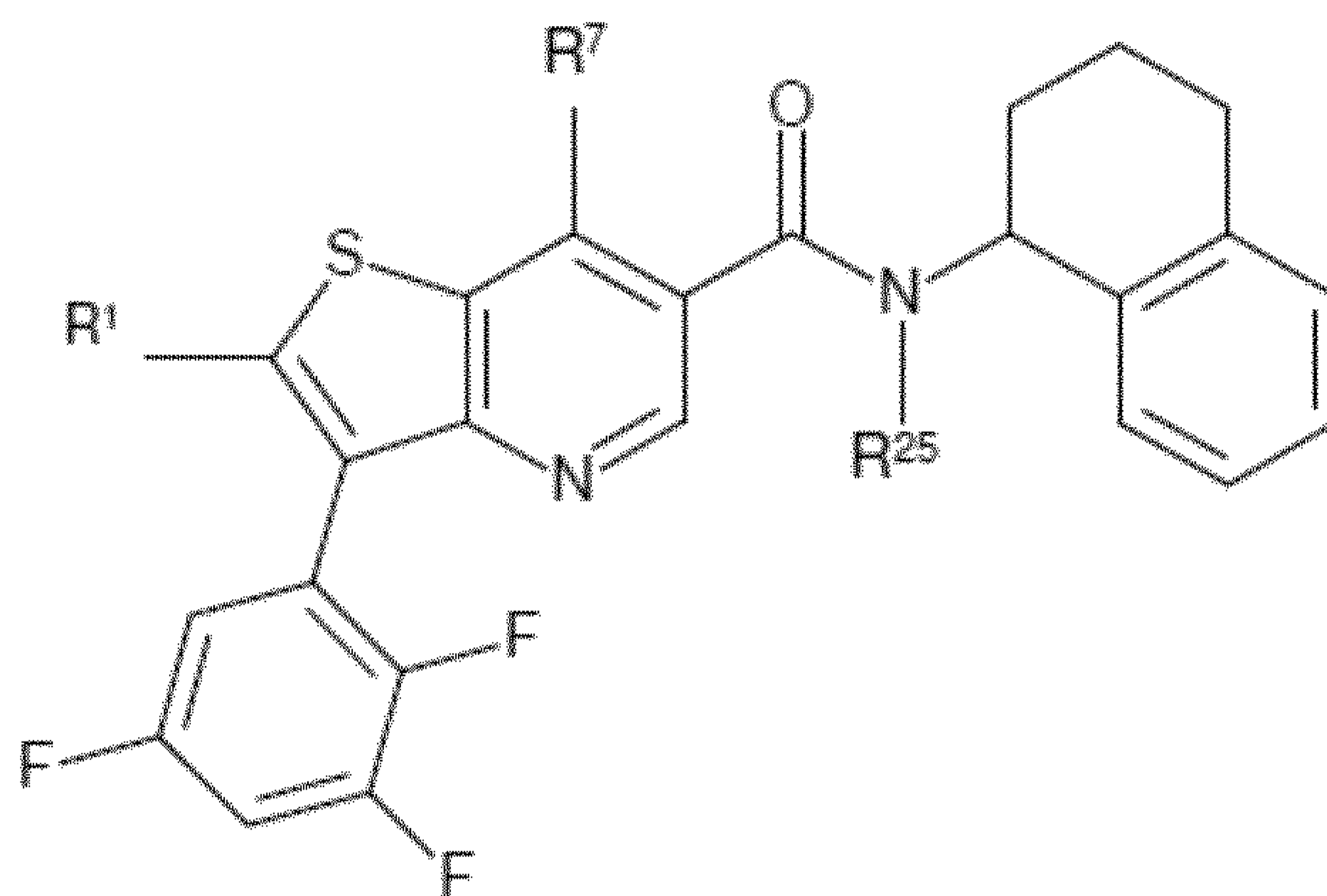
Formula (Imiii)



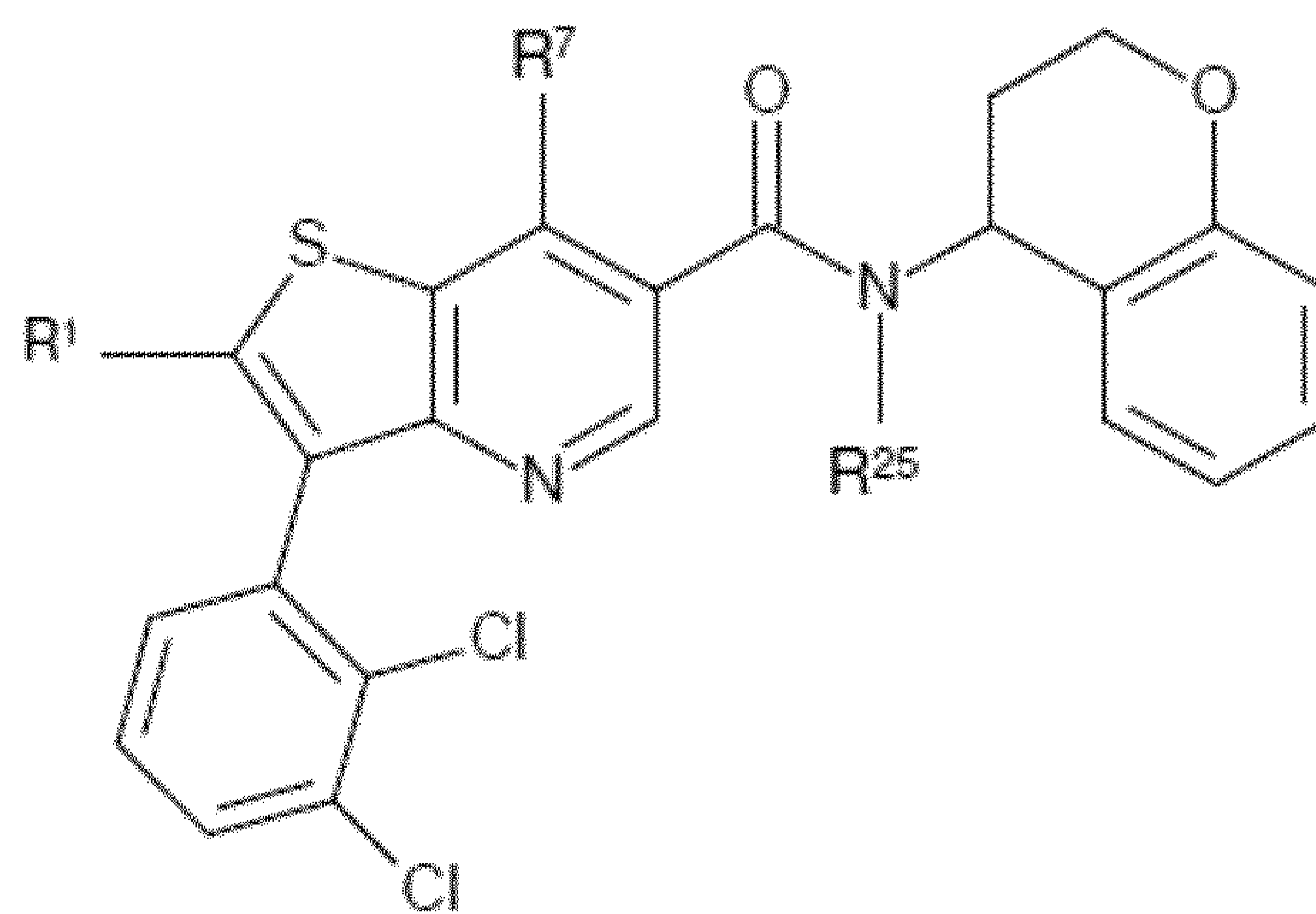
Formula (Imiv)



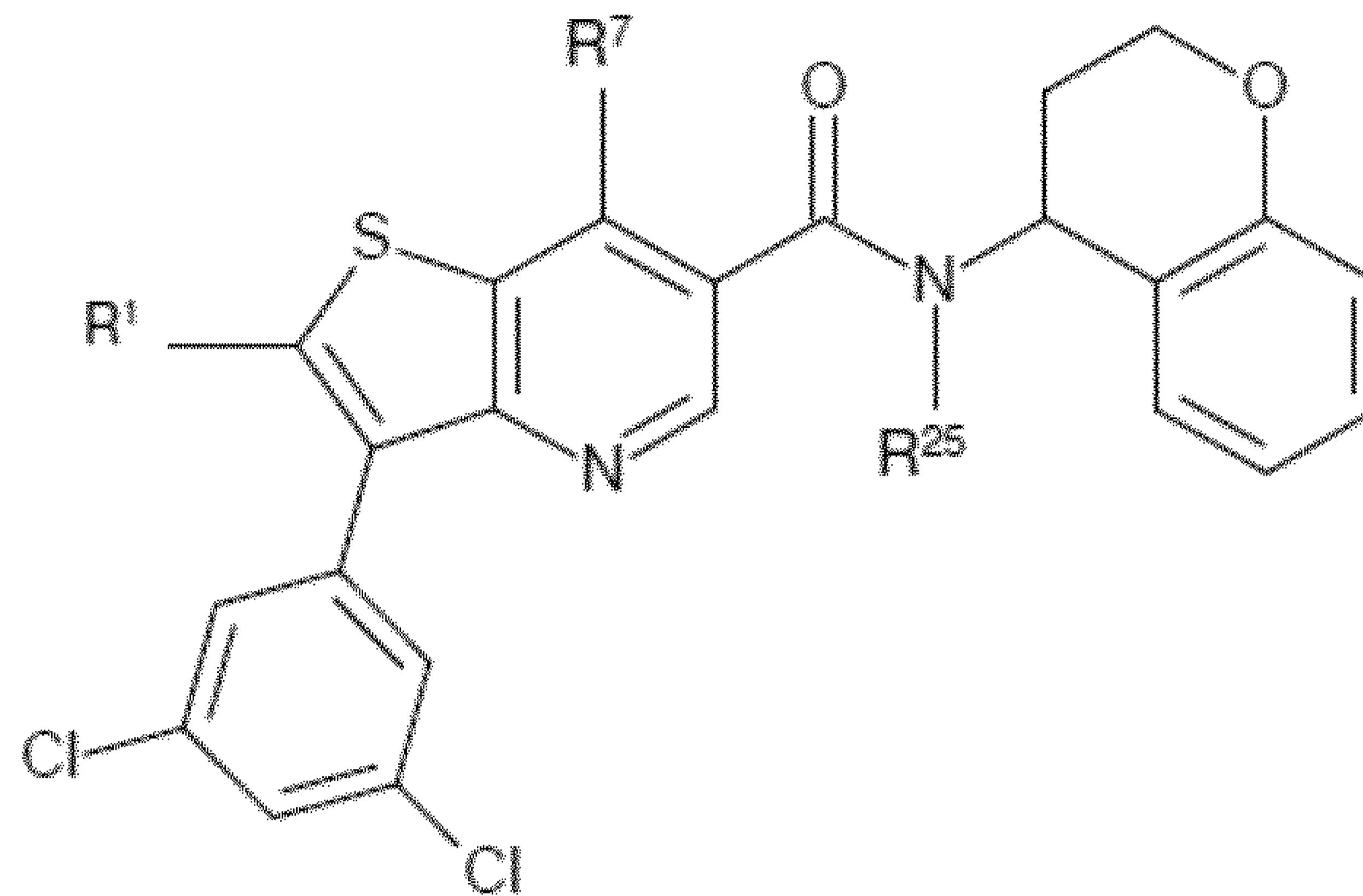
Formula (Imv)



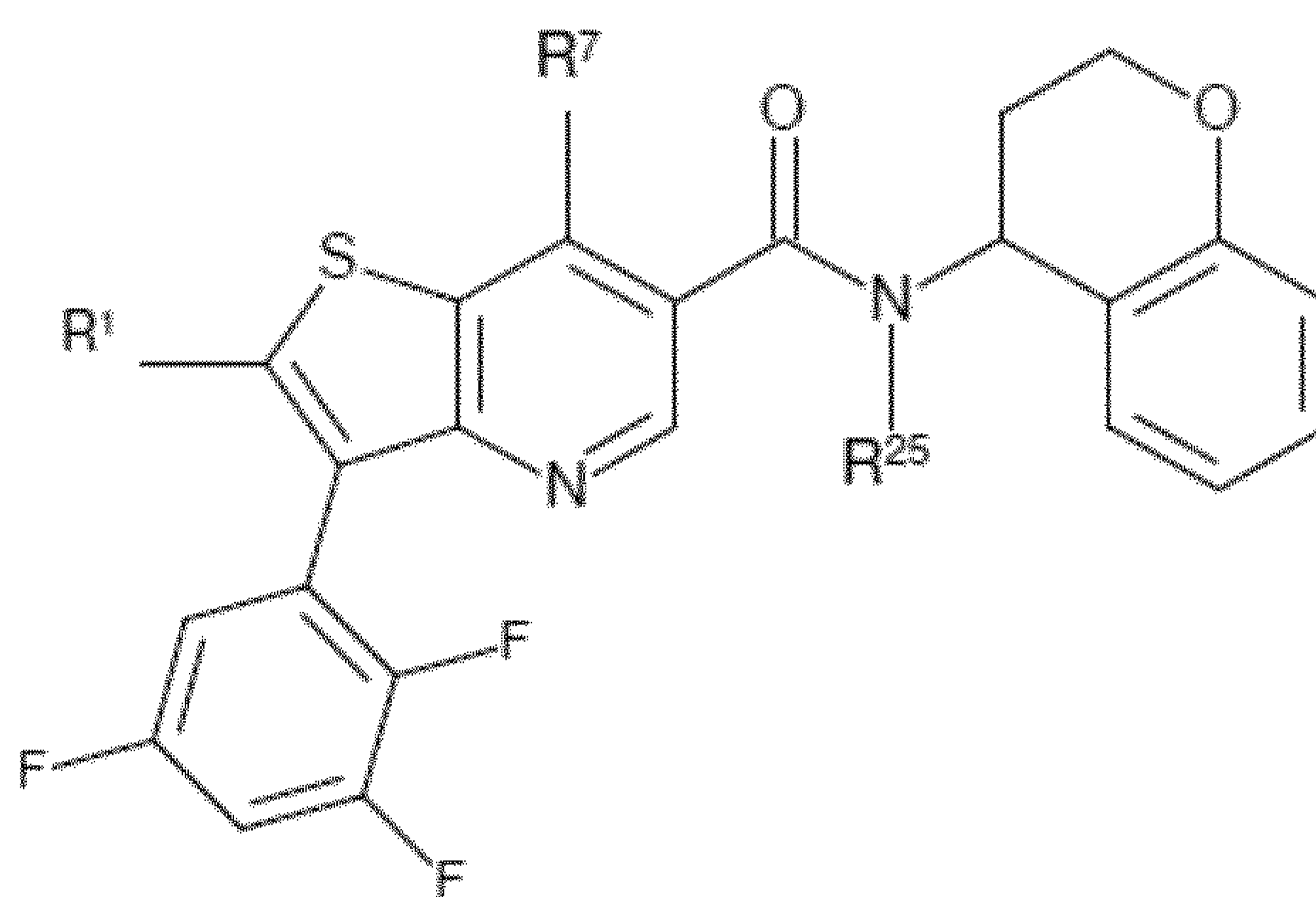
Formula (Imvi)



Formula (Imvii)



Formula (Imviii)



Formula (Imix)

- 5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Imii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imv), preferably in form of the (*S*)-enantiomer.
 15 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imviii), preferably in form of the (*S*)-enantiomer. In an

embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imix), preferably in form of the (*S*)-enantiomer.

In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms
5 containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C_{1-3} -alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

10 A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or
15 $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

R^{19} is independently selected from the group consisting of

C_{6-10} -aryl and 5 to 10-membered heteroaryl,

wherein each C_{6-10} -aryl or 5 to 10-membered heteroaryl is optionally substituted with one
20 or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl,
5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, $NR^{20}R^{21}$, $C(=O)OR^{22}$
and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

25 hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{6-10} -aryl or

R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

- 5 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

- 10 In one embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

- 15 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

- 20 R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

- 25 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In an embodiment of the invention and/or embodiments thereof

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

5 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

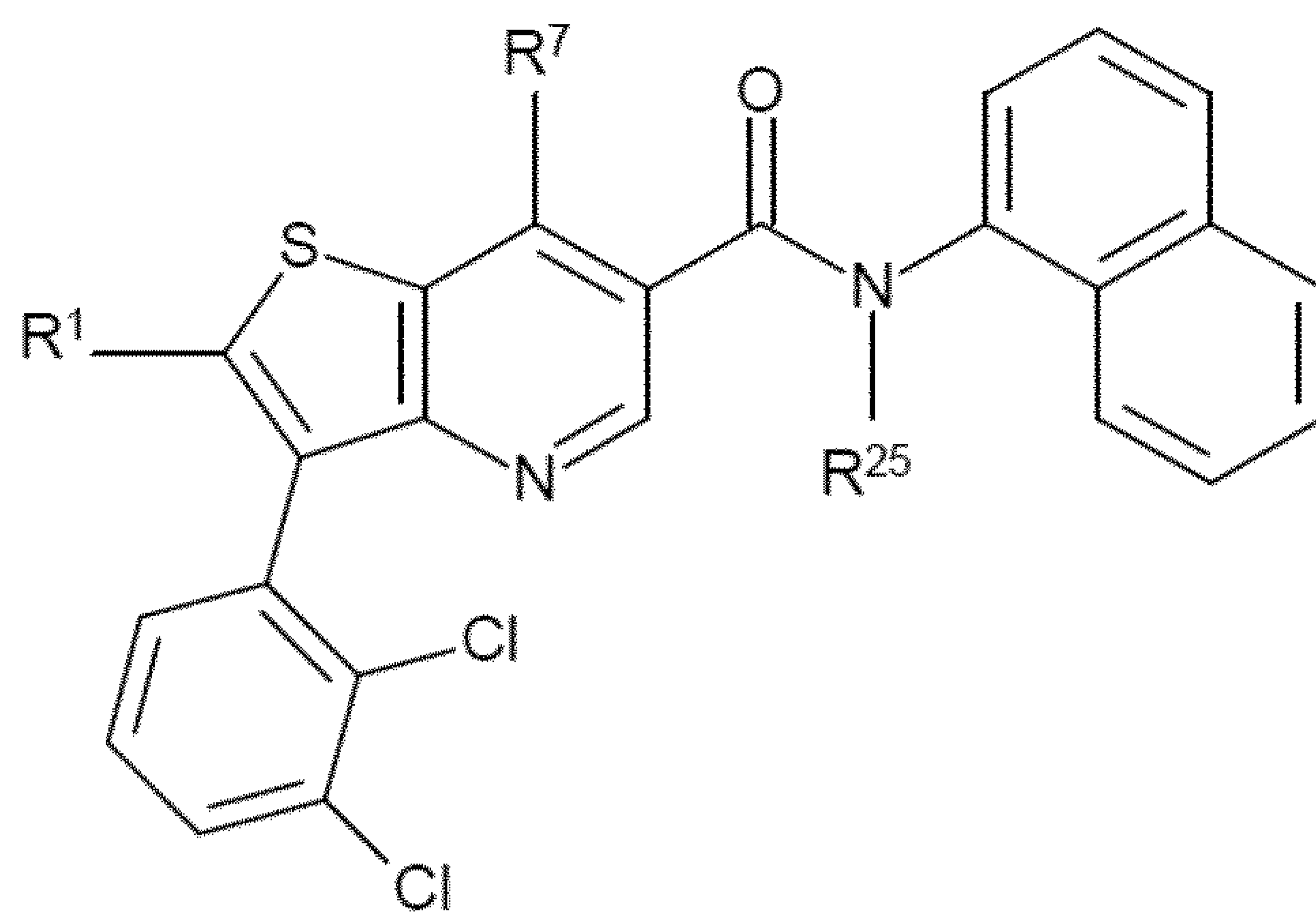
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

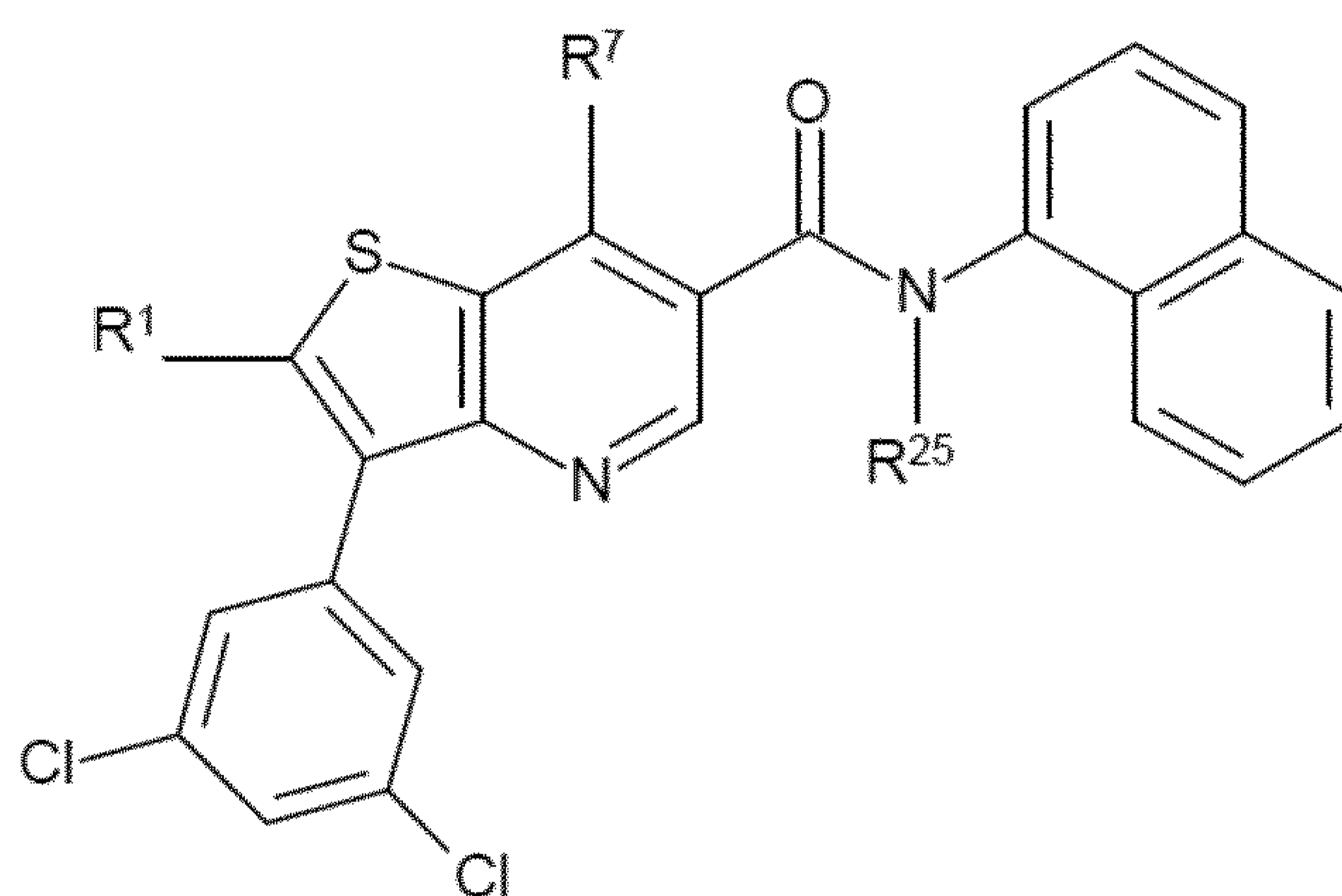
and

10 R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-
15 flurorophenyl, 3-chlorophenyl, 2,3-difluorophenyl 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorphenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.
20

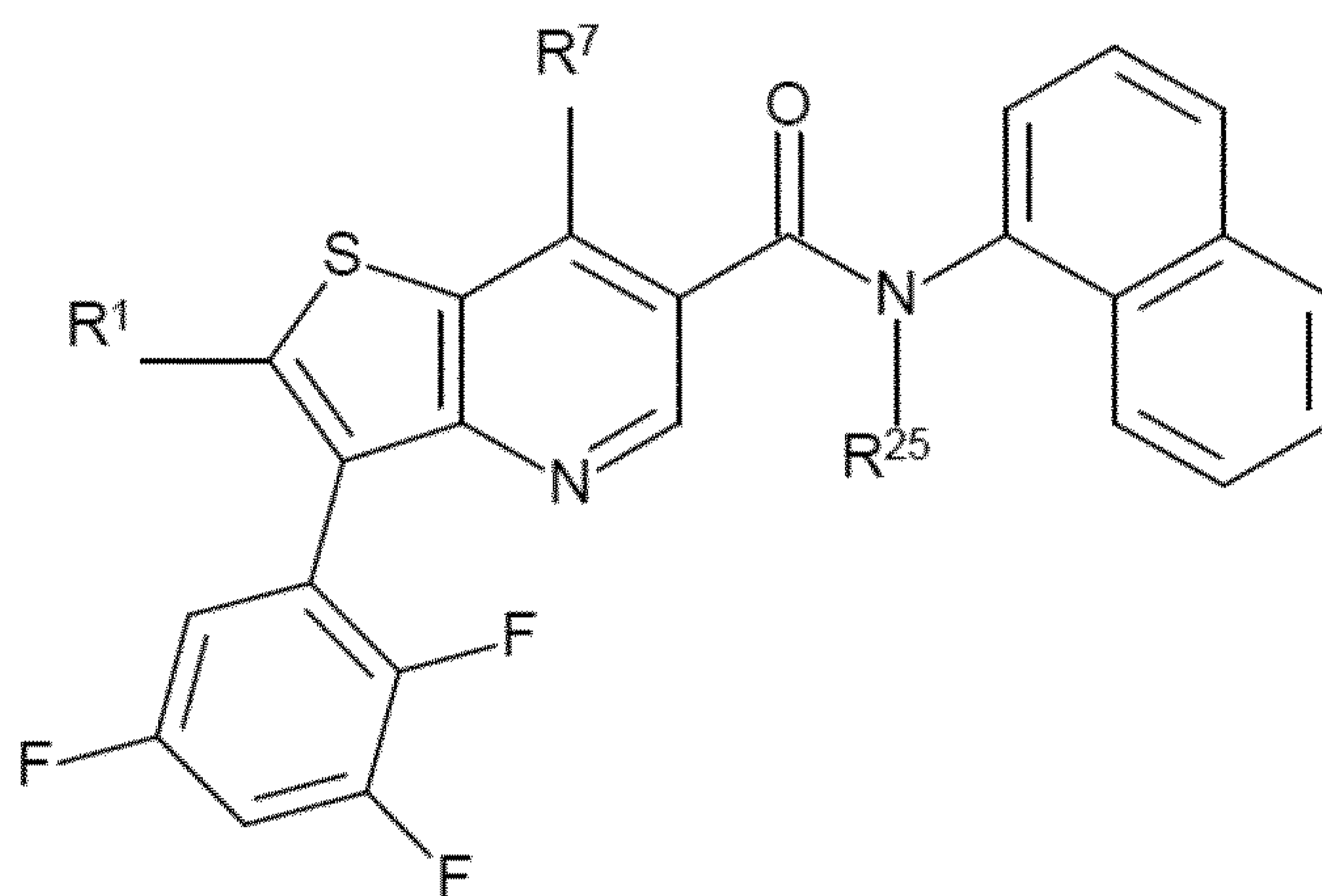
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imx), (Imxi), (Imxii), (Imxiii), (Imxiv) or (Imxv)



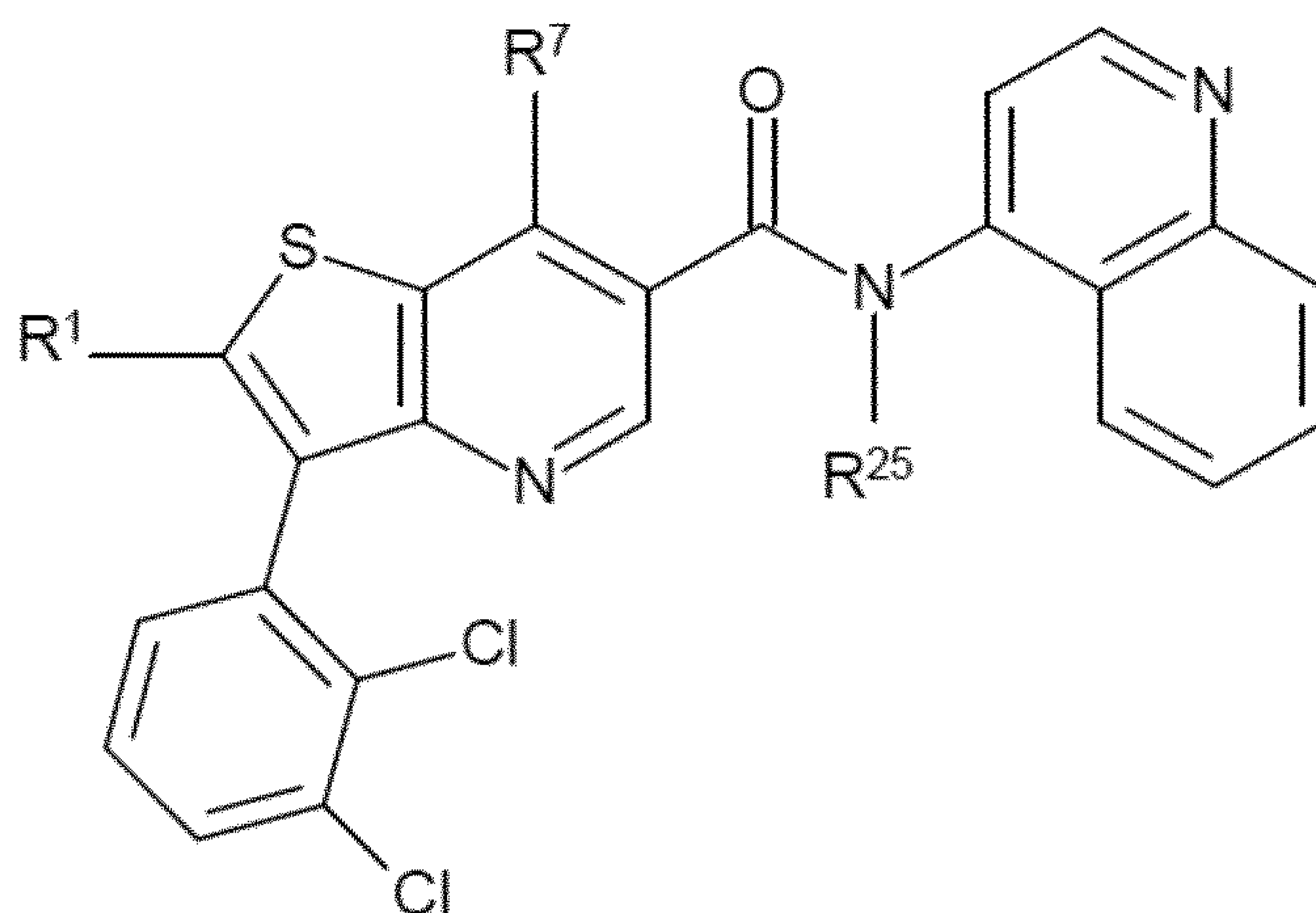
Formula (Imx)



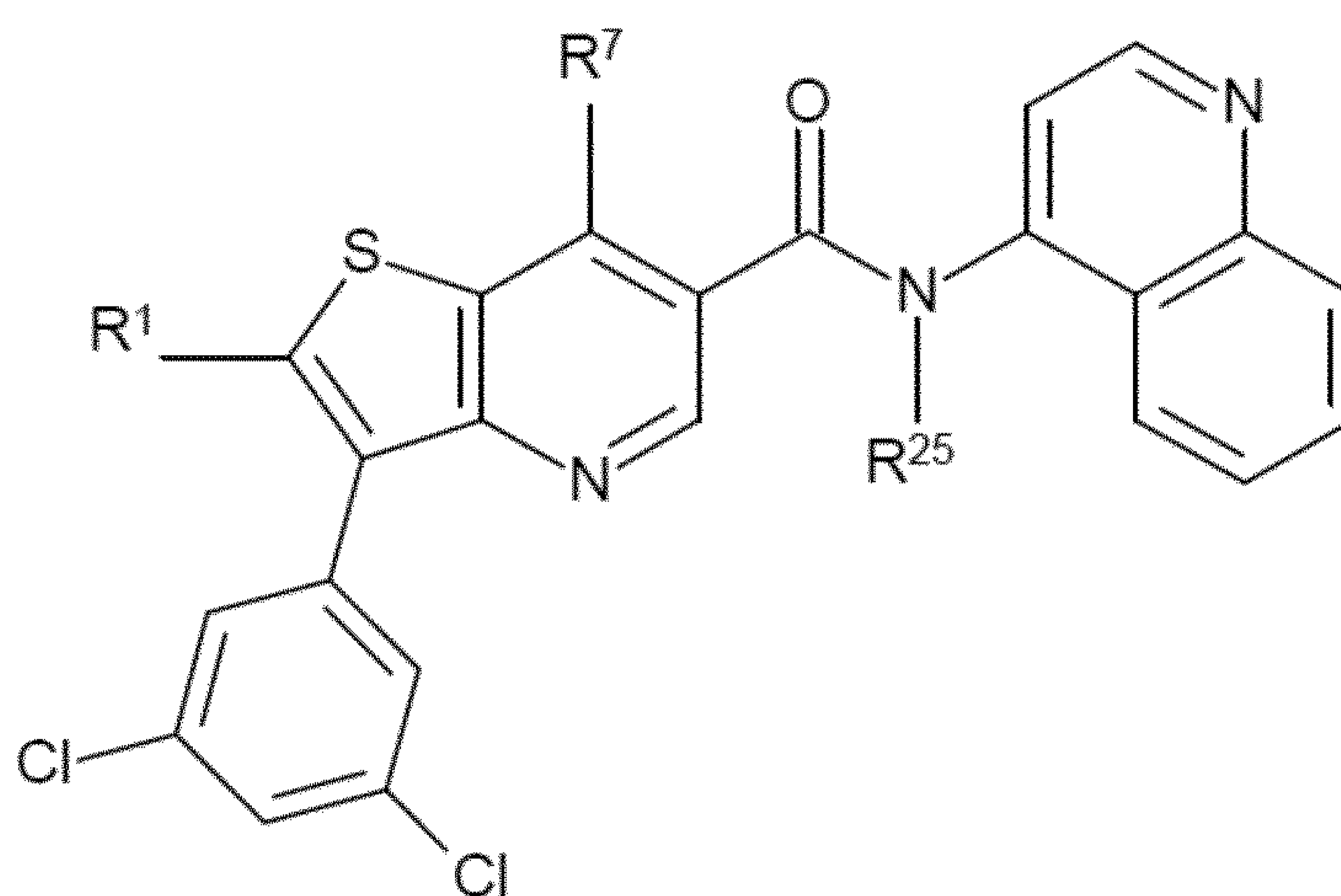
Formula (Imxi)



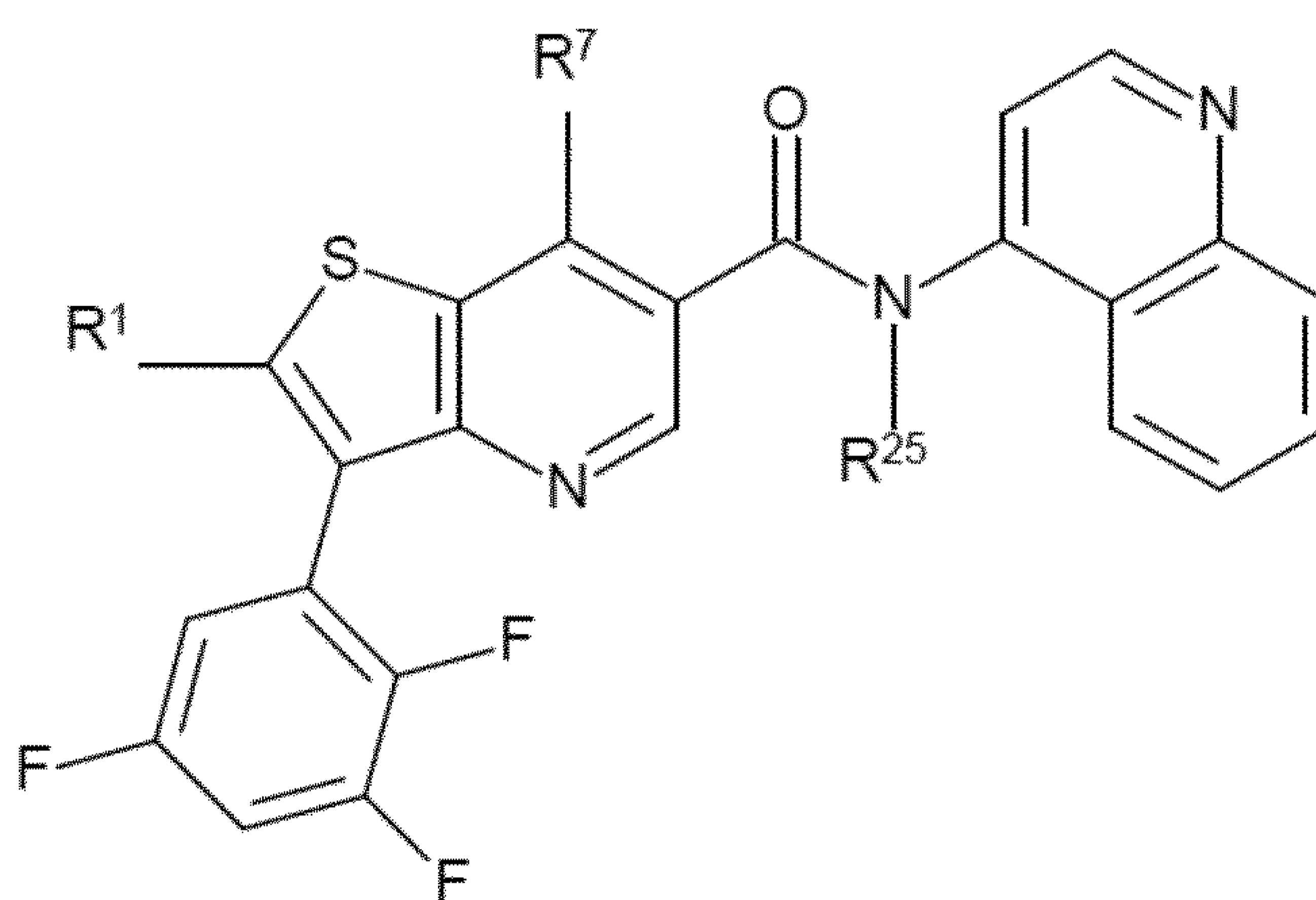
Formula (Imxii)



Formula (Imxiii)



Formula (Imxiv)



Formula (Imxv)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imx), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or

embodiments thereof, the compounds are according to Formula (Imxi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imxii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imxiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imxiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Imxv), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^{13} , R^{14} , A1, A2, A3 and A4 as well as R^{25} are defined as below.

In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

R^{25} is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

5 and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally
10 replaced by -NH- or -O-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

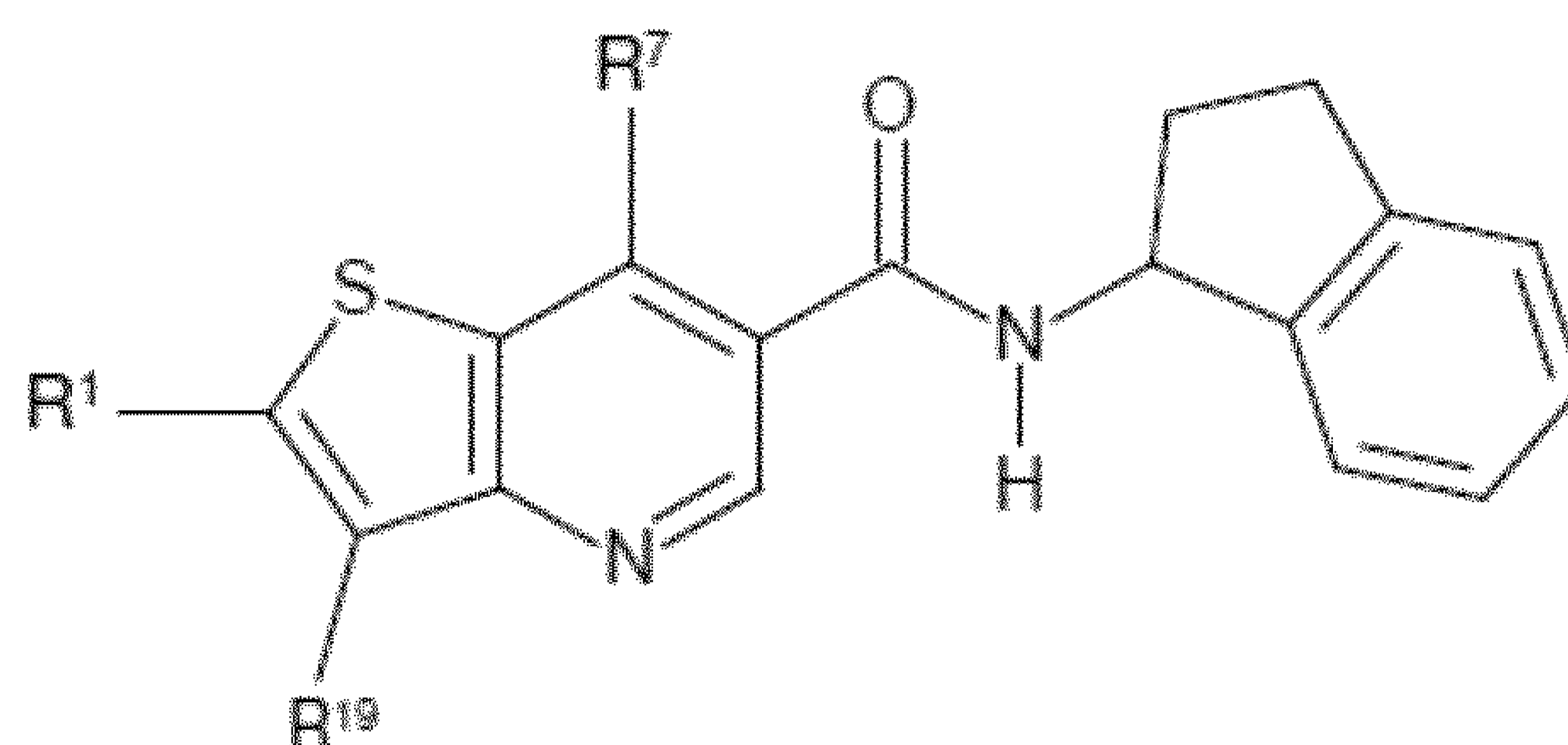
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

15 wherein none, one or two of A1, A2, A3 and A4 are N,

and

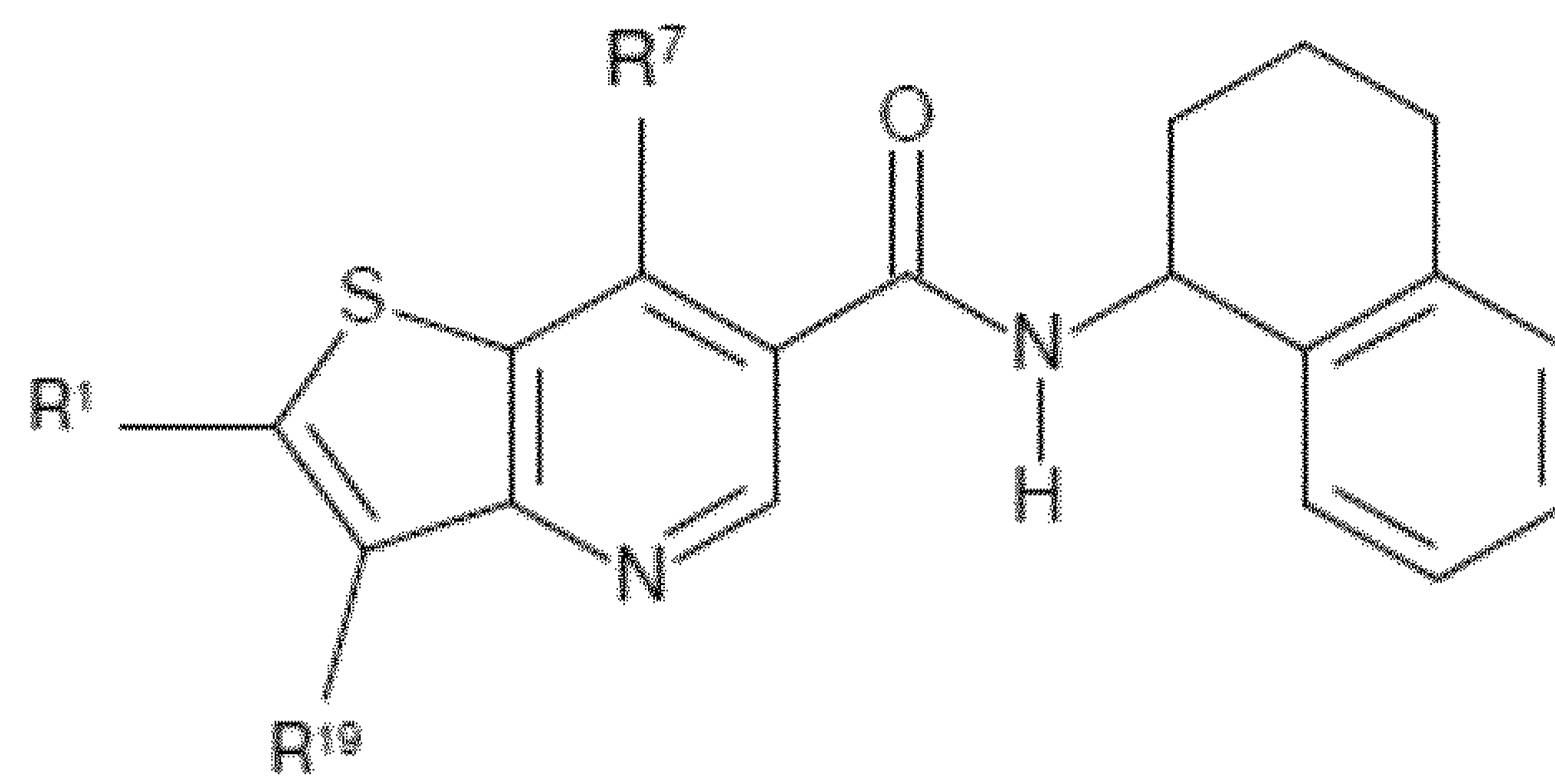
R²⁵ is hydrogen or methyl, more preferably hydrogen.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ini), (Inii), (Iniii), (Iniv), (Inv) or (Invi)

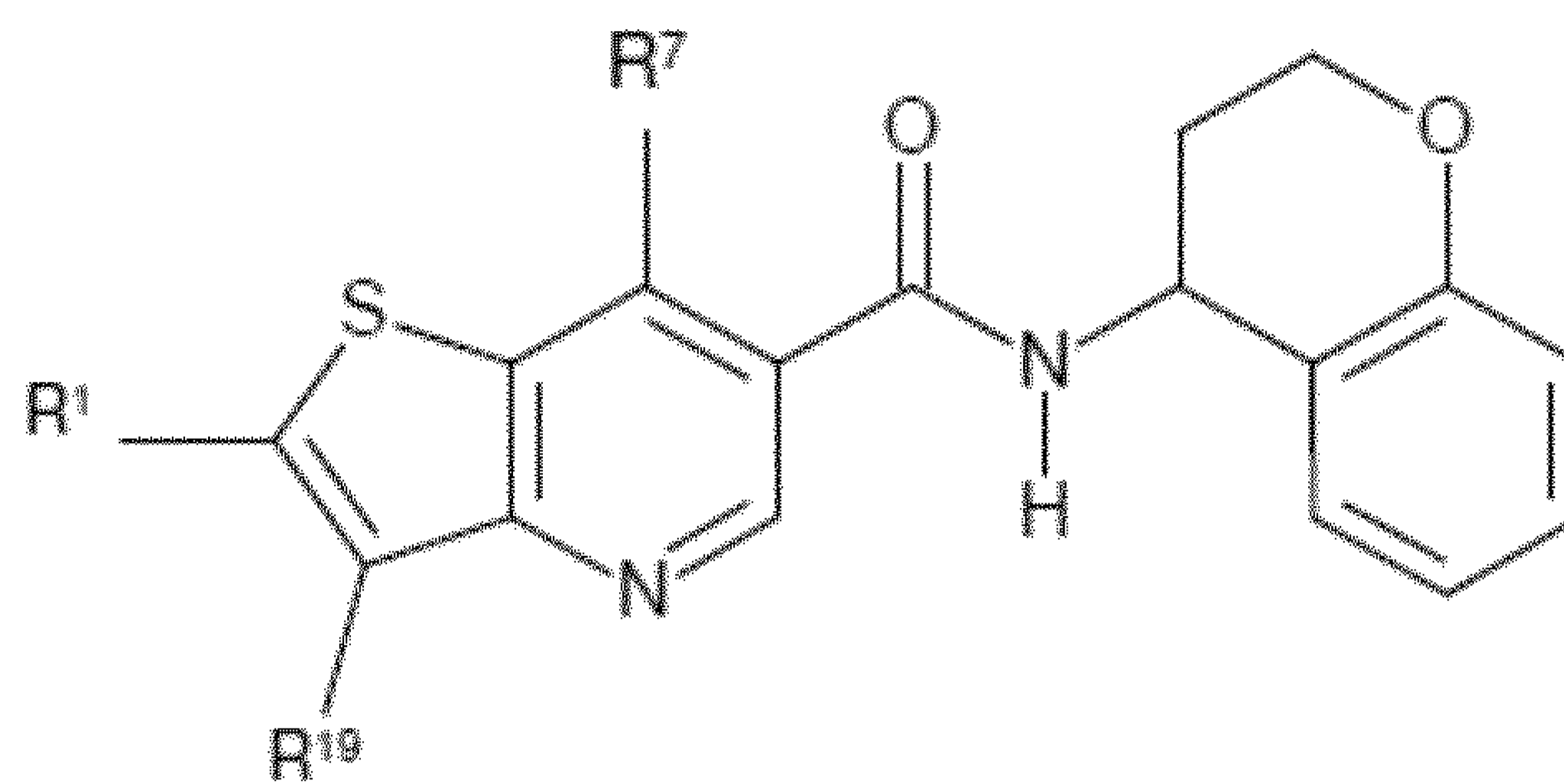


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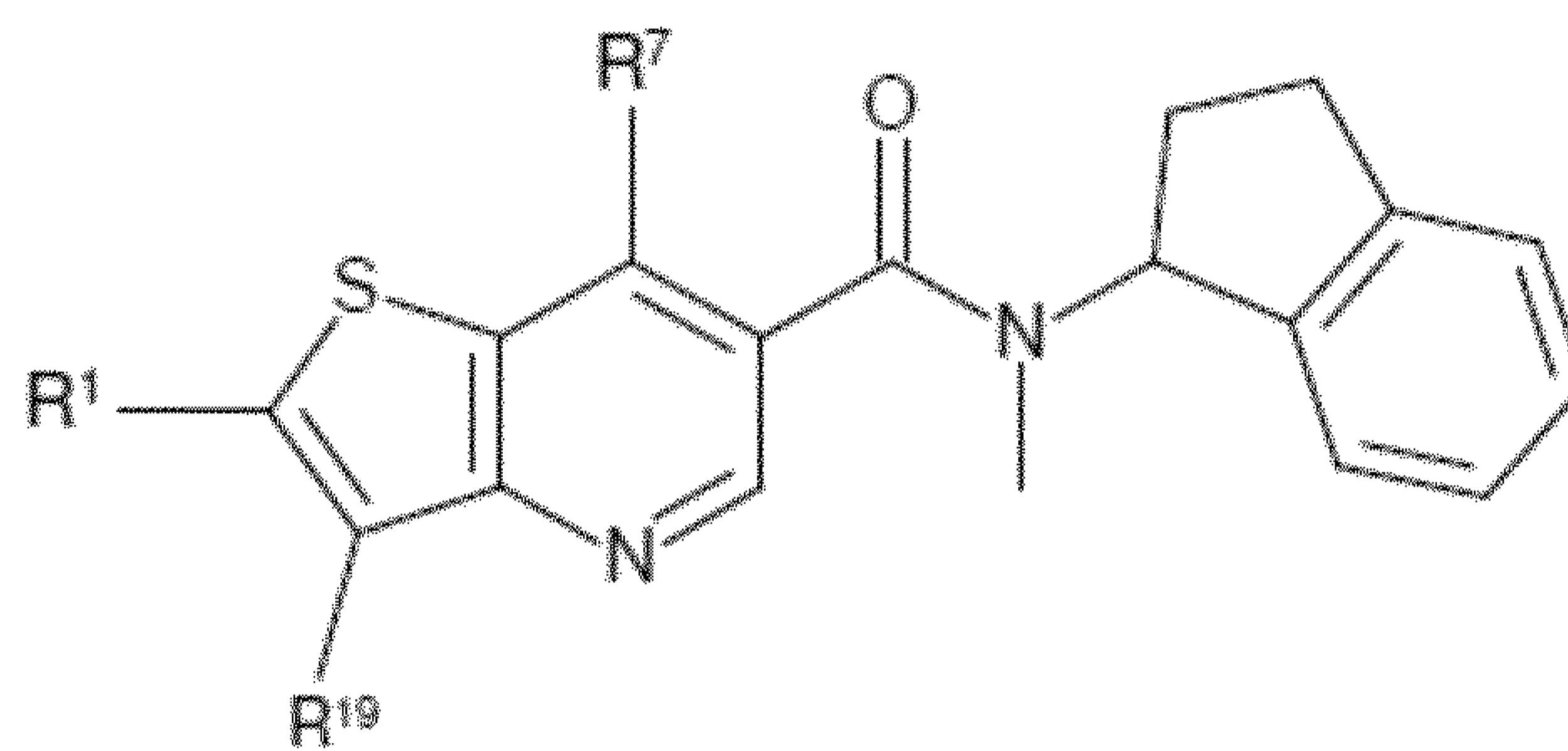
Formula (Ini)



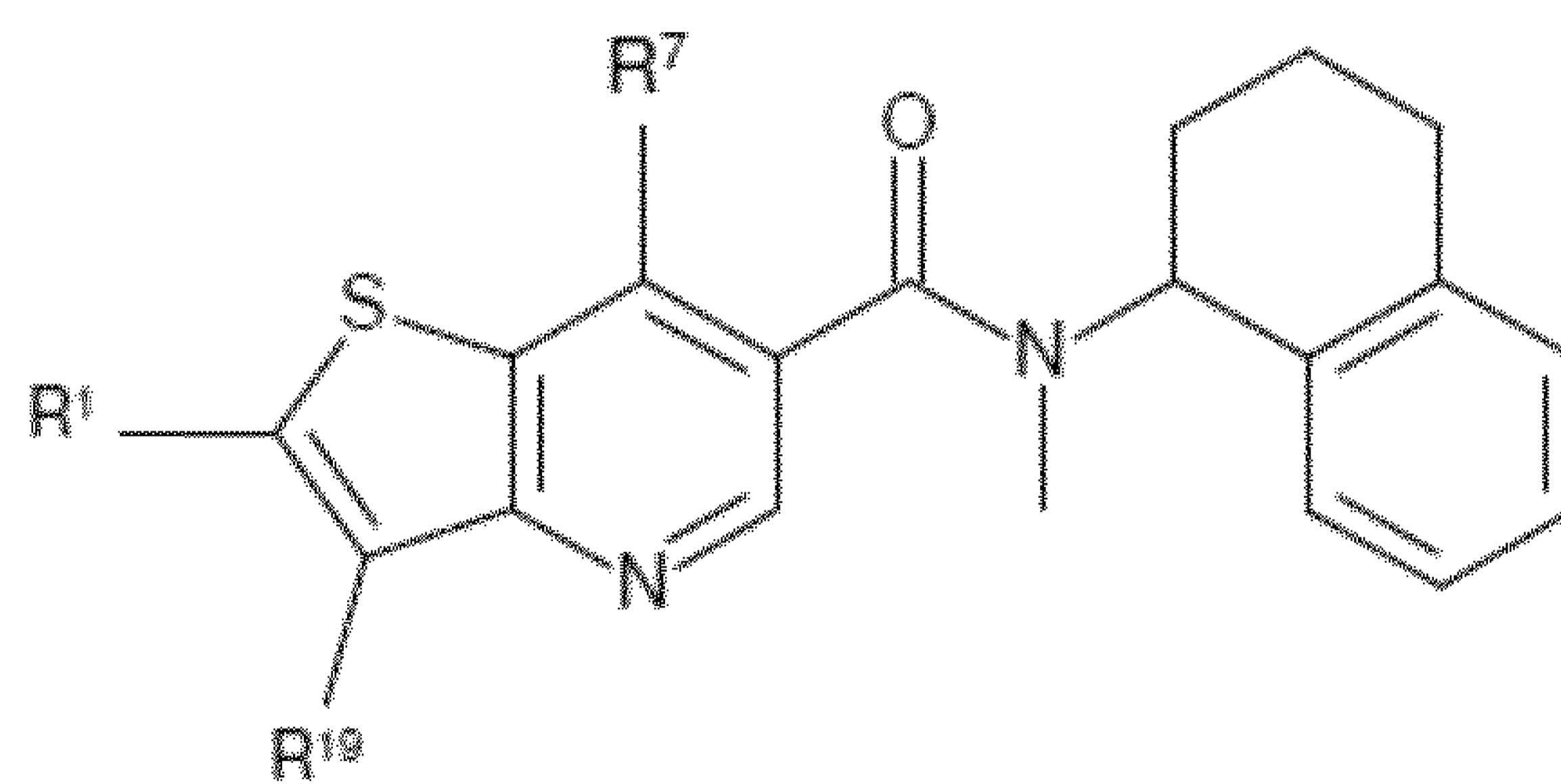
Formula (Inii)



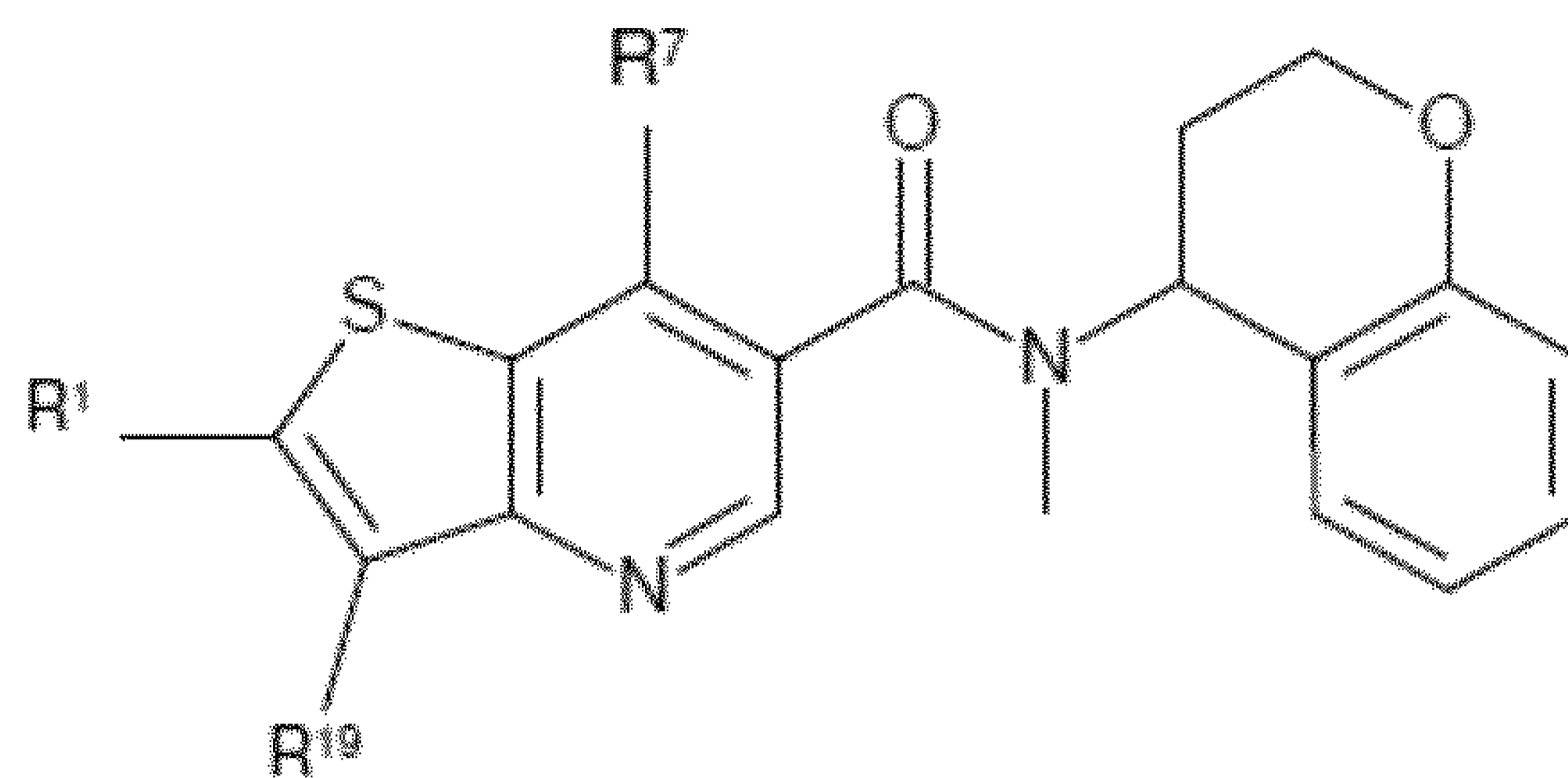
Formula (Iniii)



Formula (Iniv)



Formula (Inv)



Formula (Invi)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 and R^{19} are defined as in any of the embodiments described herein.

5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ini), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Inii), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iniii), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iniv),
 10 preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Inv), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Invi), preferably in form of the (S)-enantiomer.

15 In one embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C_{1-3} -alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

20 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or
 25 $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

5 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

10 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

15 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

20 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

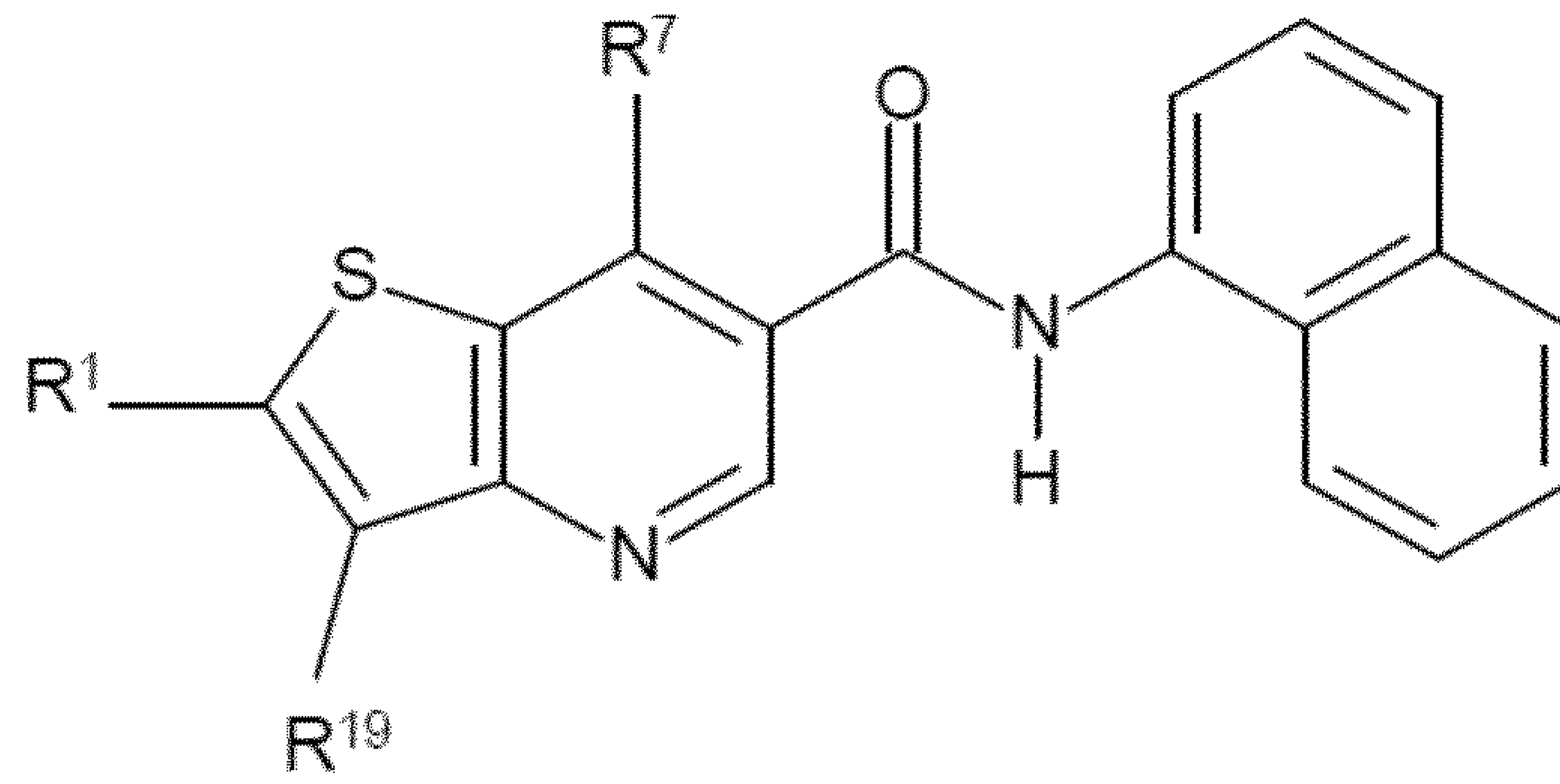
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

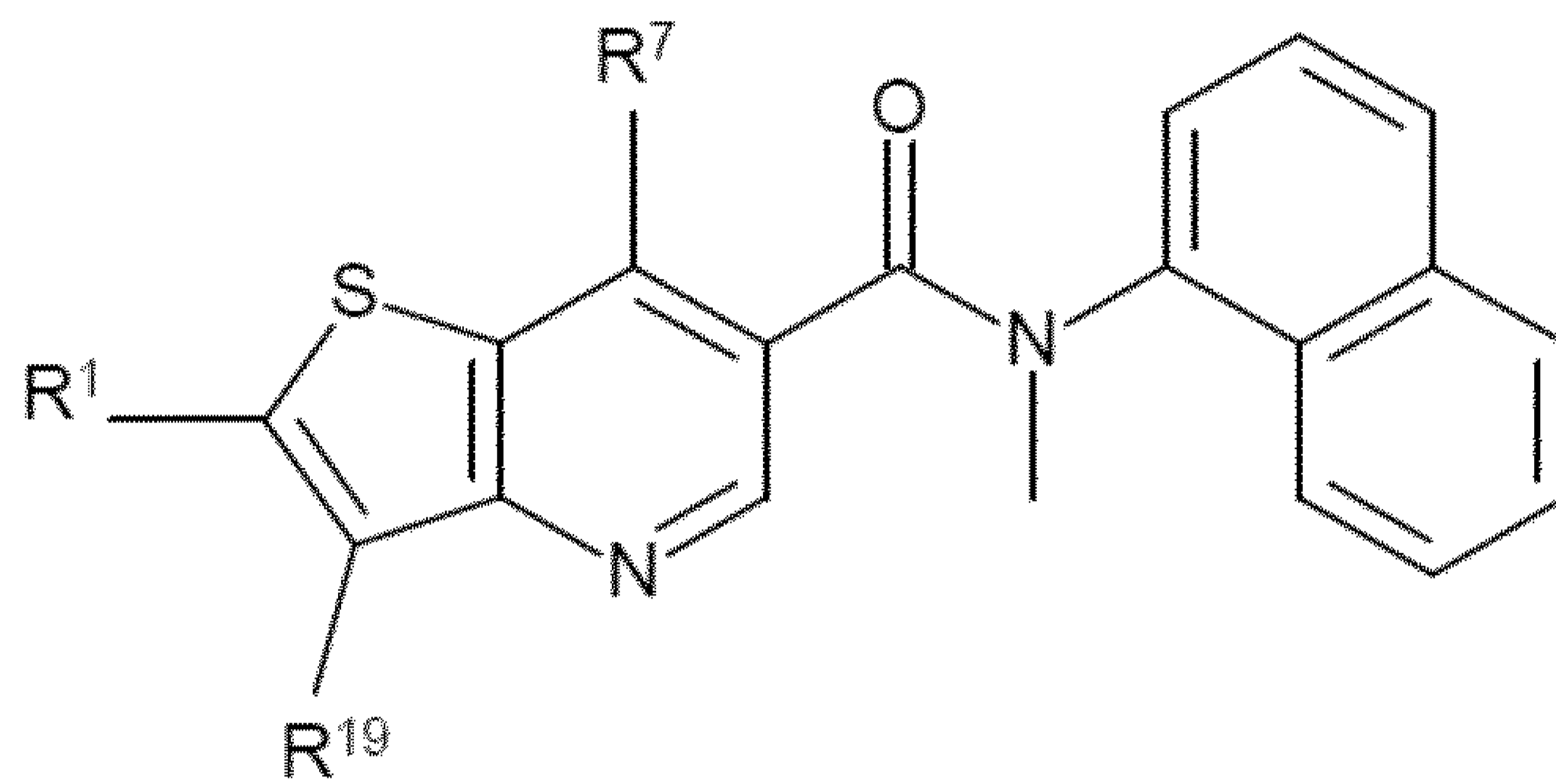
and

R²⁵ is hydrogen or methyl, more preferably hydrogen.

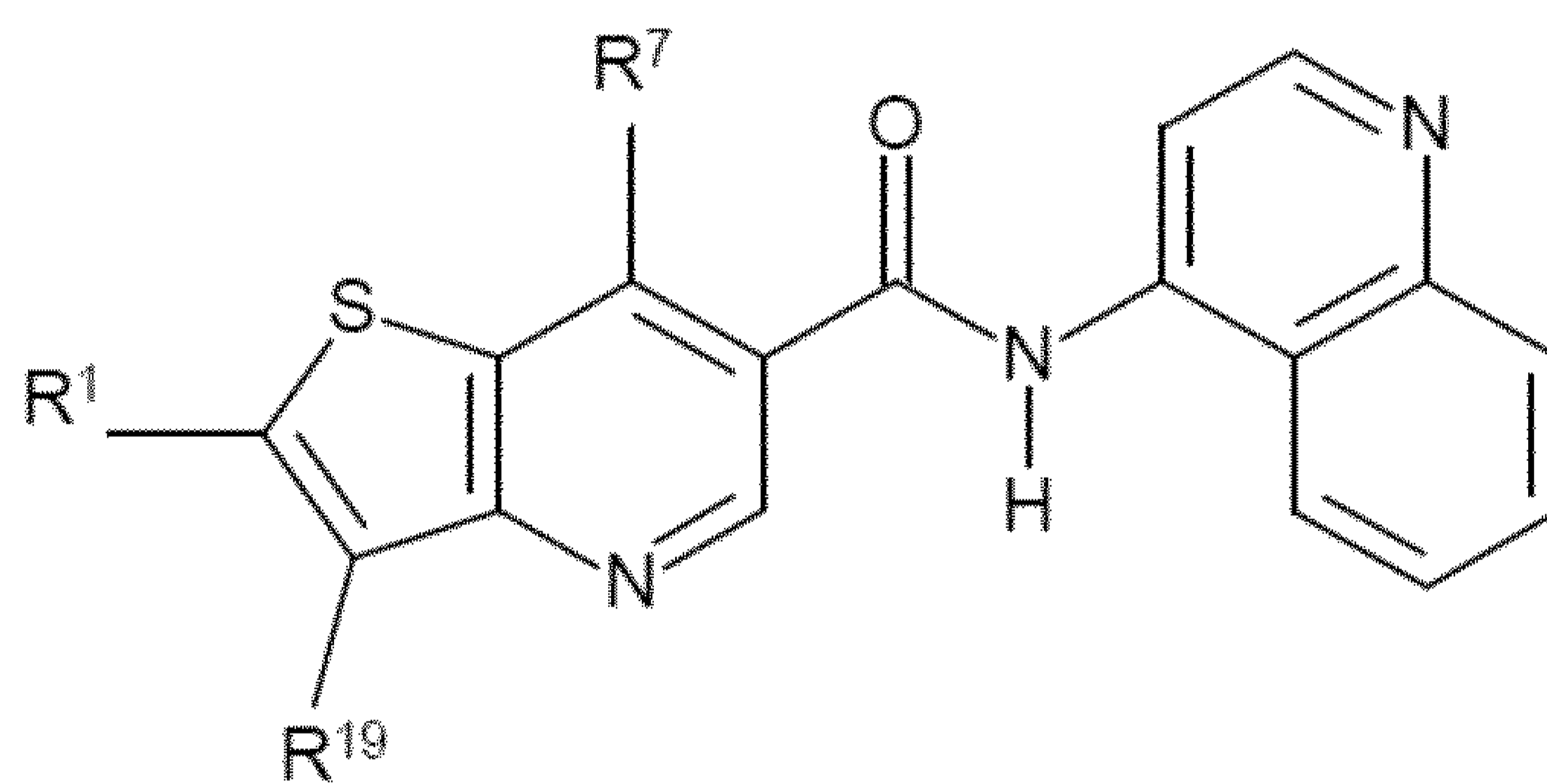
25 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Invii), (Inviii), (Inix) or (Inx)



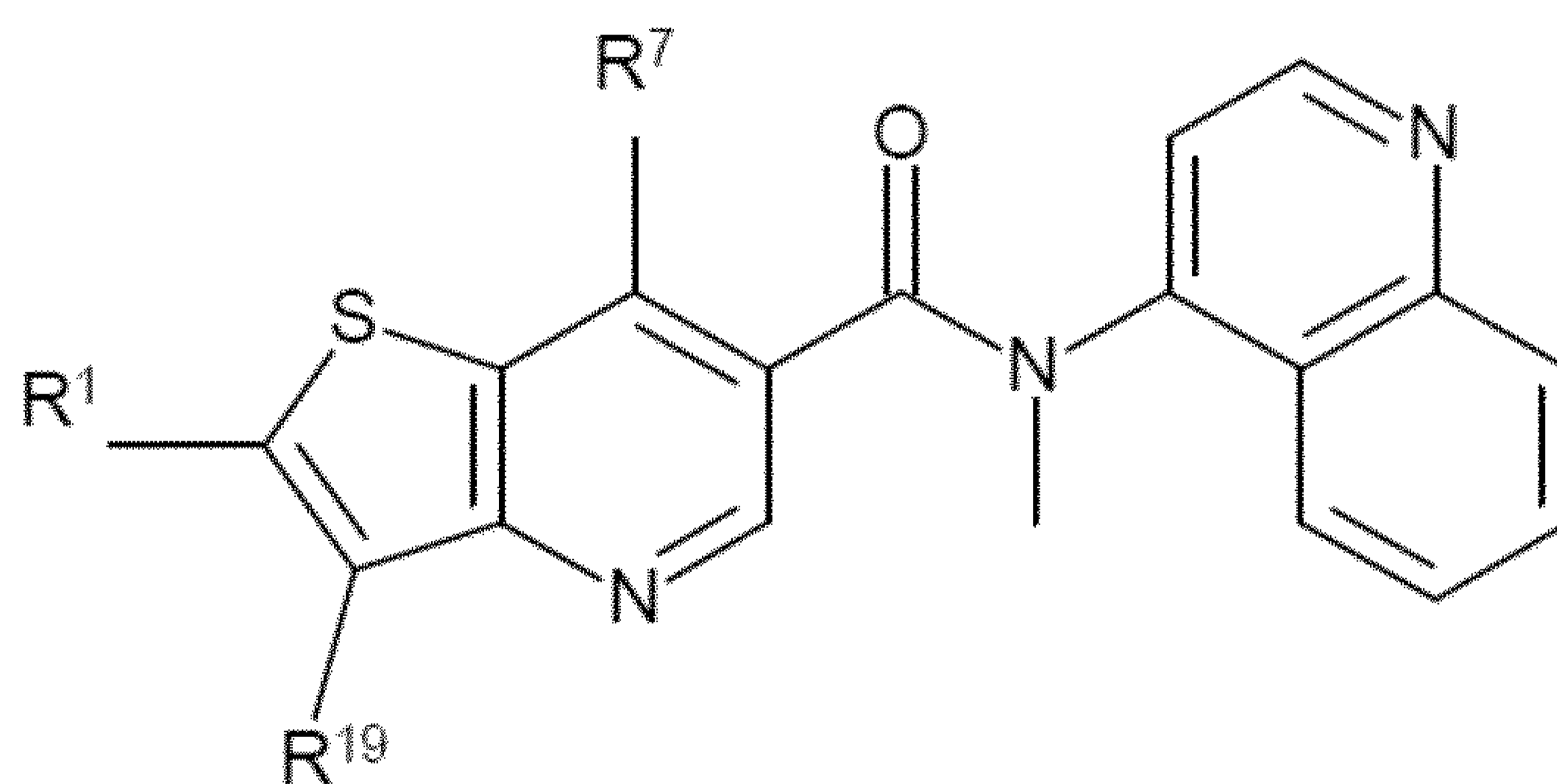
Formula (Invii)



Formula (Inviii)



Formula (Inix)



Formula (Inx)

5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures
 10 thereof, wherein R¹, R⁷ and R¹⁹ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Invii), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Inviii), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Inix), preferably in form of the (S)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Inx), preferably in form of the (S)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^{19} and R^{25} are defined as below.

In one embodiment of the invention and/or embodiments thereof,

R^{19} is independently selected from the group consisting of

C_{6-10} -aryl and 5 to 10-membered heteroaryl,

wherein each C_{6-10} -aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, $NR^{20}R^{21}$, $C(=O)OR^{22}$ and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{6-10} -aryl or

R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, or C_{6-10} -aryl or the heterocyclic ring formed by R^{20} and R^{21} together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, $NR^{20'}R^{21'}$, $C(=O)OR^{22'}$ and $C(=O)NR^{23'}R^{24'}$,

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{20'}$, $R^{21'}$, $R^{22'}$, $R^{23'}$ and $R^{24'}$ are independently selected from hydrogen and C₁₋₆-alkyl,

and

R^{25} is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

5 R^{19} is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

10 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen,

and

R^{25} is hydrogen or methyl.

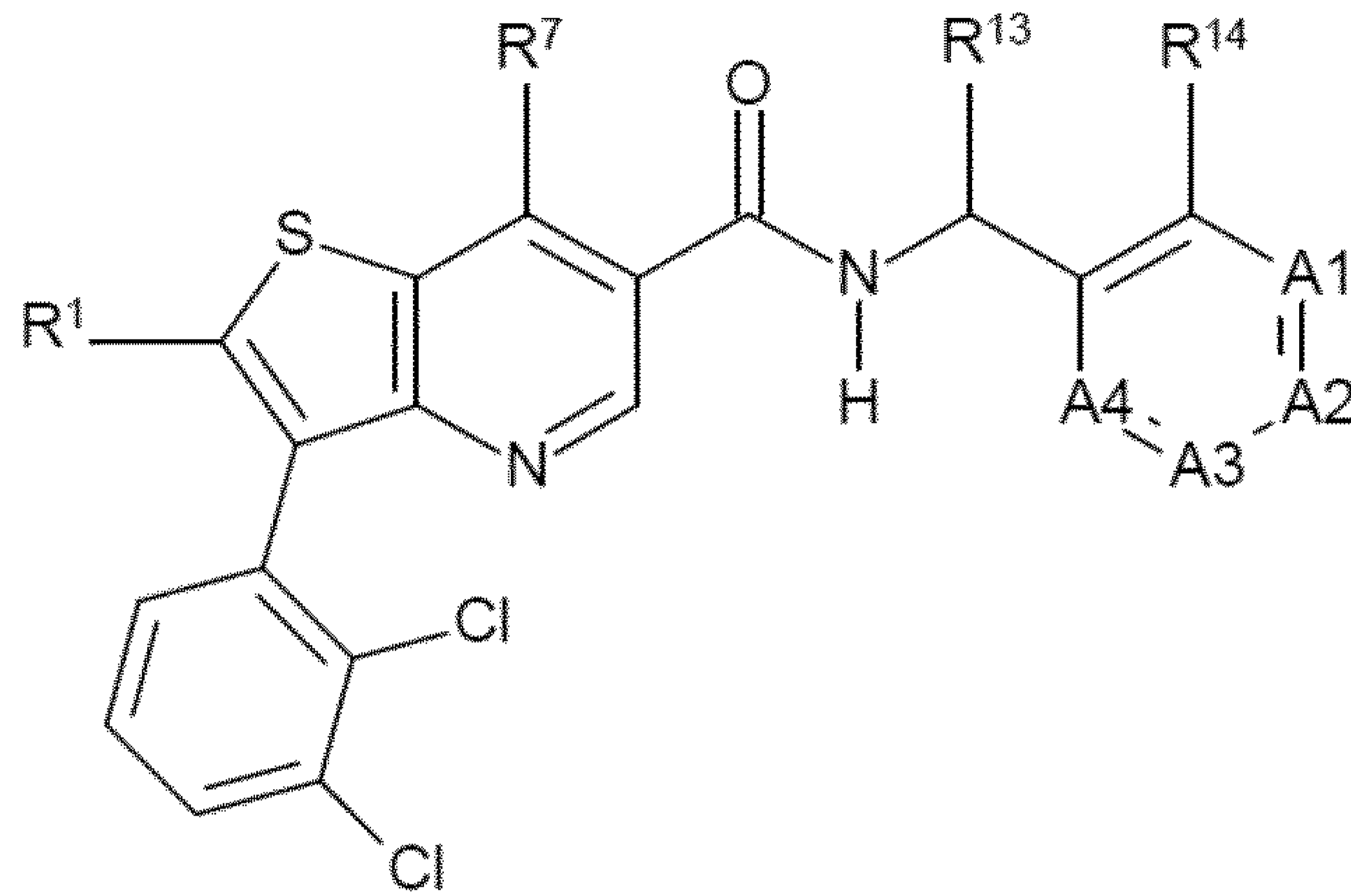
15 In one embodiment of the invention and/or embodiments thereof,

R^{19} is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl,

and

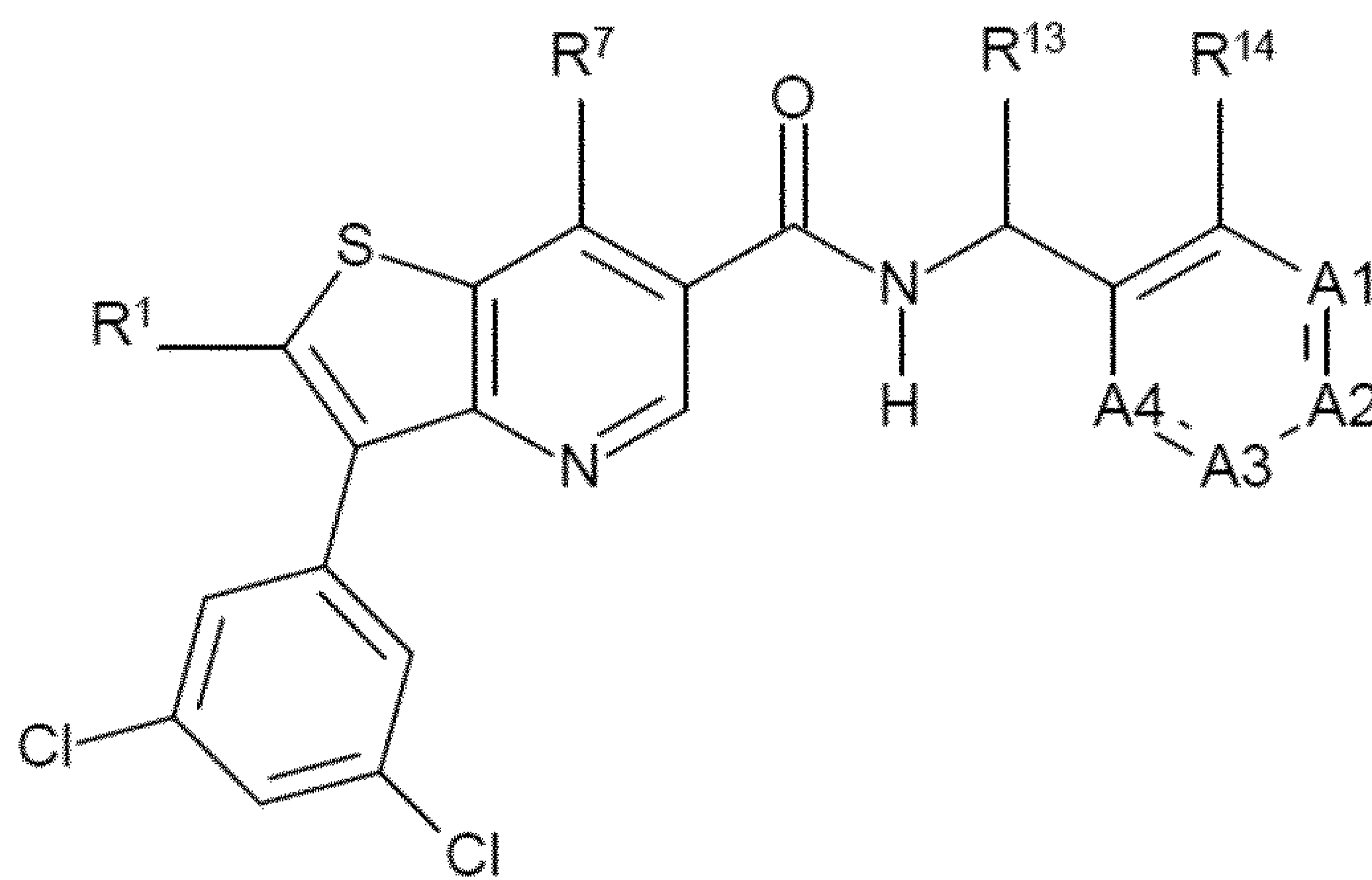
R²⁵ is hydrogen or methyl, more preferably hydrogen.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ioi), (Ioi), (Ioi), (Ioi), (Ioi) or (Ioi)

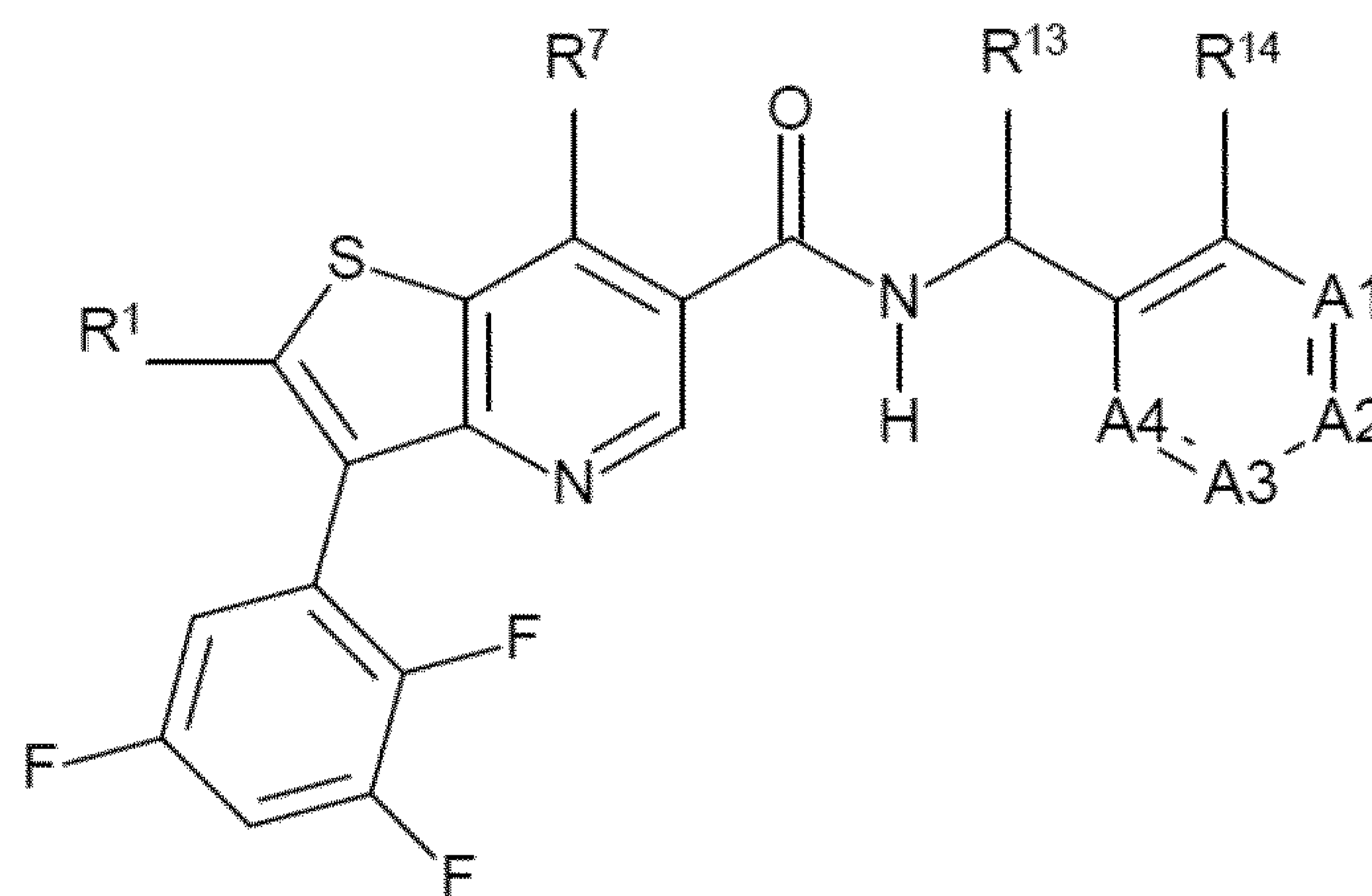


Formula (Ioi)

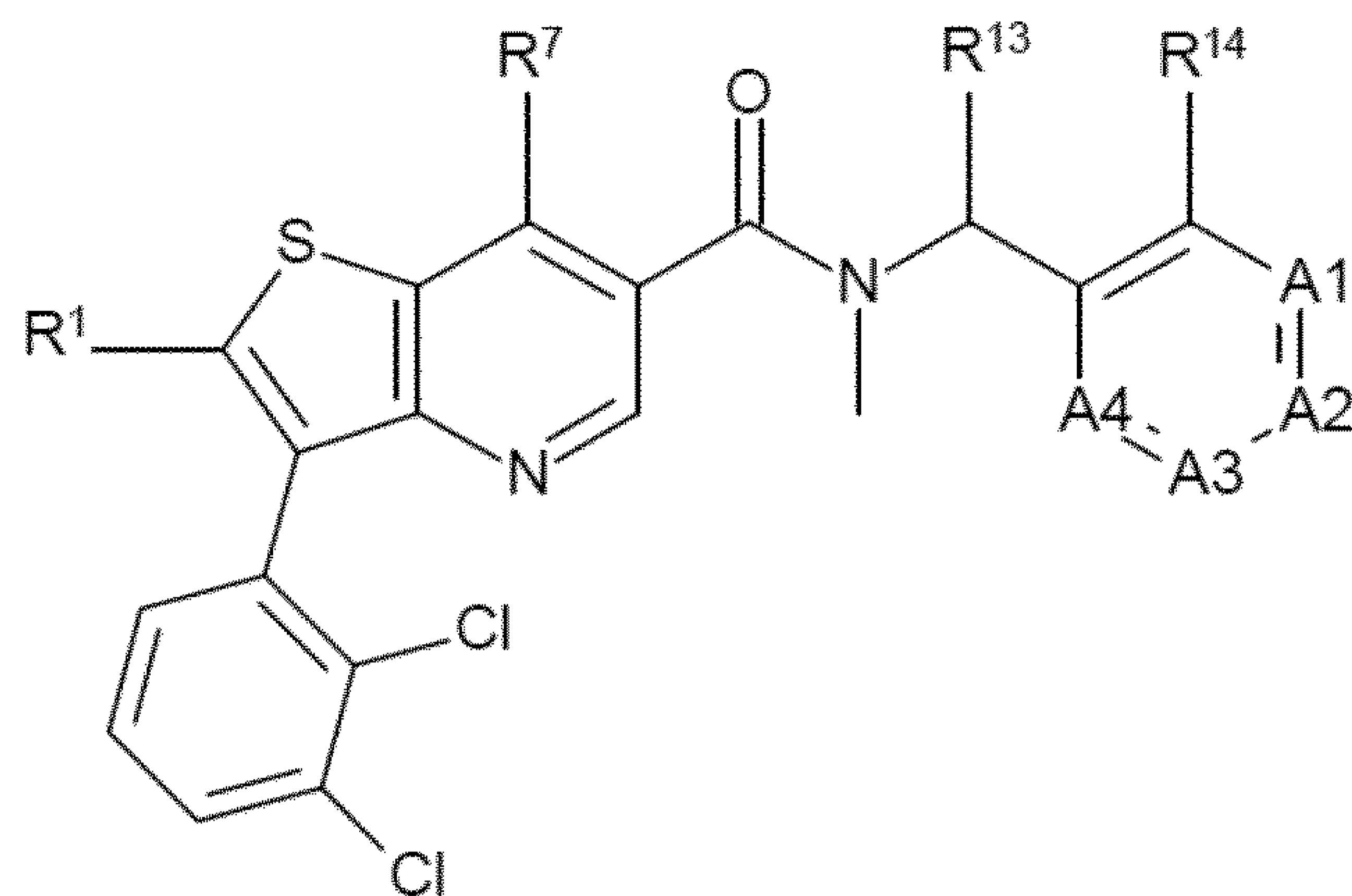
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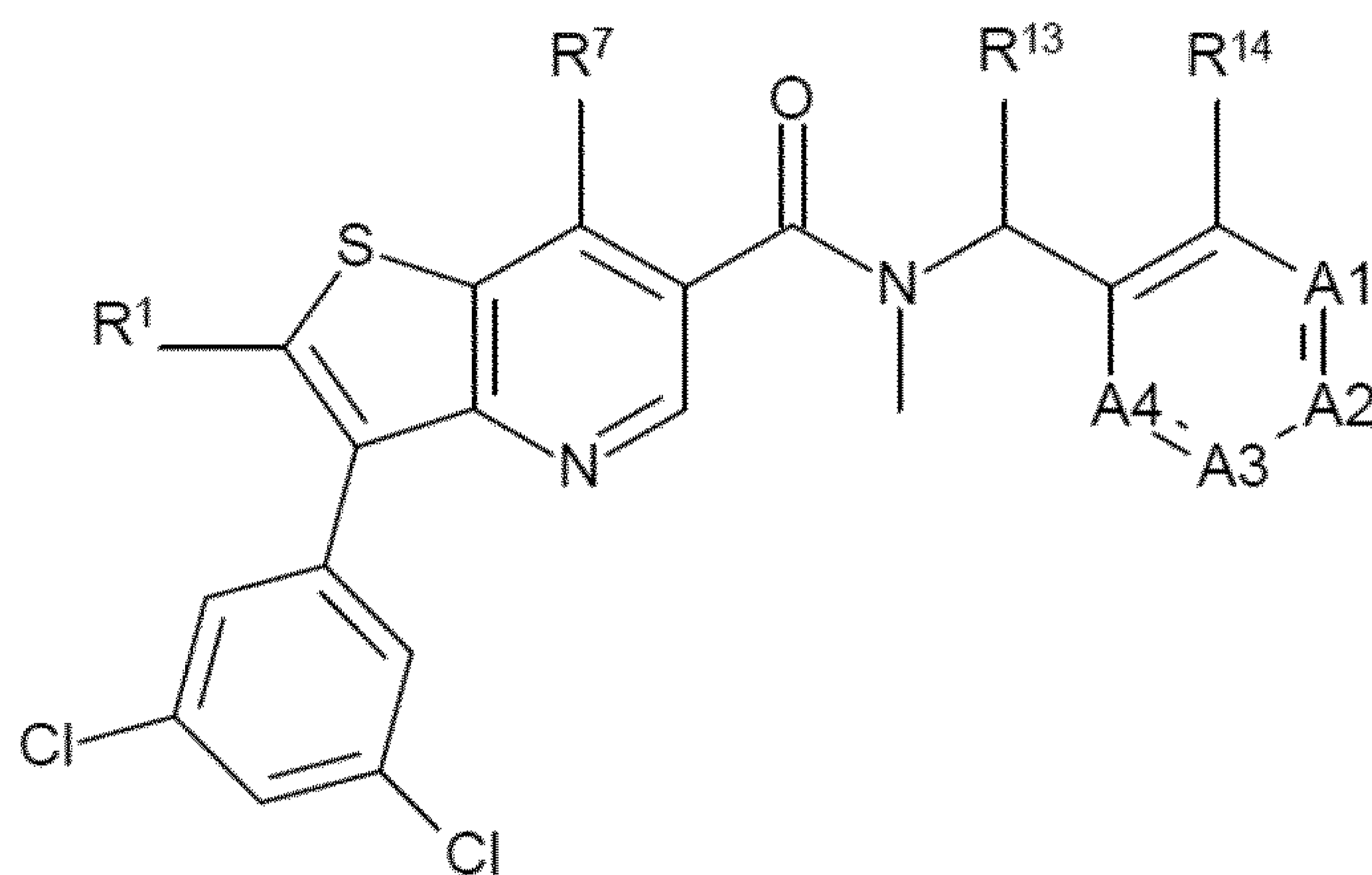
Formula (Ioi)



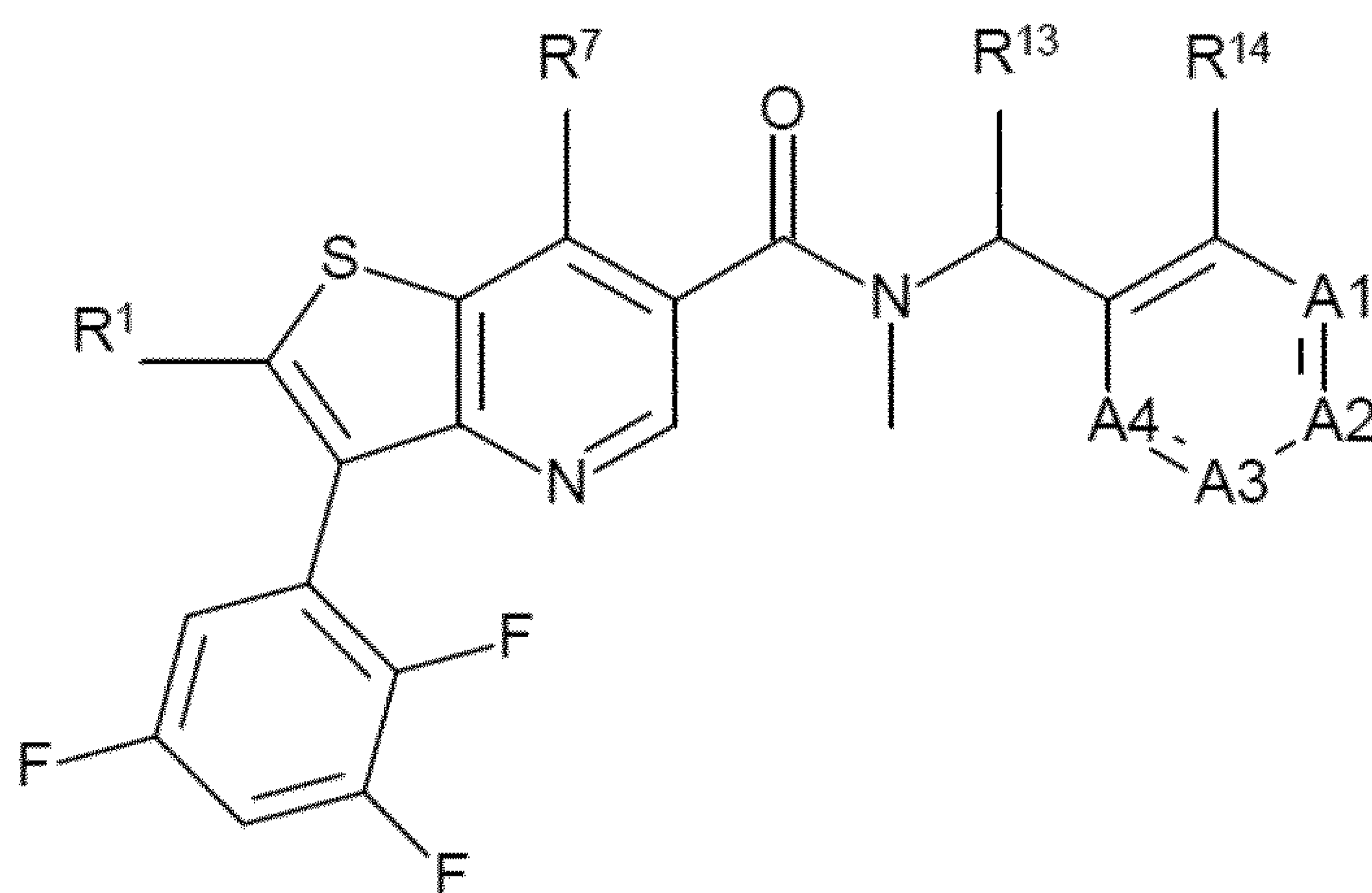
Formula (Ioi)



Formula (Ioiiv)



Formula (Ioi)



Formula (Iovi)

5

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^7 and R^{13} , R^{14} , A1, A2, A3 and A4 are defined as in any of the embodiments described herein.

- 10 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ioi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ioi), preferably in the

form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ioiiv), preferably in the form of the (*S*)-enantiomer). In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ioiiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iov), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iovi), preferably in the form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 , R^7 as well as R^{13} , R^{14} , A1, A2, A3 and A4 are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{1-6} -alkoxy,

R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

and

R^7 is independently selected from the group consisting of

5 hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently

10 selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, $NR^{8'}R^{9'}$, $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

R^8 and R^9 are independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

20 wherein the C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, $NR^{8''}R^{9''}$, $C(=O)OR^{10''}$ and $C(=O)NR^{11''}R^{12''}$;

25 R^{10} , R^{11} and R^{12} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{8''}$, $R^{9''}$, $R^{10''}$, $R^{11''}$ and $R^{12''}$ are independently selected from hydrogen and C_{1-6} -alkyl,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S,

5 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

10 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl.

In one embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^5 and R^6 are independently selected from hydrogen and C_{1-3} -alkyl,

20 $R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-3} -alkyl,

and

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, 4 to 10-membered heterocyclyl, C_{1-3} -alkoxy, hydroxy, NR^8R^9 , SR^{10} , SOR^{10} and SO_2R^{10} ,

25 wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, 4 to 10-membered heterocyclyl or C_{1-3} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

5 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

10 wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

15 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

20 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

25 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

R⁷ is independently selected from the group consisting of

5 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

10 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

15 Suitably R⁷ is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-
20 hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally
25 replaced by -NH- or -O-,

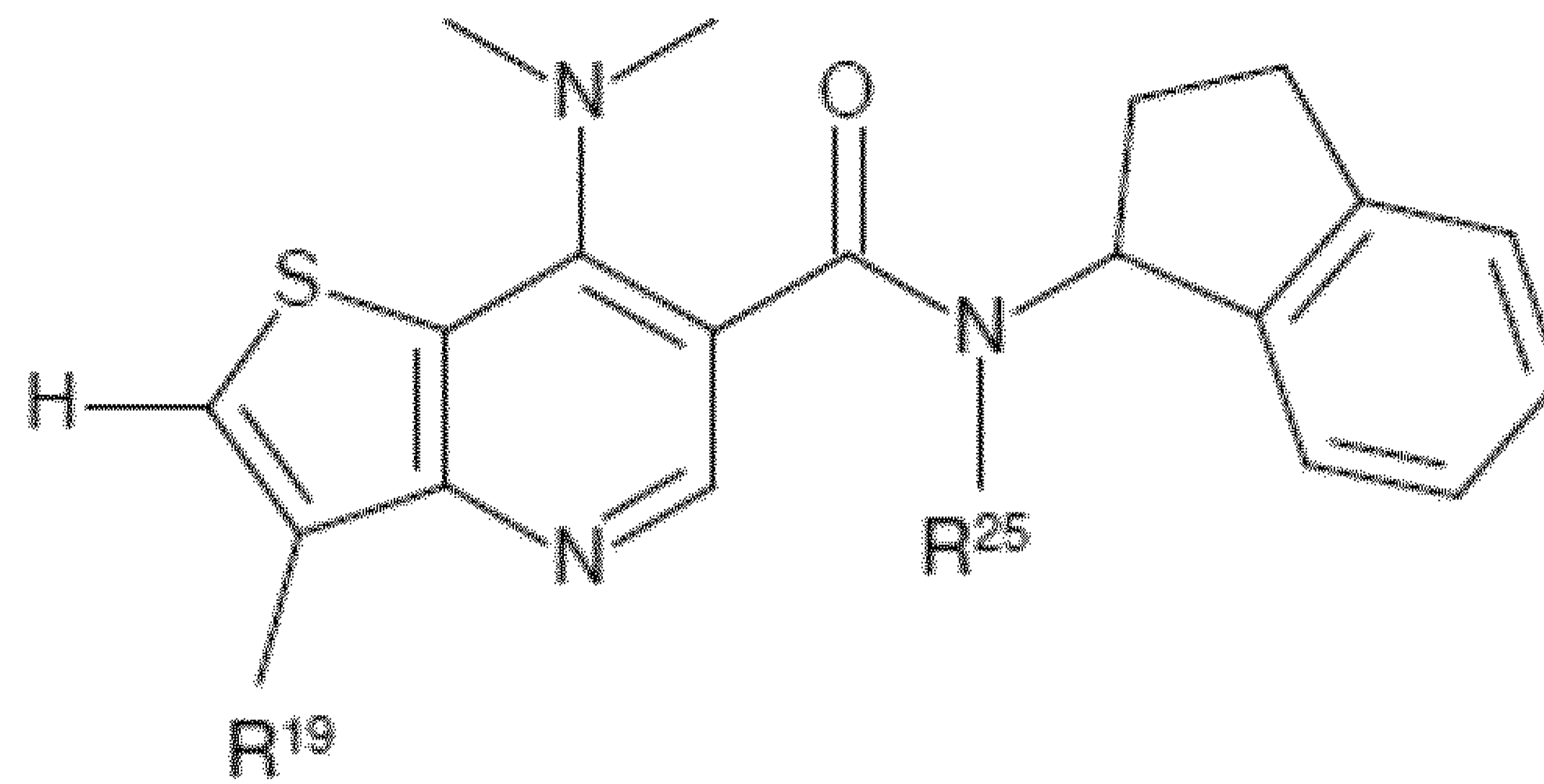
A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

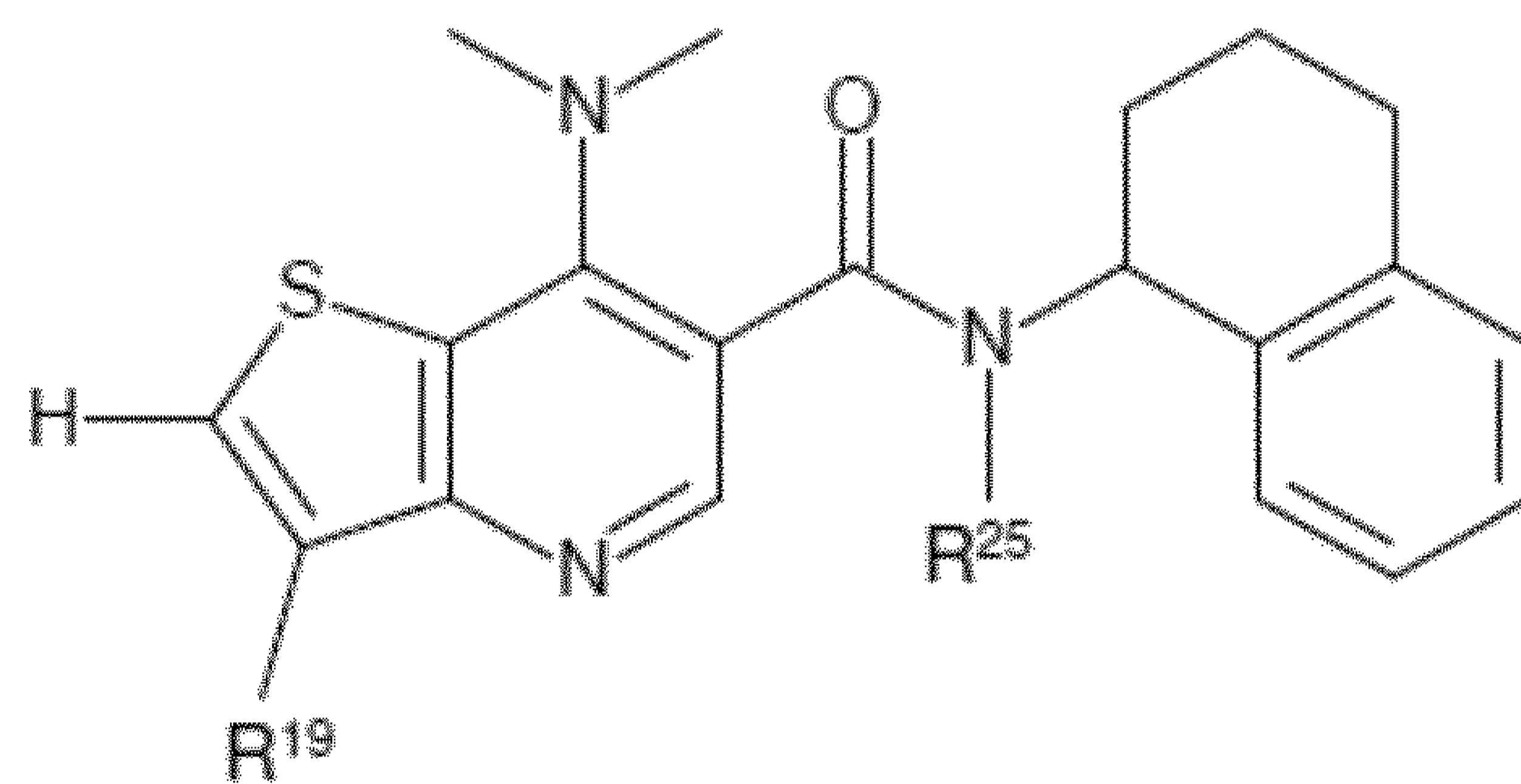
A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy, wherein none, one or two of A1, A2, A3 and A4 are N.

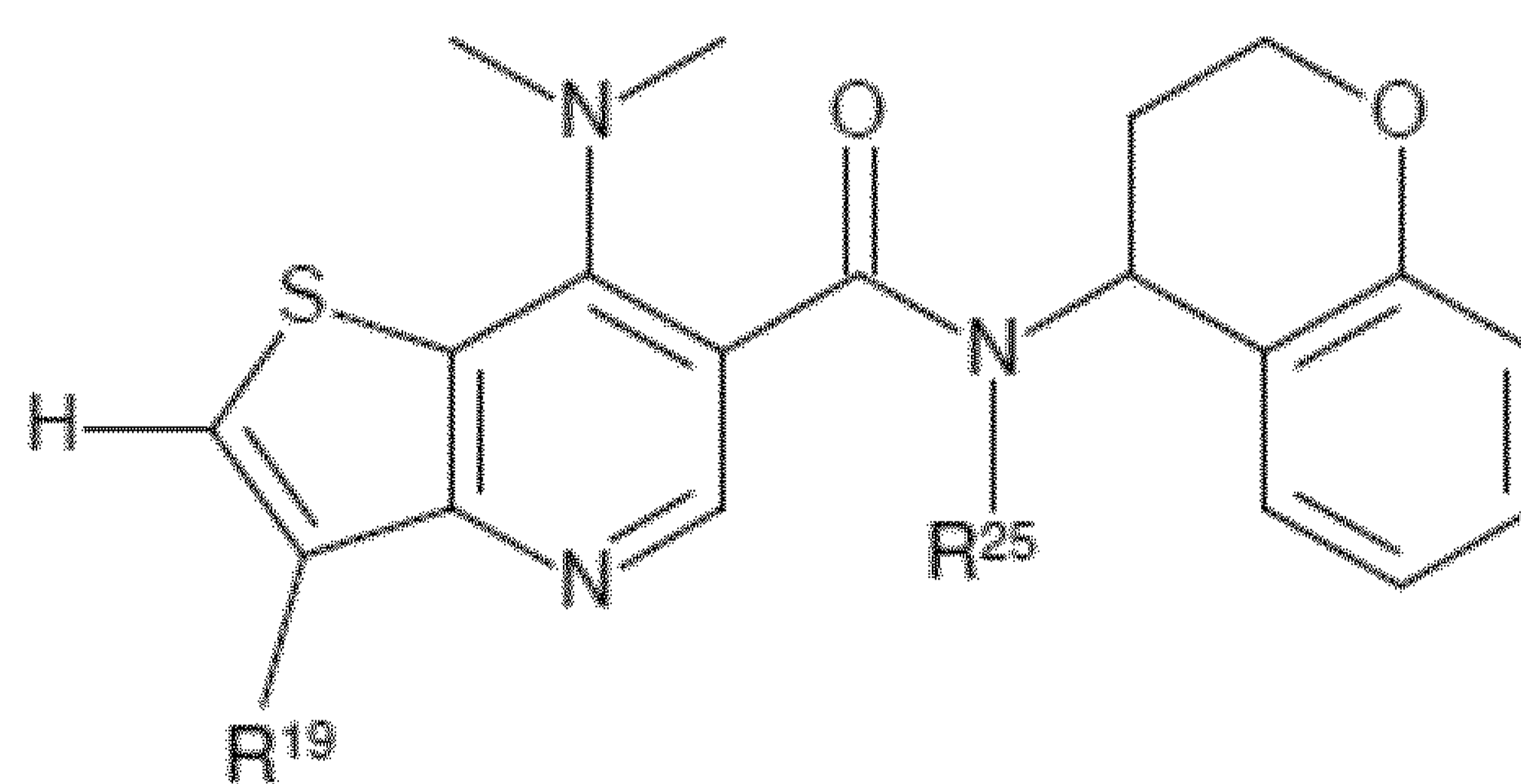
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipi), (Ipii), (Ipiii), (Ipiv), (Ipv), (Ipvi), (Ipvii), (Ipviii), (Ipix), (Ipx), (Ipxi) or (Ipxii)



Formula (Ipi)

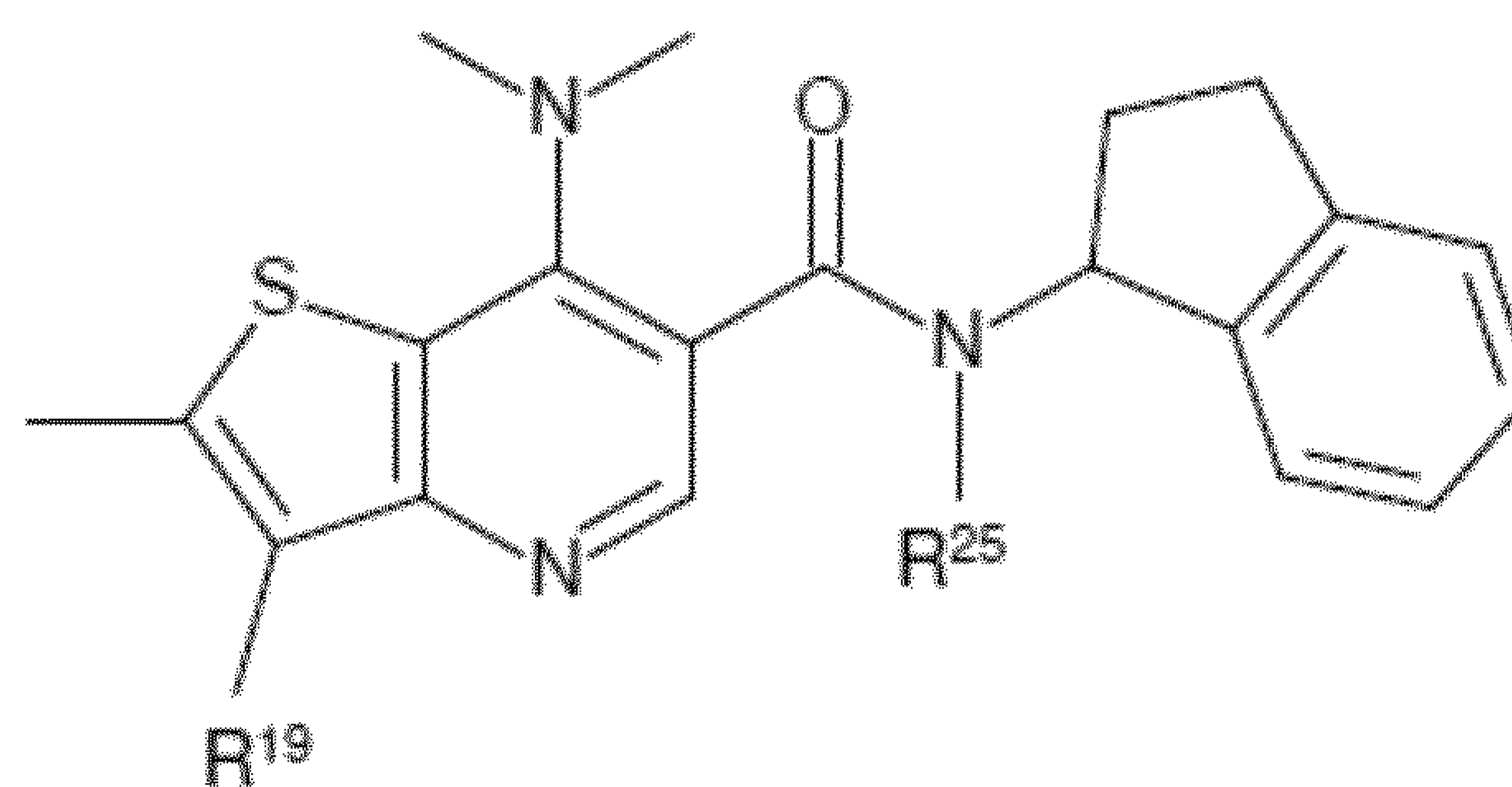


Formula (Ipii)

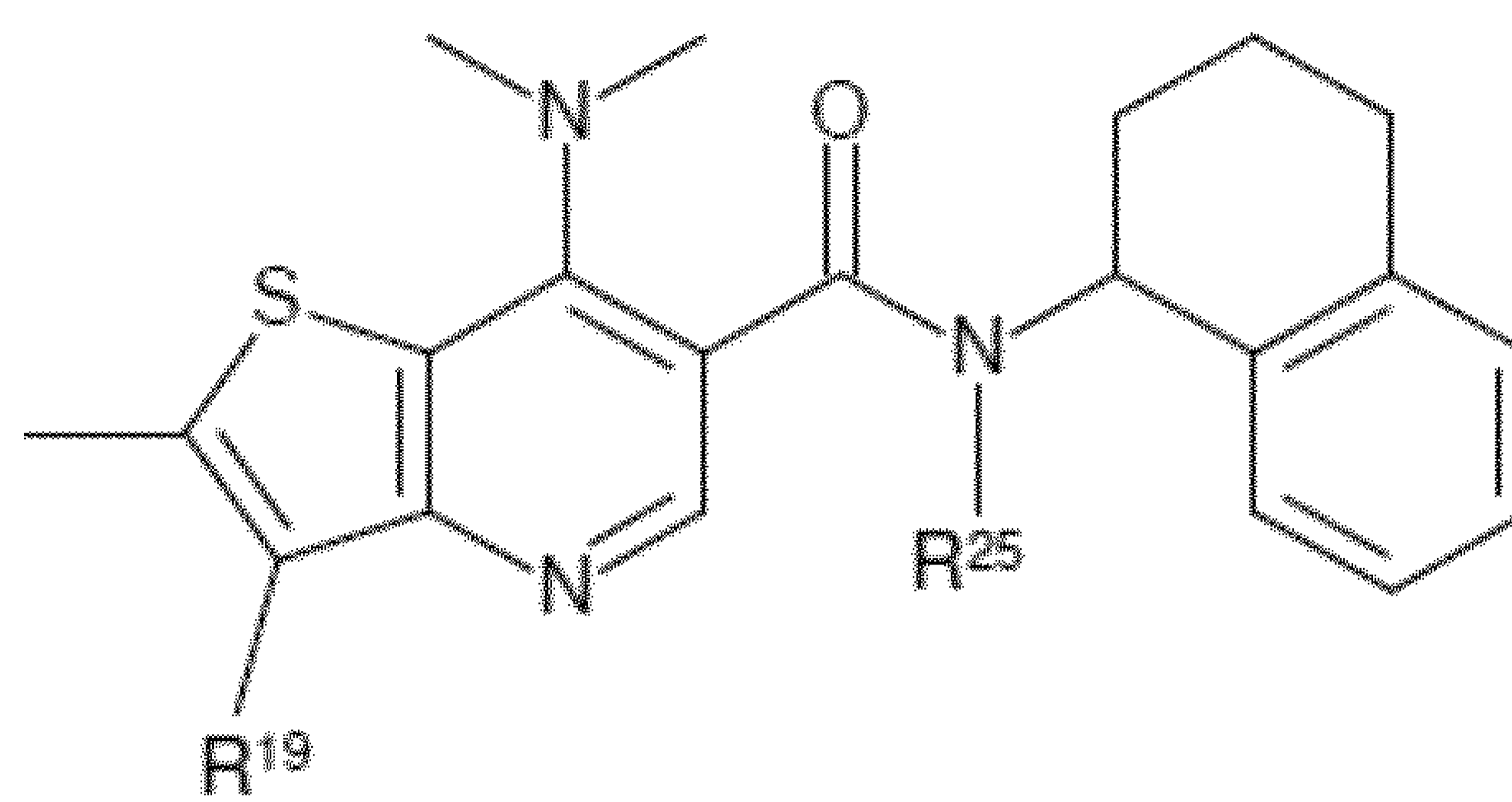


Formula (Ipiii)

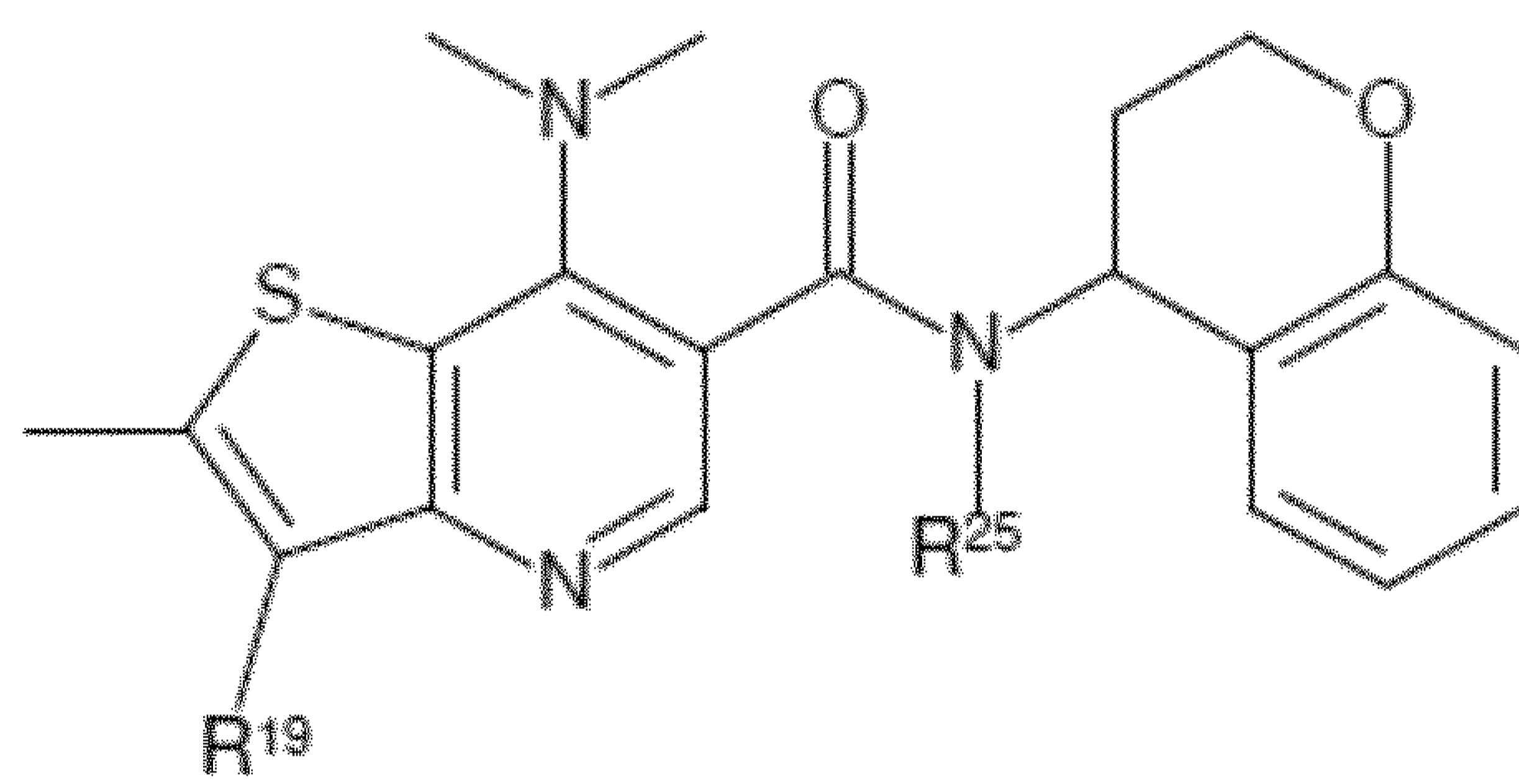
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Formula (Ixiv)

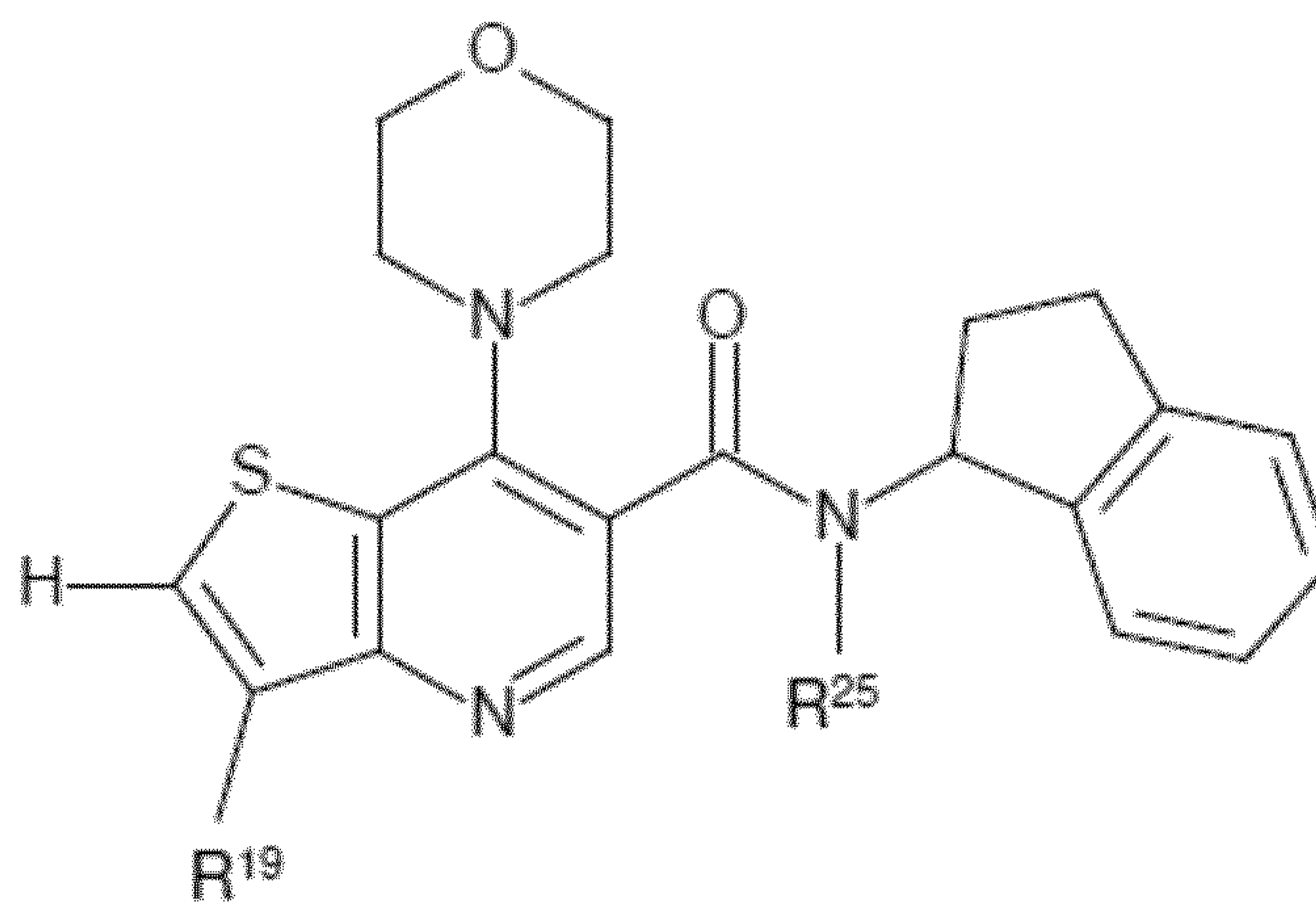


Formula (Ipv)

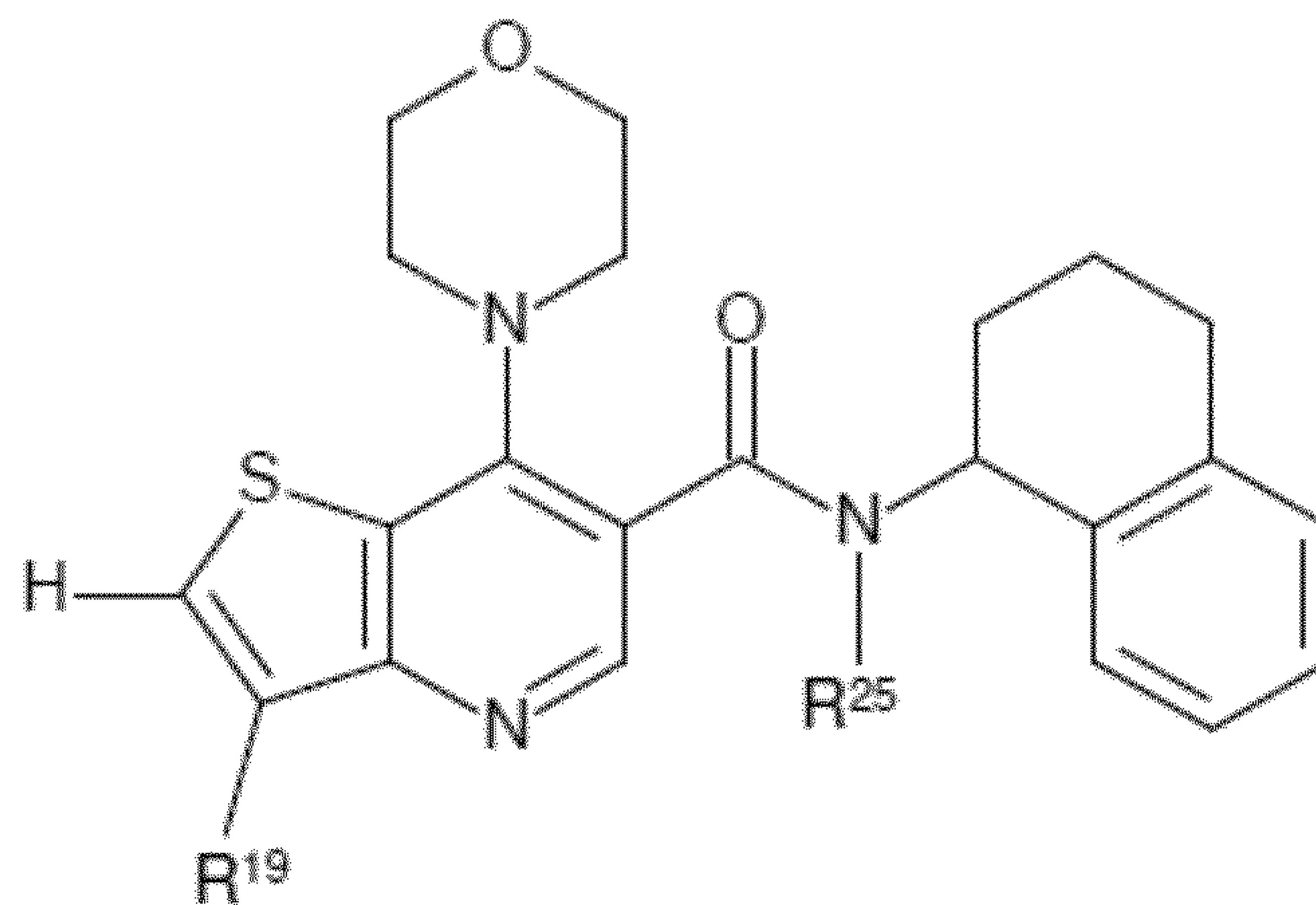


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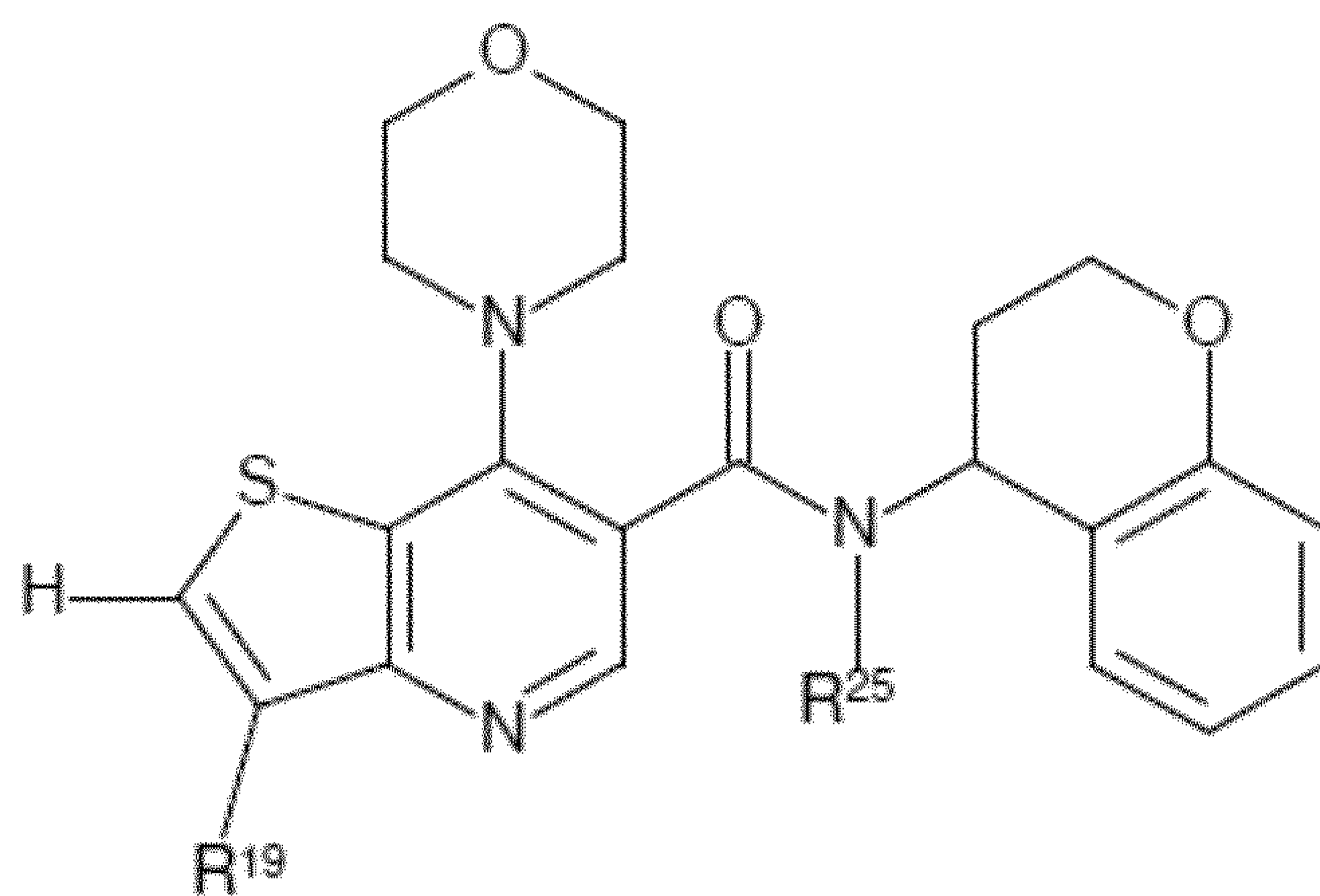
Formula (Ivii)



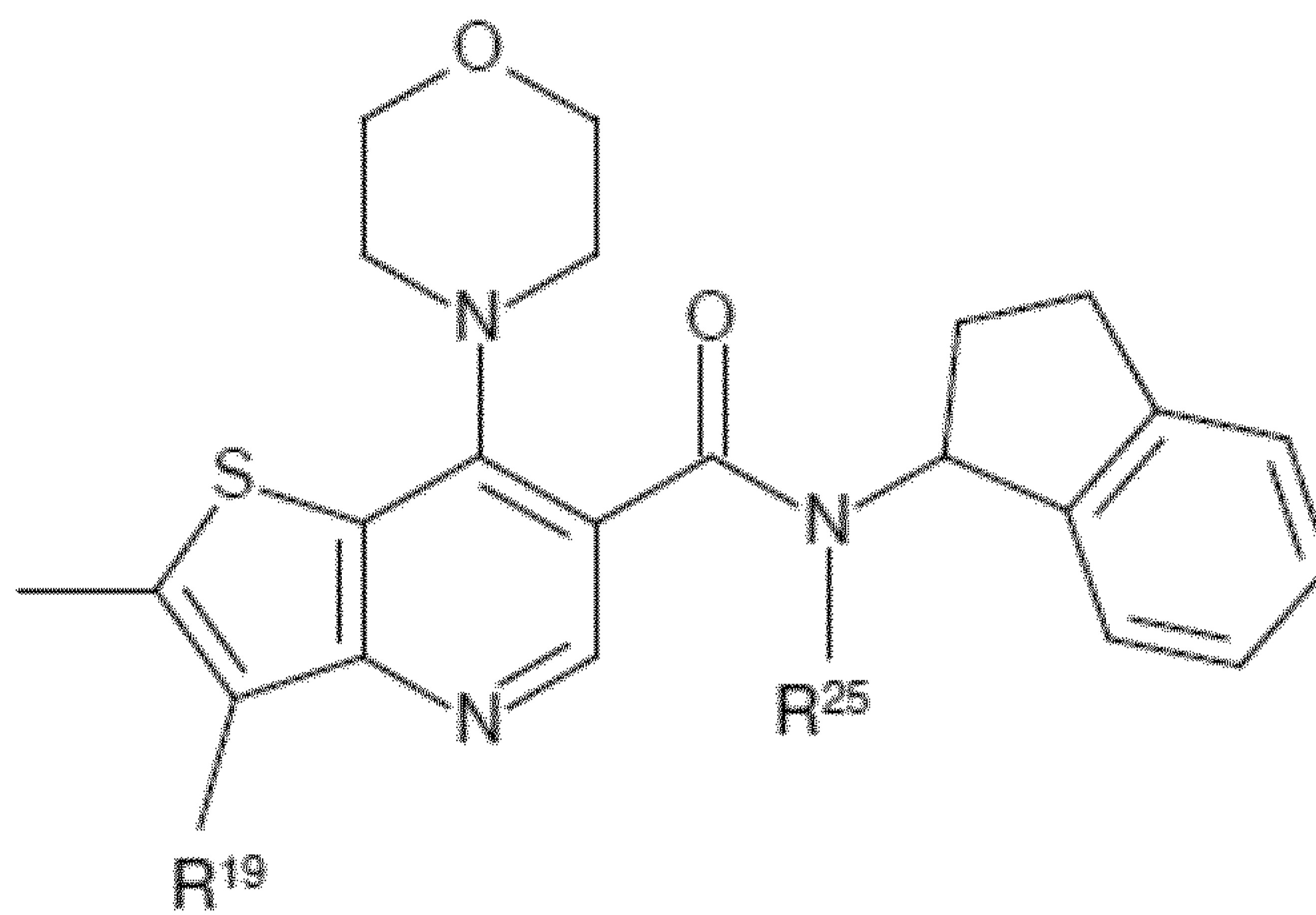
Formula (Iviii)



Formula (Ipviii)

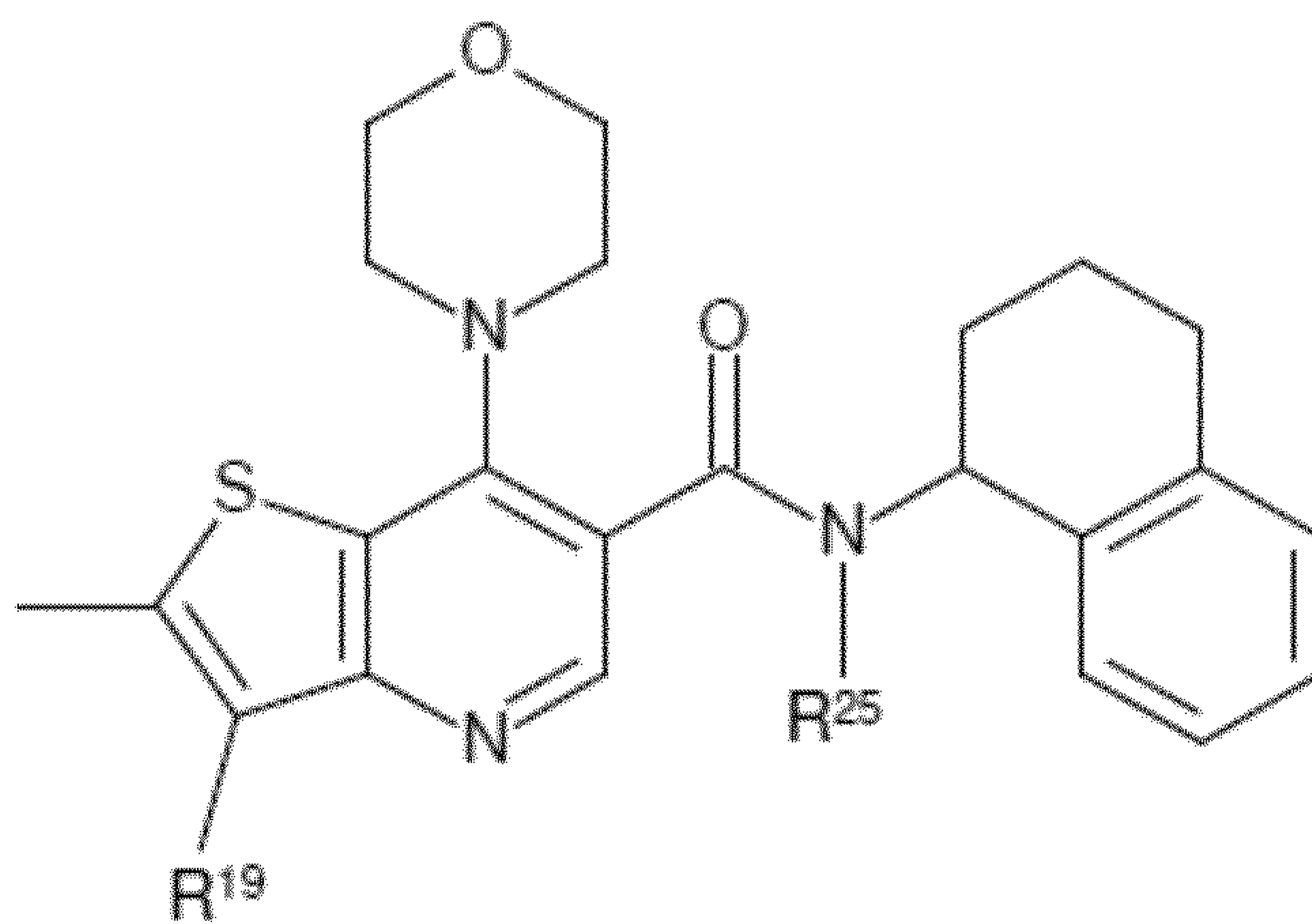


Formula (Ipix)

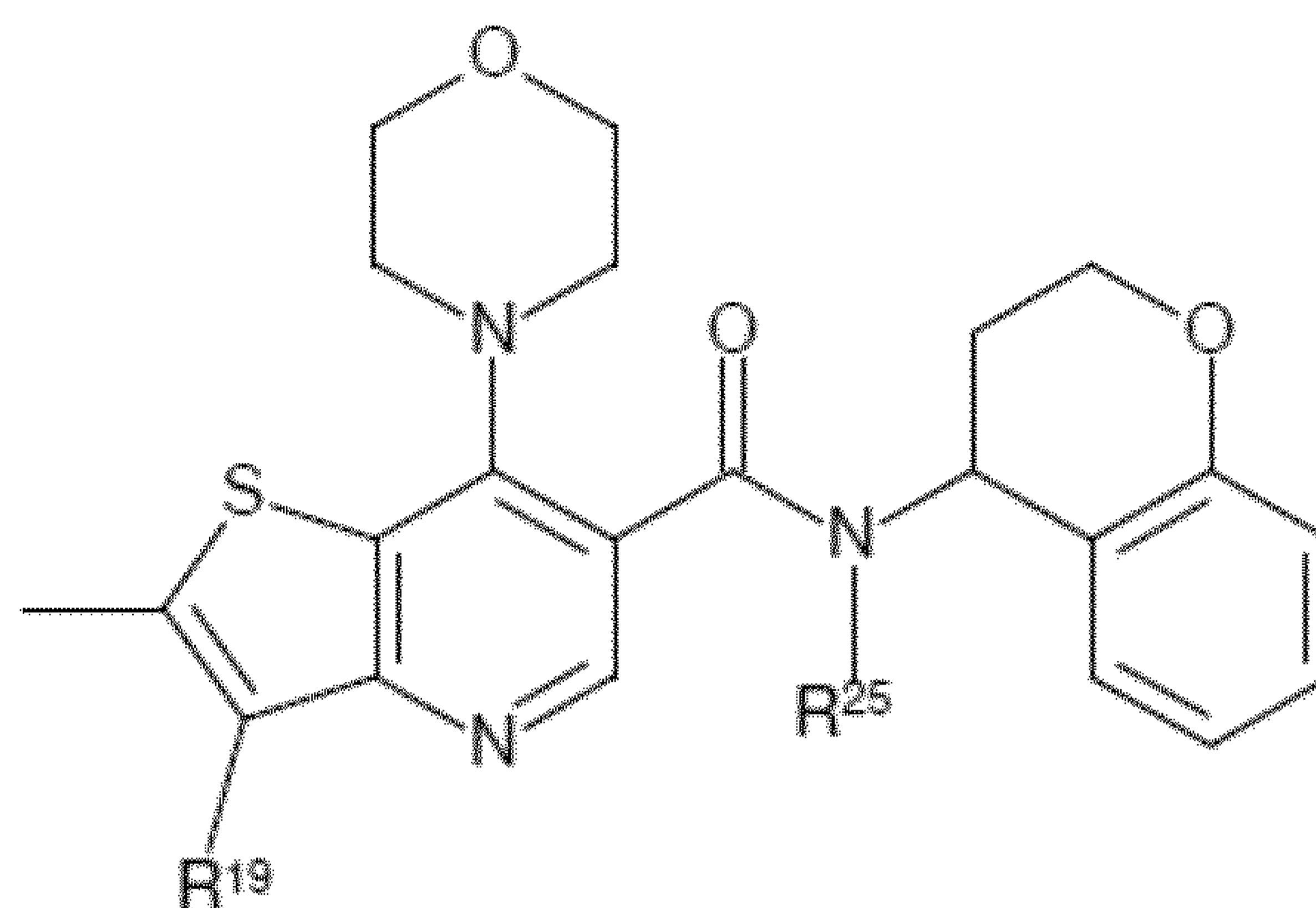


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Formula (Ipx)



Formula (Ipxi)



Formula (Ipxii)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹⁹ and R²⁵ are defined as in any of the embodiments described herein.

5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipx), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxii), preferably in the form of the (*S*)-enantiomer.

25 Optionally, in an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²R³, C(=O)OR⁴ and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3
10 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

20 and

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl, and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl,

and

R⁷ is independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

20 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group
25 consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

$R^{8''}$ and $R^{9''}$ are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

5 and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

10 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof,

15 R^1 is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

20 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R^8 and R^9 are independently selected from the group consisting of

25 hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

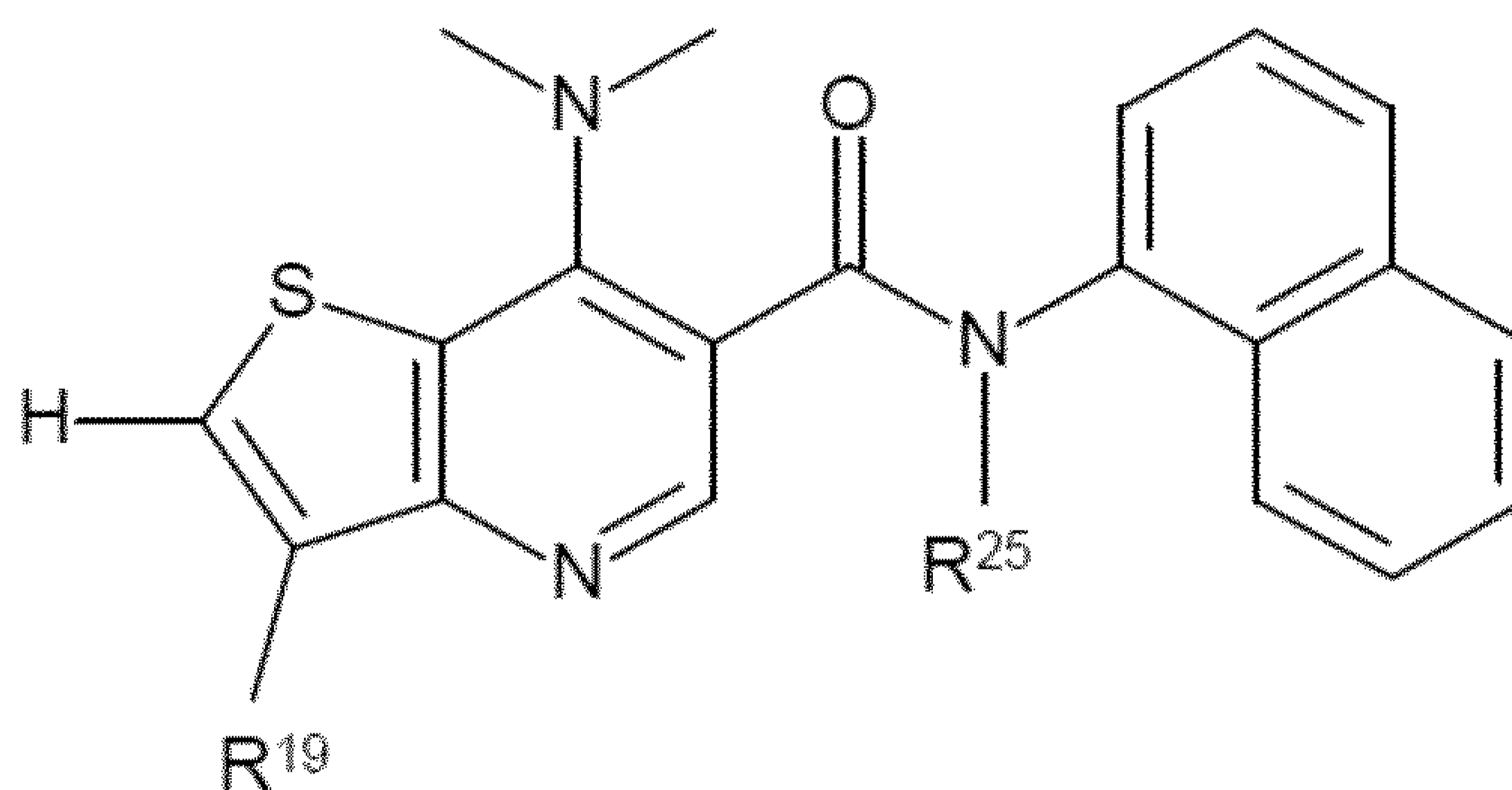
A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

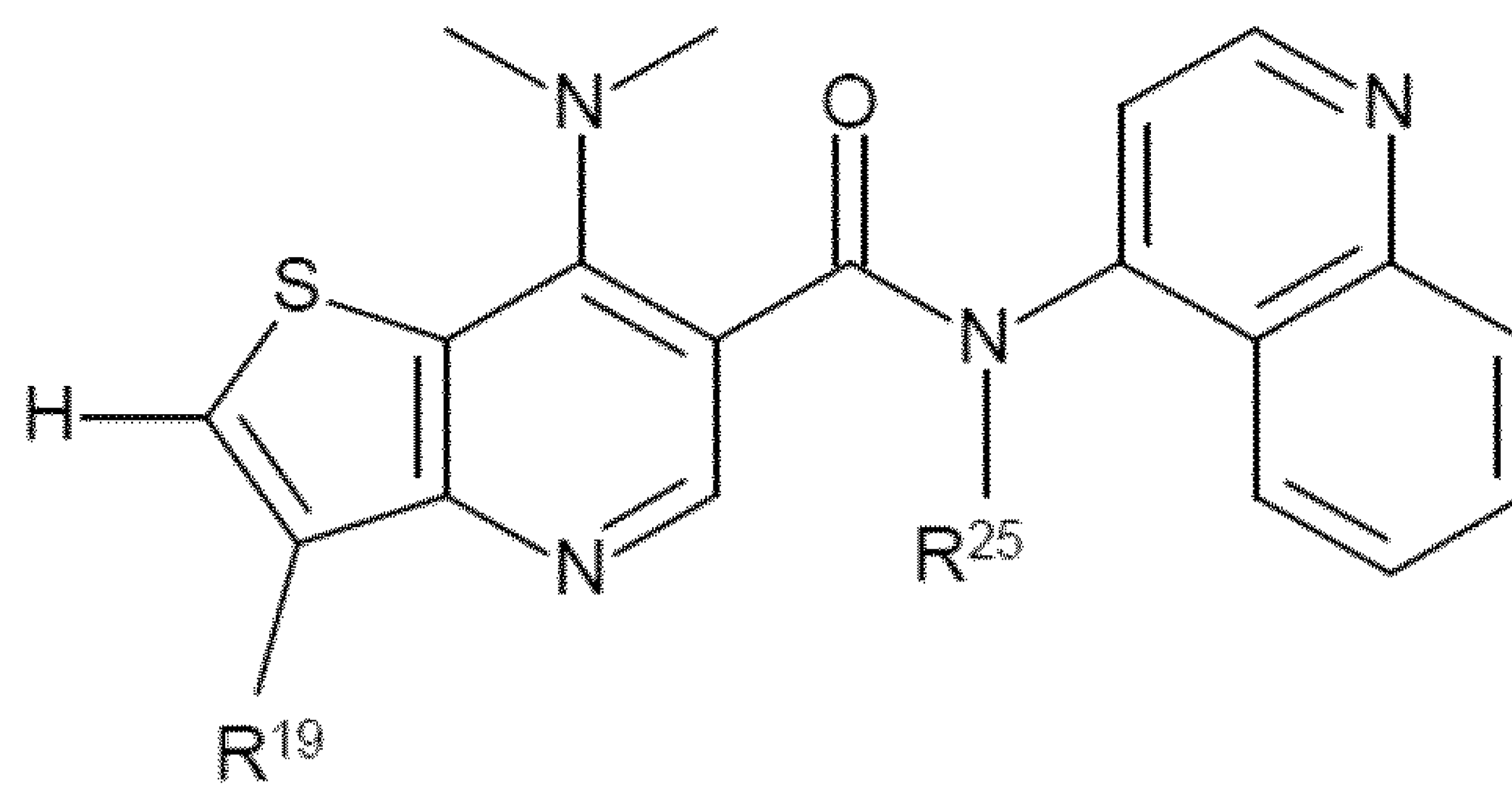
wherein none, one or two of A1, A2, A3 and A4 are N.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxiii), (Ipxiv), (Ipxv), (Ipxvi), (Ipxvii), (Ipxviii), (Ipxix) or (Ipxx)

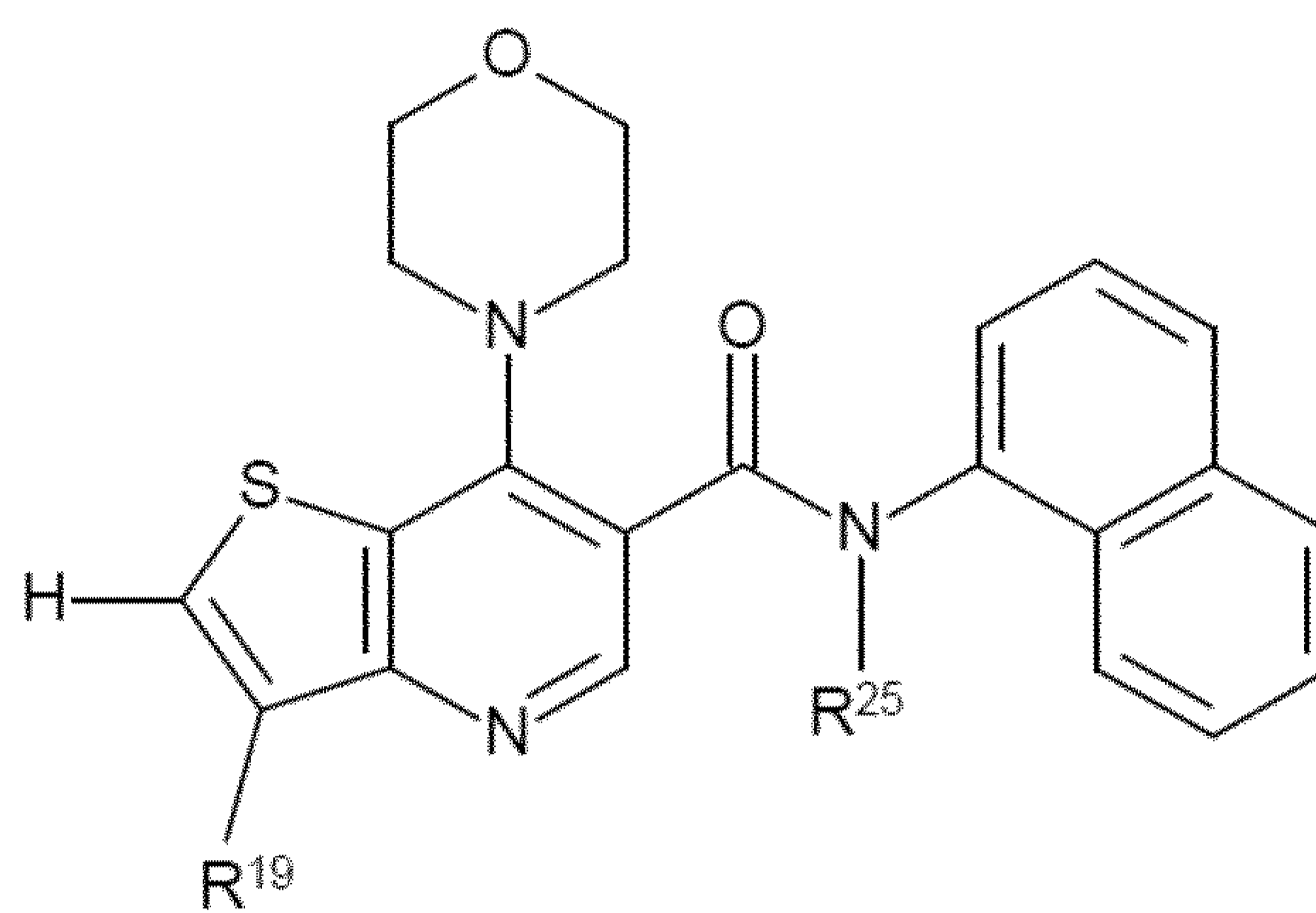


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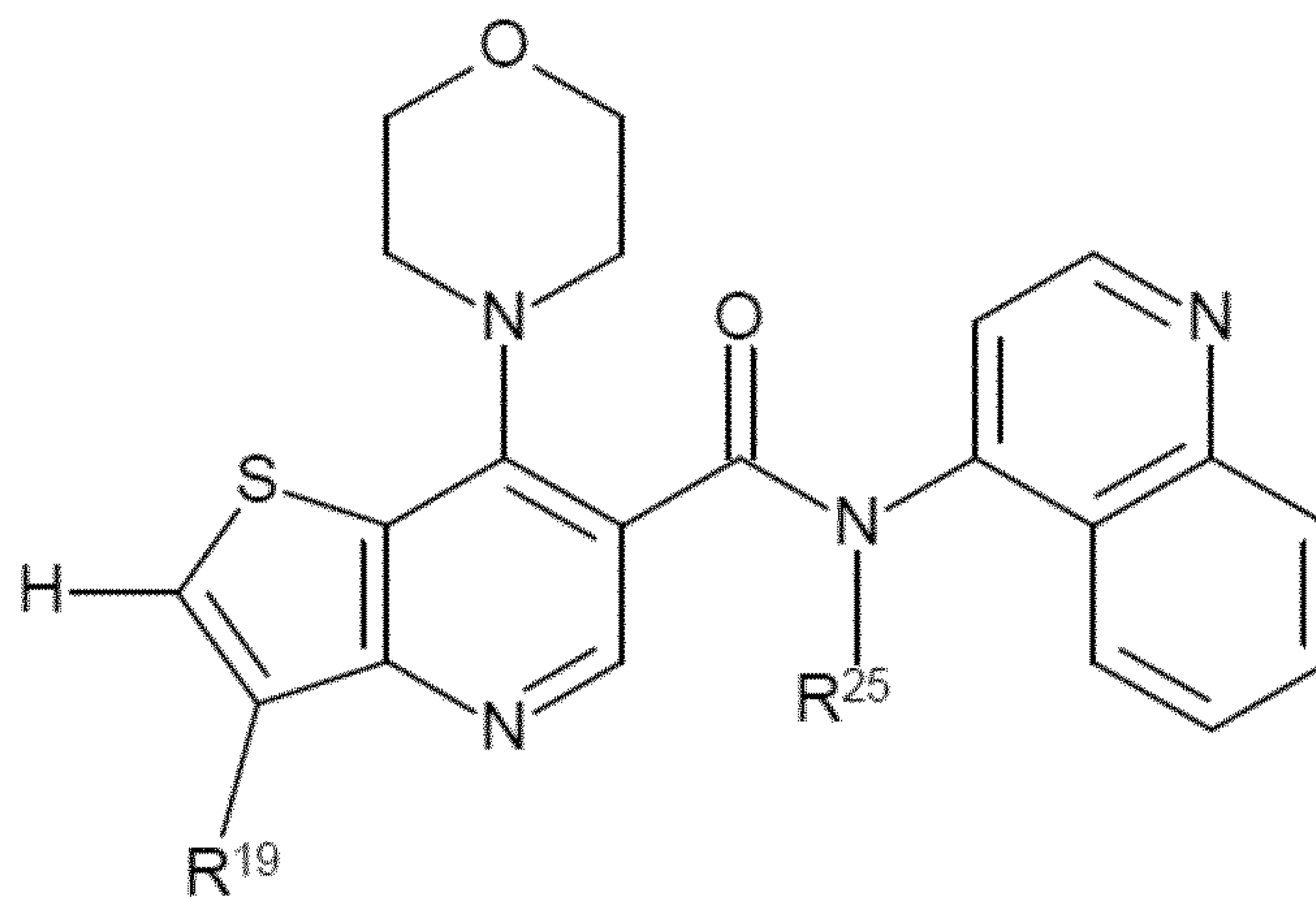
Formula (Ipxiii)



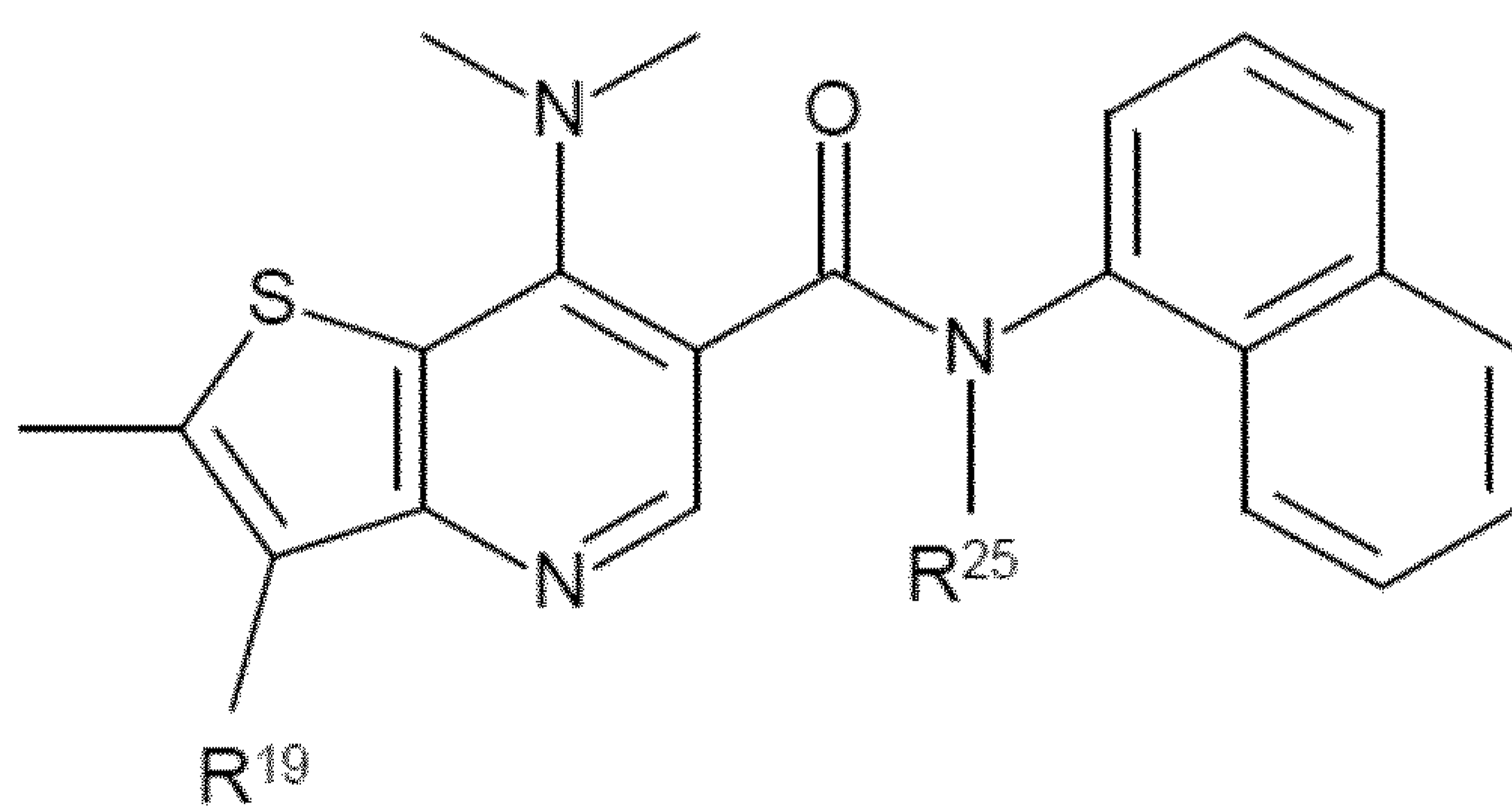
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Formula (Ipxv)

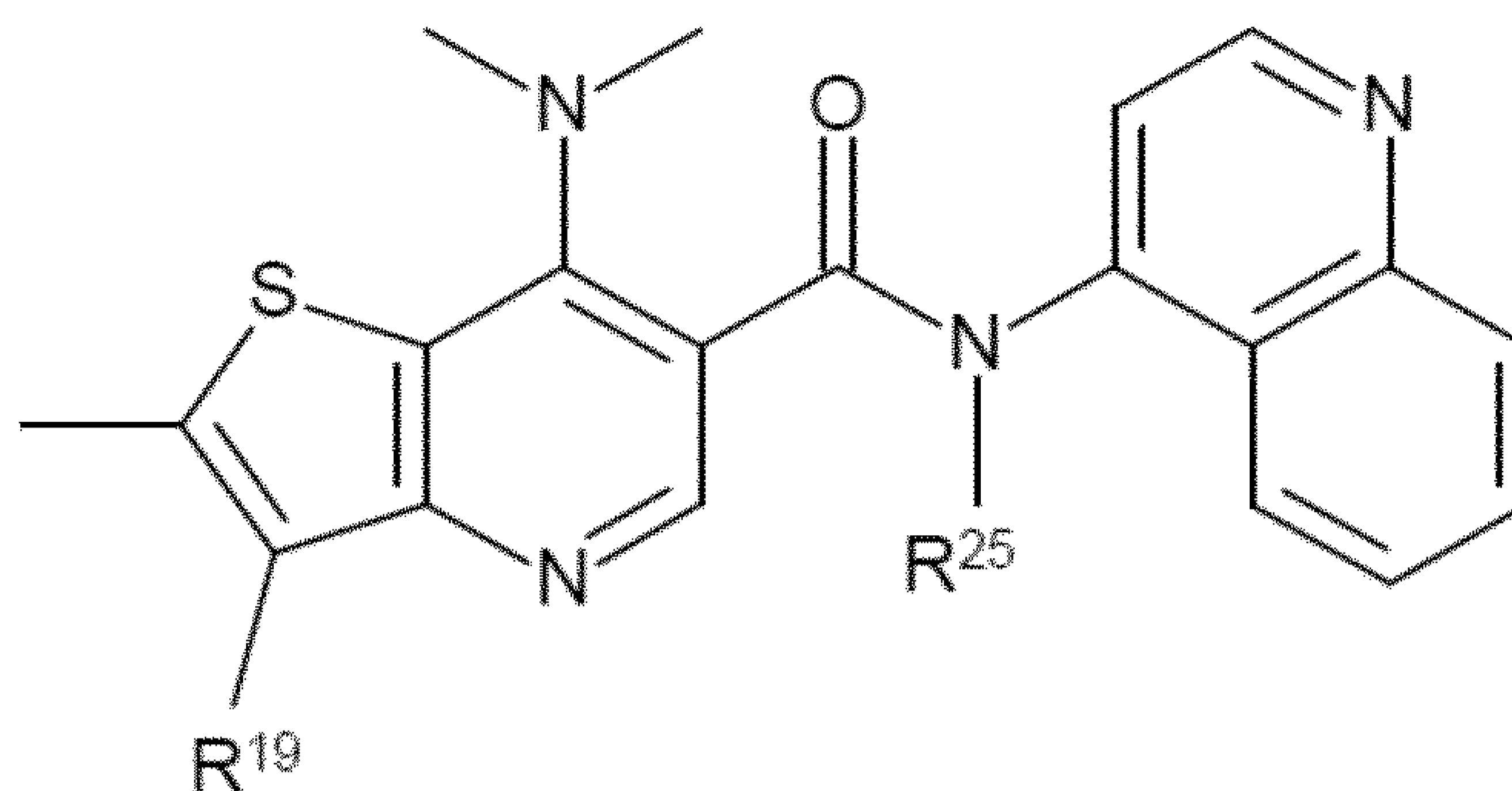


Formula (Ipxvi)

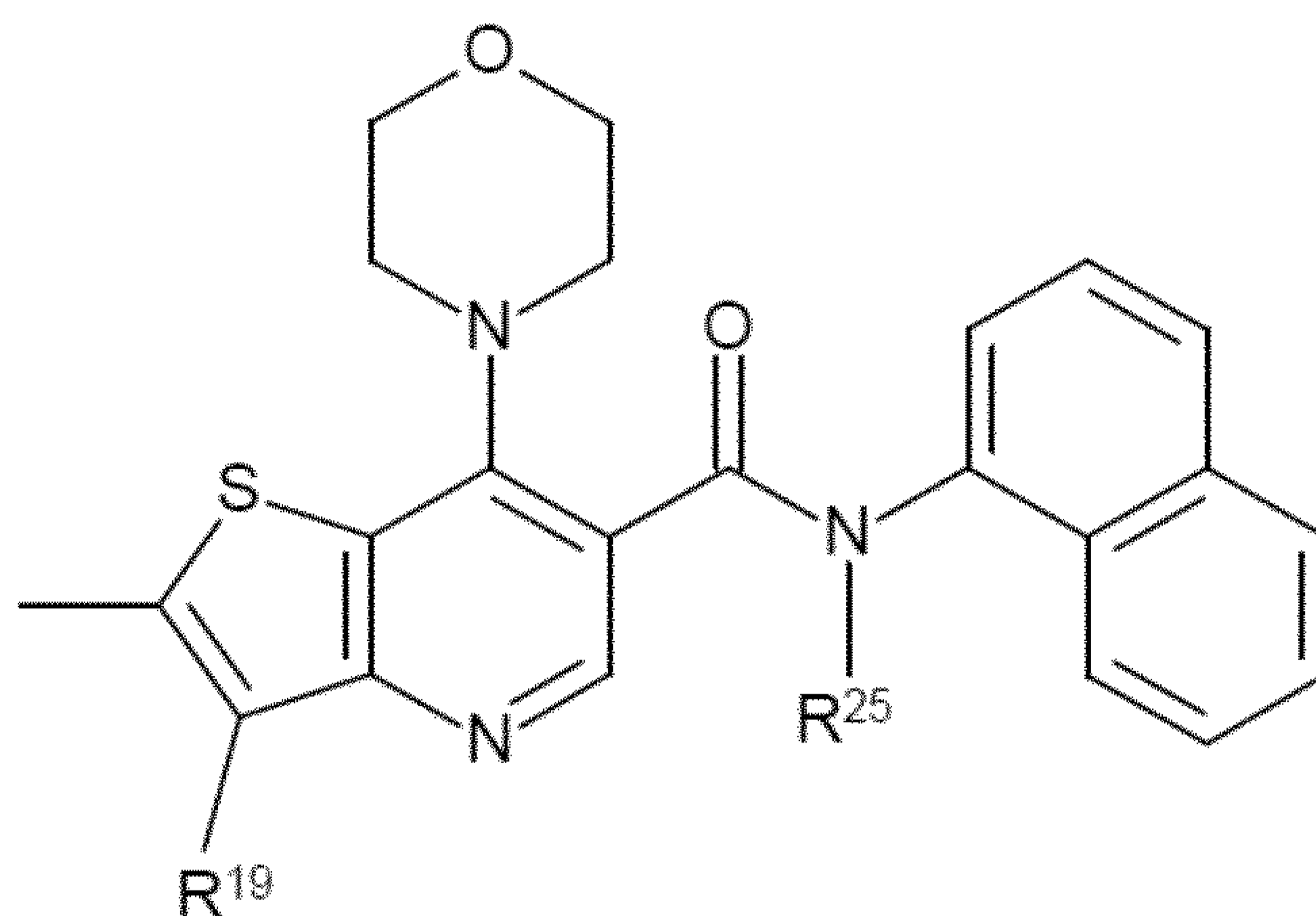


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Formula (Ipxvii)

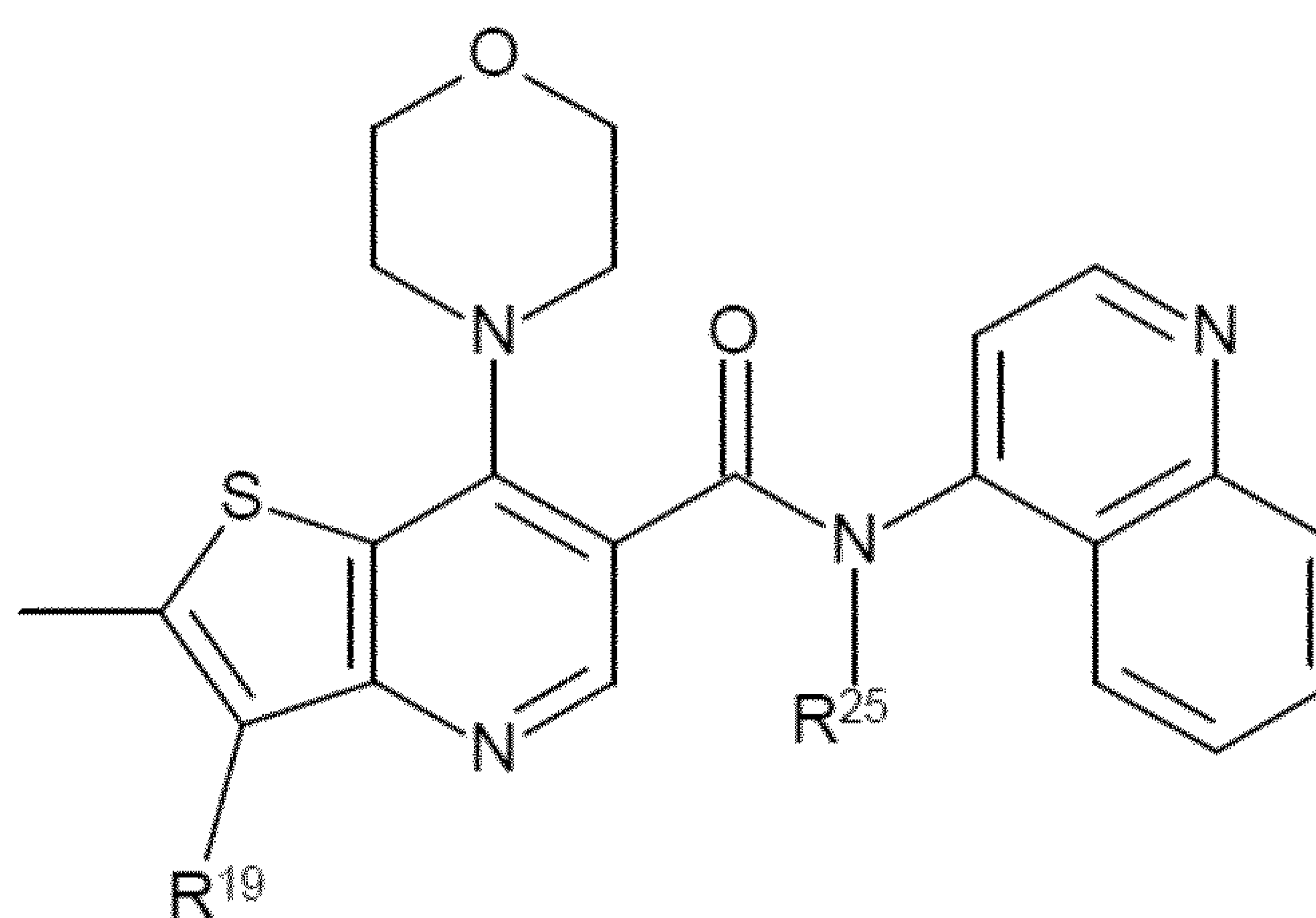


Formula (Ipxviii)



5

Formula (Ipxix)



Formula (Ipxx)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹⁹ and R²⁵ are defined as in any of the embodiments described herein.

- 10 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxv), preferably in the form of the (*S*)-enantiomer. In an

embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ipxx), preferably in the form of the (*S*)-enantiomer.

10 The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 , R^7 and R^{19} are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and NR^2R^3 ,

R^2 and R^3 are independently selected from the group consisting of

20 hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

25 wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{1-6} -alkoxy,

30 R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

and

R^7 is independently selected from the group consisting of

5 hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently

10 selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, $NR^{8'}R^{9'}$, $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

R^8 and R^9 are independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

20 wherein the C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, $NR^{8''}R^{9''}$, $C(=O)OR^{10''}$ and $C(=O)NR^{11''}R^{12''}$;

25 R^{10} , R^{11} and R^{12} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{8''}$, $R^{9''}$, $R^{10''}$, $R^{11''}$ and $R^{12''}$ are independently selected from hydrogen and C_{1-6} -alkyl,

and

R^{19} is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

10 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

20 R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

25 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl,

and

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, 4 to 10-membered heterocyclyl, C_{1-3} -alkoxy, hydroxy, NR^8R^9 , SR^{10} , SOR^{10} and SO_2R^{10} ,

5 wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, 4 to 10-membered heterocyclyl or C_{1-3} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-3} -alkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, NR^8R^9 , $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

10 R^8 and R^9 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-6} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein the C_{1-6} -alkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, hydroxy and $NR^{8''}R^{9''}$;

20 R^{10} is independently selected from hydrogen or C_{1-3} -alkyl, preferably from hydrogen, methyl or ethyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen or C_{1-3} -alkyl, preferably from hydrogen, methyl or ethyl,

$R^{8''}$ and $R^{9''}$ are independently selected from hydrogen or C_{1-3} -alkyl, preferably from hydrogen,
25 methyl or ethyl,

and

R^{19} is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

5

In an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

10 R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

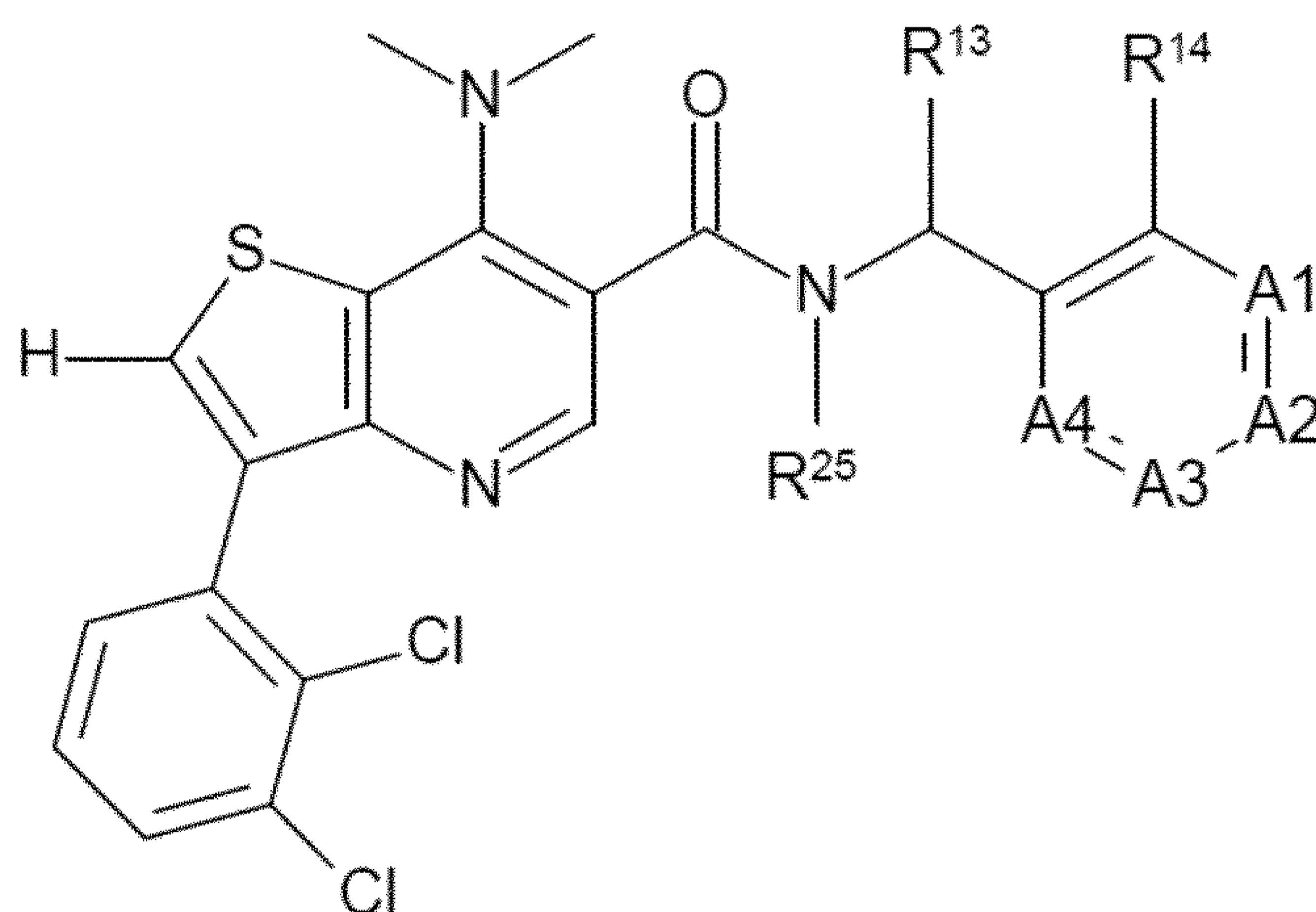
methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl and 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl,

25

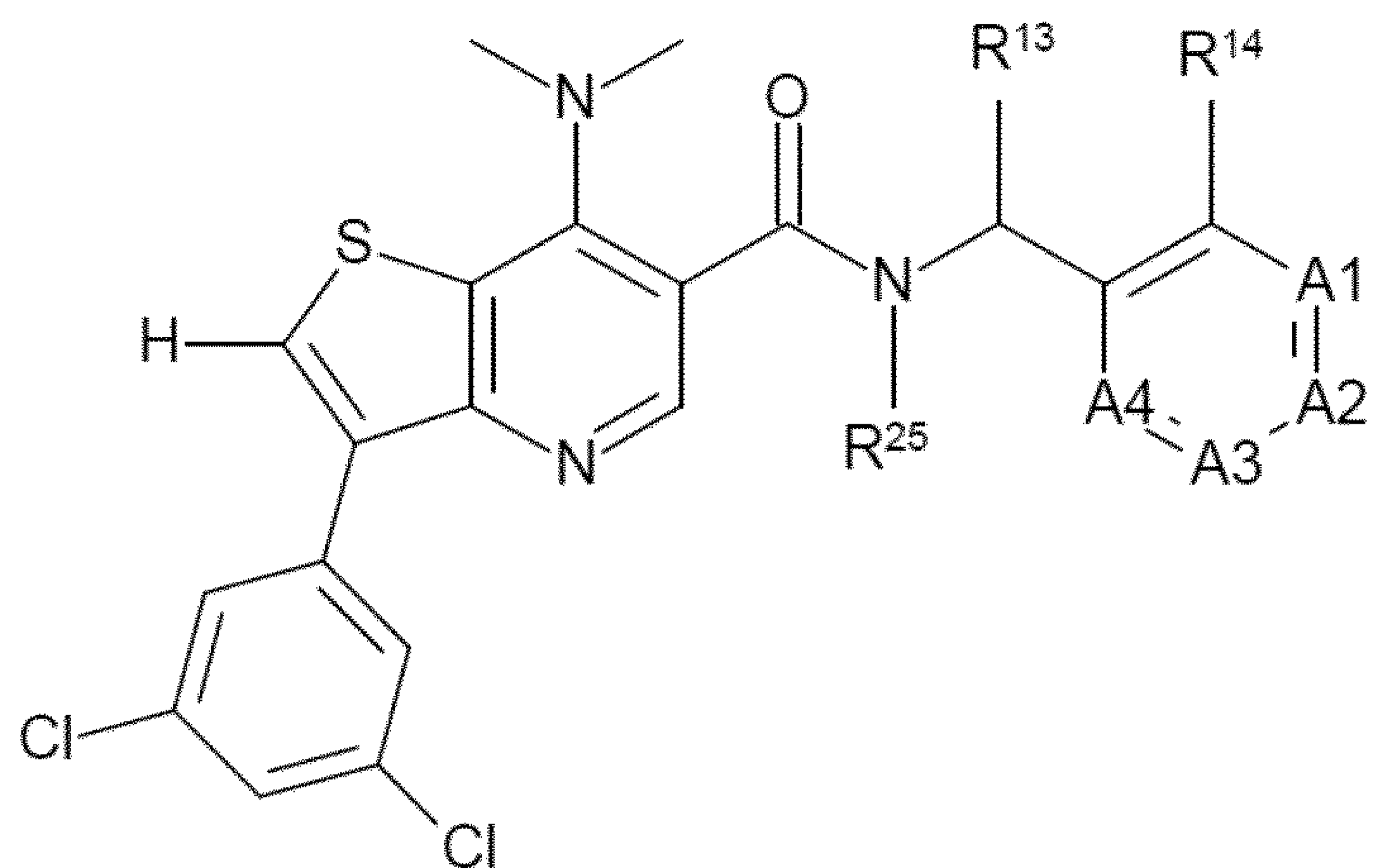
and

R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

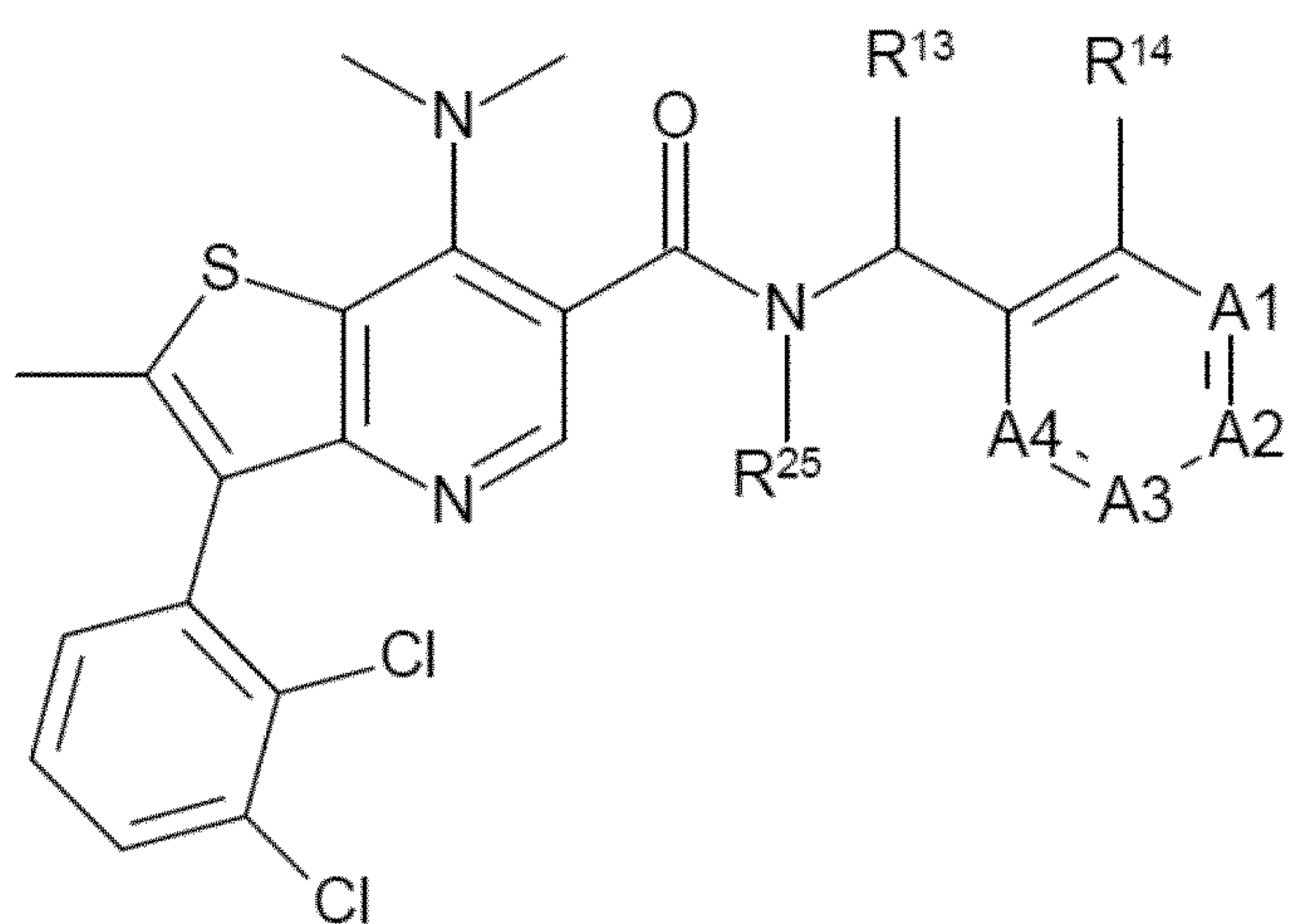
15 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqi), (Iqii), (Iqiii), (Iqiv), (Iqv), (Iqvi), (Iqvii) or (Iqviii)



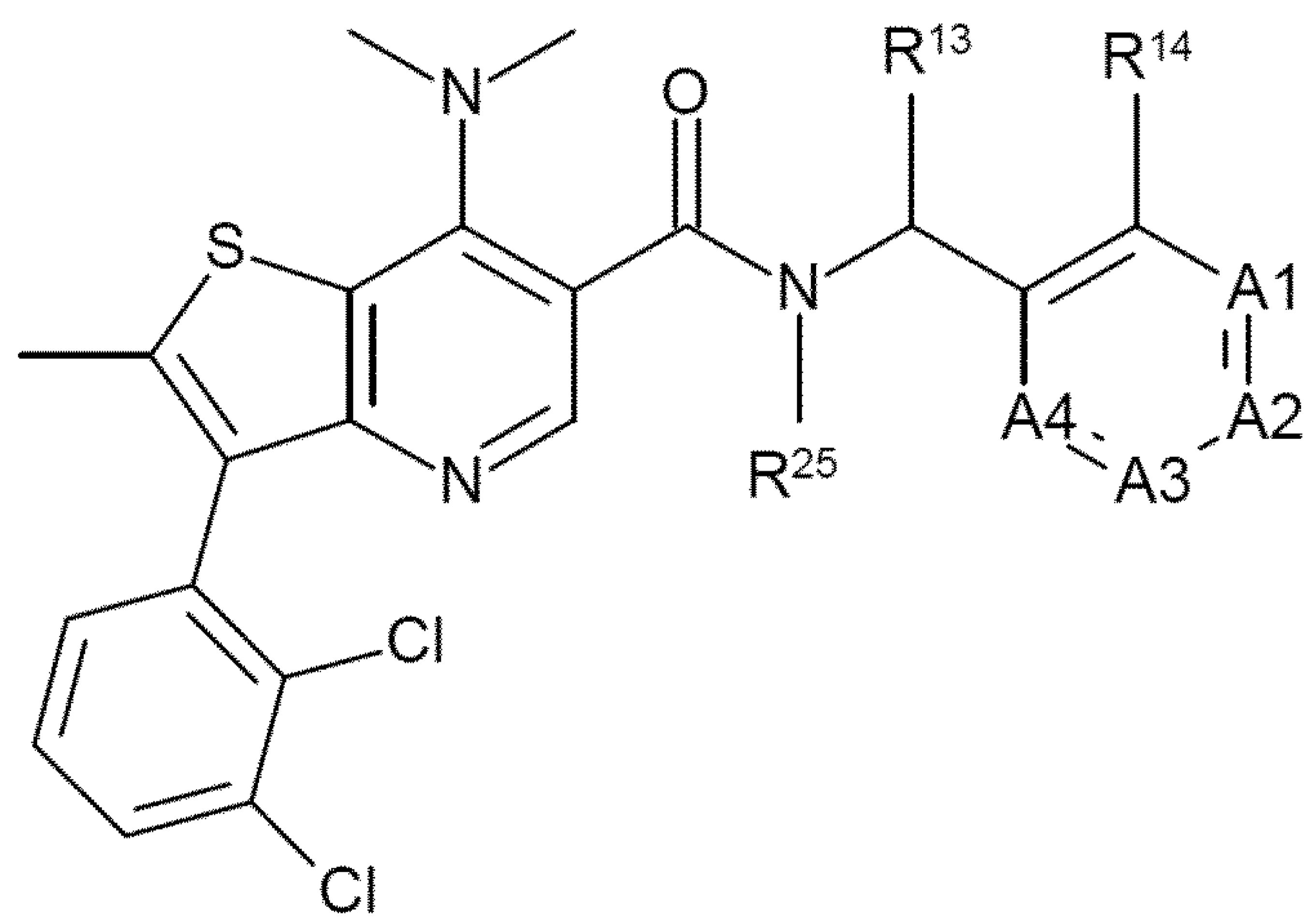
Formula (Iqi)



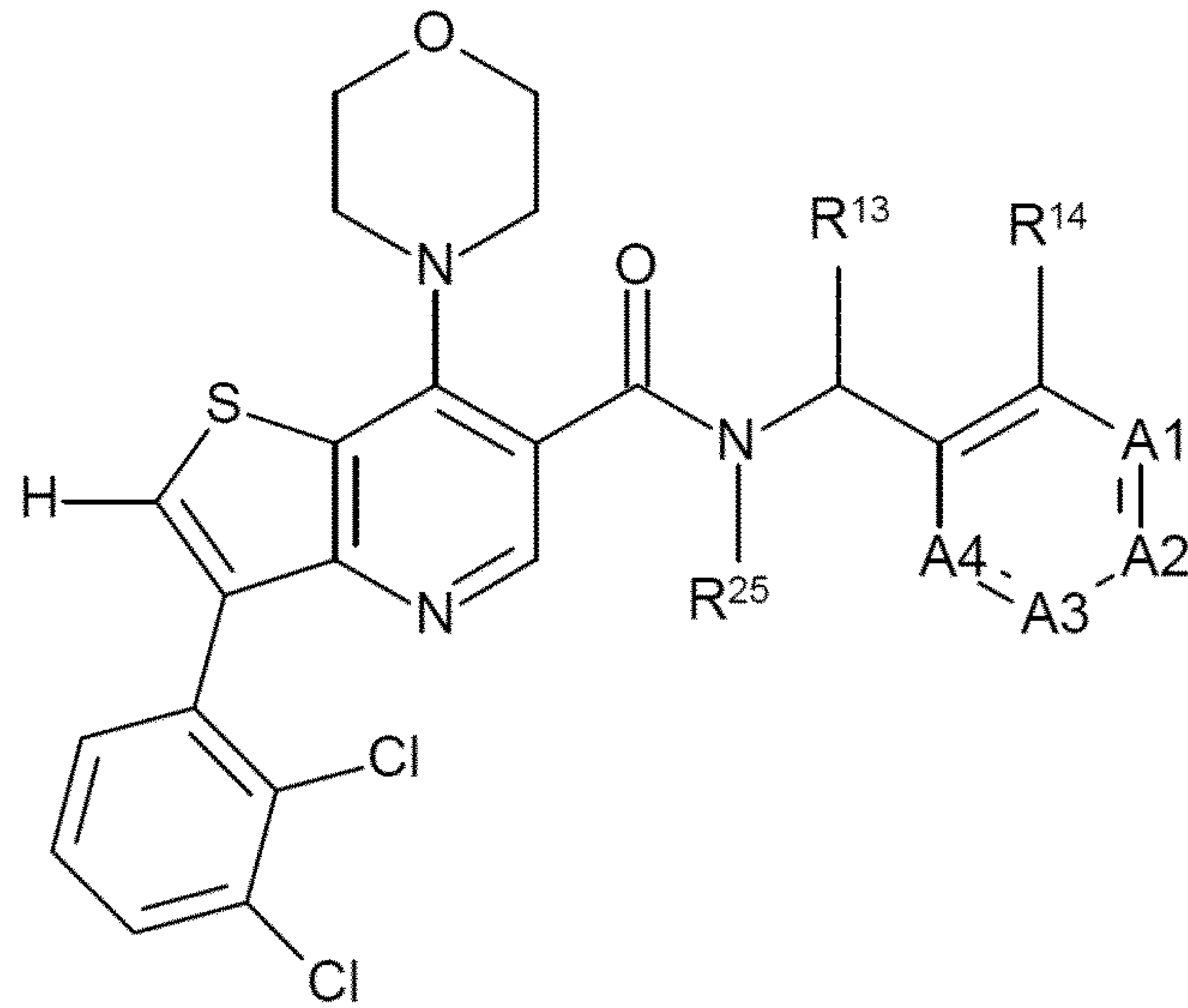
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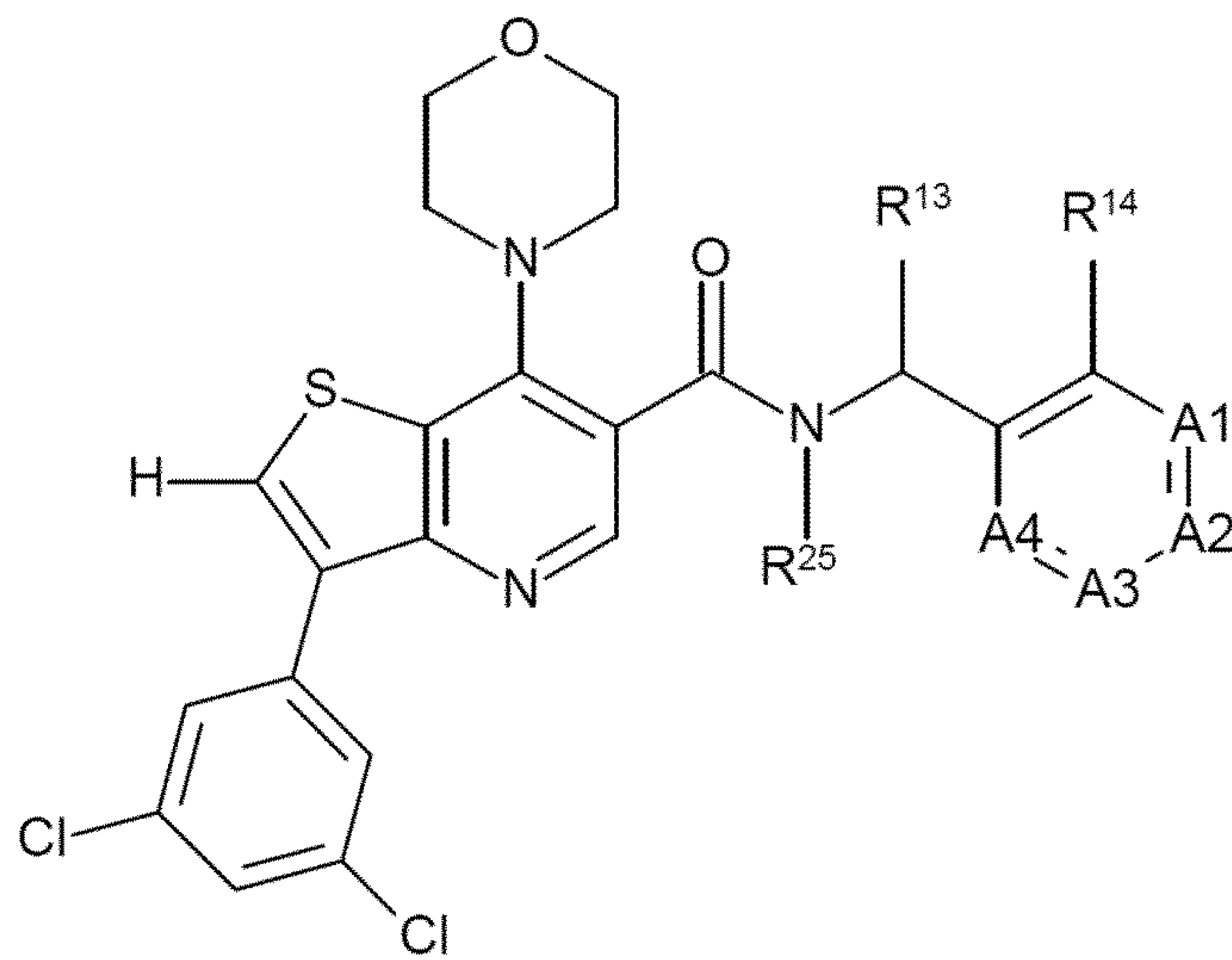
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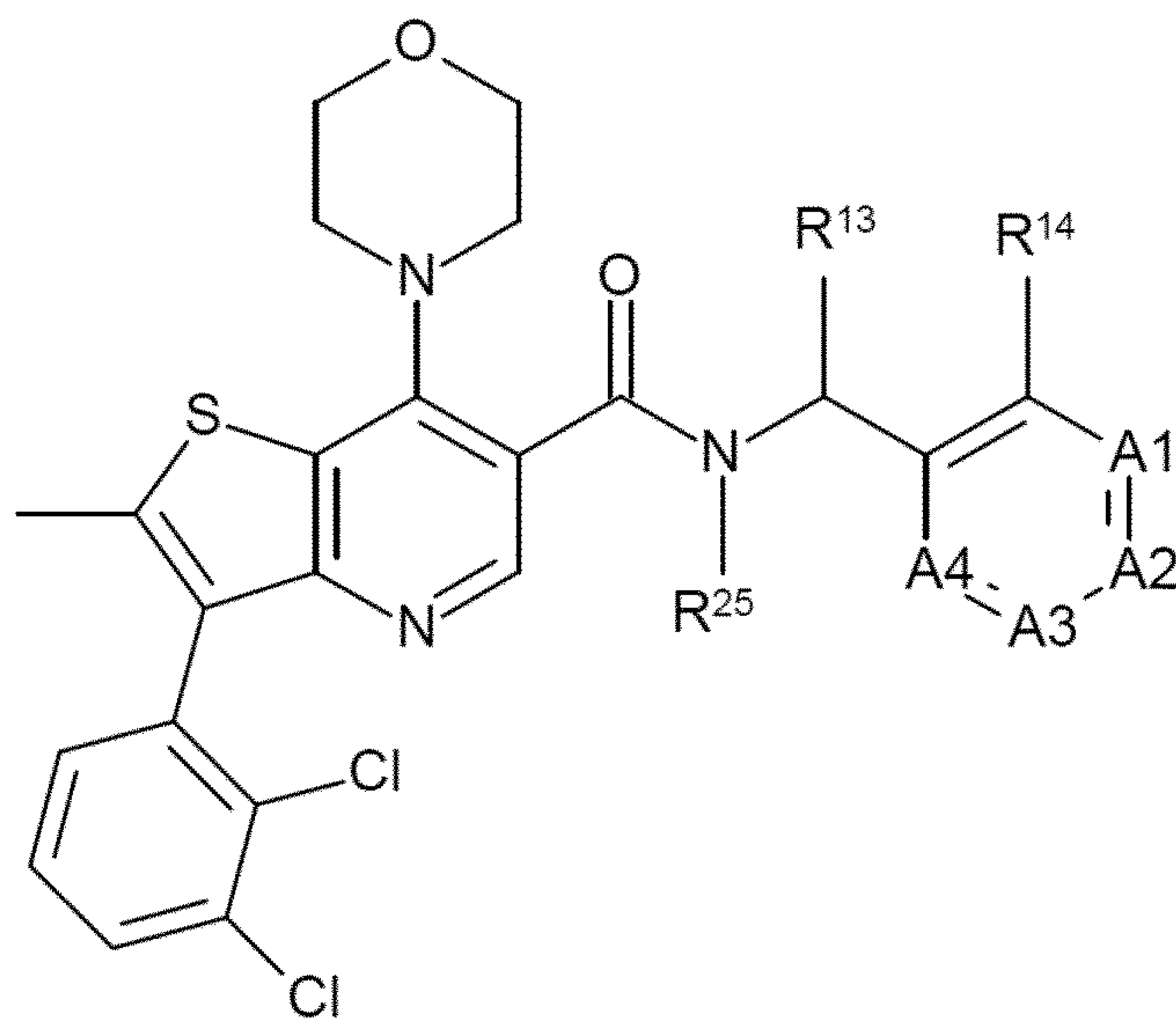
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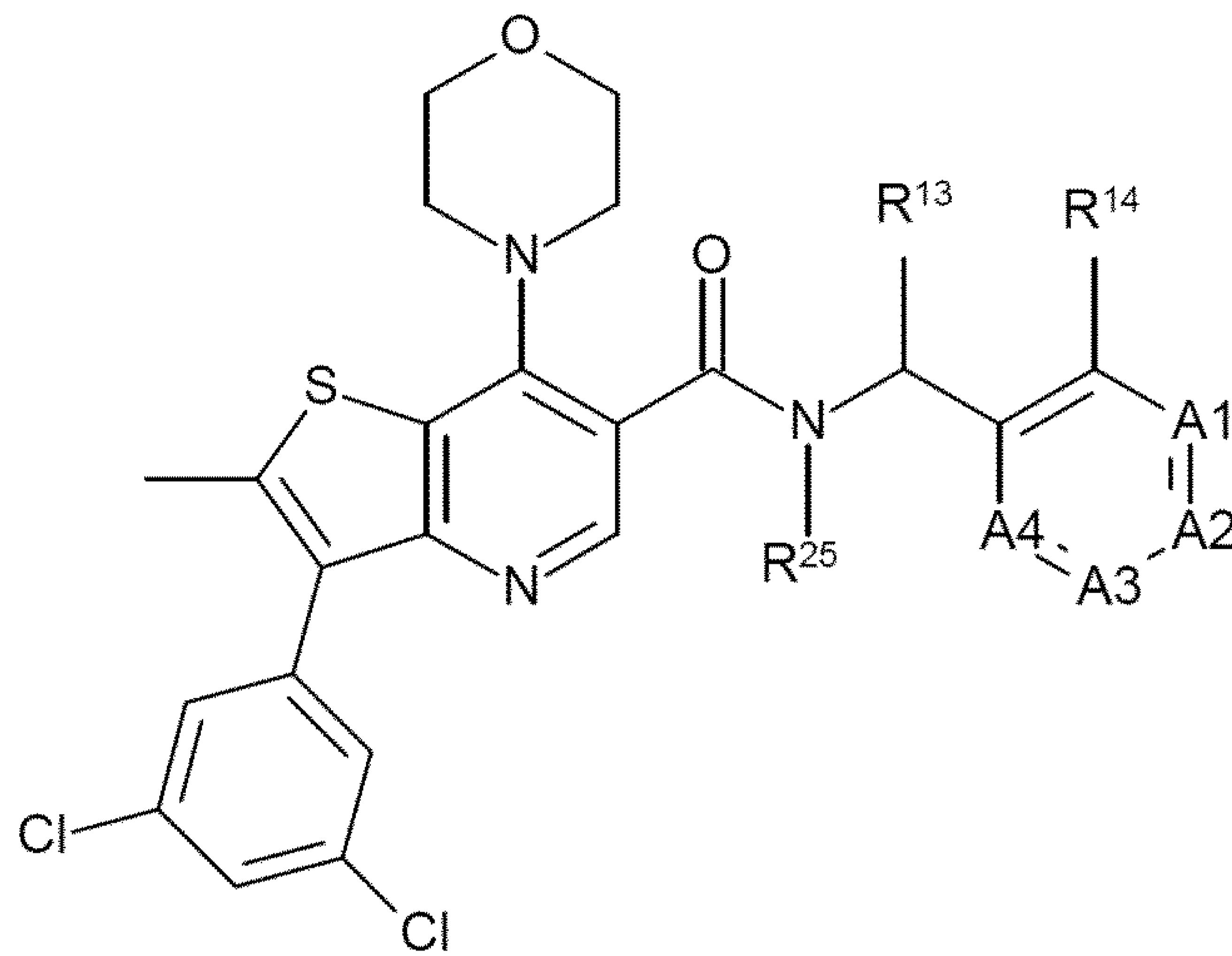
Formula (Iqv)



Formula (Iqvi)



Formula (Iqvii)



Formula (Iqviii)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^{13} , R^{14} , A1, A2, A3, A4 and R^{25} are defined as in any of the embodiments
5 described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the
10 compounds are according to Formula (Iqiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the
15 compounds are according to Formula (Iqvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iqviii), preferably in the form of the (*S*)-enantiomer.

20 The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 , R^7 and R^{25} are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²R³, C(=O)OR⁴ and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3
10 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

20 and

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl, and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl,

and

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, 4- to 10 membered heterocyclyl, C_{1-6} -alkoxy, NR^8R^9 ,

5 wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, 4- to 10 membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, and halogen,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-6} -cycloalkyl,

10 wherein the C_{1-6} -alkyl, or C_{3-6} -cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, and hydroxy.

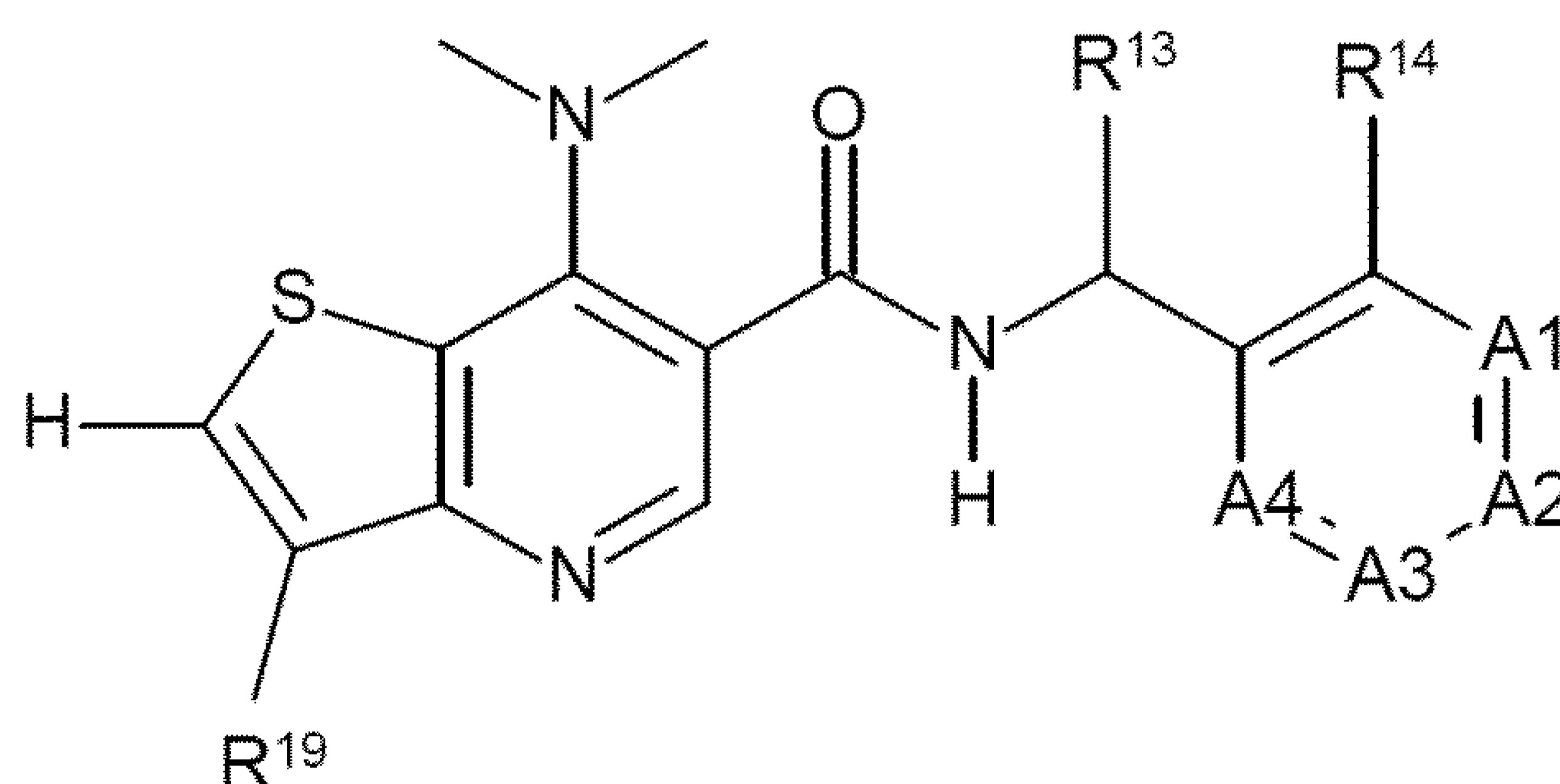
Suitably R^7 is independently selected from the group consisting of

15 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

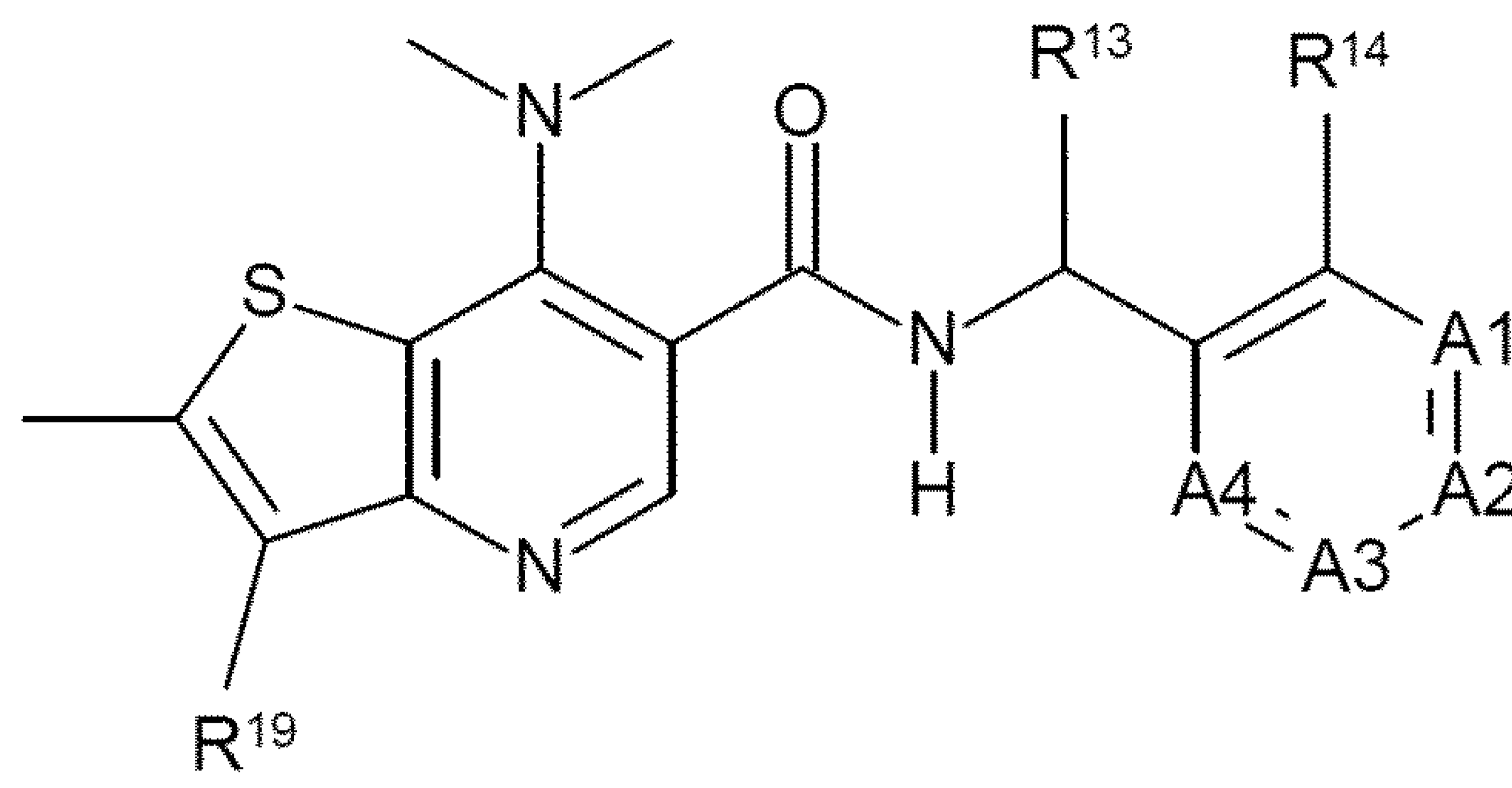
20 and

R^{25} is hydrogen or methyl, more preferably hydrogen.

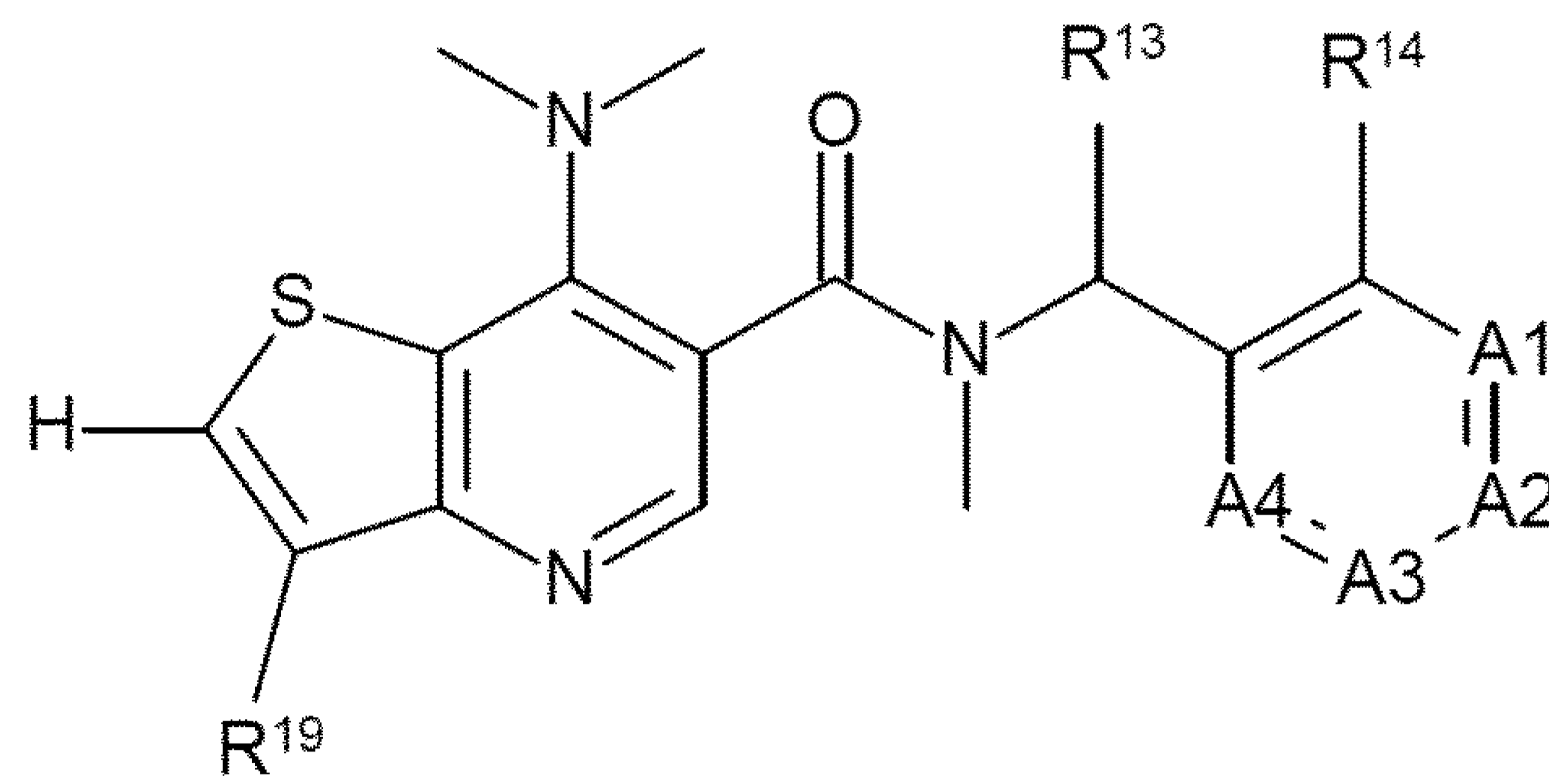
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iri), (Irii), (Iriii), (Iriv), (Irv), (Irvi), (Irvii) or (Irviii)



Formula (Iri)

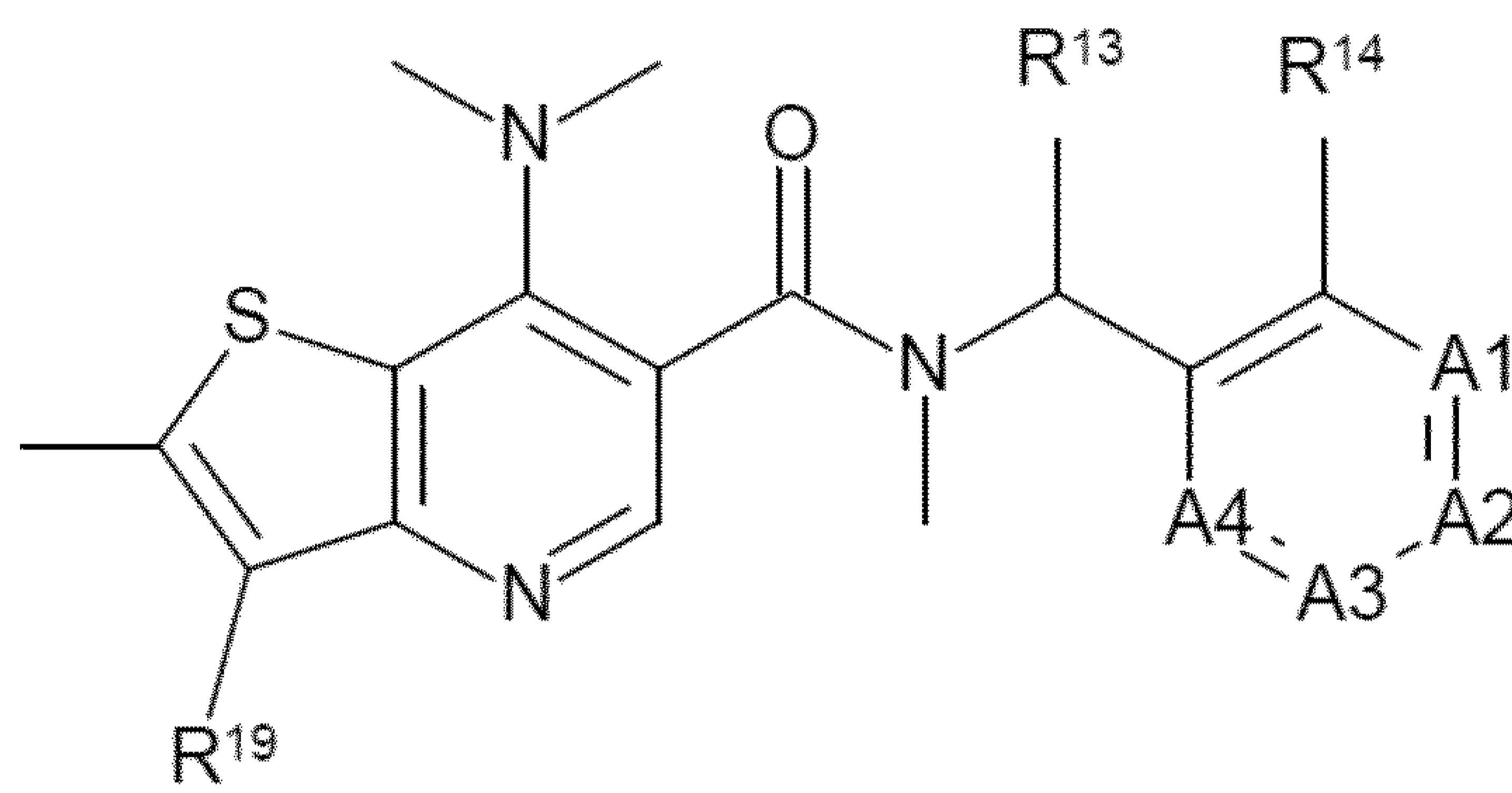


Formula (Irii)

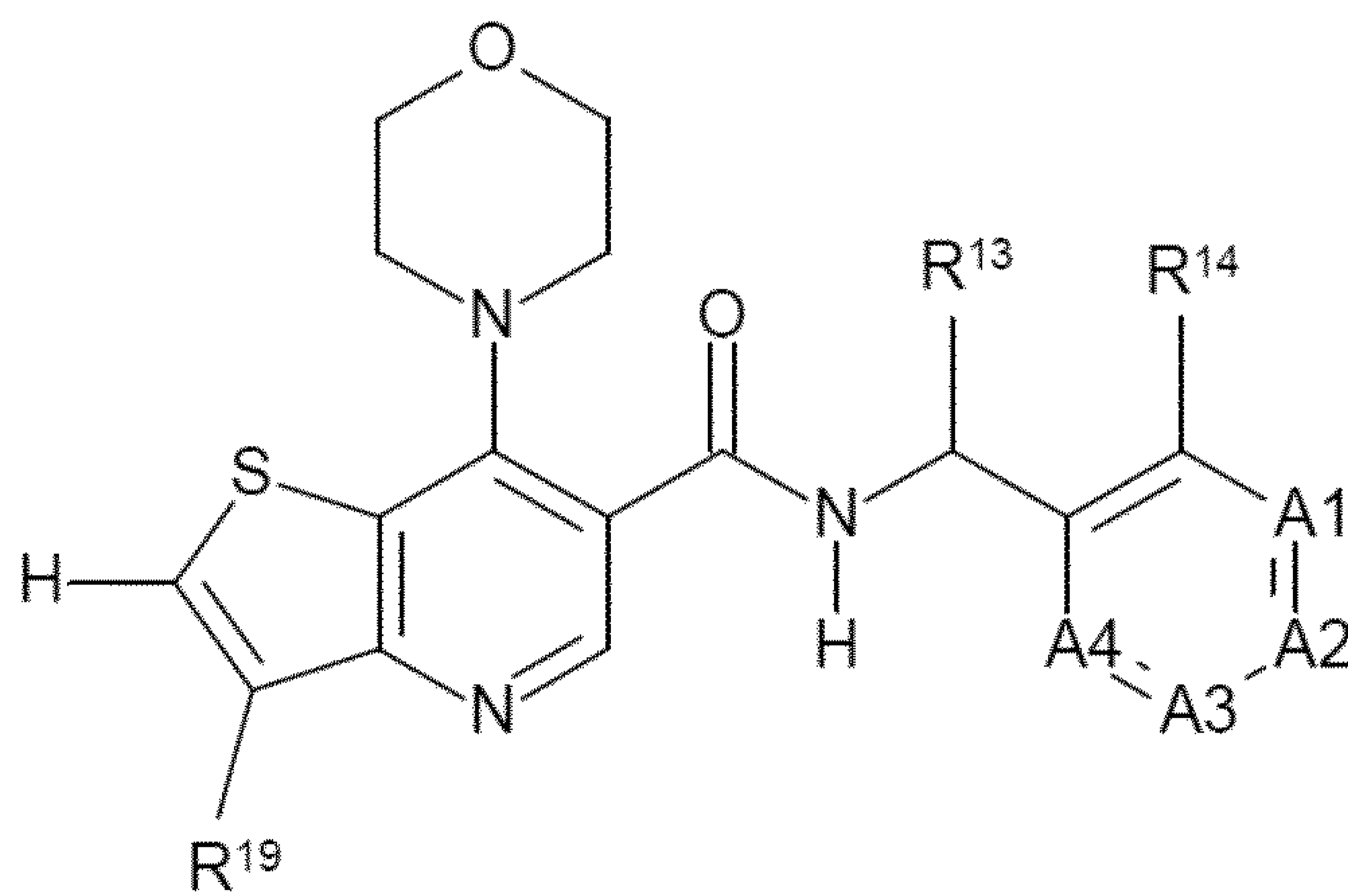


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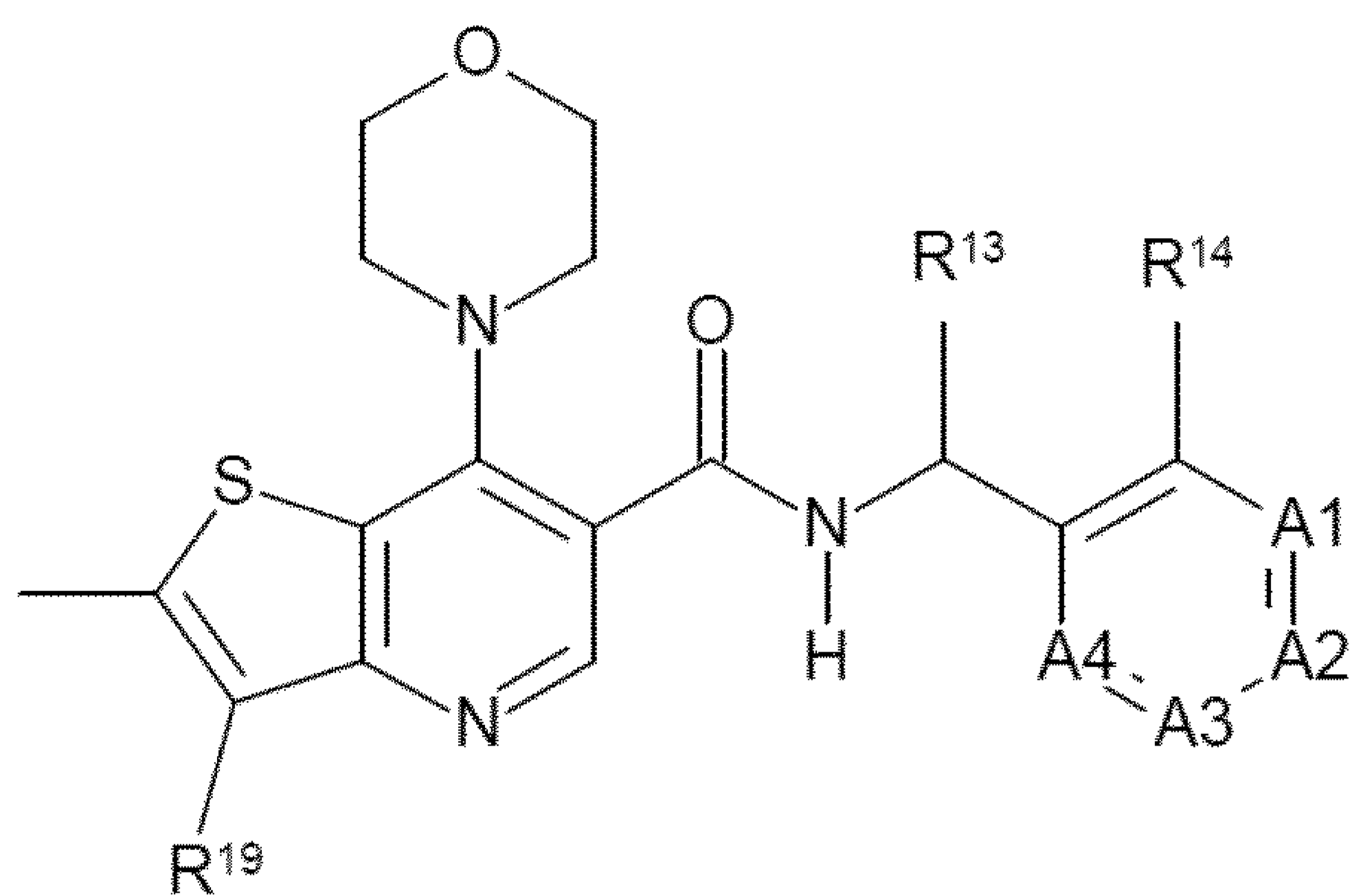
Formula (Iriii)



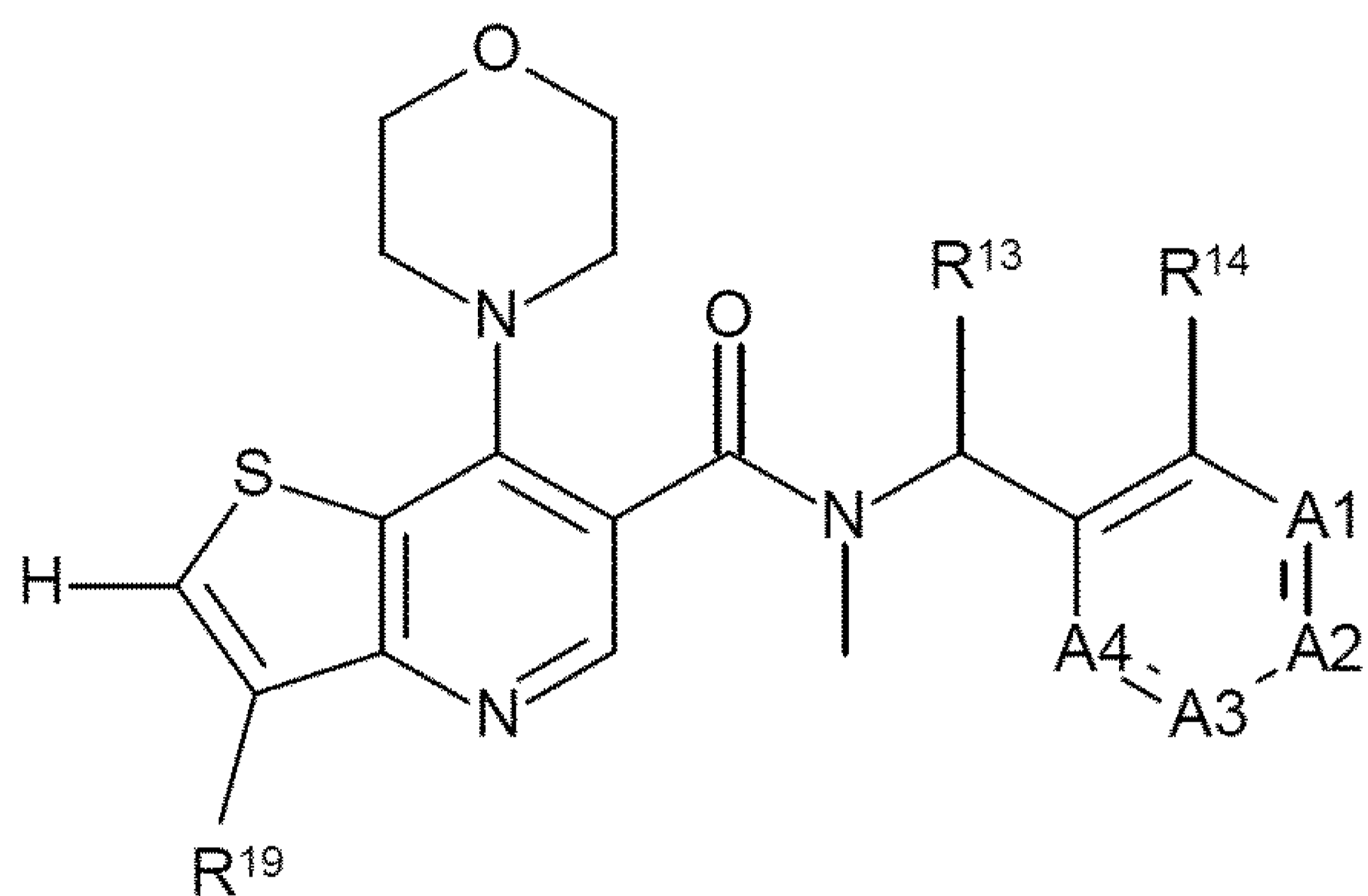
Formula (Iriv)



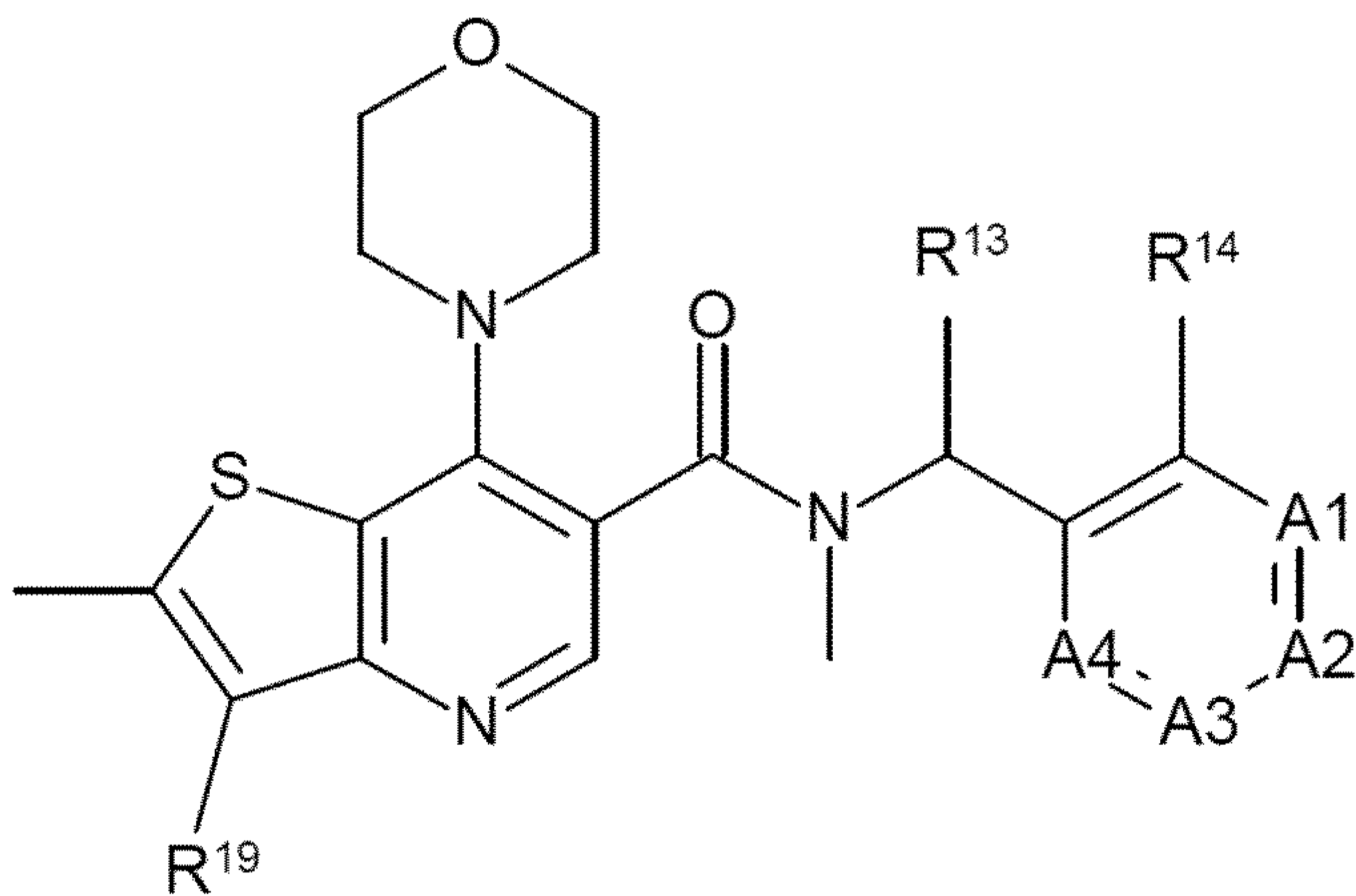
Formula (Irv)



Formula (Irvii)



Formula (Irviii)



Formula (Iri)

5

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹³, R¹⁴, A1, A2, A3, A4 and R¹⁹ are defined as in any of the embodiments described herein.

- 10 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iri), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Irii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the

compounds are according to Formula (Iriii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iriv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Irv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Irvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Irvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Irviii), preferably in the form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 , R^{13} , R^{14} , A1, A2, A3 and A4 are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²R³, C(=O)OR⁴ and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

5 and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

10 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

15 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

R^{19} is independently selected from the group consisting of

20 C_{6-10} -aryl and 5 to 10-membered heteroaryl,

wherein each C_{6-10} -aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, $NR^{20}R^{21}$, $C(=O)OR^{22}$ and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{6-10} -aryl or

R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, or C_{6-10} -aryl or the heterocyclic ring formed by R^{20} and R^{21} together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

10 C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, $NR^{20'}R^{21'}$, $C(=O)OR^{22'}$ and $C(=O)NR^{23'}R^{24'}$,

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{20'}$, $R^{21'}$, $R^{22'}$, $R^{23'}$ and $R^{24'}$ are independently selected from hydrogen and C_{1-6} -alkyl.

In one embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^5 and R^6 are independently selected from hydrogen and C_{1-3} -alkyl,

20 $R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-3} -alkyl,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

25 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more
5 substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or
more substituents independently selected from the group consisting of
halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is
10 optionally substituted with one or more halogen.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

15 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms
containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally
replaced by -NH- or -O-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

20 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

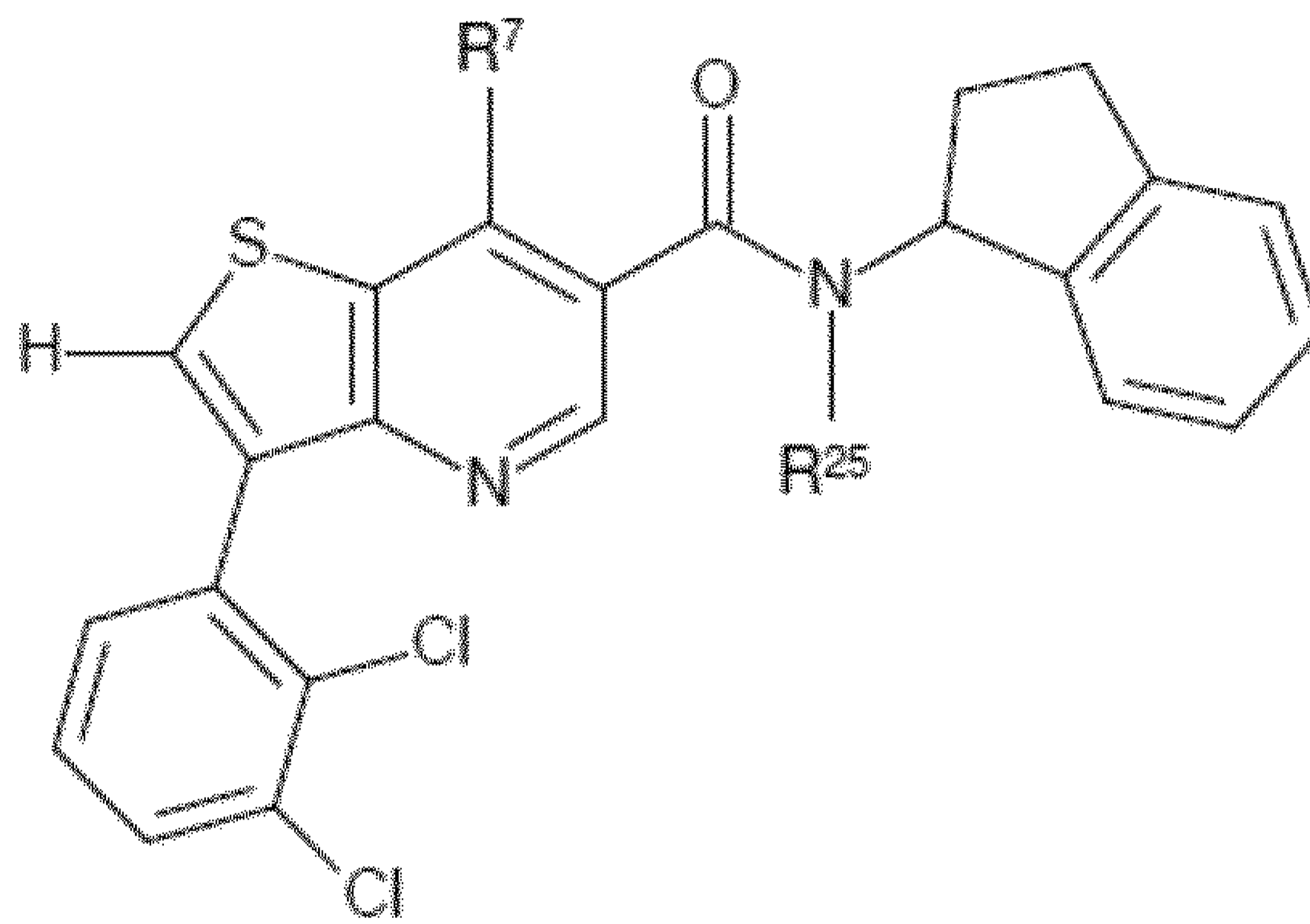
wherein none, one or two of A1, A2, A3 and A4 are N,

and

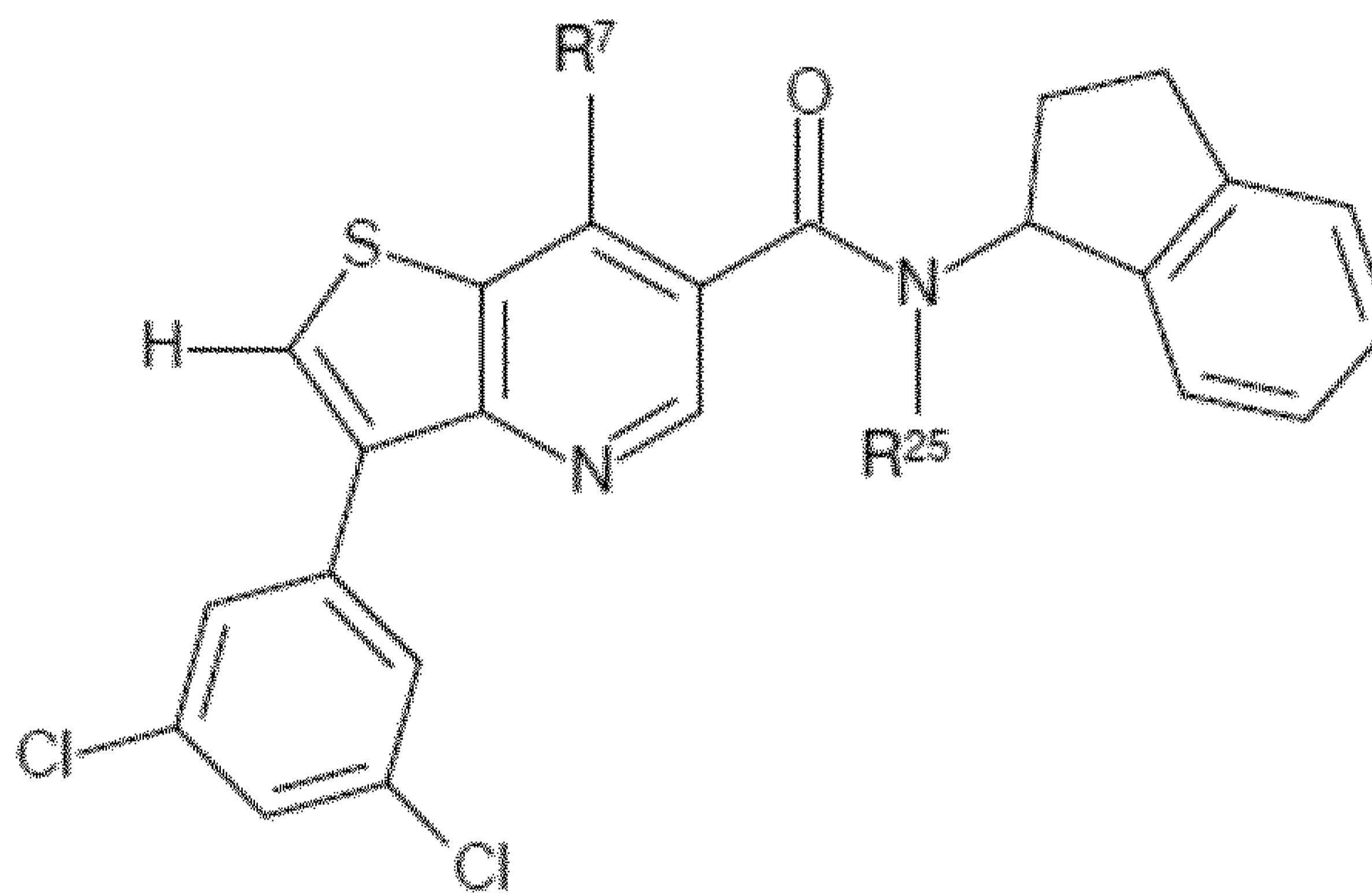
R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl,
25 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-
trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-
trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-
fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-

flurophenyl, 3-chlorophenyl, 2,3-difluorophenyl 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

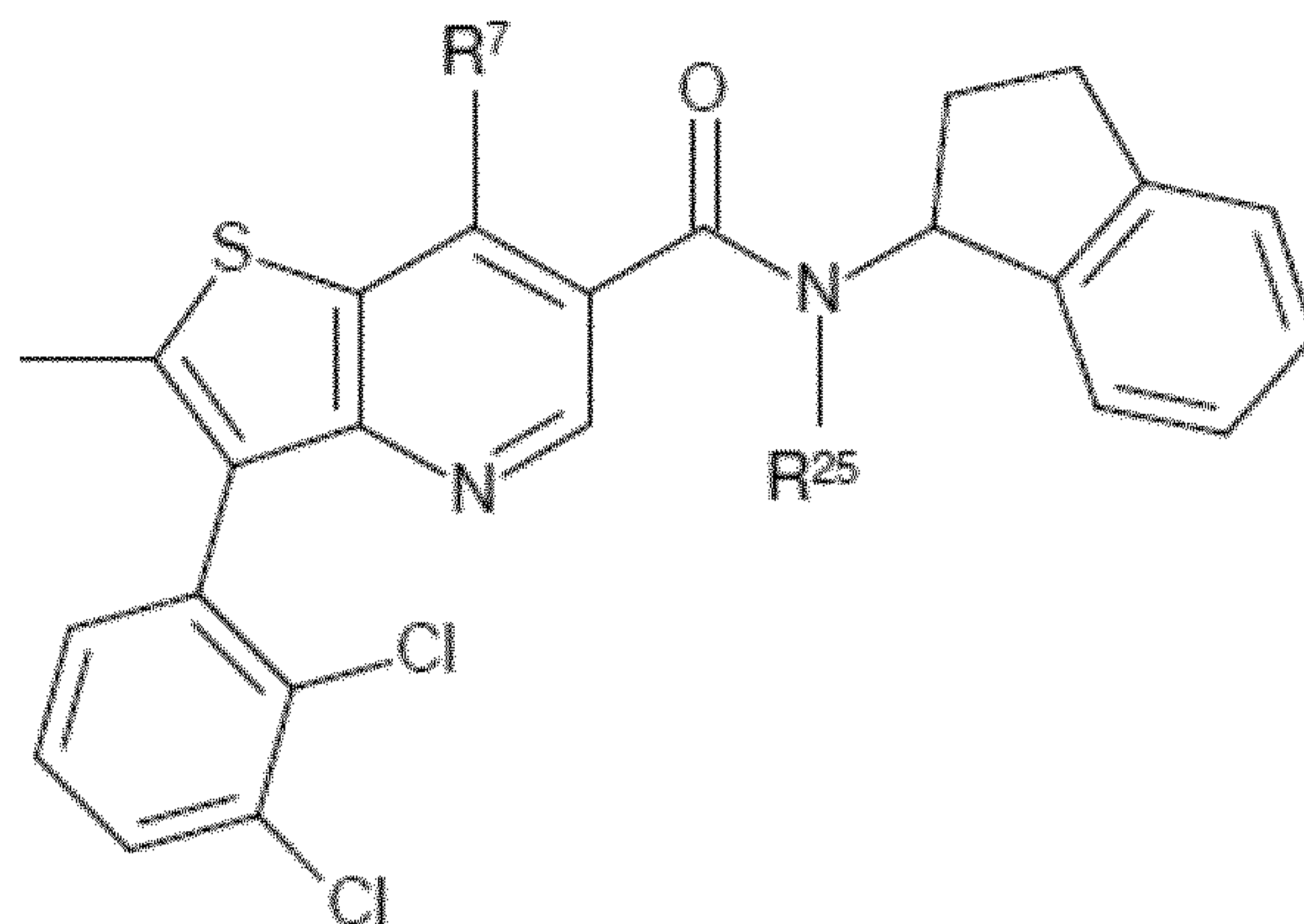
In an embodiment of the invention and/or embodiments thereof, the compounds are according to
 10 Formula (Isi), (Isii), (Isiii), (Isiv), (Isv), (Isvi), (Isvii), (Isviii), (Isix), (Isx), (Isxi) or (Isxii)



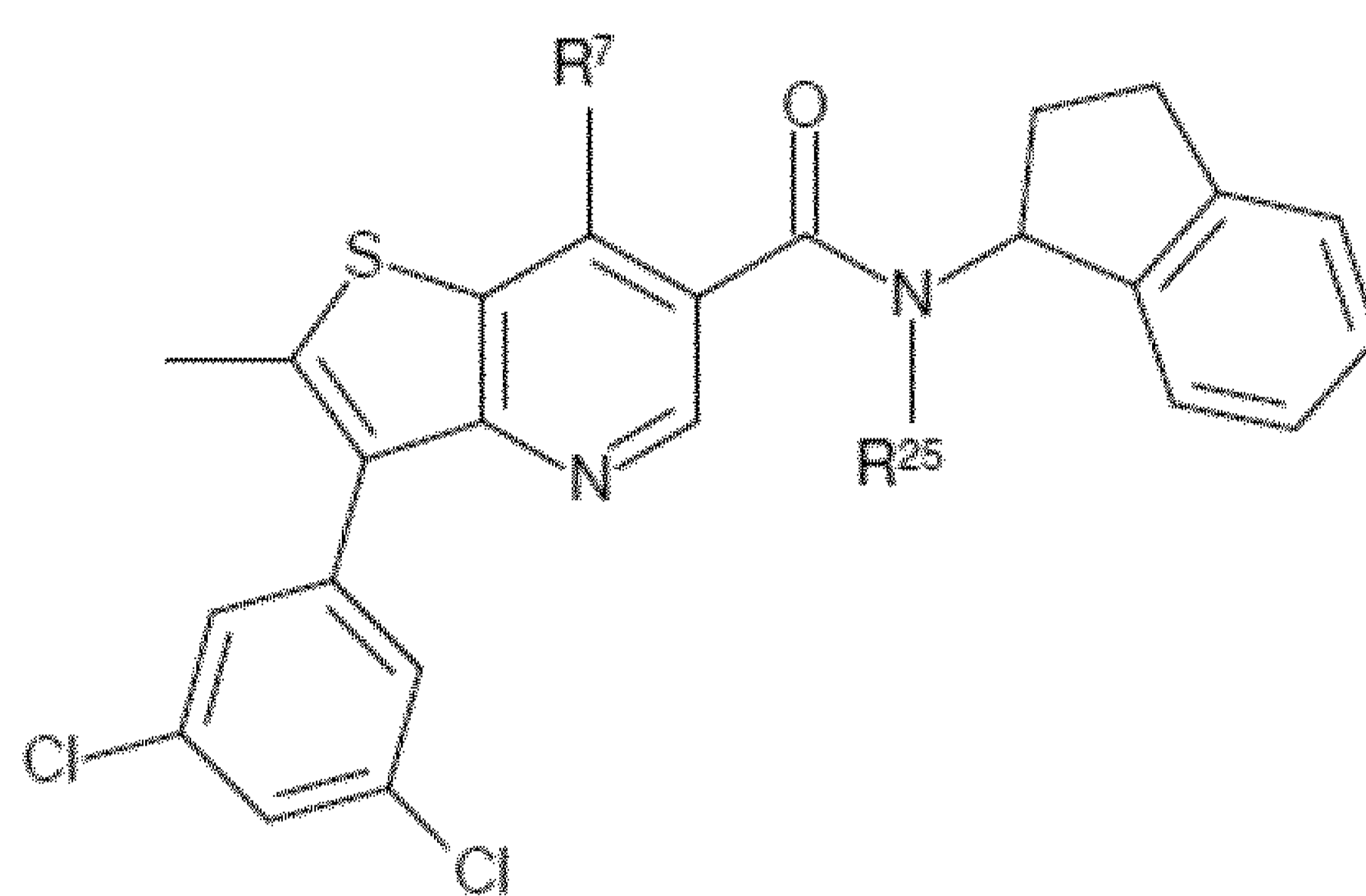
Formula (Isi)



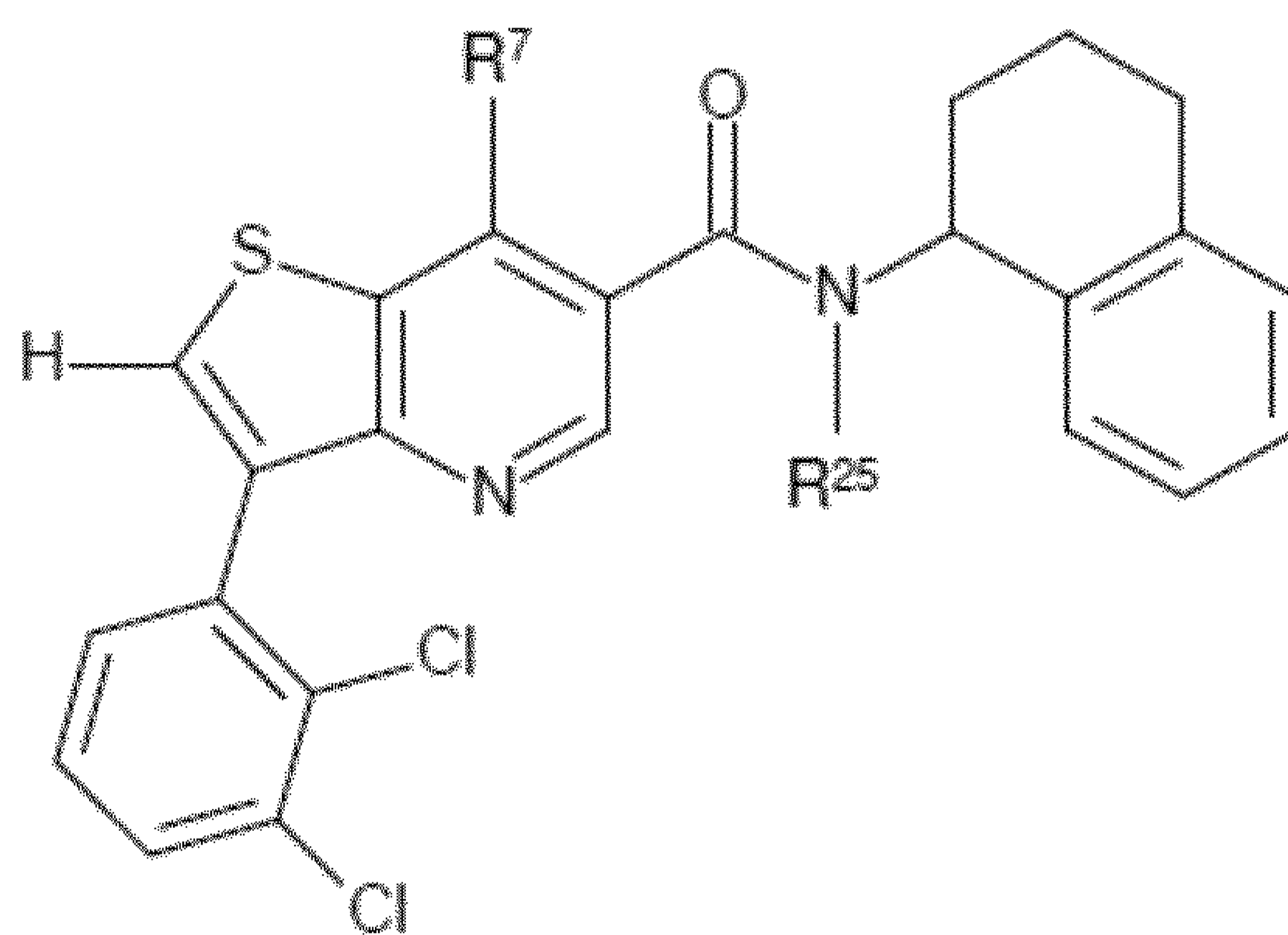
Formula (Isii)



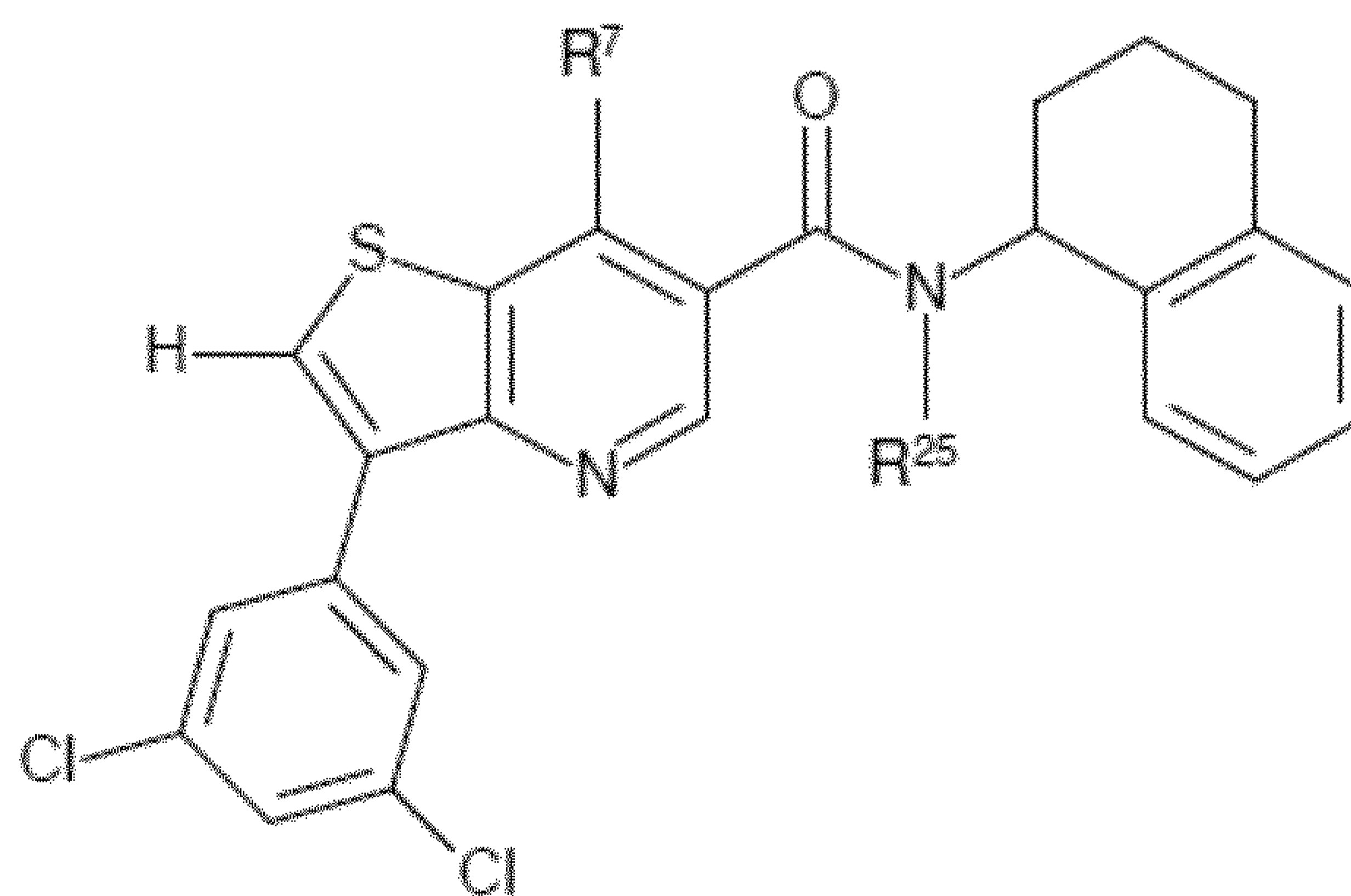
Formula (Isiii)



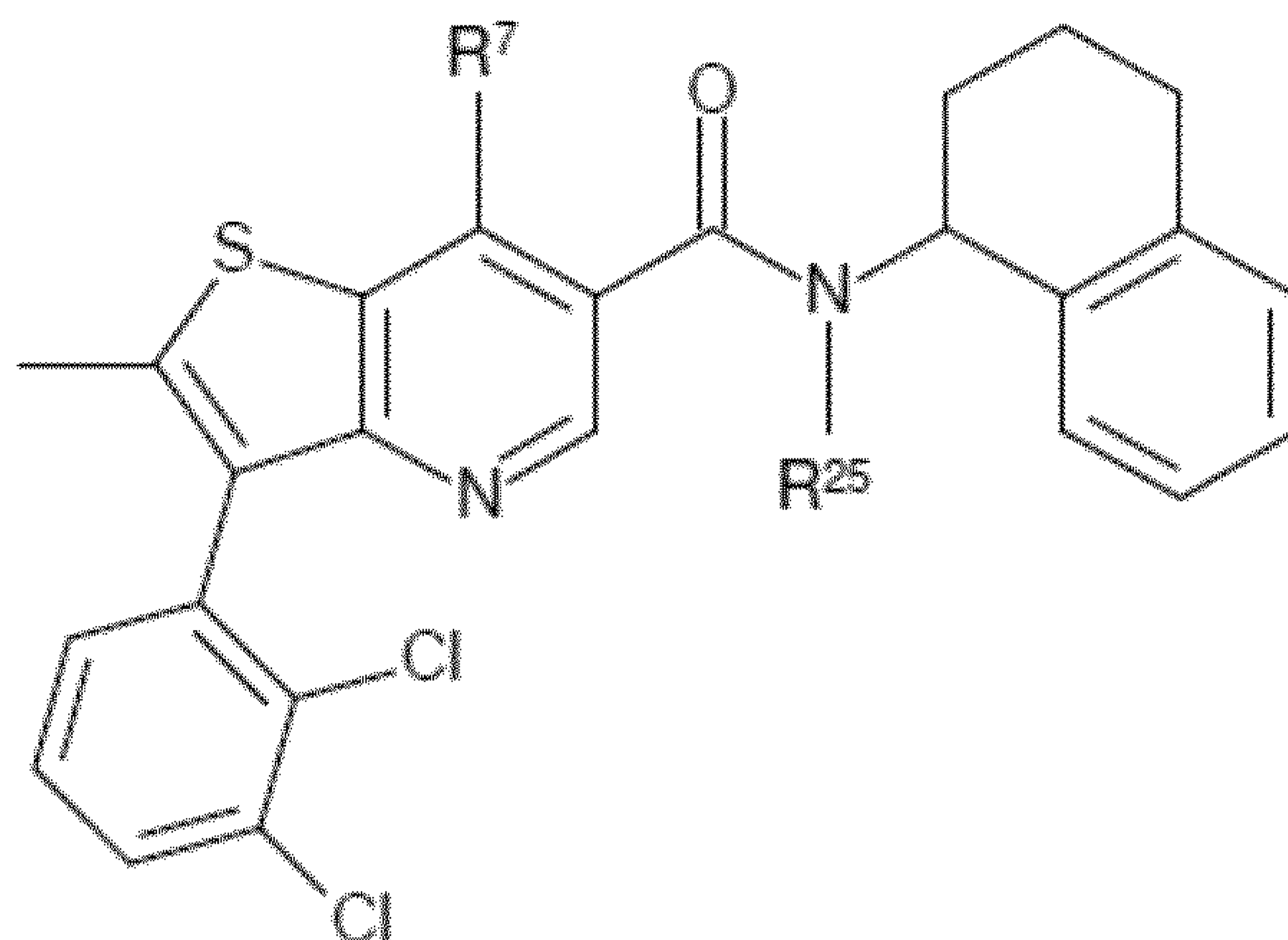
Formula (Isiv)



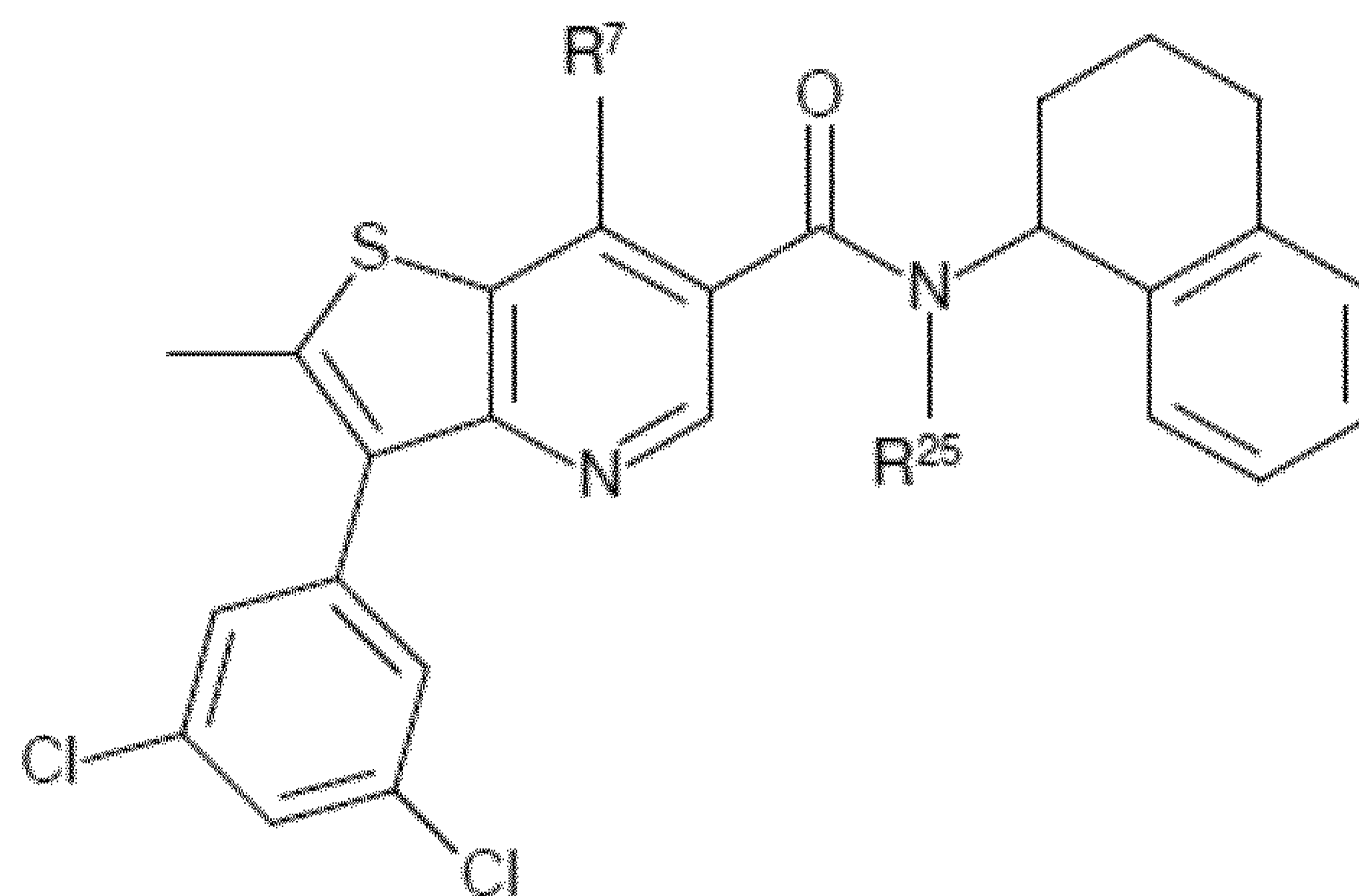
Formula (Isv)



Formula (Isvi)

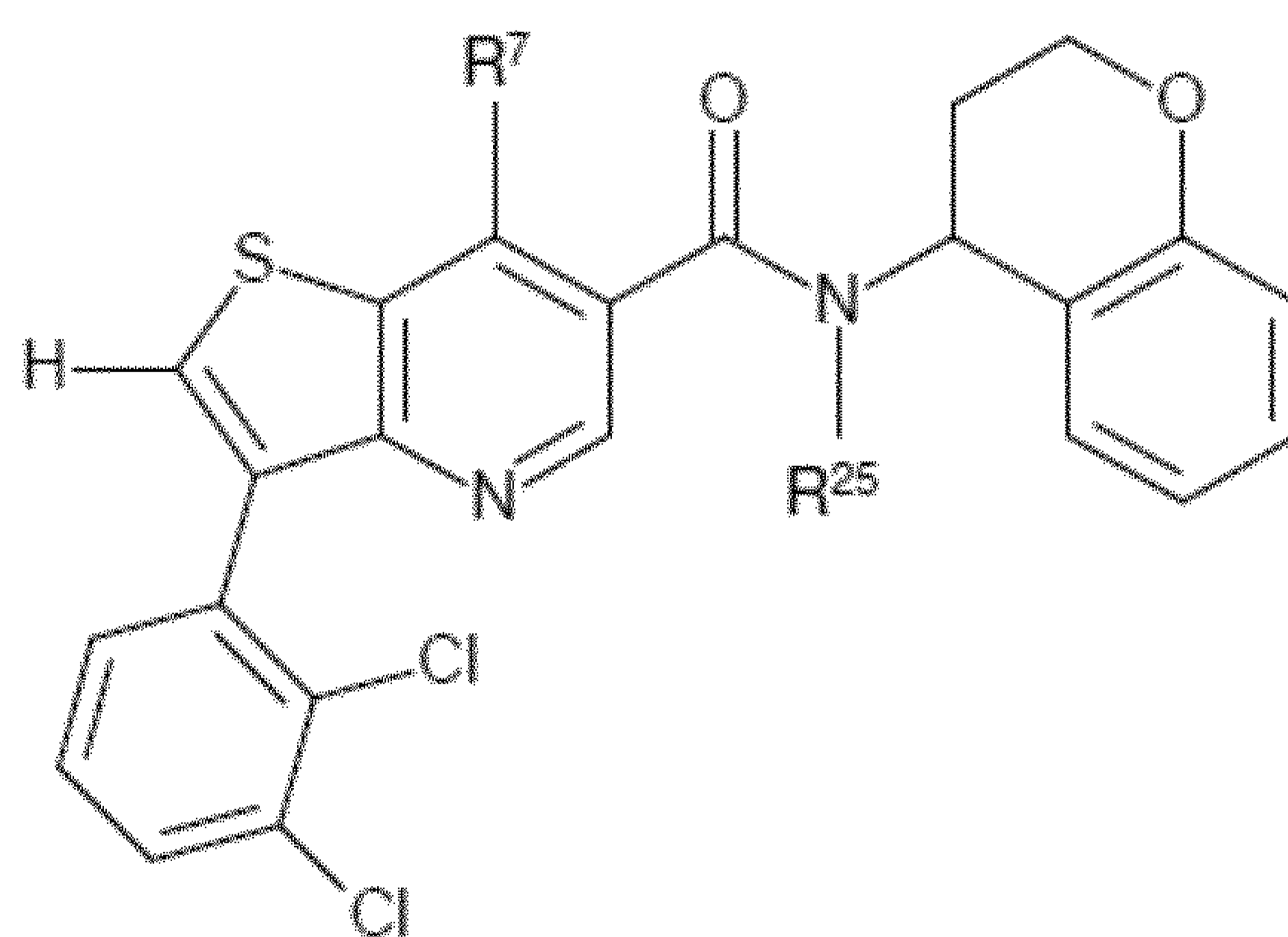


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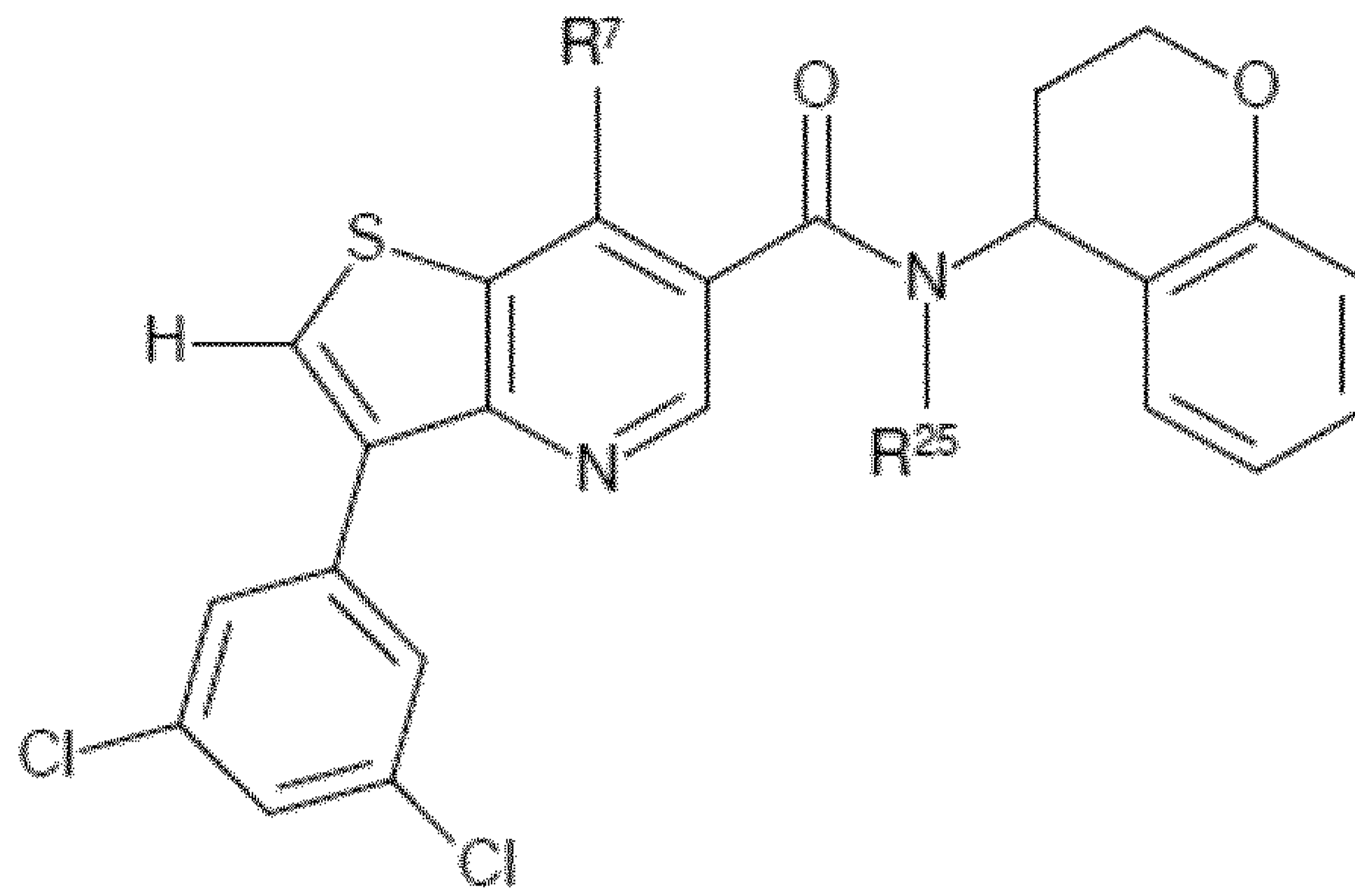


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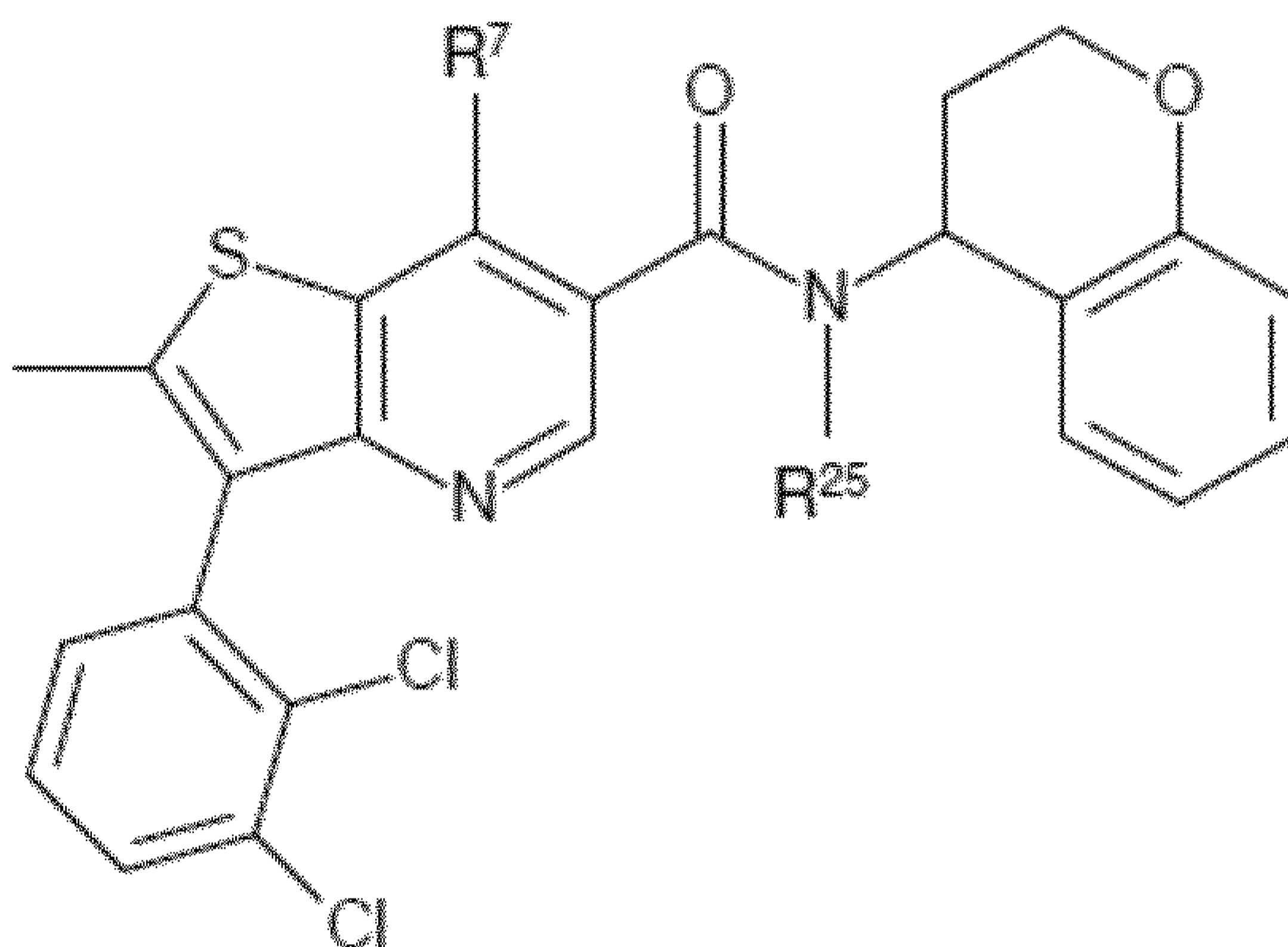
Formula (Isviii)



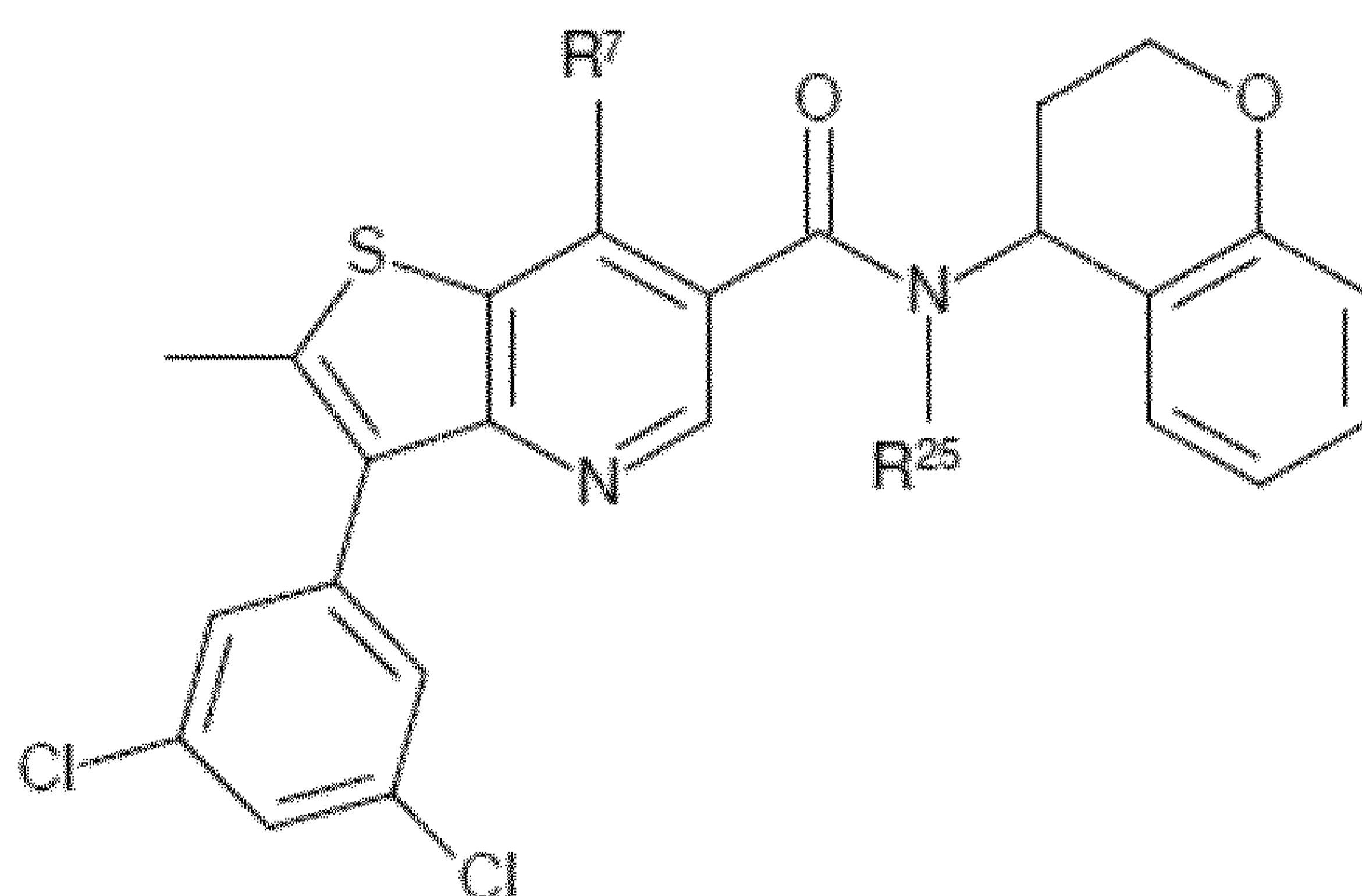
Formula (Isix)



Formula (Isx)



Formula (Isxi)



Formula (Isxii)

5

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to

Formula (Isiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxii), preferably in the form of the (*S*)-enantiomer

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and NR^2R^3 ,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

5 R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

and

10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

15 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

and

20 R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

5 wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, or C_{6-10} -aryl or the heterocyclic ring formed by R^{20} and R^{21} together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

10 C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, $NR^{20'}R^{21'}$, $C(=O)OR^{22'}$ and $C(=O)NR^{23'}R^{24'}$,

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{20'}$, $R^{21'}$, $R^{22'}$, $R^{23'}$ and $R^{24'}$ are independently selected from hydrogen and C_{1-6} -alkyl.

In one embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

15 hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^5 and R^6 are independently selected from hydrogen and C_{1-3} -alkyl,

20 $R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-3} -alkyl,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

25 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more
5 substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or
more substituents independently selected from the group consisting of
halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is
10 optionally substituted with one or more halogen.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

15 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms
containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally
replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

20 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

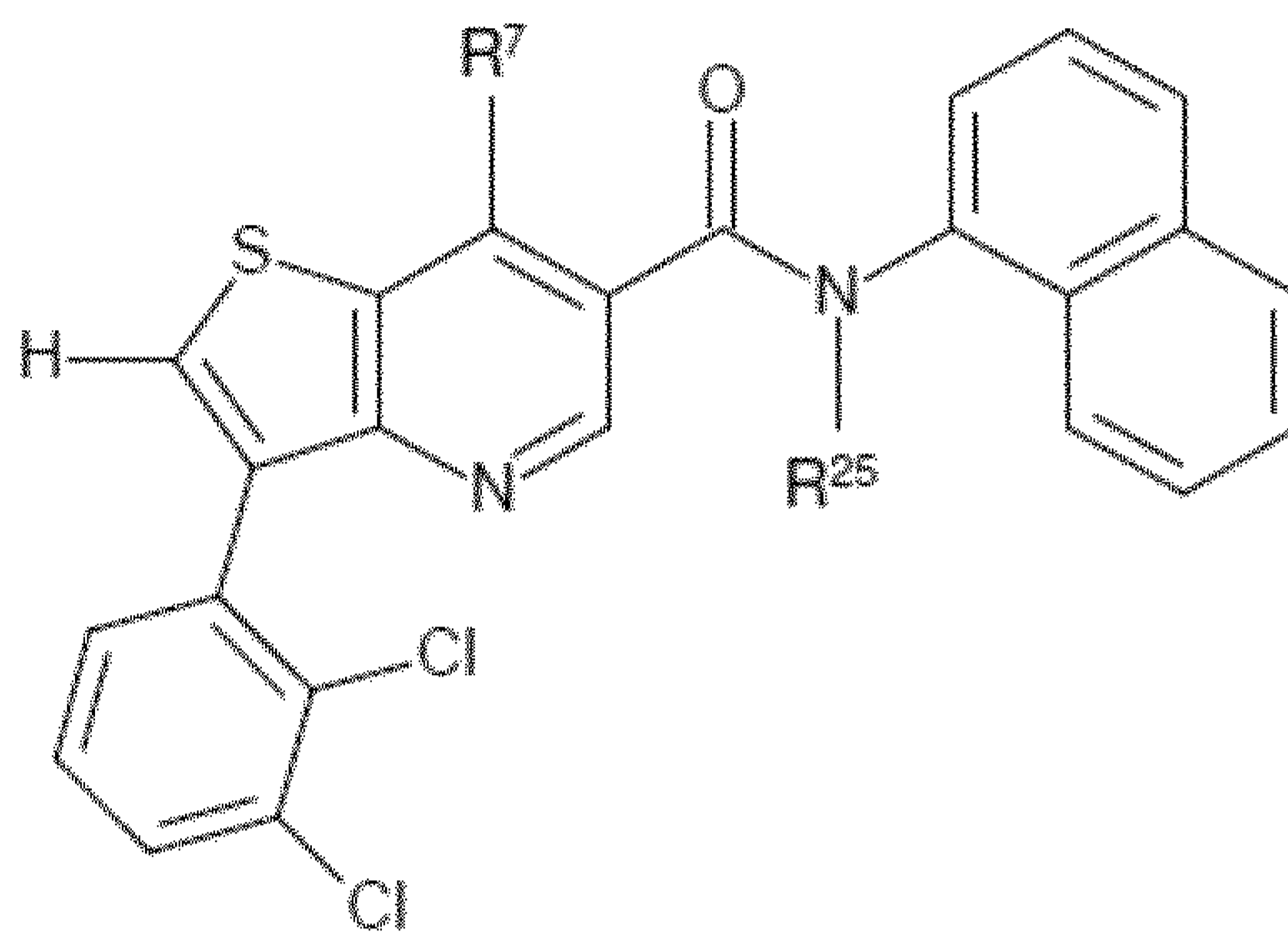
wherein none, one or two of A1, A2, A3 and A4 are N,

and

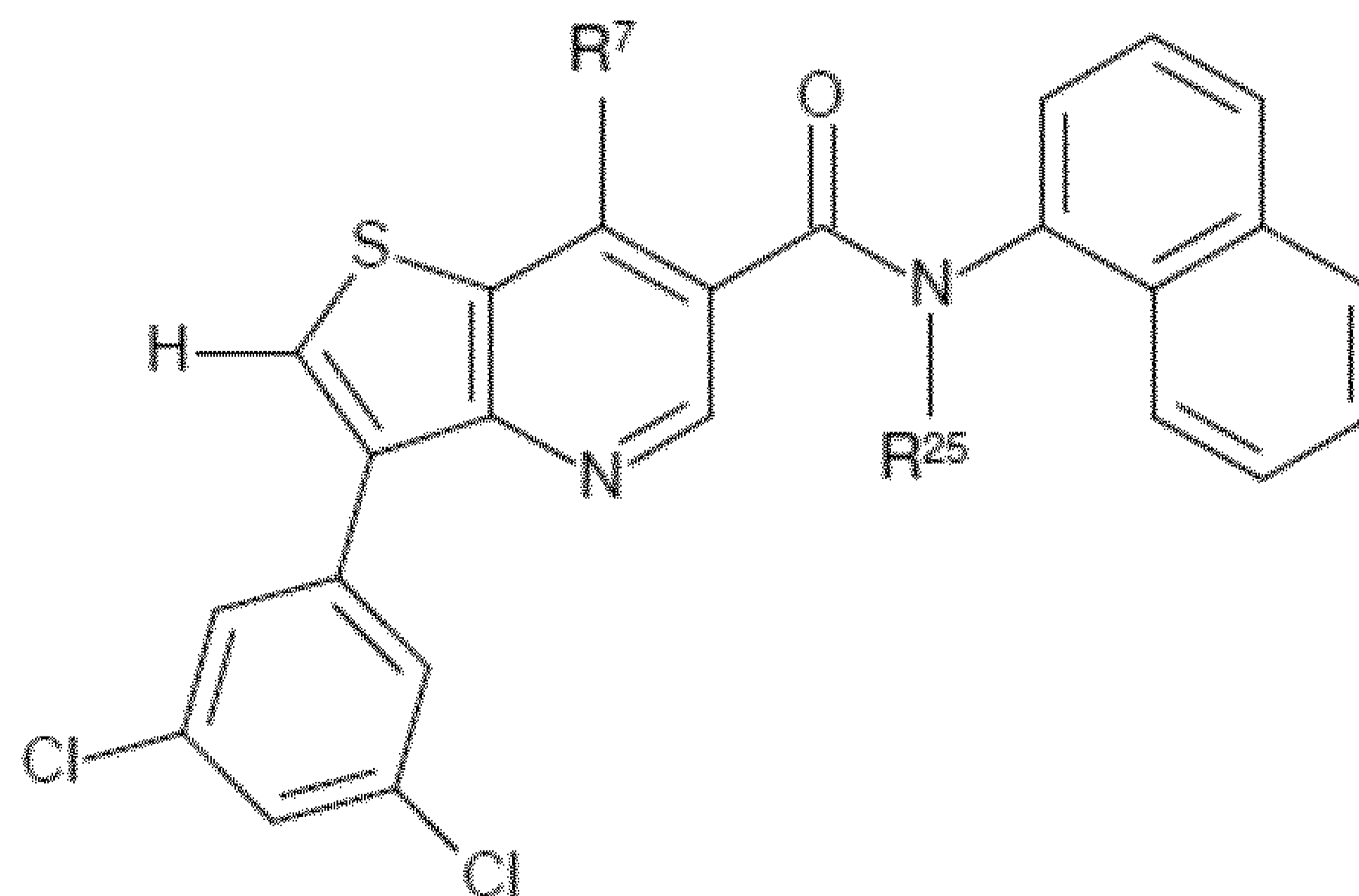
R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl,
25 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-
trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-
trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-
fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-

flurorophenyl, 3-chlorophenyl, 2,3-difluorophenyl 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

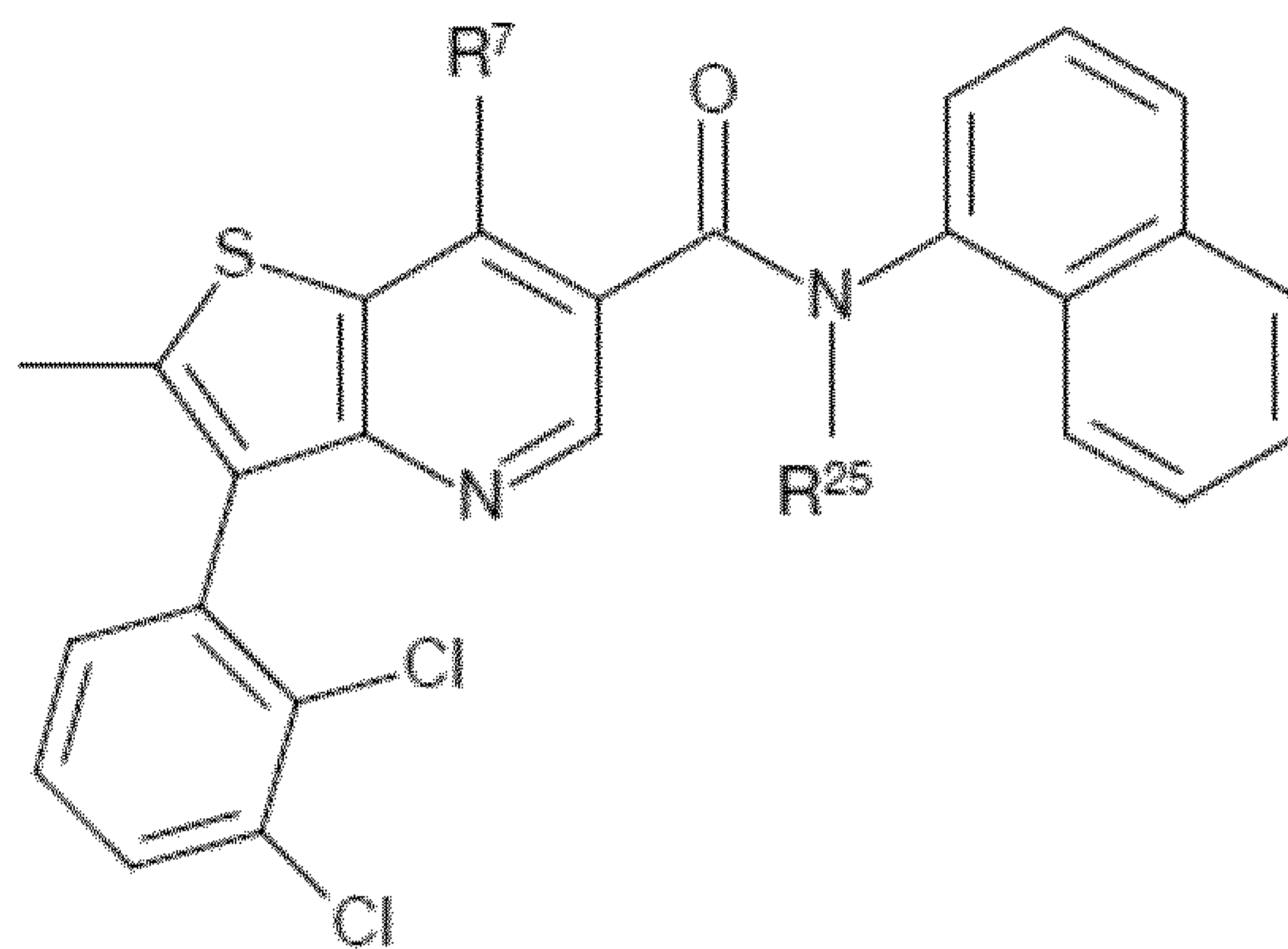
In an embodiment of the invention and/or embodiments thereof, the compounds are according to
 10 Formula (Isxiii), (Ixiv), (Isxv), (Isxvi), (Isxvii), (Isxviii), (Isxix) or (Isxx)



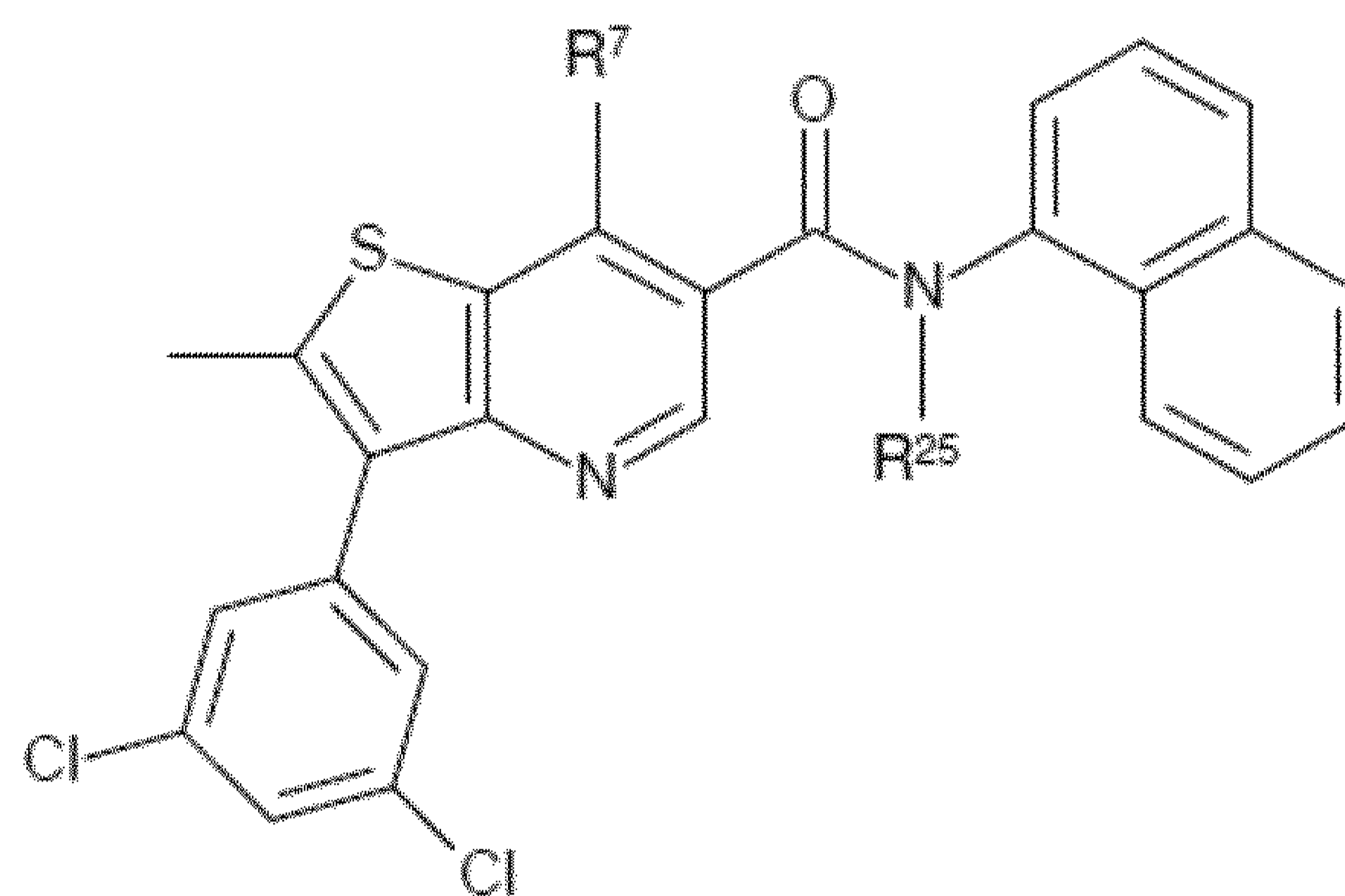
Formula (Isxiii)



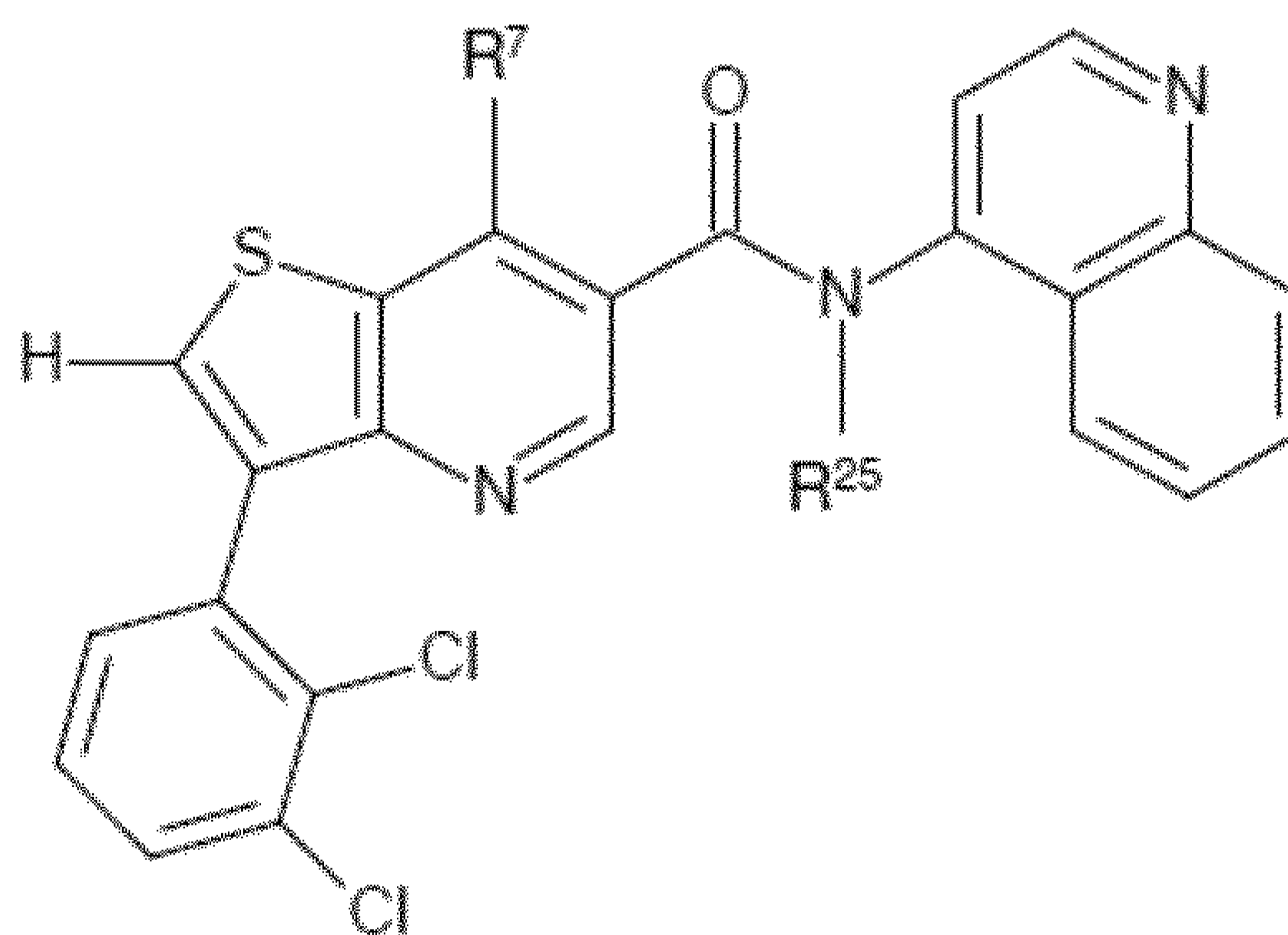
Formula (Isxiv)



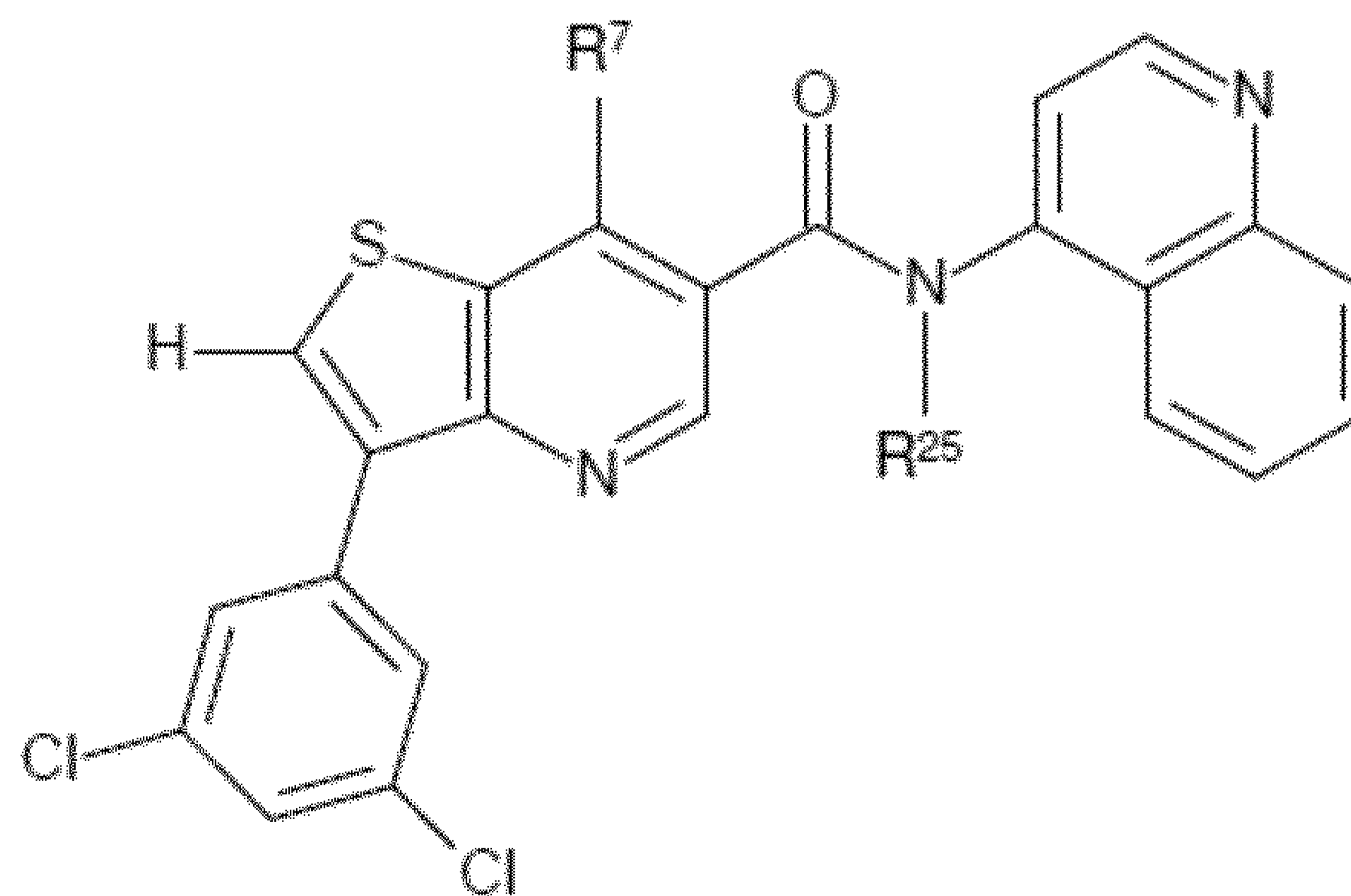
Formula (Isxv)



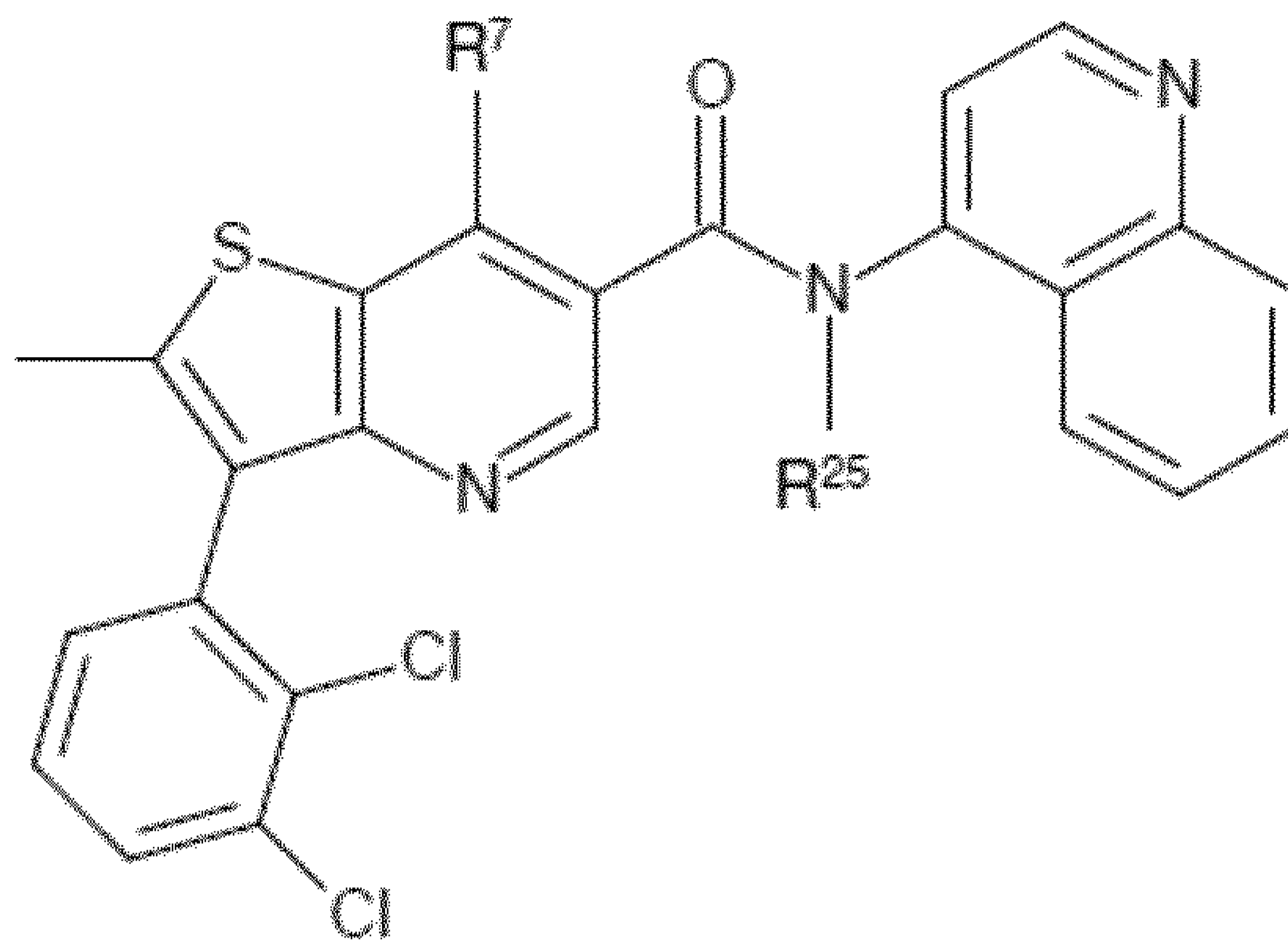
Formula (Isxvi)



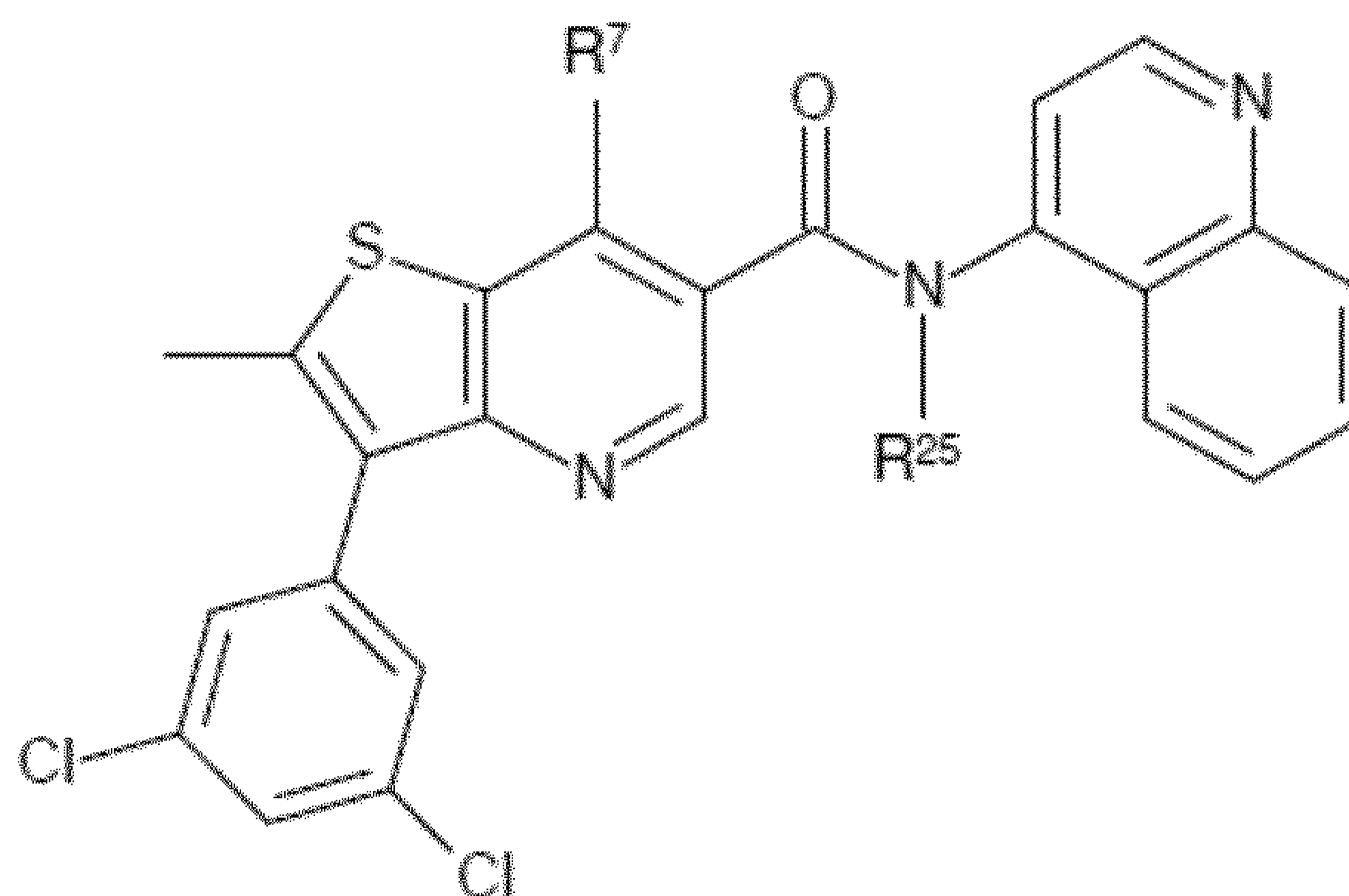
Formula (Isxvii)



Formula (Isxviii)



Formula (Isxix)



Formula (Isxx)

5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 and R^{25} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Isxx), preferably in the form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^1 , R^{13} , R^{14} , A1, A2, A3, A4 and R^{25} are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

- 5 hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

- 10 R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

- 15 wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{1-6} -alkoxy,

- 20 R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

and

- 25 R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

5 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

and

10 R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

15 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl,

and

20 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

25 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R^{25} is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof

R^1 is independently selected from the group consisting of

5 hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH- or -O-,

10 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen or C_{1-3} alkoxy,

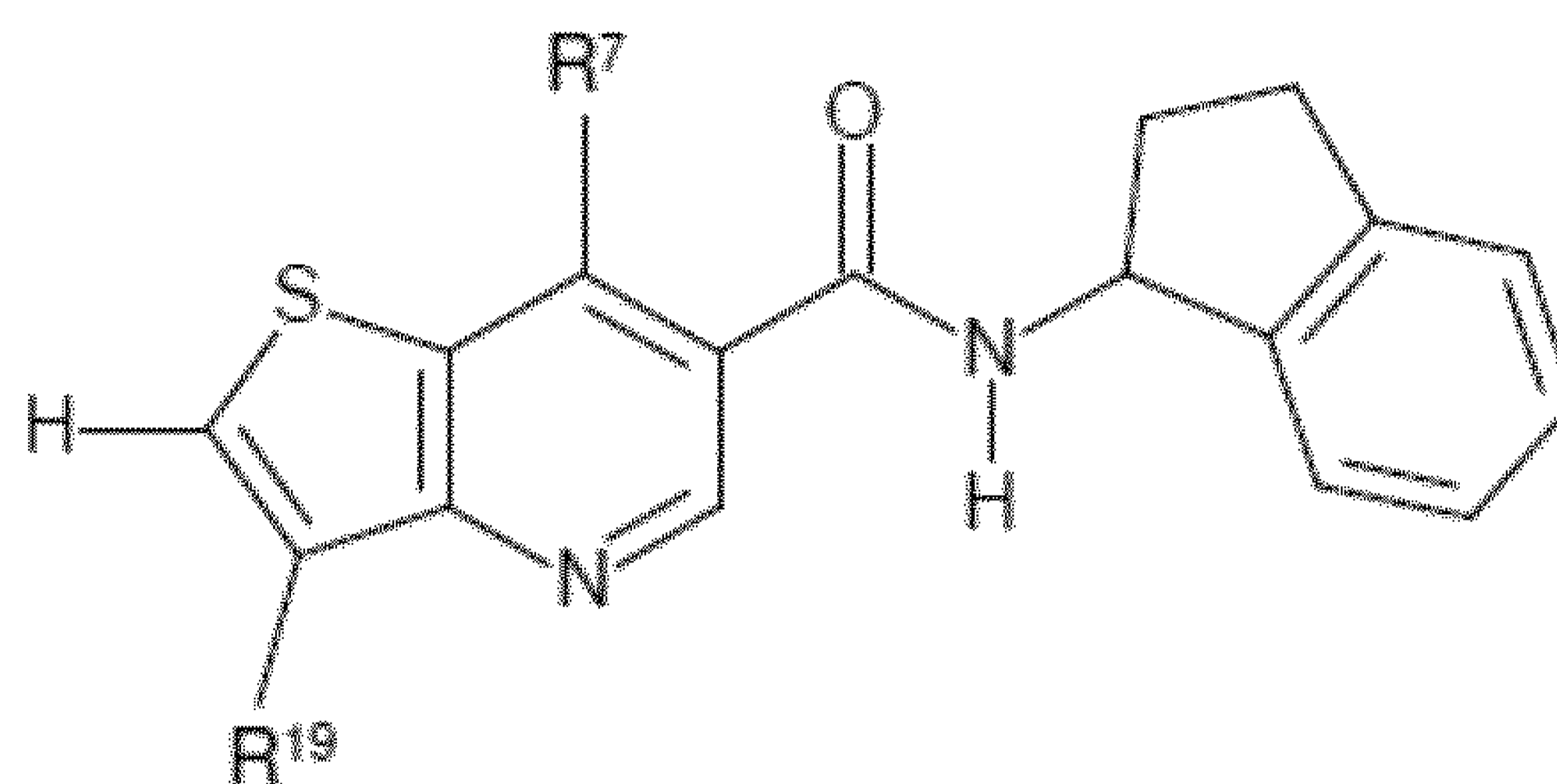
A4 is N or CR^{18} , wherein R^{18} is independently hydrogen or C_{1-3} alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

15 and

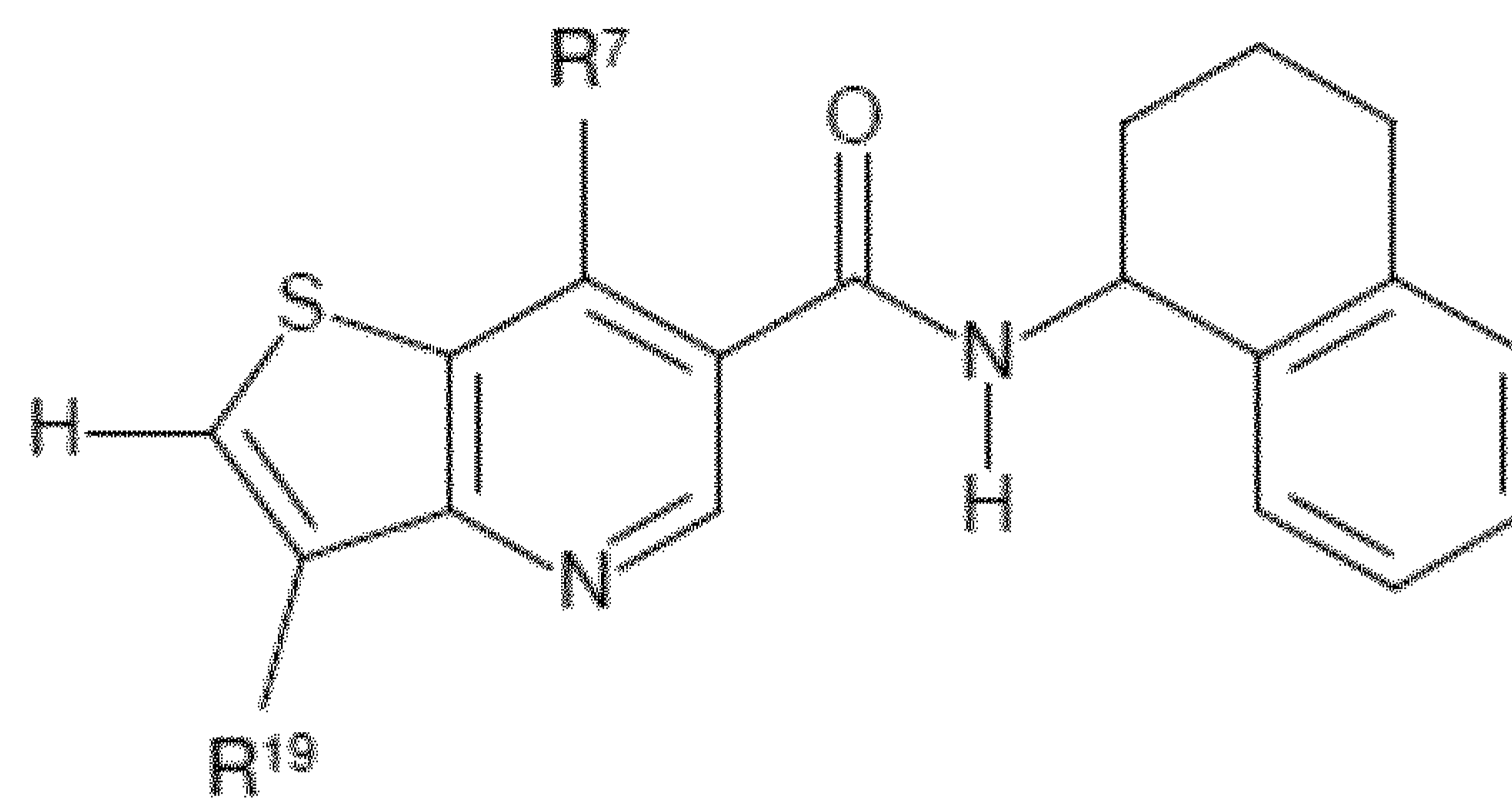
R^{25} is hydrogen or methyl, more preferably hydrogen.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iti), (Itii), (Itiii), (Itiv), (Itv), (Itvi), (Itvii), (Itviii), (Itix), (Itx), (Itxi) or (Itxii)

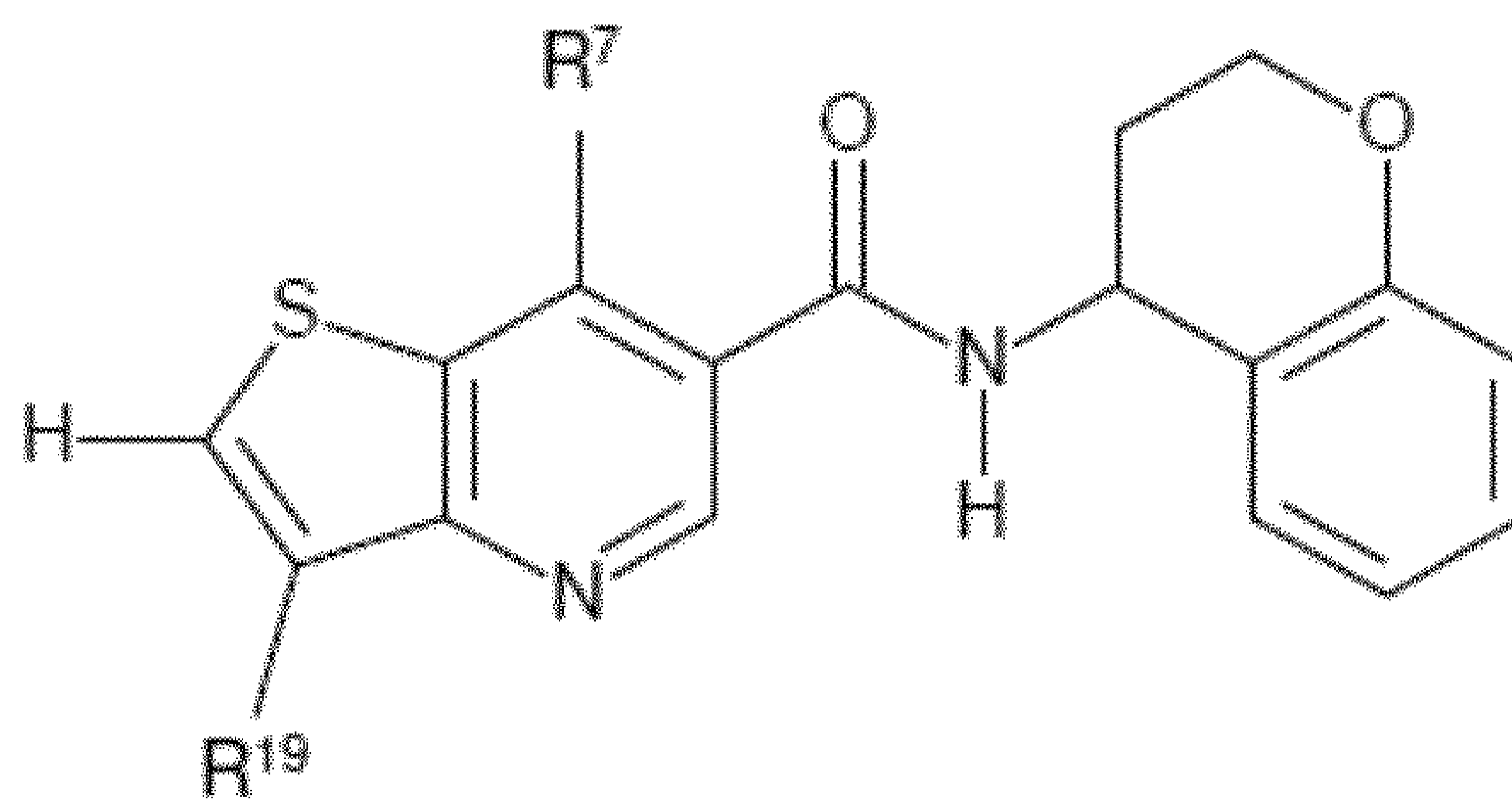


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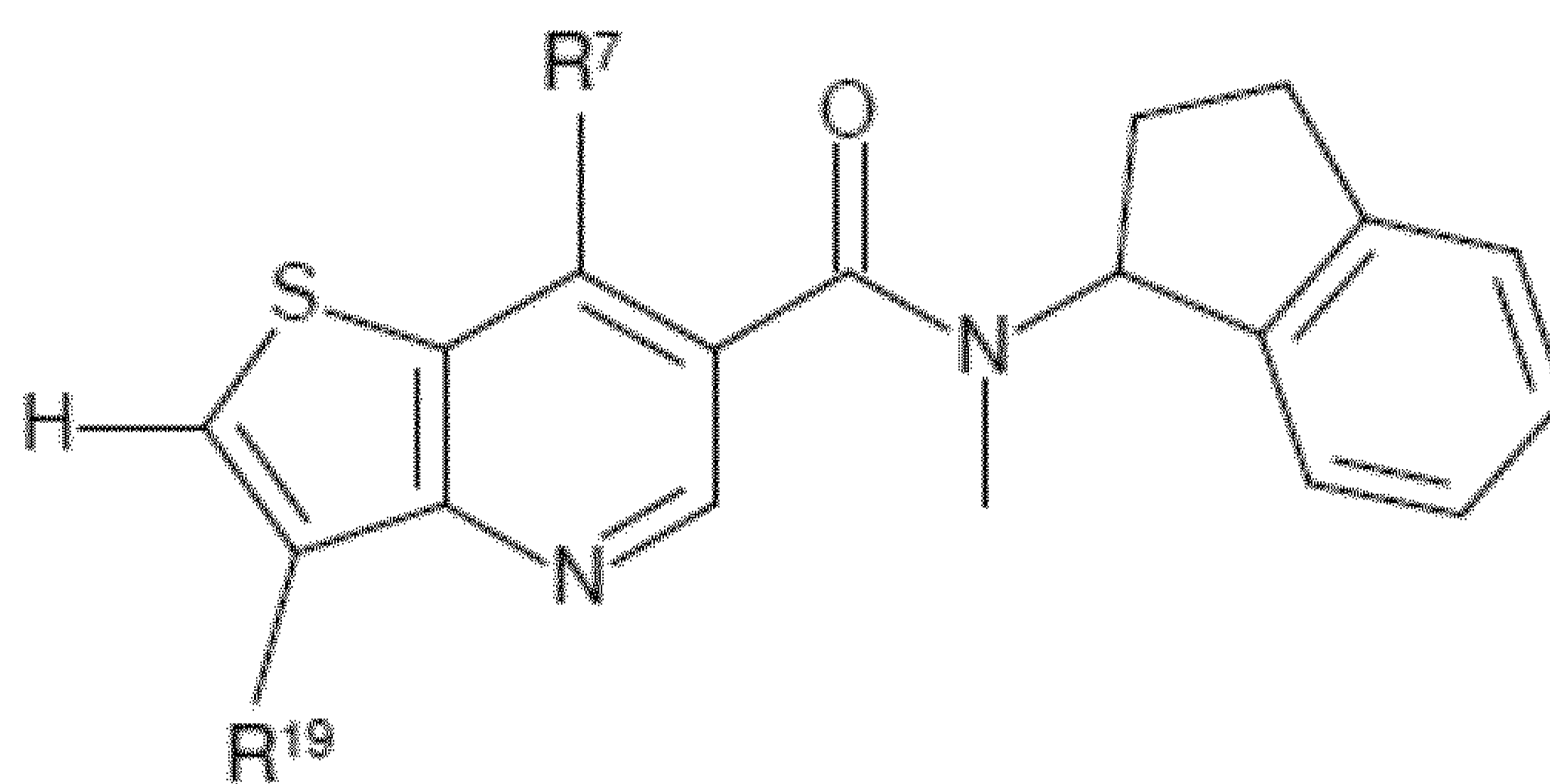
Formula (Iti)



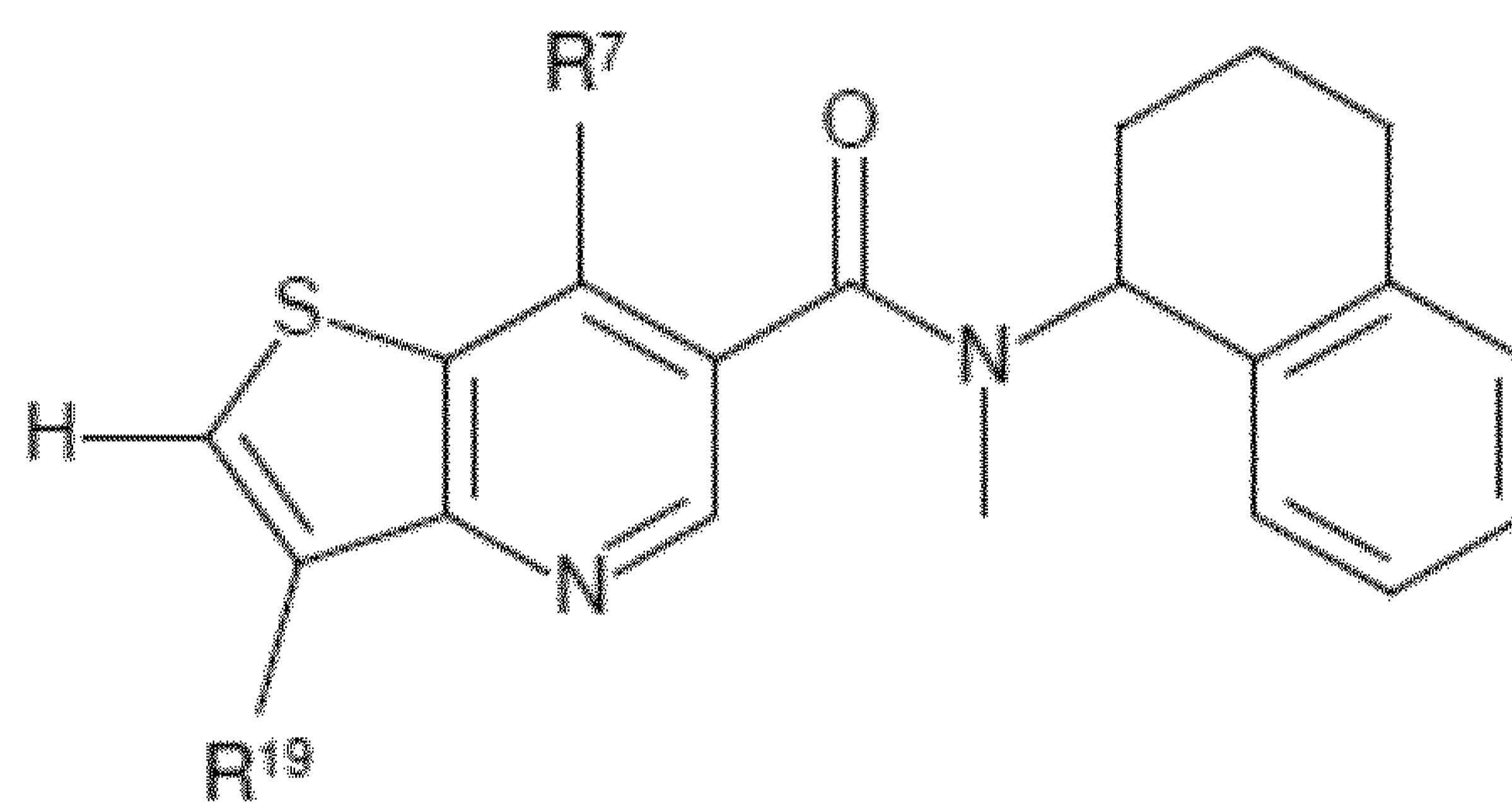
Formula (Itii)



Formula (Itiii)

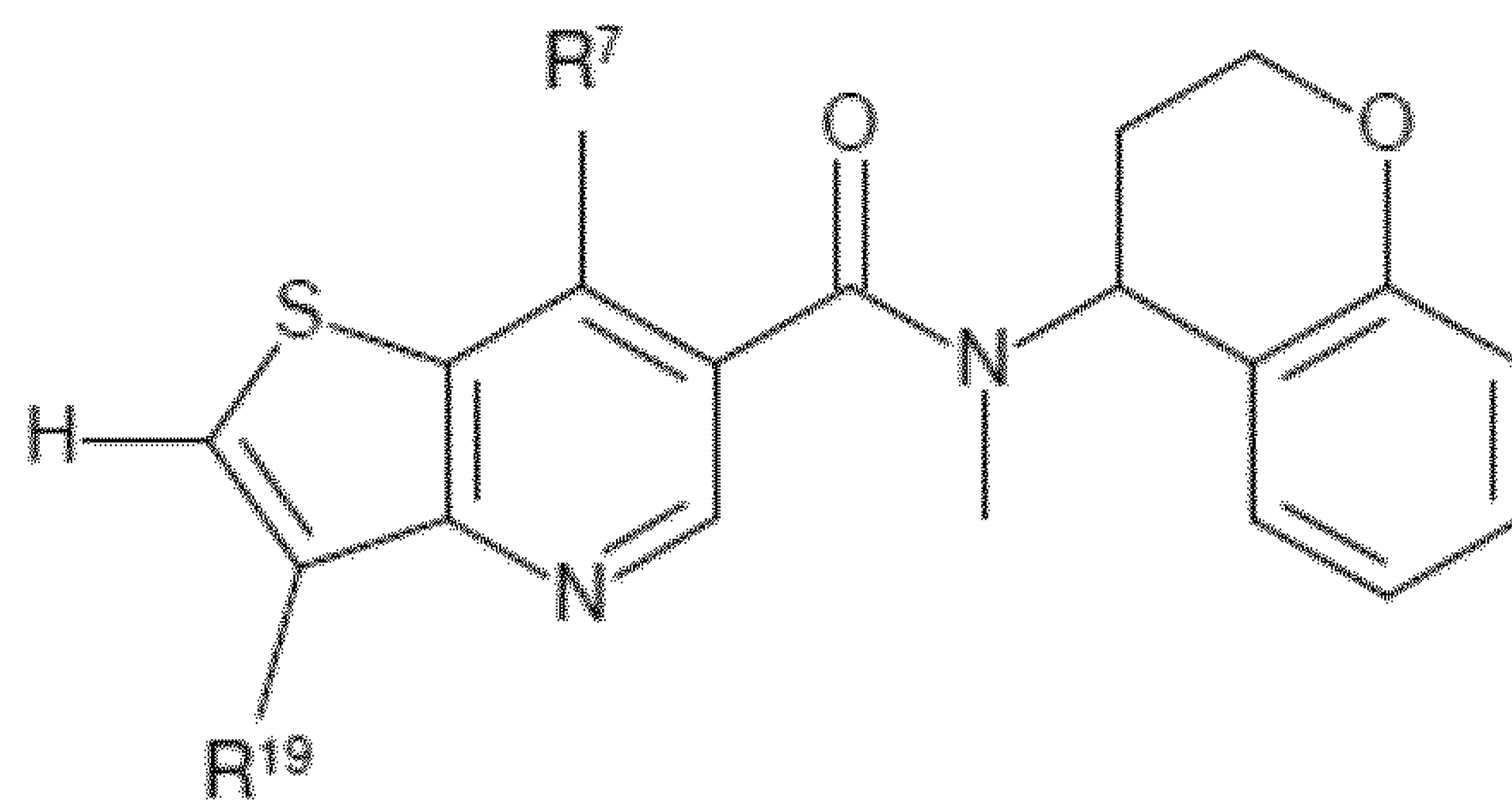


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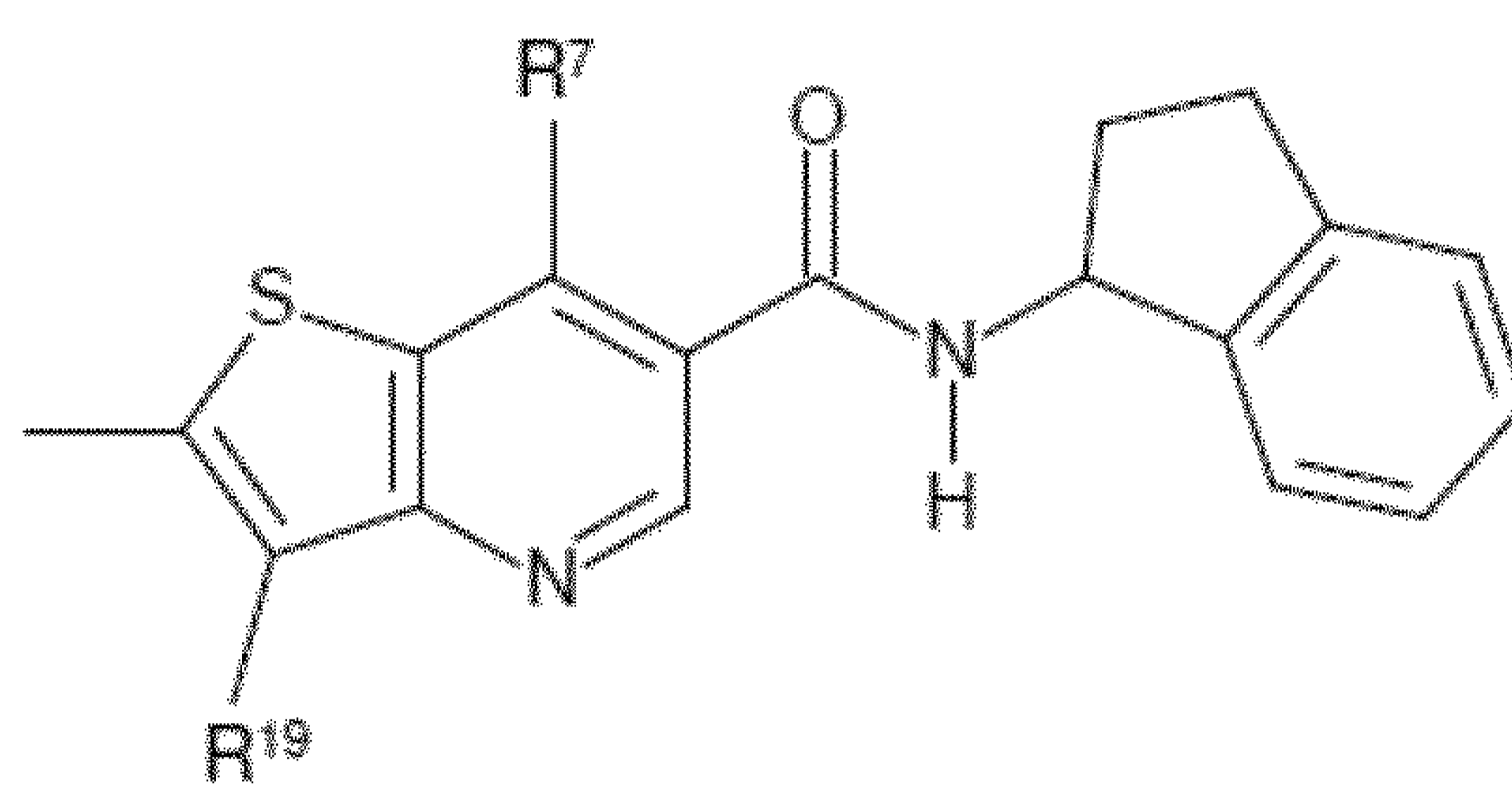


Formula (Itv)

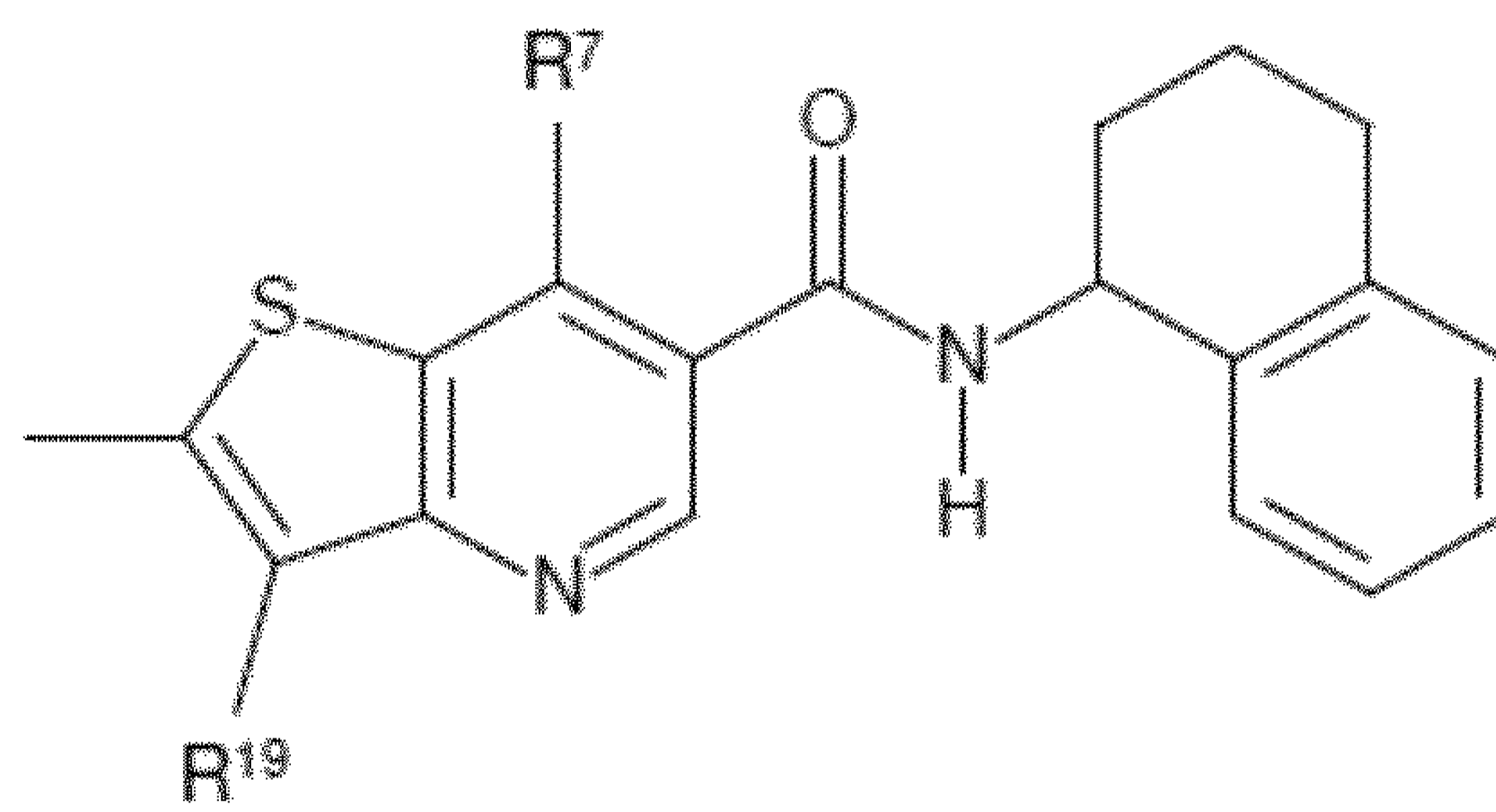
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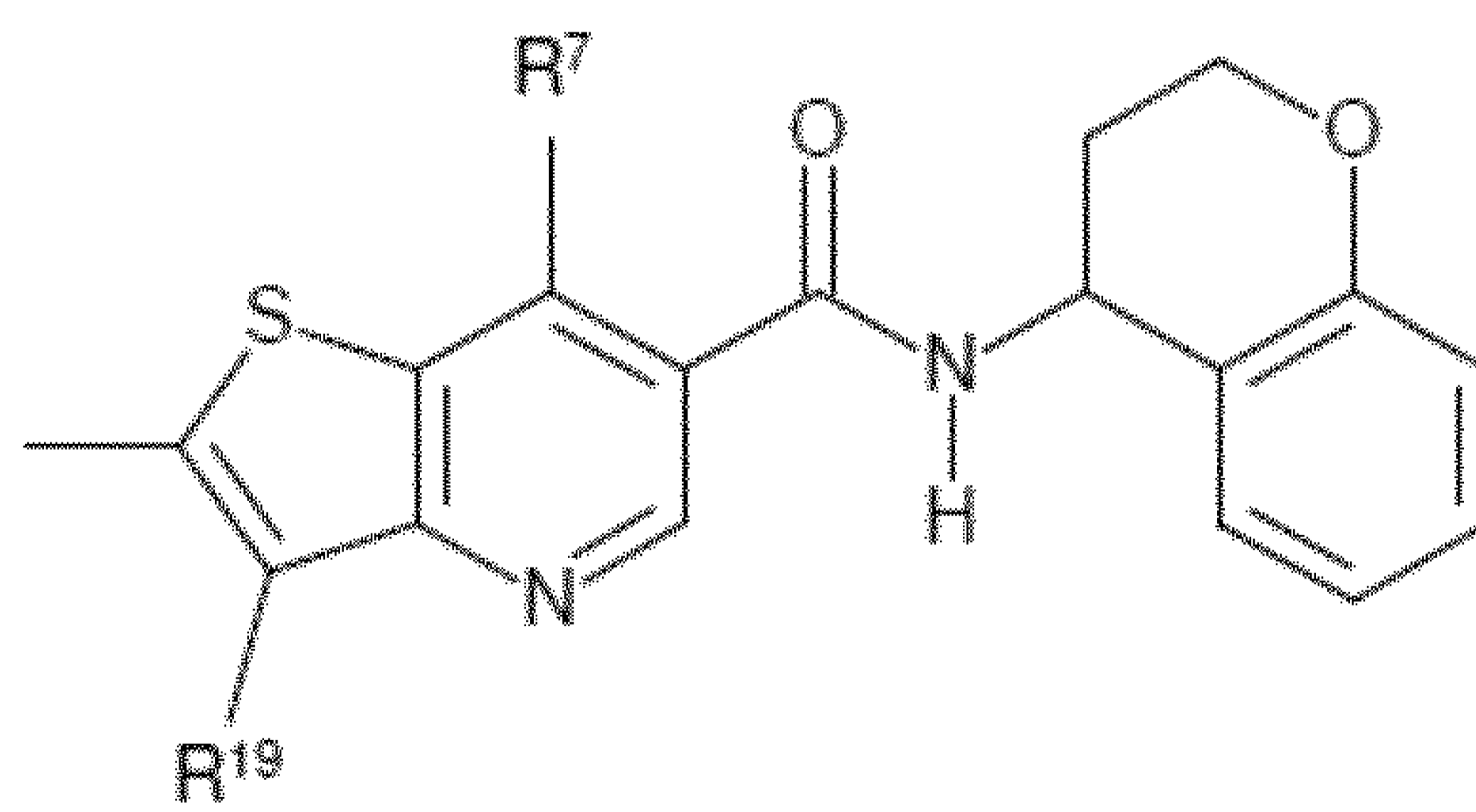
Formula (Itvi)



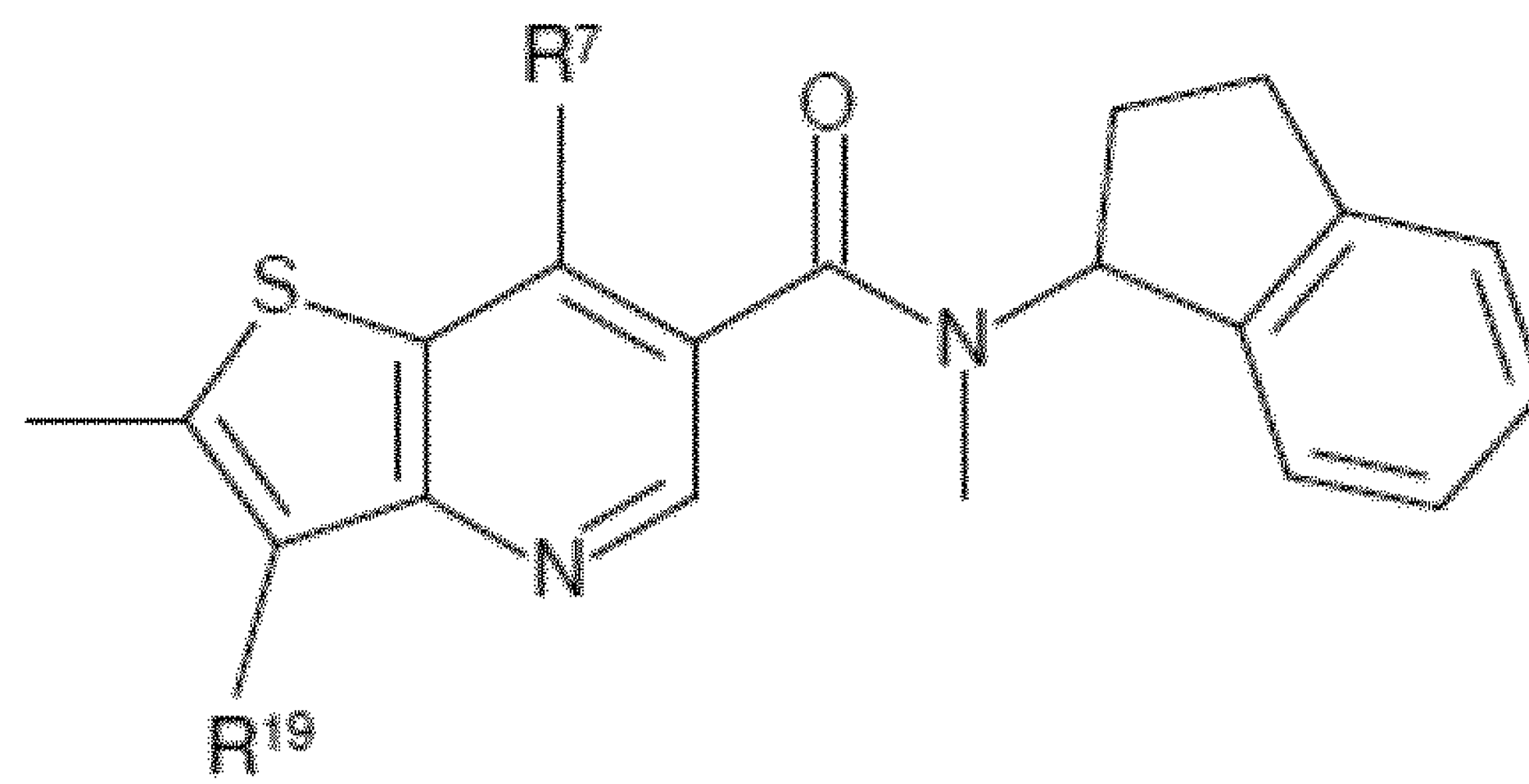
Formula (Itvii)



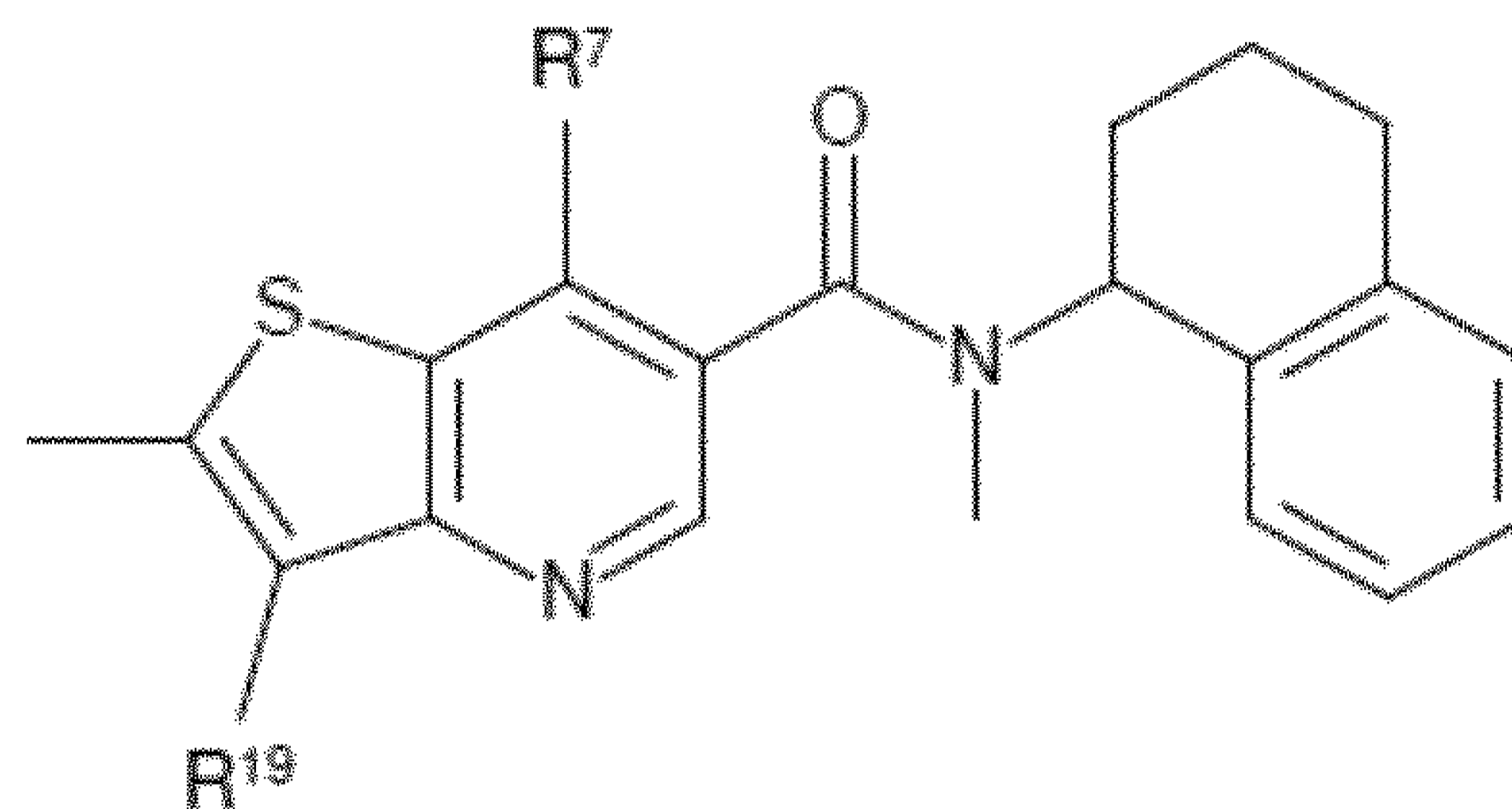
Formula (Itviii)



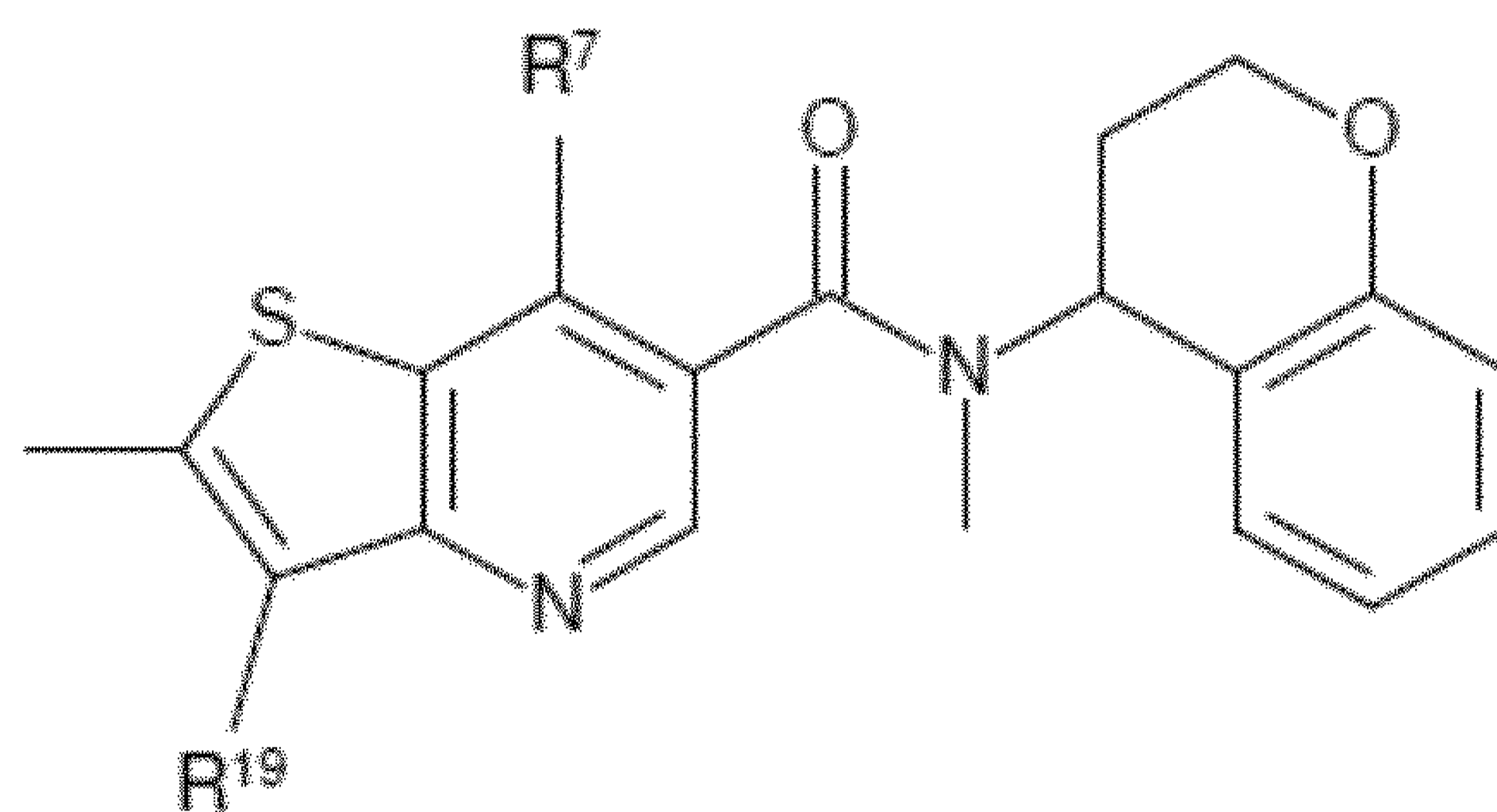
Formula (Itix)



Formula (Itx)



Formula (Itxi)



Formula (Itxii)

5

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 and R^{19} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to
 10 Formula (Iti), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itiii), preferably in the form of the (*S*)-enantiomer. In an
 15 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itvi), preferably in the form of the (*S*)-enantiomer. In an
 20 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention

and/or embodiments thereof, the compounds are according to Formula (Itviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to
5 Formula (Itx), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxii), preferably in the form of the (*S*)-enantiomer.

Optionally, in an embodiment of the invention and/or embodiments thereof,

10 R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

15 C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl and 5 to 10-membered heteroaryl, or

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3
20 further ring atoms are selected from N, S and O;

wherein each C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{1-6} -alkoxy,

R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-6} -alkyl, preferably from hydrogen and C_{1-3} -alkyl,

and

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C_{1-3} -alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
5 by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

10 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

15 R^{25} is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro and $C(=O)NR^5R^6$,

wherein each C_{1-6} -alkyl or C_{1-6} -alkoxy is optionally substituted with one or more
20 substituents independently selected from the group consisting of

C_{1-6} -alkyl, C_{1-6} -alkoxy, halogen, cyano, nitro, hydroxy and $NR^{2'}R^{3'}$,

R^5 and R^6 are independently selected from hydrogen and C_{1-3} -alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C_{1-3} -alkyl,

and

25 R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

5 and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

10 and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

15 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

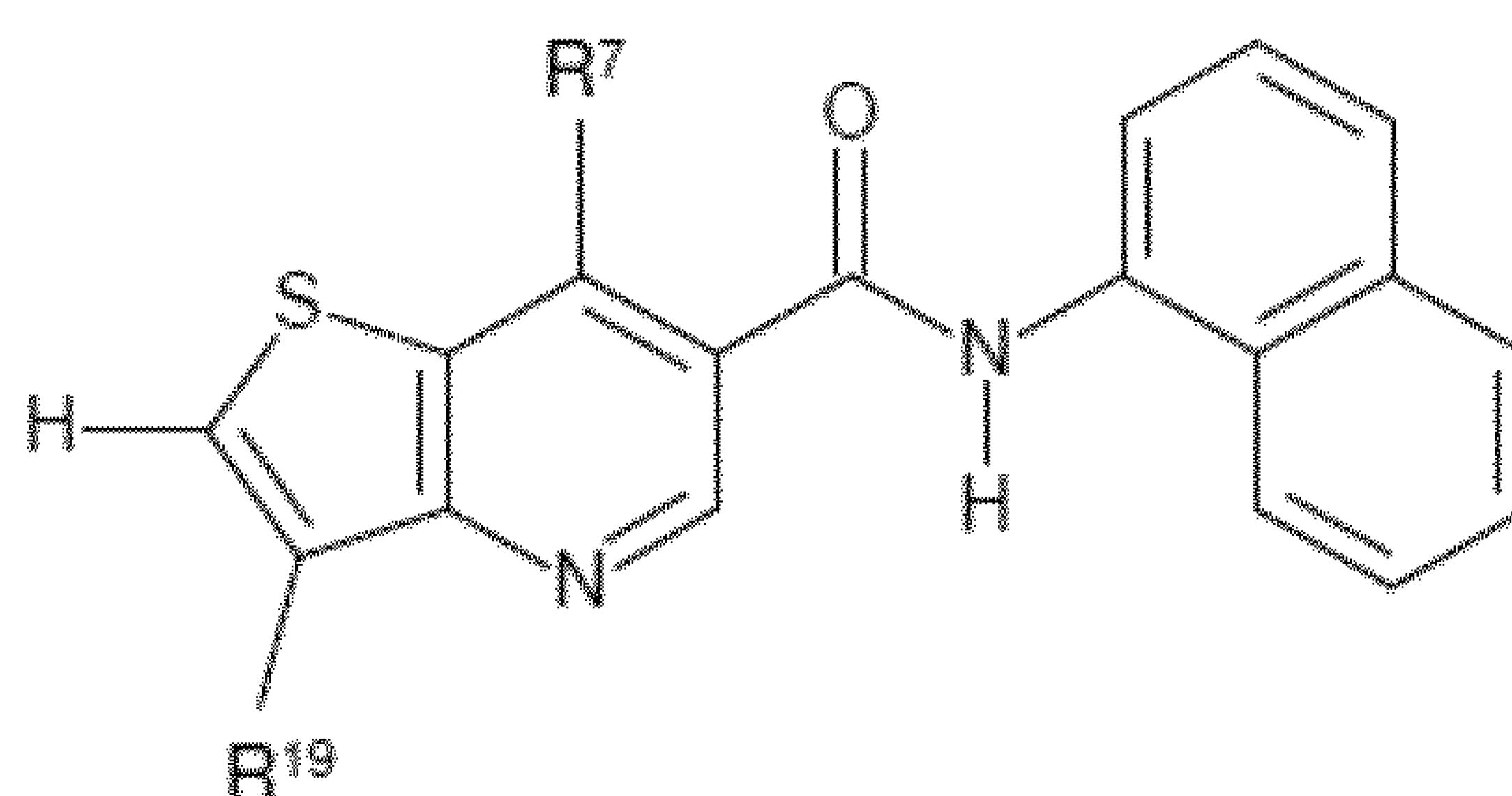
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

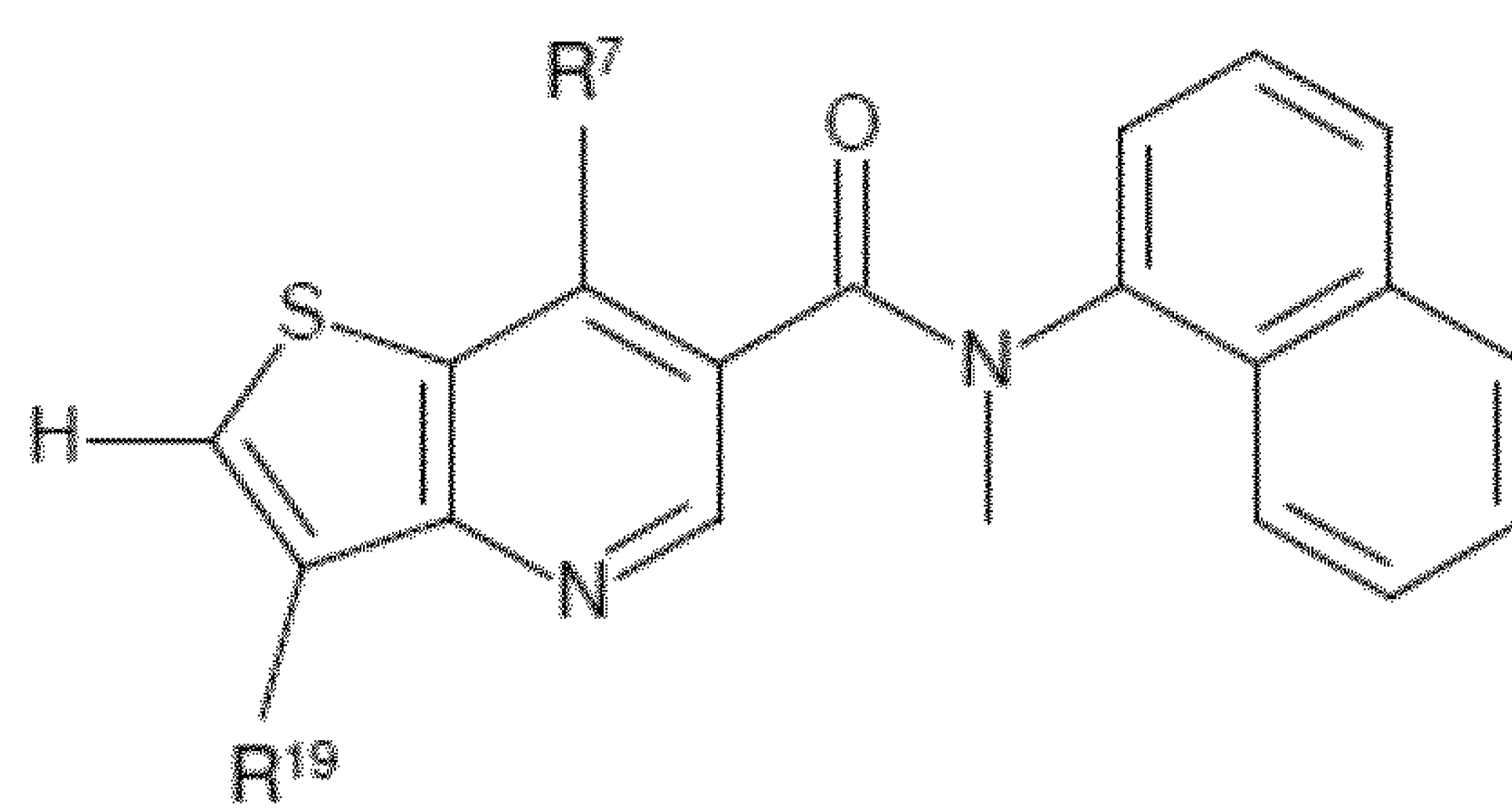
and

20 R²⁵ is hydrogen or methyl, more preferably hydrogen.

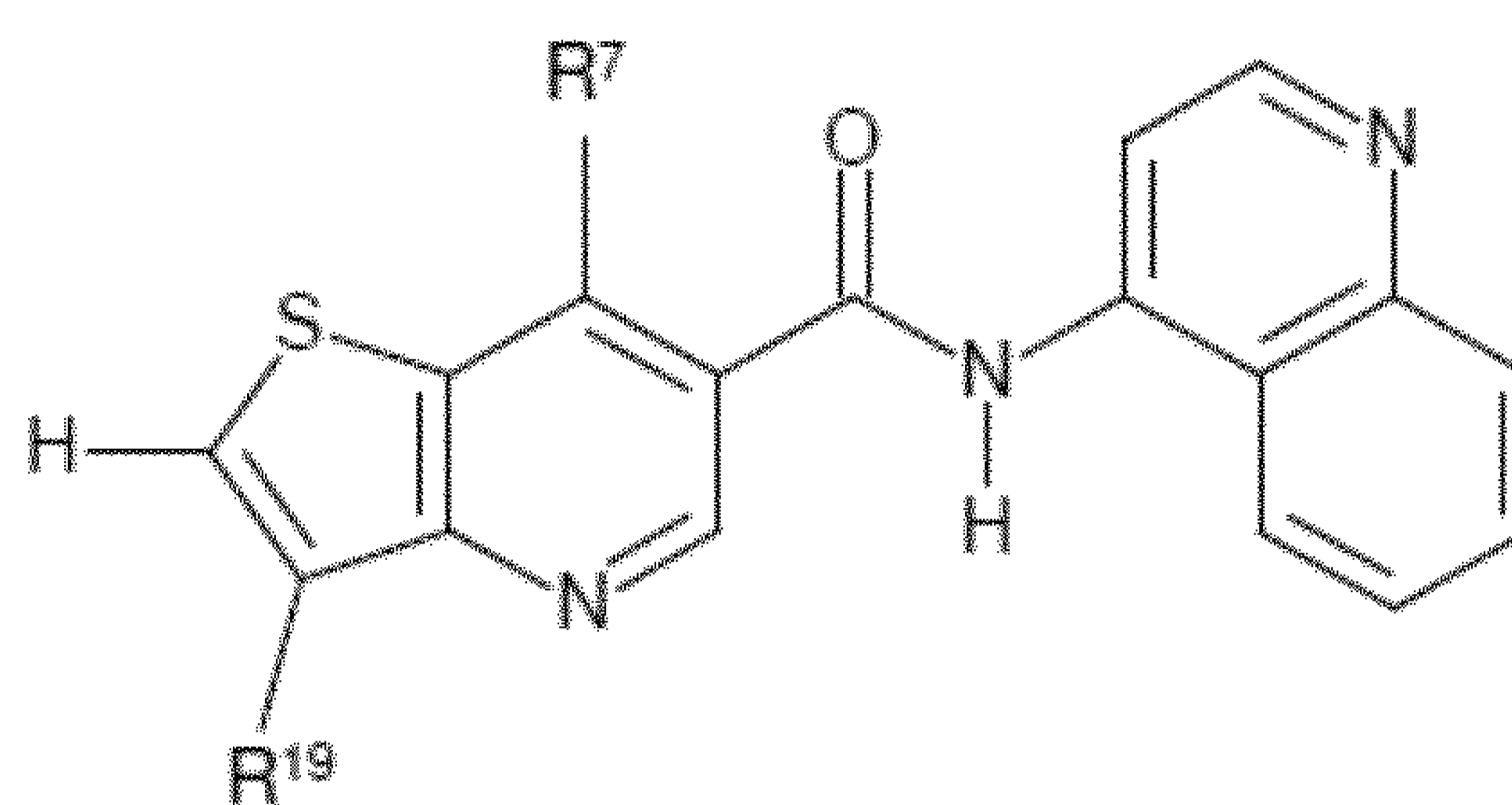
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxiii), (Itxiiii), (Itxv), (Itxvi), (Itxvii), (Itxviii), (Itxix) or (Itxx)



Formula (Ixxiii)

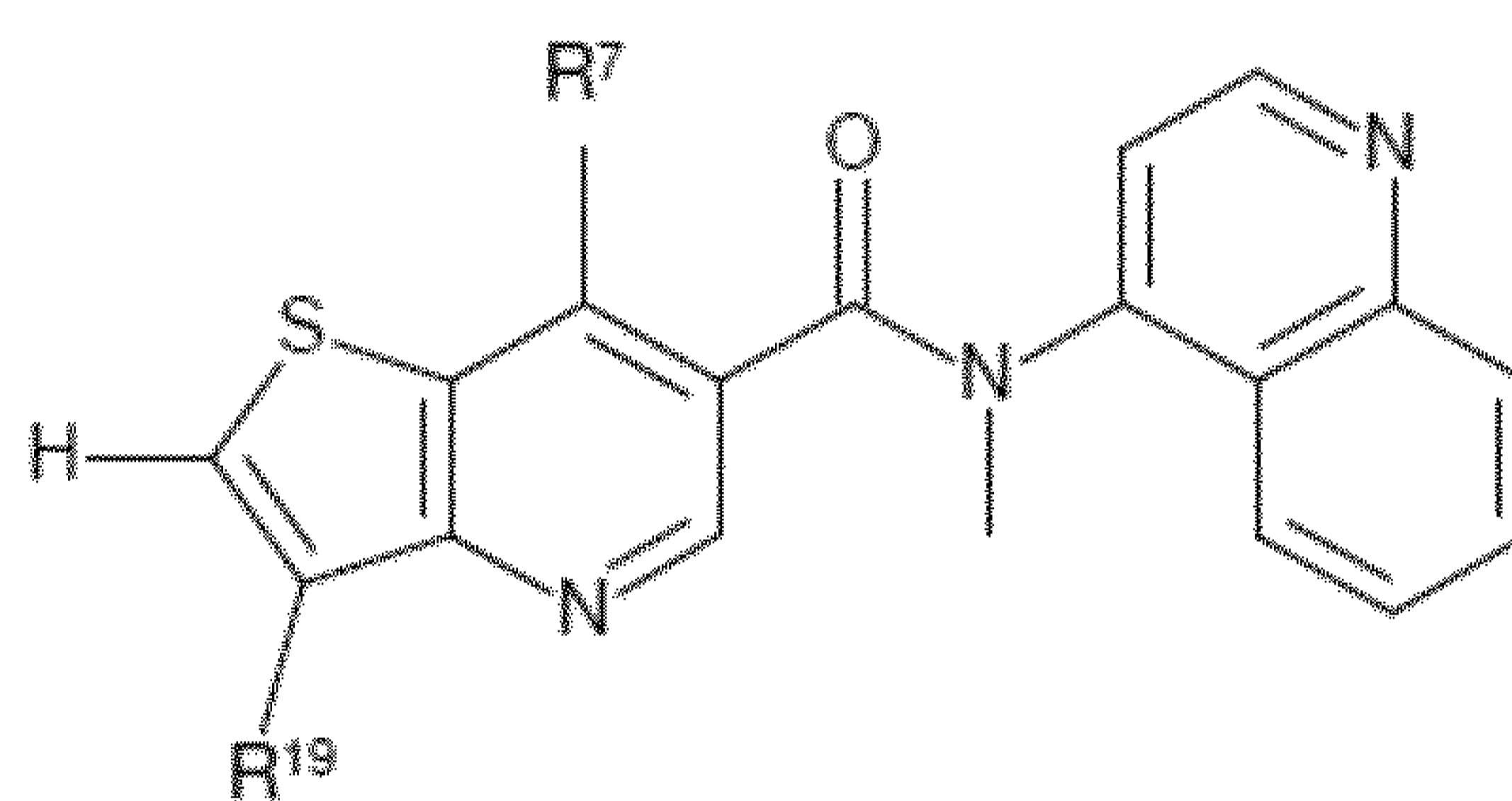


Formula (Ixxiv)

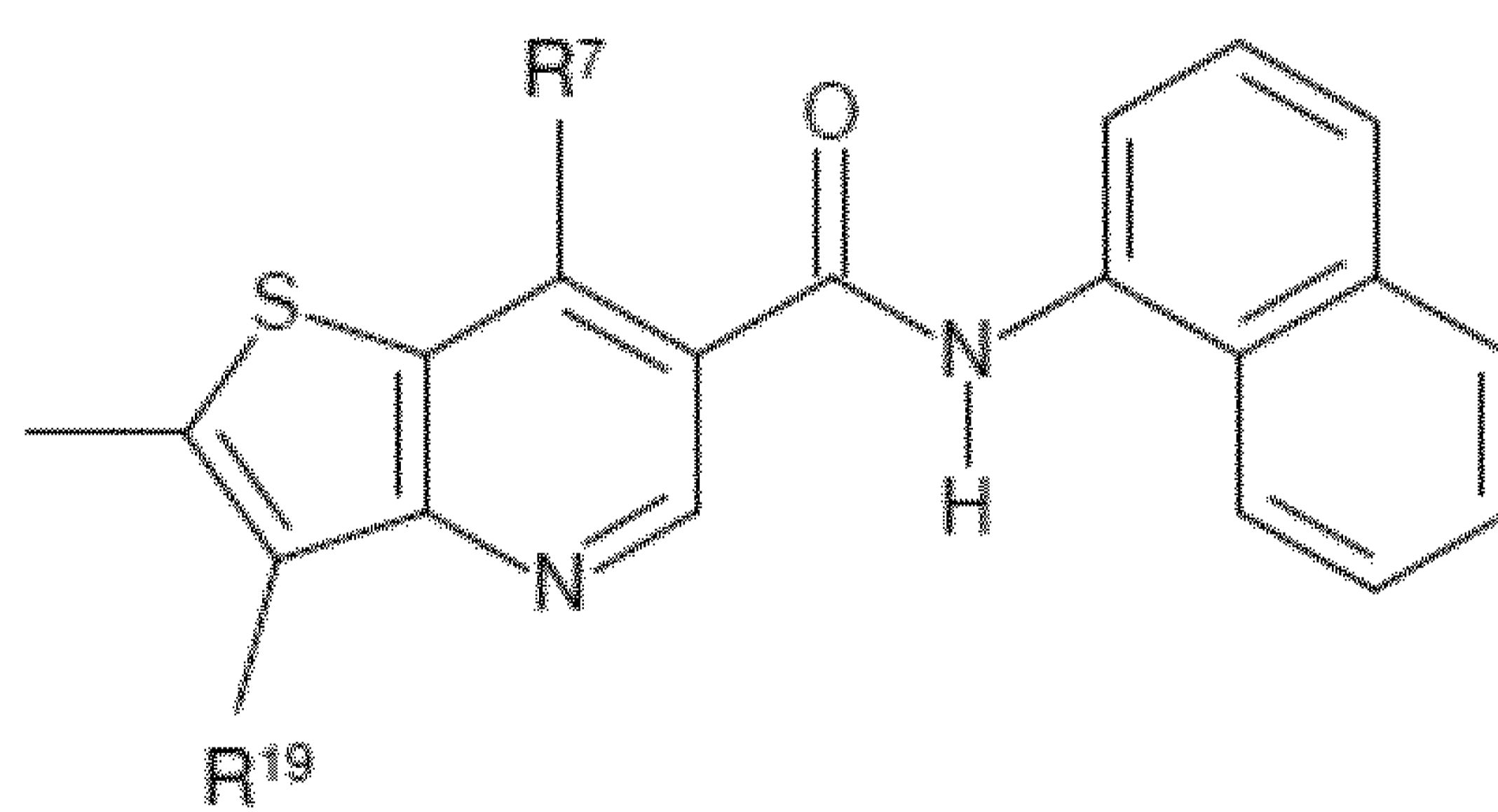


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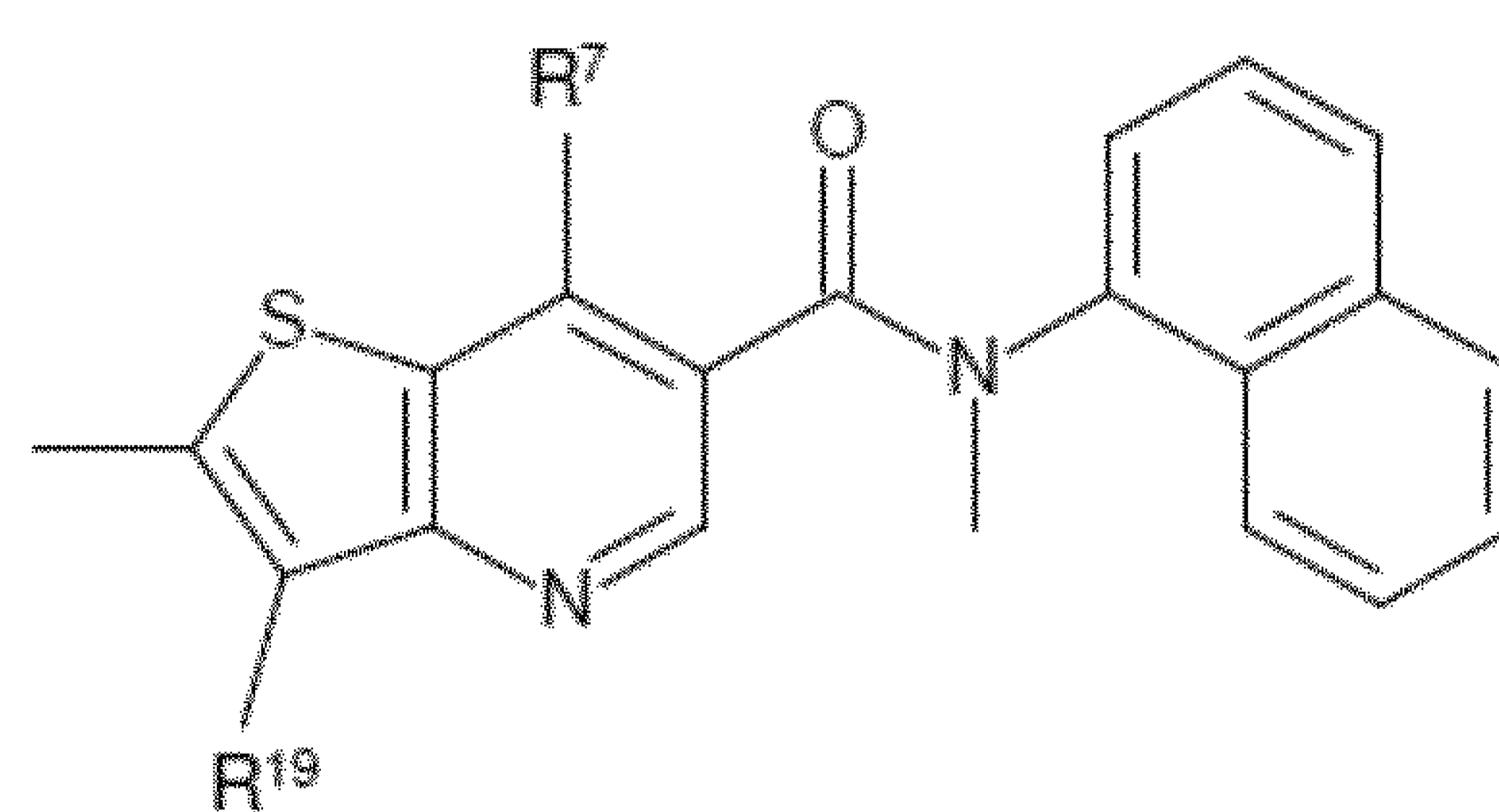
Formula (Ixxv)



Formula (Ixxvi)

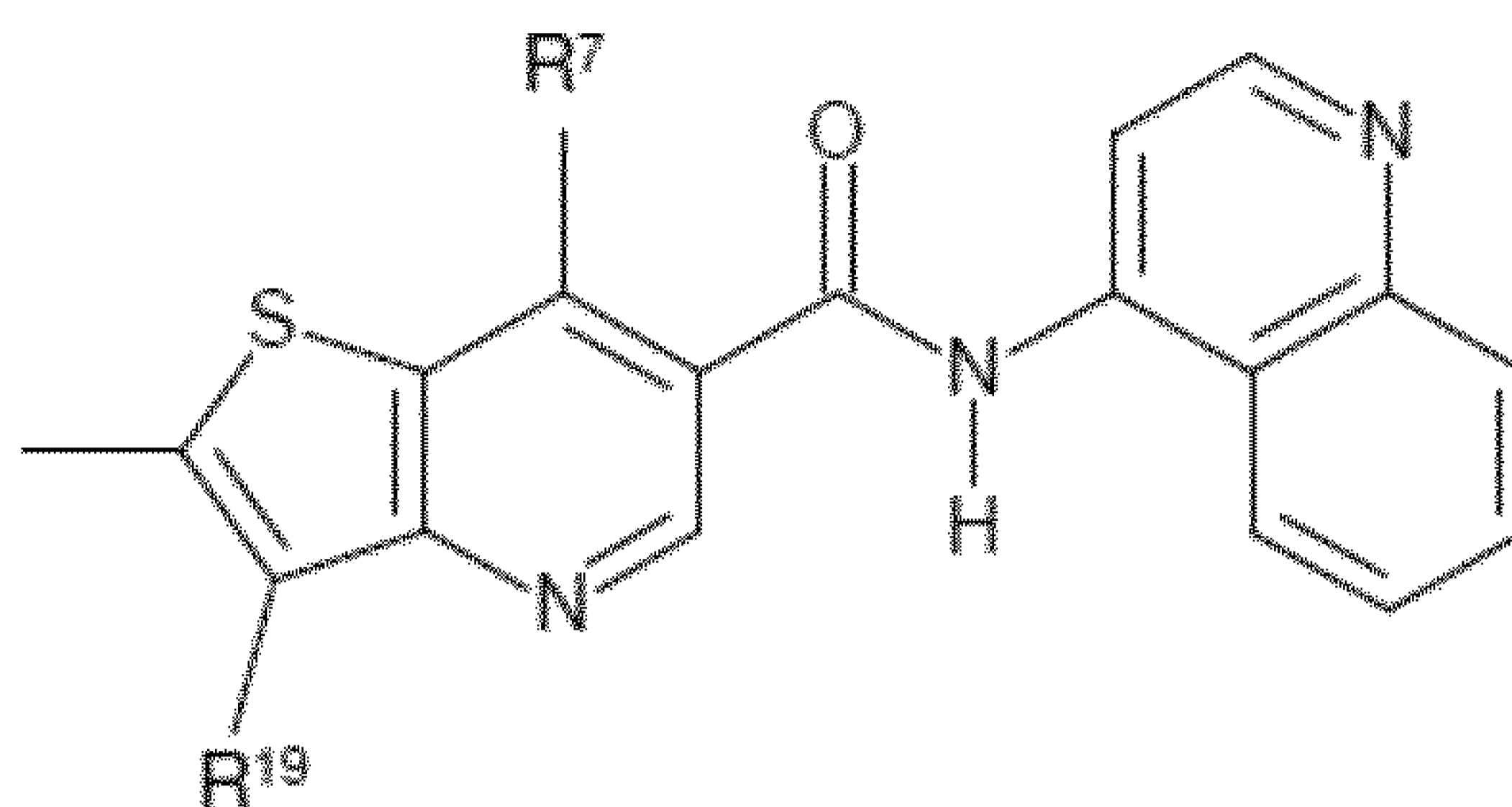


Formula (Ixxvii)

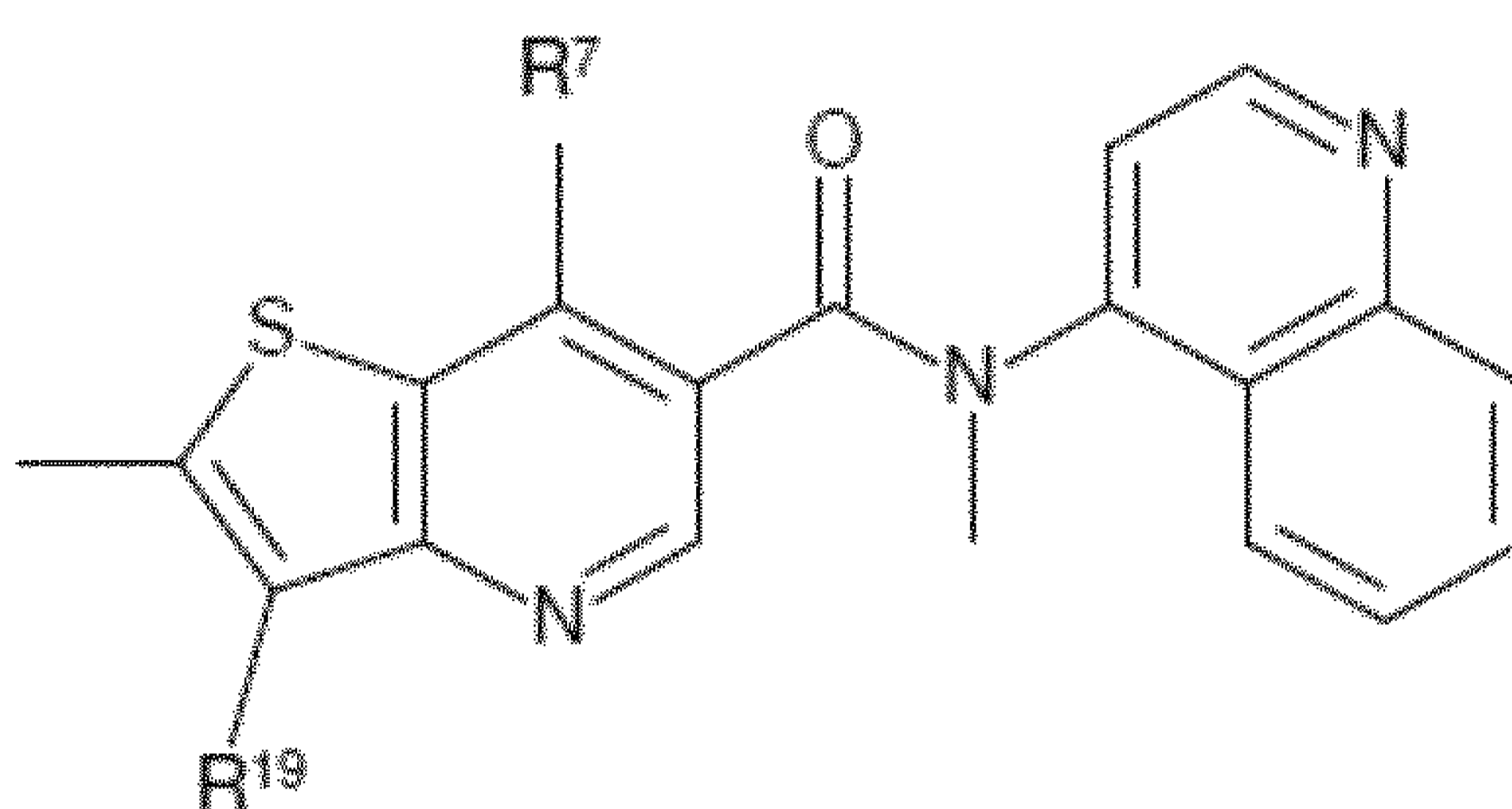


10

Formula (Itxviii)



Formula (Itxix)



5

Formula (Itxx)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R⁷ and R¹⁹ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Itxx), preferably in the form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R¹, R¹⁹ and R²⁵ are defined as below.

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²R³, C(=O)OR⁴ and C(=O)NR⁵R⁶,

5 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

10 R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O;

15 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

20 R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl, preferably from hydrogen and C₁₋₃-alkyl,

and

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

25 wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

10 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl,

and

15 R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and C(=O)NR⁵R⁶,

20 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R⁵ and R⁶ are independently selected from hydrogen and C₁₋₃-alkyl,

R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl,

and

25 R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen,

and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R¹ is independently selected from the group consisting of

hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride,

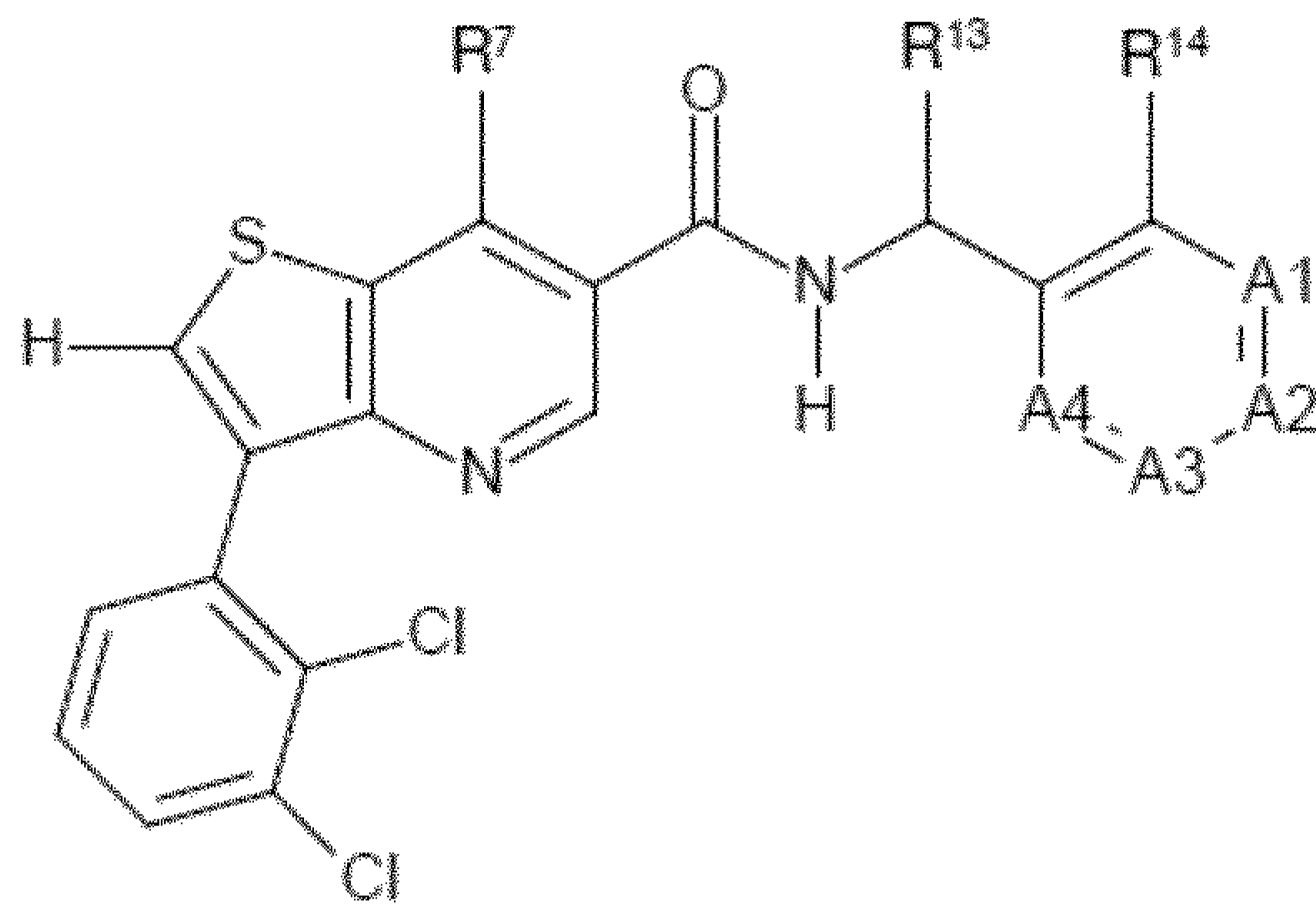
and

R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl,

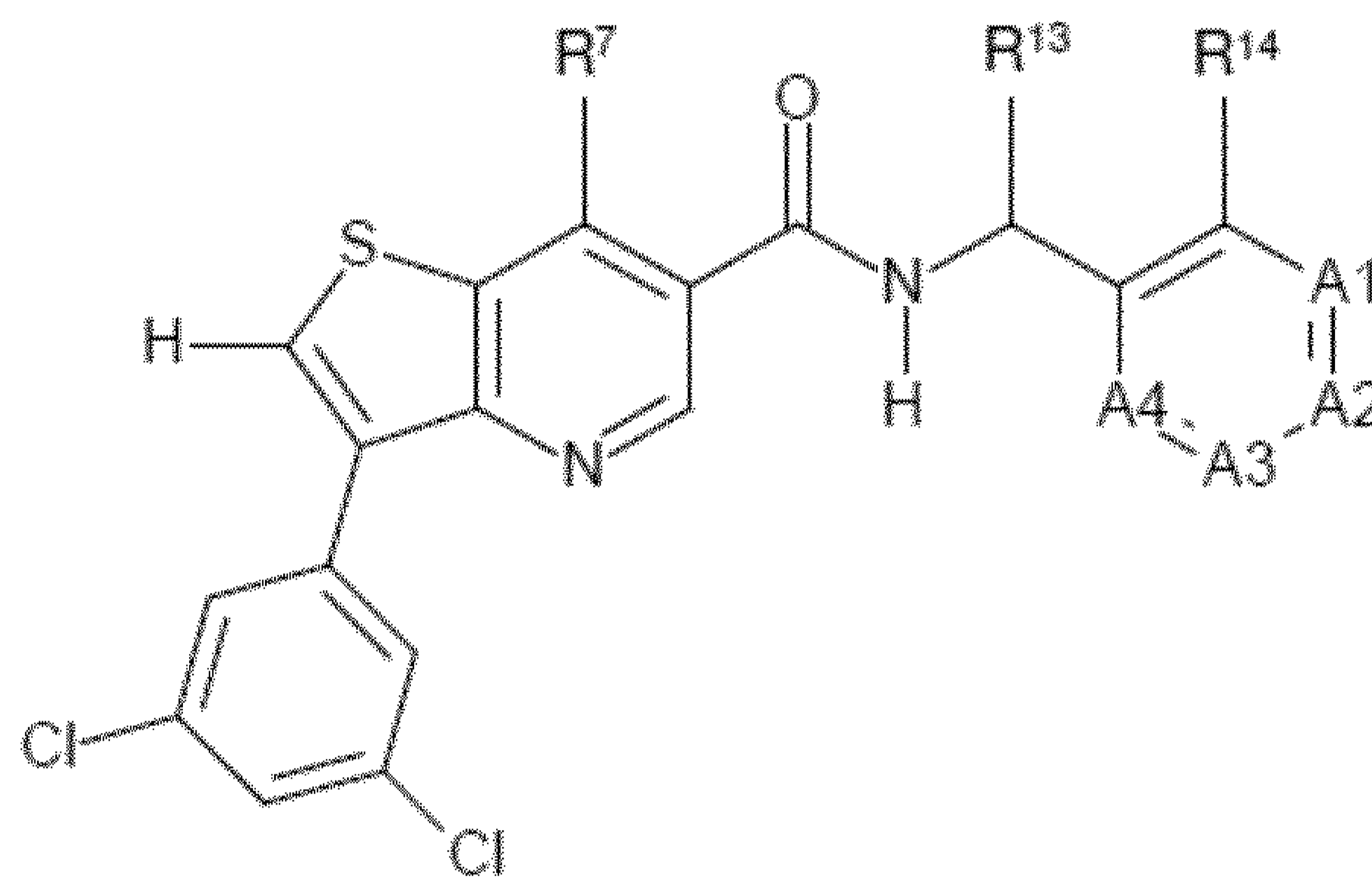
and

R²⁵ is hydrogen or methyl, more preferably hydrogen.

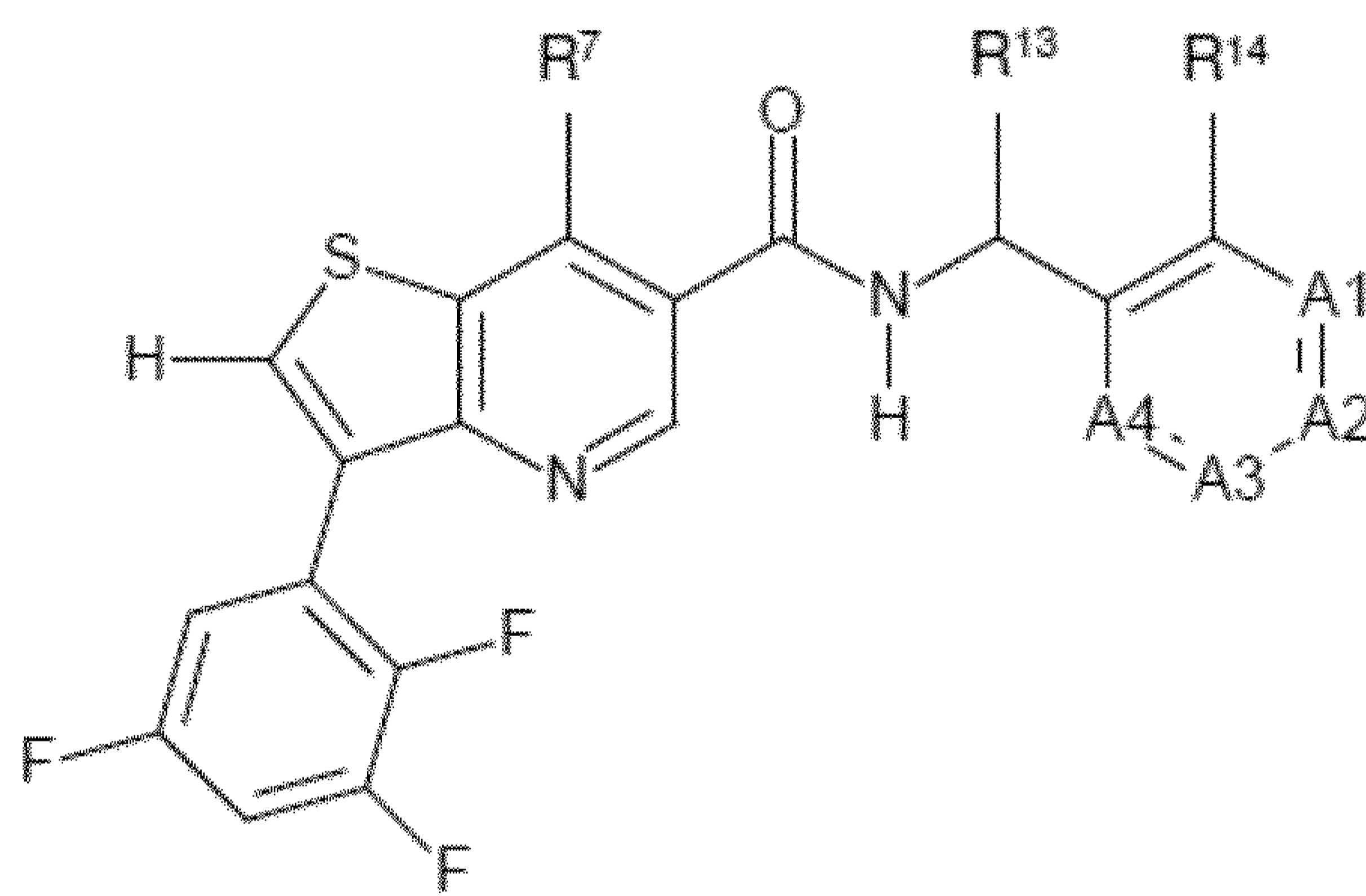
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iui), (Iuii), (Iuiii), (Iuiv), (Iuv), (Iuvi), (Iuvii), (Iuviii), (Iuix), (Iux), (Iuxi) or (Iuxii)



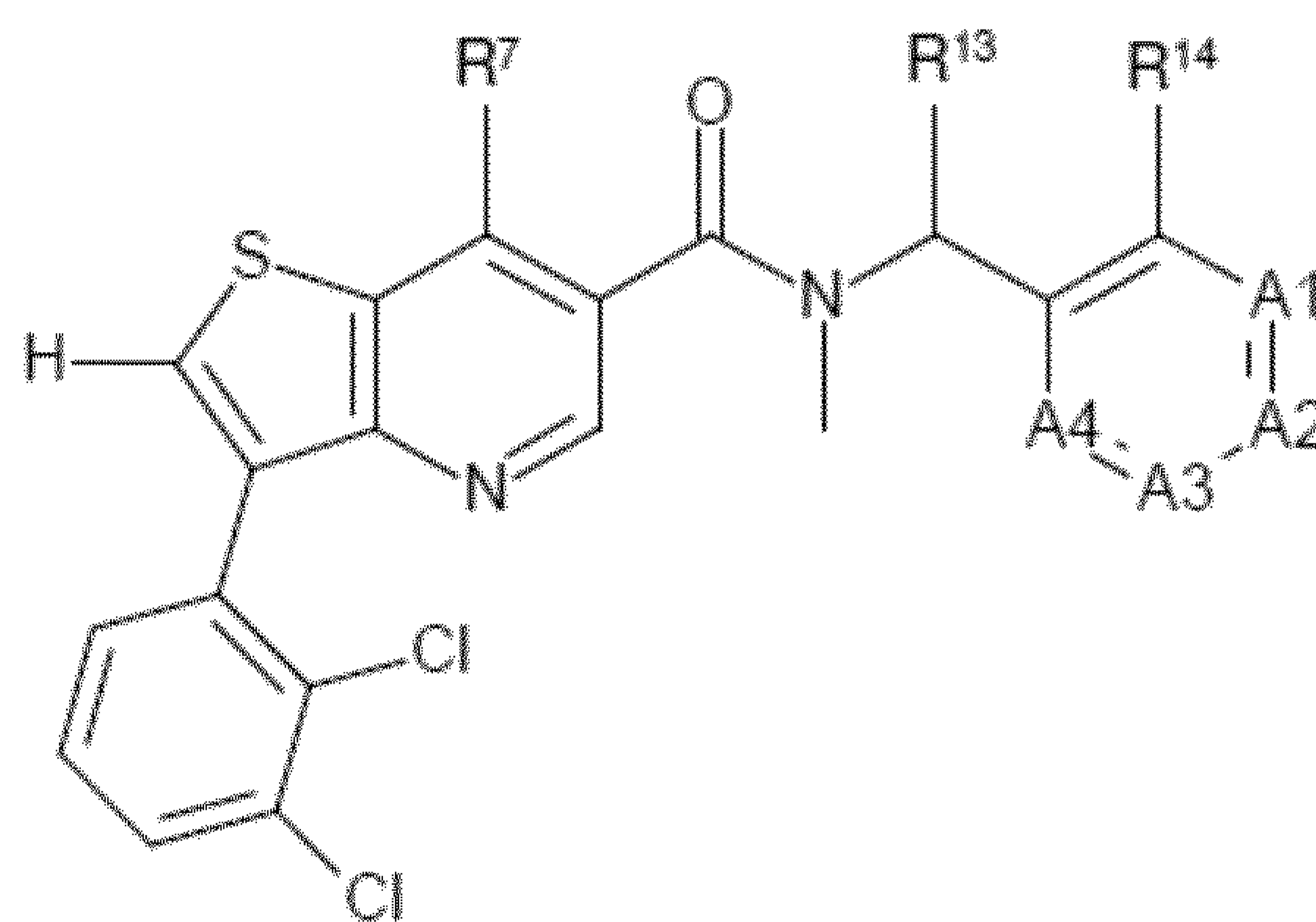
Formula (Iui)



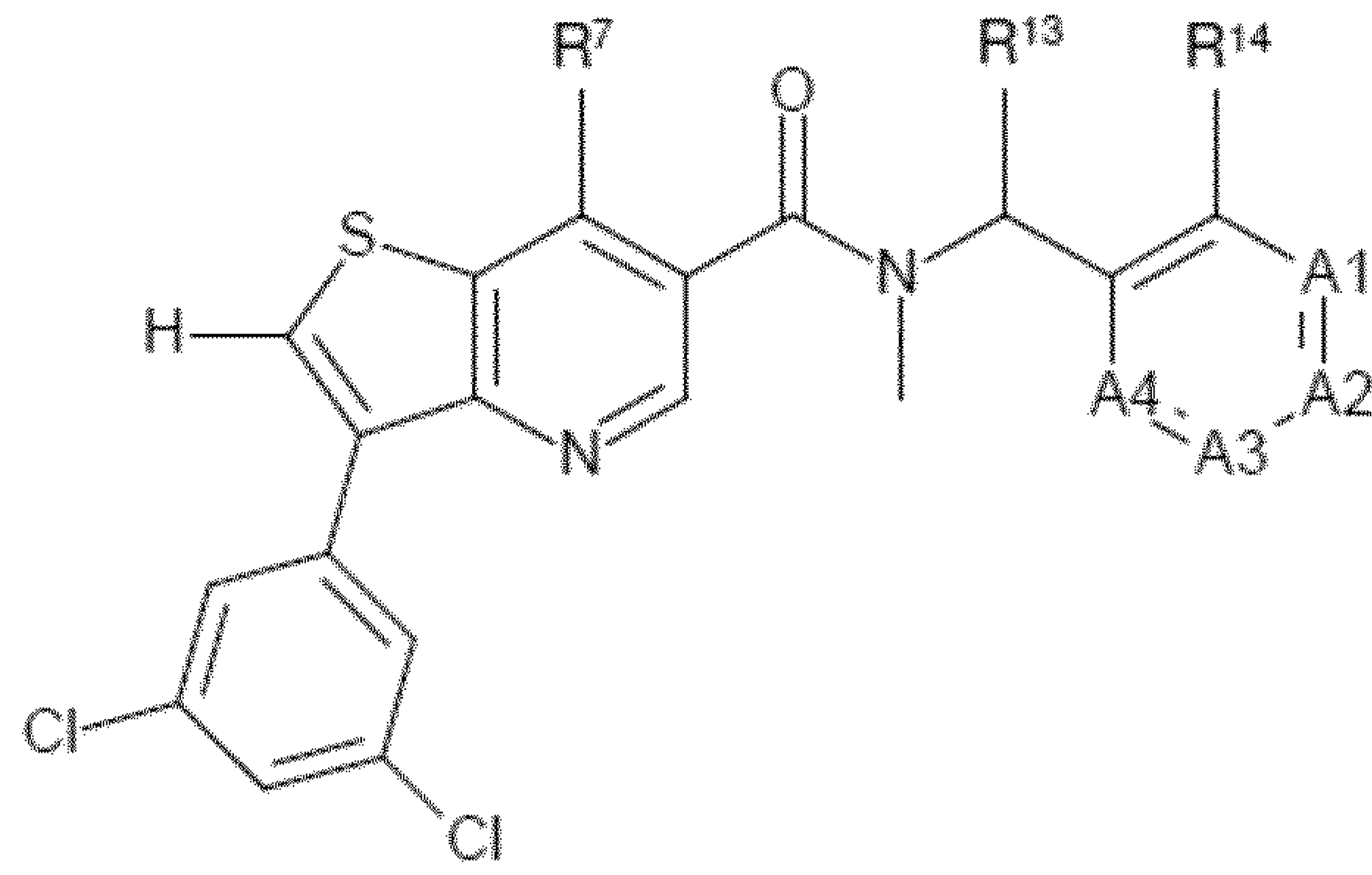
Formula (Iuii)



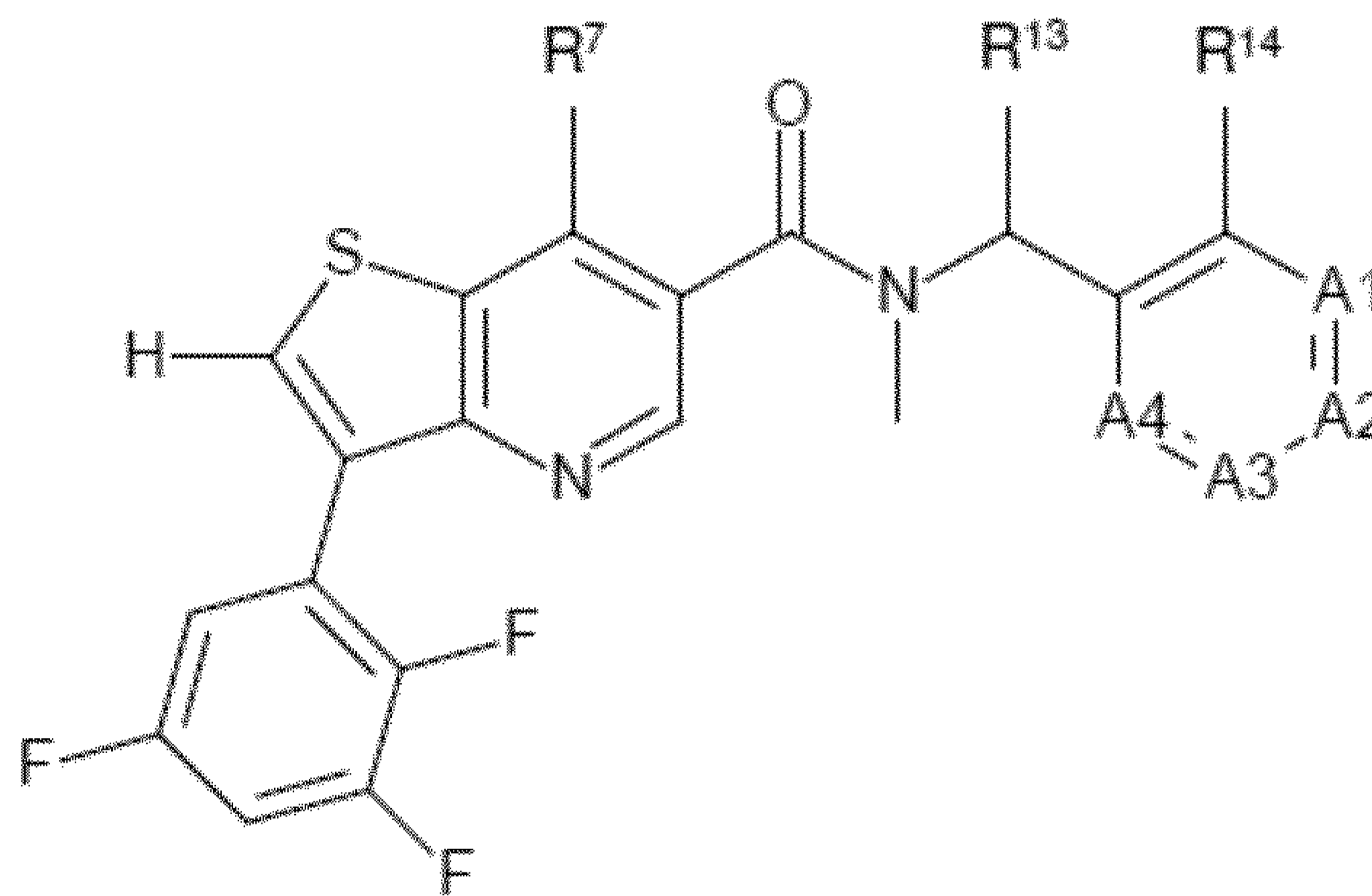
Formula (Iuiii)



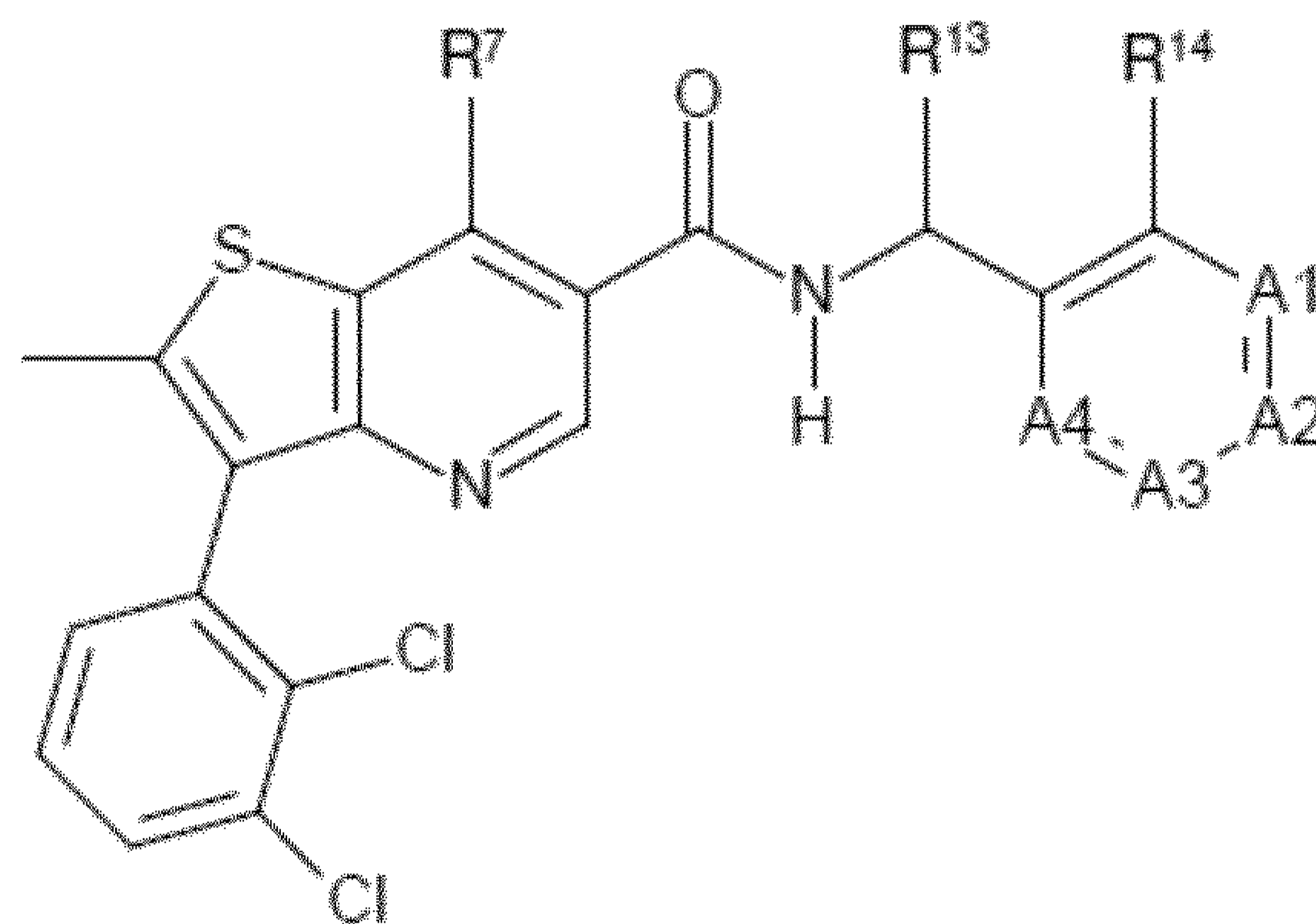
Formula (Iuiv)



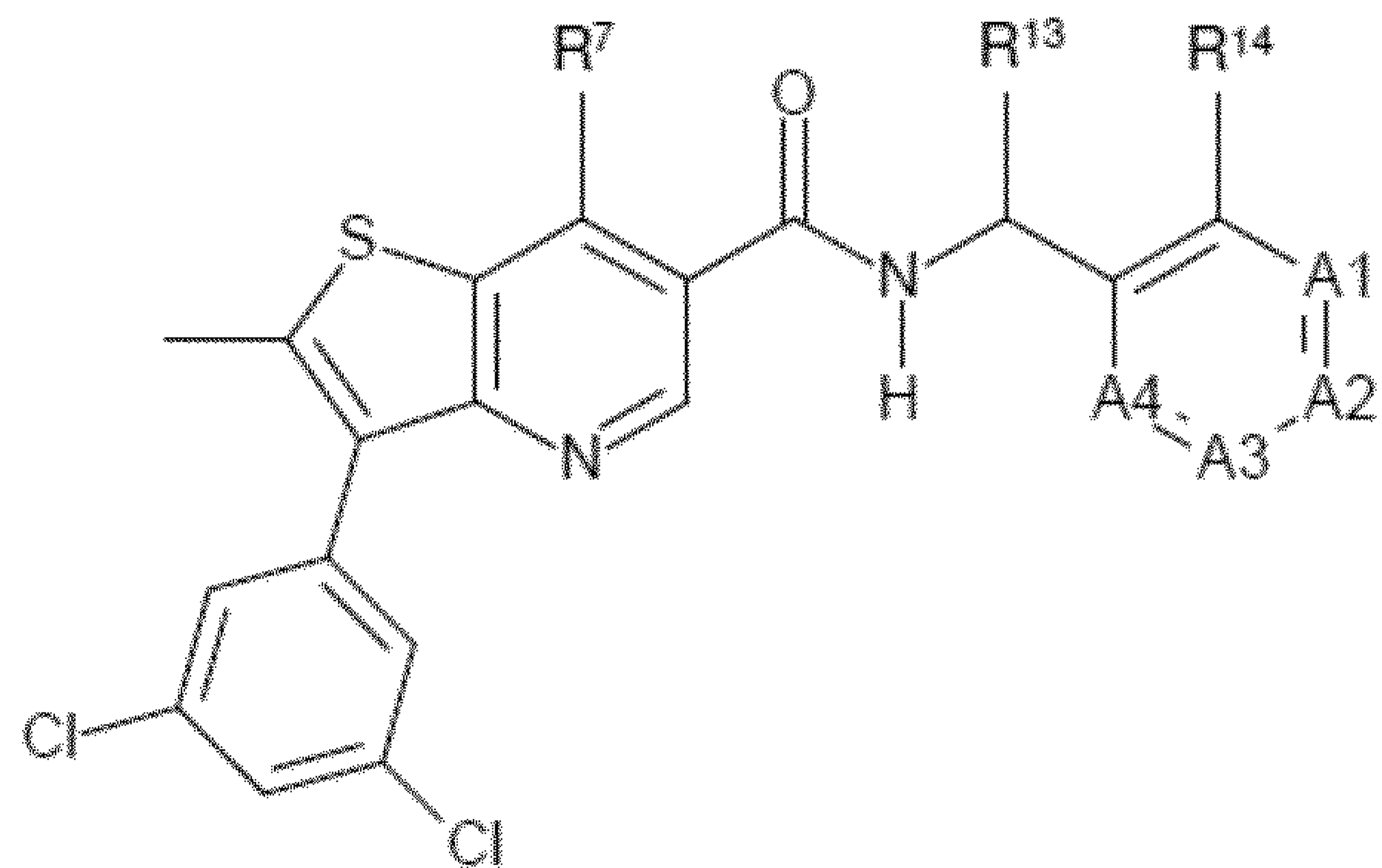
Formula (Iuv)



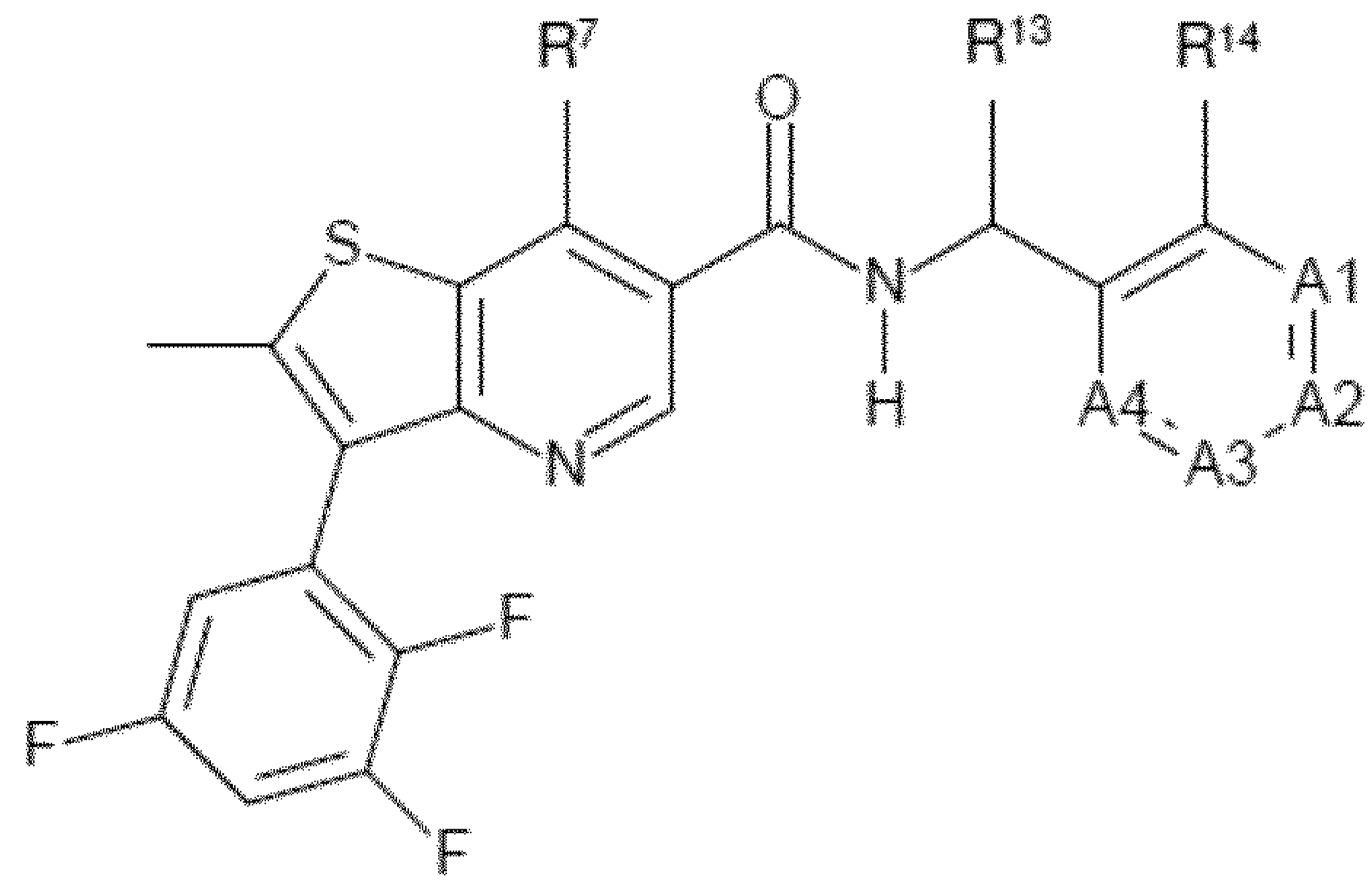
Formula (Iuvi)



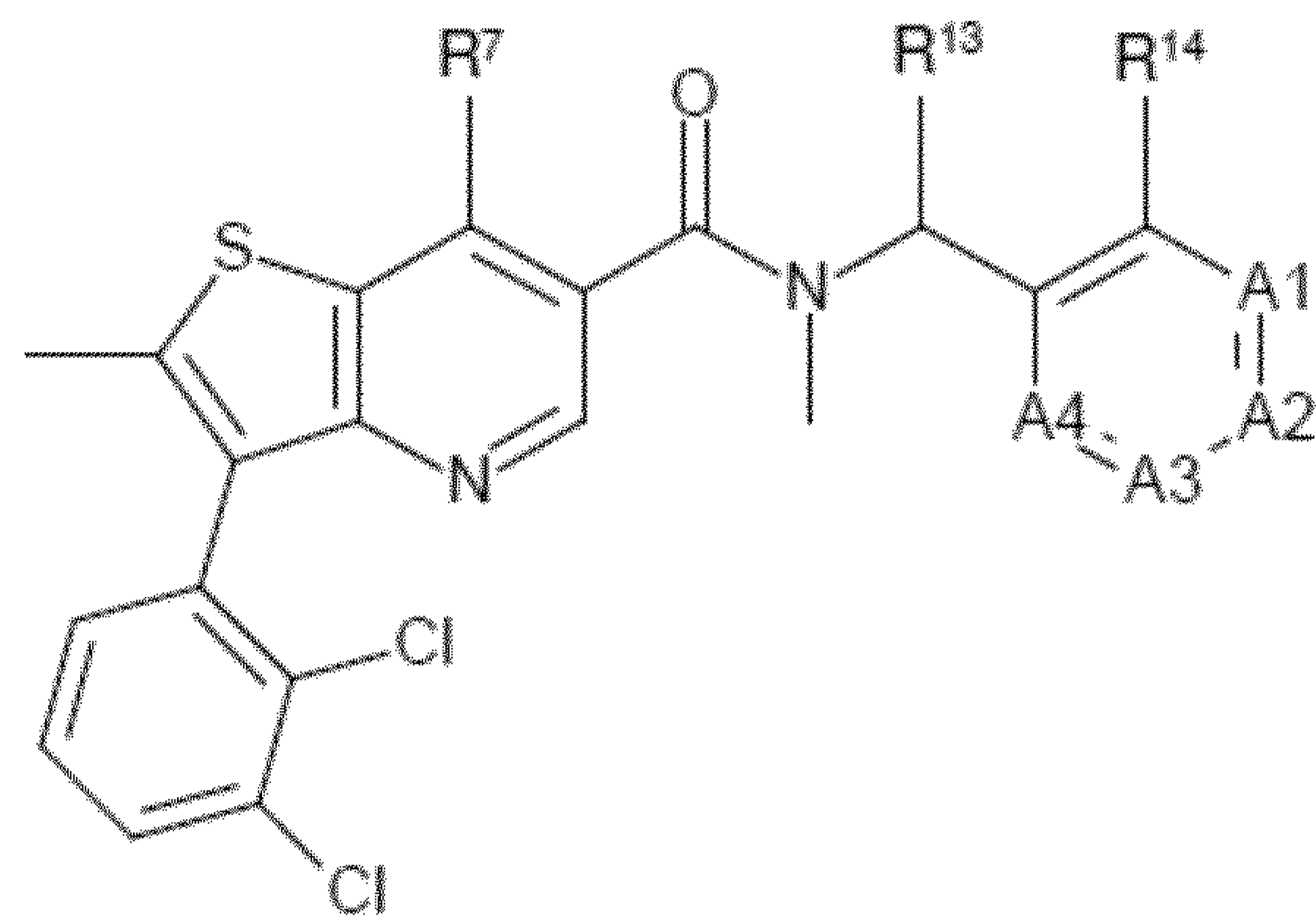
Formula (Iuvii)



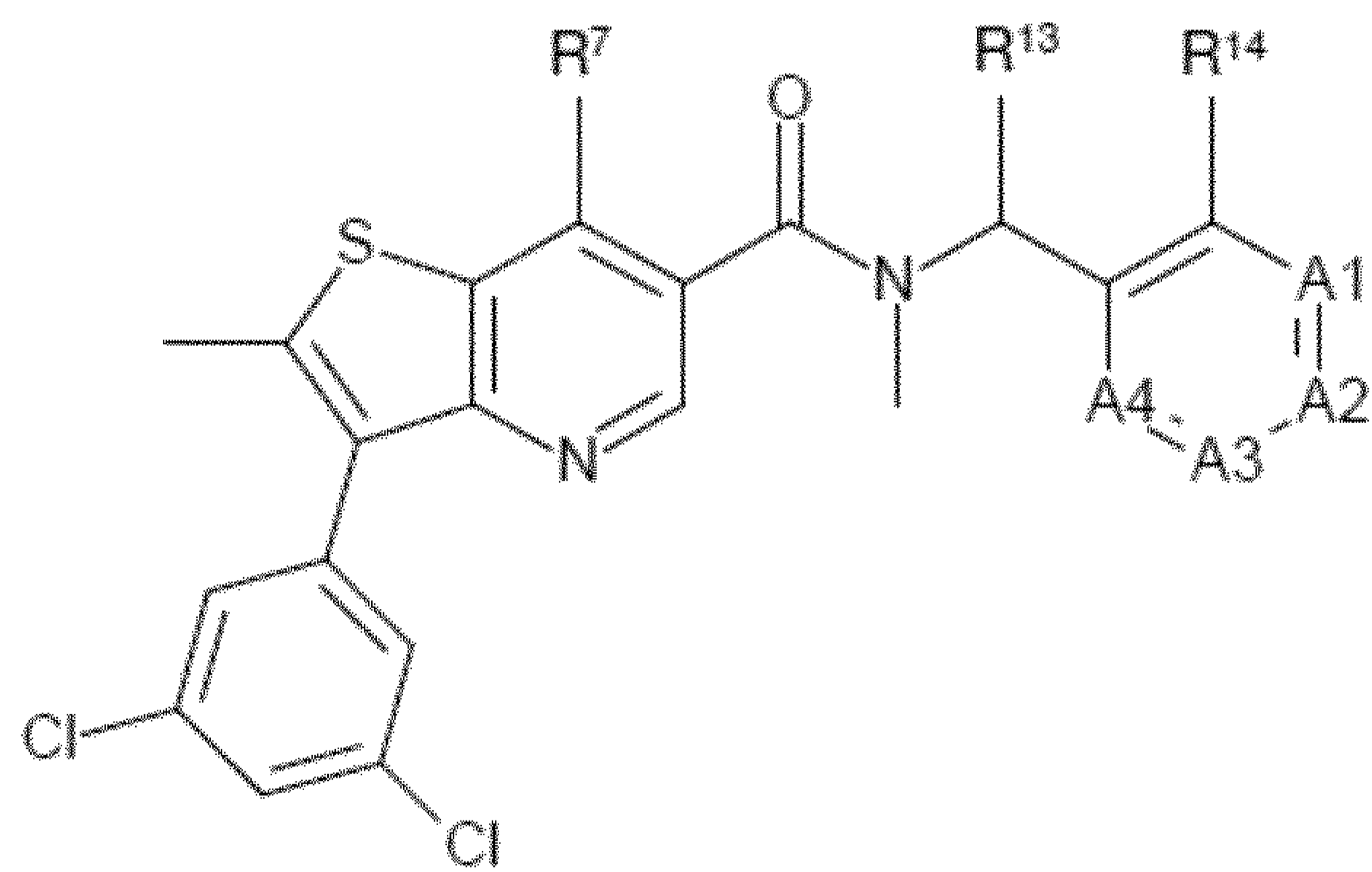
Formula (Iuviii)



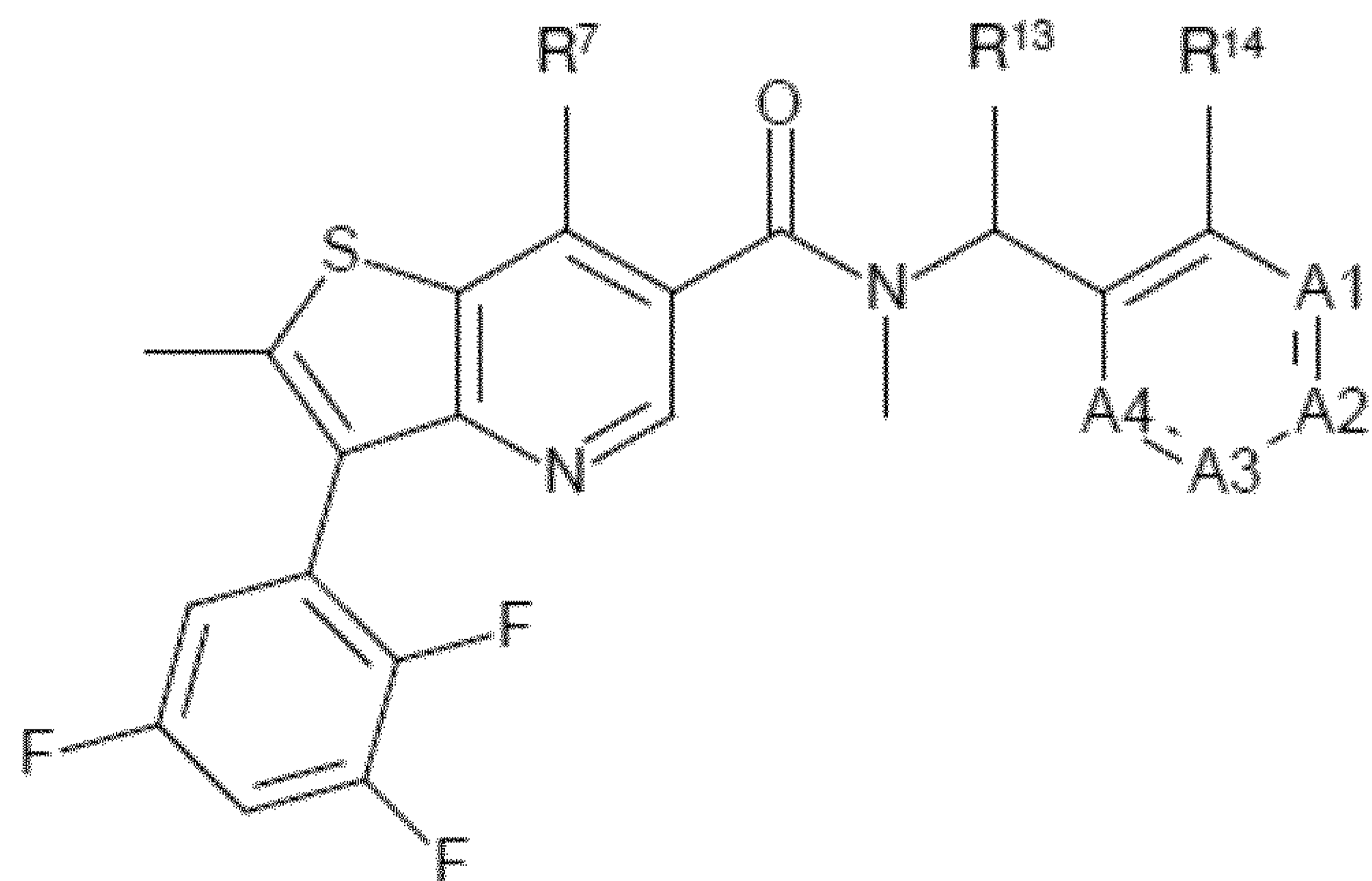
Formula (Iuix)



Formula (Ixi)



Formula(Iuxi)



5

Formula(Iuxii)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^7 and R^{13} , R^{14} , A1, A2, A3, and A4 are defined as in any of the embodiments described herein.

- 5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iui), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuiii), preferably in the form of the (*S*)-enantiomer. In an
 10 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuvi), preferably in the form of the (*S*)-enantiomer. In an
 15 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuix), preferably in the form of the (*S*)-enantiomer. In an
 20 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iux), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuxi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iuxii), preferably in the form of the (*S*)-enantiomer.
- 25 The invention provides a compound according to the invention and/or embodiments thereof, wherein R^7 , R^{13} , R^{14} , A1, A2, A3 and A4 are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

- 30 hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

10 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

20 R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

5 and

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

15 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

20 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

25 R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

In one embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

5 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

10 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

20 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

5 R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

10 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

15 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

20 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

25 Suitably R⁷ is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino,

dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

5 and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH- or -O-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

10 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

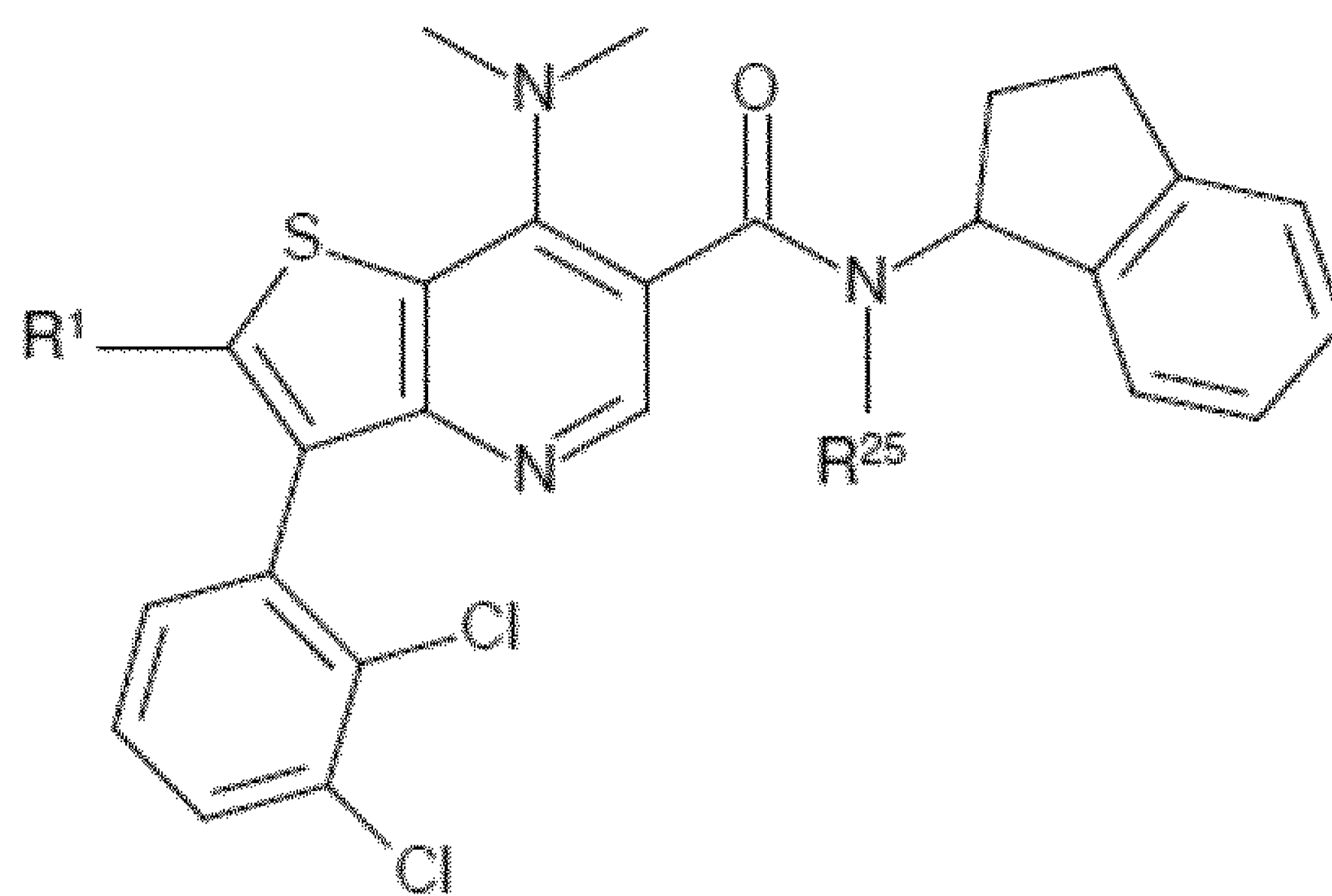
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

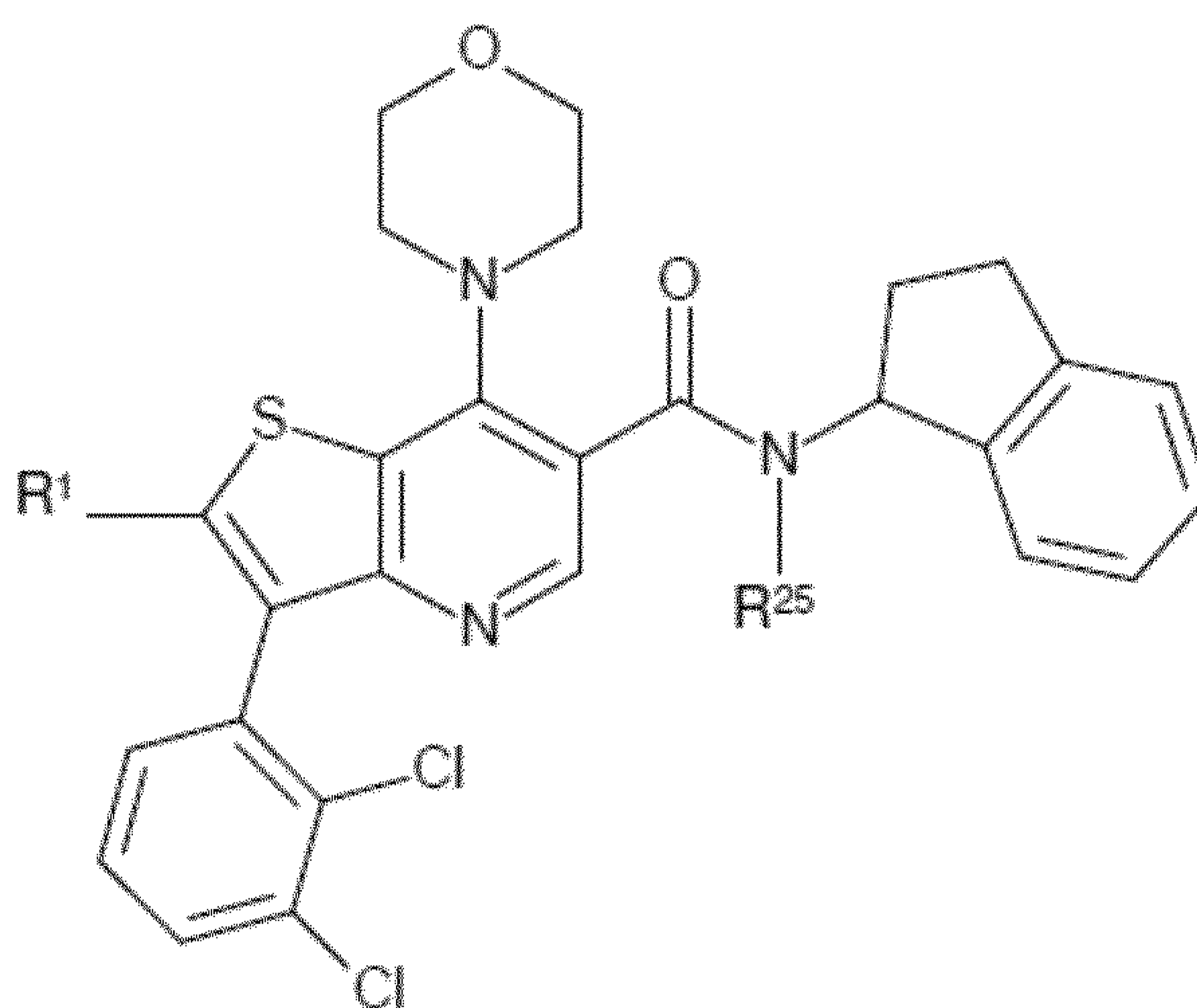
and

15 R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-
20 fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.
25

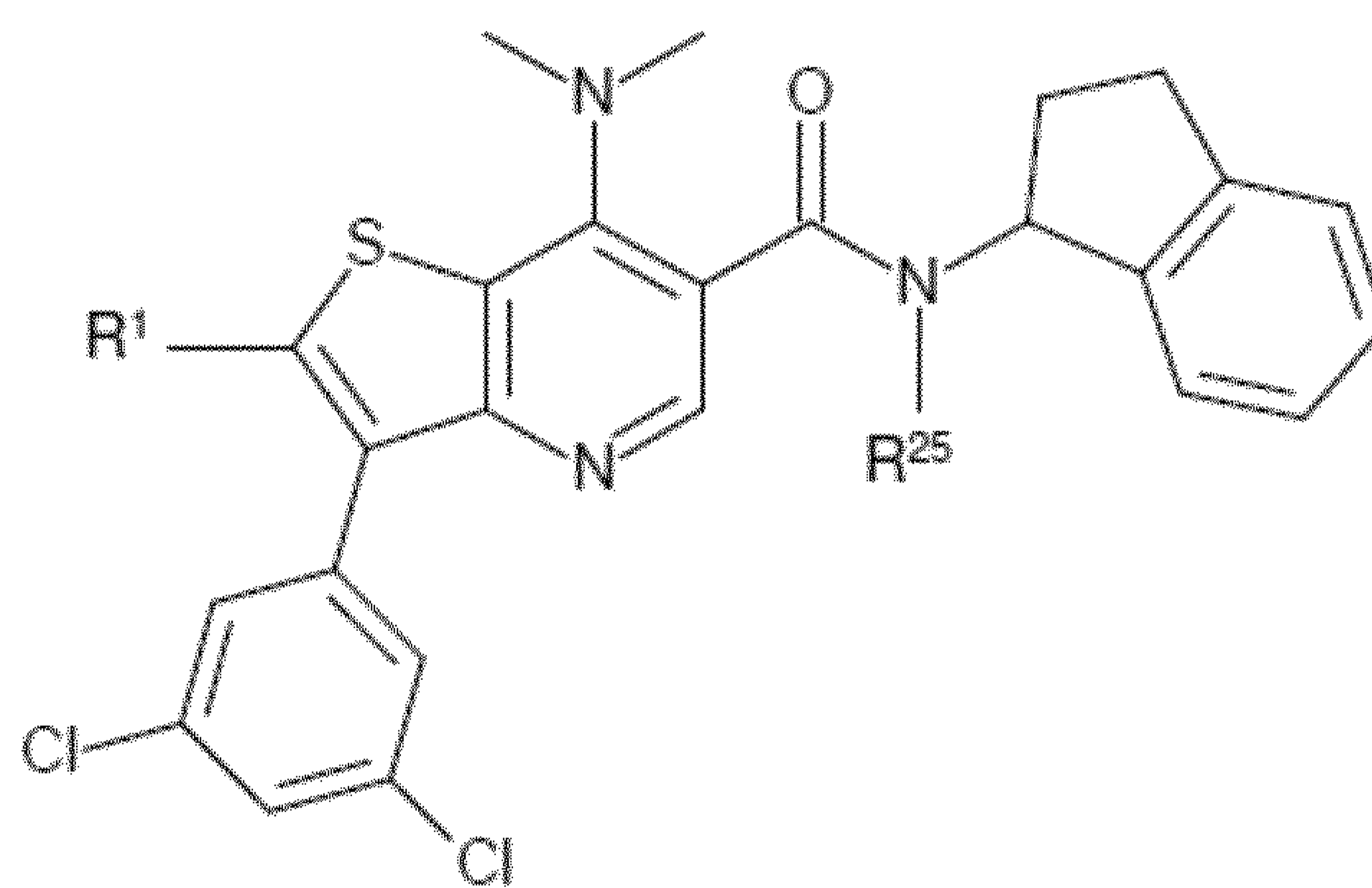
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivi), (Ivii), (Iviii), (Ivix), (Ivx), (Ivxi) or (Ivxii)



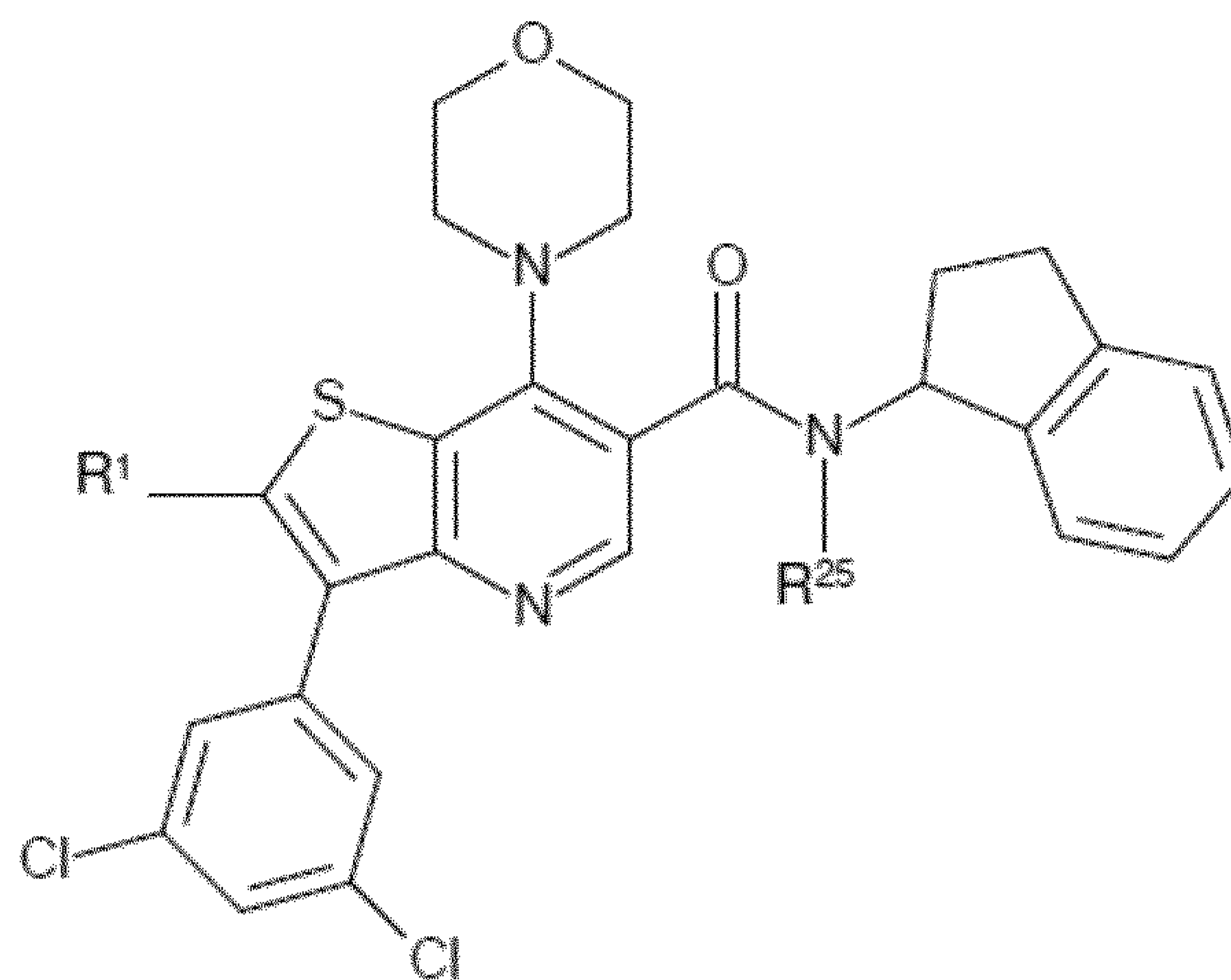
Formula (Ivi)



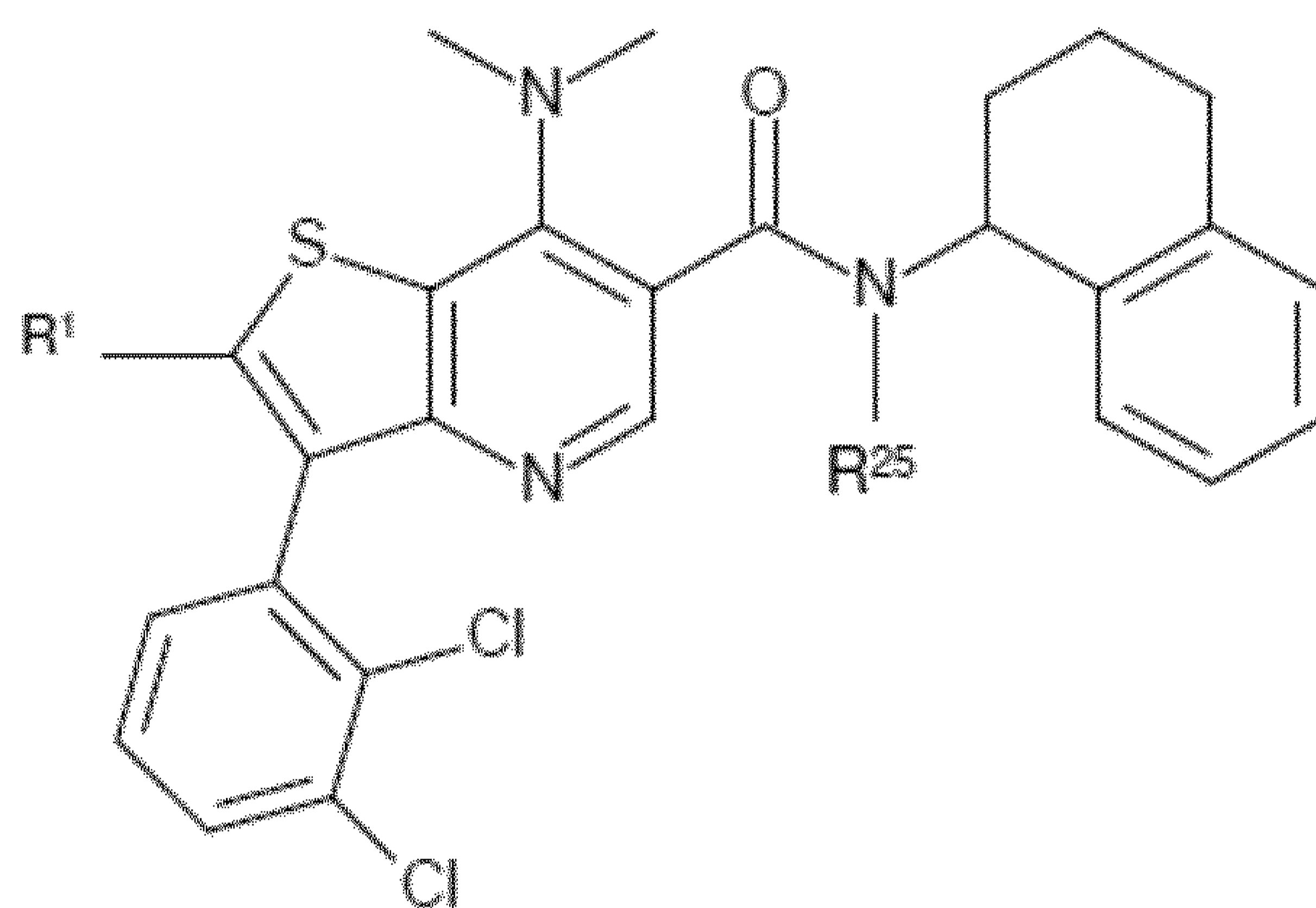
Formula (Ivii)



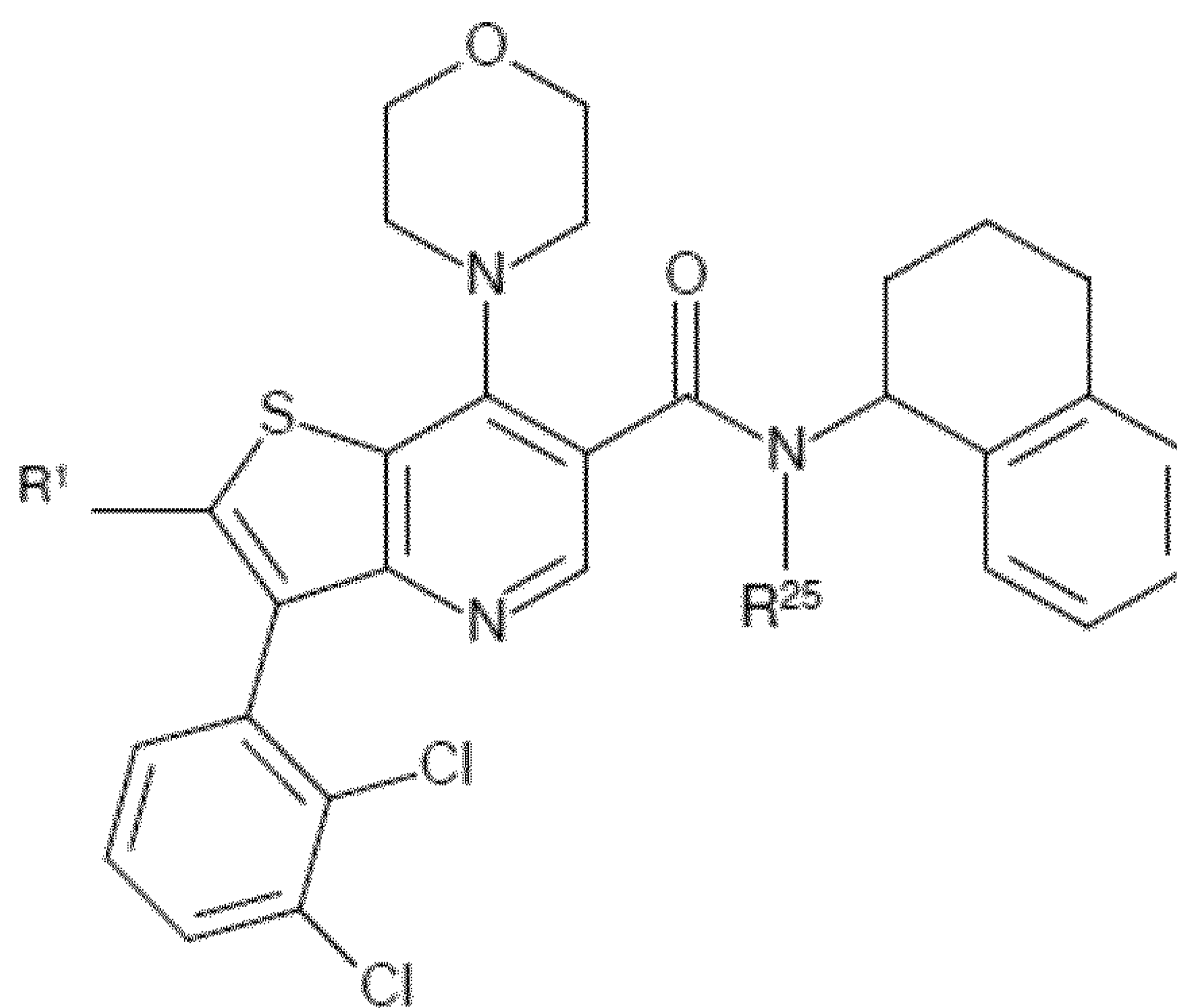
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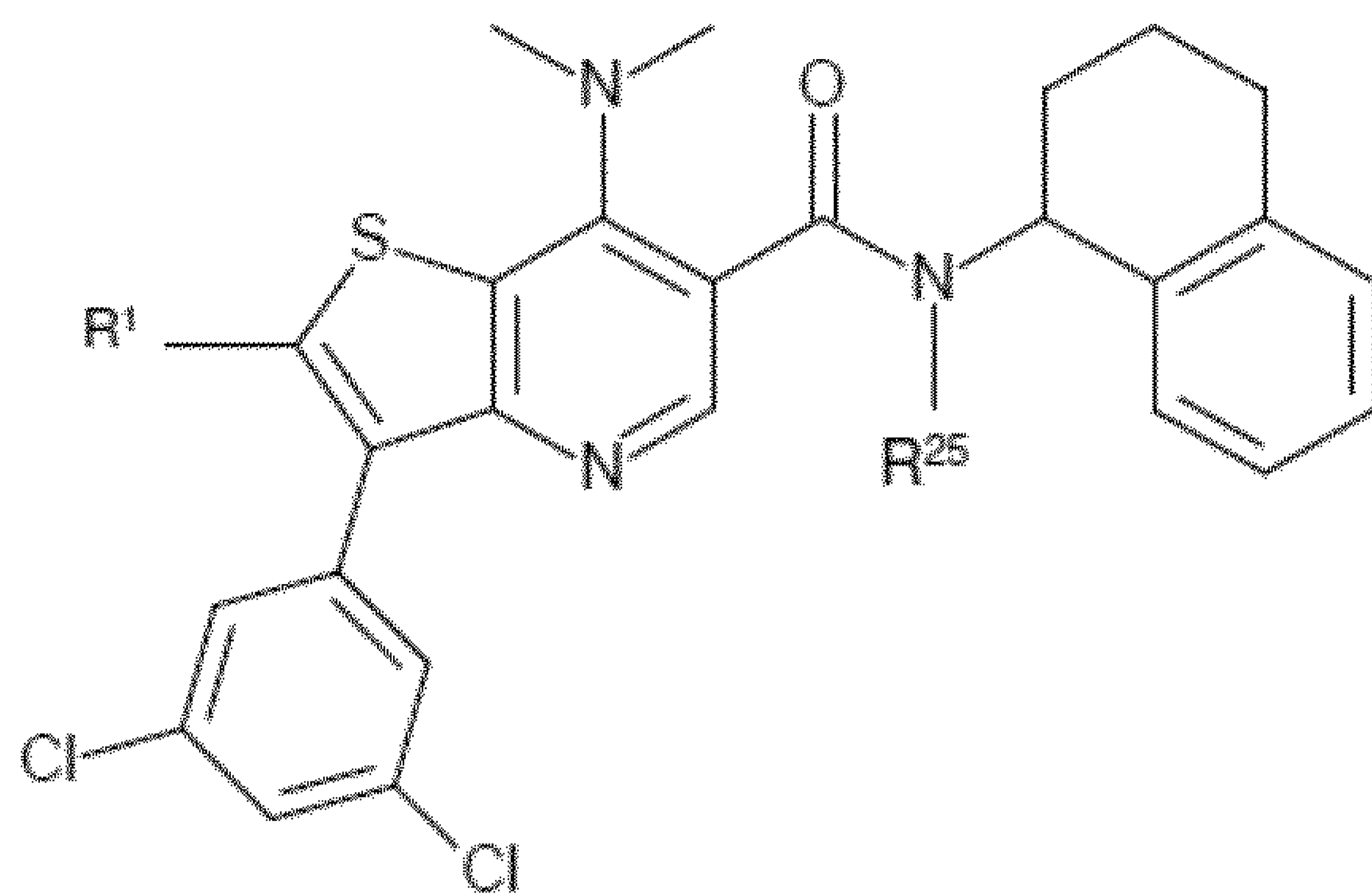
Formula (Iviv)



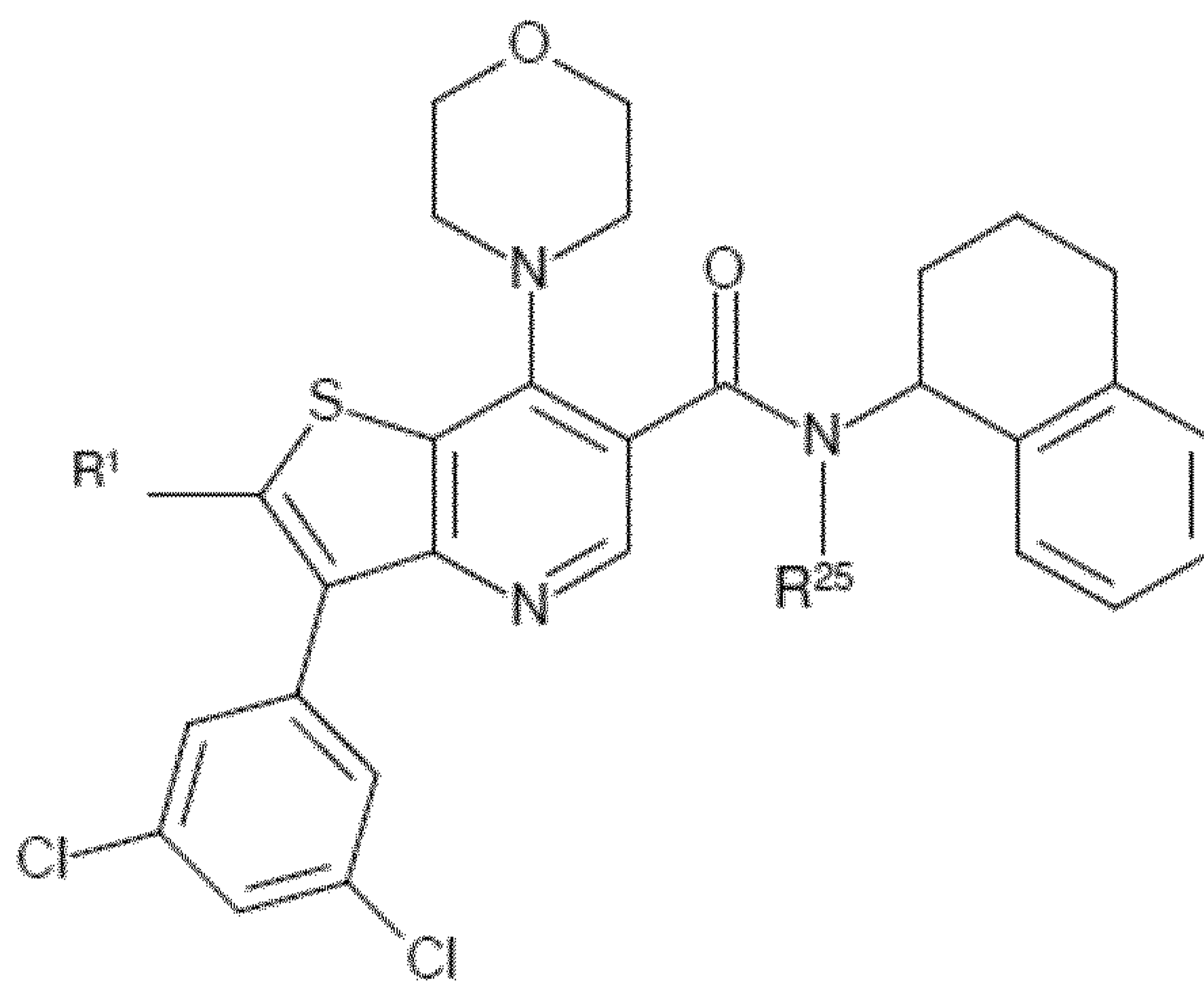
Formula (Ivv)



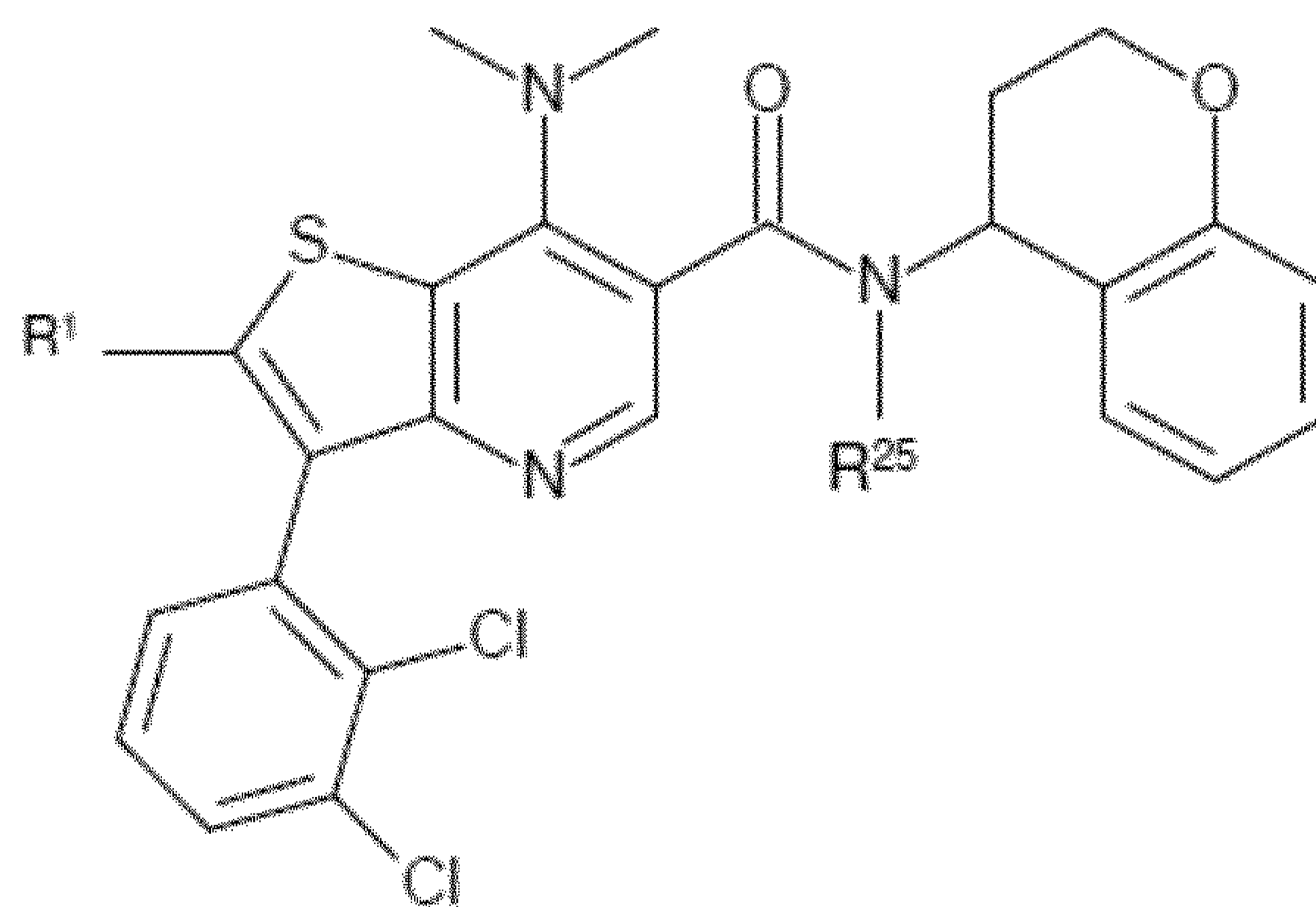
Formula (Ivvi)



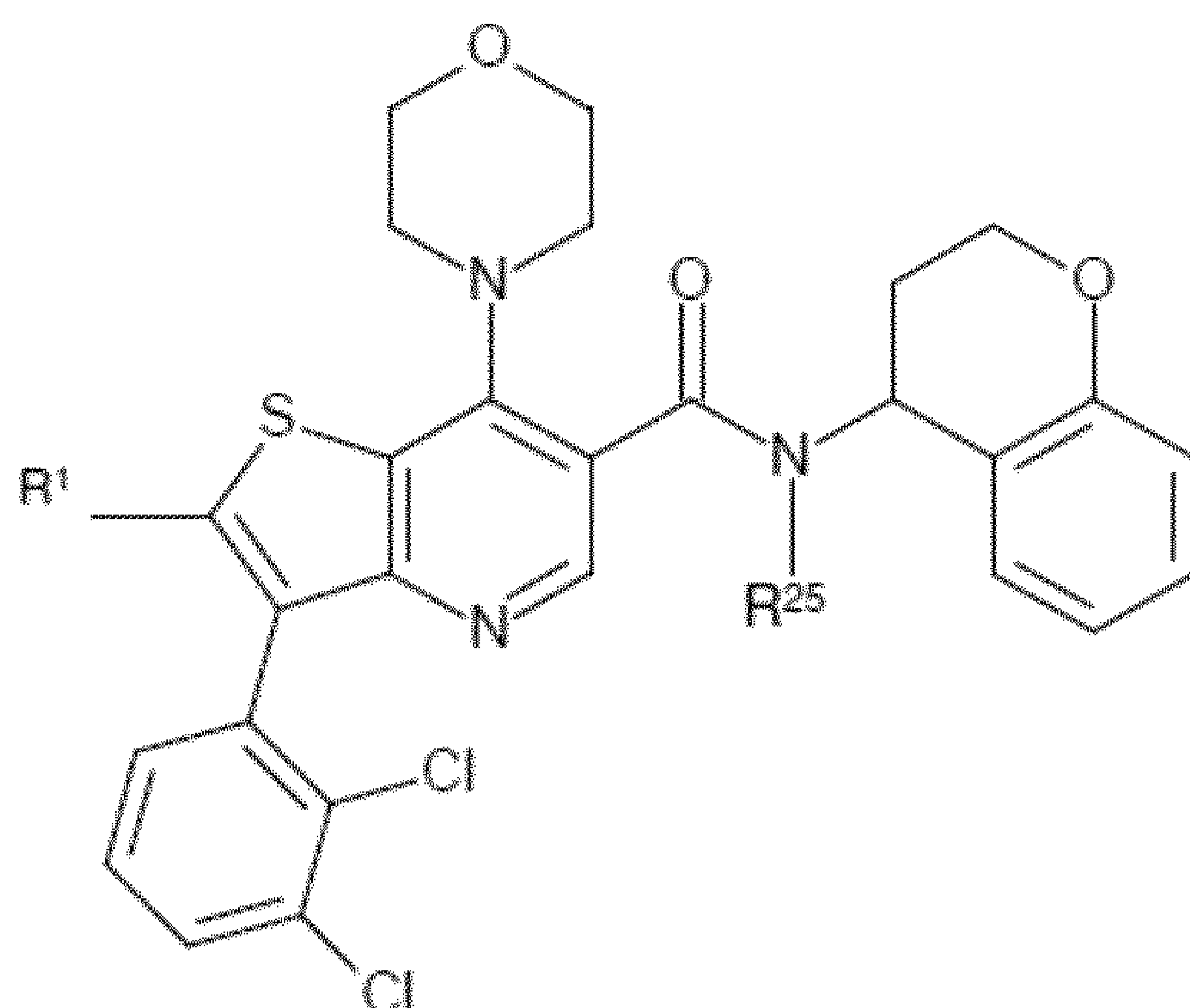
Formula (Iv vii)



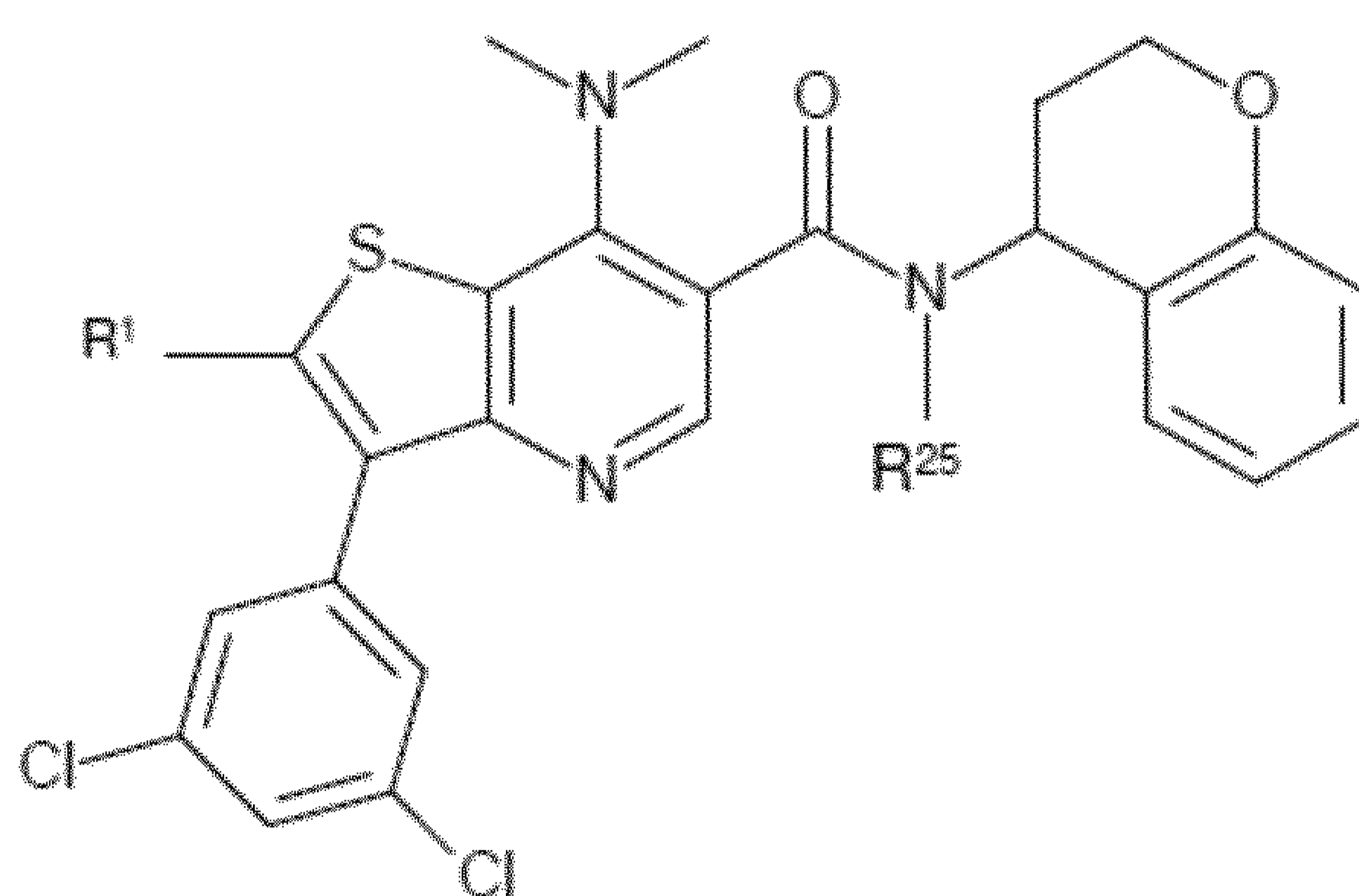
Formula (Iv viii)



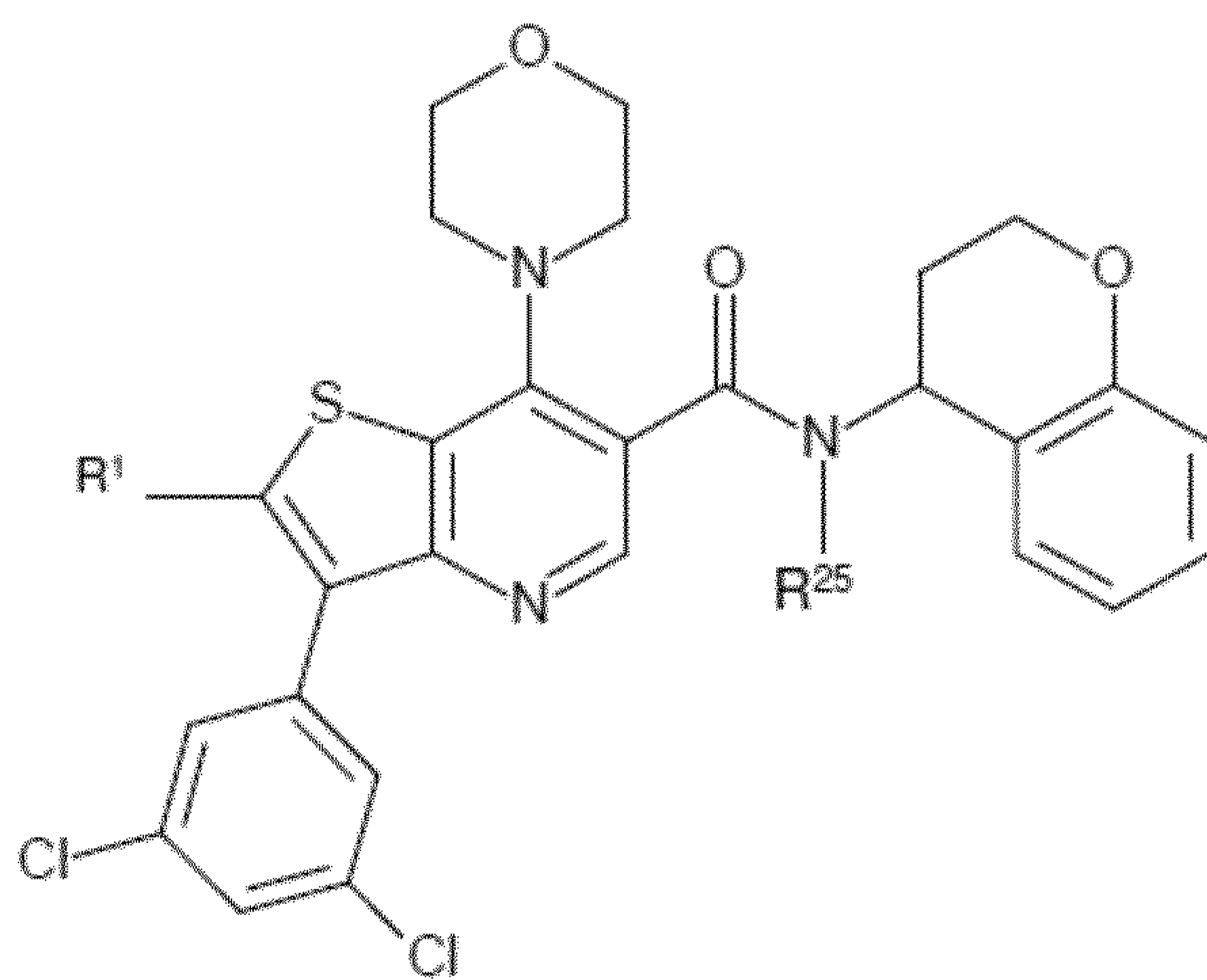
Formula (Iv ix)



Formula (Ivx)



Formula (Ivxi)



Formula (Ivxi)

5

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹ and R²⁵ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivii), preferably in the

10

form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iviv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iviii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivx), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxii), preferably in the form of the (*S*)-enantiomer.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, NR^8R^9 , $C(=O)OR^{10}$ and $C(=O)NR^{11}R^{12}$,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

10 R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,
R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,
R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,
and

15 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

20 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

25 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

and

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

10 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

20 In one embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or
10 ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

15 and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A₁ is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

20 A₂ is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A₃ is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A₄ is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A₁, A₂, A₃ and A₄ are N,

and

25 R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

5 In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

10 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

15 wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

20 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

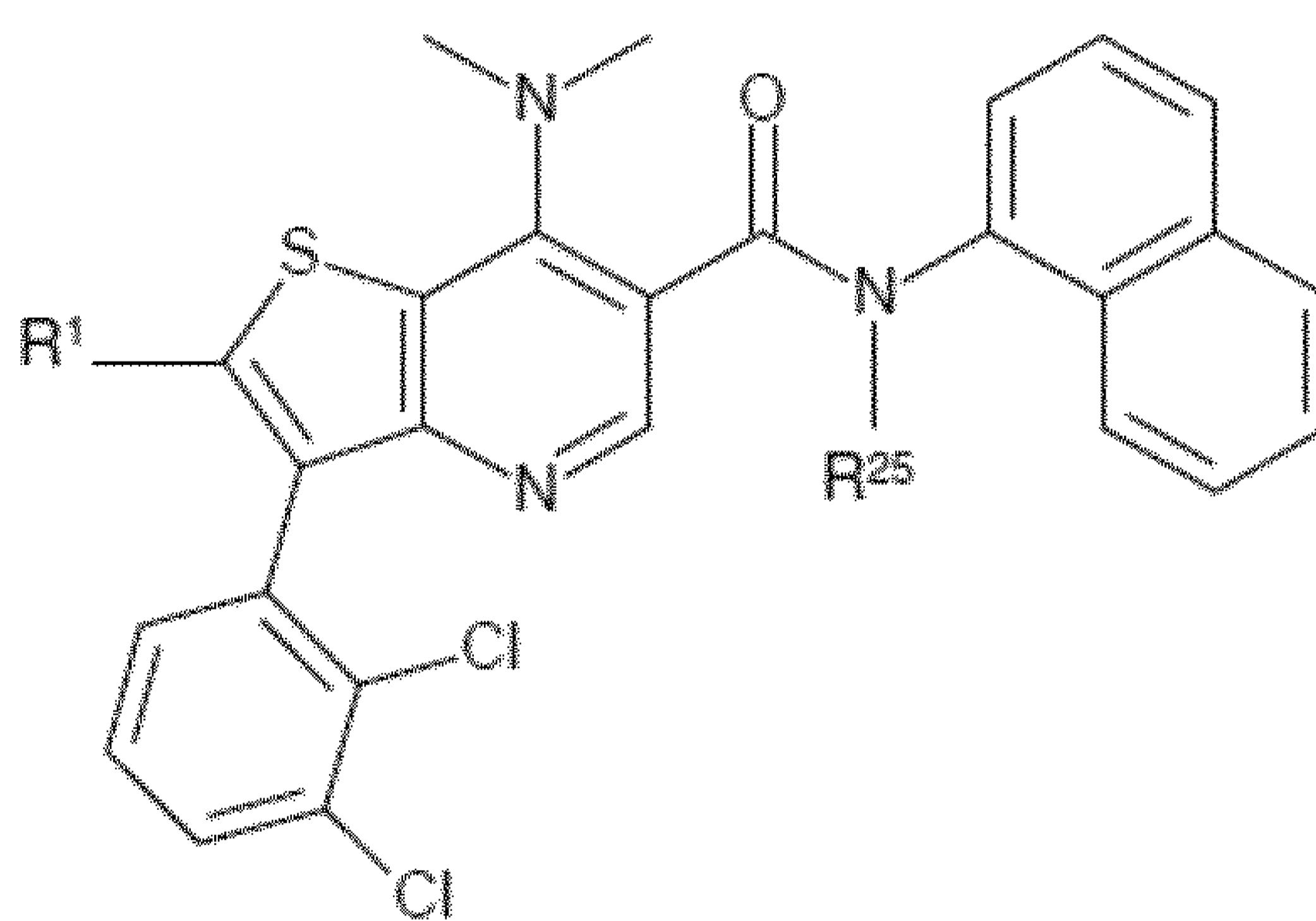
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

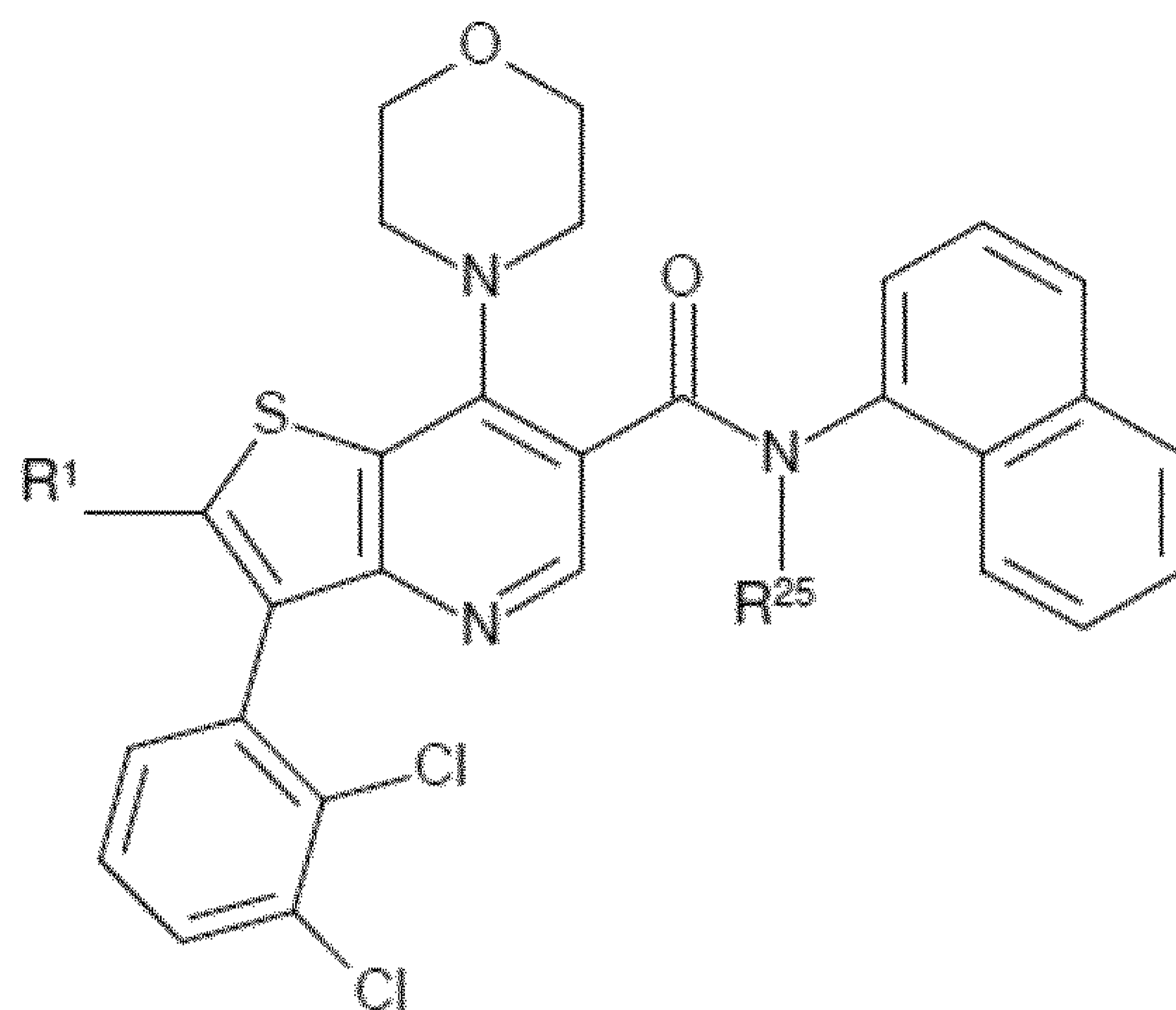
and

- 5 R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl.

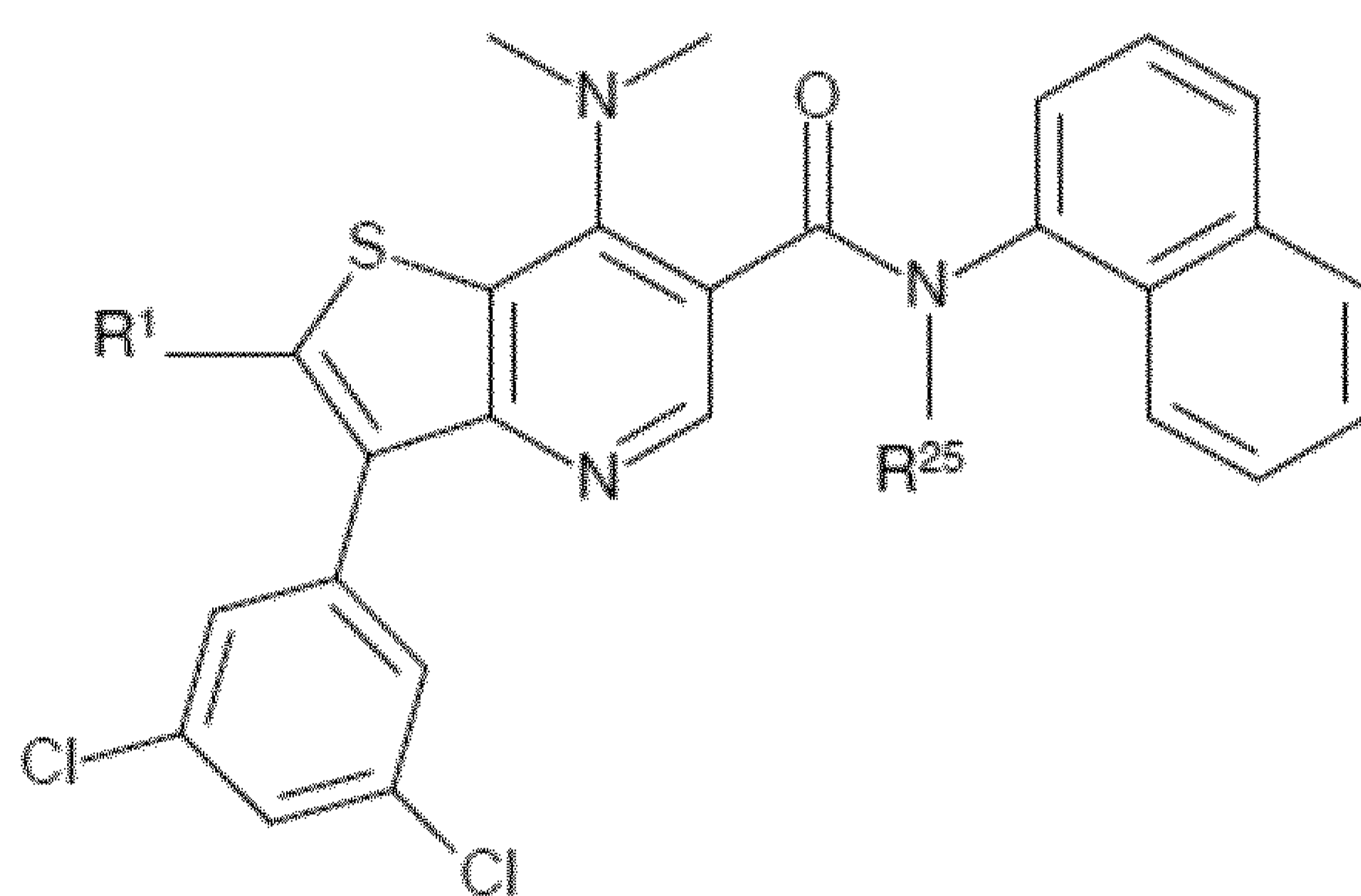
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxxiii), (Ivxxiv), (Ivxxv), (Ivxxvi), (Ivxxvii), (Ivxxviii), (Ivxxix) or (Ivxxx)



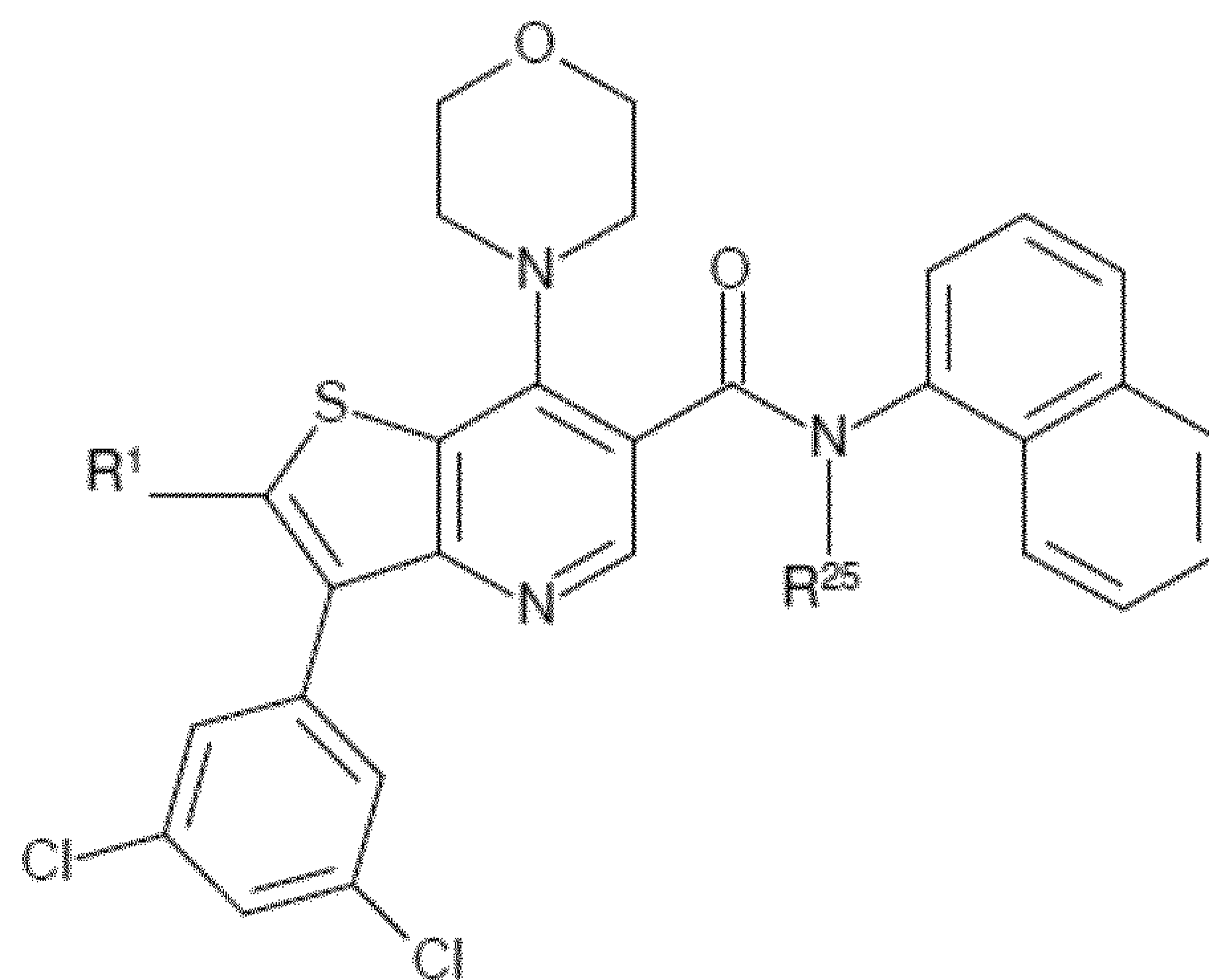
Formula (Ivxxiii)



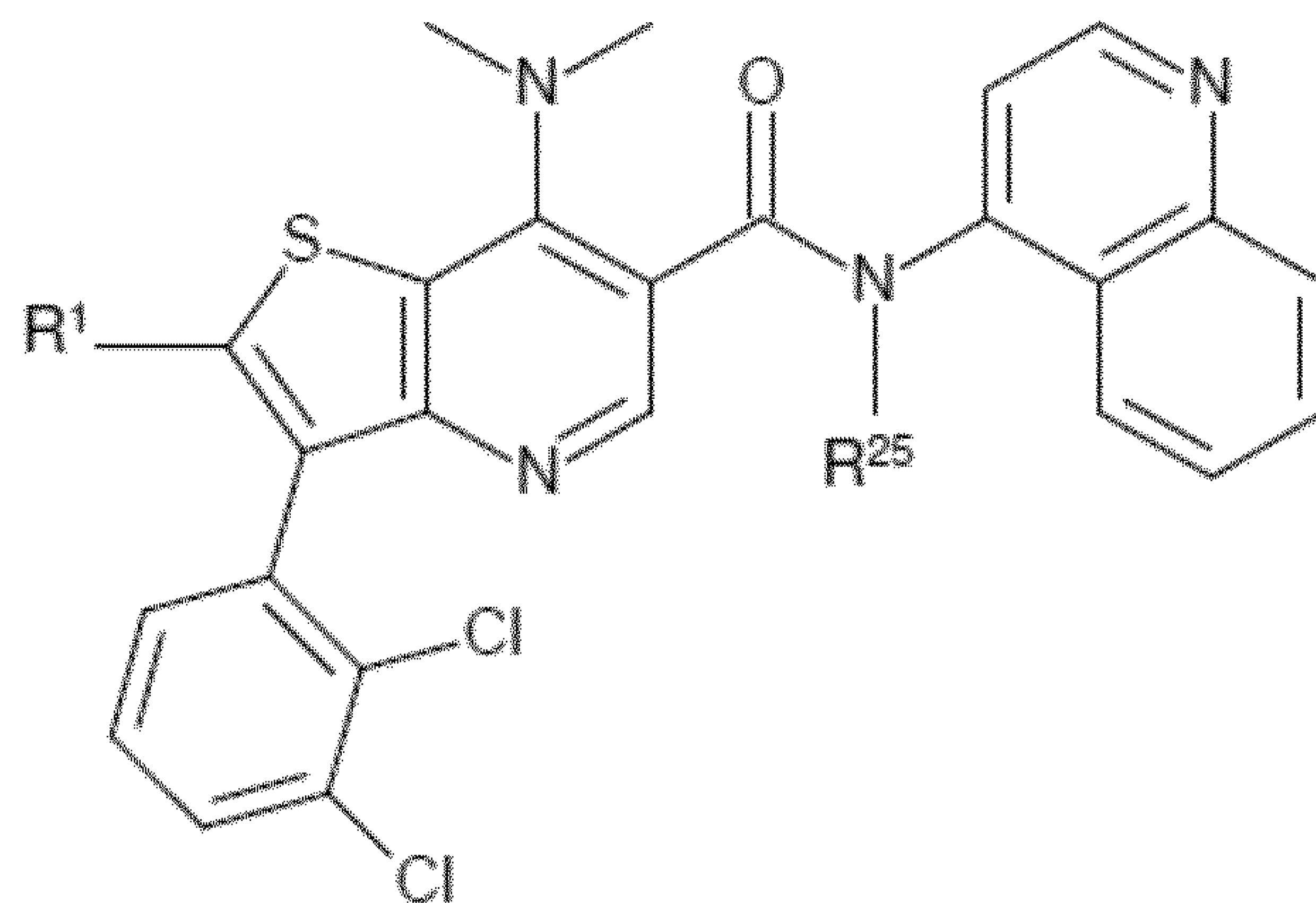
Formula (Ivxiv)



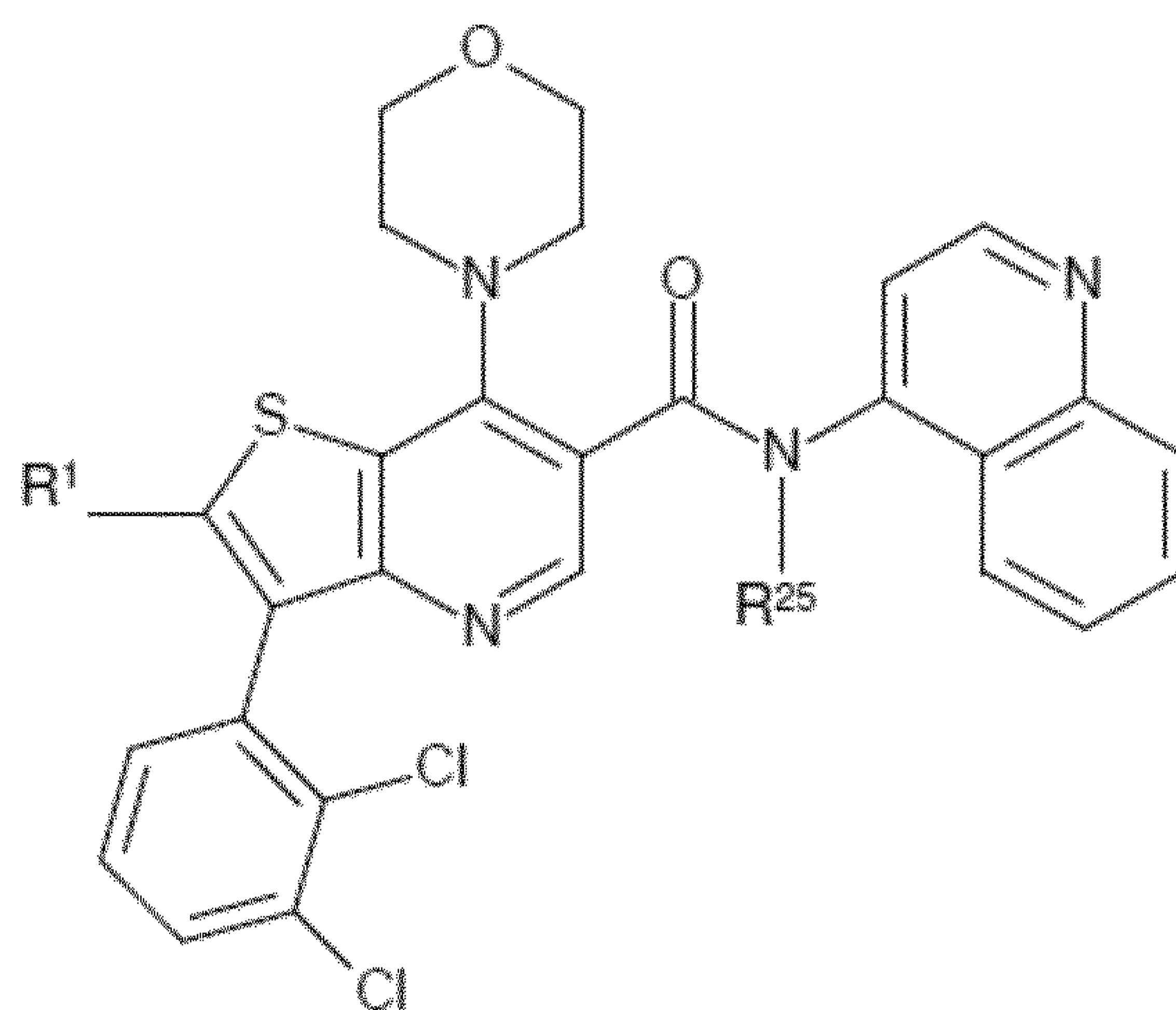
Formula (Iv xv)



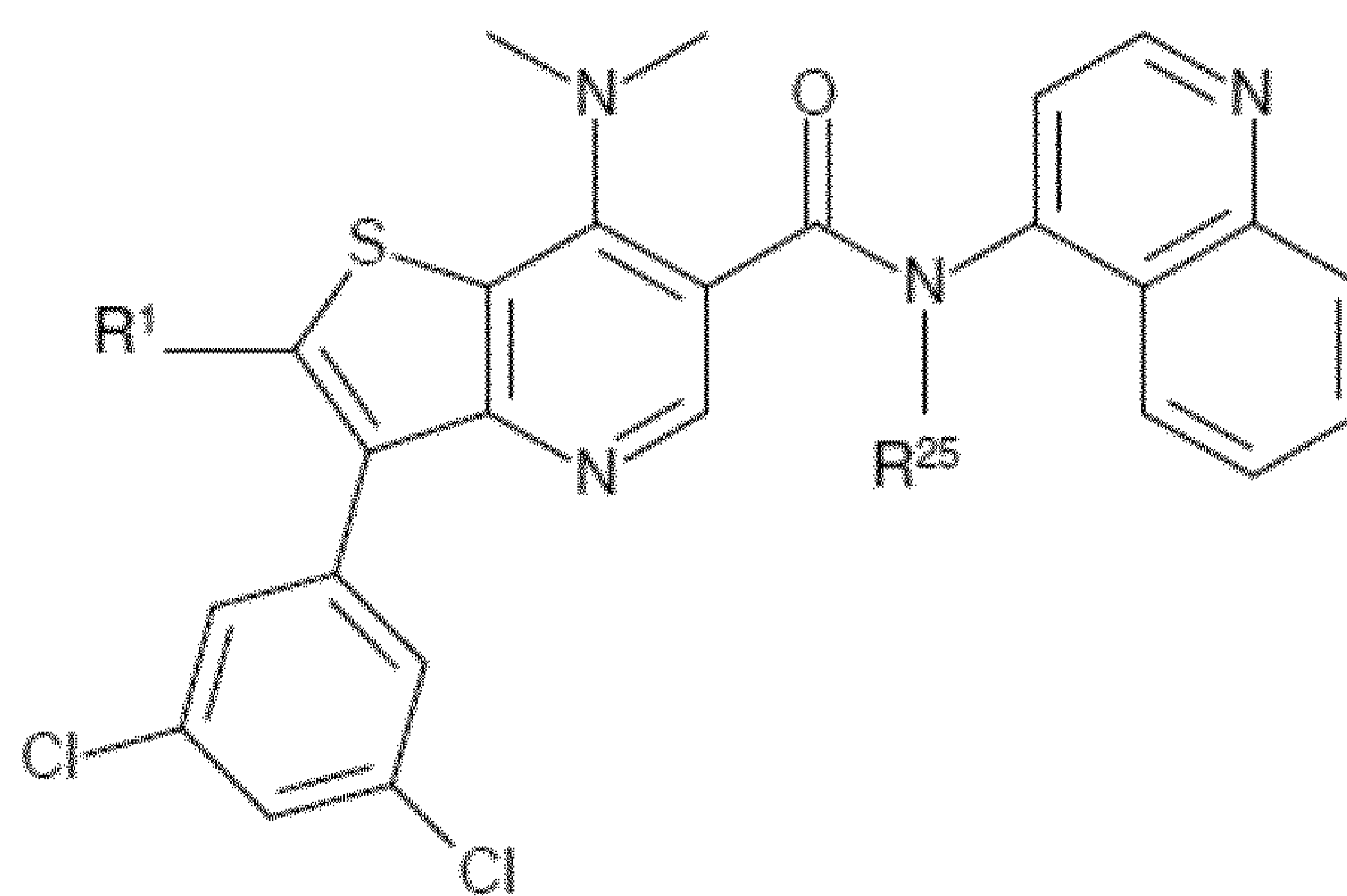
Formula (Iv xvi)



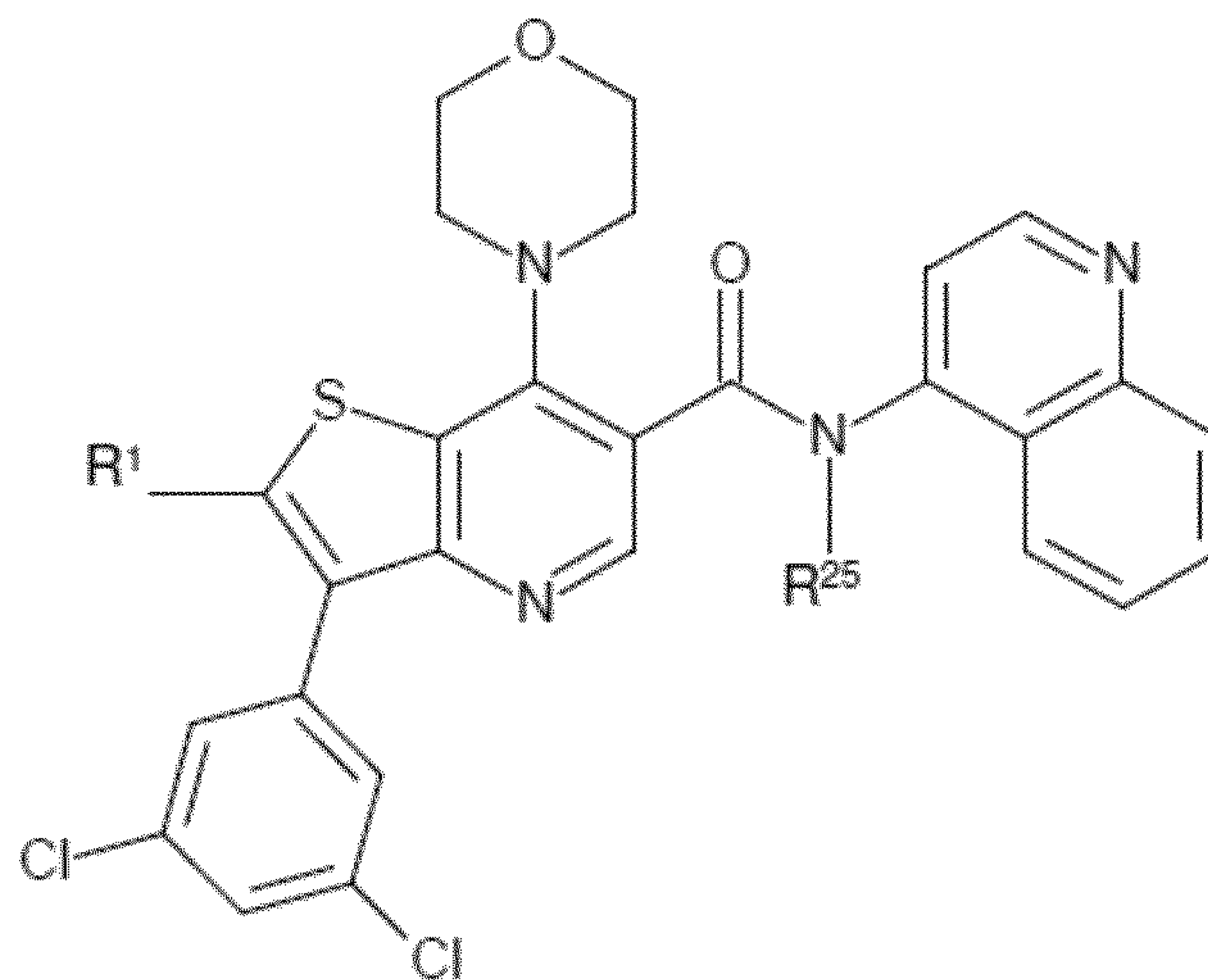
Formula (Iv xvii)



Formula (Iv xviii)



Formula (Iv xix)



Formula (Ivxx)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 and R^{25} are defined as in any of the embodiments described herein.

- 5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxiii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxiv), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxv), preferably in the form of the (*S*)-enantiomer. In an
- 10 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxvi), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxvii), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxviii), preferably in the form of the (*S*)-enantiomer. In an
- 15 embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxix), preferably in the form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ivxx), preferably in the form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof, wherein R^7 , R^{13} , R^{14} , A1, A2, A3, A4 and R^{25} are defined as below.

20

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

5 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

5 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

and

10 R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

15 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

20 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

25 wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

5 R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

15 wherein none, one or two of A1, A2, A3 and A4 are N,

and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof

R⁷ is independently selected from the group consisting of

20 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

25 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

- 5 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-
10 hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1-yl,

and

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH- or -O-,

- 15 A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

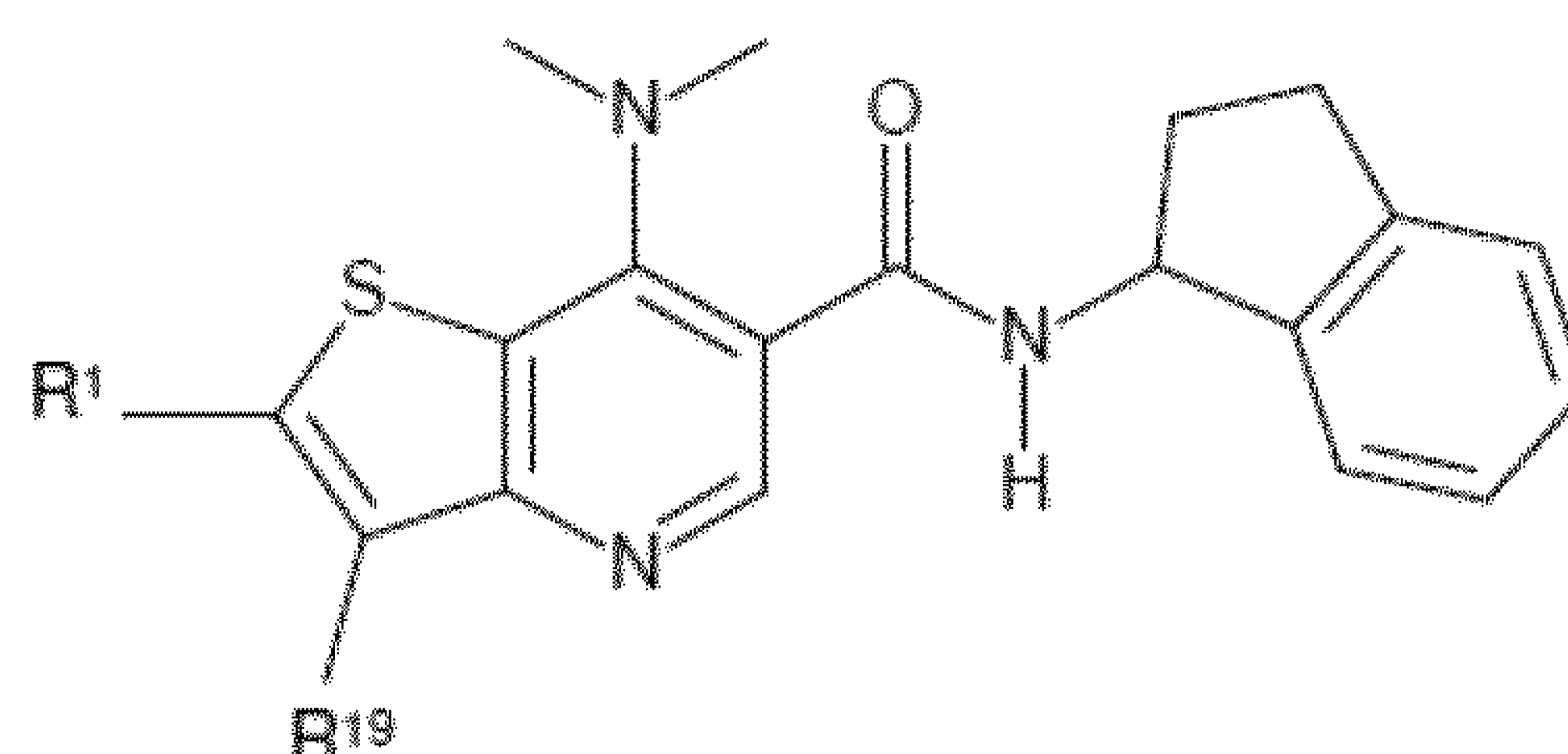
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

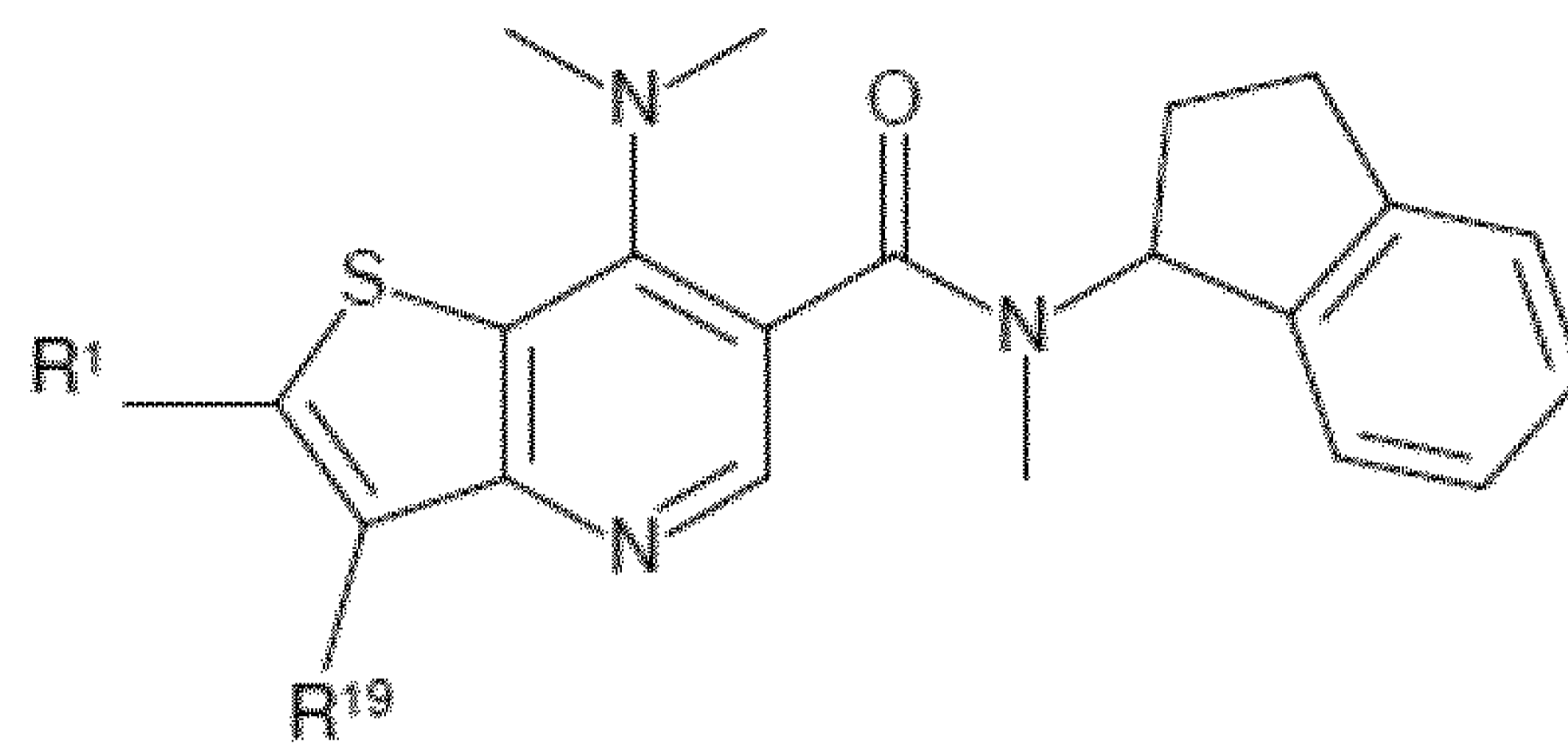
- 20 and

R²⁵ is hydrogen or methyl, more preferably hydrogen.

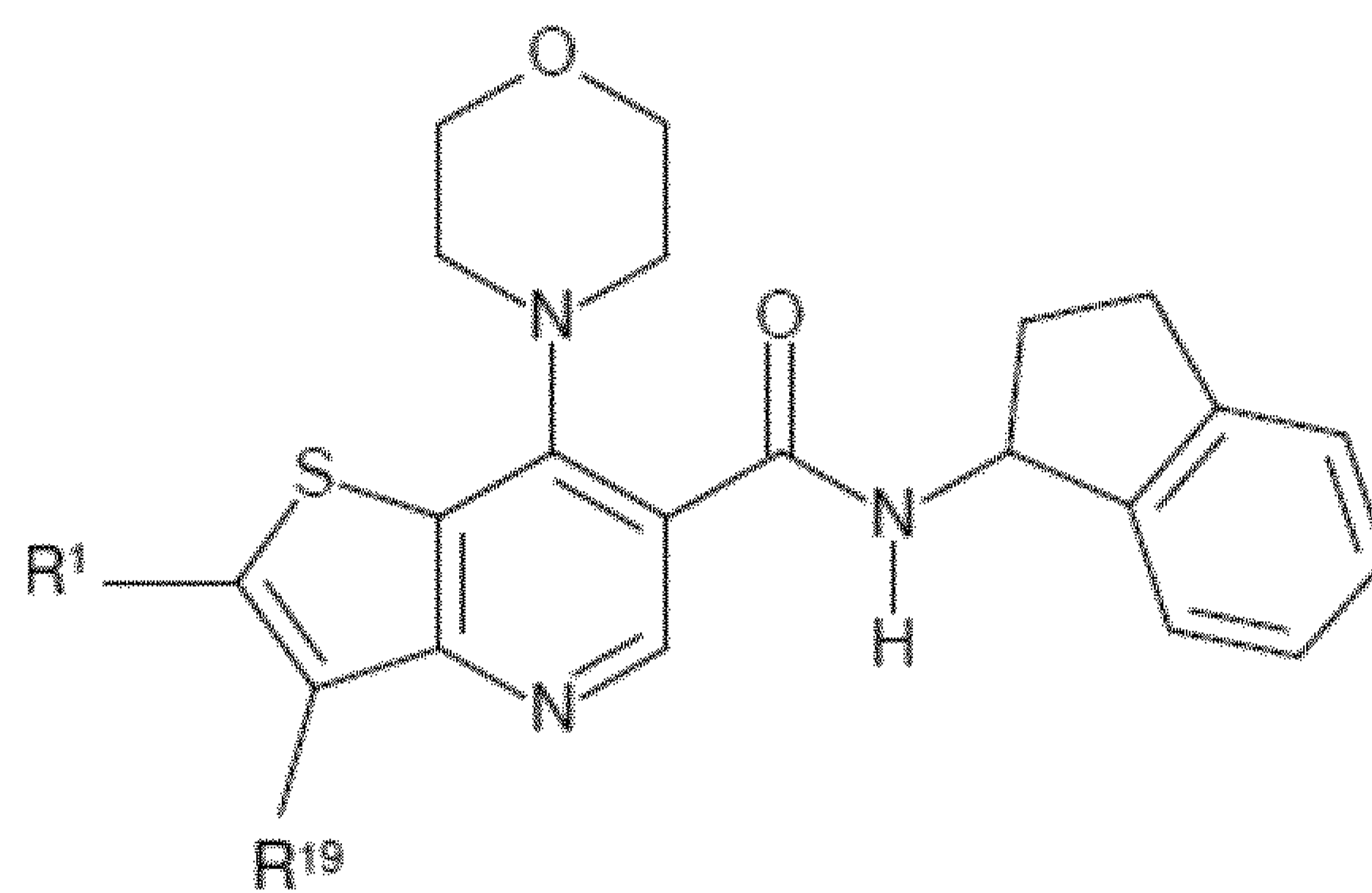
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwi), (Iwii), (Iwiii), (Iwiv), (Iwv), (Iwvi), (Iwvii), (Iwviii), (Iwix), (Iwx), (Iwxi) or (Iwxii)



Formula (Iwi)

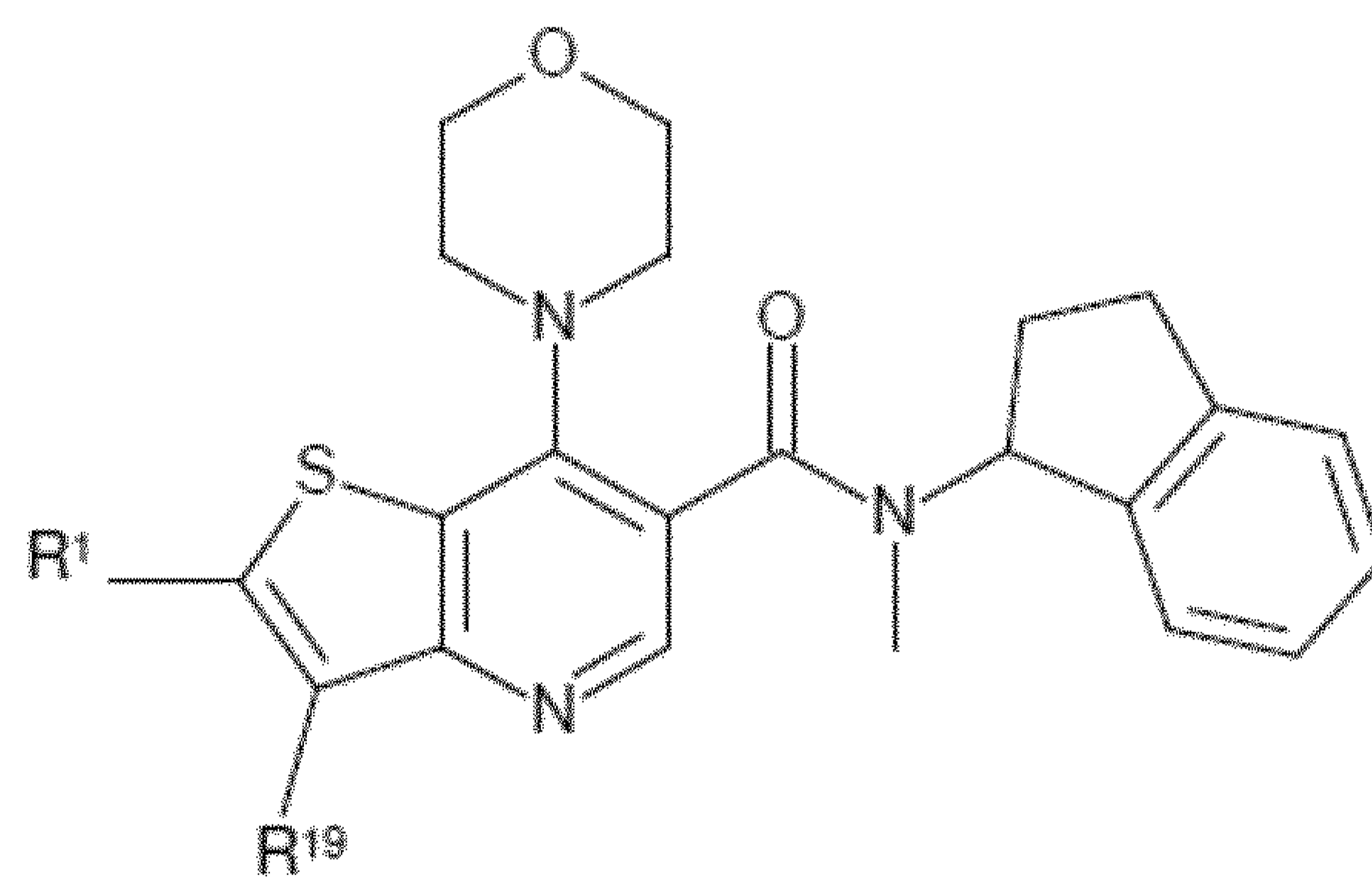


Formula (Iwii)

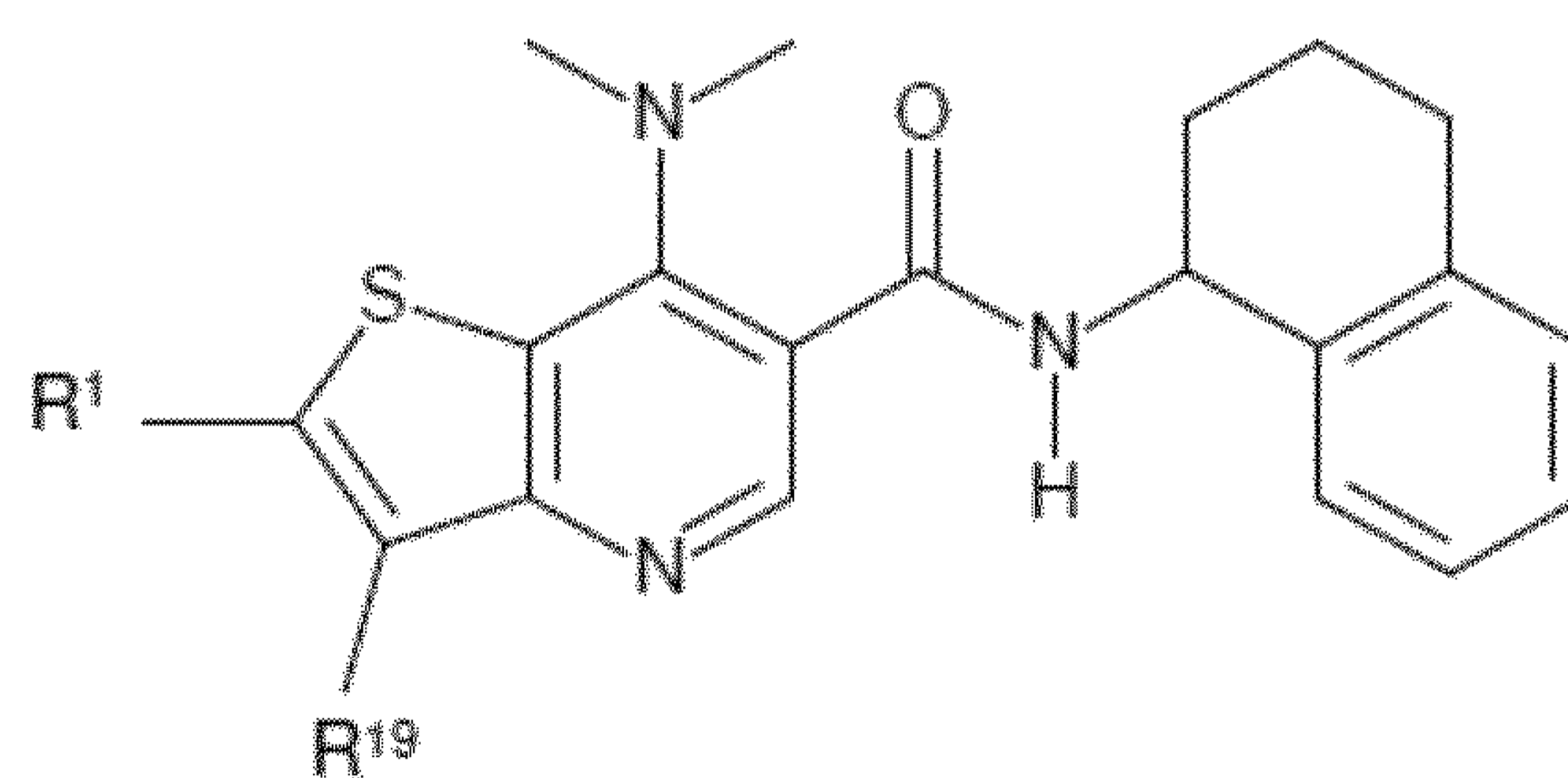


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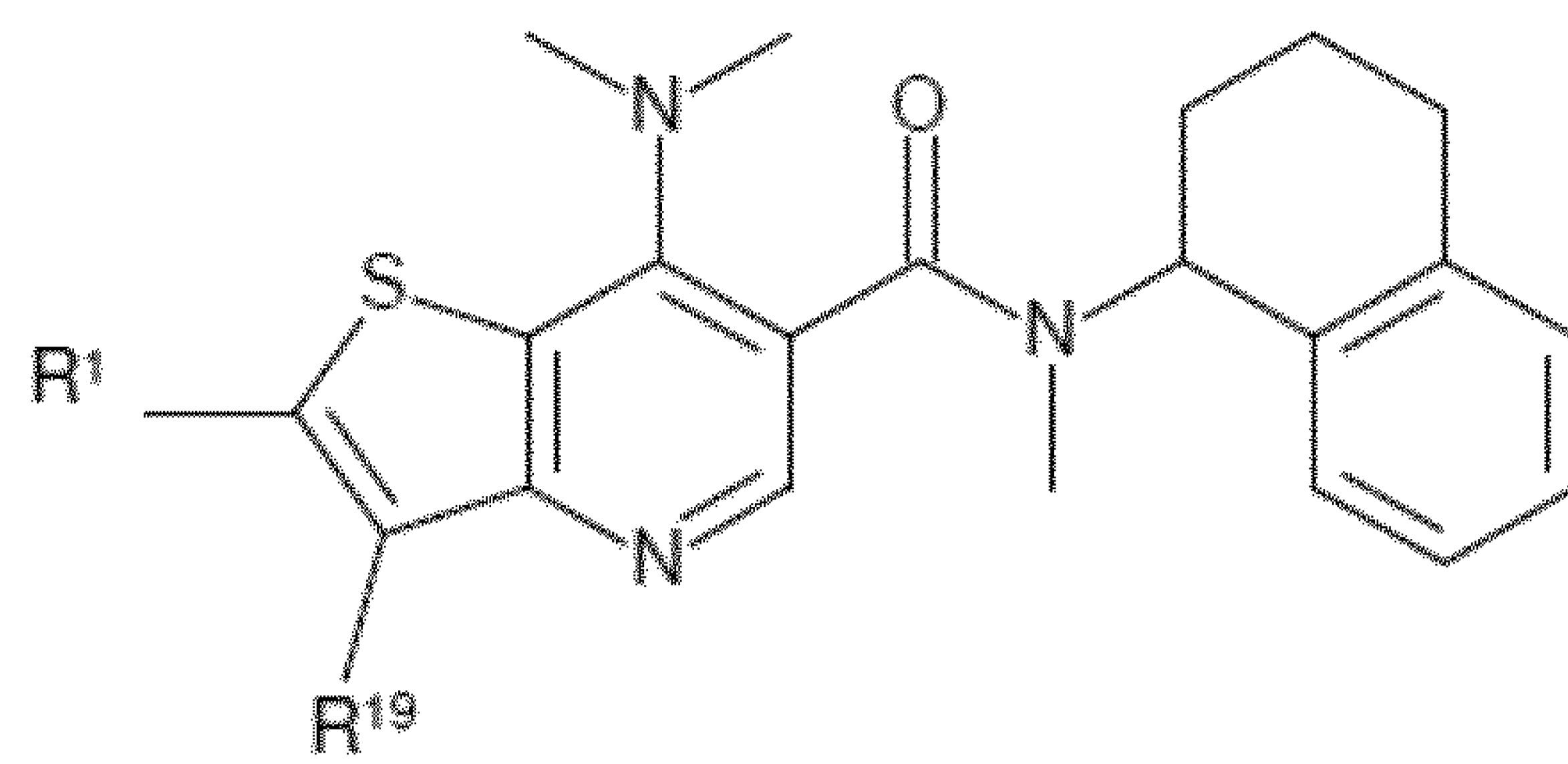
Formula (Iwiii)



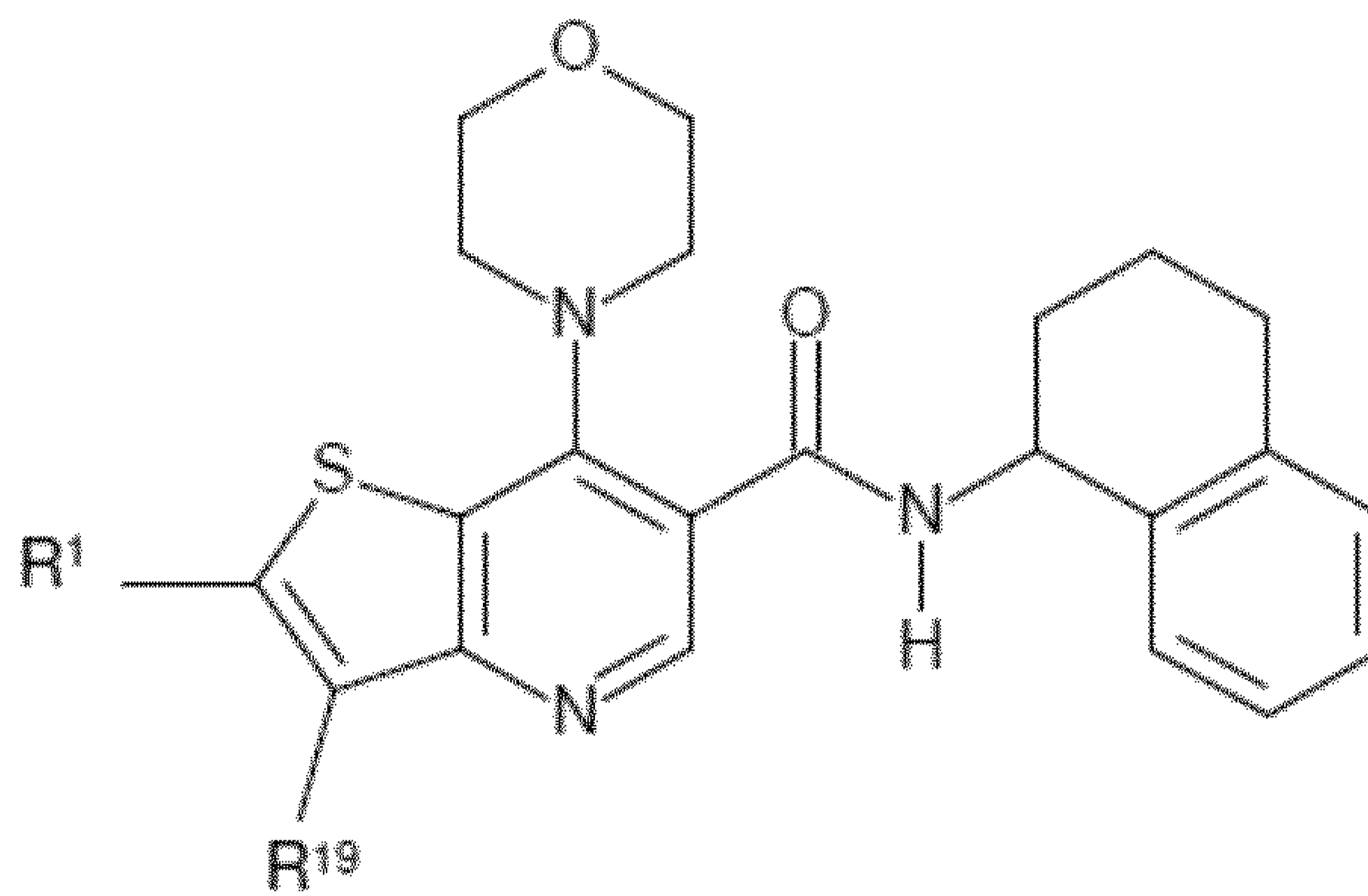
Formula (Iwiv)



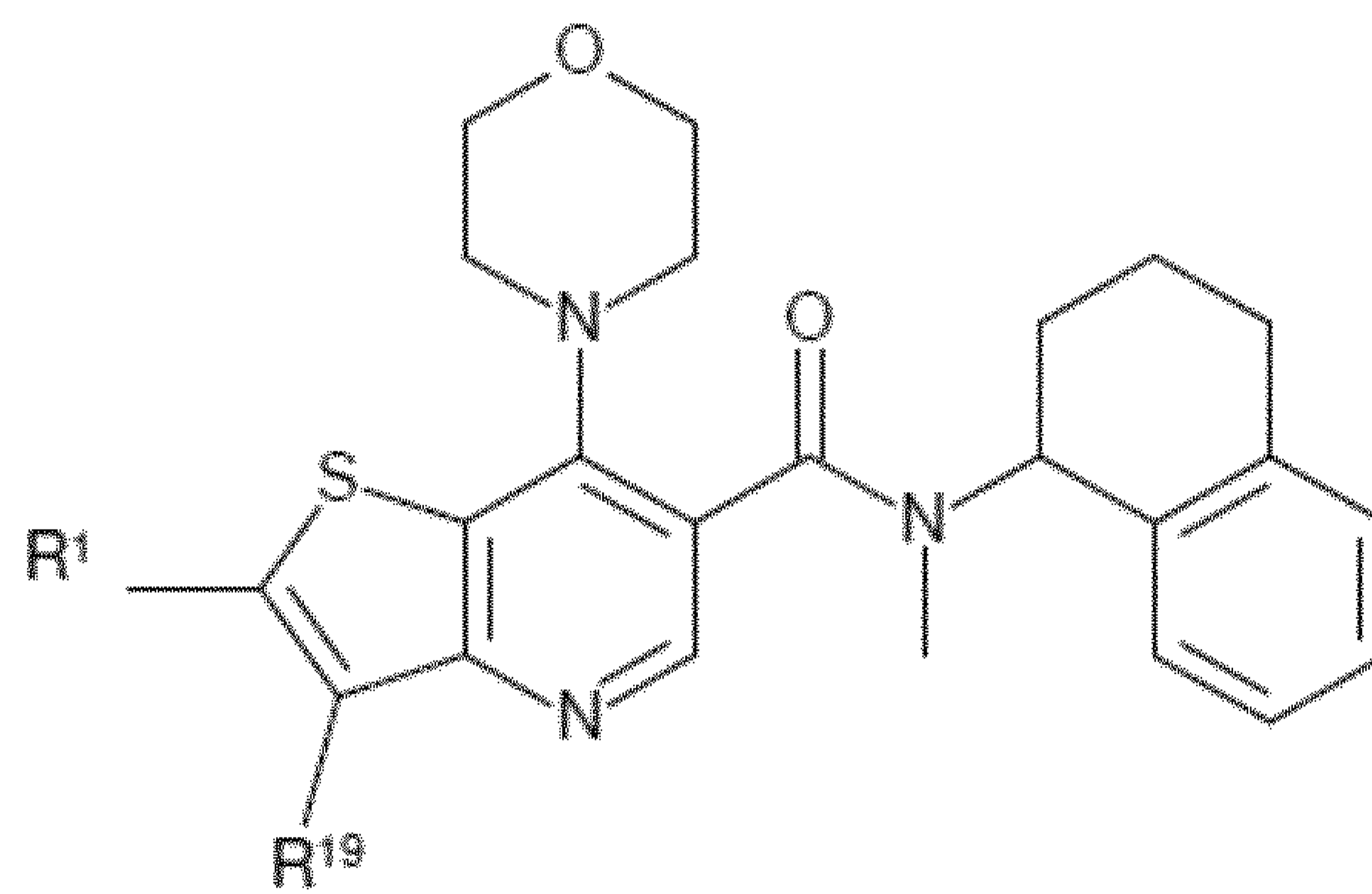
Formula (Iwv)



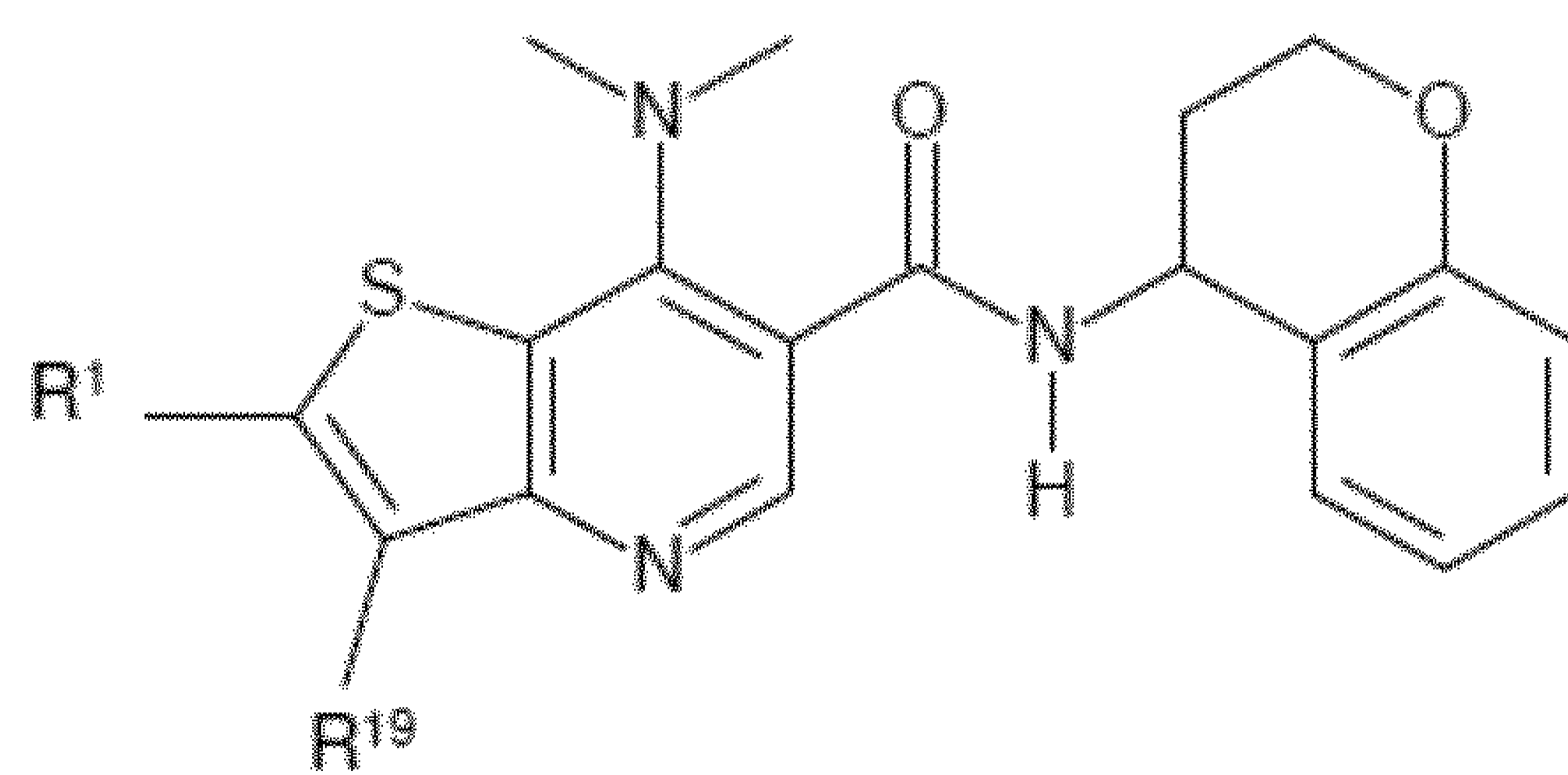
Formula (Iwvi)



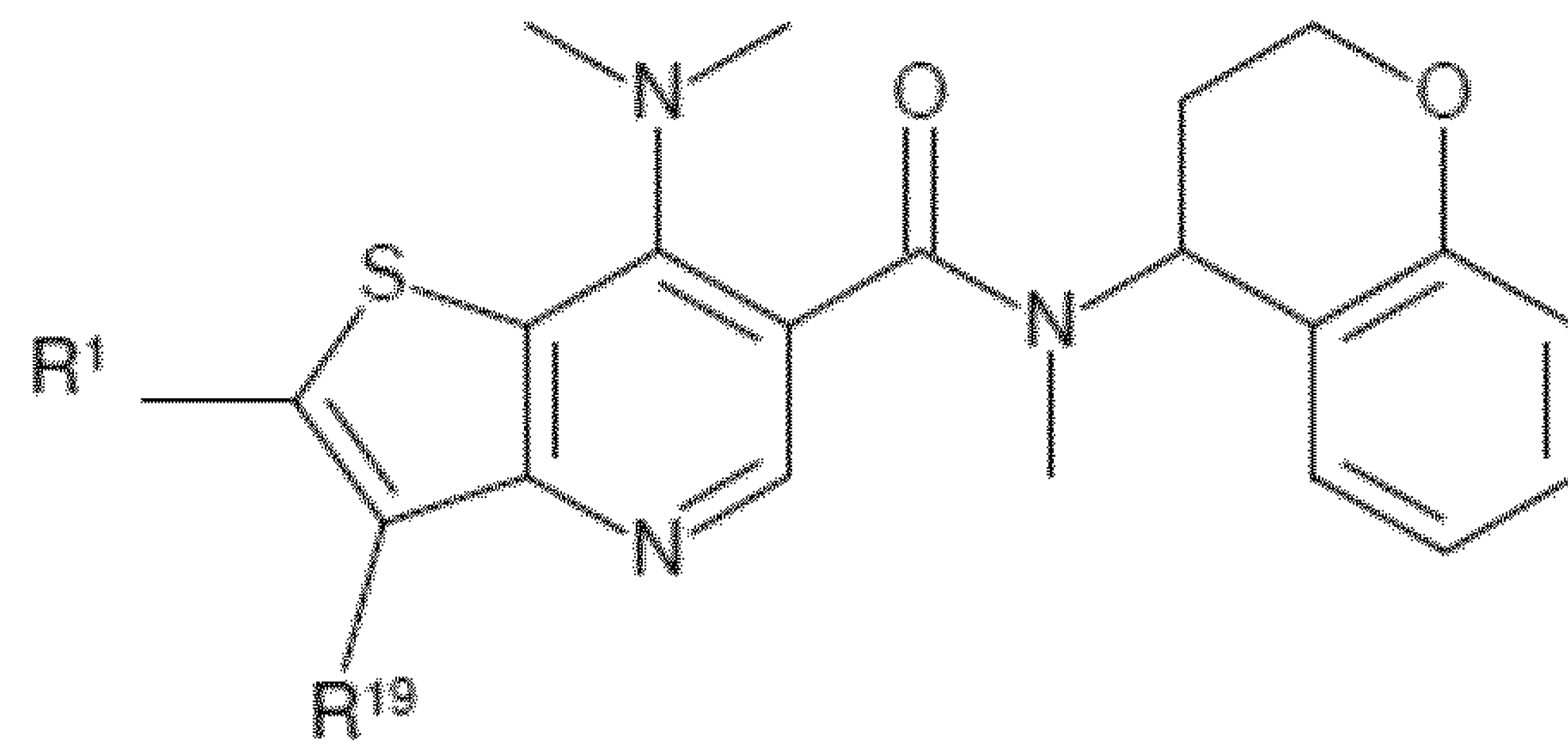
Formula (Iwvii)



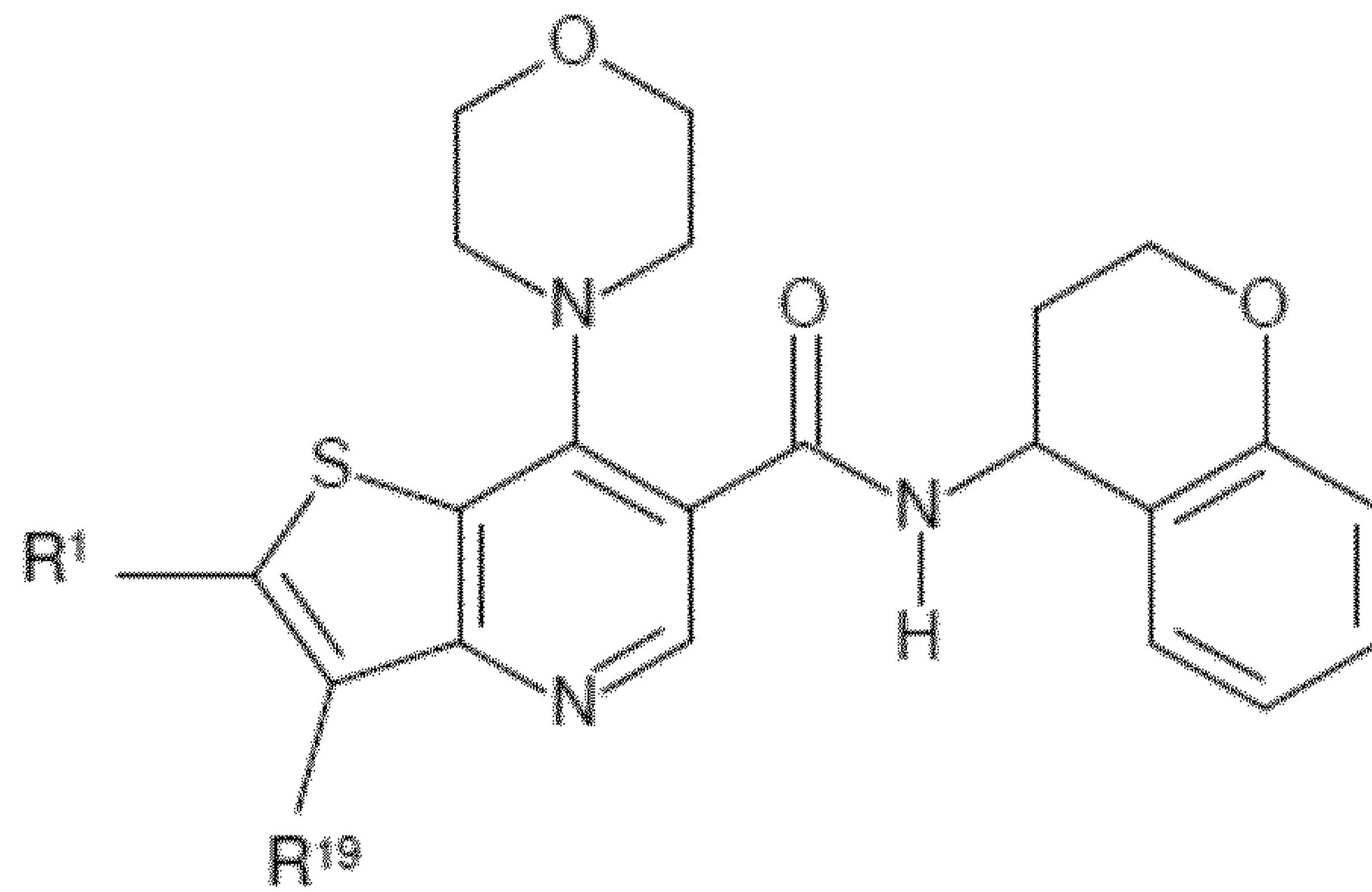
Formula (Iwviii)



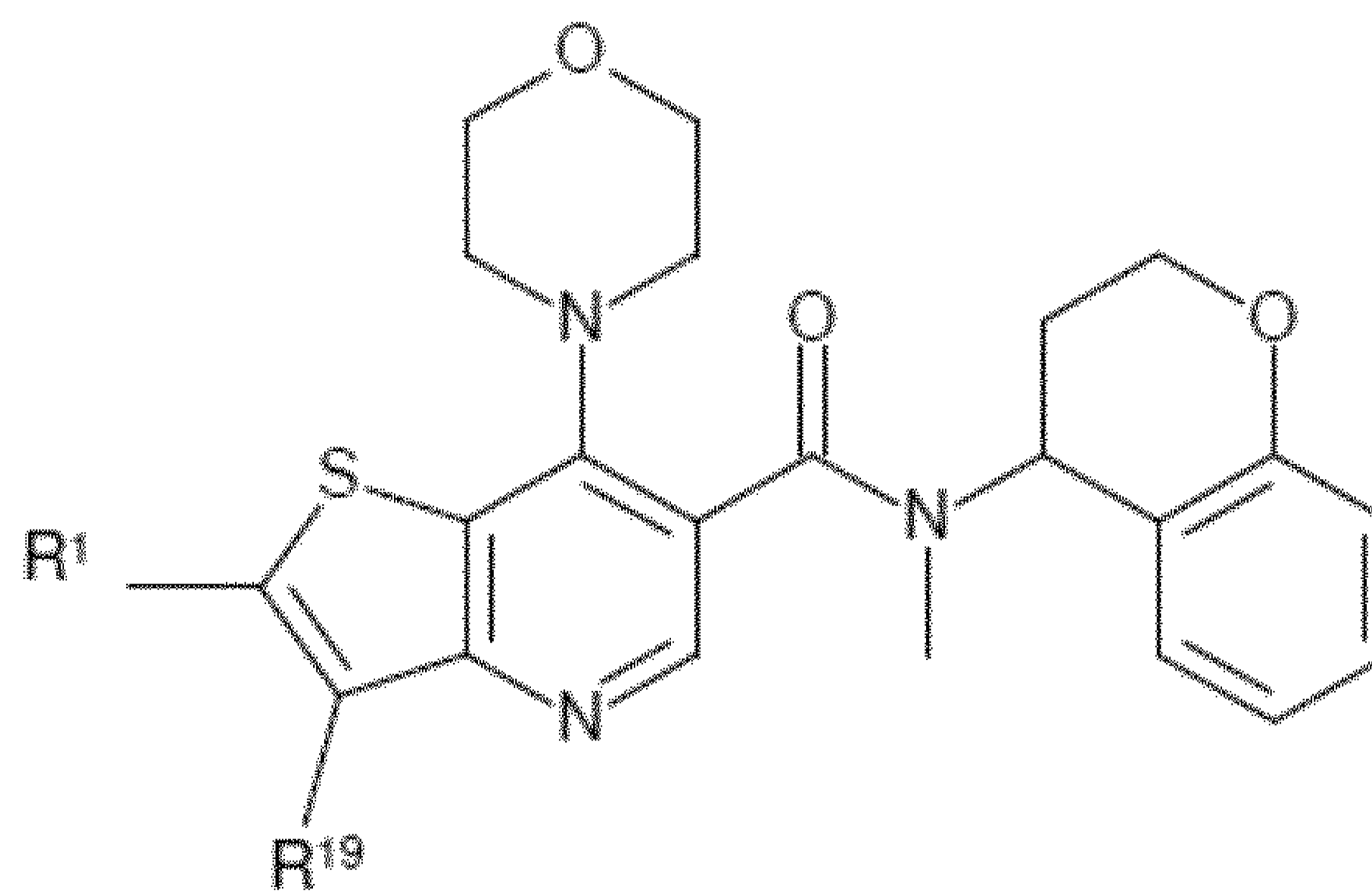
Formula (Iwix)



Formula (Iwx)



Formula (Iwxi)



Formula (Iwxii)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹ and R¹⁹ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Iwii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwiv),
 15 preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwv), preferably in form of the (*S*)-enantiomer.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwviii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwix), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwx), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwxi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwxii), preferably in form of the (*S*)-enantiomer.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, NR^8R^9 , $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 4 to 10-membered heterocyclyl or C_{1-6} -alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{3-10} -cycloalkyl, 5 to 10-membered heterocyclyl, C_{1-6} -alkoxy, halogen, cyano, hydroxy, oxo, $NR^{8'}R^{9'}$, $C(=O)OR^{10'}$ and $C(=O)NR^{11'}R^{12'}$,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the

N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

- 5 R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,
 R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,
 R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,
 and

- 10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

- 15 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

- 20 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

- 25 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

10 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

20 R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof

5 R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

20 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl, 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

and

25 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

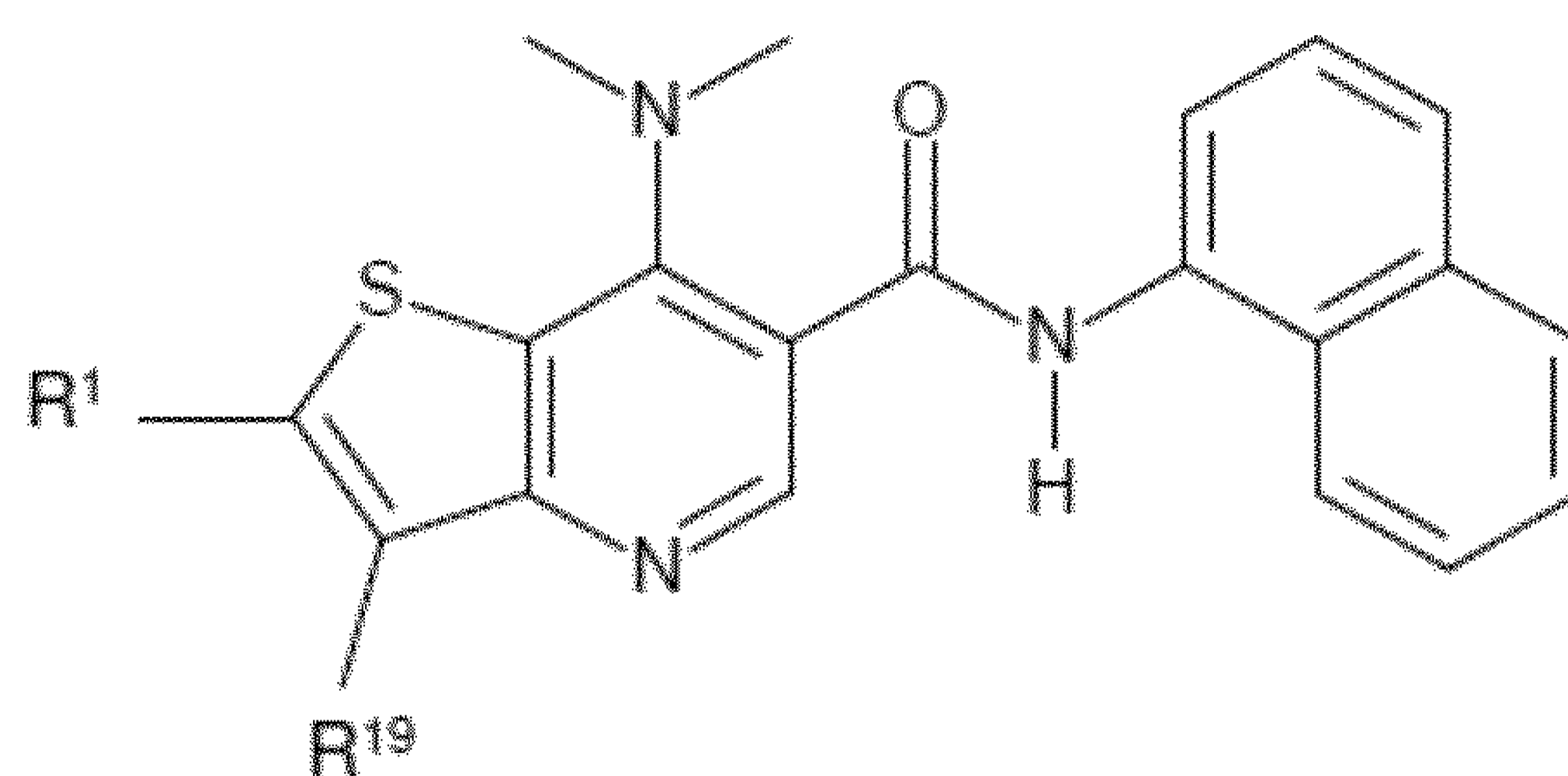
A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

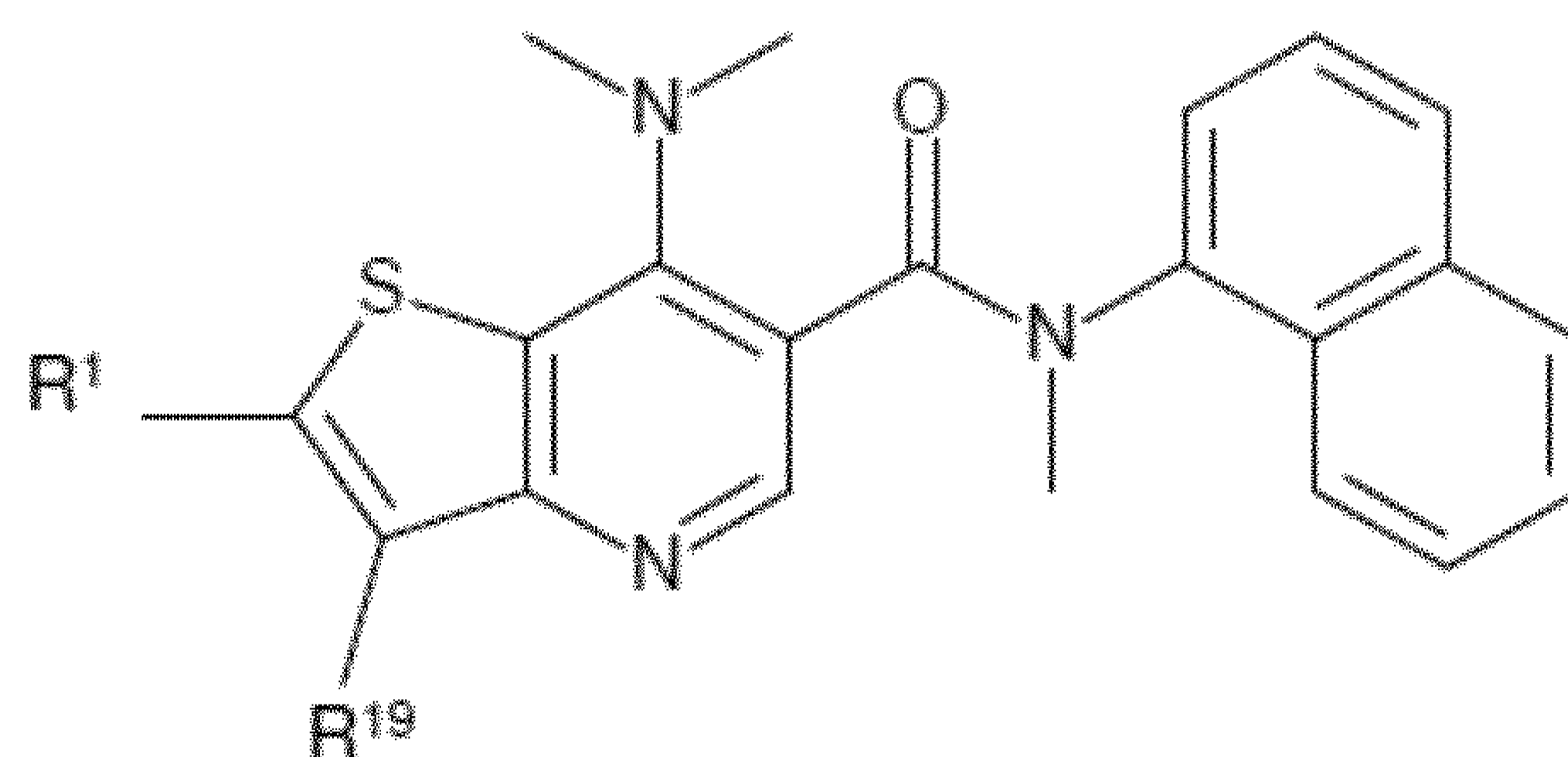
and

5 R²⁵ is hydrogen or methyl, more preferably hydrogen.

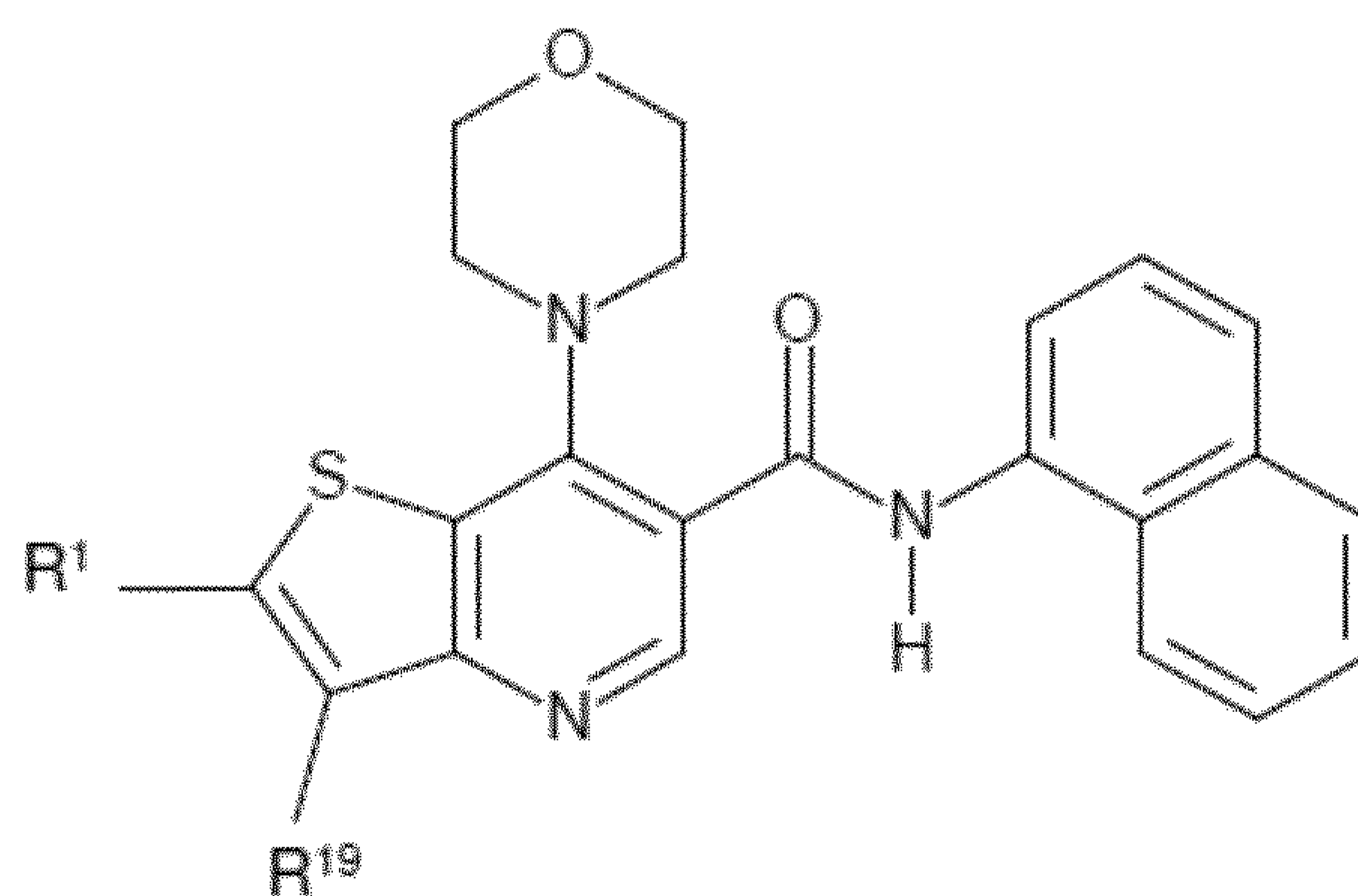
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iwxiii), (Iwxiv), (Iwxv), (Iwxvi), (Iwxvii), (Iwxviii), (Iwxix) or (Iwxx)



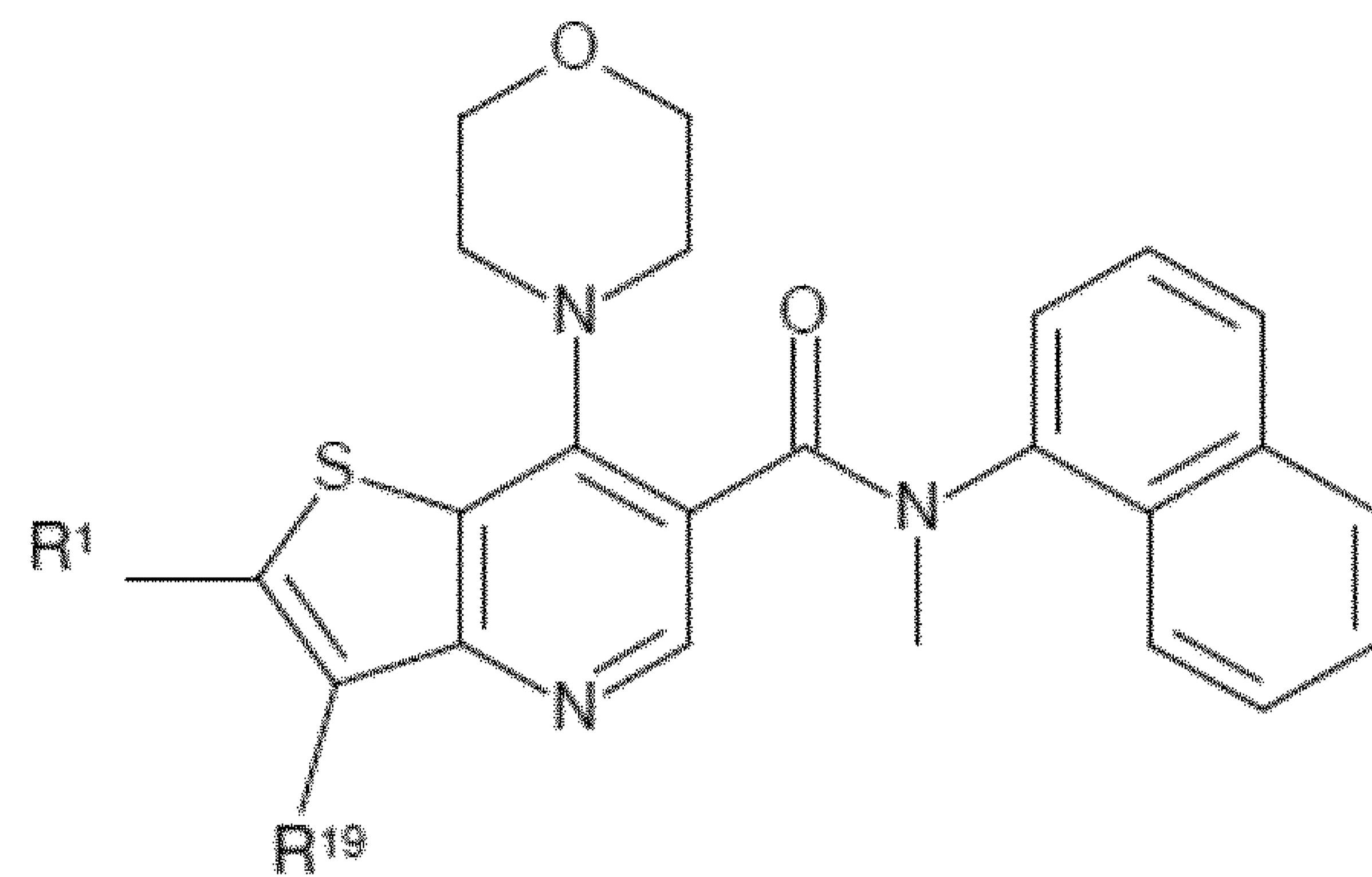
Formula (Iwxiii)



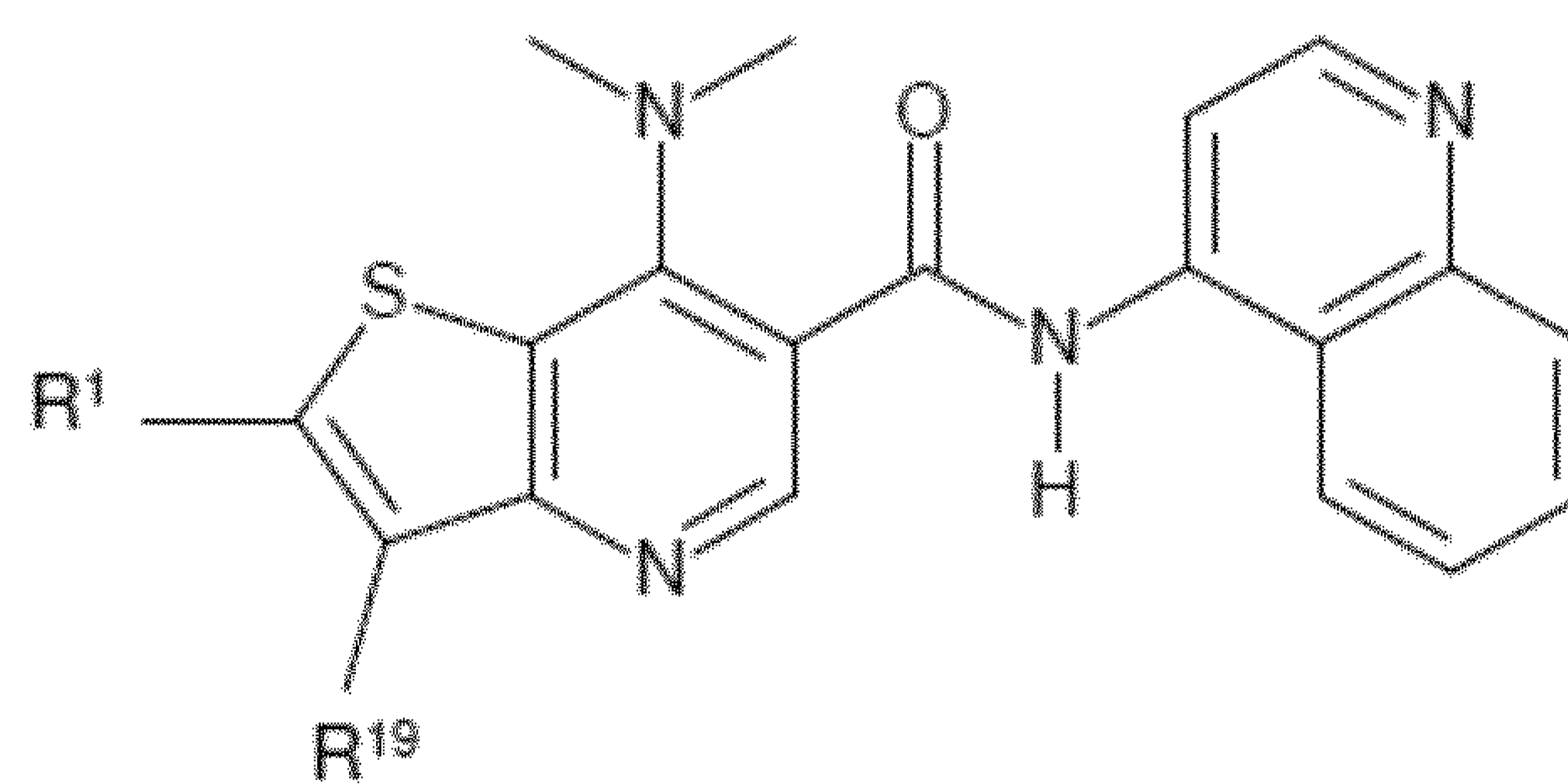
Formula (Iwxiv)



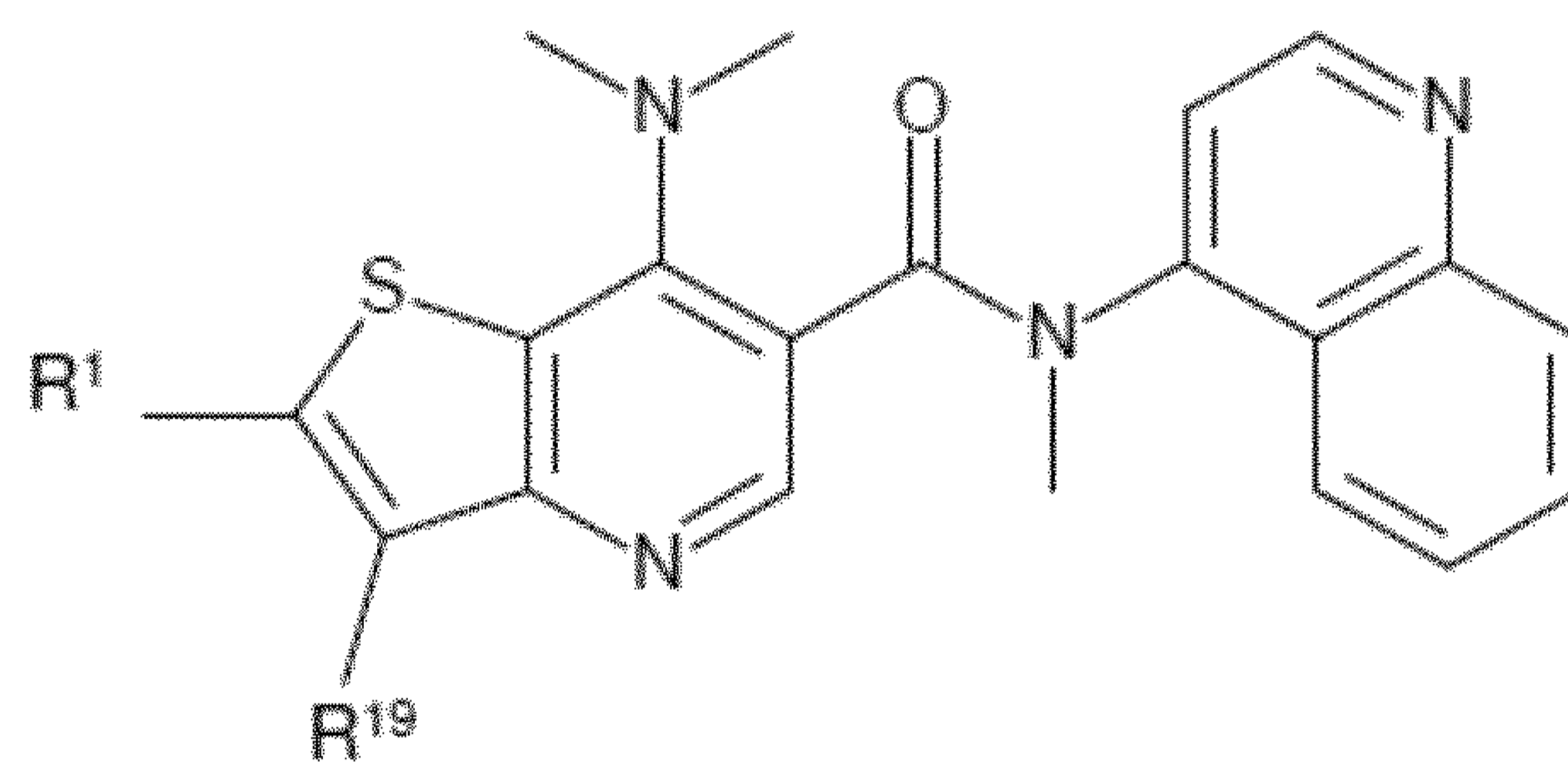
Formula (Iwxv)



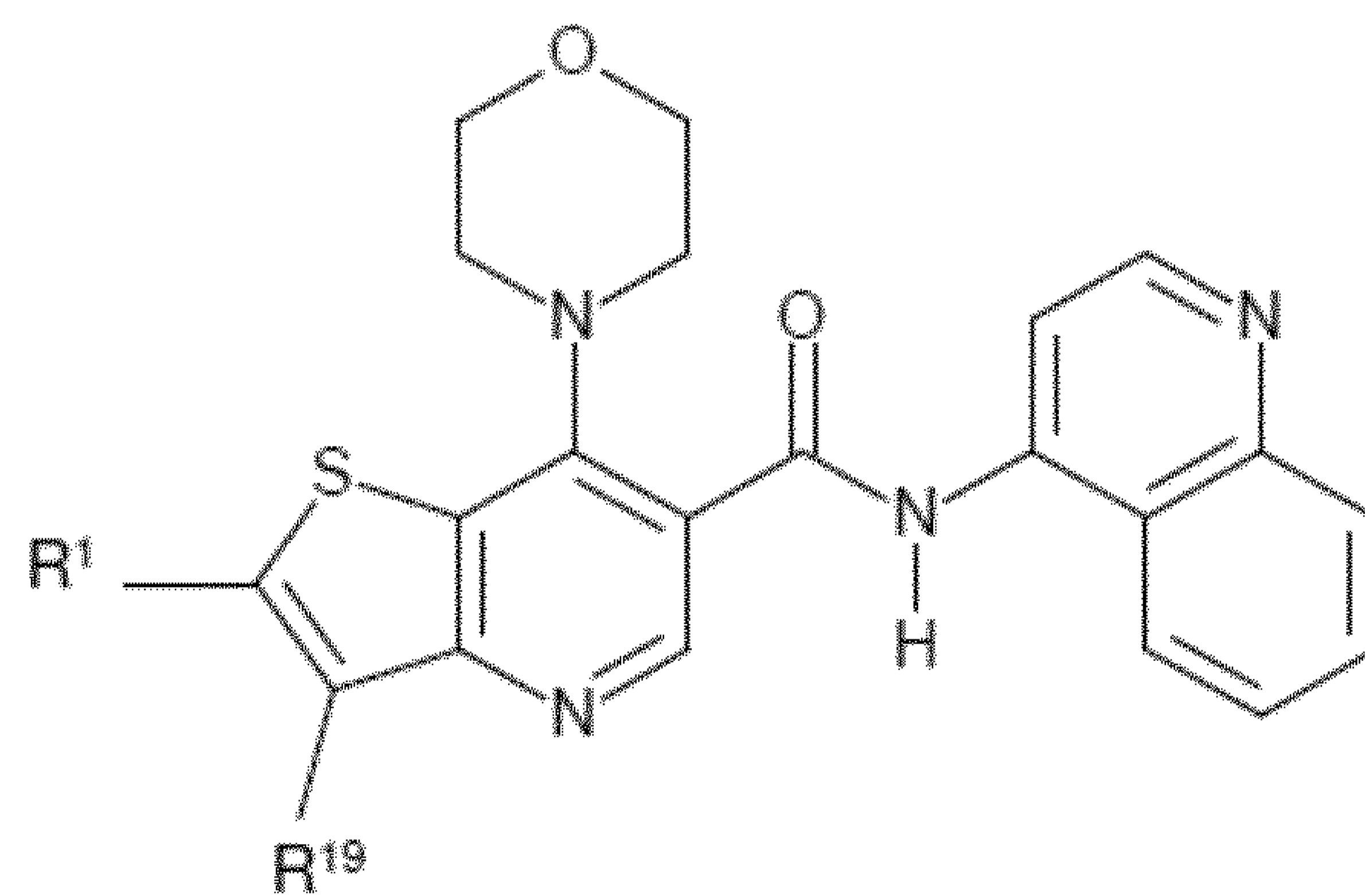
Formula (Iwxvi)



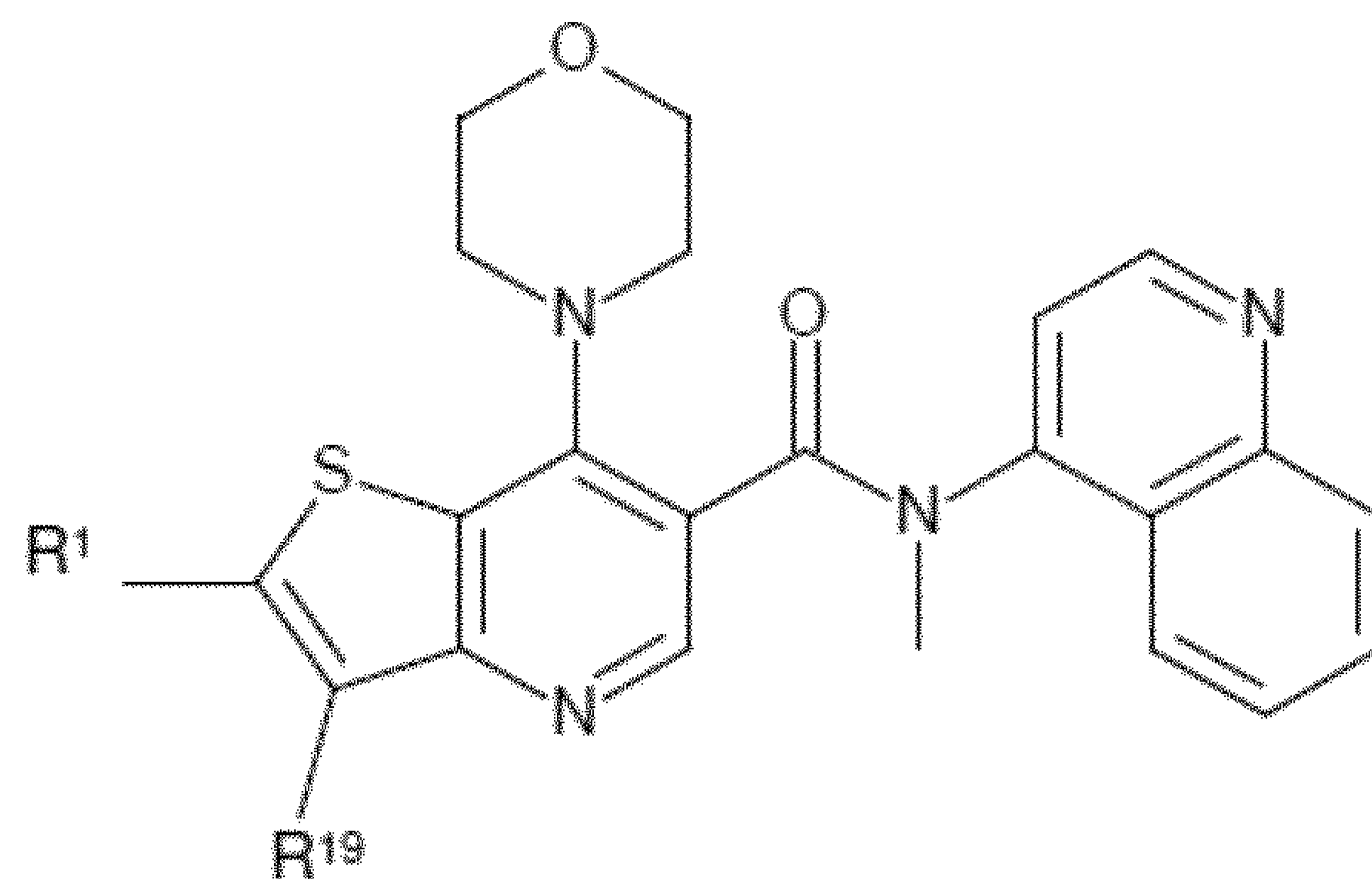
Formula (Iwxvii)



Formula (Iwxviii)



Formula (Iwxix)



Formula (Iwxx)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures
 5 thereof, wherein R^1 and R^{19} are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to
 Formula (Iwxiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention
 and/or embodiments thereof, the compounds are according to Formula (Iwxiv), preferably in form
 of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the
 10 compounds are according to Formula (Iwxv), preferably in form of the (*S*)-enantiomer. In an
 embodiment of the invention and/or embodiments thereof, the compounds are according to
 Formula (Iwxvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention
 and/or embodiments thereof, the compounds are according to Formula (Iwxvii), preferably in form
 of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the
 15 compounds are according to Formula (Iwxviii), preferably in form of the (*S*)-enantiomer. In an
 embodiment of the invention and/or embodiments thereof, the compounds are according to
 Formula (Iwxvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention
 and/or embodiments thereof, the compounds are according to Formula (Iwxix), preferably in form
 of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the
 20 compounds are according to Formula (Iwxx), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof,
 wherein R^7 , R^{19} and R^{25} are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

5 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4 to 10-membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl and 5 to 10-membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

15 wherein the C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)OR^{10''} and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

and

25 R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

5 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

10 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl,

and

R²⁵ is hydrogen or methyl.

20 In one embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl, C₁₋₃-alkoxy, hydroxy, NR⁸R⁹, SR¹⁰, SOR¹⁰ and SO₂R¹⁰,

25 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4 to 10-membered heterocyclyl or C₁₋₃-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₃-alkyl, 5 to 10-membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''};

10 R¹⁰ is independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen, methyl or ethyl,

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₃-alkyl, preferably from hydrogen,
15 methyl or ethyl,

and

R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen,

25 and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

Suitably R⁷ is independently selected from the group consisting of

15 methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino, hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl and 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl,

and

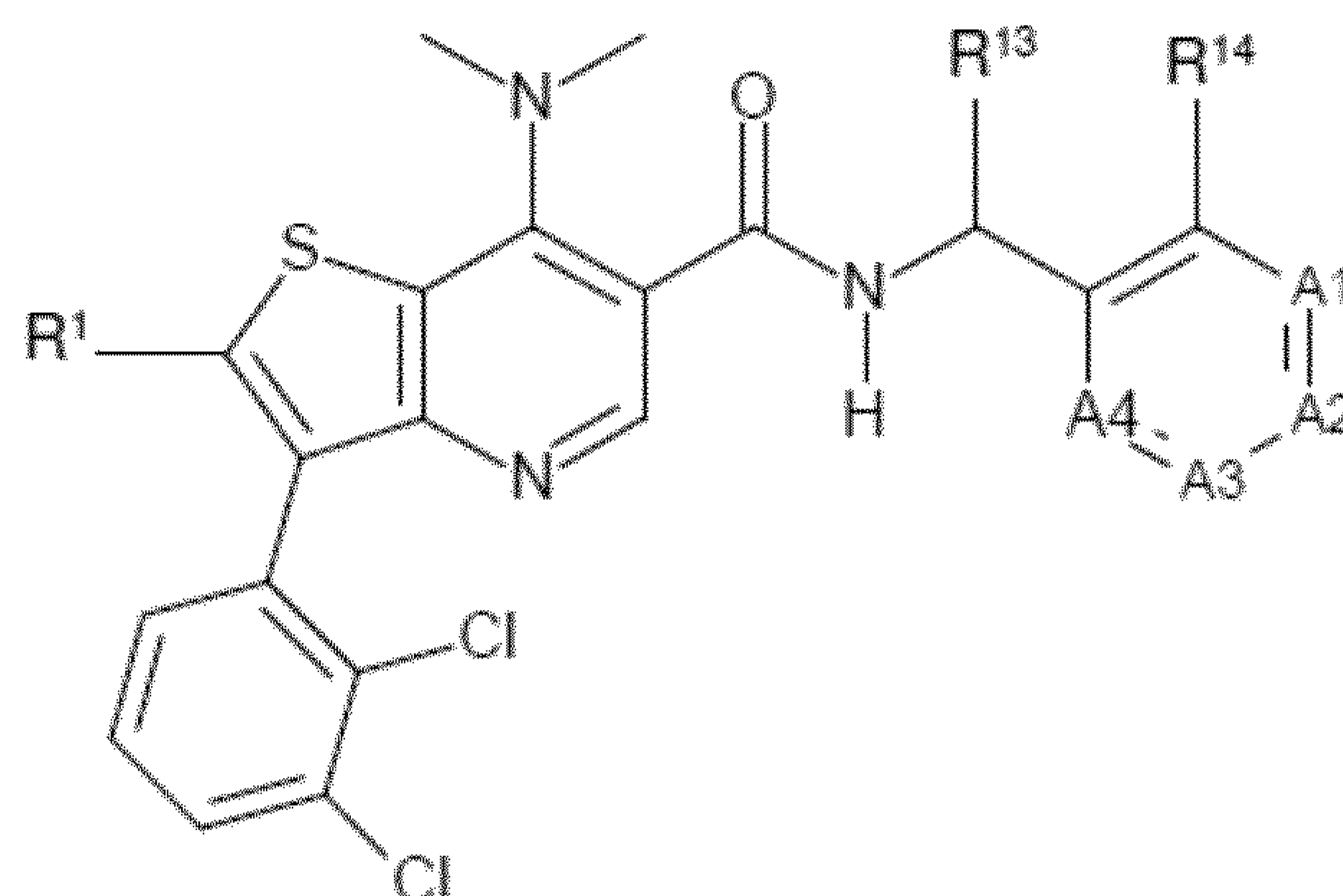
20 R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, and
 25 preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl,
 30 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl,

3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl,

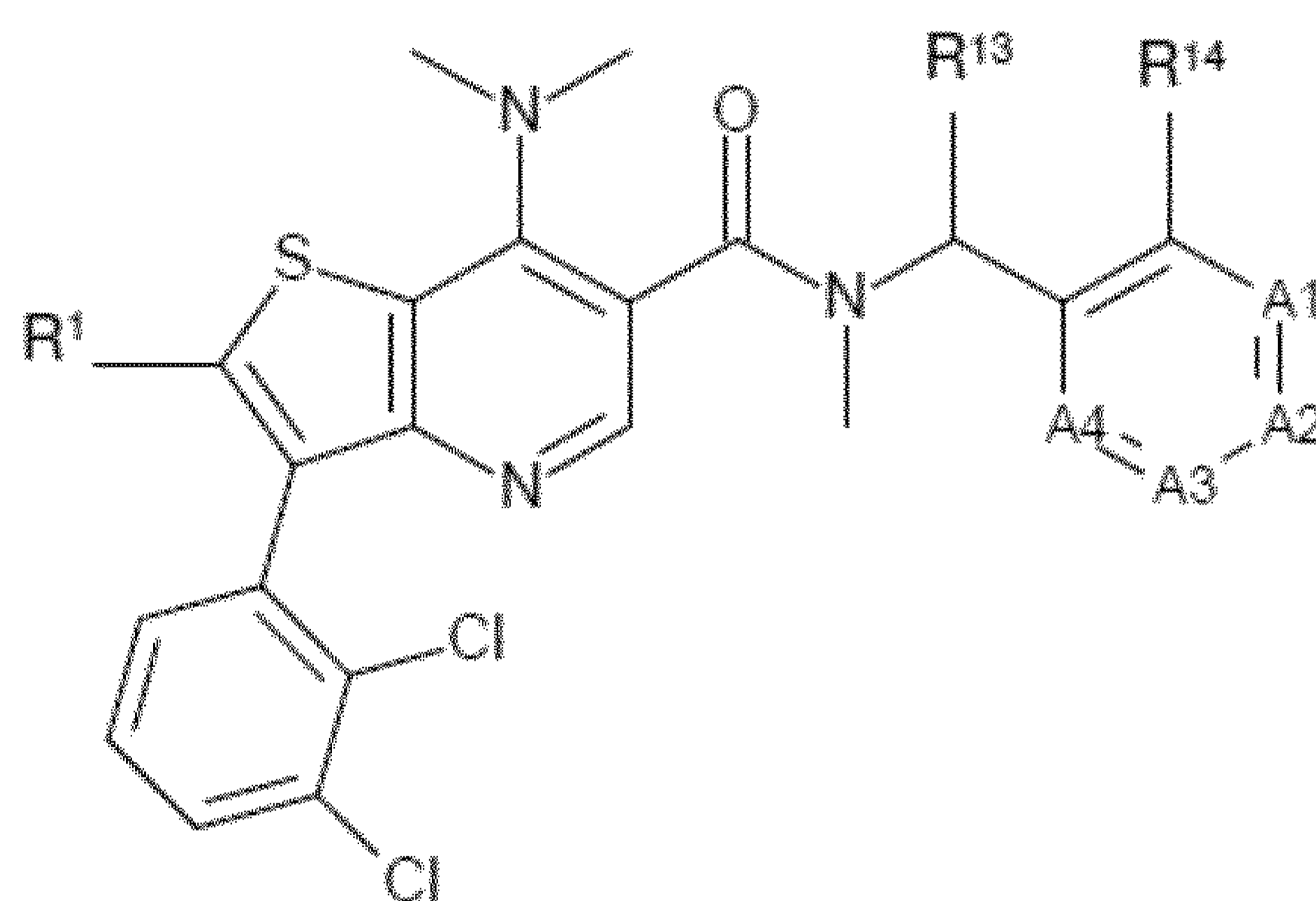
and

R²⁵ is hydrogen or methyl, more preferably hydrogen.

- 5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixi), (Ixi), (Ixi), (Ixiv), (I xv), (I xvi), (I xvii) or (I xviii),

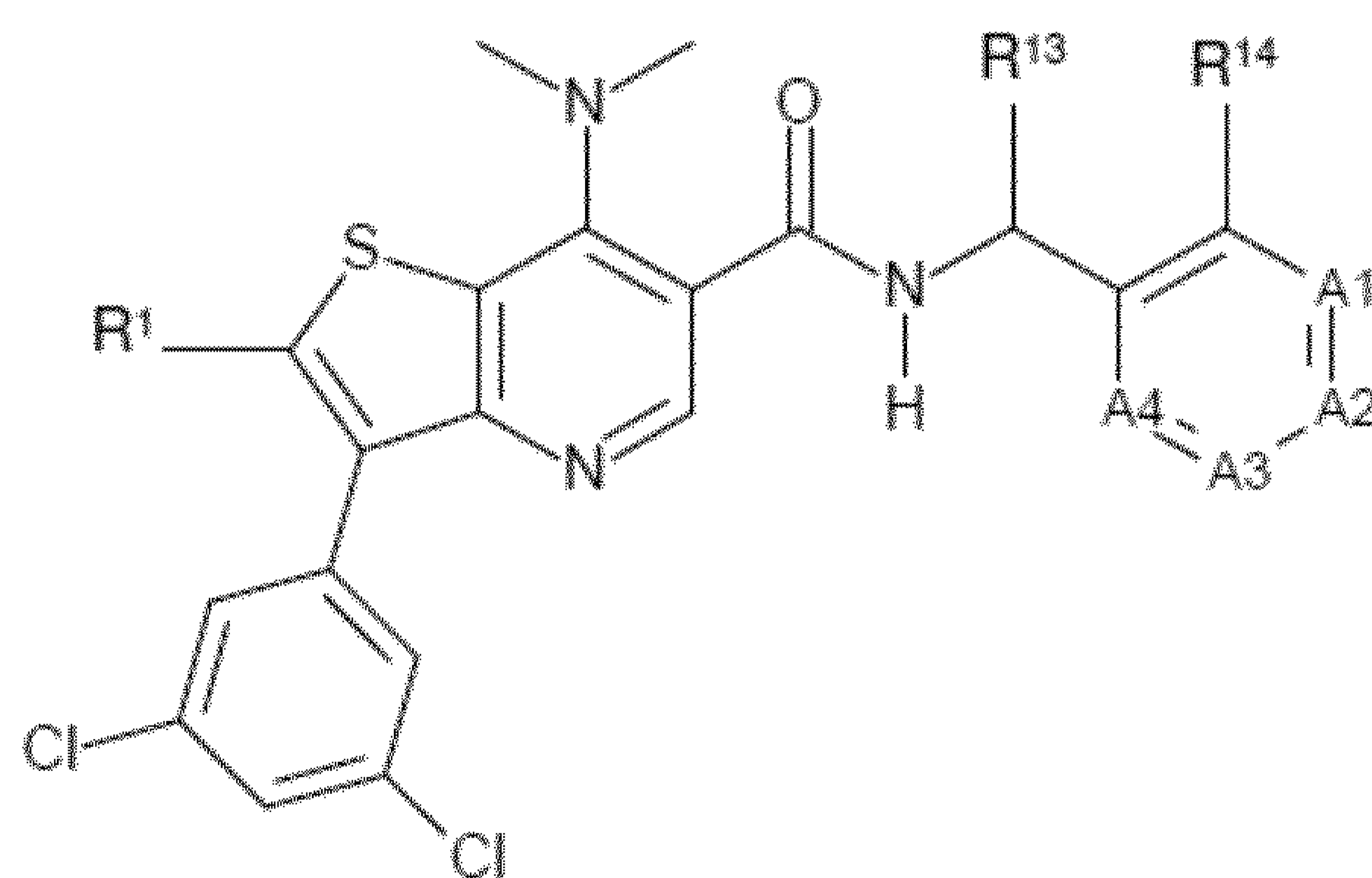


Formula (Ixi)

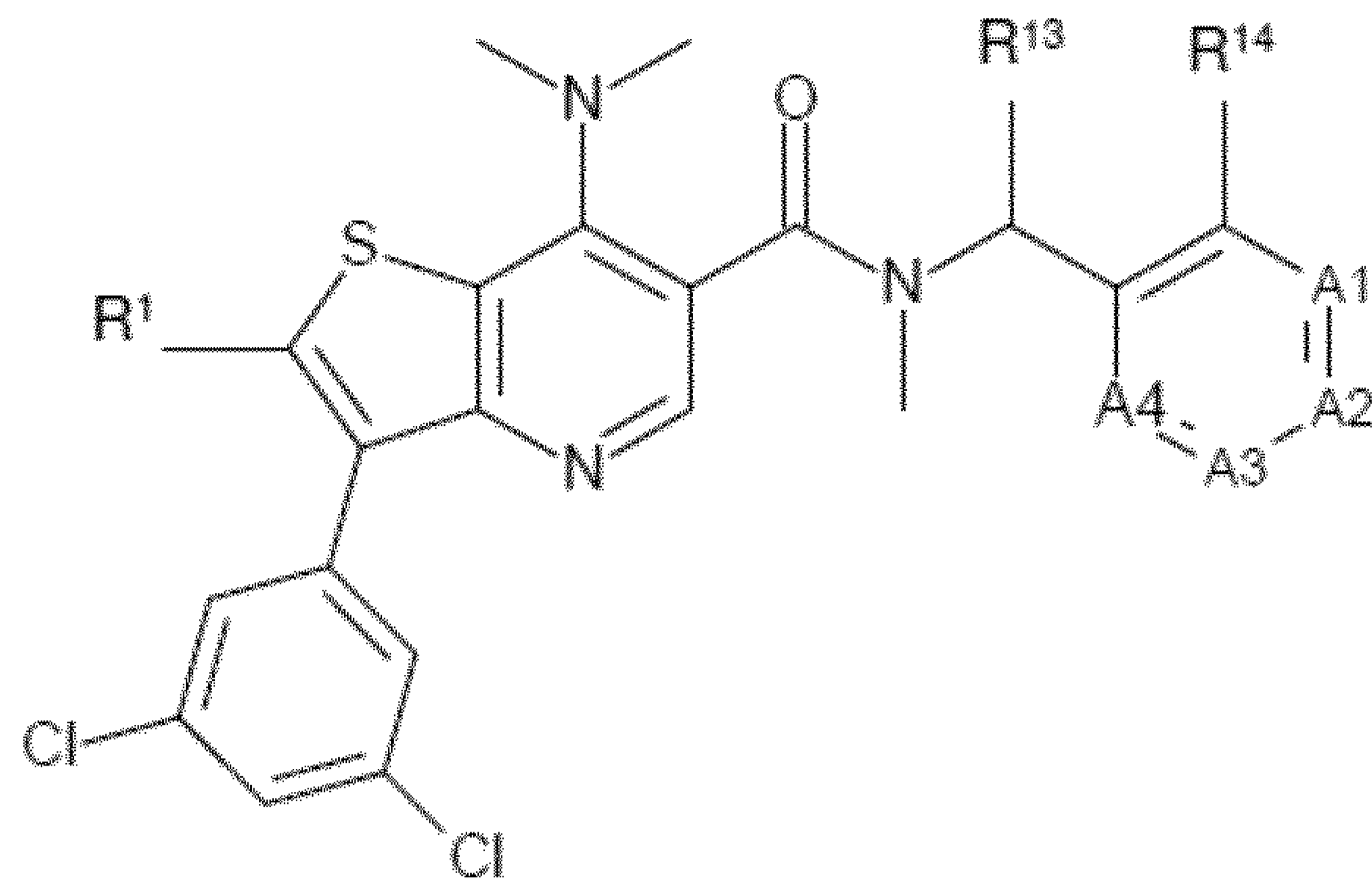


Formula (Ixi)

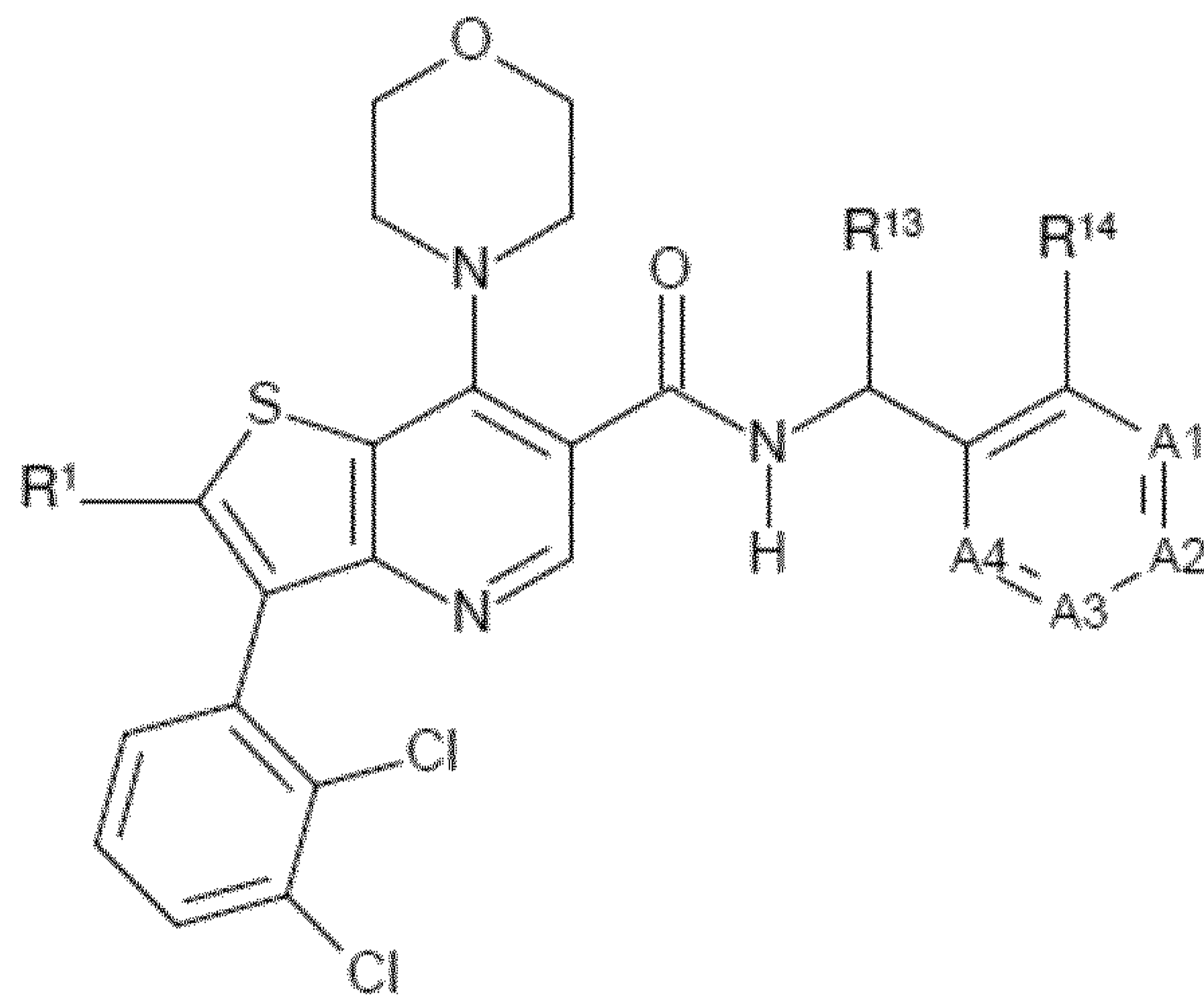
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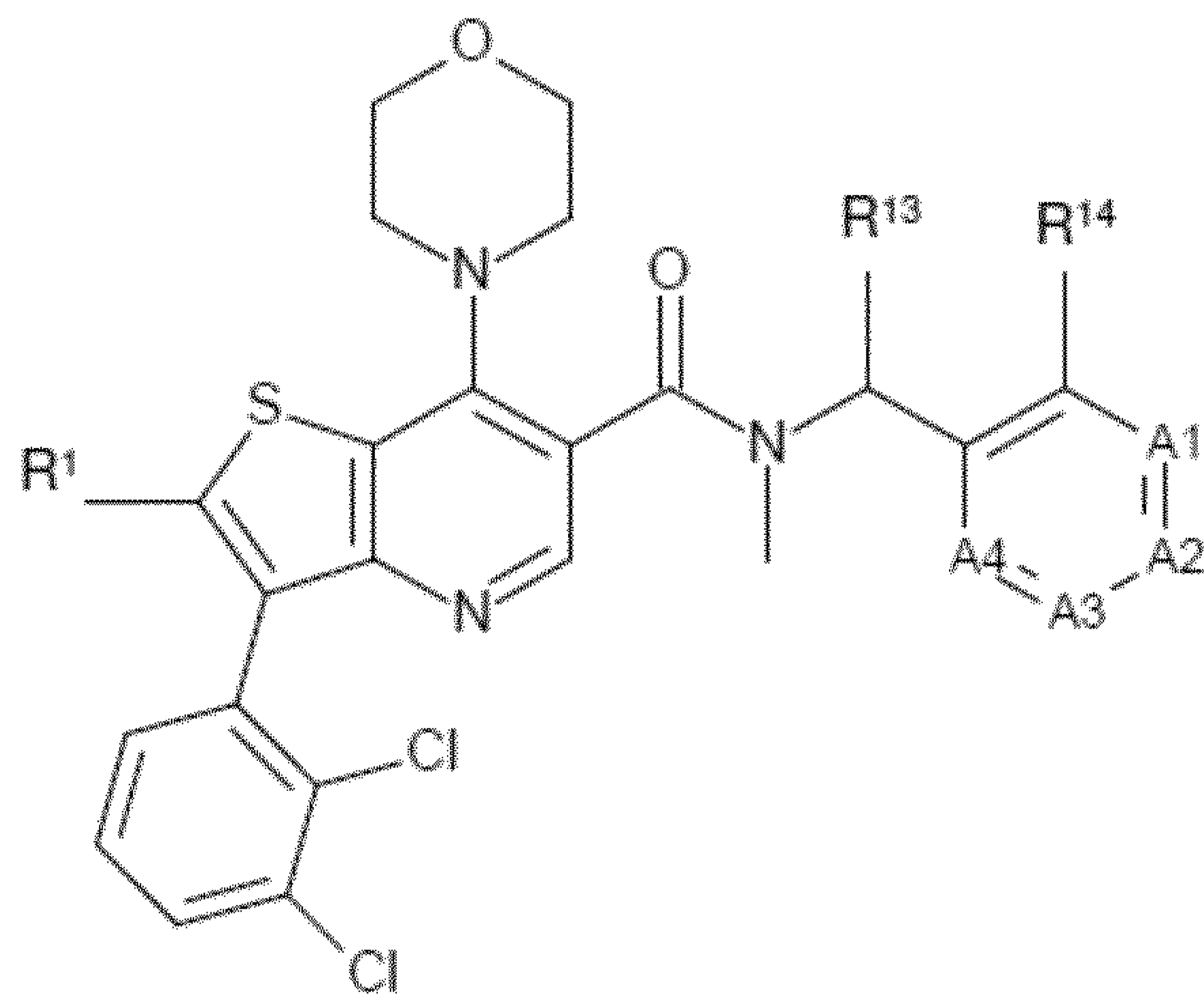
Formula (Ixi)



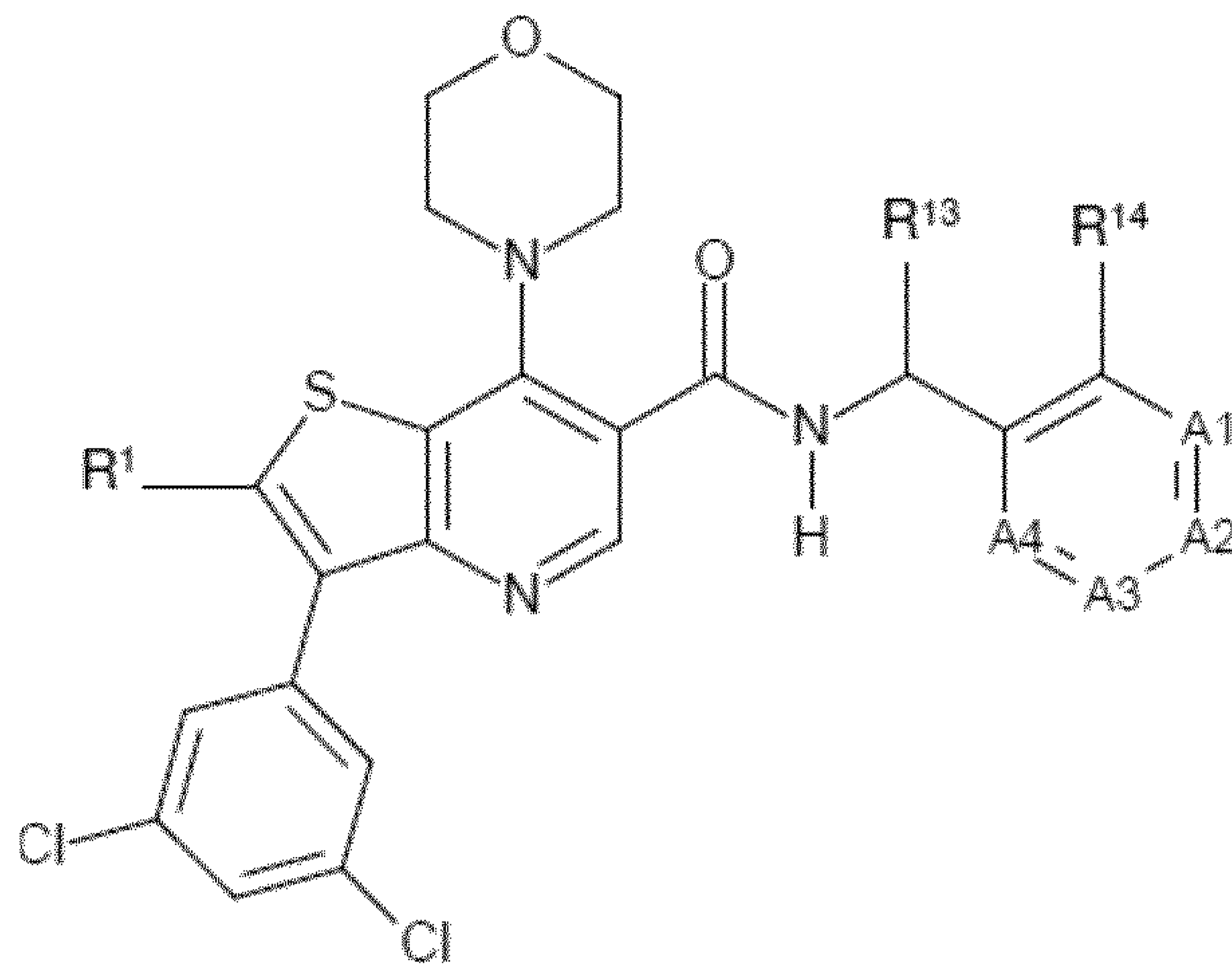
Formula (Ixiv)



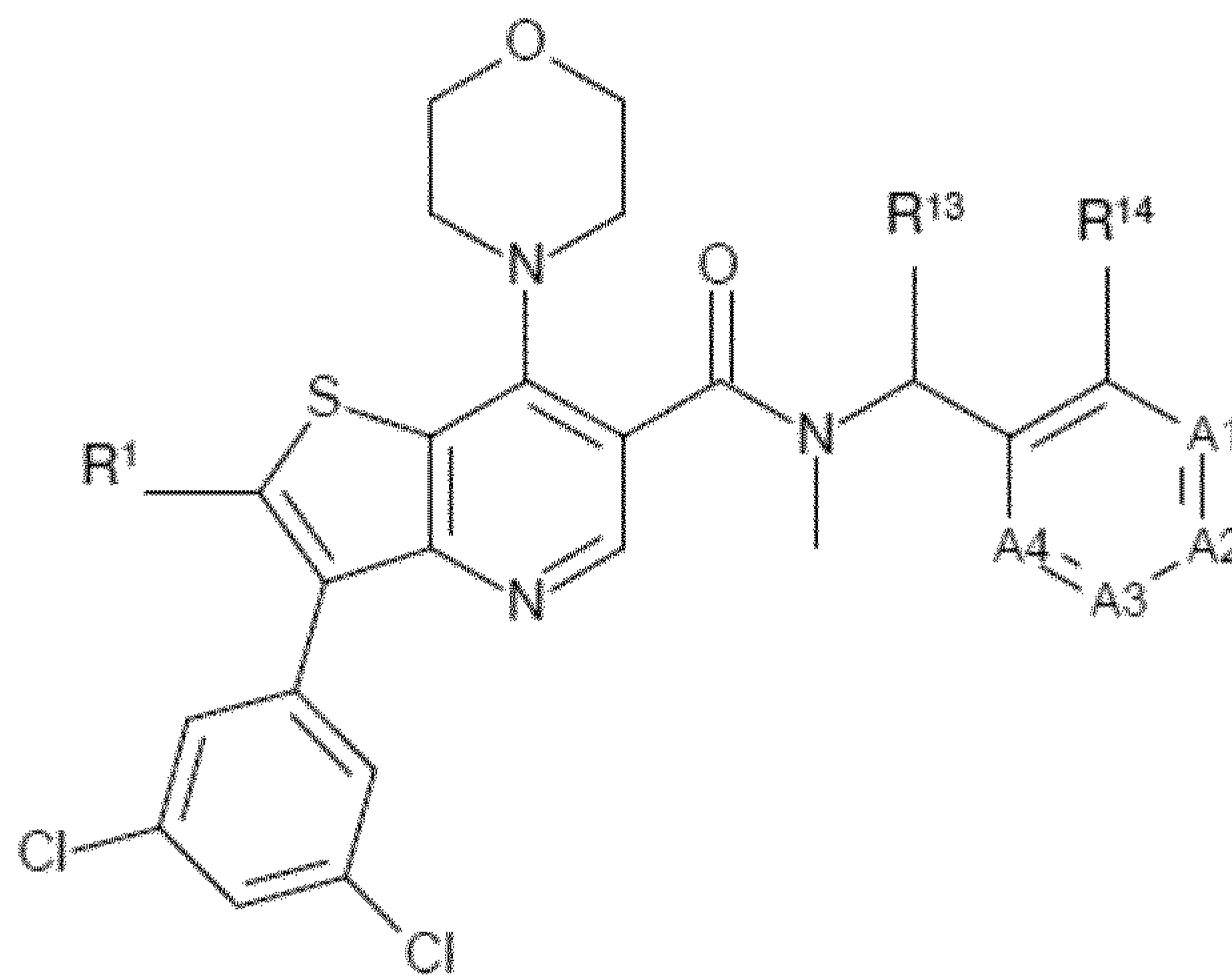
Formula (Ixv)



Formula (Ixvi)



Formula (I xvii)



Formula (I xviii)

5 or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 , R^{13} , R^{14} , A1, A2, A3, and A4 are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (I xi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (I xii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (I xiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (I xiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments
 15 thereof, the compounds are according to Formula (I xv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (I xvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or

embodiments thereof, the compounds are according to Formula (I xvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (I xviii), preferably in form of the (*S*)-enantiomer.

The invention provides a compound according to the invention and/or embodiments thereof,
5 wherein R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are defined as below.

Optionally, in an embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms
containing saturated ring, wherein the saturated ring is optionally substituted with one or more C_{1-3} -
alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
10 by -NH-, -O-, -S(O)-, -S(O)₂- or -S-,

A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or
 $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or
 $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

15 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or
 $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or
 $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

and

20 R^{19} is independently selected from the group consisting of

C_{6-10} -aryl and 5 to 10-membered heteroaryl,

wherein each C_{6-10} -aryl or 5 to 10-membered heteroaryl is optionally substituted with one
or more substituent(s) independently selected from the group consisting of

25 C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{1-6} -alkoxy, 5 to 10-membered heterocyclyl, C_{6-10} -aryl,
5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, $NR^{20}R^{21}$, $C(=O)OR^{22}$
and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl and C_{6-10} -aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

5 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

10 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl,

and

R²⁵ is hydrogen or methyl.

15 In one embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

20 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

25 R¹⁹ is a 5 to 10-membered heteroaryl

wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen,

5 and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof,

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally
10 replaced by -NH- or -O-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen or C₁₋₃ alkoxy,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen or C₁₋₃ alkoxy,

15 wherein none, one or two of A1, A2, A3 and A4 are N,

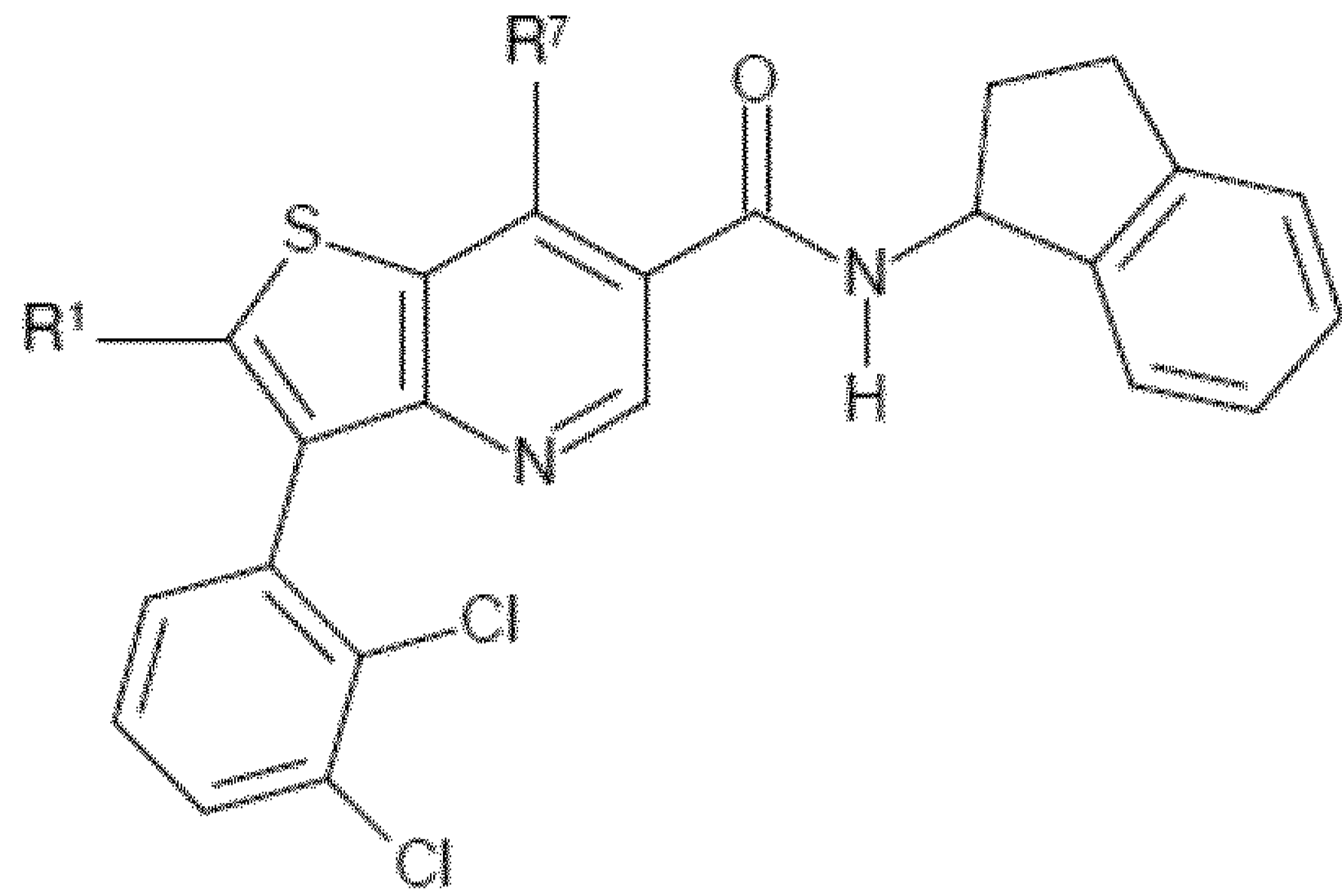
and

R¹⁹ is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl,

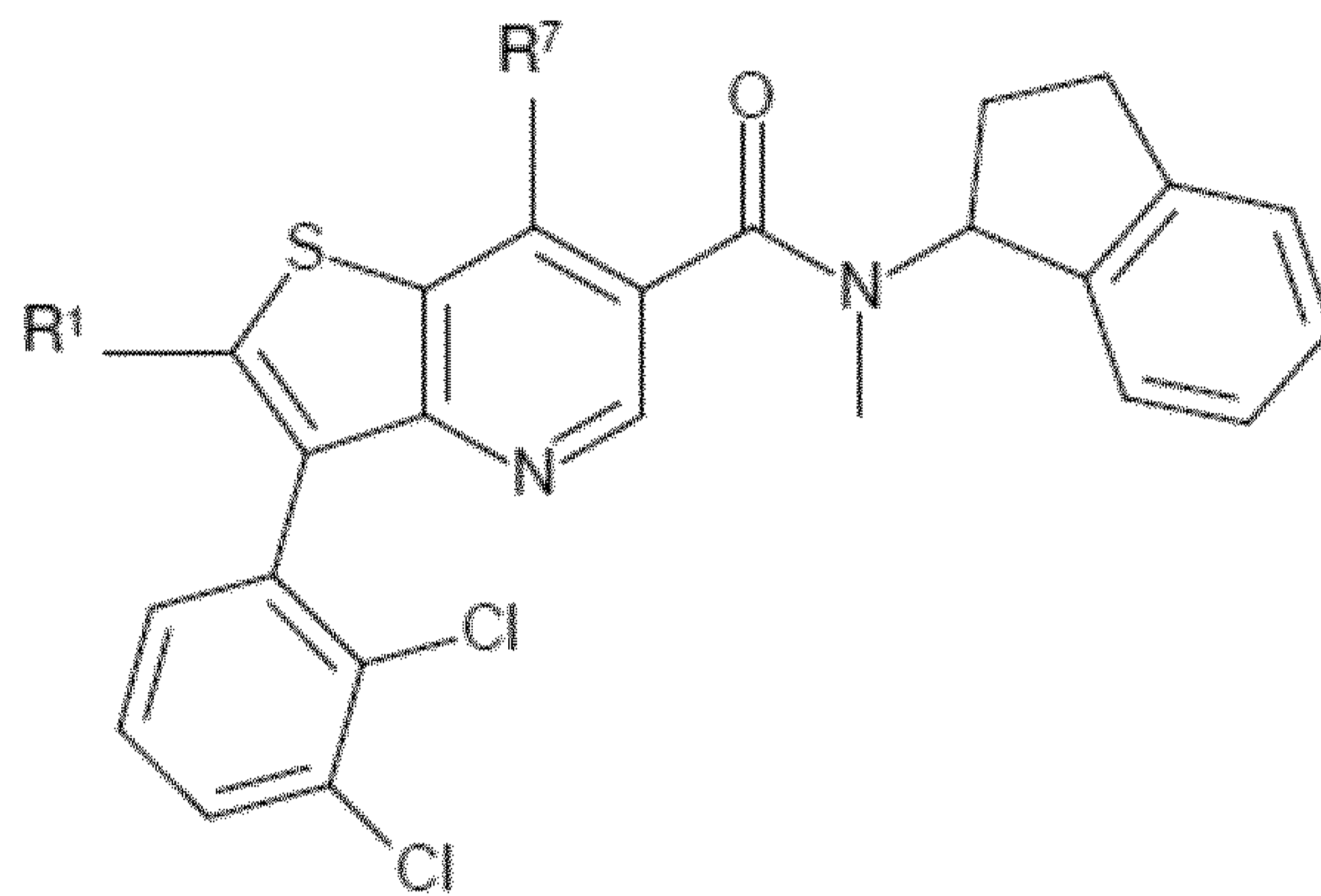
30 and

R²⁵ is hydrogen or methyl, more preferably hydrogen.

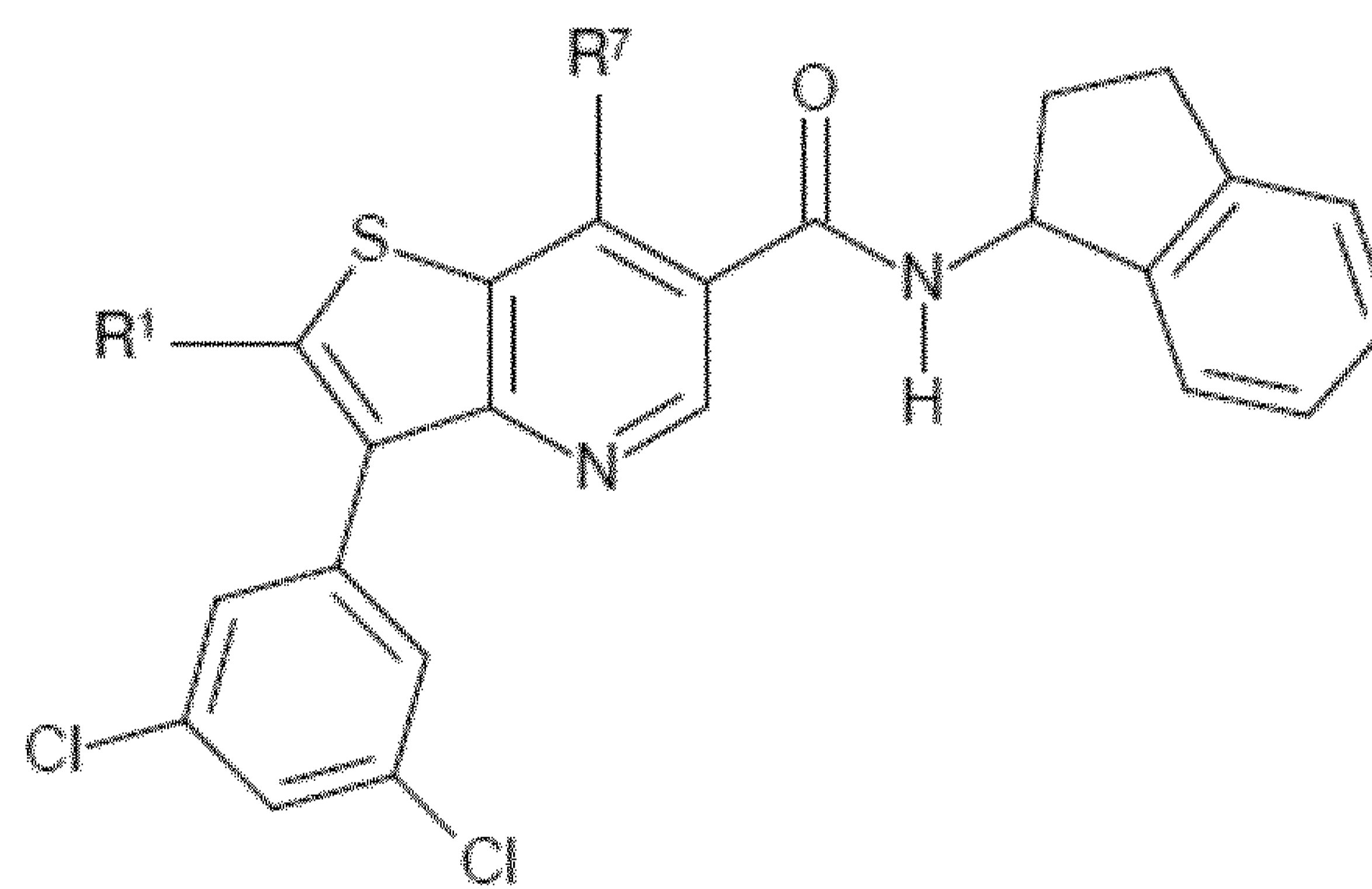
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyi), (Iyii), (Iyiii), (Iyiv), (Iyv), (Iyvi), (Iyvii), (Iyviii), (Iyix), (Iyx), (Iyxi) or (Iyxii)



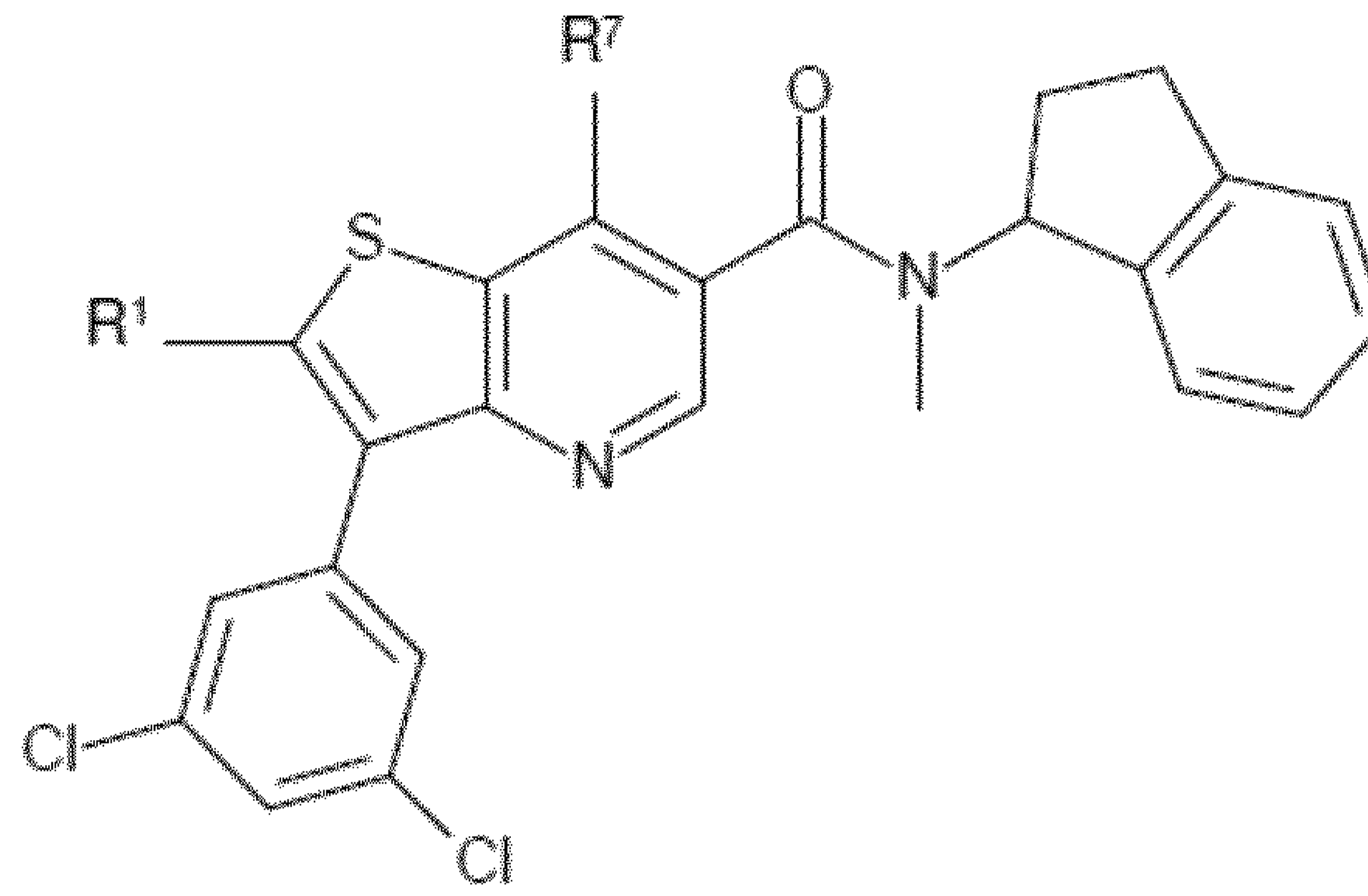
Formula (Iyi)



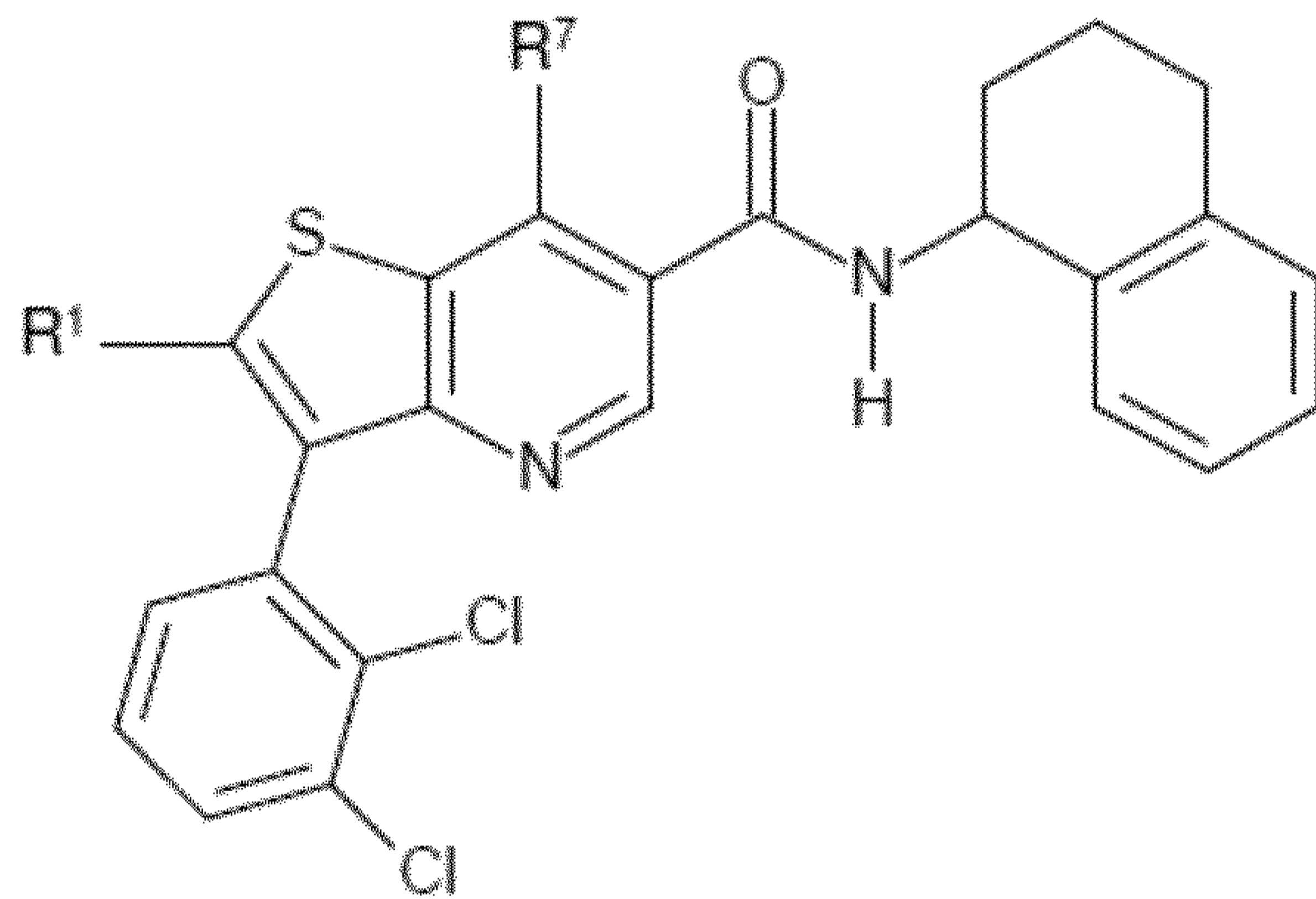
Formula (Iyiii)



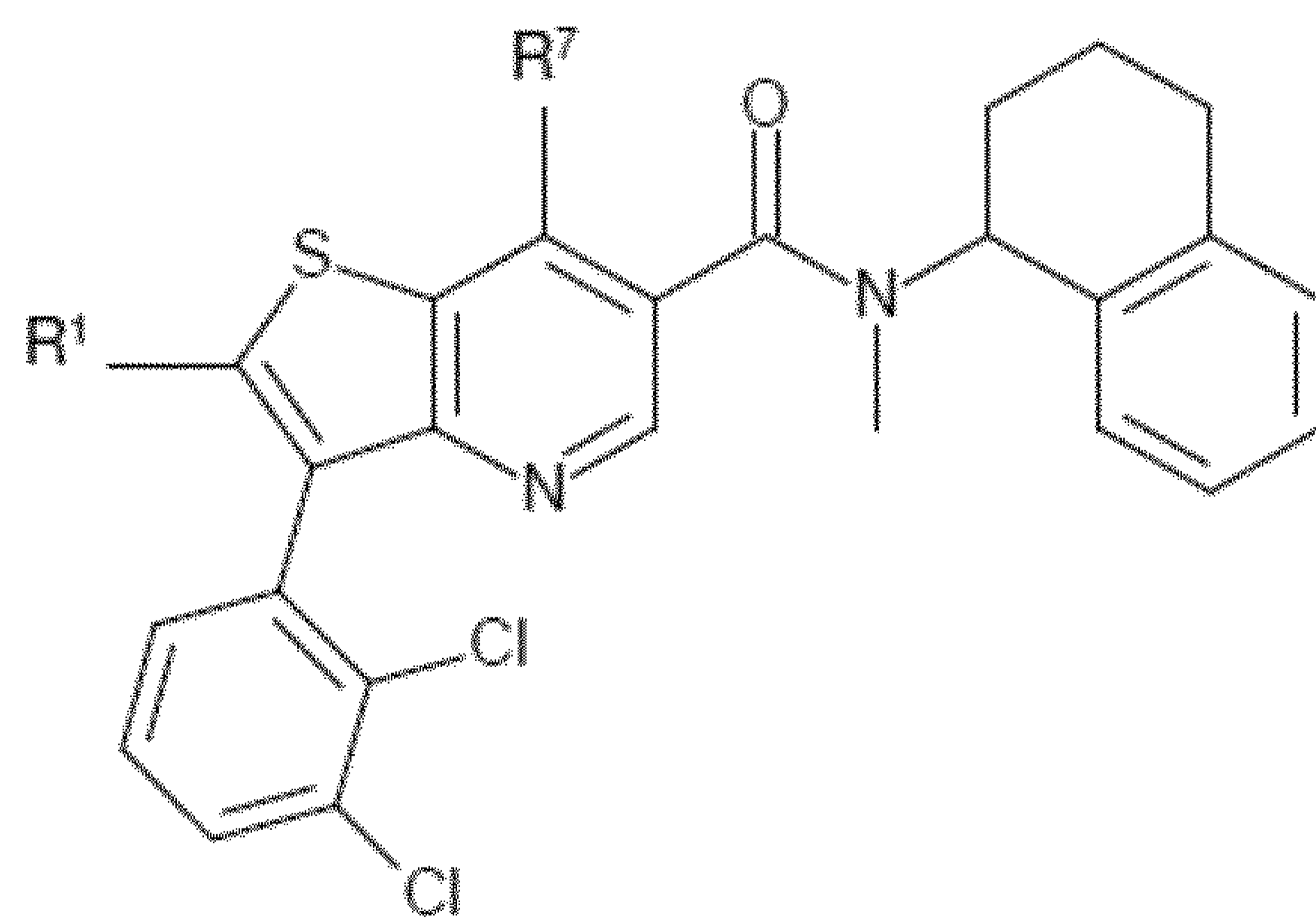
Formula (Iyiii)



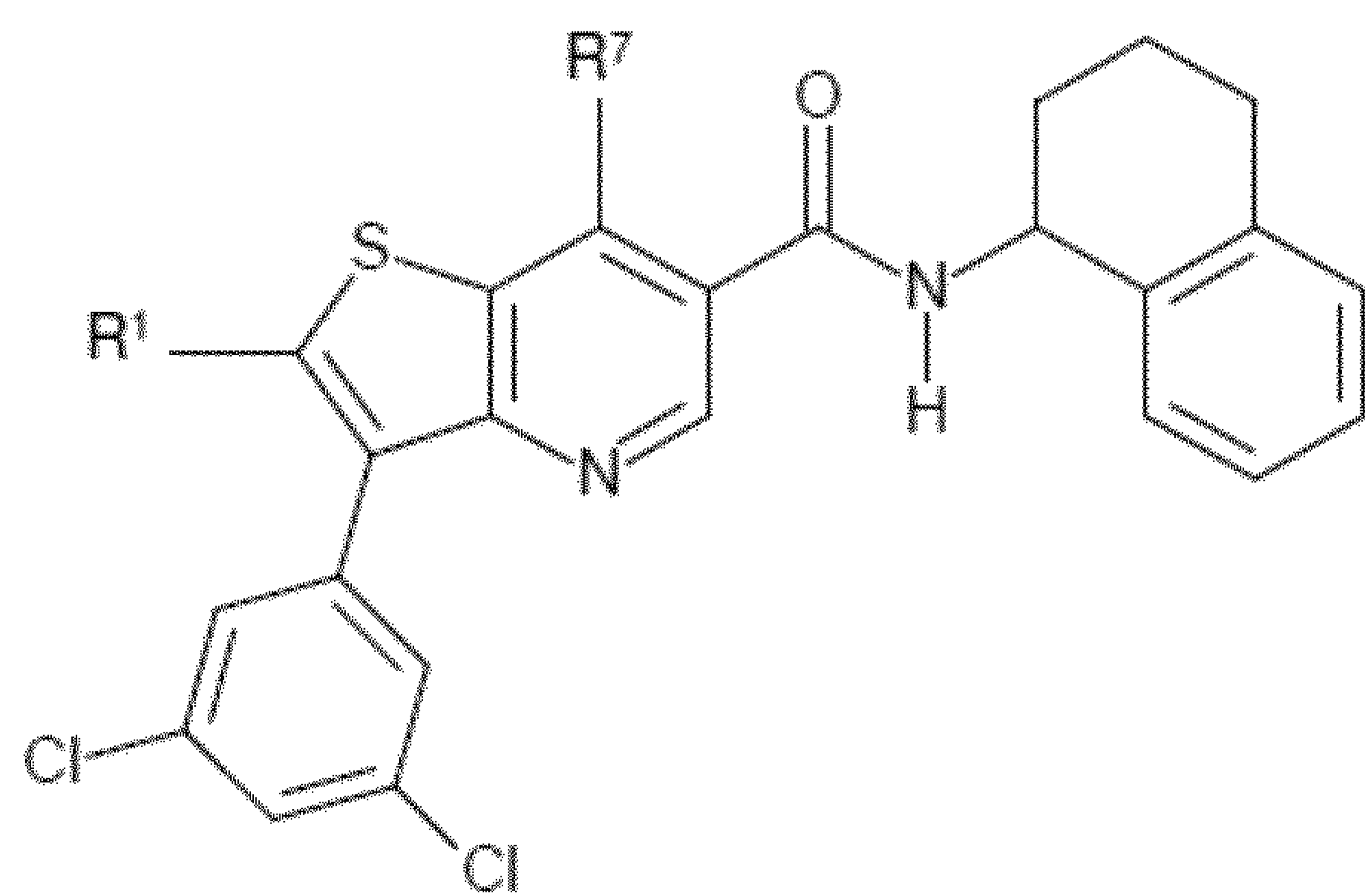
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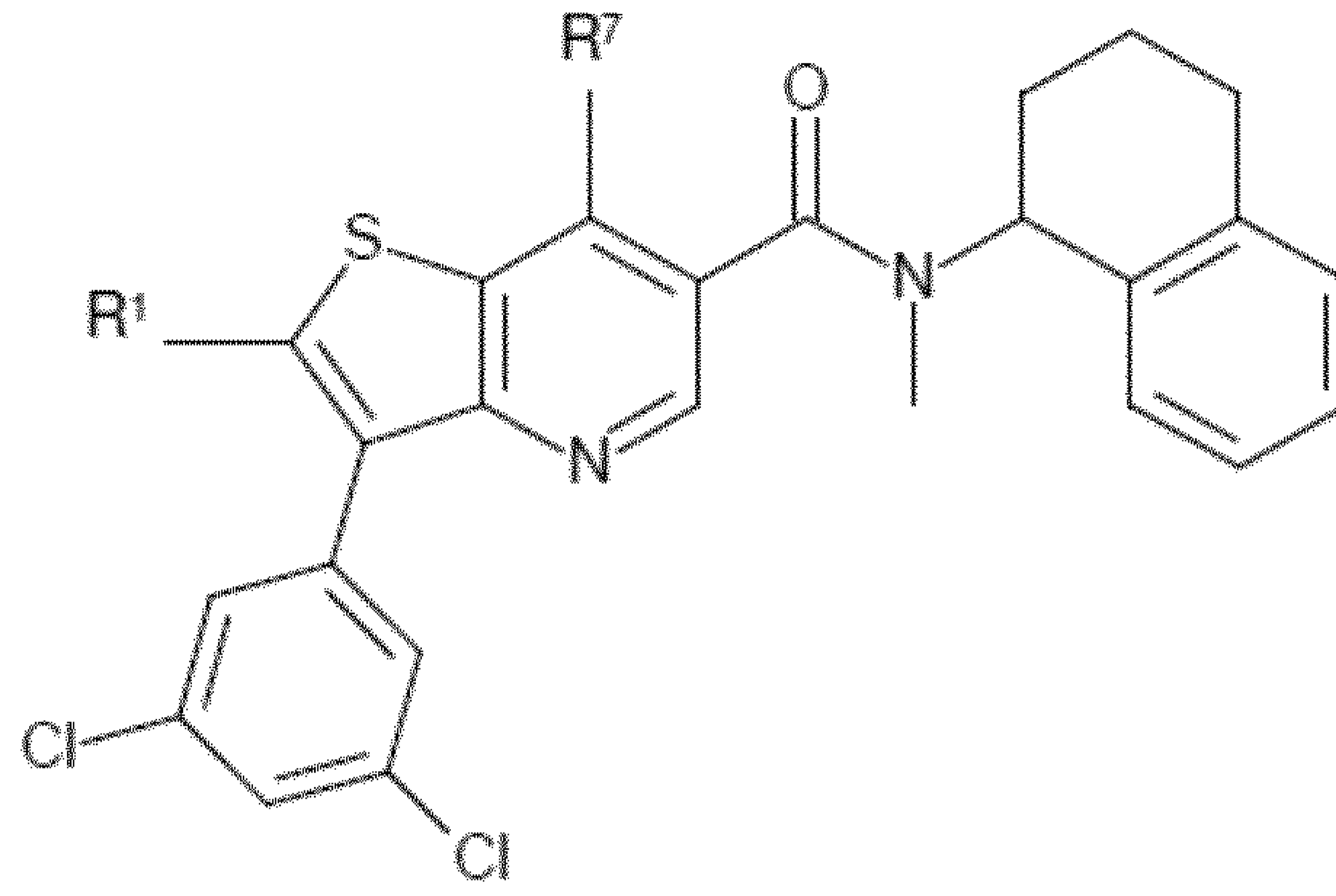
Formula (Iyv)



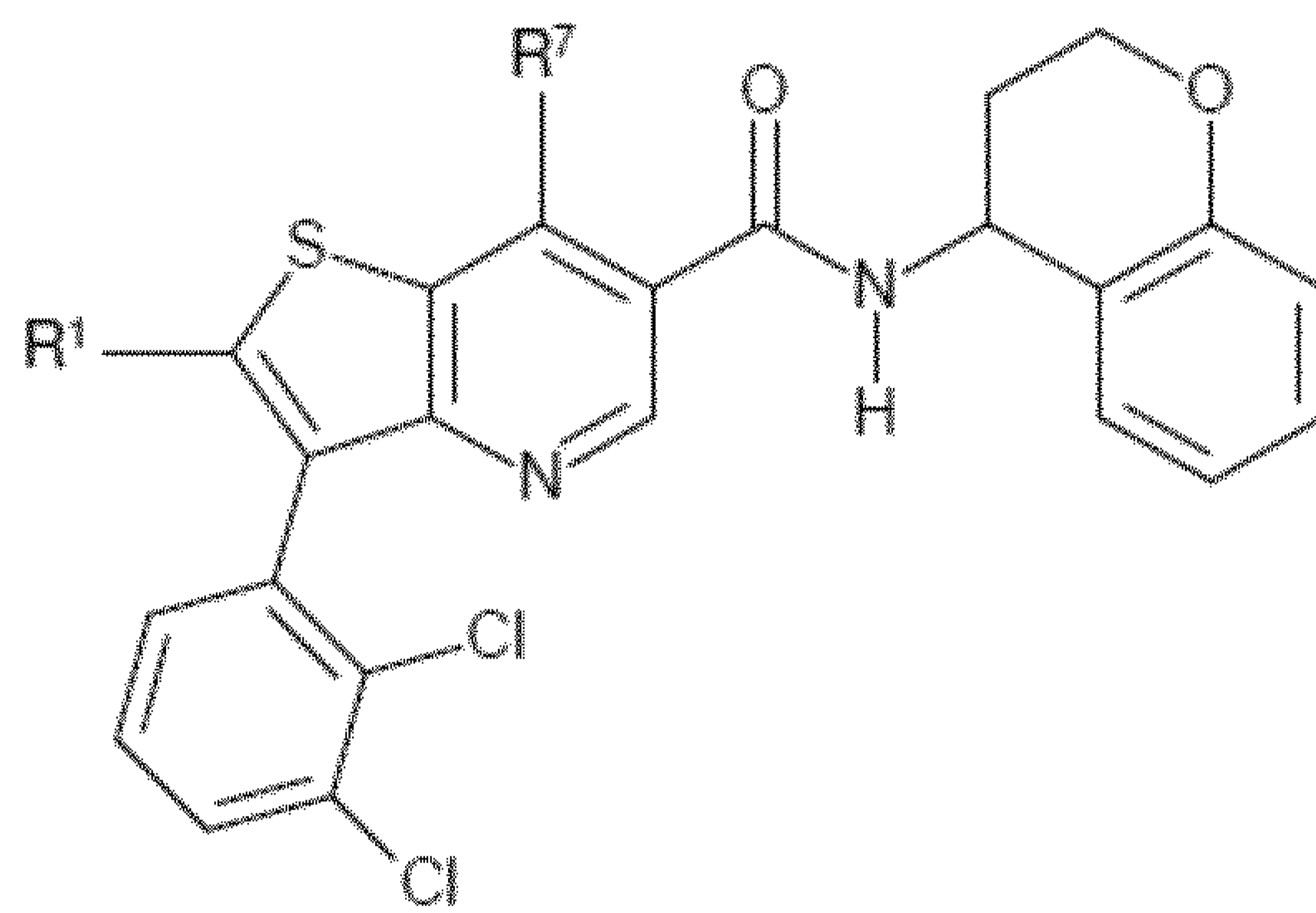
Formula (Iyvi)



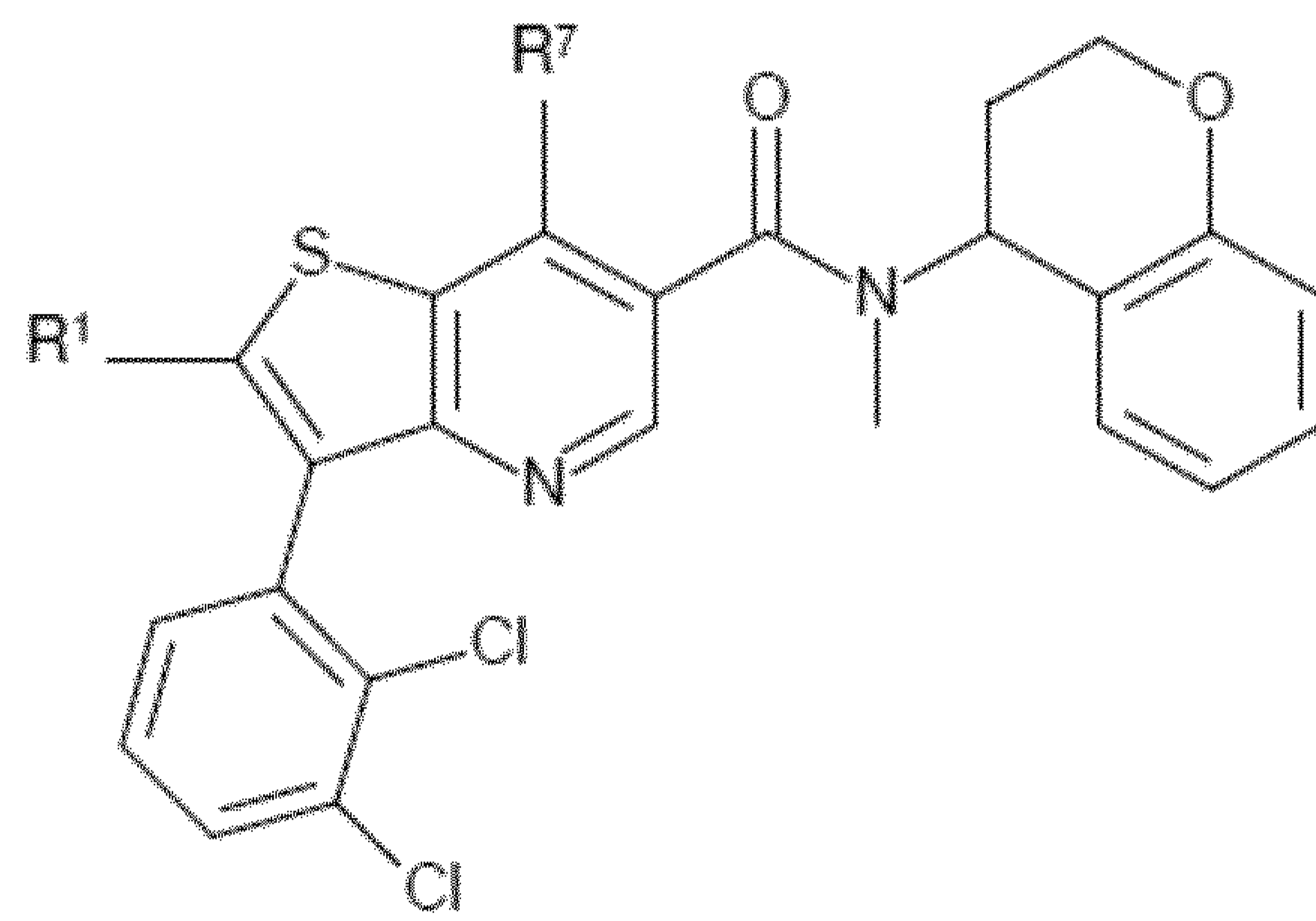
Formula (Iyvii)



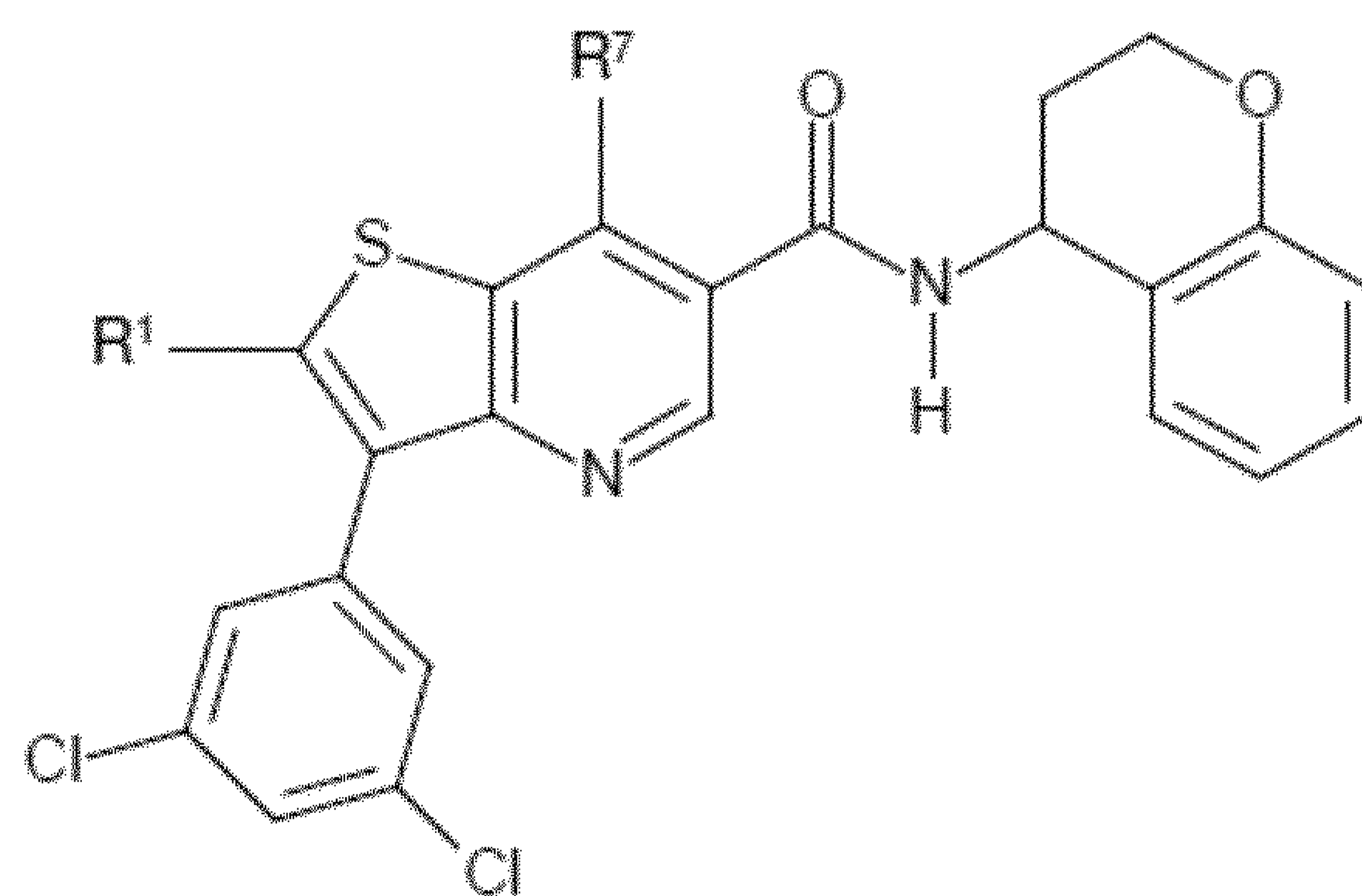
Formula (Iyviii)



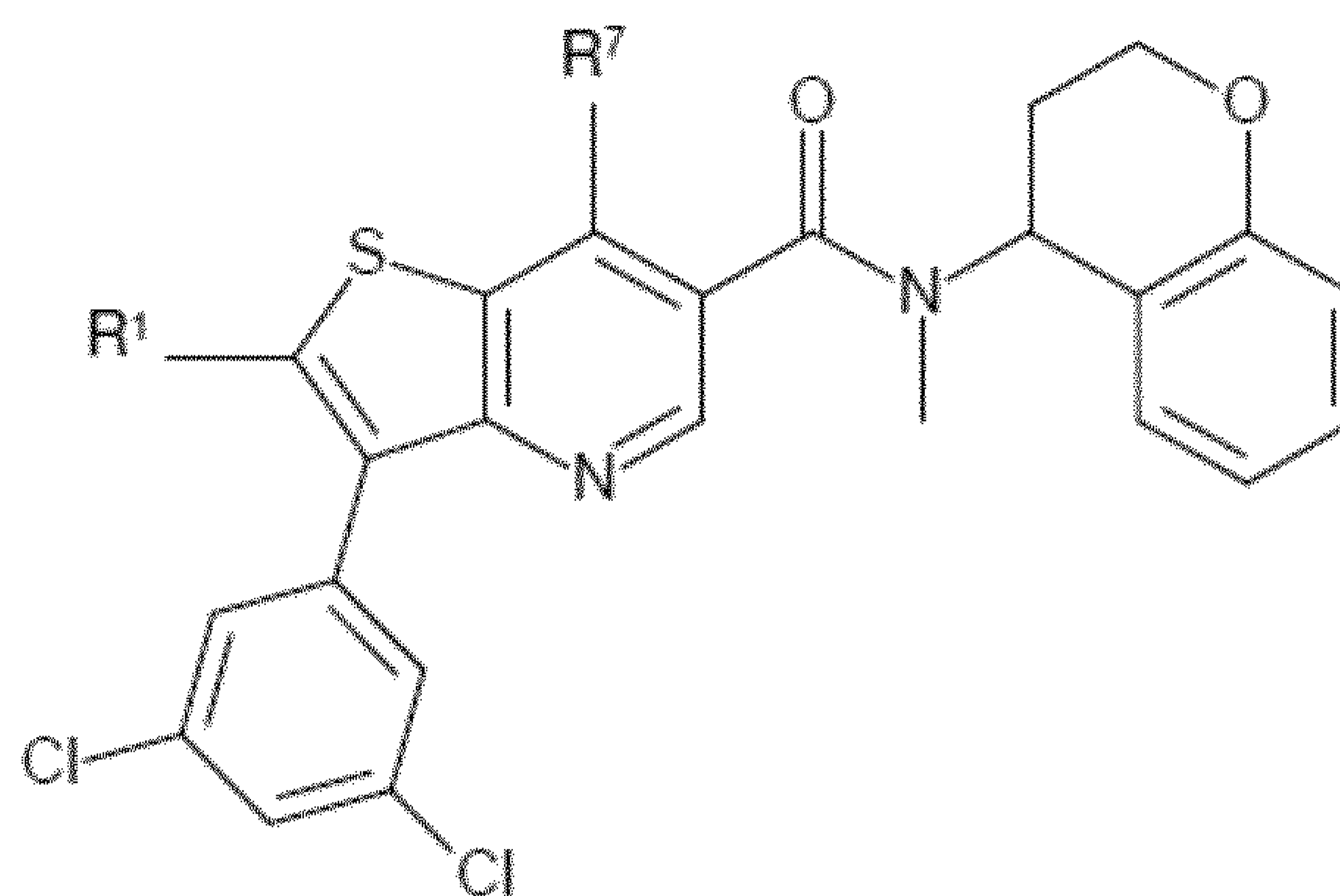
Formula (Iyix)



Formula (Iyx)



Formula (Iyxi)



Formula (Iyxii)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R^1 and R^7 are defined as in any of the embodiments described herein.

5 In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 10 embodiments thereof, the compounds are according to Formula (Iyvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyviii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyix), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyx), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyxi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or
 20 embodiments thereof, the compounds are according to Formula (Iyxii), preferably in form of the (*S*)-enantiomer.

25 Optionally, in an embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more

C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

5 A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

10 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

and

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5 to 10-membered heteroaryl,

15 wherein each C₆₋₁₀-aryl or 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

20 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

25 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, 5 to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5 to 10-membered heteroaryl, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'},

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

5 R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl,

and

R²⁵ is hydrogen or methyl.

In one embodiment of the invention and/or embodiments thereof,

10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

15 A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, C₁₋₃ alkyl or C₁₋₃ alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

and

R¹⁹ is a 5 to 10-membered heteroaryl

20 wherein the 5 to 10-membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one
25 or more halogen,

and

R²⁵ is hydrogen or methyl.

In an embodiment of the invention and/or embodiments thereof,

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N- or -S-,

5 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen or C_{1-3} alkoxy,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen or C_{1-3} alkoxy,

A3 is N or CR^{17} , wherein R^{17} is independently hydrogen or C_{1-3} alkoxy,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen or C_{1-3} alkoxy,

wherein none, one or two of A1, A2, A3 and A4 are N,

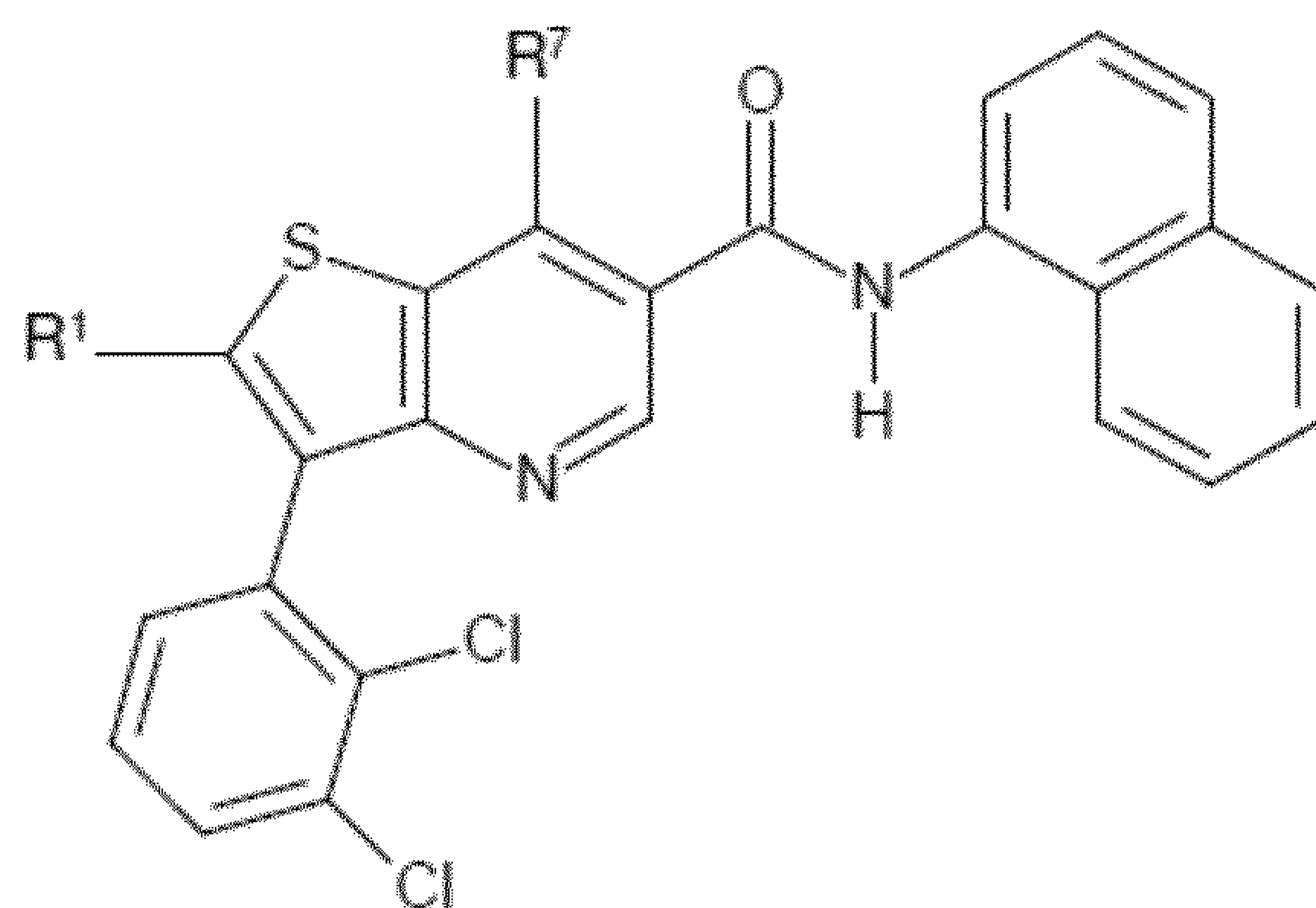
10 and

R^{19} is independently selected from 3,5-dichlorophenyl, 2,3-dichlorophenyl, 2,3,5-trifluorophenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 2,3-dimethylphenyl, 3-chlorophenyl, 3-trifluoromethoxyphenyl, 3-dimethylaminophenyl, 3,5-difluorophenyl, 2,3-difluorophenyl, 3,4,5-trifluorophenyl, 2-fluoro-3-chlorophenyl, 2-fluoro-5-trifluoromethylphenyl, naphth-1-yl, 2-
15 fluoro-5-chlorophenyl, 3-fluoro-5-trifluoromethylphenyl, and 2,3,5-trichlorophenyl, preferably 3-fluorophenyl, 3-chlorophenyl, 2,3-difluorophenyl, 3,5-difluorophenyl, 2,3-dichlorophenyl, 3,5-dichlorophenyl, 2-chloro-3-fluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 3-chloro-5-fluorophenyl, 5-chloro-2-fluorophenyl, 3,4,5-trifluorophenyl, 2,3,5-trifluorophenyl, 3,5-dichloro-4-fluorophenyl and 3,4,5-trichlorophenyl, more preferably 3-chlorophenyl, 2,3-
20 dichlorophenyl, 3,5-dichlorophenyl, 3,5-difluorophenyl, 2,3,5-trifluorophenyl, 3,4,5-trifluorophenyl, 3-chloro-2-fluorophenyl, 5-chloro-3-fluorophenyl, 5-chloro-3-fluorophenyl, 3,5-dichloro-4-fluorophenyl, in particular 2,3,5-trifluorophenyl, 2,3-dichlorophenyl and 3,5-dichlorophenyl,

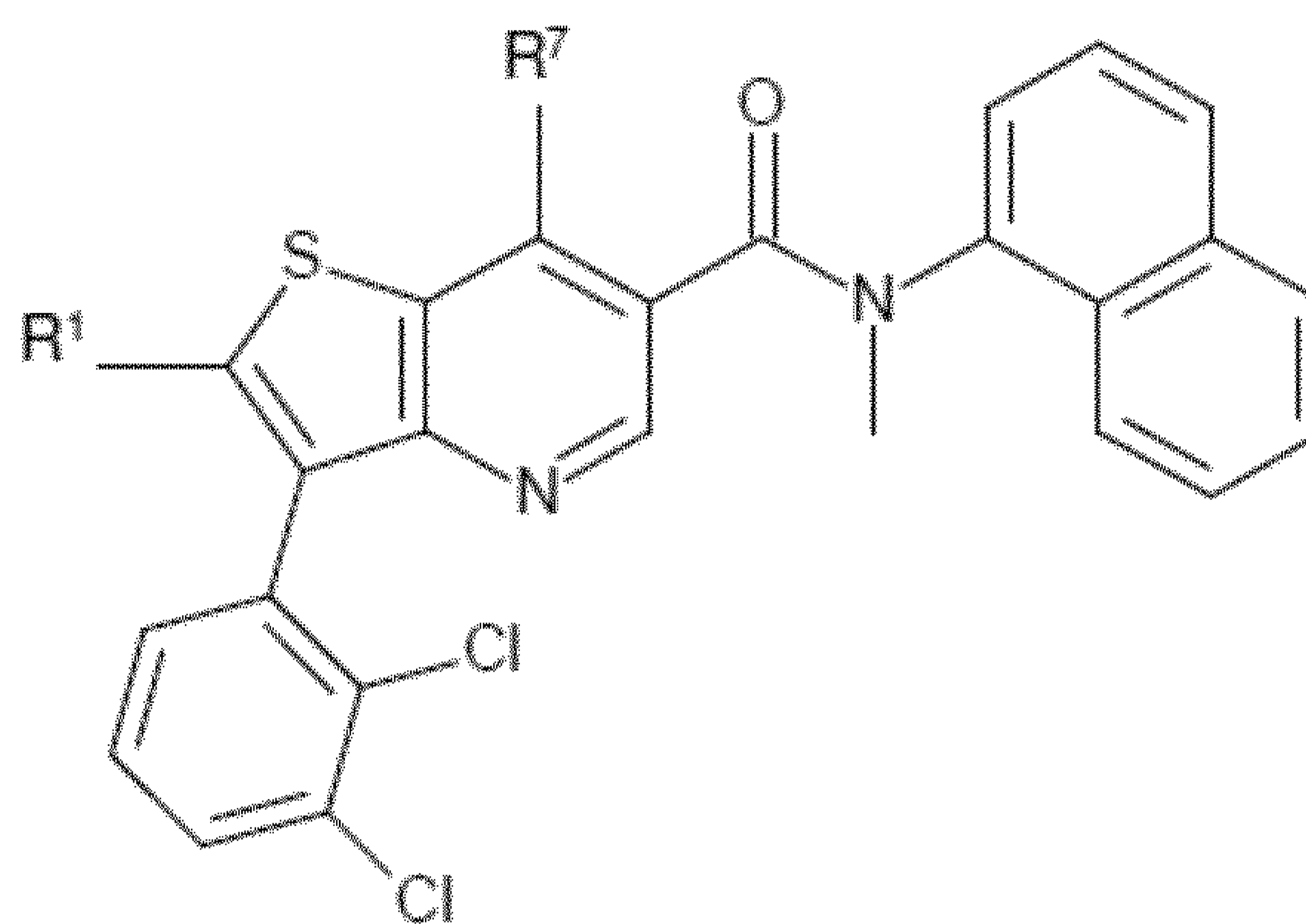
and

25 R^{25} is hydrogen or methyl, more preferably hydrogen.

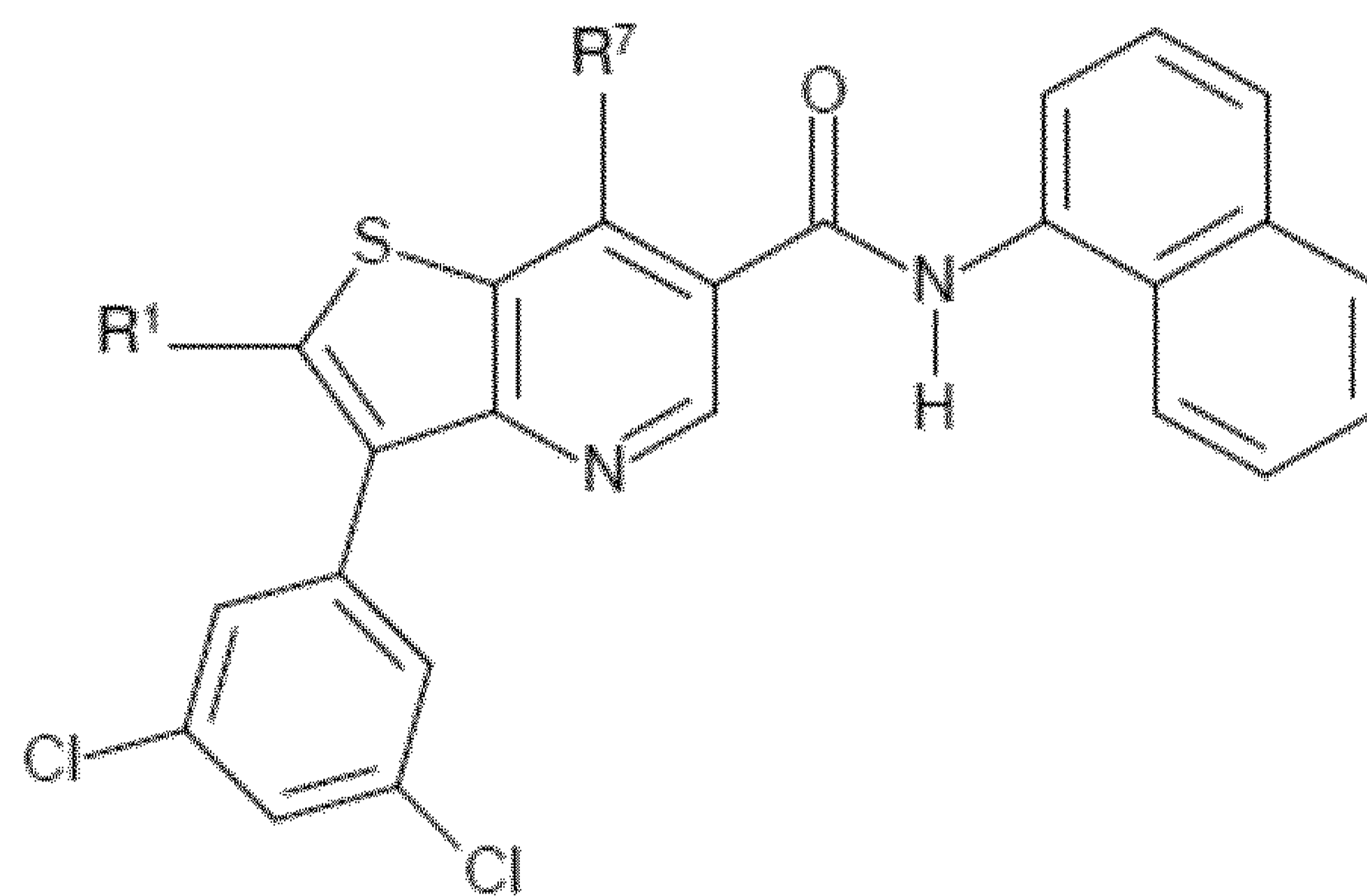
In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Iyxi), (Iyxii), (Iyxiii), (Iyxiv), (Iyxv), (Iyxvi), (Iyxvii), (Iyxviii), (Iyxix) or (Iyxx)



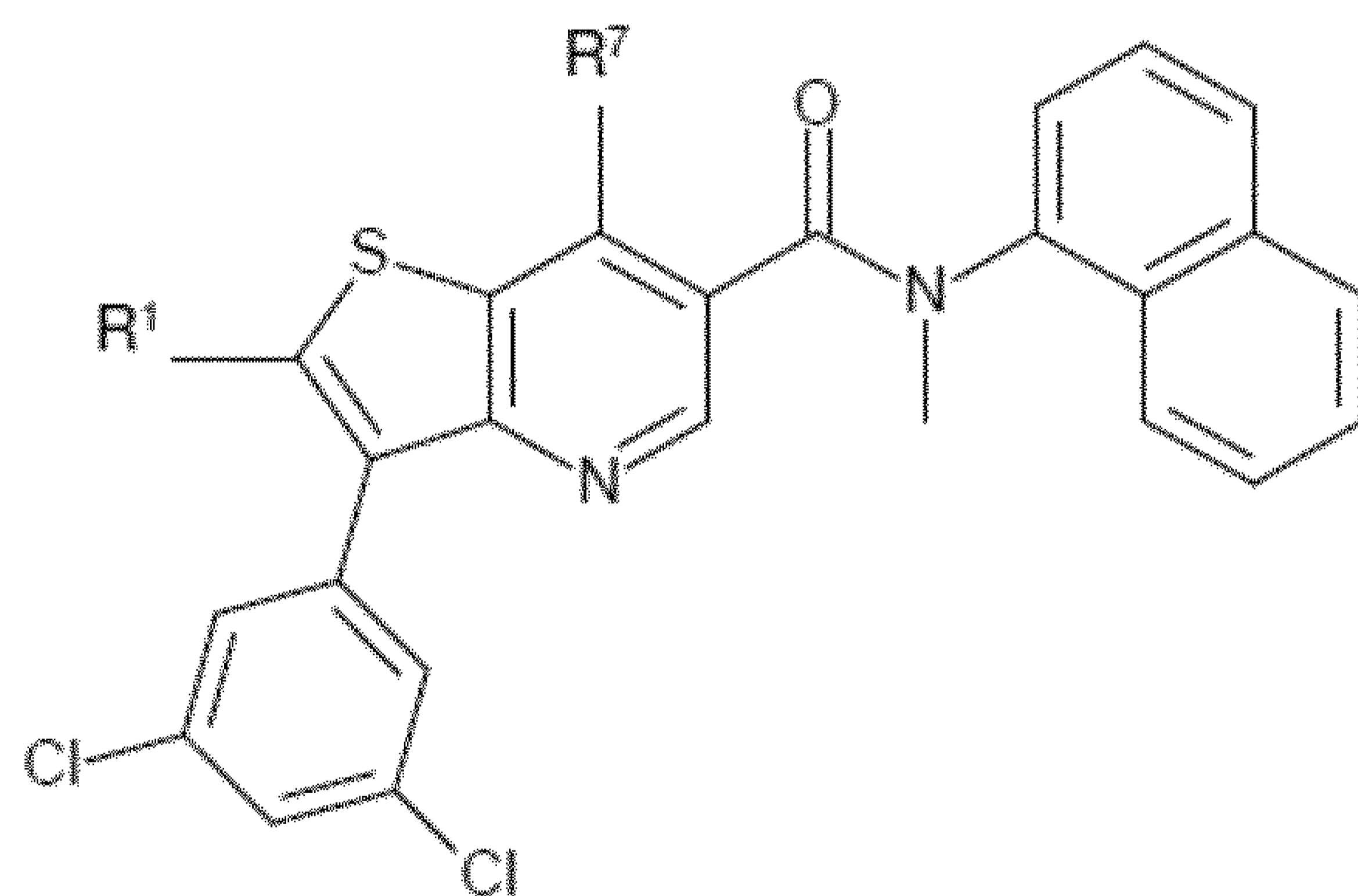
Formula (Iyxiii)



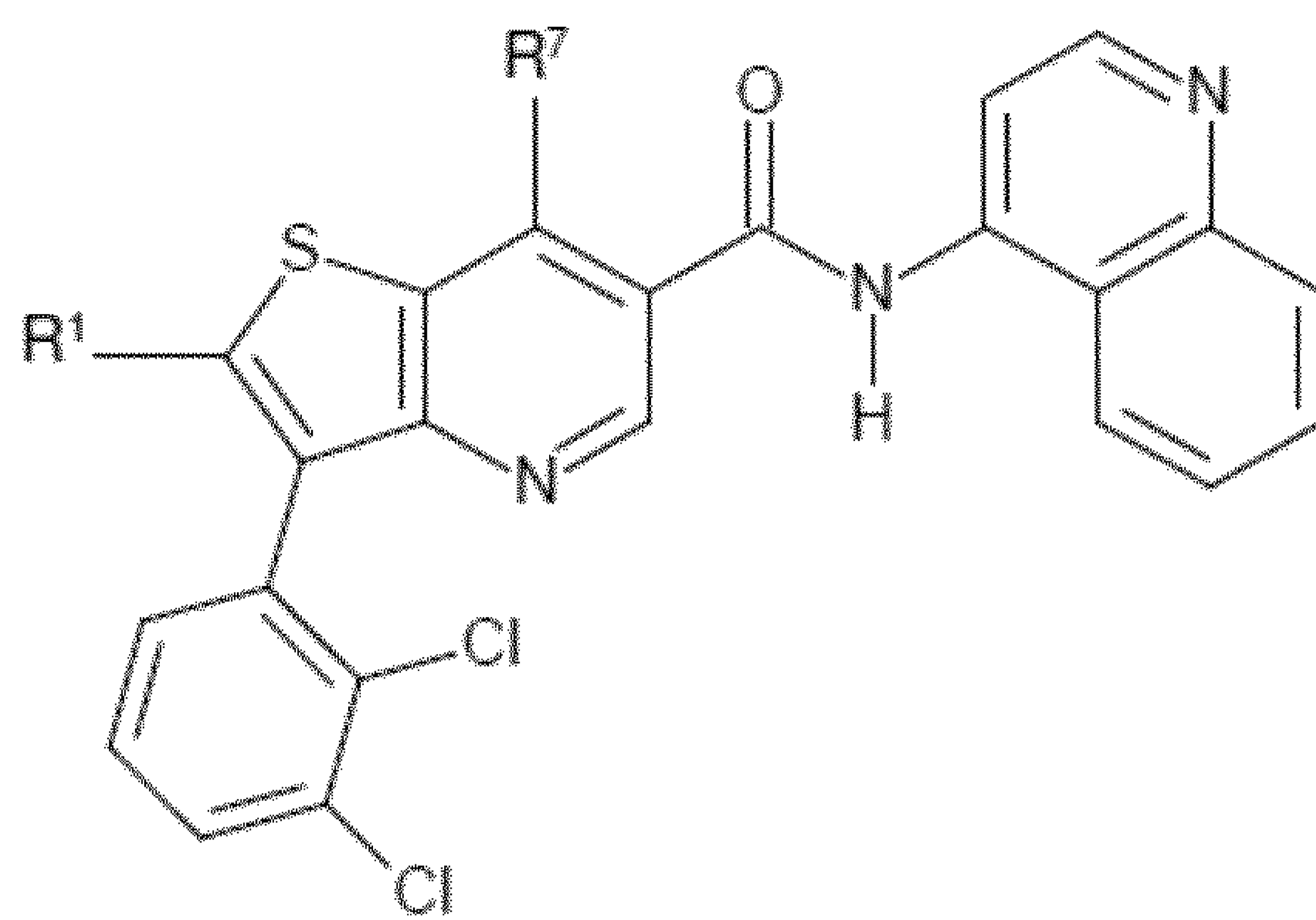
Formula (Iyxiv)



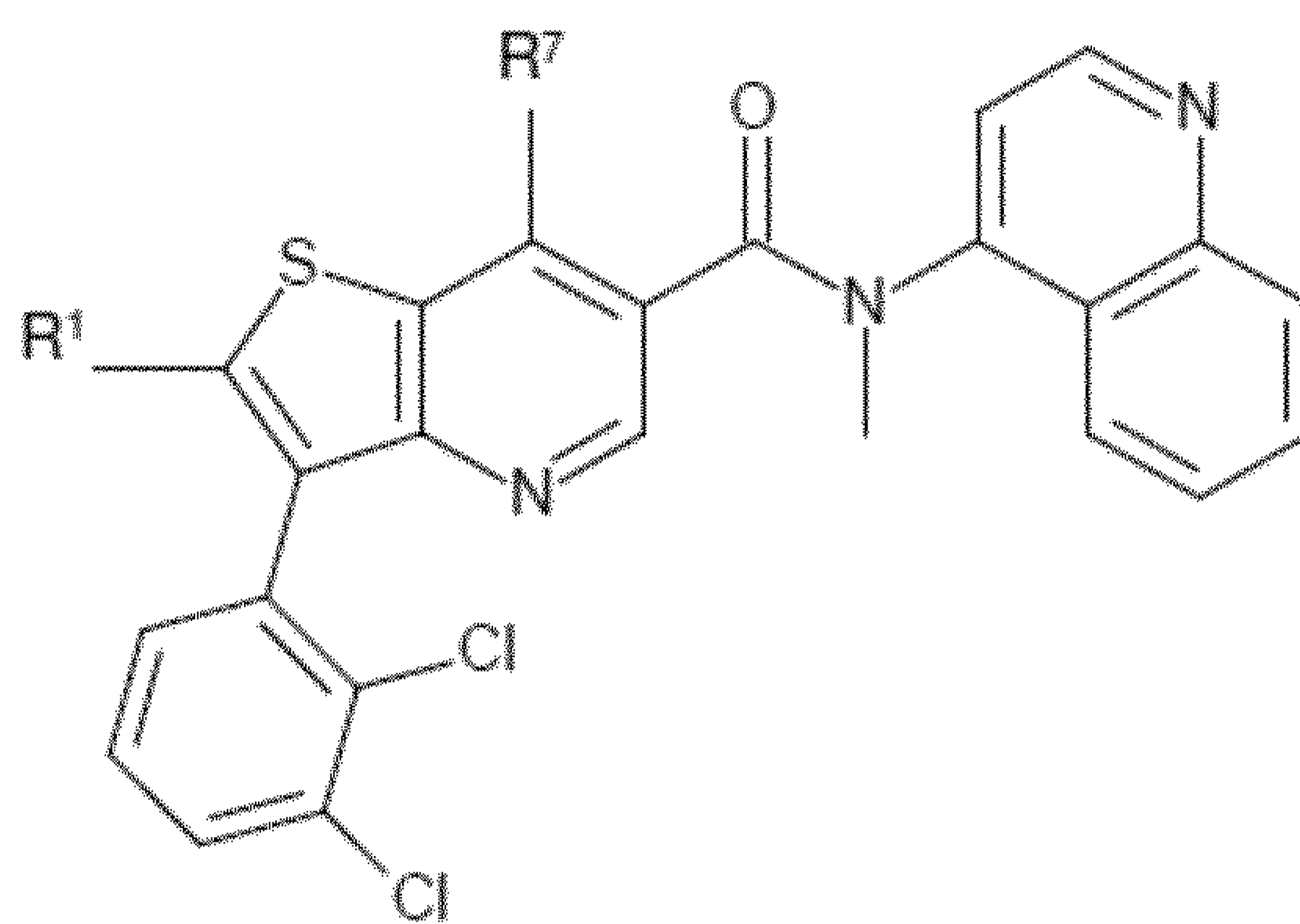
Formula (Iyxv)



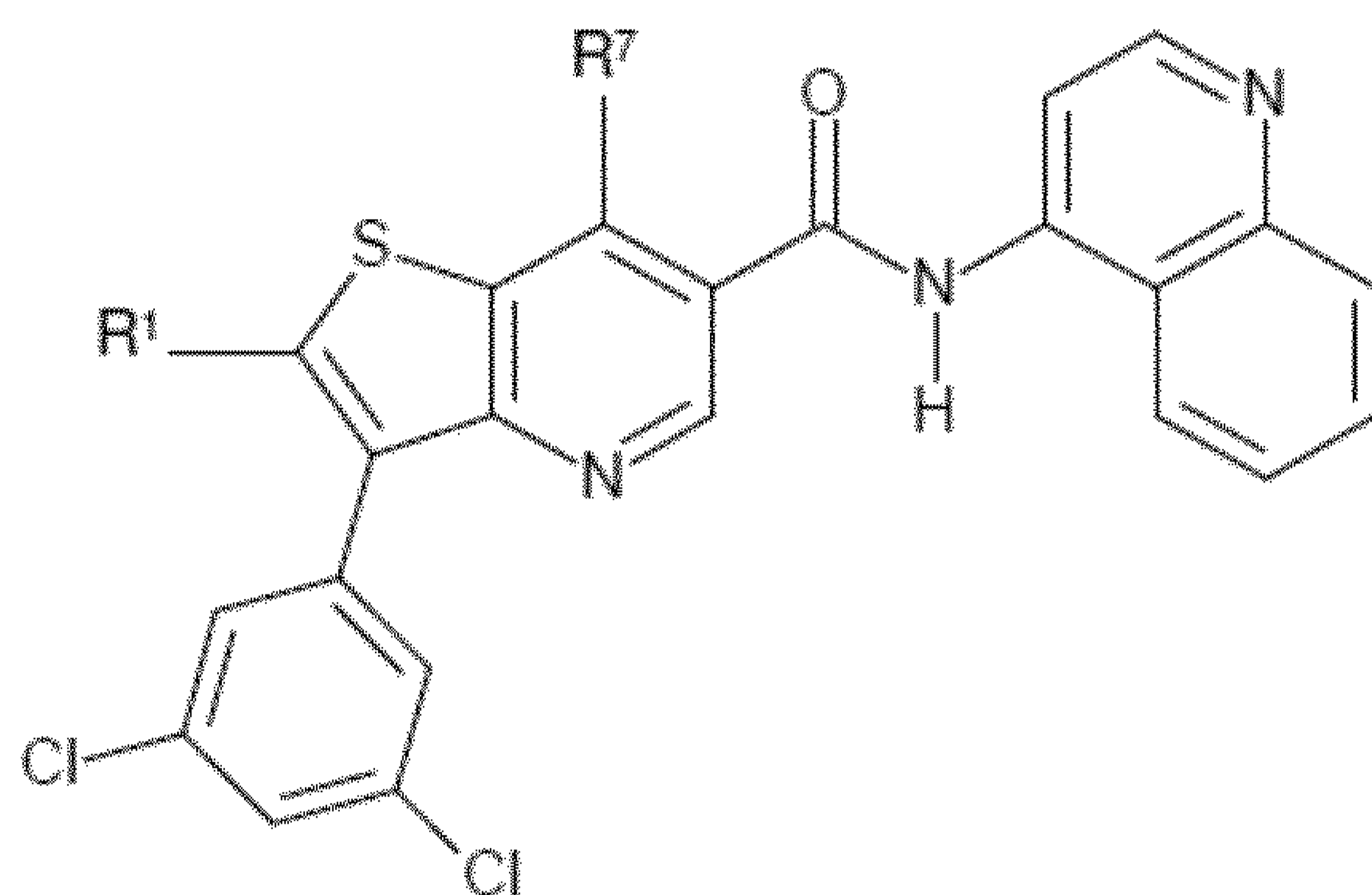
Formula (Iyxvi)



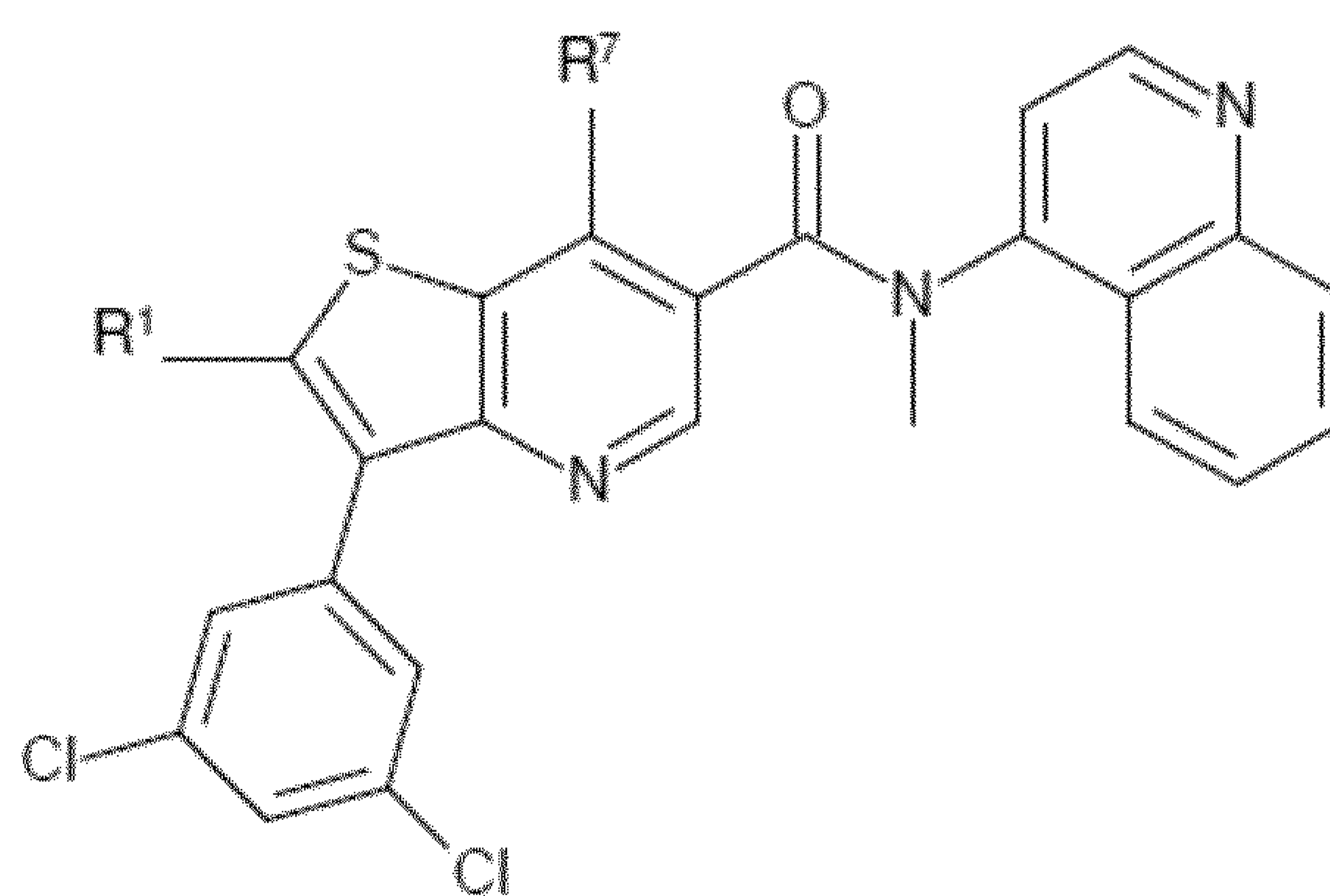
Formula (Iyxvii)



Formula (Iyxviii)



Formula (Iyxi)



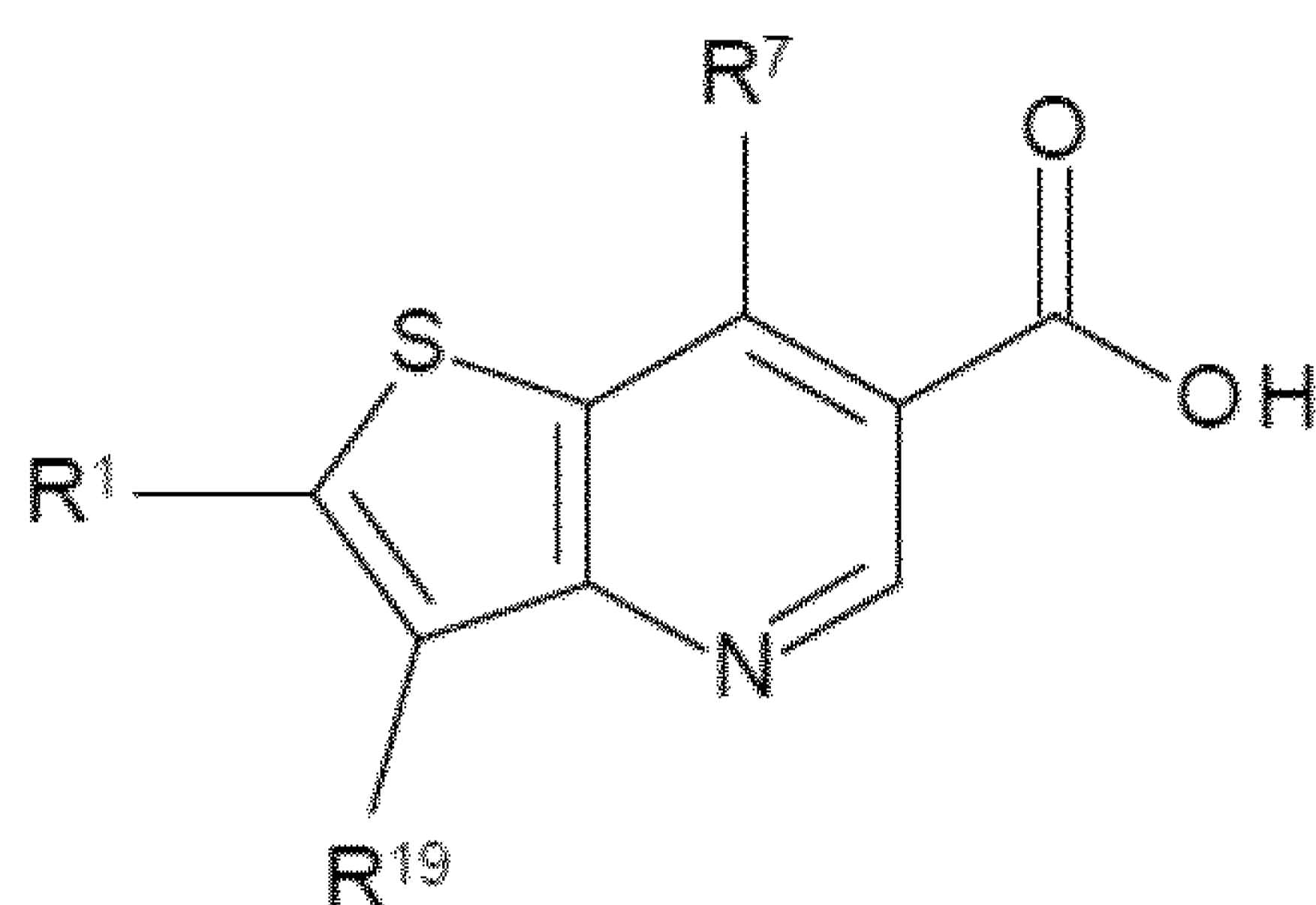
Formula (Iyxx)

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof, wherein R¹ and R⁷ are defined as in any of the embodiments described herein.

In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxiii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxiv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxv), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxvi), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxvii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxviii), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxix), preferably in form of the (*S*)-enantiomer. In an embodiment of the invention and/or embodiments thereof, the compounds are according to Formula (Ixxx), preferably in form of the (*S*)-enantiomer.

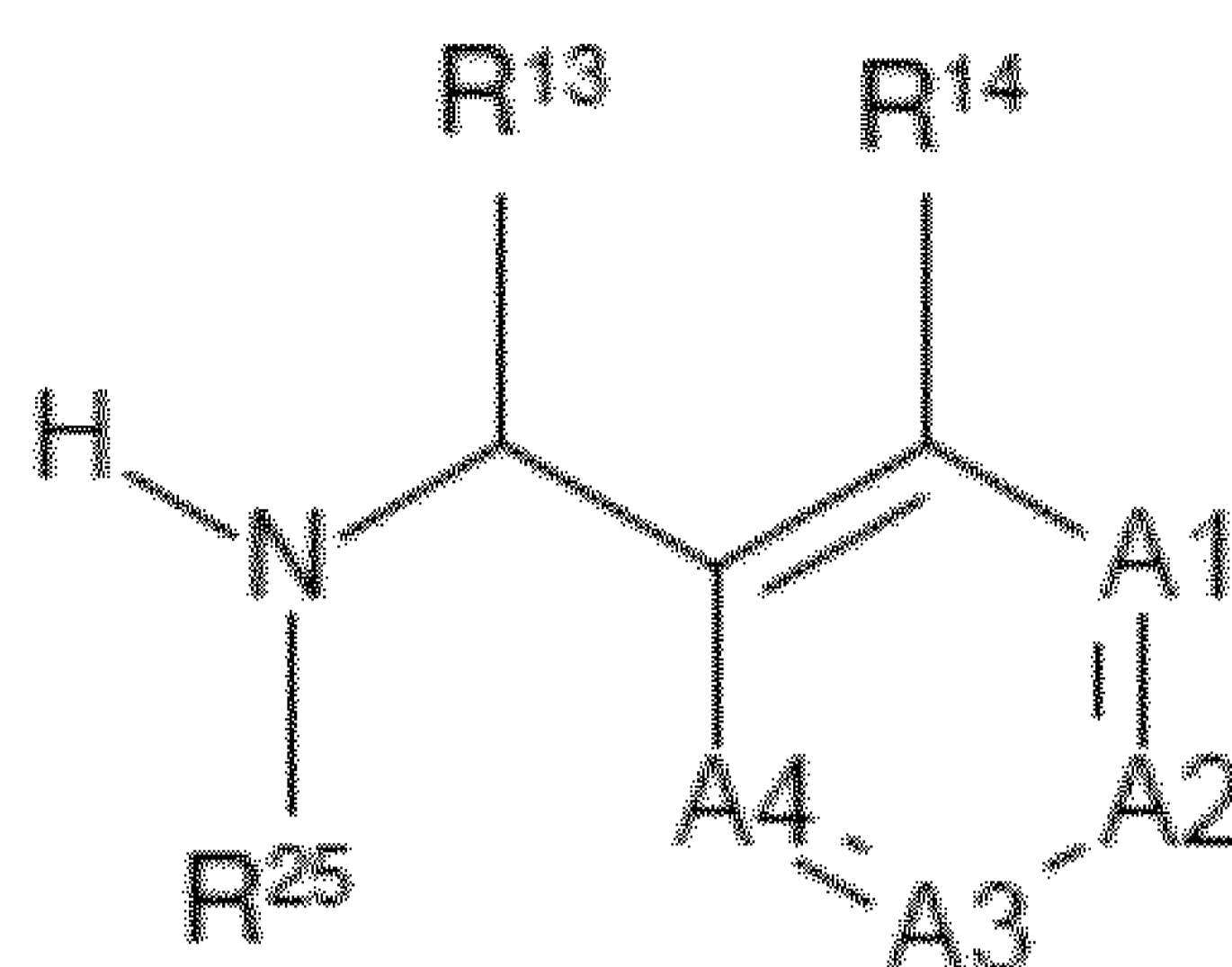
The compound according to invention can be considered as an "active" agent, which in this context is regarded as a substance that will inhibit the growth of helminths such as *Dirofilaria*, in particular *Dirofilaria immitis*. The term "inhibiting the growth" indicates that the rate of increase in the numbers of a population of a helminth is reduced. Thus, the term includes situations in which the helminth population increases but at a reduced rate, as well as situations where the growth of the population is stopped, as well as situations where the numbers of the helminth in the population are reduced or the population is even eliminated.

Further, the present invention provides a process for preparing the compound according to Formula (I) comprising the step of reacting a compound of Formula (A)



Formula (A)

with a compound of Formula (B)



Formula (B)

5 wherein

R^1 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR²R³, COOH, C(=O)OR⁴, SR⁴, SOR⁴, SO₂R⁴,
 10 SO₂NR⁵R⁶ and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR^{2'}R^{3'}, C(=O)OR^{4'}, SR^{4'}, SOR^{4'}, SO₂R^{4'}, SO₂NR^{5'}R^{6'} and C(=O)NR^{5'}R^{6'},

R^2 and R^3 are independently selected from the group consisting of

20 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl and C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

25 R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl or C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{2''}R^{3''}, C(=O)OR^{4''}, SR^{4''}, SOR⁴, SO₂R^{4''}, SO₂NR^{5''}R^{6''} and C(=O)NR^{5''}R^{6''},

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{2'}, R^{3'}, R^{4'}, R^{5'} and R^{6'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{2''}, R^{3''}, R^{4''}, R^{5''} and R^{6''} are independently selected from hydrogen and C₁₋₆-alkyl,

R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 4- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR⁸R⁹, COOH, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰, SO₂NR¹¹R¹² and C(=O)NR¹¹R¹²,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 4- to 10-membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'}, SR^{10'}, SOR^{10'}, SO₂R^{10'}, SO₂NR^{11'}R^{12'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl, C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl or C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{8''}R^{9''}, C(=O)OR^{10''}, SR^{10''}, SOR^{10''}, SO₂R^{10''}, SO₂NR^{11''}R^{12''} and C(=O)NR^{11''}R^{12''},

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

R¹³ is hydrogen or C₁₋₃ alkyl,

R¹⁴ is hydrogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, NR^{14'}R^{14''}, wherein R^{14'} and R^{14''} are independently C₁₋₃-alkyl or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

R^{13} and R^{14} together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C_{1-3} -alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

5 A1 is N or CR^{15} , wherein R^{15} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{15'}R^{15''}$, wherein $R^{15'}$ and $R^{15''}$ are independently C_{1-3} -alkyl,

A2 is N or CR^{16} , wherein R^{16} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{16'}R^{16''}$, wherein $R^{16'}$ and $R^{16''}$ are independently C_{1-3} -alkyl,

10 A3 is N or CR^{17} , wherein R^{17} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{17'}R^{17''}$, wherein $R^{17'}$ and $R^{17''}$ are independently C_{1-3} -alkyl,

A4 is N or CR^{18} , wherein R^{18} is independently hydrogen, halogen, C_{1-3} alkyl, C_{1-3} alkoxy, or $NR^{18'}R^{18''}$, wherein $R^{18'}$ and $R^{18''}$ are independently C_{1-3} -alkyl,

R^{19} is independently selected from the group consisting of C_{6-10} -aryl and 5- to 10- membered heteroaryl,

15 wherein each C_{6-10} -aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, C_{1-6} -alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, $NR^{20}R^{21}$, $C(=O)OR^{22}$, SR^{22} , SOR^{22} , SO_2R^{22} , $SO_2NR^{23}R^{24}$ and $C(=O)NR^{23}R^{24}$,

R^{20} and R^{21} are independently selected from the group consisting of

25 hydrogen, C_{1-6} -alkyl, C_{3-10} -cycloalkyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy- C_{1-6} -alkyl, C_{1-6} -alkyl substituted with C_{6-10} -aryl, C_{1-6} -alkyl substituted with 5- to 10- membered heteroaryl, or

R^{20} and R^{21} together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

30 wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy or C_{1-6} -

alkylmercapto or the heterocyclic ring formed by R^{20} and R^{21} together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

5 C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, $NR^{20'}R^{21'}$, $C(=O)OR^{22'}$, $SR^{22'}$, $SOR^{22'}$, $SO_2R^{22'}$, $SO_2NR^{23'}R^{24'}$, and $C(=O)NR^{23'}R^{24'}$,

R^{22} , R^{23} and R^{24} are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{20'}$, $R^{21'}$, $R^{22'}$, $R^{23'}$ and $R^{24'}$ are independently selected from hydrogen and C_{1-6} -alkyl,

10 R^{25} is independently selected from hydrogen and C_{1-6} -alkyl,

to obtain the compound according to Formula (I).

In an embodiment of the invention and/or embodiments thereof, as far as R^1 , R^7 , R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are concerned, the same applies as described above with regard to the compound according to the invention.

15 The compounds of Formula (A) and Formula (B) are either commercially or synthetically available.

In an embodiment of the invention and/or embodiments thereof, the carboxylic acid of Formula (A) and the amine according to Formula (B) can be submitted to form the corresponding amide group in an organic solvent in the presence of a coupling agent.

20 A coupling agent can be regarded as a substance generally facilitating the formation of an ester or an amide. The coupling agent reacts with a carboxy group by forming a reactive intermediate which is subsequently further reacted with an alcohol or an amine to form the final product, i.e. an ester or an amide.

25 Examples of coupling agents include, but are not limited to, carbodiimides such as N,N'-dicyclohexylcarbodiimide (DCC), diisopropylcarbodiimide (DIC), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDCxHCl) and N-Cyclohexyl-N'-(2-morpholinoethyl)carbodiimid-methyl-p-toluolsulfonat (CMC), Phosphonium salts such as Benzotriazol-1-yl-oxytripyrrolidino-phosphoniumhexafluorophosphat (PyBOP), aminium salts such as 3-[bis(dimethyl-

amino)methylumyl]-3*H*-benzotriazol-1-oxid-hexafluorosphat (HBTU) and carbonyldiimidazole (CDI).

In an embodiment of the invention and/or embodiments thereof, the coupling agent is selected from *N,N'*-dicyclohexylcarbodiimide (DCC), diisopropylcarbodiimide (DIC), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDCxHCl) and carbonyldiimidazole (CDI). More preferably the coupling agent is 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride.

Organic solvents are known to the skilled person.

A suitable organic solvent for the process according to the present invention can for example be acetonitrile, dioxane, tetrahydrofuran (THF) and dimethylformamide (DMF), dimethyl sulfoxide (DMSO), preferably dimethylformamide (DMF).

In an embodiment of the invention and/or embodiments thereof, the process can be carried out in the presence of an auxiliary alkaline compound. Suitable alkaline compounds include, but are not limited to, pyridines such as 4-(dimethylamino) pyridine (DMAP), amidines such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and amines such as triethylamine and diisopropylethylamine (DIPEA), preferably 4-(dimethylamino) pyridine (DMAP).

In an embodiment of the invention and/or embodiments thereof, the process can be carried out at a temperature of 5° to 120°C, preferably at 20 to 100°C.

In an alternative embodiment of the invention and/or embodiments thereof, the carboxylic acid according to Formula (A) can be reacted with thionyl chloride or oxalyl chloride, preferably oxalyl chloride, to form the corresponding acid chloride. Subsequently the corresponding acid chloride can be submitted to a reaction with the amine according to Formula (B) to obtain the compound of Formula (I).

In an alternative embodiment of the invention and/or embodiments thereof, the alternative process can be carried out in an organic solvent and/or in the presence of an auxiliary alkaline compound.

A suitable organic solvent can for example be acetonitrile, toluene, dioxane, tetrahydrofuran, chloroform or dichloromethane.

As far as the auxiliary alkaline compound is concerned, the same applies as described above, preferred are pyridine, DMAP, triethylamine and diisopropylethylamine.

Further, the invention provides a veterinary composition comprising the compound according to the invention and one or more physiologically acceptable excipient(s).

Veterinary compositions of the present invention and/or embodiments thereof comprise a therapeutically effective amount of a compound of the present invention and/or embodiments thereof formulated together with one or more physiologically acceptable excipient(s).

Physiologically acceptable excipients are known in the art. For example, they are described in "Gennaro, Remington: The Science and Practice of Pharmacy" (20th Edition, 2000). All such physiologically acceptable excipients must be substantially pharmaceutically or veterinary pure and non-toxic in the amounts employed and must be compatible with the active ingredients.

10 In one preferred embodiment of the invention and/or embodiments thereof the one or more physiologically acceptable excipient(s) is selected from carriers, binders, antioxidants, buffers, sugar components, surfactants, lubricants, stabilizers, flow agents, disintegration agents and preservatives and mixtures thereof.

As used herein, the term "carrier" means a non-toxic, inert, solid, semi-solid or liquid filler or diluent carrying/encapsulating material of any type. Some examples of materials that can serve as physiologically acceptable carriers are, but are not limited to, sugars such as lactose, glucose and sucrose; starches such as corn starch and potato starch ; cellulose and its derivatives such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate ; powdered tragacanth; malt; gelatine; talc; excipients such as cocoa butter and suppository waxes; oils such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; esters such as ethyl oleate and ethyl laurate; agar.

A binder is a substance which is capable of making other substances stick together. The binder is a component that, in case binder is a polymer, preferably has a melting temperature or a glass transition temperature (T_g) in the range of 25 to 100°C, preferably 35 to 85°C, in particular 40 to 70°C. The glass transition temperature is the temperature at which a polymer becomes brittle as it cools down and soft as it heats up. This means that hydrophilic polymers become soft at temperatures above the glass transition temperature (T_g) and become plastically deformable without breaking. The glass transition temperature or melting point are determined via methods known by the skilled person.

30 In one preferred embodiment of the invention and/or embodiments thereof the binder is selected from polyethylene glycol, polypropylene glycol, polyethylene glycol-polypropylene glycol copolymer, microcrystalline wax, glycerol monostearate, hydrogenated castor oil, polyethylene

glycol glycerol hydroxystearate, polysaccharides, polyvinylpyrrolidone, polyvinyl alcohol, poly(meth)acrylates, polyvinylpyrrolidone-polyacetate copolymer and mixtures thereof.

Antioxidants are substances that are used to inhibit oxidation. Antioxidants suitable to be comprised in the present soft chewable veterinary dosage form include, but are not limited to, ascorbic acid, glutathione, tocopherol and its esters, tert-butylhydroquinone (TBHQ), butyl hydroxy anisole (BHA also referred to as 2-tert-butyl-4-hydroxy anisole, 3-tert-butyl-4-hydroxy anisole or a mixture thereof) and butyl hydroxy toluene (BHT also referred as 2,6-di tert-butyl 4-methyl phenol). It is preferred that the antioxidant is present in the conglomerate. In one preferred embodiment of the invention and/or embodiments thereof antioxidants comprised in the veterinary dosage form may be in the range of 0.001 to 1.00 weight %.

Buffers are substances to maintain/adjust the pH value of a product. Non-limiting examples of buffers are hydrogen carbonate salts, dihydrogen phosphate salts, hydrogen phosphate salts.

Sugar components are used to sweeten the taste of a product. They comprise natural sugars (carbohydrates) as well as sugar substitutes. In one preferred embodiment of the invention and/or embodiments thereof buffers comprised in the veterinary dosage form may be in the range of 1 to 10 weight %.

Surfactants can be regarded as substances lowering the interfacial tension between two phases. Common surfactants are alkylsulfates (for example sodium lauryl sulfate), alkyl trimethyl ammonium salts, alcohol ethoxylates and the like. In one preferred embodiment of the invention and/or embodiments thereof surfactants comprised in the veterinary dosage form may be in the range of 0.1 to 10.0 weight %.

Lubricants generally can be regarded as substances which are suitable to reduce friction, such as static friction, sliding friction and rolling friction. The lubricant is preferably a stearate or fatty acid, more preferably an earth alkali metal stearate, such as magnesium stearate. In one preferred embodiment of the invention and/or embodiments thereof lubricants comprised in the veterinary dosage form may be in the range of 0.1 to 10.0 weight %.

A stabiliser is a physiologically acceptable excipient which helps to preserve the product. Examples include, but are not limited to, alginates, carrageen, gelatine, pectin and natural gums. In one preferred embodiment of the invention and/or embodiments thereof surfactants comprised in the veterinary dosage form may be in the range of 0.01 to 3.0 weight %.

Flow agents, also referred to as glidants, can be used to improve the flowability. Traditionally, talc was used as glidant but is nowadays nearly fully replaced by colloidal silica. In one

preferred embodiment of the invention and/or embodiments thereof flow agents comprised in the veterinary dosage form may be in the range of 1 to 3 weight %.

Disintegration agents, also referred to as disintegrants, are compounds which enhance the ability of the dosage form, preferably the ability of the tablet, when in contact with a liquid, preferably water, to break into smaller fragments. Non-limiting examples of disintegration agents include sodium carboxymethyl starch, sodium starch glycolate, cross-linked polyvinyl pyrrolidone, sodium carboxymethyl glycolate, preferably sodium starch glycolate. In one preferred embodiment of the invention and/or embodiments thereof surfactants comprised in the veterinary dosage form may be in the range of 1.0 to 7.0 weight %.

Preservatives are substances that can be added to prevent decomposition by microbial growth or by undesirable chemical changes. Non-limiting examples include lactic acid, benzoic acid benzoates and hydroxybenzoates. In one preferred embodiment of the invention and/or embodiments thereof surfactants comprised in the veterinary dosage form may be in the range of 0.01 to 1.0 weight %.

The compounds according to this invention may be administered in various dosage forms. The term "dosage form" means that the compounds according to this invention are formulated into a product suitable for administering to the animal via the envisaged dosage route. Such dosage forms are sometimes referred to herein as formulations or pharmaceutical compositions.

The pharmaceutical compositions of this invention and/or embodiments thereof can be administered to animals orally, rectally, intravaginally, parenterally, topically, buccally or nasally.

In one preferred embodiment of the invention and/or embodiments thereof dosage forms useful for oral administration can be liquid or solid dosage forms.

Liquid dosage forms of the compounds are generally solutions, suspensions or emulsions. A solution is a mixture of two or more components that form a single phase that is homogeneous down to the molecular level. A suspension consists of insoluble solid particles dispersed in a liquid medium, with the solid particles accounting for about 0.5% to about 30% of the suspension. The liquid may be aqueous, oily or both. An emulsion is a heterogeneous dispersion of one immiscible liquid in another; it relies on an emulsifying agent for stability. A dry powder (or granule) for reconstitution is mixed and reconstituted with a diluent (e.g. water) as a solution, or as a suspension immediately prior to dosing such as by injection. The principal advantage of this dosage form is that it overcomes the problem of instability in solution or suspension.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, micro-emulsions, solutions, suspensions, syrups, drenches in feed or drinking water formulations and elixirs. A drench is a liquid oral formulation that is administered directly into the mouth/throat of an animal, especially a dog, by means of a “drench gun” or syringe or another suitable device.

5 When the composition is administered in the animal recipient's drinking water or as a drench, it may be convenient to use a solution or suspension formulation. This formulation can, for example, be a concentrated suspension that is mixed with water or a dry preparation that is mixed and suspended in the water. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing
10 agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils (in particular cottonseed, groundnut, corn, germ, olive castor and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitane and mixtures thereof. Besides inert diluents, the oral compositions can also include adjuvants such as wetting
15 agents, emulsifying and suspending agents, sweetening, flavouring and perfuming agents.

Solid dosage forms for oral administration include capsules, tablets, dragées, pills, powders and granules, chewable treats, premixes and medicated blocks. In such solid dosage forms, the active compound is mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose,
20 sucrose, glucose, mannitol, and silicic acid; b) binders such as, for example, carboxymethyl-cellulose, alginates, gelatine, polyvinyl pyrrolidinone, sucrose and acacia; c) humectants such as glycerol; d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates and sodium carbonate; e) solution retarding agents such as paraffin; f) absorption accelerators such as quaternary ammonium compounds; g) wetting agents such as,
25 for example, acetyl alcohol and glycerol monostearate; h) absorbents such as kaolin and bentonite clay and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

The active compounds can also be in micro-encapsulated form with one or more excipients as
30 noted above. The solid dosage forms of tablets, dragées, capsules, pills and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the pharmaceutical formulating art such as enteric coatings, release-controlling coatings and other well-known coatings. In such solid dosage forms the active compound may be admixed with at least one inert diluent such as sucrose, lactose or starch. Such dosage forms may also comprise, as

is normal practice, additional substances other than inert diluents, e.g. tableting lubricants and other tableting aids such as magnesium stearate and microcrystalline cellulose. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. They may optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally in a delayed manner. Examples of such embedding compositions include polymeric substances and waxes.

Solid compositions of a similar type may also be employed as fillers in soft and hard gelatine capsules using such excipients as lactose as well as high molecular weight polyethylene glycols and the like.

10 Solid oral formulations are either administered directly to an animal (tablet, capsule) or mixed with the feed or via medicated feed blocks.

When the oral formulation is administered via a non-human animal's feed, it may for example be fed as a discrete feed or as a chewable treat. Alternatively (or additionally), it may for example be intimately dispersed in the animal recipient's regular feed, used as a top dressing or in the form of solid pellets, paste or liquid that is added to the finished feed. When the oral formulation is administered as a feed additive, it may be convenient to prepare a "premix" in which the oral formulation is dispersed in a small amount of a liquid or solid carrier. This "premix" is, in turn, dispersed in the animal's regular feed using for example a conventional mixer.

15 In one preferred embodiment of the invention and/or embodiments thereof dosage forms useful for rectal and vaginal administration can be regarded as semi solid dosage forms.

Compositions for rectal or vaginal administration can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax which are solid at ambient temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

25 In one preferred embodiment of the invention and/or embodiments thereof the dosage forms are useful for parenteral administrations. One dosage route (administration route) is the parenteral, especially injection administration (e.g. subcutaneous injection, intravenous injection, intramuscular injection etc.). Parenteral formulations and delivery systems for non-oral routes comprise liquids (e.g. solutions, suspensions, emulsions and dry powders for reconstitution), semi-solids and solids (e.g. implants). The majority of implants that are used in veterinary medicine are compressed tablets or dispersed matrix systems in which the drug is uniformly dispersed within a

nondegradable polymer or alternatively extrusion products. In one embodiment the compounds of the current invention are administered subcutaneously.

Injectable formulations, for example sterile injectable aqueous or oleaginous suspensions, may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution, suspension or emulsion in a nontoxic parenterally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose, any bland fixed oil can be employed, including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid are used in the preparation of injectables.

The injectable formulations can be sterilized, for example by filtration through a bacterial-retaining filter or by incorporating sterilizing agents in the form of sterile solid compositions that can be dissolved or dispersed in sterile water or other sterile injectable media prior to use.

In order to prolong the effect of a drug, it is often desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the drug then depends on its rate of dissolution that, in turn, may depend on crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered drug form may be accomplished by dissolving or suspending the drug in an oil vehicle. Injectable depot forms are made by forming microencapsulation matrices of the drug in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations may also be prepared by entrapping the drug in liposomes or microemulsions that are compatible with body tissues.

In one preferred embodiment of the invention and/or embodiments thereof dosage forms useful for topical administration (also referred to as transdermal administration) of a compound of this invention include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants or patches. The active component is admixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives or buffers as may be required. Ophthalmic formulations, ear drops and the like are also contemplated as being within the scope of this invention.

The ointments, pastes, creams and gels may contain, in addition to an active compound of this invention, excipients such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide or mixtures thereof.

- 5 Compounds of the invention may also be formulated for use as topical powders and sprays that can contain, in addition to the compounds of this invention, excipients such as lactose, talc, silicic acid, aluminium hydroxide, calcium silicates and polyamide powder or mixtures of these substances.

Sprays can additionally contain customary propellants such as chlorofluorohydrocarbons.

- 10 Transdermal patches have the added advantage of providing controlled delivery of a compound to the body. Such dosage forms can be made by dissolving or dispensing the compound in the proper medium. Absorption enhancers can also be used to increase the flux of the compound across the skin.

- 15 The rate can be controlled by either providing a rate controlling membrane or by dispersing the compound in a polymer matrix or gel.

In one preferred embodiment of the invention and/or embodiments thereof dosage forms useful for buccal administration of a compound of this invention include orally disintegrating tablets (ODT), films, sublingual drops, lozenges, effervescent buccal tablets, toothpaste and mouthwash.

- 20 In one preferred embodiment of the invention and/or embodiments thereof dosage forms useful for nasal administration of a compound of this invention include liquid aerosols or inhalable dry powders. Liquid aerosol formulations may be nebulized predominantly into particle sizes that can be delivered to the terminal and respiratory bronchioles.

Liquid aerosol and inhalable dry powder formulations are preferably delivered throughout the endobronchial tree to the terminal bronchioles and eventually to the parenchymal tissue.

- 25 Aerosolized formulations of the invention may be delivered using an aerosol-forming device, such as a jet, vibrating porous plate or ultrasonic nebulizer, preferably selected to allow the formation of aerosol particles having a mass medium average diameter predominantly between 1 to 5 μm .

- 30 Further, the formulation preferably has a balanced osmolarity ionic strength and chloride concentration and the smallest aerosolizable volume able to deliver an effective dose of the compounds of the invention to the site of the infection. Additionally, the aerosolized Formulation

preferably does not impair negatively the functionality of the airways and does not cause undesirable side effects.

Aerosolization devices suitable for the administration of aerosol formulations of the invention include for example jet, vibrating porous plate, ultrasonic nebulizers and energized dry powder inhalers that are able to nebulize the formulation of the invention into aerosol particles predominantly in the size range of 1-5 μm . Predominantly in this application means that at least 70% but preferably more than 90% of all generated aerosol particles are in the 1 to 5 μm range. A jet nebulizer works by air pressure to break a liquid solution into aerosol droplets. Vibrating porous plate nebulizers work by using a sonic vacuum produced by a rapidly vibrating porous plate to extrude a solvent droplet through a porous plate. An ultrasonic nebulizer works by a piezoelectric crystal that shears a liquid into small aerosol droplets.

The concentration of the compounds according to this invention in the applied dosage form may vary widely depending on for example the dosage route. In general, the concentration of the present compound or embodiments thereof in the formulation according to the present invention or embodiments thereof is from 1 to 70% by weight, based on the total weight of the formulation. In some embodiments the concentration is from 1 to 50% by weight or from 10 to 50% by weight. In other embodiments, the concentration is from 35 to 65% by weight, from 40 to 60% by weight, from 45 to 55% by weight or about 50% by weight.

Preferred concentrations of the compound according to the present invention or embodiments thereof dissolved in drinking water are from 0.01 to 0.05% weight by volume, particularly 0.01 to 0.025%, and in-feed from 100 to 400 ppm (g/metric ton), particularly 100 to 200 ppm.

In a preferred embodiment of the invention or embodiments thereof the veterinary compositions of the present invention and/or embodiments thereof comprise a therapeutically effective amount of a compound of the present invention and/or embodiments thereof as the single active agent.

In a preferred embodiment of the invention or embodiments thereof the veterinary compositions of the present invention and/or embodiments thereof comprise a therapeutically effective amount of a compound of the present invention and/or embodiments thereof in combination with one or more other known active agent(s). These one or more other known active agent(s) may be of a similar spectrum as the present compound to synergistically enhance treatment of the infections covered by the spectrum of the present compound. Alternatively, these one or more other known active agent(s) may be of a different spectrum as the present compound, when multiple parasitic organisms are suspected in which another agent of a different spectrum may be required in addition

to the present compound. The treatment can involve administering a composition having the present compound and one or more further known active agent(s) or administration of the inventive compounds followed by or preceded by administration of one or more additional active agent(s).

Particular combinations comprise a) one or more compounds according to this invention with b) one or more pharmaceutically acceptable active compounds which differ in structure from component a). The active compounds b) are preferably anthelmintic compounds, more preferably selected from the group consisting of avermectins (e.g., ivermectin, selamectin, doramectin, abamectin, emamectin and eprinomectin); milbemycins (moxidectin and milbemycin oxime); probenzimidazoles (e.g., febantel, netobimin, and thiophanate); benzimidazole derivatives, such as a thiazole benzimidazole derivative (e.g., thiabendazole and cambendazole) or a carbamate benzimidazole derivatives (e.g., fenbendazole, albendazole (oxide), mebendazole, oxfendazole, parbendazole, oxibendazole, flubendazole, and triclabendazole); an imidazothiazole (e.g., levamisole and tetramisole); a tetrahydropyrimidine (morantel and pyrantel), organophosphates (e.g., trichlorphon, haloxon, dichlorvos, and naphthalophos); salicylanilides (e.g., closantel, oxyclozanide, rafoxanide, and niclosamide); nitrophenolic compounds (e.g., nitroxynil and nitroscanate); benzenedisulphonamides (e.g., clorsulon); pyrazineisoquinolines (e.g., praziquantel and epsiprantel); heterocyclic compounds (e.g., piperazine, diethylcarbamazine, dichlorophen, and phenothiazine); arsenicals (e.g., thiacetarsamide, melorsamine, and arsenamide); cyclooctadepsipeptides (e.g., emodepside, PF1022A); paraherquamides (e.g., derquantel, paraherquanide); and amino-acetonitrile compounds (e.g. monepantel, AAD 1566); tribendimidine (amidine compound); amidine compounds (e.g., amidantel and tribendimidin), including all pharmaceutically acceptable forms, such as salts, solvates or N-oxides.

The compounds as described in this specification can be combined with pharmaceutically acceptable insecticides or acaricides. Such pharmaceutically acceptable insecticides and acaricides include, for example, acetamiprid, acetoprole, amitraz, amidoflumet, avermectin, azadirachtin, bifenthrin, bifenazate, broflanilide, buprofezin, bistrifluron, chlorfenapyr, chlorfluazuron, chlorantraniliprole, chlorpyrifos, chromafenozide, clothianidin, cyantraniliprole, cyflumetofen, 13-cyfluthrin, cyhalothrin, Acyhalothrin, cymiazole cypermethrin, cyromazine, deltamethrin, demiditraz, diafenthiuron, diazinon, diflubenzuron, dimefluthrin, dinotefuran, emamectin, esfenvalerate, ethiprole, fenoxycarb, fenpropathrin, fenvalerate, fipronil, flonicamid, flubendiamide, flucythrinate, tau-fluvalinate, flufenoxuron, halofenozide, hexaflumuron, imidacloprid, indoxacarb, lufenuron, metaflumizone, methoprene, metofluthrin, methoxyfenozide, nitenpyram, novaluron, noviflumuron, permethrin, phosmet, profluthrin, protrifenbute, pymetrozine, pyrafluprole, pyrethrin, pyridalyl, pyrifluquinazon, pyriprole, pyriproxyfen,

rotenone, ryanodine, sisapronil, spinetoram, spinosad, spiroadiclofen, spiromesifen, spirotetramat, sulfoxaflor, tebufenozide, tebufenpyrad, teflubenzuron, tefluthrin, tetrachlorvinphos, tetramethylfluthrin, thiacloprid, thiamethoxam, tigolaner, tolfenpyrad, tralomethrin, and triflumuron. General references discussing antiparasitic agents, such as insecticides and acaricides, include, for example, The Pesticide Manual, 18th Edition, J. A. Turner, Ed., British Crop Protection Council Publications, U.K. (2018).

The compounds as described in this specification can be combined with pharmaceutically acceptable insect growth regulators. Such pharmaceutically acceptable insect growth regulators include, for example, methoprene, pyriproxyfen, tetrahydroazadirachtin, chlorfluazuron, cyromazine, diflubenzuron, fluazuron, flucycloxuron, flufenoxuron, hexaflumuron, lufenuron, ifenuron, tebufenozide, and triflumuron. These compounds tend to provide both initial and sustained treatment of parasite infections at all stages of insect development, including eggs, on the animal subject, as well as within the environment of the animal subject.

The compounds as described in this specification can be combined with pharmaceutically acceptable anti-protozoals. Such pharmaceutically acceptable anti-protozoals include, for example, triazintriones like, for example, toltrazuril and ponazuril and triazindiones such as clazuril, diclazuril and letrazuril. In some contemplated embodiments, the compounds are administered with dihydroazole compounds, such as, for example, compounds discussed in WO 2010/75591.

In some contemplated embodiments, the compounds of the present invention are administered with anthelmintic proteins, such as, for example Bacillus thuringensiscrystal proteins e.g. described in WO 2010/053517.

In some contemplated embodiments, the compounds are administered with pyridylmethanamine derivatives, such as, for example, pyridylmethanamine derivatives discussed in EP0539588 WO2007/115643.

In some contemplated embodiments, the compounds is administered with nodulisporic acids and derivatives thereof, such as, for example, compounds discussed in US5,399,582; US5,945,317; US5,962,499; US5,834,260; US6,221,894; or US5,595,991; or WO1996/29073.

In some contemplated embodiments, the compounds are administered with isoxazoline compounds (e.g., sarolaner, fluralaner, lotilaner, afoxolaner, fluxametamide, isocycloseram)

Other antiparasitic compounds contemplated to be useful in combination therapies with the compounds include, for example, imidazo[1,2-b] pyridazine compounds discussed in US2005-

0182059; 1-(4-Mono and dihalomethylsulphonylphenyl)-2-acylamino-3-fluoropropanol compounds discussed US7,361,689; trifluoromethanesulfonamide oxime ether compounds discussed in US7,312,248; n-[(phenyloxy)phenyl]-1, 1, 1-trifluoromethanesulfonamide and n-[(phenylsulfanyl)phenyl]-1, 1, 1-trifluoromethanesulfonamide compounds discussed in US2006-
5 0281695; and 2-phenyl-3-(1 H-pyrrol-2-yl)acrylonitrile compounds discussed in US2006/0128779; azole compounds discussed in WO2017/192385, WO2019/170626, WO2019/197468, WO2019/201835, WO2019/206799, WO2019/215198, WO2020/053364, WO2020/053365, WO2020/070049, WO2020/079198, WO2020/094363, WO2020/169445, WO2020/193341, WO2020/201079, WO2020/201398, WO2020/208036, WO2020/212235, and
10 WO2020/219871.

Further aspects regarding the formulation of drugs and various excipients are found for example in Gennaro, A.R., et al., eds., Remington: The Science and Practice of Pharmacy (Lippincott Williams & Wilkins, 20th Ed., 2000). Moreover, methods of formulation are well known in the art and are disclosed for example in Remington: The Science and Practice of Pharmacy, Mack
15 Publishing Company, Easton, Pa., 19th Edition (1995).

As indicated above, the compound according to the invention can be considered as an "active" agent, which is regarded as a substance that will inhibit the growth of helminths such as *Dirofilaria*, in particular *Dirofilaria immitis*. The term "inhibiting the growth" indicates that the rate of increase in the numbers of a population of a helminth is reduced.

20 It is understood that the term "treating" or "treatment" used herein includes prophylactic, metaphylactic and therapeutic or curative treatment. Prophylactic or metaphylactic treatment, i.e. deworming, is commonly used to prevent helminth infection so to control parasitic infections in animals. In addition, helminths can infect humans and therefore pose a threat to human health as well. Prophylactic treatments comprise treatments which are done at regular intervals such as 1-6
25 times per year, or 2-4 times per year or 1-4 per month, or even continuous such as via the drinking water. Metaphylactic treatment comprise treatment of all animal e.g. in the same area, when a number of animals is diagnosed to prevent the spread of the parasite to the other animals. Metaphylactic and prophylactic treatment may also occur seasonal, e.g. when the vector is especially active.

30

In therapeutic or curative treatment the compounds are administered after clinical diagnosis. In this method, there is reduced expenses for anthelmintics, possibility of selection for resistance is

significantly reduced if only some animals are treated and this will ensure the presence of a susceptible parasite population within the herd or flock, but its disadvantage is that, it requires regular monitoring which increases labour input. In a preferred embodiment the compounds according to this invention are used to treat a helminth infection, such as an infection caused by one or more helminths selected from the group consisting of a) cestodes: *e.g. Anaplocephala* spp.; *Dipylidium* spp.; *Diphyllobothrium* spp.; *Echinococcus* spp.; *Moniezia* spp.; *Taenia* spp.; b) trematodes *e.g. Dicrocoelium* spp.; *Fasciola* spp.; *Paramphistomum* spp.; *Schistosoma* spp.; or c) nematodes, *e.g. Acanthocheilonema* spp.; *Ancylostoma* spp.; *Aneator* spp.; *Ascaridia* spp.; *Ascaris* spp.; *Brugia* spp.; *Bunostomum* spp.; *Capillaria* spp.; *Chabertia* spp.; *Cooperia* spp.; *Cyathostomum* spp.; *Cylicocyclus* spp.; *Cylicodontophorus* spp.; *Cylicostephanus* spp.; *Craterostomum* spp.; *Dictyocaulus* spp.; *Dipetalonema* spp.; *Dirofilaria* spp.; *Dracunculus* spp.; *Enterobius* spp.; *Filaroides* spp.; *Habronema* spp.; *Haemonchus* spp.; *Heterakis* spp.; *Hyostromylus* spp.; *Metastrongylus* spp.; *Meullerius* spp.; *Necator* spp.; *Nematodirus* spp.; *Nippostrongylus* spp.; *Oesophagostomum* spp.; *Onchocerca* spp.; *Oncocercidae* spp.; *Ostertagia* spp.; *Oxyuris* spp.; *Parascaris* spp.; *Stephanurus* spp.; *Strongylus* spp.; *Syngamus* spp.; *Toxocara* spp.; *Strongyloides* spp.; *Teladorsagia* spp.; *Toxascaris* spp.; *Trichinella* spp.; *Trichuris* spp.; *Trichostrongylus* spp.; *Triodontophorus* spp.; *Uncinaria* spp., and/or *Wuchereria* spp.; preferably nematodes; in particular *Dirofilaria* spp.; *Haemonchus* spp.; *Ascaridia* spp.; *Strongylus* spp.; especially *Dirofilaria immitis*.

In particular the compounds according to the present invention or the veterinary composition according to present invention are administered to treat or prevent disorders/diseases caused by one or more helminths selected from the group consisting a) nematodes: *Ostertagia ostertagi*, *Cooperia oncophora*, *Cooperia punctata*, *Trichostrongylus axei*, *Haemonchus placei*, *Haemonchus contortus*, *Nematodirus helvetianus*, *Nematodirus spathiger*, *Trichostrongylus colubriformis*, *Trichostrongylus circumcincta*, *Oesophagostomum venulosum*, *Chabertia ovina*, *Dictyocaulus viviparous*, *Dictyocaulus filaria*, *Dirofilaria immitis*, *Dirofilaria repens*; b) Trematodes: *Fasciola hepatica*, *Fascioloides magna*, *Dicrocoelium dentriticum*, *Paramphistomum cervi*, c) Cestodes: *Moniezia expansa*.

The present invention provides the compounds according to the invention or the veterinary composition according to the present invention for use as a medicament. In a preferred embodiment the compounds according to the invention or the veterinary composition according to the present invention are suitable for use as a medicament for the treatment of helminthiasis and in particular heartworm disease.

The compounds according to the present invention or the veterinary composition according to the present invention are used to make a medicament. In a preferred embodiment the compounds according to the present invention or the veterinary composition according to the present invention are used to make a medicament for the treatment of helminthiasis and in particular heartworm disease.

Further, the invention provides the use of the compound according to the present invention or the veterinary composition according to the present invention for the manufacture of a medicament.

Further, the invention provides the use of the compounds of the present invention or the veterinary composition according to the present invention for the manufacture of a medicament for the treatment of helminthiasis and in particular heartworm disease. Preferably, the compounds of the present invention or the veterinary composition according to the present invention are used for the manufacture of a medicament for the treatment of helminthiasis and in particular heartworm disease.

Moreover, the present invention provides the compounds according to the present invention or the composition of the present invention for use in the treatment of disorders/diseases caused by helminths, preferably by one or more helminths selected from the group consisting of a) cestodes: *e.g.* *Anaplocephala* spp.; *Dipylidium* spp.; *Diphyllobothrium* spp.; *Echinococcus* spp.; *Moniezia* spp.; *Taenia* spp.; b) trematodes *e.g.* *Dicrocoelium* spp.; *Fasciola* spp.; *Paramphistomum* spp.; *Schistosoma* spp.; or c) nematodes, *e.g.* *Acanthocheilonema* spp.; *Ancylostoma* spp.; *Aneator* spp.; *Ascaridia* spp.; *Ascaris* spp.; *Brugia* spp.; *Bunostomum* spp.; *Capillaria* spp.; *Chabertia* spp.; *Cooperia* spp.; *Cyathostomum* spp.; *Cylicocyclus* spp.; *Cylicodontophorus* spp.; *Cylicostephanus* spp.; *Craterostomum* spp.; *Dictyocaulus* spp.; *Dipetalonema* spp.; *Dirofilaria* spp.; *Dracunculus* spp.; *Enterobius* spp.; *Filaroides* spp.; *Habronema* spp.; *Haemonchus* spp.; *Heterakis* spp.; *Hyostromylus* spp.; *Metastrongylus* spp.; *Meullerius* spp.; *Necator* spp.; *Nematodirus* spp.; *Nippostrongylus* spp.; *Oesophagostomum* spp.; *Onchocerca* spp.; *Oncocercidae* spp.; *Ostertagia* spp.; *Oxyuris* spp.; *Parascaris* spp.; *Stephanurus* spp.; *Strongylus* spp.; *Syngamus* spp.; *Toxocara* spp.; *Strongyloides* spp.; *Teladorsagia* spp.; *Toxascaris* spp.; *Trichinella* spp.; *Trichuris* spp.; *Trichostrongylus* spp.; *Triodontophorus* spp.; *Uncinaria* spp., and/or *Wuchereria* spp.; more preferably nematodes, in particular *Dirofilaria* spp.; *Haemonchus* spp.; *Ascaridia* spp.; *Strongylus* spp and *Oesophagostomun dentatum*, especially *Dirofilaria immitis*.

In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of filariasis and in particular heartworm disease. In a preferred embodiment of the invention or

embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are *Dirofilaria* spp., more in particular *Dirofilaria repens* or *Dirofilaria immitis*.

5 In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of haemonchosis. In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are *Haemonchus* spp. and in particular *Haemonchus placei* and *Haemonchus contortus*.

10 In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of ascaridiasis. In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are *Ascaridia galli*.

15 In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of oesophagostomiasis. In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are
20 *Oesophagostomum* spp. and in particular *Oesophagostomum venulosum* and *Oesophagostomum dentatum*.

In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of *Trichostrongylus* infection. In a preferred embodiment of the invention or embodiments thereof,
25 the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are *Trichostrongylus* spp. and in particular *Trichostrongylus axei* and *Trichostrongylus colubriformis*.

In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of
30 Ostertagiosis. In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the

treatment of disorders/diseases caused by helminths, wherein the helminths are *Ostertagia* spp. and in particular *Ostertagia ostertagi*.

In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of
5 *Cooperia* infection. In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are *Cooperia* spp. and in particular *Cooperia oncophora*.

In a preferred embodiment of the invention or embodiments thereof, the compounds according to
10 the present invention or the composition of the present invention are for use in the treatment of Nematodiriasis. In a preferred embodiment of the invention or embodiments thereof, the compounds according to the present invention or the composition of the present invention are for use in the treatment of disorders/diseases caused by helminths, wherein the helminths are *Nematodirus* spp. and in particular *Nematodirus helvetianus*, *Nematodirus spathiger*.

15 It is contemplated that the compounds according to this invention and compounds corresponding to the use according to the invention may be used to treat animals, including humans and non-human animals, especially non-human mammals. Such non-human mammals include, for example, livestock mammals (*e.g.*, swine, livestock ruminants like bovines, sheep, goats, etc.), laboratory mammals (*e.g.*, mice, rats, jirds, etc.), companion mammals (*e.g.*, dogs, cats, equines,
20 etc.), and wild and zoo mammals (*e.g.*, buffalo, deer, etc.). It is contemplated that the compounds also are suitable to treat non-mammals, such as poultry (*e.g.*, turkeys, chickens, ducks, etc.) and fish (*e.g.*, salmon, trout, koi, etc.).

In the following the use of the compounds as disclosed and covered by the general structures disclosed in this application for use in the treatment of heartworm disease, especially if associated
25 with *Dirofilaria*, in particular *Dirofilaria immitis*, is sometimes referred to as “use according to the invention”.

It has been shown by the inventors that the compounds of the current invention as disclosed and defined earlier are especially suitable for the treatment of heartworm disease, especially in dogs.

The compounds according to the present invention or the veterinary composition according to
30 present invention are administered to treat or prevent disorders/diseases caused by one or more helminths selected from the group consisting of a) cestodes: *e.g.* *Acanthocheilonema* spp.; *Anaplocephala* spp.; *Dipylidium* spp.; *Diphyllobothrium* spp.; *Echinococcus* spp.; *Moniezia* spp.;

Taenia spp.; b) trematodes e.g. *Dicrocoelium* spp.; *Fasciola* spp.; *Paramphistomum* spp.;
Schistosoma spp.; or c) nematodes, e.g. *Ancylostoma* spp.; *Aneator* spp.; *Ascaridia* spp.; *Ascaris*
spp.; *Brugia* spp.; *Bunostomum* spp.; *Capillaria* spp.; *Chabertia* spp.; *Cooperia* spp.;
5 *Cyathostomum* spp.; *Cylicocyclus* spp.; *Cylicodontophorus* spp.; *Cylicostephanus* spp.;
Craterostomum spp.; *Dictyocaulus* spp.; *Dipetalonema* spp.; *Dirofilaria* spp.; *Dracunculus* spp.;
Enterobius spp.; *Filaroides* spp.; *Habronema* spp.; *Haemonchus* spp.; *Heterakis* spp.;
Hyostromylus spp.; *Metastrongylus* spp.; *Meullerius* spp. *Necator* spp.; *Nematodirus* spp.;
Nippostrongylus spp.; *Oesophagostomum* spp.; *Onchocerca* spp.; *Oncocercidae* spp.; *Ostertagia*
10 spp.; *Oxyuris* spp.; *Parascaris* spp.; *Stephanurus* spp.; *Strongylus* spp.; *Syngamus* spp.; *Toxocara*
spp.; *Strongyloides* spp.; *Teladorsagia* spp.; *Toxascaris* spp.; *Trichinella* spp.; *Trichuris* spp.;
Trichostrongylus spp.; *Triodontophorus* spp.; *Uncinaria* spp., and/or *Wuchereria* spp.; more
preferably nematodes, in particular *Dirofilaria* spp.; *Haemonchus* spp.; *Ascaridia* spp.; *Strongylus*
spp. and *Oesophagostomum dentatum*, especially *Dirofilaria immitis*. More preferably, the
15 compounds according to the present invention or the veterinary composition according to present
invention are administered to treat or prevent heartworm disease.

In particular the compounds according to the present invention or the veterinary composition
according to present invention are administered to treat or prevent disorders/diseases caused by
one or more helminths selected from the group consisting a) nematodes: *Ostertagia ostertagi*,
Cooperia oncophora, *Cooperia punctata*, *Trichostrongylus axei*, *Haemonchus placei*,
20 *Haemonchus contortus*, *Nematodirus helvetianus*, *Nematodirus spathiger*, *Trichostrongylus*
colubriformis, *Trichostrongylus circumcincta*, *Oesophagostomum venulosum*, *Chabertia ovina*,
Dictyocaulus viviparus, *Dictyocaulus filaria*, *Dirofilaria immitis*, *Dirofilaria repens*; b)
Trematodes: *Fasciola hepatica*, *Fascioloides magna*, *Dicrocoelium dentriticum*,
Paramphistomum cervi, c) Cestodes: *Monezia expansa*.

25 The term “treatment” as used herein refers to reversing, alleviating, inhibiting the progress of a
disease, disorder or condition. In case of the heartworm disease, this means that the clinical
symptoms (reduced function of lung, heart, liver and/or kidney) are alleviated. Prophylactic use is
expressly contemplated, especially in the treatment of heartworm. It is advantageous to
prophylactically treat helminth infection by deworming.

30 The term “treatment” as used herein also refers to inhibiting the growth, migration or survival of
larval stages of helminths such as *Dirofilaria*, especially *Dirofilaria immitis*, after these larval
stages have been transmitted to a mammalian host by the bite of a vector such as a mosquito.

Thus, the invention provides a method of treating a disease caused by helminths which comprises administering to an animal, in particular a dog, a therapeutically effective amount of a compound according to the present invention or the composition according to the present invention. In other words, the invention provides a method of treating filariasis and especially heartworm disease
5 comprising administering a therapeutically effective amount of a compound according to the invention or the composition according to the present invention to a mammal, in particular a dog, in need thereof.

The invention is also directed to a method for treating an animal with diseases caused by a nematode comprising administering to the subject in need thereof an effective amount of a
10 compound according to the present invention or a composition according to the present invention and/or embodiments thereof, wherein the helminth is a nematode and is at least one selected from the group of *Dirofilaria* spp., in particular *Dirofilaria immitis*. Suitably the subject is a mammal, in particular a dog or a cat, especially a dog.

The invention is also directed to a method for treating a mammal, preferably a dog, suffering from
15 a disease caused by a helminth, in particular a nematode, comprising administering to the subject in need thereof an effective amount of a compound according to the present invention or the composition according to the present invention and/or embodiments thereof, wherein the nematode is at least one selected from the group of *Dirofilaria*, in particular *Dirofilaria immitis*.

In a preferred embodiment the compounds according to this invention are used to treat a disease
20 caused by nematodes in an animal, wherein the nematode is at least one of helminths such as *Dirofilaria*, in particular *Dirofilaria immitis*, comprising administering an effective amount of a compound according to the invention to the animal in need thereof.

According to the treatment by the compounds of the present invention and/or embodiments thereof, diseases caused by helminths, in particular nematodes, especially *Dirofilaria*, more
25 especially *Dirofilaria immitis*, are treated or prevented in a mammal, in particular a dog, by administering to the animal a therapeutically effective amount of a compound of the invention in such amounts and for such time as is necessary to achieve the desired result.

A "therapeutically effective amount" of a compound of the invention and/or embodiments thereof means a sufficient amount of the compound according to the present invention or the composition
30 according to the present invention for treating heartworm disease, at a reasonable benefit/risk ratio applicable to any medical treatment. It will be understood, however, that the total daily usage of a compound according to the invention and a composition according to present invention will be

decided by the attending physician or veterinary doctor within the scope of sound medical judgment. The specific therapeutically effective dose level for any particular animal will depend on a variety of factors including the disorder being treated and the severity of the disorder; the activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the animal; the time of administration, route of administration and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed; and like factors well known in the medical arts.

When the compound according to this invention is administered orally or parenterally by subcutaneous injection, the total dose is preferably greater than about 0.001 mg/kg (i.e. 0.001 milligram of compound according to this invention per kilogram body weight of the treated animal). In some such embodiments, the total dose is from about 0.001 to about 200 mg/kg, from about 0.01 to about 20 mg/kg, from about 0.1 to about 10 mg/kg or from about 1 to about 20 mg/kg. The same dose range may be suitable for other dosage routes. The desired dose, however, may be less in some instances where the compound according to this invention is administered intravenously.

Protection is preferably for at least 7 days, more preferably for at least 10 days, more preferably for at least 2 weeks, more preferably for at least 3 weeks, more preferably for at least 4 weeks. The protection is for 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20 weeks or more. Preferably the protection is for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 months or more.

The dose used to control diseases caused by a helminth such as *Dirofilaria immitis* might vary with the compound, the severity of the disease and the age, weight and condition of the animal, in particular the dog. The total dose required for several days' protection will generally, however, be in the range of from about 0.1 to about 200 mg/kg bodyweight and preferably will be in the range of from about 1 to about 100 mg/kg. Preferably protection is for at least seven days, more preferably at least 2 weeks, more preferably at least 1 month, and even more preferably for at least 1, 2, 3, 4,5, or 6 months.

Protection for up to about seven days can be provided by a single dose; the length of protection will depend on the dose given. The total dose can also be divided into smaller doses given at intervals, such as once daily for two to seven days. Obviously, other suitable dosage regimens can be constructed.

Especially preferred is the use of the compounds according to the present invention or the composition according to the present invention in dogs. The compounds according to the present invention or the composition according to the present invention can be used in animals of different weights, including animals of a weight higher than 35 kg.

5 Other exemplary animals that can be treated with the compounds according to the present invention or the composition according to the present invention are smaller pets such as cats. In one embodiment the compounds according to the present invention or the composition according to the present invention are used to treat diseases such as severe lung disease, heart failure and damage to other inner organs caused by *Dirofilaria*, more especially *Dirofilaria immitis*.

10 In one embodiment, the animal that is treated is a dog and the disease that is treated is heartworm disease.

In a preferred embodiment of the invention or embodiments thereof a single administration of a composition according to this invention is sufficient to treat or prevent a disease caused by helminth, such as a nematode, in particular *Dirofilaria immitis*, or at least to diminish the clinical
15 symptoms in the diseased animal. This can be called “one shot” administration. Although the administration of such a “one shot” single dose is very suitable, it is contemplated that multiple doses can be used, e.g. two administrations 12-24 hours apart or alternatively two administrations 48-72 hours apart.

Factors affecting the preferred dosage may include for example the disease to be treated, the type
20 (e.g. species and breed), age, size, sex, diet, activity and condition of the of the diseased animal, the dosage route, pharmacological considerations such as the activity, efficacy, pharmacokinetic and toxicology profiles of the particular compound according to the present invention and the composition administered and whether the compound according to the present invention is administered as part of a combination of active ingredients. Thus, the preferred amount of the
25 compound according to this invention can vary and can therefore deviate from the typical dosages set forth above. Determining such dosage adjustments is generally within the skill of those in the art. The effective dosage will vary; for example, for prophylactic treatment relatively low doses may be be administered over an extended time or relatively high doses may be administered in a single treatment. The formulation type selected for a dosage form in any instance will depend on
30 the particular purpose envisaged and the physical, chemical and biological properties of the compound according to this invention.

The veterinary compositions, the uses as medicament and uses in the treatment of diseases caused by helminths, in particular nematodes, especially *Dirofilaria immitis*, and methods according to the present invention encompass methods wherein a compound according to this invention is the sole active ingredient administered to the recipient animal. It is contemplated, however, that the veterinary compositions, the uses as medicament and uses in the treatment of diseases caused by nematodes, in particular *Dirofilaria immitis*, and methods according to the present invention also encompass combination therapies wherein a compound is administered in combination with one or more other pharmaceutically acceptable active ingredient(s). The other active ingredient(s) may be, for example, one or more other compounds according to this invention. Alternatively (or additionally), the other active ingredient(s) may be one or more pharmaceutically acceptable compound(s) that are not compounds according to this invention. The other active ingredient(s) may target the same and/or different diseases or conditions.

Contemplated active ingredient(s) that may be administered in combination with the compounds according to the present invention include, for example, antibacterials, anti-inflammatories, pharmaceutically acceptable anthelmintics, insecticides and acaricides, insect growth regulators, hormones, immunostimulants, dermatological preparations (e.g. antiseptics and disinfectants) and immunobiologicals (e.g. vaccines and antisera) for disease prevention.

Particular combinations comprise a) one or more compounds according to this invention with b) one or more pharmaceutically acceptable active compounds which differ in structure from component a). The active compounds b) are preferably anthelmintic compounds, more preferably selected from the group consisting of avermectins (e.g., ivermectin, selamectin, doramectin, abamectin, emamectin and eprinomectin); milbemycins (moxidectin and milbemycin oxime); probenzimidazoles (e.g., febantel, netobimin, and thiophanate); benzimidazole derivatives, such as a thiazole benzimidazole derivative (e.g., thiabendazole and cambendazole) or a carbamate benzimidazole derivatives (e.g., fenbendazole, albendazole (oxide), mebendazole, oxfendazole, parbendazole, oxibendazole, flubendazole, and triclabendazole); an imidazothiazole (e.g., levamisole and tetramisole); a tetrahydropyrimidine (morantel and pyrantel), organophosphates (e.g., trichlorphon, haloxon, dichlorvos, and naphthalophos); salicylanilides (e.g., closantel, oxyclozanide, rafoxanide, and niclosamide); nitrophenolic compounds (e.g., nitroxynil and nitroscanate); benzenedisulphonamides (e.g., clorsulon); pyrazineisoquinolines (e.g., praziquantel and epsiprantel); heterocyclic compounds (e.g., piperazine, diethylcarbamazine, dichlorophen, and phenothiazine); arsenicals (e.g., thiacetarsamide, melorsamine, and arsenamide); cyclooctadepsipeptides (e.g., emodepside, PF1022A); paraherquamides (e.g., derquantel, paraherquanide); and amino-acetonitrile compounds (e.g. monepantel, AAD 1566);

tribendimidine (amidine compound); amidine compounds (e.g., amidantel and tribendimidin), including all pharmaceutically acceptable forms, such as salts, solvates or N-oxides.

The compounds as described in this specification can be combined with pharmaceutically acceptable insecticides or acaricides. Such pharmaceutically acceptable insecticides and acaricides include, for example, acetamiprid, acetoprole, amitraz, amidoflumet, avermectin, azadirachtin, bifenthrin, bifenazate, broflanilide, buprofezin, bistrifluron, chlorfenapyr, chlorfluazuron, chlorantraniliprole, chlorpyrifos, chromafenozide, clothianidin, cyantraniliprole, cyflumetofen, 13-cyfluthrin, cyhalothrin, Acyhalothrin, cymiazole cypermethrin, cyromazine, deltamethrin, demiditraz, diafenthiuron, diazinon, diflubenzuron, dimefluthrin, dinotefuran, emamectin, esfenvalerate, ethiprole, fenoxycarb, fenpropathrin, fenvalerate, fipronil, flonicamid, flubendiamide, flucythrinate, tau-fluvalinate, flufenoxuron, halofenozide, hexaflumuron, imidacloprid, indoxacarb, lufenuron, metaflumizone, methoprene, metofluthrin, methoxyfenozide, nitenpyram, novaluron, noviflumuron, permethrin, phosmet, profluthrin, protrifenbute, pymetrozine, pyrafluprole, pyrethrin, pyridalyl, pyrifluquinazon, pyriprole, pyriproxyfen, rotenone, ryanodine, sisapronil, spinetoram, spinosad, spirodiclofen, spiromesifen, spirotetramat, sulfoxaflor, tebufenozide, tebufenpyrad, teflubenzuron, tefluthrin, tetrachlorvinphos, tetramethylfluthrin, thiacloprid, thiamethoxam, tigolaner, tolfenpyrad, tralomethrin, and triflumuron. General references discussing antiparasitic agents, such as insecticides and acaricides, include, for example, The Pesticide Manual, 18th Edition, J. A. Turner, Ed., British Crop Protection Council Publications, U.K. (2018).

The compounds as described in this specification can be combined with pharmaceutically acceptable insect growth regulators. Such pharmaceutically acceptable insect growth regulators include, for example, methoprene, pyriproxyfen, tetrahydroazadirachtin, chlorfluazuron, cyromazine, diflubenzuron, fluazuron, flucycloxuron, flufenoxuron, hexaflumuron, lufenuron, ifenuron, tebufenozide, and triflumuron. These compounds tend to provide both initial and sustained treatment of parasite infections at all stages of insect development, including eggs, on the animal subject, as well as within the environment of the animal subject.

The compounds as described in this specification can be combined with pharmaceutically acceptable anti-protozoals. Such pharmaceutically acceptable anti-protozoals include, for example, triazintriones like, for example, toltrazuril and ponazuril and triazindiones such as clazuril, diclazuril and letrazuril. In some contemplated embodiments, the compounds are administered with dihydroazole compounds, such as, for example, compounds discussed in WO 2010/75591.

In some contemplated embodiments, the compounds of the present invention are administered with anthelmintic proteins, such as, for example *Bacillus thuringiensis* crystal proteins e.g. described in WO 2010/053517.

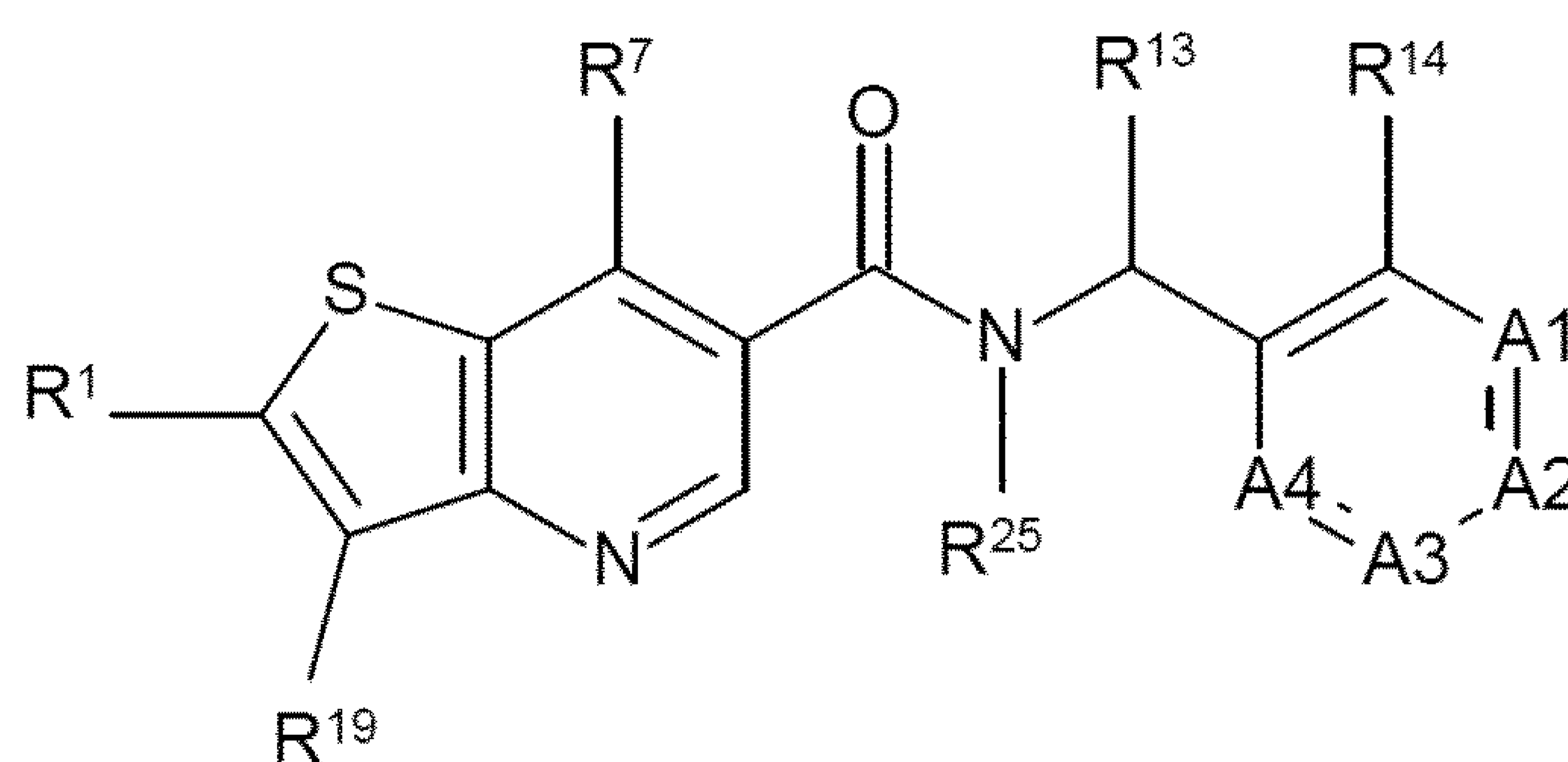
In some contemplated embodiments, the compounds are administered with pyridylmethamine derivatives, such as, for example, pyridylmethamine derivatives discussed in EP0539588 WO2007/115643.

In some contemplated embodiments, the compounds is administered with nodulisporic acids and derivatives thereof, such as, for example, compounds discussed in US5,399,582; US5,945,317; US5,962,499; US5,834,260; US6,221,894; or US5,595,991; or WO1996/29073.

In some contemplated embodiments, the compounds are administered with isoxazoline compounds (e.g., sarolaner, fluralaner, lotilaner, afoxolaner, fluxametamide, isocycloseram)

Other antiparasitic compounds contemplated to be useful in combination therapies with the compounds include, for example, imidazo[1,2-b] pyridazine compounds discussed in US2005-0182059; 1-(4-Mono and dihalomethylsulphonylphenyl)-2-acylamino-3-fluoropropanol compounds discussed US7,361,689; trifluoromethanesulfonamide oxime ether compounds discussed in US7,312,248; n-[(phenyloxy)phenyl]-1, 1, 1-trifluoromethanesulfonamide and n-[(phenylsulfanyl)phenyl]-1, 1, 1-trifluoromethanesulfonamide compounds discussed in US2006-0281695; and 2-phenyl-3-(1 H-pyrrol-2-yl)acrylonitrile compounds discussed in US2006/0128779; azole compounds discussed in WO2017/192385, WO2019/170626, WO2019/197468, WO2019/201835, WO2019/206799, WO2019/215198, WO2020/053364, WO2020/053365, WO2020/070049, WO2020/079198, WO2020/094363, WO2020/169445, WO2020/193341, WO2020/201079, WO2020/201398, WO2020/208036, WO2020/212235, and WO2020/219871.

In embodiment 1 the present invention is directed to a compound of Formula (I)



25

Formula (I)

wherein

R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR²R³, COOH, C(=O)OR⁴, SR⁴, SOR⁴, SO₂R⁴,
 5 SO₂NR⁵R⁶ and C(=O)NR⁵R⁶,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR^{2'}R^{3'}, C(=O)OR^{4'}, SR^{4'}, SOR^{4'}, SO₂R^{4'}, SO₂NR^{5'}R^{6'} and C(=O)NR^{5'}R^{6'},

R² and R³ are independently selected from the group consisting of

15 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl and C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

20 R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl or C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group
 25 consisting of
 30

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{2''}R^{3''}, C(=O)OR^{4''}, SR^{4''}, SOR⁴, SO₂R^{4''}, SO₂NR^{5''}R^{6''} and C(=O)NR^{5''}R^{6''},

5 R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{2'}, R^{3'}, R^{4'}, R^{5'} and R^{6'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{2''}, R^{3''}, R^{4''}, R^{5''} and R^{6''} are independently selected from hydrogen and C₁₋₆-alkyl,

R⁷ is independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 4- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR⁸R⁹, COOH, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰, SO₂NR¹¹R¹² and C(=O)NR¹¹R¹²,

15 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 4- to 10- membered heterocyclyl, C₆₋₁₀ aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'}, SR^{10'}, SOR^{10'}, SO₂R^{10'}, SO₂NR^{11'}R^{12'} and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

25 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl and C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10-membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl or C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{8''}R^{9''}, C(=O)OR^{10''}, SR^{10''}, SOR^{10''}, SO₂R^{10''}, SO₂NR^{11''}R^{12''} and C(=O)NR^{11''}R^{12''},

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

R¹³ is hydrogen or C₁₋₃ alkyl,

R¹⁴ is hydrogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, NR^{14'}R^{14''}, wherein R^{14'} and R^{14''} are independently C₁₋₃-alkyl or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

5 R¹⁹ is independently selected from the group consisting of C₆₋₁₀-aryl and 5- to 10- membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

10 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR²⁰R²¹, C(=O)OR²², SR²², SOR²², SO₂R²², SO₂NR²³R²⁴ and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

15 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl, C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

20 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

25 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{20'}R^{21'}, C(=O)OR^{22'}, SR^{22'}, SOR^{22'}, SO₂R^{22'}, SO₂NR^{23'}R^{24'} and C(=O)NR^{23'}R^{24'},

30 R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{20'}$, $R^{21'}$, $R^{22'}$, $R^{23'}$ and $R^{24'}$ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{25} is independently selected from hydrogen and C₁₋₆-alkyl,

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof.

5 In embodiment 2 the present invention is directed to a compound according to embodiment 1, wherein R^1 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR^2R^3 , $C(=O)OR^4$ and $C(=O)NR^5R^6$,

10 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^2R^3 ,

R^2 and R^3 are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

15 R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O,

20 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R^4 , R^5 and R^6 are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{2'}$ and $R^{3'}$ are independently selected from hydrogen and C₁₋₆-alkyl.

25 In embodiment 3 the present invention is directed to a compound according to embodiment 1 or 2, wherein R^1 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy and halogen,

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy and NR^{2'}R^{3'},

wherein R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl.

In embodiment 4 the present invention is directed to a compound according to anyone of embodiments 1 to 3, wherein R¹ is independently selected from the group consisting of

5 hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride, preferably selected from the group consisting of hydrogen, and methyl.

In embodiment 5 the present invention is directed to a compound according to any one of embodiments 1 to 4, wherein R⁷ is independently selected from the group consisting of

10 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'}, and C(=O)NR^{11'}R^{12'},

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10 membered heterocyclyl and 5- to 10 membered heteroaryl, or

20 R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

25 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10 membered heterocyclyl, and 5- to 10 membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)-OR^{10''} and C(=O)NR^{11''}R^{12''};

R^{10} , R^{11} and R^{12} are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen and C₁₋₆-alkyl,

$R^{8''}$, $R^{9''}$, $R^{10''}$, $R^{11''}$ and $R^{12''}$ are independently selected from hydrogen and C₁₋₆-alkyl.

In embodiment 6 the present invention is directed to a compound according to any one of
5
embodiments 1 to 5, wherein R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, hydroxy,
NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

10
wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, 5- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR⁸R⁹, C(=O)OR¹⁰ and C(=O)NR¹¹R¹²,

R^8 and R^9 are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl, and 5- to 10 membered heteroaryl, or

15
 R^8 and R^9 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

20
wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl, and 5- to 10 membered heteroaryl or the heterocyclic ring formed by R^8 and R^9 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''},

R^{10} , R^{11} and R^{12} are independently selected from hydrogen or C₁₋₆-alkyl,

$R^{8'}$, $R^{9'}$, $R^{10'}$, $R^{11'}$ and $R^{12'}$ are independently selected from hydrogen or C₁₋₆-alkyl.

25
 $R^{8''}$ and $R^{9''}$ are independently selected from hydrogen or C₁₋₆-alkyl.

In embodiment 7 the present invention is directed to a compound according to any one of
embodiments 1 to 6, wherein R^7 is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

5 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

10 In embodiment 8 the present invention is directed to a compound according to any one of embodiments 1 to 7, wherein R⁷ is independently selected from the group consisting of

methyl, ethyl, isopropyl, isopropenyl, methoxy, ethoxy, isopropoxy, hydroxy, methyl sulfoxyl, methyl sulfonyl, methylthio, amino, methylamino, ethylamino, isopropylamino, dimethylamino, isopropylmethylamino, cyclopropylamino, 2-hydroxyethylmethylamino,
 15 hydroxyethylamino, methoxyethylamino, morpholin-4-yl, 4-methylpiperazin-1-yl, 3-hydroxy-pyrrolidin-1-yl, 3-fluoroazetidin-1-yl and 3,3-difluoroazetidin-1-yl, 4-oxo-1-piperidyl, azetidin-1-yl, tetrahydro-2H-pyran-4-yl, piperidin-1-yl, and 4,4-difluoropiperidin-1yl.

20 In embodiment 9 the present invention is directed to a compound according to any one of embodiments 1 to 8, wherein

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
 25 by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

5 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl.

In embodiment 10 the compound according to any one of embodiments 1 to 9, wherein

10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally
15 replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

20 A3 is CR¹⁷, wherein R¹⁷ is hydrogen,

A4 is CR¹⁸, wherein R¹⁸ is hydrogen.

In embodiment 11 the compound according to any one of embodiments 1 to 10, wherein

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally
25 replaced by -NH-, -O- or -S-,

A1 is CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is CR¹⁷, wherein R¹⁷ is hydrogen,

A4 is CR¹⁸, wherein R¹⁸ is hydrogen.

In embodiment 12 the present invention is directed to a compound according to any one of embodiments 1 to 11, wherein none, one or two of residues A1, A2, A3 and A4 is N.

5 In embodiment 13 the present invention is directed to a compound according to any one of embodiments 1 to 12, wherein R¹⁹ is independently selected from the group consisting of

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5- to 10- membered heteroaryl,

10 wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

15 R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

20 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

25 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'}

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

In embodiment 14 the present invention is directed to a compound according to any one of embodiments 1 to 13, wherein R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5- to 10- membered heteroaryl

5 wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

10 wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

In embodiment 15 the present invention is directed to a compound according to any one of embodiments 1 to 14, wherein R¹⁹ is C₆₋₁₀-aryl,

15 wherein the C₆₋₁₀-aryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, halogen, C₁₋₆-alkoxy cyano and nitro wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy is optionally substituted with one or more halogen.

In embodiment 16 the present invention is directed to a compound according to any one of embodiments 1 to 14, wherein R¹⁹ is C₆₋₁₀-aryl,

20 wherein the C₆₋₁₀-aryl is phenyl substituted with one, two or three substituents independently selected from the group consisting of

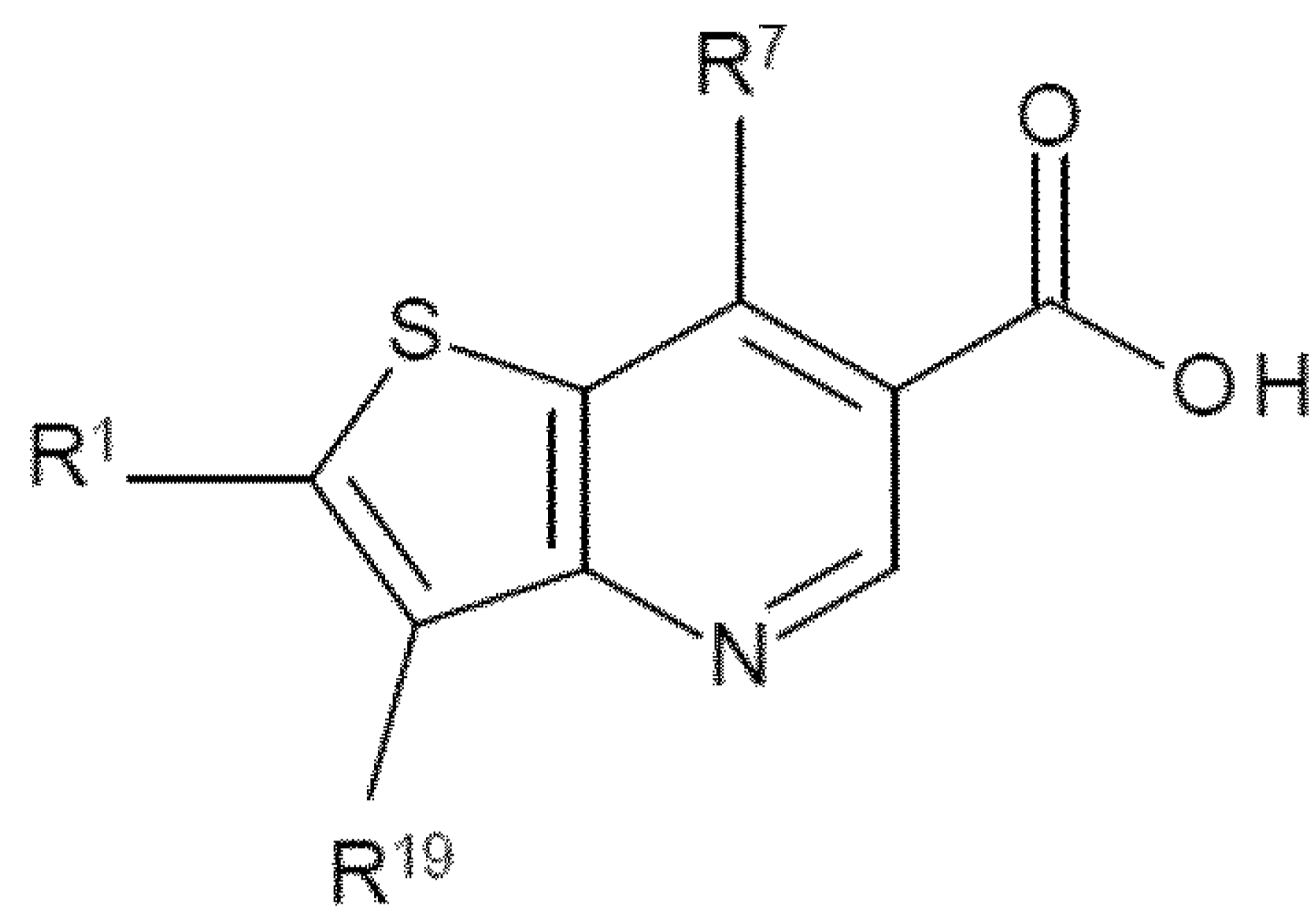
fluoride, chloride bromide, trifluoromethyl and trifluoromethoxy.

25 In embodiment 17 the present invention is directed to a compound according to any one of embodiments 1 to 16, wherein R²⁵ is hydrogen.

In embodiment 18 the present invention is directed to a compound according to any one of the embodiments as described herein being present in form of the (*S*)-enantiomer.

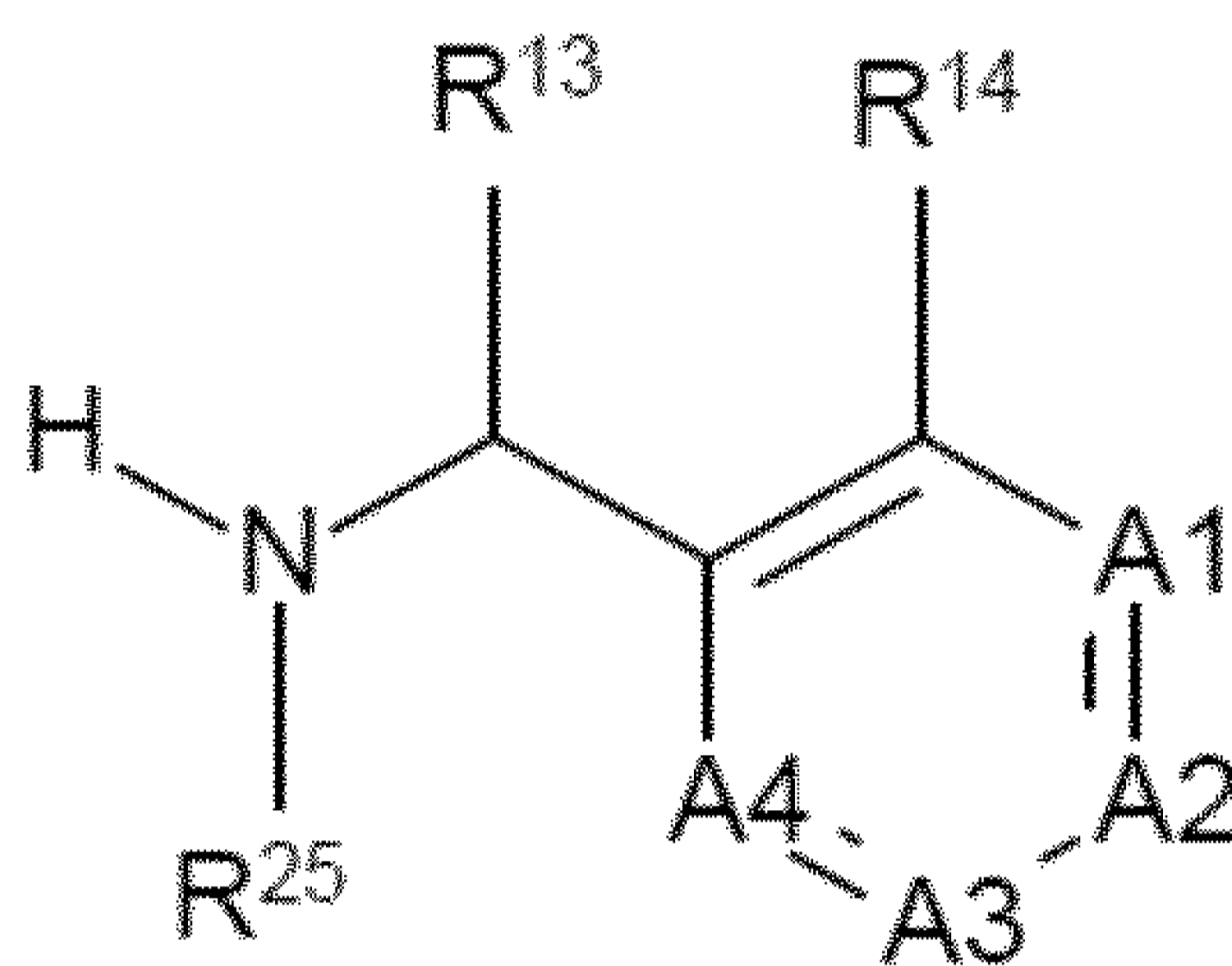
In embodiment 19 the present invention is directed to a process for preparing the compound according to Formula (I) comprising the step of

reacting a compound of Formula (A)



Formula (A)

with a compound of Formula (B)



Formula (B)

wherein R^1 , R^7 , R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are defined as in any one of embodiments as described herein,

to obtain the compound according to Formula (I).

- 5
- 10 In embodiment 20 the present invention is directed to a veterinary composition comprising
- compound according to Formula (I) according to any one of embodiments as described herein, and
 - one or more physiologically acceptable excipient(s).

15 In embodiment 21 the present invention is directed to a veterinary composition according to embodiment 20, wherein the one or more physiologically acceptable excipient(s) are selected from carriers, fillers, flavours, binders, antioxidants, buffers, sugar components, lubricants, surfactants, stabilizers, flow agents, disintegration agents and preservatives and mixtures thereof.

20 In embodiment 22 the present invention is directed to a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of the embodiments as described herein for use as a medicament.

In embodiment 23 the present invention is directed to a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of embodiments as described herein for use in the treatment of disorders/diseases caused by helminths.

5 In embodiment 24 the present invention is directed to a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of embodiments as described herein for use according to embodiment 23, wherein the disease is the heartworm disease.

10 In embodiment 25 the present invention is directed to a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of embodiments as described herein for use according to embodiment 23 or 24, wherein the helminths are *Dirofilaria immitis*.

15 In embodiment 26 the present invention is directed to a method of treating a disease caused by helminths which comprises administering to an animal, in particular a dog, a therapeutically effective amount of a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of embodiments as described herein.

20 In embodiment 27 the present invention is directed to a method of treating filariasis and especially heartworm disease comprising administering a therapeutically effective amount of a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of embodiments as described herein to a mammal, in particular a dog, in need thereof.

25 In embodiment 28 the present invention is directed to a method for treating an animal with diseases caused by a nematode comprising administering to the subject in need thereof an effective amount of a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition according to any one of embodiments as described herein, wherein the helminth is a nematode and is at least one selected from the group of *Dirofilaria* spp., in particular *Dirofilaria immitis*. Suitably the subject is a mammal, in particular a dog or a cat, especially a dog.

30 In embodiment 29 the present invention is directed to a method for treating a mammal, preferably a dog, suffering from a disease caused by a helminth, in particular a nematode, comprising administering to the subject in need thereof an effective amount of a compound according to Formula (I) according to any one of embodiments as described herein or a veterinary composition

according to any one of embodiments as described herein, wherein the nematode is at least one selected from the group of *Dirofilaria*, in particular *Dirofilaria immitis*.

Features of the invention have been described in embodiments in the present application; however, for brevity not all combinations of the features are literally described. Combinations of features as
5 described above are, however, expressly considered to be part of the invention.

Experimental Part**Analytics - HPLC Methods***Method 1*Chromatographic system:

- 5 Column: Xbridge BEH C18 Waters, 2.1x50 mm, 2.5 μ
- Oven: 40°C
- Eluents: Solvent A: water / HCO₂H (0.05%); Solvent B: acetonitrile / HCO₂H (0.05%)
- Flow: 0.8 ml / min
- Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	98	2
1.2	0	100
1.7	0	100
1.8	98	2

- 10 Run time: 2.2 min + 0.5 min equilibration time

*Method 2*Chromatographic system:

- Column: Xbridge BEH C18 Waters, 2.1x50 mm, 2.5 μ
- Oven: 40°C
- 15 Eluents: Solvent A: water / NH₃ (0.1%); Solvent B: acetonitrile
- Flow: 0.8 ml / min
- Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	98	2
1.2	0	100
1.7	0	100
1.8	98	2

- Run time: 2.2 min + 0.5 min equilibration time

Method 3

Chromatographic system:Column: Xbridge BEH Phenyl Waters, 2.1x50 mm, 2.5 μ

Oven: 40°C

Eluents: Solvent A: water / HCO₂H (0.05%); Solvent B: acetonitrile / HCO₂H (0.05%)

5 Flow: 0.8 ml / min

Gradient:

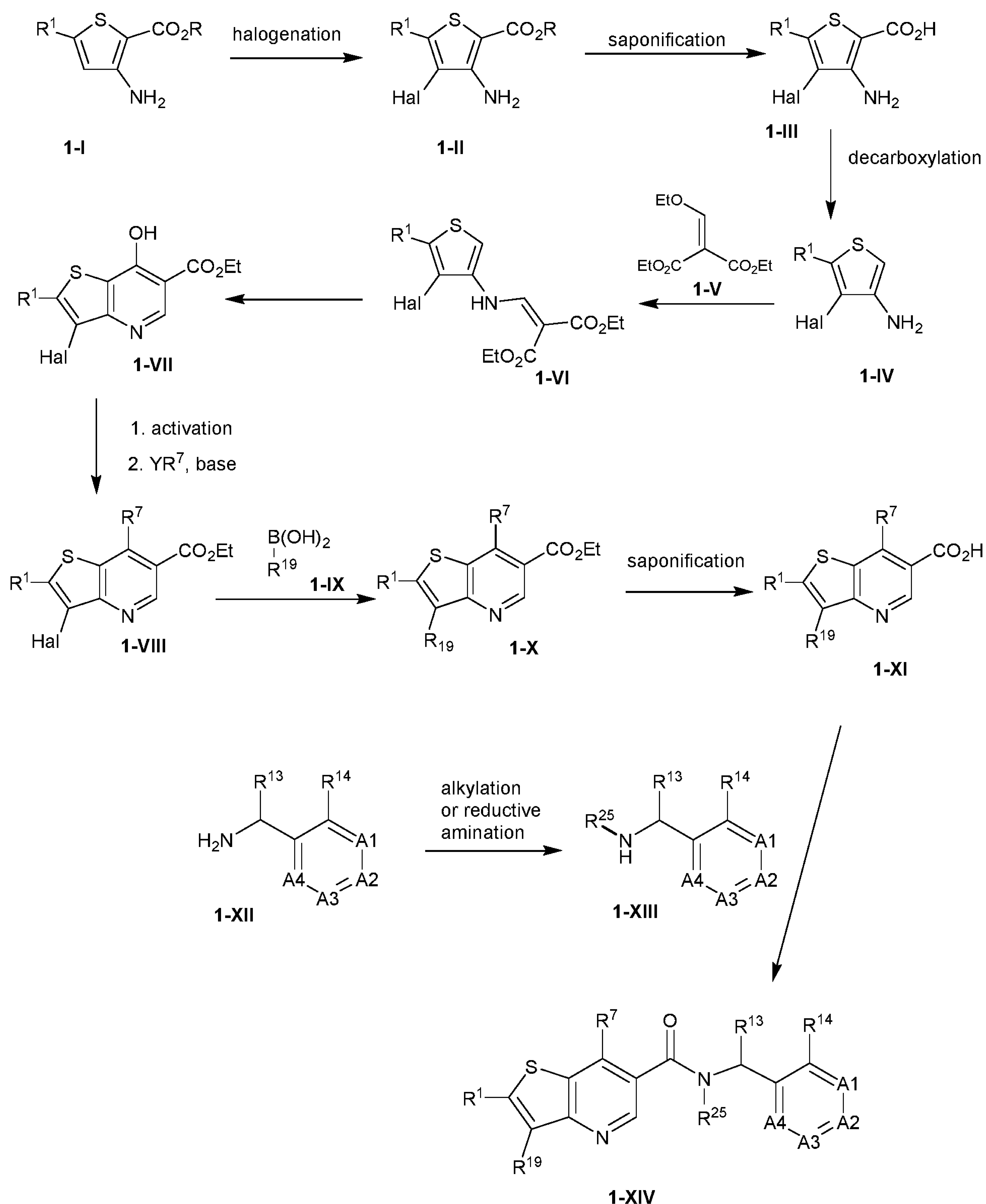
Time [min]	Solvent A [%]	Solvent B [%]
0.0	98	2
1.2	0	100
1.7	0	100
1.8	98	2

Run time: 2.2 min + 0.5 min equilibration time

10 General synthetic procedures

The compounds of the current invention can be synthesized as shown in Scheme 1 below:

Scheme 1:



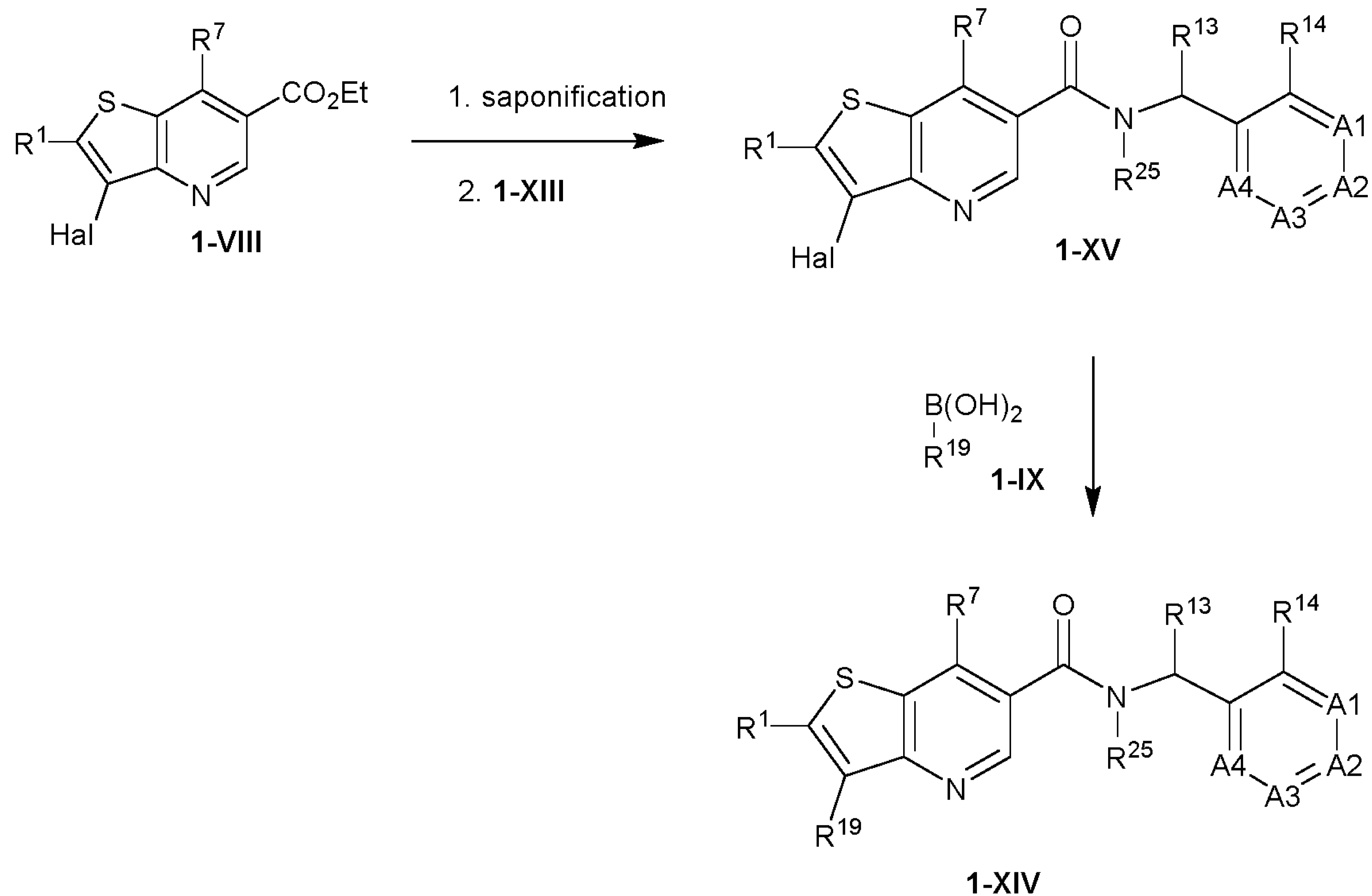
A 3-amino-2-alkoxycarbonylthiophene **1-I** is halogenated in the 4-position, preferably brominated. This can be achieved by heating with hydrobromic acid in dimethyl sulfoxide or by treatment with NBS in carbon tetrachloride, optionally with the addition of a radical initiator like dibenzoyl peroxide. Thiophene compounds **1-I** are commercially available or can be synthesized as described in, for example, Synth. Commun. 2014 (44), 1002-1006. The ester in the halo

compound **1-II** is hydrolyzed by treatment with aqueous base, for example sodium or potassium hydroxide in water. Heating of the thiophene carboxylic acid **1-III** under acidic conditions, for example in acetic or hydrochloric acid gives, under decarboxylation, the amino thiophene **1-IV**. This is condensed with diethyl ethoxymethylenemalonate **1-V** and the resulting enamine
5 compound **1-VI** is cyclized by heating, for example by refluxing in a mixture of biphenyl and biphenylether (Dowtherm A) to give the thienopyridine **1-VII** as described in US2004/0138449. Compounds **1-III**, **1-IV** and **1-VI** can be isolated, or the sequence of **1-III** to **1-VII** can be performed in one pot.

The 4-hydroxy group is activated, for example by converting to a halogen, preferably a chloride
10 by treatment with thionyl chloride. Alternatively, the hydroxy is esterified, for example by esterification with triflic acid anhydride. This is followed by treatment with a nucleophile YR^7 to yield the 4-substituted thienopyridine **1-VIII**. In case R^7 is an amino substituent, YR^7 is preferably an amine, in case R^7 is an alkoxy substituent, YR^7 is preferably an alkoxide. A Suzuki-type coupling with the boronic acid **1-IX** as described in, for example, Tetrahedron 58(48), 9633-9695,
15 2002 gives **1-X**. As an alternative to the free boronic acid **1-IX** an analogous boronic ester might be used, for example a pinacol ester.

Ester hydrolysis by treatment with aqueous base gives the thienopyridine carboxylic acid **1-XI**. Amine **1-XIII** is acylated with the thienopyridine carboxylic acid **1-XI** to give the amide **1-XIV**. Acylation can be performed by activation of **1-X** as acid chloride or use of a coupling reagent like
20 HATU or DCC followed by treatment with **1-XIII** in the presence of a base like triethylamine. Conditions for acylation reactions are described in, for example, volume E22a of Methods of Organic Chemistry (Houben-Weyl), Synthesis of Peptides and Peptidomimetics, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 2002. **1-XIII** can be a primary amine ($R^{25} = H$) or a secondary amine ($R^{25} = \text{alkyl}$), in the latter case R^{25} can be introduced by reductive amination of
25 the primary amine **1-XII**.

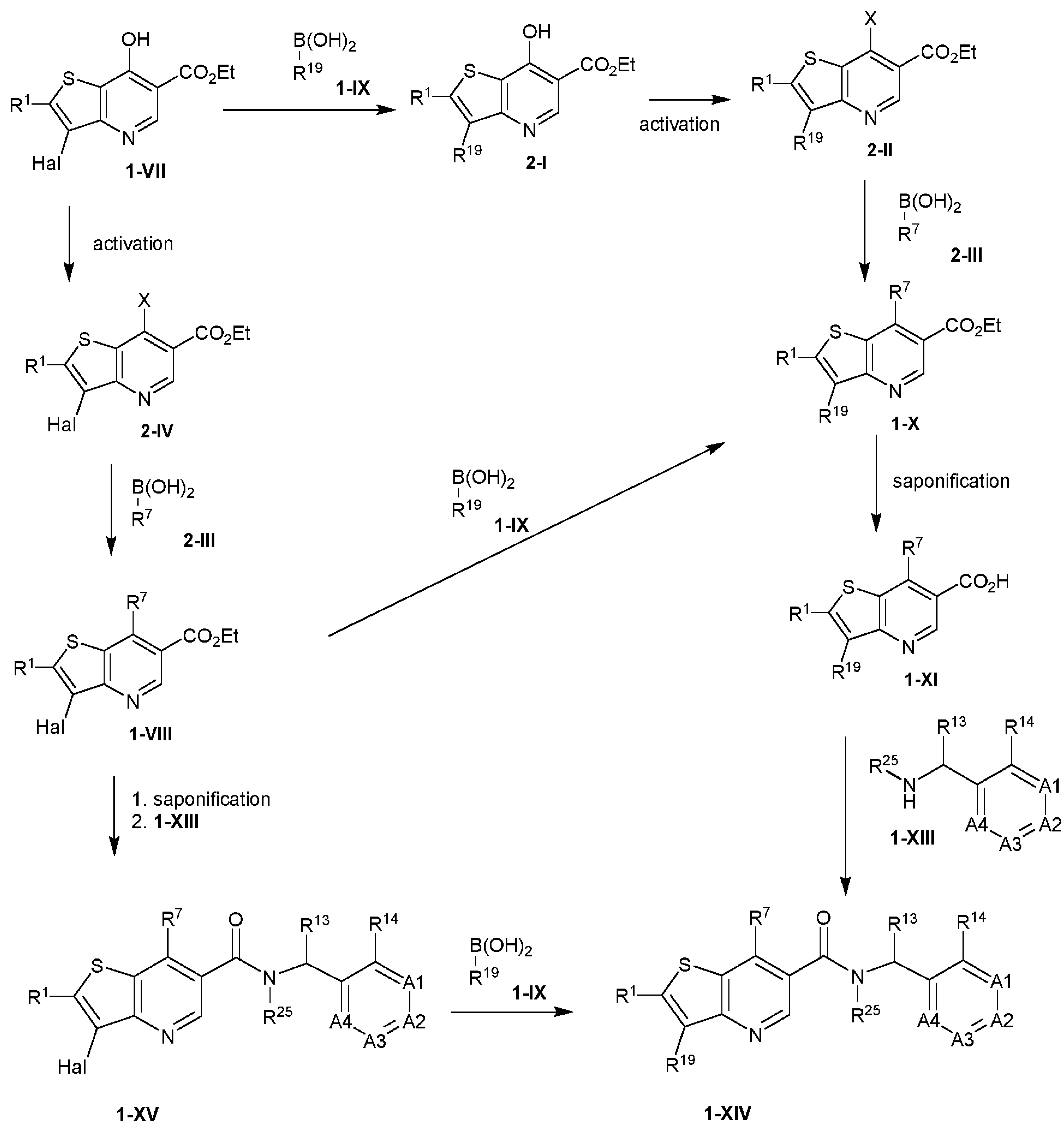
Alternatively, the thienopyridine **1-VIII** can be subjected to saponification followed by coupling with the amino compound **1-XIII** to give the amide **1-XV** as shown below:



Suzuki-type coupling with the boronic acid **1-IX** gives the amide **1-XIV**.

Alternatively, compounds of Formula I, for example where R^7 is an alkyl or alkenyl group, can be synthesized as shown in scheme 2.

Scheme 2



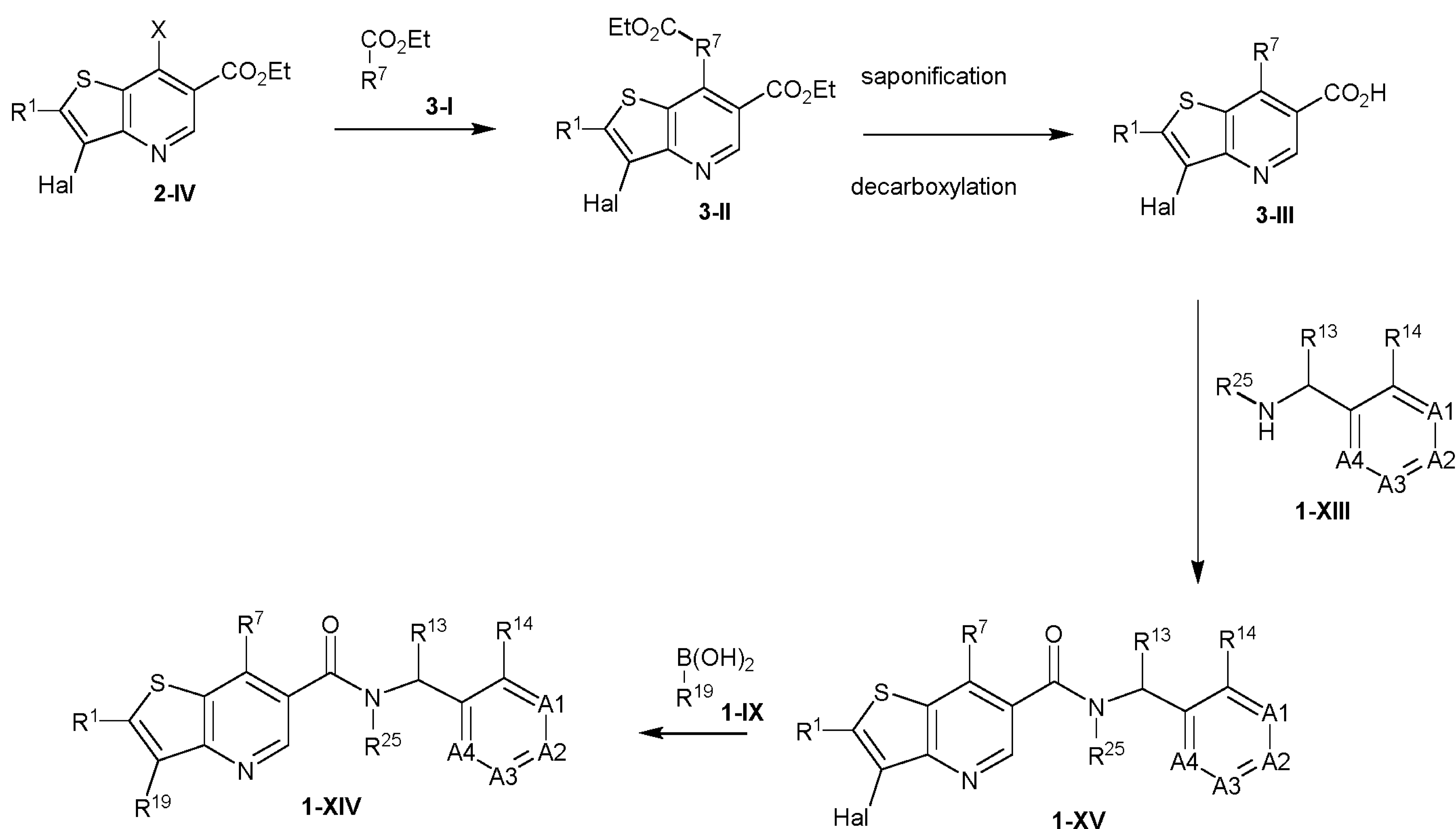
4-Hydroxythienopyridine **1-VII** undergoes a Suzuki-type coupling with a boronic acid **1-IX** as described in Scheme 1 to yield **2-I**. The 4-hydroxygroup is activated to give **2-II**, for example by treatment with a chlorinating agent like thionyl chloride ($X=Cl$) or phosphoryl bromide ($X=Br$) or by treatment with triflic acid anhydride ($X = OSO_2CF_3$). The activated **2-II** is reacted with an alkyl- or alkenyl boronic acid **2-III** as described in, for example, ChemMedChem, 2014, 9(4), 719-723 followed by saponification with aqueous base to give the carboxylic acid **1-XI**. Acylation of the amine **1-XIII** with **1-XI** as described in Scheme 1 gives the amide **1-XIV**.

Alternative reaction sequences are also possible, for example where activation of **1-VII** is followed by Suzuki-type coupling to give the ester **1-VIII**. This can then be coupled with the boronic acid

1-IX to give the ester **1-X**. Or **1-VIII** can be subjected to saponification followed by amide coupling to give **1-XV** which upon Suzuki-type coupling with **1-IX** gives compound **1-XIV**.

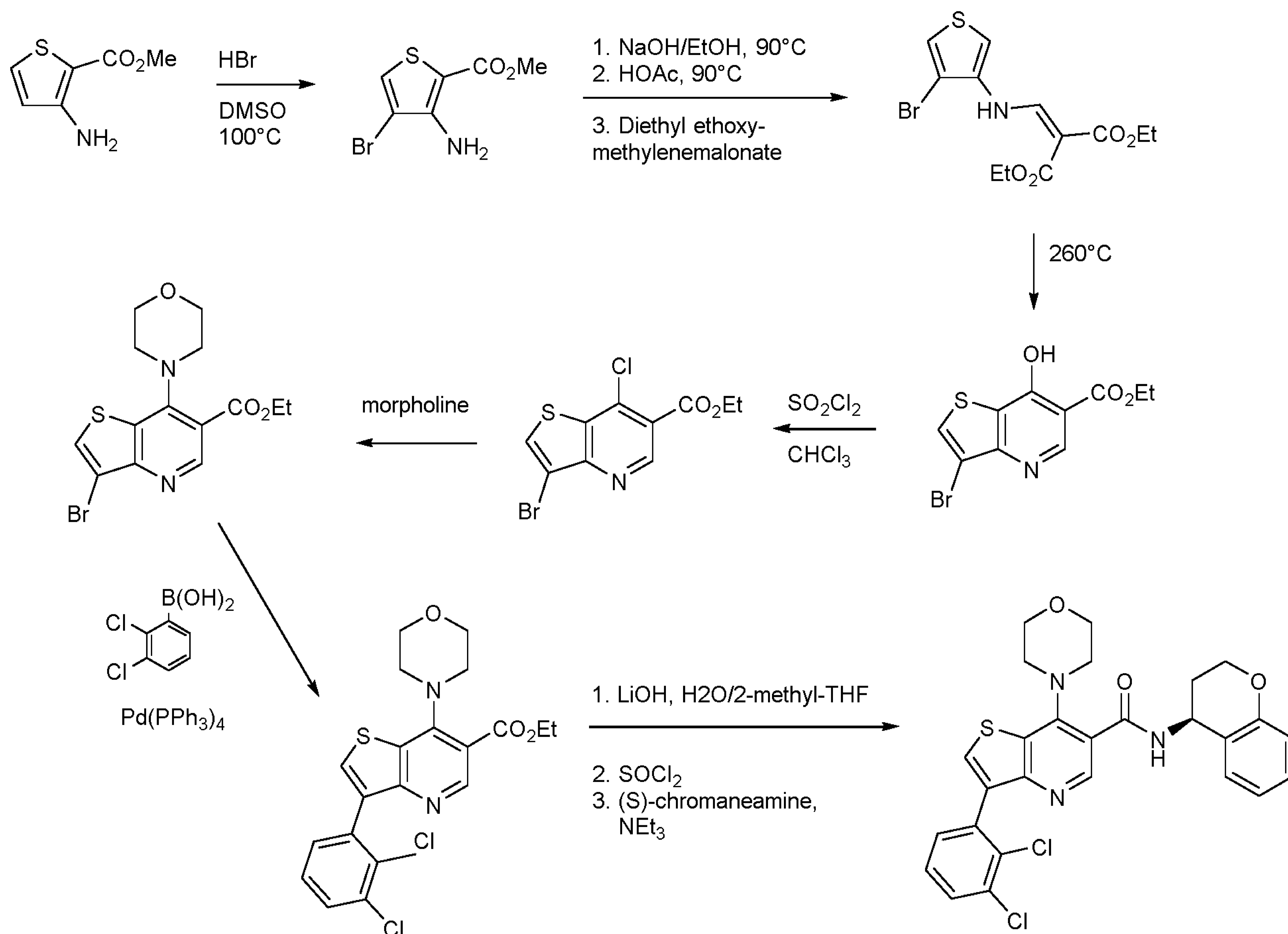
An activated ester compound **2-IV** can be alkylated with another ester compound like **3-I**, for example when R^7 represents a cycloalkyl or heterocycloalkyl like a tetrahydropyran (Scheme 3). In the presence of a base like LDA or LHMDS **3-I** is deprotonated in the position alpha to the ester group and can substitute X in **2-IV**. Saponification by aqueous base followed by decarboxylation as described in, for example, WO2019/215182 leads to the acid **3-III** that can be coupled with the amine **1-XIII** followed by a Suzuki-type coupling with **1-IX** to give the amide **1-XIV**.

10 Scheme 3:



15

Synthetic procedures – specific compounds

Synthesis of (*S*)-N-(chroman-4-yl)-3-(2,3-dichlorophenyl)-7-morpholinothieno[3,2-*b*]pyridine-6-carboxamide (example 4)

5 1. Methyl 3-amino-4-bromothiophene-2-carboxylate

Methyl 3-aminothiophene-2-carboxylate (25.7 g, 163 mmol) was dissolved in DMSO (35 ml). At 20°C hydrogen bromide (18.50 ml, 163 mmol) was added and the solution was stirred at 90°C for 3h and then at 100°C for 20h. The reaction mixture was diluted with 500 ml aqueous sodium hydrogen carbonate (5 %) and extracted twice with dichloromethane (500 ml). The combined
 10 extracts were washed with 2x 500 ml water, dried over Na₂SO₄, filtered and evaporated. The residue was purified by chromatography (silica, eluting with a gradient of n-pentane/ethyl acetate) to yield a solid. MS: 237.9 (M+1).

2. Diethyl 2-(((4-bromothiophen-3-yl)amino)methylene)malonate

Methyl 3-amino-4-bromothiophene-2-carboxylate (6.10 g, 25.8 mmol) was dissolved in ethanol
 15 (20 ml). Aqueous sodium hydroxide (1M, 31.0 ml) was added and the mixture was stirred at 90°C for 0.5h. After cooling to room temperature acetic acid (2 ml) was added and the mixture was

stirred at 90°C for 0.5h. After cooling to room temperature, diethyl ethoxymethylenemalonate (5.22 ml, 25.8 mmol) was added and the resulting mixture was stirred overnight at room temperature. It was diluted with 300 ml water, the precipitate was isolated by filtration and washed with 3x 100 ml water to give the product as a solid. MS: 349 (M+1).

5 3. Ethyl 3-bromo-7-hydroxythieno[3,2-b]pyridine-6-carboxylate

Dowtherm A (40 ml) was heated to reflux (260°C). Diethyl 2-(((4-bromothiophen-3-yl)amino)methylene)malonate (8.2 g, 23.55 mmol) was added and the mixture was stirred at 260°C for 45 min. After cooling to 90°C n-heptane was added (300 ml). After further cooling to 23°C (room temperature), the precipitate was isolated by filtration and washed with 2x 100 ml n-
10 heptane. The resulting solid was suspended in 70 ml ethyl acetate, filtered and washed with 70 ml ethyl acetate followed by 70 ml n-heptane to give the product as a solid. MS: 303.9 (M+1).

4. Ethyl 3-bromo-7-chlorothieno[3,2-b]pyridine-6-carboxylate

Ethyl 3-bromo-7-hydroxythieno[3,2-b]pyridine-6-carboxylate (2.80 g, 9.27 mmol) was suspended in chloroform (28 ml). A small drop DMF and thienyl chloride (0.812 ml, 11.12 mmol) were added
15 and the mixture was stirred under reflux for 40h. After cooling to 23°C (room temperature) the mixture was slowly added to 80 ml saturated aqueous sodium hydrogen carbonate solution, and extracted with 50 ml dichloromethane. The extract was dried over Na₂SO₄, filtered and evaporated. The resulting residue was purified first by chromatography (silica, eluting with a gradient of n-pentane/ethyl acetate) and afterwards by stirring the raw product with a mixture of 50 ml ethyl
20 acetate and 100 ml n-pentane. After 2h the solid was isolated by filtration and washed with 100 ml n-pentane to give the product as a solid. MS: 321.9 (M+1)

5. Ethyl 3-bromo-7-morpholinothieno[3,2-b]pyridine-6-carboxylate

Ethyl 3-bromo-7-chlorothieno[3,2-b]pyridine-6-carboxylate (0.435 g, 1.36 mmol) was dissolved in morpholine (5.0 ml, 58.0 mmol) and the mixture was stirred at 23°C (room temperature) for 1h.
25 Dichloromethane (30 ml) was added, the mixture was washed with water (3x 100 ml) and concentrated under reduced pressure. The residue was purified by chromatography (silica, eluting with a gradient of n-pentane/ethyl acetate) to give the product as a solid. MS: 373.0 (M+1).

6. Ethyl 3-(2,3-dichlorophenyl)-7-morpholinothieno[3,2-b]pyridine-6-carboxylate

Ethyl 3-bromo-7-morpholinothieno[3,2-b]pyridine-6-carboxylate (0.5 g, 1.35 mmol), (3,5-
30 dichlorophenyl)boronic acid (540 mg, 2.83 mmol) and potassium carbonate (465 mg, 3.37 mmol) were combined under argon with dioxane (20 ml) and water (10 ml). Pd(PPh₃)₄ (78 mg, 0.067

mmol) was added and the mixture was stirred for 60 min at 90°C. Afterwards the mixture was extracted with dichloromethane (2x 50 ml), the combined extracts were concentrated under reduced pressure and the residue was purified by chromatography (silica, eluting with a gradient of n-pentane/ethyl acetate). The product was obtained as a solid. MS: 437.0 (M+1).

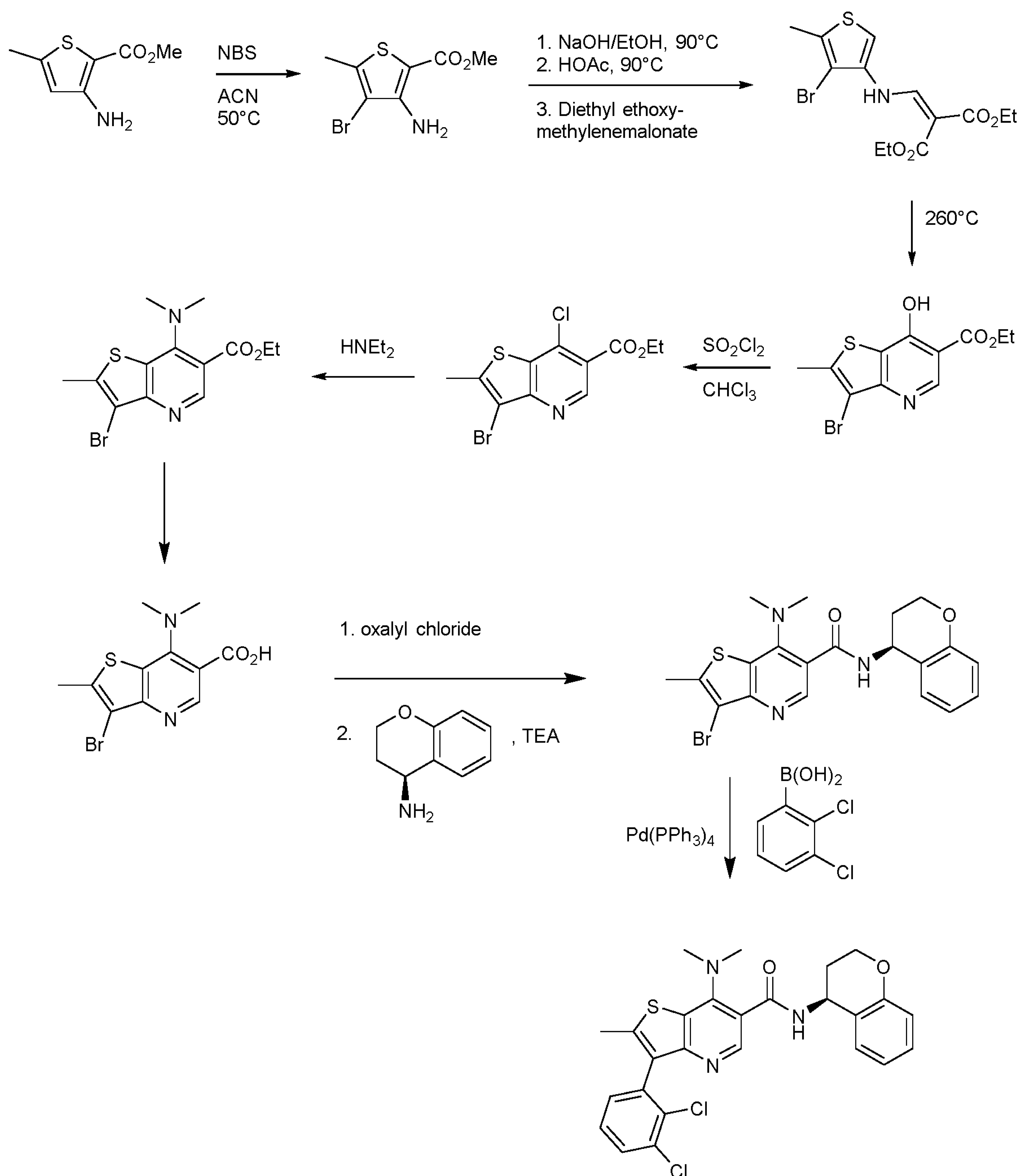
5 7. 3-(2,3-dichlorophenyl)-7-morpholinothieno[3,2-b]pyridine-6-carboxylic acid

Ethyl 3-(2,3-dichlorophenyl)-7-morpholinothieno[3,2-b]pyridine-6-carboxylate (530 mg, 1.21 mmol) and lithium hydroxide hydrate (530 mg, 13.06 mmol) were combined with water (5.5 ml) and 2-methyltetrahydrofuran (5.5 ml) and the mixture was stirred at 90°C. After 30 min additional 2-methyltetrahydrofuran (5.5 ml) was added and stirring was continued at 90°C. After 24h 1,4-
10 dioxane (5.3 ml) was added, stirring was continued at 110°C for 6 hours. The mixture was cooled to room temperature and HCl (1M, 13 ml) was added. The mixture was concentrated under reduced pressure and the residue obtained was used as such in the next step. MS: 409.0 (M+1)

8. (S)-N-(chroman-4-yl)-3-(2,3-dichlorophenyl)-7-morpholinothieno[3,2-b]pyridine-6-carboxamide

15 Thionyl chloride (2 ml, 27.4 mmol) was added to a stirred mixture of 3-(2,3-dichlorophenyl)-7-morpholinothieno[3,2-b]pyridine-6-carboxylic acid (152 mg, 0.371 mmol) and a small drop DMF in dichloromethane (4 ml) and the mixture was stirred at room temperature. After 45 min additional thionyl chloride (1 ml, 13.70 mmol) was added and stirring was continued overnight. The mixture was concentrated under reduced pressure, dichloromethane (4 ml), triethylamine (0.13 ml, 0.93
20 mmol) and (S)-chroman-4-amine hydrochloride (83 mg, 0.45 mmol) were added and the mixture was stirred at room temperature overnight. Water (10 ml) and dichloromethane (10 ml) were added, the phases were separated and the aqueous phase was extracted again with dichloromethane. The combined organic phases were concentrated under reduced pressure, and the residue was purified by chromatography (silica, eluting with a gradient of n-pentane / ethyl
25 acetate). The obtained solid residue was stirred for 5 min in a 1:2 mixture of ethyl acetate and n-pentane (5 ml), filtered and washed with a 1:2 mixture of ethyl acetate and n-pentane (2 x 5 ml) followed by n-pentane (5 ml). The product was obtained as a solid. MS: 540.1 (M+1).

Synthesis of (S)-N-(chroman-4-yl)-3-(2,3-dichlorophenyl)-7-dimethylamino-2-methylthieno[3,2-b]pyridine-6-carboxamide (example 36)



1. Methyl 3-amino-4-bromo-5-methylthiophene-2-carboxylate

Methyl 3-amino-5-methylthiophene-2-carboxylate (53.8 g, 314 mmol) was dissolved in acetonitrile (1047 ml) and stirred at 50 °C. NBS (67.1 g, 377 mmol) was added in portions and stirring was continued for 45 min. The reaction mixture was quenched by addition of saturated aqueous Na₂SO₃ and extracted with EtOAc (2x10mL). The combined extracts were washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (silica, gradient n-pentane/EtOAc 100:1 to 80:20) to yield a yellow solid. MS: 250.2 (M+1).

10 2. Diethyl 2-(((4-bromo-5-methylthiophen-3-yl)amino)methylene)malonate

A 1L flask was charged with methyl 3-amino-4-bromo-5-methylthiophene-2-carboxylate (45.5 g, 182 mmol) and ethanol (182 ml). Sodium hydroxide (1 M, 218 ml) was added and the mixture was heated to 90 °C. After two hours heating was stopped and the mixture was allowed to reach room temperature and then cooled to 0°C. Acetic acid (15.79 ml, 273 mmol) was added to give a white
5 turbid mixture, which was heated to 90°C. After 90 min the mixture was allowed to reach room temperature, diethyl ethoxymethylenemalonate (36.8 ml, 182 mmol) was added and the resulting turbid mixture was stirred overnight at ambient temperature. The resulting precipitate was isolated by filtration, washed with water (500mL) and EtOH (100mL) to give a yellow solid, which was dried under reduced pressure. MS: 364.0 (M+1).

10 3. Ethyl 3-bromo-7-hydroxy-2-methylthieno[3,2-b]pyridine-6-carboxylate

Dowtherm A (300 ml) was heated to 260 °C in a 250mL round-bottom flask. Diethyl 2-(((4-bromo-5-methylthiophen-3-yl)amino)methylene)malonate (58.7 g, 162 mmol) was added carefully into the hot solution and stirring was continued at 260°C. After 3 hours the mixture was cooled to 90°C, transferred into an Erlenmeyer flask, diluted with n-heptane (300mL) and stirred at room
15 temperature for 1 hour. The resulting precipitate was isolated by filtration, washed with n-pentane (5x100mL) and the resulting solid was dried under reduced pressure. MS: 316.3 (M+1).

4. Ethyl 3-bromo-7-chloro-2-methylthieno[3,2-b]pyridine-6-carboxylate

A 500mL flask was charged with ethyl 3-bromo-7-hydroxy-2-methylthieno[3,2-b]pyridine-6-carboxylate (21.8 g, 69.0 mmol) and chloroform (200 ml). DMF (0.02 ml) and thionyl chloride
20 (10.06 ml, 138 mmol) were added, the mixture was heated to reflux and stirred overnight. The mixture was allowed to cool to room temperature and concentrated under reduced pressure. The residue was dissolved in dichloromethane, washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (silica, gradient of n-pentane/EtOAc 100:1 to 2:1) to yield a solid. MS: 334.3
25 (M+1).

5. Ethyl 3-bromo-7-(dimethylamino)-2-methylthieno[3,2-b]pyridine-6-carboxylate

A 50mL flask was charged with ethyl 3-bromo-7-chloro-2-methylthieno[3,2-b]pyridine-6-carboxylate (2.0 g, 6.0 mmol) and chloroform (20 ml). Triethylamine (1.25 ml, 9.0 mmol) followed by dimethylamine (2M in THF, 4.50 ml, 9.00 mmol) were added and the mixture was
30 heated to 85°C. Stirring was continued for 8 hours at 85°C, then heating was stopped and stirring was continued overnight. The mixture was poured into water (300 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (3x 100mL). The combined

organic phases were washed with water and brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (silica, gradient of DCM/EtOAc 100:1 to 80:20) to yield an oil. MS: 343.3 (M+1).

6. 3-Bromo-7-(dimethylamino)-2-methylthieno[3,2-b]pyridine-6-carboxylic acid

5 Ethyl 3-bromo-7-(dimethylamino)-2-methylthieno[3,2-b]pyridine-6-carboxylate (3.60 g, 10.5 mmol) and lithium hydroxide (2.012 g, 84 mmol) were dissolved in a mixture of 1,4-dioxane (31.5 ml) and water (10.5 ml) and the resulting mixture was heated to 110°C. After stirring for 3 hours at this temperature the mixture was allowed to reach room temperature. Concentrated hydrochloric acid (8.75 ml, 105 mmol) was added dropwise at 0 °C and the mixture was stirred at room
10 temperature overnight. The mixture was concentrated under reduced pressure, the residue was suspended in cold THF and the resulting precipitate was isolated by filtration to give a solid. MS: 316 (M+1).

7. (*S*)-3-bromo-N-(chroman-4-yl)-7-(dimethylamino)-2-methylthieno[3,2-b]pyridine-6-carboxamide

15 A 100mL flask was charged with 3-bromo-7-(dimethylamino)-2-methylthieno[3,2-b]pyridine-6-carboxylic acid (1.779 g, 5.25 mmol) in dichloromethane (26.2 ml) and DMF (0.026 ml). Oxalyl chloride (2.298 ml, 26.3 mmol) was added at 0°C and the mixture was stirred at room temperature. After 3 hours additional oxalyl chloride (2.298 ml, 26.3 mmol) was added at 0°C and the mixture was stirred at room temperature for 3 days. The mixture was concentrated under reduced pressure
20 to yield crude acid chloride that was used directly. The crude acid chloride was suspended in dichloromethane (26 ml), TEA was added (8.78 ml, 63.0 mmol) followed by (*S*)-chroman-4-amine hydrochloride (1.170 g, 6.30 mmol) and the resulting mixture was stirred at room temperature. After 3.5 hours the mixture was diluted with DCM, washed with saturated aqueous NaHCO₃ (3x 50mL) and brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was
25 purified by column chromatography (silica, gradient of DCM/EtOAc 100:0 to 80:20) to yield a solid. MS: 446.4 (M+1).

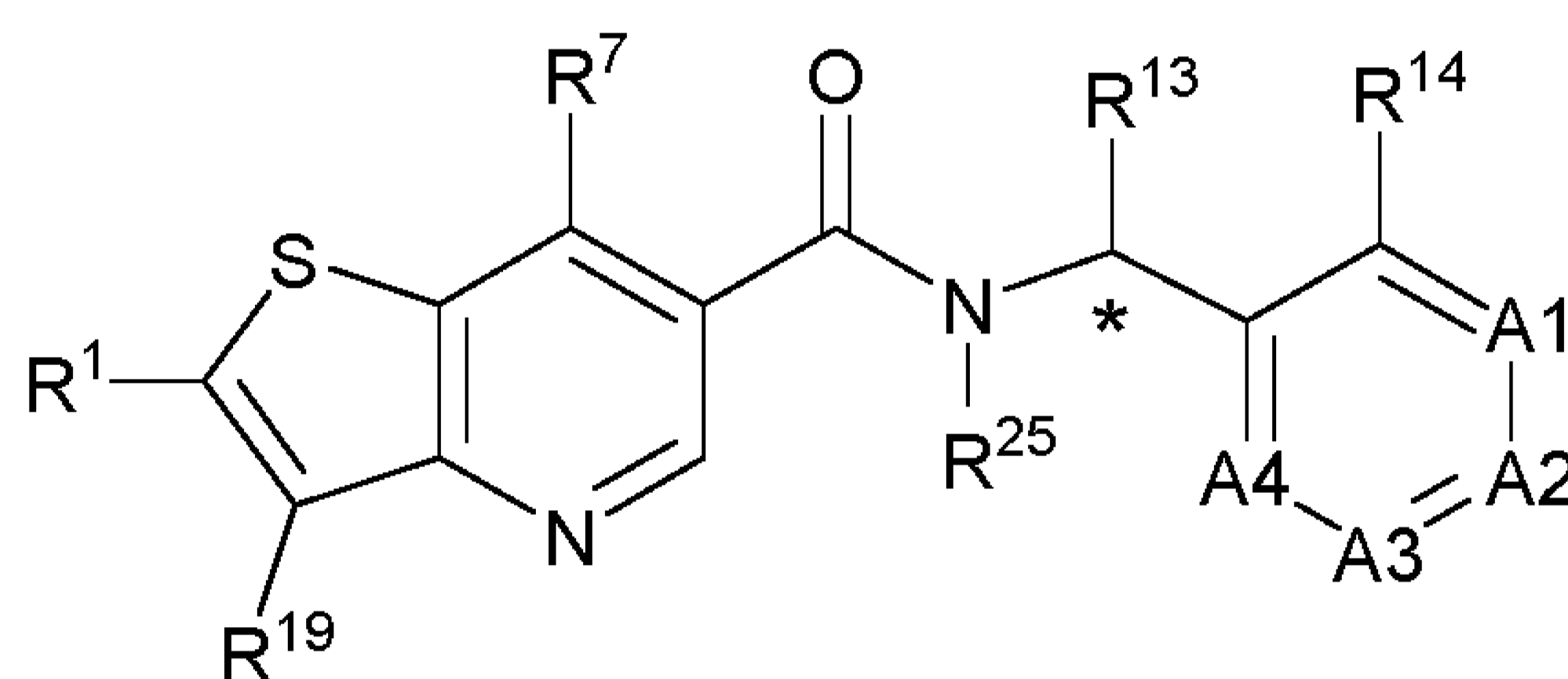
8. (*S*)-N-(chroman-4-yl)-3-(2,3-dichlorophenyl)-7-dimethylamino-2-methylthieno[3,2-b]pyridine-6-carboxamide

A 20 mL vial was charged with (*S*)-3-bromo-N-(chroman-4-yl)-7-(dimethylamino)-2-methylthieno[3,2-b]pyridine-6-carboxamide (400 mg, 0.896 mmol), 2,3-dichlorophenylboronic acid (256 mg, 1.344 mmol), tetrakis(triphenylphosphine)palladium (104 mg, 0.090 mmol) and sodium carbonate (304 mg, 2.87 mmol). The vial was evacuated and refilled with Argon (3 cycles).
30

A mixture of 1,4-dioxane (12 ml) and water (3.00 ml) was purged with argon, added to the solids and the resulting slurry was heated to 100 °C with stirring. After 4 hours the mixture was allowed to reach room temperature, poured into water and extracted several times with dichloromethane. The combined extracts were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (silica, gradient of DCM/EtOAc 100:0 to 70:30) to yield a solid. MS: 512.5 (M+1).

Table A: Examples

Table A below provides for each of the exemplified compounds of Formula (I) the structure, wherein in all exemplified compounds A1 to A4 are CH. The nature of R¹³ can have the consequence that the adjacent carbon (marked *) becomes asymmetric. In this case “R/S” denotes the absolute configuration at the asymmetric carbon marked with (*) in Formula (I).



Formula (I)

Table A:

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
1	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
2	H	morpholin-4-yl	CH ₃	H	(S)	3,5-dichlorophenyl	H
3	H	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
4	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
5	H	morpholin-4-yl	CH ₃	H	(S)	2,3-dichlorophenyl	H
6	H	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
7	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
8	H	dimethylamino	CH ₃	H	(S)	3,5-dichlorophenyl	H
9	H	dimethylamino	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
10	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
11	H	dimethylamino	CH ₃	H	(S)	2,3-dichlorophenyl	H
12	H	dimethylamino	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
13	H	morpholin-4-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
14	H	morpholin-4-yl	=CH-CH=CH-			2,3-dichlorophenyl	H
15	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
16	H	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	2,3,5-trifluorophenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
17	H	4-methylpiperazin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
18	H	4-methylpiperazin-1-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
19	H	4-methylpiperazin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
20	H	4-methylpiperazin-1-yl	-CH ₂ -CH ₂ -O-			2,3-dichlorophenyl	H
21	H	dimethylamino	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
22	H	dimethylamino	=CH-CH=CH-			2,3-dichlorophenyl	H
23	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
24	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
25	H	dimethylamino	-CH ₂ -CH ₂ -		(S)	2,3,5-trifluorophenyl	H
26	H	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
27	H	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -O-			2,3-dichlorophenyl	H
28	H	dimethylamino	-CH ₂ -CH ₂ -O-			2,3-dichlorophenyl	H
29	H	4-methylpiperazin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
30	H	4-methylpiperazin-1-yl	-CH ₂ -CH ₂ -CH ₂ -			3,5-dichlorophenyl	H
31	H	dimethylamino	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
32	H	morpholin-4-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
33	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
34	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
35	CH ₃	dimethylamino	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
36	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
37	CH ₃	dimethylamino	=CH-CH=CH-			2,3-dichlorophenyl	H
38	CH ₃	dimethylamino	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
39	H	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
40	H	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
41	H	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -		(S)	2,3,5-trifluorophenyl	H
42	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
43	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3-methoxyphenyl	H
44	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dimethylphenyl	H
45	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
46	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
47	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
48	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-methoxyphenyl	H
49	H	morpholin-4-yl	=CH-CH=CH-			3,5-dichlorophenyl	H
50	H	dimethylamino	=CH-CH=CH-			3,5-dichlorophenyl	H
51	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
52	H	4-oxo-1-piperidyl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
53	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
54	CH ₃	dimethylamino	=CH-CH=CH-			3,5-dichlorophenyl	H
55	CH ₃	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
56	CH ₃	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
57	CH ₃	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
58	CH ₃	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
59	CH ₃	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
60	CH ₃	3,3-difluoroazetidid-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
61	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
62	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
63	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
64	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
65	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
66	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
67	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
68	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
69	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
70	CH ₃	morpholin-4-yl	=CH-CH=CH-			3,5-dichlorophenyl	H
71	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
72	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
73	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
74	CH ₃	morpholin-4-yl	=CH-CH=CH-			2,3-dichlorophenyl	H
75	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-dimethylphenyl	H
76	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
77	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
78	H	dimethylamino	-CH ₂ -O-			2,3-dichlorophenyl	H
79	H	morpholin-4-yl	-CH ₂ -O-			2,3-dichlorophenyl	H
80	H	morpholin-4-yl	-CH ₂ -O-			3-chlorophenyl	H
81	H	morpholin-4-yl	-CH ₂ -O-			3,5-dichlorophenyl	H
82	H	methoxyethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
83	H	azetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
84	H	azetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
85	H	azetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
86	H	cyclopropylamino	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
87	H	cyclopropylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
88	H	cyclopropylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
89	H	cyclopropylamino	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
90	H	azetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
91	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
92	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
93	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
94	H	hydroxyethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
95	H	2-hydroxyethylmethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
96	H	dimethylamino	-CH ₂ -O-			3,5-dichlorophenyl	H
97	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethoxyphenyl	H
98	H	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-dimethylaminophenyl	H
99	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
100	H	morpholin-4-yl	-CH ₂ -O-		(S)	3,5-dichlorophenyl	H
101	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
102	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
103	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
104	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
105	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethoxyphenyl	H
106	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
107	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
108	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
109	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethoxyphenyl	H
110	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	2,3,5-trifluorophenyl	H
111	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3,5-difluorophenyl	H
112	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3-trifluoromethylphenyl	H
113	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3-trifluoromethoxyphenyl	H
114	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	2,3,5-trifluorophenyl	H
115	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	3,5-difluorophenyl	H
116	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	3-trifluoromethylphenyl	H
117	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	3-trifluoromethoxyphenyl	H
118	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
119	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
120	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	2,3,5-trifluorophenyl	H
121	H	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3-trifluoromethoxyphenyl	H
122	H	morpholin-4-yl	-CH ₂ -O-		(S)	2,3-dichlorophenyl	H
123	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
124	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethylphenyl	H
125	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
126	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-difluorophenyl	H
127	H	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethoxyphenyl	H
128	H	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	3,5-difluorophenyl	H
129	H	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3,4,5-trifluorophenyl	H
130	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-difluorophenyl	H
131	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-trifluoromethoxyphenyl	H
132	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
133	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
134	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -		(S)	2,3-difluorophenyl	H
135	CH ₃	dimethylamino	-CH ₂ -CH ₂ -		(S)	2,3-difluorophenyl	H
136	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-difluorophenyl	H
137	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-difluorophenyl	H
138	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	2,3-difluorophenyl	H
139	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -		(S)	3,5-difluorophenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
140	H	methoxy	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
141	H	methoxy	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
142	H	ethoxy	-CH ₂ -CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
143	H	ethoxy	-CH ₂ -CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
144	H	methoxy	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
145	H	methoxy	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
146	H	ethoxy	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
147	H	ethoxy	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
148	H	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
149	H	methoxy	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
150	H	methoxy	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
151	H	ethoxy	-CH ₂ -CH ₂ -		(S)	2,3-dichlorophenyl	H
152	H	ethoxy	-CH ₂ -CH ₂ -		(S)	3,5-dichlorophenyl	H
153	H	3,3-difluoroazetidin-1-yl	-CH ₂ -O-			2,3-dichlorophenyl	H
154	H	3,3-difluoroazetidin-1-yl	-CH ₂ -O-			3,5-dichlorophenyl	H
155	H	3-fluoroazetidin-1-yl	-CH ₂ -O-			2,3-dichlorophenyl	H
156	H	3-fluoroazetidin-1-yl	-CH ₂ -O-			3,5-dichlorophenyl	H
157	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
158	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
159	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
160	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
161	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
162	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
163	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
164	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
165	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
166	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
167	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
168	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
169	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichlorophenyl	H
170	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	3,5-dichlorophenyl	H
171	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trifluorophenyl	H
172	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
173	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
174	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
175	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
176	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
177	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
178	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
179	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
180	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
181	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
182	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
183	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
184	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
185	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
186	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
187	CH ₃	piperidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
188	CH ₃	piperidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
189	CH ₃	piperidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
190	CH ₃	piperidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
191	CH ₃	piperidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
192	CH ₃	piperidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
193	CH ₃	4,4-difluoropiperidin-1yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
194	CH ₃	4,4-difluoropiperidin-1yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
195	CH ₃	4,4-difluoropiperidin-1yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
196	CH ₃	4,4-difluoropiperidin-1yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-3-chlorophenyl	H
197	CH ₃	4,4-difluoropiperidin-1yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-trifluoromethylphenyl	H
198	CH ₃	4,4-difluoropiperidin-1yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
199	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
200	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
201	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
202	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
203	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
204	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
205	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2,5-dichlorophenyl	H
206	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
207	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
208	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
209	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
210	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
211	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
212	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2-fluoro-5-chlorophenyl	H
213	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H
214	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H
215	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H
216	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H
217	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H
218	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
219	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2-chloro-5-trifluoromethylphenyl	H
220	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
221	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
222	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
223	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
224	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
225	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
224	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	3-fluoro-5-trifluoromethylphenyl	H
225	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
226	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
227	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
228	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
229	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
230	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
231	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2,3,5-trichlorophenyl	H
232	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
233	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
234	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
235	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
236	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
237	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
238	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	naphth-1-yl	H
239	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
240	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
241	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
242	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
243	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
244	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
245	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2,3-dichloro-4-pyridyl	H
246	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
247	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
248	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
249	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
250	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
251	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
252	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-3-chlorophenyl	H
253	CH ₃	dimethylamino	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H
254	CH ₃	morpholin-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H
255	CH ₃	3-fluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H
256	CH ₃	3,3-difluoroazetidin-1-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H
257	CH ₃	tetrahydro-2H-pyran-4-yl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H

No	R ¹	R ⁷	R ¹³	R ¹⁴	R/S	R ¹⁹	R ²⁵
258	CH ₃	ethyl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H
259	CH ₃	isopropyl	-CH ₂ -CH ₂ -O-		(S)	2-methyl-5-chlorophenyl	H
260	H	methoxy	=CH-CH=-CH-			2,3-dichlorophenyl	H
261	H	methoxy	=CH-CH=-CH-			3,5-dichlorophenyl	H
262	H	ethoxy	=CH-CH=-CH-			2,3-dichlorophenyl	H
263	H	ethoxy	=CH-CH=-CH-			3,5-dichlorophenyl	H
264	H	dimethylamino	=CH-CH=-CH-			3,5-dichlorophenyl	H
265	H	morpholino	=CH-CH=-CH-			3,5-dichlorophenyl	H
266	CH ₃	dimethylamino	=CH-CH=-CH-			3,5-dichlorophenyl	H
267	CH ₃	morpholino	=CH-CH=-CH-			2,3-dichlorophenyl	H
268	CH ₃	morpholino	=CH-CH=-CH-			3,5-dichlorophenyl	H
269	CH ₃	3,3-difluoroazetid-1-yl	=CH-CH=-CH-			2,3-dichlorophenyl	H
270	CH ₃	3,3-difluoroazetid-1-yl	=CH-CH=-CH-			3,5-dichlorophenyl	H
271	CH ₃	3-fluoroazetid-1-yl	=CH-CH=-CH-			2,3-dichlorophenyl	H
272	CH ₃	3-fluoroazetid-1-yl	=CH-CH=-CH-			3,5-dichlorophenyl	H
273	H	dimethylamino	=CH-CH=-N-			2,3-dichlorophenyl	H
274	H	dimethylamino	=CH-CH=-N-			3,5-dichlorophenyl	H
275	H	morpholino	=CH-CH=-N-			2,3-dichlorophenyl	H
276	H	morpholino	=CH-CH=-N-			3,5-dichlorophenyl	H
277	H	dimethylamino	=CH-S-			2,3-dichlorophenyl	H
278	H	dimethylamino	=CH-S-			3,5-dichlorophenyl	H
279	H	morpholino	=CH-S-			2,3-dichlorophenyl	H
280	H	morpholino	=CH-S-			3,5-dichlorophenyl	H

Table B: analytical data

Table B shows the calculated molecular weight (MW) (gram/mol), the observed MS signal (m/z), the HPLC retention time (Rt) in minutes, and the HPLC-method as described in above (“Analytical: HPLC-Methods”) used for analysis.

Table B

No	HPLC Method	HPLC Rt	mass signal	MW
1	1	1.337	540.1	540.5
2	1	1.343	512.0	512.5
3	1	1.350	524.0	524.5
4	1	1.262	540.1	540.5
5	1	1.274	512.1	512.5
6	1	1.280	524.0	524.5
7	1	1.180	498.0	498.4
8	1	1.183	470.0	470.4
9	1	1.232	482.0	482.4
10	1	0.944	498.0	498.4
11	1	0.935	470.0	470.4
12	1	0.964	482.0	482.4
13	1	1.193	538.0	538.5

No	HPLC Method	HPLC Rt	mass signal	MW
14	1	1.183	534.0	534.5
15	1	1.150	526.1	525.5
16	1	1.179	510.1	509.5
17	1	0.831	553.1	553.5
18	1	0.960	551.1	551.5
19	1	0.923	553.1	553.5
20	2	1.175	553.0	553.5
21	2	1.270	496.1	496.5
22	2	0.981	492.0	492.4
23	1	1.080	484.1	483.5
24	1	1.125	508.1	507.6
25	2	1.214	468.1	467.5
26	1	1.139	546.0	546.4
27	1	1.135	546.0	546.4
28	2	1.204	498.0	498.4
29	2	1.333	537.1	537.5
30	2	1.388	551.1	551.5
31	2	1.386	496.0	496.5
32	2	1.374	538.0	538.5
33	1	1.029	496.0	496.5
34	1	0.951	496.1	496.5
35	1	0.973	510.0	510.5
36	1	0.919	512.1	512.5
37	1	1.005	506.0	506.4
38	1	1.083	510.1	510.5
39	1	1.132	530.0	530.4
40	1	1.136	532.0	531.5
41	2	1.230	516.0	515.5
42	1	1.226	540.1	539.6
43	1	1.061	502.1	501.6
44	1	1.043	500.1	499.6
45	2	1.198	508.1	507.6
46	1	0.903	466.1	465.5
47	2	1.244	498.1	497.5
48	1	0.866	460.1	459.6
49	1	1.344	534.0	534.5
50	1	1.296	492.0	492.4
51	1	1.012	466.0	465.5
52	1	1.167	552.0	552.5
53	1	1.109	512.0	512.5
54	1	1.213	506.0	506.4
55	1	1.185	558.0	558.5
56	1	1.137	560.0	560.4
57	1	1.151	544.0	544.4

No	HPLC Method	HPLC Rt	mass signal	MW
58	1	1.311	558.0	558.5
59	1	1.255	560.0	560.4
60	1	1.211	544.0	544.4
61	1	1.014	540.0	540.5
62	1	1.010	542.0	542.5
63	1	0.997	526.0	526.5
64	1	1.079	540.0	540.5
65	3	0.977	542.0	542.5
66	3	0.983	526.0	526.5
67	1	1.363	552.0	552.5
68	1	1.294	554.0	554.5
69	1	1.308	538.0	538.5
70	1	1.341	548.0	548.5
71	1	1.239	552.0	552.5
72	1	1.172	554.0	554.5
73	1	1.186	538.0	538.5
74	1	1.226	548.0	548.5
75	2	1.207	458.2	457.6
76	1	1.299	546.0	546.4
77	1	1.329	530.0	530.4
78	1	0.961	484.0	484.4
79	1	1.143	526.0	526.4
80	1	1.190	492.0	492.0
81	2	1.288	526.0	526.4
82	1	1.075	514.0	513.5
83	1	0.883	478.1	477.5
84	1	0.876	496.1	495.5
85	1	0.905	478.0	477.5
86	1	1.182	478.0	477.5
87	1	1.060	478.1	477.5
88	1	1.147	496.0	495.5
89	1	1.196	510.1	509.5
90	1	0.920	510.1	509.5
91	1	0.883	496.0	495.5
92	1	1.033	496.0	495.5
93	1	1.010	528.1	527.5
94	1	0.879	500.0	499.5
95	1	1.084	514.0	513.5
96	1	1.173	484.0	484.4
97	1	1.102	514.1	513.5
98	2	1.197	473.2	472.6
99	1	0.956	512.0	512.4
100	1	1.285	526.0	526.4
101	1	1.102	528.0	528.4

No	HPLC Method	HPLC Rt	mass signal	MW
102	1	0.960	498.1	497.5
103	1	0.904	480.1	479.5
104	1	0.965	512.1	511.6
105	1	0.965	528.1	527.6
106	1	1.121	540.1	539.6
107	1	1.106	522.1	521.6
108	1	1.202	554.1	553.6
109	1	1.187	570.1	569.6
110	1	1.139	524.1	523.6
111	1	1.124	506.0	505.6
112	1	1.179	538.1	537.6
113	1	1.201	554.1	553.6
114	1	1.030	482.1	481.5
115	1	1.010	464.1	463.5
116	1	1.068	496.1	495.6
117	1	1.080	512.1	511.6
118	1	1.195	512.0	512.4
119	1	1.038	514.0	513.5
120	1	1.031	498.0	497.5
121	1	1.285	540.0	539.6
122	1	1.144	526.0	526.4
123	1	1.091	514.0	513.5
124	1	1.225	546.0	545.5
125	1	1.192	514.0	513.5
126	1	1.217	498.0	497.5
127	1	1.239	562.0	561.5
128	1	1.226	492.0	491.6
129	1	1.232	526.0	525.5
130	1	0.991	480.1	479.5
131	1	1.018	544.1	543.5
132	1	1.136	522.0	521.6
133	1	0.961	480.0	479.5
134	1	1.124	506.0	505.6
135	1	1.000	464.1	463.5
136	1	0.926	510.0	509.5
137	1	0.945	510.0	509.5
138	1	0.958	494.0	493.5
139	1	0.978	494.0	493.5

Biological examples**In vitro assay: *Ascaridia galli* and *Oesophagostimum dentatum***

Ascaridia galli (intestinal roundworm of chicken), larval stage 3 ("L3"); and *Oesophagostimum dentatum* (nodular worm of swine), larval stages 3 and 4 (respectively "L3" and "L4") where
 5 suspended in a nutrient medium and distributed to 96 well plates with 20 larvae per well. The wells were spiked DMSO solutions of the compounds with declining concentration. The anthelmintic effects were determined by microscopic examination and defined by the minimum effective concentration ("MEC"), which is the concentration by which at least one of the larvae shows mortality, a change in motility or a change in progression of development.

10 The following compounds showed an MEC of 50 μM or less against *Ascaridia galli* L3: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 17, 21, 23, 24, 25, 26, 27, 28, 29, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 68, 69, 71, 72, 73, 75, 78, 79, 81, 83, 85, 86, 87, 88, 89, 91, 94, 95, 97, 98, 99

The following compounds showed an MEC of 10 μM or less against *Ascaridia galli* L3: 1, 3, 4, 5,
 15 6, 7, 9, 10, 12, 13, 15, 16, 21, 23, 24, 26, 27, 28, 32, 33, 34, 36, 39, 40, 41, 43, 44, 45, 46, 51, 53, 55, 56, 57, 58, 59, 62, 63, 65, 66, 68, 71, 72, 73, 75, 79, 85, 91, 99

The following compounds showed an MEC of 50 μM or less against *Oesophagostimum dentatum*
 L3: 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36,
 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67,
 20 68, 69, 70, 71, 72, 73, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 88, 91, 92, 93, 94, 95, 96, 97, 98, 99, 101.

The following compounds showed an MEC of 10 μM or less against *Oesophagostimum dentatum*
 L3: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 38,
 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68,
 25 69, 70, 71, 72, 73, 75, 76, 79, 81, 83, 84, 85, 91, 92, 95, 96, 97, 99.

The following compounds showed an MEC of 50 μM or less against *Oesophagostimum dentatum*
 L4: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36,
 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66,
 67, 68, 69, 71, 72, 73, 75, 76, 77, 78, 79, 82, 83, 84, 85, 91, 92, 95, 97, 98, 99, 100

30 The following compounds showed an MEC of 10 μM or less against *Oesophagostimum dentatum*
 L4: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 38,

39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 71, 72, 73, 75, 78, 79, 83, 84, 85, 91, 92, 95, 97, 98, 99.

In vitro assay: *Haemonchus contortus*

Solutions of compounds with declining concentrations in DMSO were prepared, diluted with
5 nutrient medium and distributed to 96 well microtiterplates. Exsheathed L3 larvae of *Haemonchus contortus* were incubated for 20 min at 37°C in a water bath, separated by centrifugation and added to the wells with 300 Larvae/well. After incubation for 7 days motility was assessed by automated microscopy. Ivermectin was used as positive control, DMSO as negative control and ED₅₀ values were calculated which represent the concentration for an individual compound that reduces
10 motility by 50% with respect to the positive control.

The following compounds showed an ED₅₀ value below 50 µM against *Haemonchus contortus*: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 21, 23, 25, 26, 27, 28, 32, 33, 34, 35, 36, 38, 39, 41, 42, 43, 44, 45, 46, 48, 51, 53, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 69, 71, 72, 73, 75, 76, 78, 79, 81, 83, 84, 85, 91, 92, 93, 97, 99, 102, 103, 104, 105, 106, 107, 108, 110, 111, 113, 114.

15 The following compounds showed an ED₅₀ value below 10 µM against *Haemonchus contortus*: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 21, 23, 25, 26, 27, 28, 32, 33, 34, 35, 36, 38, 39, 41, 42, 43, 44, 45, 46, 48, 51, 53, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 69, 71, 72, 73, 75, 76, 78, 79, 81, 83, 84, 85, 91, 92, 93, 97, 99, 102, 103, 104, 105, 106, 107, 108, 110, 111, 113, 114.

20 **In vitro assay: *Dirofilaria immitis* L1**

Approximately 500 *D. immitis* microfilaria were added to a microtiter plate containing a nutrient medium and the test compound in DMSO at varying concentrations. After incubation for 3 days, activity was evaluated as reduction in motility as compared to DMSO as negative control. Compounds were tested in duplicates. Based on the concentration response curves EC₅₀ values
25 were calculated.

The following compounds showed an EC₅₀ value below 10 µM: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 38, 39, 40, 41, 42, 43, 44, 45, 46, 48, 51, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 91, 92, 94, 95, 97, 98, 99, 102, 103, 104, 105, 106, 107, 108,
30 109, 110, 111, 112, 113, 114, 115, 116, 117.

The following compounds showed an EC₅₀ value below 1 µM: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 38, 39, 40, 41, 42, 43, 44, 45, 46, 48, 51, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 81, 82, 83, 84, 85, 91, 92, 94, 95, 97, 98, 99, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117.

5

The following compounds showed an EC₅₀ value below 0.1 µM: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 21, 23, 24, 25, 26, 27, 28, 32, 33, 34, 35, 36, 38, 39, 40, 41, 42, 44, 45, 46, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 71, 72, 73, 75, 76, 78, 79, 84, 85, 91, 92, 95, 97, 99, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117.

10

In vitro assay: *Dirofilaria immitis* L4

10 larvae L4 of *D. immitis* were added to a microtiter plate containing a nutrient medium and the test compound in DMSO at varying concentrations. After incubation for 3 days, activity was evaluated as reduction in motility as compared to DMSO as negative control. Compounds were tested in duplicates. Based on the concentration response curves EC₅₀ values were calculated.

15

The following compounds showed an EC₅₀ value below 10 µM: 1, 4, 10, 12.

The following compounds showed an EC₅₀ value below 1 µM: 1, 4, 10, 12.

The following compounds showed an EC₅₀ value below 0.1 µM: 1, 4, 10, 12.

20 In vitro assay: *Acanthocheilonema viteae* L1

Approximately 500 *A. viteae* microfilaria were added to a microtiter plate containing a nutrient medium and the test compound in DMSO at varying concentrations. After incubation for 3 days, activity was evaluated as reduction in motility as compared to DMSO as negative control. Compounds were tested in duplicates. Based on the concentration response curves EC₅₀ values were calculated.

25

The following compounds showed an EC₅₀ value below 10 µM: 1, 3, 7, 10, 13, 15, 16, 17, 23, 24, 25, 26, 36, 42, 45, 46, 53, 56, 62, 72.

The following compounds showed an EC₅₀ value below 1 µM: 1, 3, 7, 10, 13, 15, 16, 23, 24, 25, 26, 36, 42, 45, 46, 53, 56, 62, 72.

30 The following compounds showed an EC₅₀ value below 0.1 µM: 1, 3, 7, 10, 13, 15, 16, 23, 24, 25, 26, 36, 46, 53, 56, 62, 72.

In vitro assay: agonistic activity at *C. elegans* slo-1a

A CHO K1 cell line stably transfected with the *Caenorhabditis elegans* slo-1a (accession no Y51A2D.19a) was established. Cells were seeded in microtiter plates (black 384-well MTP, clear bottom) in a concentration of 10,000 cells/well in 25 μ l medium and cultured for 20 to 24 hours at 37°C and 5% CO₂. After incubation, 25 μ l of FMP-dye Blue-Tyrodé's was added to each well and incubated at room temperature for 30 min. Ten minutes after addition of 12.5 μ l compound solution, the plates are transferred to the FLIPR for measurement.

For the membrane potential measurements, the plates were placed in the FLIPR Penta (Molecular Devices). The baseline measurement of the fluorescence was started for 20 sec (Exc. 510-545 nm, Emm. 565-625 nm). Potential channel opening measurement was started by addition of 25 μ l of KCl -Tyrodé (final assay concentration of the KCl-Tyrodé: 70 mM KCl, 2 mM CaCl₂, 1 mM MgCl₂, 0.8 mM NaH₂PO₄, 5 mM Glucose, 28 mM Hepes, pH 7.4, including the voltage sensitive dye). The complete measurement takes 150 s.

EC₅₀ values were determined in triplicate utilizing compound dilution series. The data were determined at least in two independent tests. The data were proceeded by using the ActivityBase XE Runner software (IDBS) for curve fitting and calculation of the half-maximal effective concentration.

The following compounds showed an EC₅₀ value below 10 μ M: 1, 2, 3, 4, 7, 8, 9, 10, 11, 12, 15, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 38, 39, 41, 42, 46, 47, 48, 51, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 71, 72, 73, 74, 75, 78, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113.

The following compounds showed an EC₅₀ value below 1 μ M: 1, 3, 4, 7, 9, 10, 11, 12, 21, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 38, 39, 42, 46, 48, 53, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 71, 72, 73, 75, 85, 91, 95, 97, 98, 99, 102, 103, 104, 105, 106, 107, 108, 110, 111, 112, 113.

In vitro assay: agonistic activity at the human Maxi K channel (BK channel)

A CHO K1 cell line was stably transfected with the KCNMA1 (KCa1.1, U11058) and beta1 (KCNMB1) subunits of the human Maxi K channel (Ponte et al, Molecular Pharmacology 2012, 81(4), 567-577).

Cells were seeded in microtiter plates (black 384-well MTP, clear bottom) in a concentration of 20,000 cells/well in 25 μ l medium and cultured for 20 to 24 hours at 37°C and 5% CO₂. After incubation, 25 μ l of FMP-dye Blue-Tyrode's was added to each well and incubated at room temperature for 30 min. Ten minutes after addition of 12.5 μ l compound solution, the plates are
5 transferred to the FLIPR for measurement.

For the membrane potential measurements, plates were placed in the FLIPR Penta (Molecular Devices). The baseline measurement of the fluorescence was started for 20 sec (Exc. 510-545 nm, Emm. 565-625 nm). Potential channel opening measurement was started by addition of 25 μ l KCl-Tyrode (final assay concentration of the KCl-Tyrode: 70mM KCl, 2 mM CaCl₂, 1 mM MgCl₂,
10 0.8 mM NaH₂PO₄, 5 mM Glucose, 28 mM Hepes, pH 7.4, including the voltage sensitive dye). The complete measurement takes 150 s.

EC₅₀ values were determined in triplicate utilizing compound dilution series. The data were determined at least in two independent tests. The data were proceeded by using the ActivityBase XE Runner software (IDBS) for curve fitting and calculation of the half-maximal effective
15 concentration.

The following compounds showed an EC₅₀ value between 5 and 10 μ M: 4, 6, 13

The following compounds showed an EC₅₀ value above 30 μ M: 1, 2, 3, 5, 7, 8, 9, 10, 11, 12, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66,
20 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113.

In vivo assay: efficacy against *Haemonchus contortus* in jirds

Compounds according to this invention were tested in vivo using *Haemonchus contortus* in jirds (*Meriones unguiculatus*). The jirds were orally infected with approximately 1500 third-stage
25 larvae of *Haemonchus contortus*. Ten days after infection, the jirds in the treatment groups were treated once either orally or subcutaneously with compounds at a dose of 10 mg per kg bodyweight. For treatment, compounds were dissolved in a mixture of 10% Transcutol, 10% Cremophor EL and 80% physiological sodium chloride solution. Three days after treatment, the jirds were necropsied, and the larvae burden in the stomach was determined. The efficacy was
30 defined as the reduction of the mean larvae count in the infected jirds of the treatment group in comparison to the infected jirds in an untreated control group (negative control).

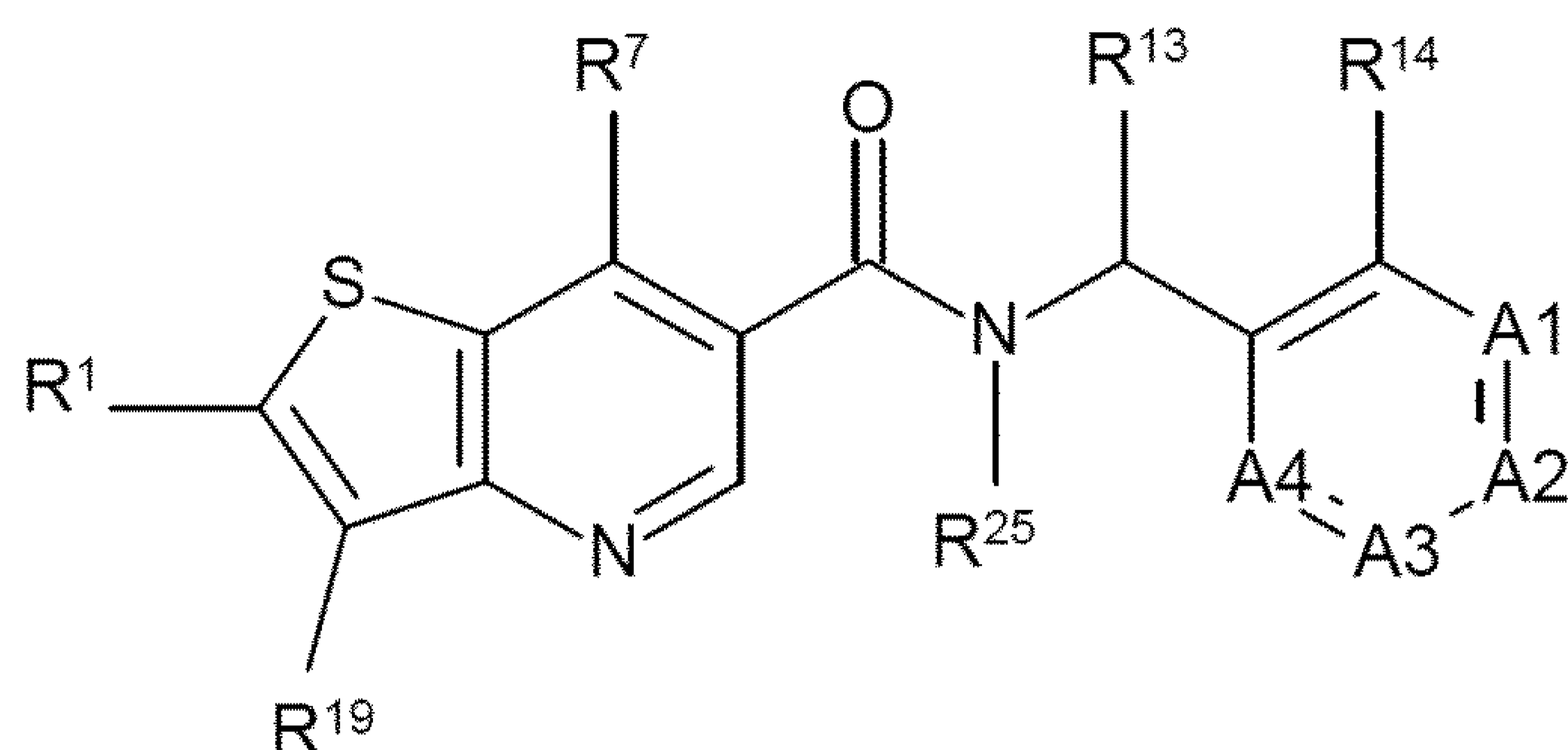
The following compounds reduced the *Haemonchus contortus* count by at least 80% when

administered orally or subcutaneously at 10 mg/kg bw.: 10, 36, 53, 56, 62, 65, 68, 72, 102.

Thus, it can be seen from the present results that the present compounds are effective as far as the treatment of nematodes, especially *Dirofilaria*, is concerned, while the potential for target-related adverse reactions in the host such as mammal (e.g. a human being) is low.

Claims

1. Compound of Formula (I)



Formula (I)

5

wherein

R^1 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, C_{1-6} -alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR^2R^3 , $COOH$, $C(=O)OR^4$, SR^4 , SOR^4 , SO_2R^4 , $SO_2NR^5R^6$ and $C(=O)NR^5R^6$,

10

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy or C_{1-6} -alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15

C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, C_{1-6} -alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, $NR^{2'}R^{3'}$, $C(=O)OR^{4'}$, $SR^{4'}$, $SOR^{4'}$, $SO_2R^{4'}$, $SO_2NR^{5'}R^{6'}$ and $C(=O)NR^{5'}R^{6'}$,

20 R^2 and R^3 are independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy- C_{1-6} -alkyl, C_{1-6} -alkyl substituted with C_{3-10} -cycloalkyl, C_{1-6} -alkyl substituted with 5- to 10- membered heterocyclyl, C_{1-6} -alkyl substituted with C_{6-10} -aryl and C_{1-6} -alkyl substituted with 5- to 10- membered heteroaryl, or

25

R^2 and R^3 together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10-membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy- C_{1-6} -alkyl, C_{1-6} -alkyl substituted with C_{3-10} -cycloalkyl, C_{1-6} -alkyl substituted with 5- to 10- membered heterocyclyl, C_{1-6} -alkyl substituted with C_{6-10} -aryl or C_{1-6} -alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R^2 and R^3 together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, $NR^{2''}R^{3''}$, $C(=O)OR^{4''}$, $SR^{4''}$, SOR^4 , $SO_2R^{4''}$, $SO_2NR^{5''}R^{6''}$ and $C(=O)NR^{5''}R^{6''}$,

R^4 , R^5 and R^6 are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{2'}$, $R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{6'}$ are independently selected from hydrogen and C_{1-6} -alkyl,

$R^{2''}$, $R^{3''}$, $R^{4''}$, $R^{5''}$ and $R^{6''}$ are independently selected from hydrogen and C_{1-6} -alkyl,

R^7 is independently selected from the group consisting of

hydrogen, C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 4- to 10- membered heterocyclyl, C_{6-10} aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, C_{1-6} -alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR^8R^9 , $COOH$, $C(=O)OR^{10}$, SR^{10} , SOR^{10} , SO_2R^{10} , $SO_2NR^{11}R^{12}$ and $C(=O)NR^{11}R^{12}$,

wherein each C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 4- to 10-membered heterocyclyl, C_{6-10} aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy or C_{1-6} -alkylmercapto, is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C_{1-6} -alkyl, C_{2-6} -alkenyl, C_{2-6} -alkynyl, C_{3-10} -cycloalkyl, 5- to 10- membered heterocyclyl, C_{6-10} -aryl, 5- to 10- membered heteroaryl, C_{1-6} -alkoxy, C_{1-6} -alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, oxo, NR^8R^9 , $C(=O)OR^{10'}$, $SR^{10'}$, $SOR^{10'}$, $SO_2R^{10'}$, $SO_2NR^{11'}R^{12'}$ and $C(=O)NR^{11'}R^{12'}$,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl and C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₃₋₁₀-cycloalkyl, C₁₋₆-alkyl substituted with 5- to 10- membered heterocyclyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl or C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{8''}R^{9''}, C(=O)OR^{10''}, SR^{10''}, SOR^{10''}, SO₂R^{10''}, SO₂NR^{11''}R^{12''} and C(=O)NR^{11''}R^{12''},

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl,

R¹³ is hydrogen or C₁₋₃ alkyl,

R¹⁴ is hydrogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, NR^{14'}R^{14''}, wherein R^{14'} and R^{14''} are independently C₁₋₃-alkyl or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋

$_3$ -alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more
5 C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or
10 NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{17'}R^{17''}, wherein R^{17'} and R^{17''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy, or NR^{18'}R^{18''}, wherein R^{18'} and R^{18''} are independently C₁₋₃-alkyl,

15 R¹⁹ is independently selected from the group consisting of C₆₋₁₀-aryl and 5- to 10- membered heteroaryl,

wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, C₁₋₆-alkylmercapto, halogen, cyano, nitro, hydroxy, mercapto, NR²⁰R²¹, C(=O)OR²², SR²², SOR²², SO₂R²², SO₂NR²³R²⁴ and C(=O)NR²³R²⁴,

R²⁰ and R²¹ are independently selected from the group consisting of

25 hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy-C₁₋₆-alkyl, C₁₋₆-alkyl substituted with C₆₋₁₀-aryl, C₁₋₆-alkyl substituted with 5- to 10- membered heteroaryl, or

30 R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy or C₁₋₆-alkylmercapto or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more

5

substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, carbonyl, halogen, cyano, hydroxy, mercapto, NR^{20'}R^{21'}, C(=O)OR^{22'}, SR^{22'}, SOR^{22'}, SO₂R^{22'}, SO₂NR^{23'}R^{24'} and C(=O)NR^{23'}R^{24'},

10 R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl,

R²⁵ is independently selected from hydrogen and C₁₋₆-alkyl,

or a stereoisomer, physiologically acceptable salt, ester, solvate, polymorph, prodrug and mixtures thereof.

15 2. The compound according to claim 1, wherein R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²R³, C(=O)OR⁴ and C(=O)NR⁵R⁶,

20

wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituents independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy and NR^{2'}R^{3'},

R² and R³ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl and 5 to 10-membered heteroaryl, or

25 R² and R³ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2 or 3 further ring atoms are selected from N, S and O,

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl or 5 to 10-membered heteroaryl or the heterocyclic ring formed by R² and R³ together with the N atom to which they are

attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₁₋₆-alkoxy,

R⁴, R⁵ and R⁶ are independently selected from hydrogen and C₁₋₆-alkyl,

5 R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₆-alkyl.

3. The compound according to claim 1 or 2, wherein R¹ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₁₋₆-alkoxy and halogen,

10 wherein each C₁₋₆-alkyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy and NR^{2'}R^{3'},

wherein R^{2'} and R^{3'} are independently selected from hydrogen and C₁₋₃-alkyl.

4. The compound according to any one of claims 1 to 3, wherein R¹ is independently selected from the group consisting of

15 hydrogen, methyl, trifluoromethyl, ethyl, methoxy, ethoxy, fluoride and chloride, preferably selected from the group consisting of hydrogen, and methyl.

5. The compound according to any one of claims 1 to 4, wherein R⁷ is independently selected from the group consisting of

20 hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, C₃₋₁₀-cycloalkyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

25 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR⁸R⁹, C(=O)OR¹⁰, and C(=O)NR¹¹R¹²,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10 membered heterocyclyl and 5- to 10 membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3
5 further ring atoms are selected from N, S and O;

wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₆₋₁₀-aryl, 5- to 10 membered heterocyclyl, and 5- to 10 membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group
10 consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{8''}R^{9''}, C(=O)-OR^{10''}
and C(=O)NR^{11''}R^{12''};

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen and C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen and C₁₋₆-alkyl,

15 R^{8''}, R^{9''}, R^{10''}, R^{11''} and R^{12''} are independently selected from hydrogen and C₁₋₆-alkyl.

6. The compound according to any one of claims 1 to 5, wherein R⁷ is independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, hydroxy, NR⁸R⁹, C(=O)OR¹⁰, SR¹⁰, SOR¹⁰, SO₂R¹⁰ and C(=O)NR¹¹R¹²,

20 wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, 5- to 10 membered heterocyclyl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, oxo, NR^{8'}R^{9'}, C(=O)OR^{10'} and C(=O)NR^{11'}R^{12'},

25 R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl, C₆₋₁₀-aryl, and 5- to 10 membered heteroaryl, or

R⁸ and R⁹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 1 ring atom is N and wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

wherein the C₁₋₆-alkyl, C₆₋₁₀-aryl, and 5- to 10 membered heteroaryl or the heterocyclic ring formed by R⁸ and R⁹ together with the N atom to which they are attached is optionally substituted with one or more substituent(s) independently selected from the group consisting of

5 C₁₋₆-alkyl, C₁₋₆-alkoxy, hydroxy and NR^{8''}R^{9''},

R¹⁰, R¹¹ and R¹² are independently selected from hydrogen or C₁₋₆-alkyl,

R^{8'}, R^{9'}, R^{10'}, R^{11'} and R^{12'} are independently selected from hydrogen or C₁₋₆-alkyl.

R^{8''} and R^{9''} are independently selected from hydrogen or C₁₋₆-alkyl.

7. The compound according to any one of claims 1 to 6, wherein R⁷ is independently selected
10 from the group consisting of

hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl, C₁₋₆-alkoxy, NR⁸R⁹,

wherein each C₁₋₆-alkyl, C₂₋₆-alkenyl, 4- to 10 membered heterocyclyl or C₁₋₆-alkoxy is optionally substituted with one or more substituent(s) independently selected from the group consisting of

15 C₁₋₆-alkyl, C₁₋₆-alkoxy, and halogen,

R⁸ and R⁹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₆-cycloalkyl,

wherein the C₁₋₆-alkyl, or C₃₋₆-cycloalkyl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

20 C₁₋₆-alkyl, C₁₋₆-alkoxy, and hydroxy.

8. The compound according to any one of claims 1 to 7, wherein

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein the saturated ring is optionally substituted with one or more C₁₋₃-alkyl or =O, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced
25 by -NH-, -O-, -S(O)-, -S(O)₂- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein the unsaturated ring is optionally substituted with one or more C₁₋₃-alkyl, and/or wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is N or CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is N or CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

5 A3 is N or CR¹⁷, wherein R¹⁷ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A4 is N or CR¹⁸, wherein R¹⁸ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl.

9. The compound according to any one of claims 1 to 8, wherein

10 R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally replaced by -NH-, -O- or -S-, or

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing unsaturated ring, wherein one or more of the ring-forming carbon atoms are optionally
15 replaced by -NH-, -N=, =N-, -O- or -S-,

A1 is CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

20 A3 is CR¹⁷, wherein R¹⁷ is hydrogen,

A4 is CR¹⁸, wherein R¹⁸ is hydrogen.

10. The compound according to any one of claims 1 to 9, wherein

R¹³ and R¹⁴ together with the atoms to which they are attached form a 5 or 6- carbon atoms containing saturated ring, wherein one or more of the ring-forming carbon atoms are optionally
25 replaced by -NH-, -O- or -S-,

A1 is CR¹⁵, wherein R¹⁵ is independently hydrogen, halogen C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{15'}R^{15''}, wherein R^{15'} and R^{15''} are independently C₁₋₃-alkyl,

A2 is CR¹⁶, wherein R¹⁶ is independently hydrogen, halogen, C₁₋₃ alkyl, C₁₋₃ alkoxy or NR^{16'}R^{16''}, wherein R^{16'} and R^{16''} are independently C₁₋₃-alkyl,

A3 is CR¹⁷, wherein R¹⁷ is hydrogen,

A4 is CR¹⁸, wherein R¹⁸ is hydrogen.

11. The compound according to any one of claims 1 to 10, wherein none, one or two of residues A1, A2, A3 and A4 is N.

5 12. The compound according to any one of claims 1 to 11, wherein R¹⁹ is independently selected from the group consisting of

R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5- to 10- membered heteroaryl,

10 wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, halogen, cyano, nitro, hydroxy, NR²⁰R²¹, C(=O)OR²² and C(=O)NR²³R²⁴,

15 R²⁰ and R²¹ are independently selected from the group consisting of

hydrogen, C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl and C₆₋₁₀-aryl or

R²⁰ and R²¹ together with the N atom to which they are attached form a saturated or unsaturated heterocyclic ring having 3 to 12 ring atoms, wherein 0, 1, 2, or 3 further ring atoms are selected from N, S and O;

20 wherein each C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, C₁₋₆-alkoxy, or C₆₋₁₀-aryl or the heterocyclic ring formed by R²⁰ and R²¹ together with the N atom to which they are attached is optionally substituted with one or more substituents independently selected from the group consisting of

25 C₁₋₆-alkyl, C₃₋₁₀-cycloalkyl, 5- to 10- membered heterocyclyl, C₆₋₁₀-aryl, 5- to 10- membered heteroaryl, C₁₋₆-alkoxy, halogen, cyano, hydroxy, NR^{20'}R^{21'}, C(=O)OR^{22'} and C(=O)NR^{23'}R^{24'}

R²², R²³ and R²⁴ are independently selected from hydrogen and C₁₋₆-alkyl,

R^{20'}, R^{21'}, R^{22'}, R^{23'} and R^{24'} are independently selected from hydrogen and C₁₋₆-alkyl.

13. The compound according to any one of claims 1 to 12, wherein R¹⁹ is independently selected from the group consisting of

C₆₋₁₀-aryl and 5- to 10- membered heteroaryl

wherein each C₆₋₁₀-aryl or 5- to 10- membered heteroaryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, C₁₋₆-alkoxy, halogen, cyano, nitro and hydroxy,

wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more substituents independently selected from the group consisting of halogen, cyano, hydroxy, preferably each C₁₋₆-alkyl, C₁₋₆-alkoxy, is optionally substituted with one or more halogen.

14. The compound according to any one of claims 1 to 13, wherein R¹⁹ is C₆₋₁₀-aryl,

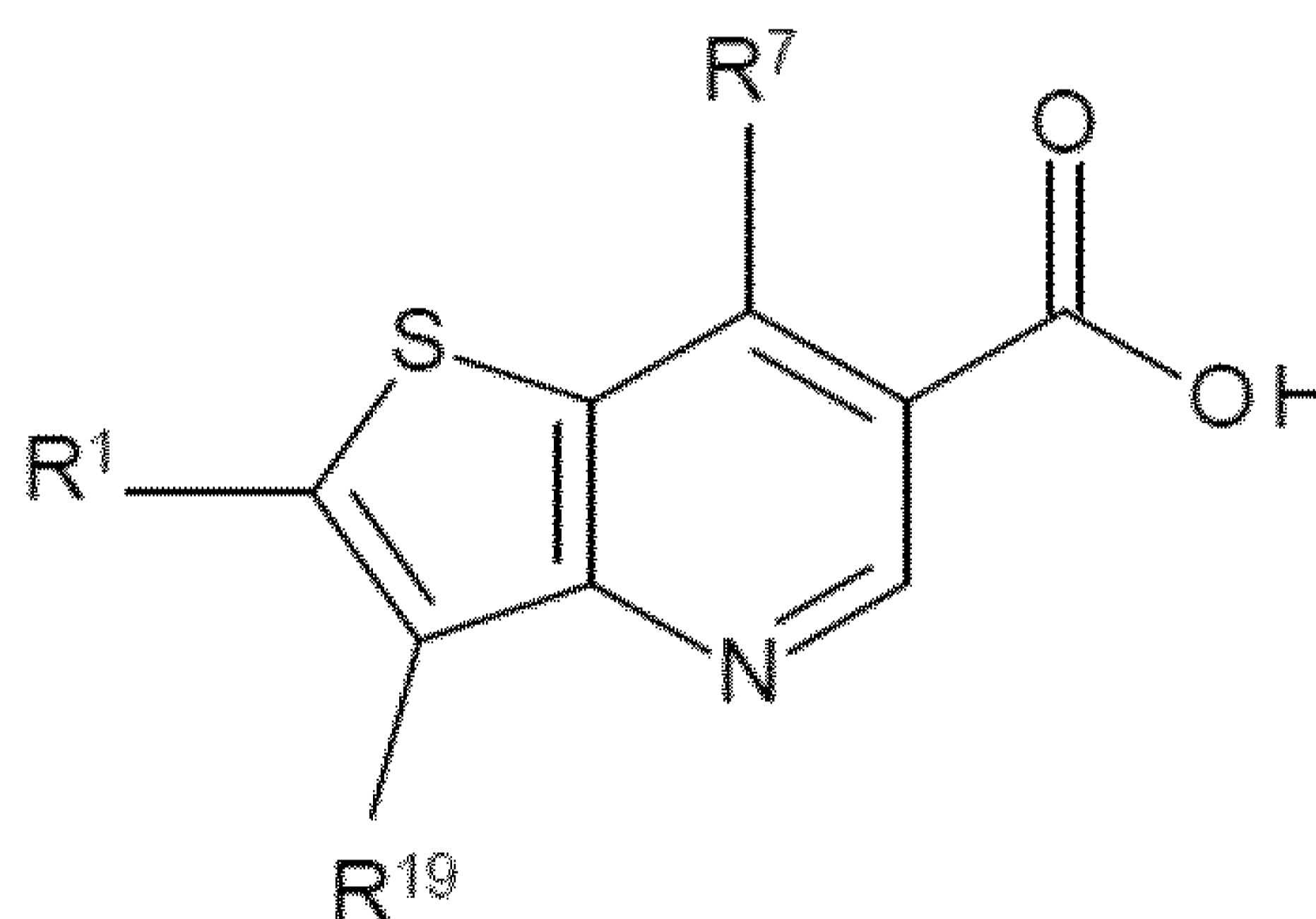
wherein the C₆₋₁₀-aryl is optionally substituted with one or more substituent(s) independently selected from the group consisting of

C₁₋₆-alkyl, halogen, C₁₋₆-alkoxy cyano and nitro wherein each C₁₋₆-alkyl, C₁₋₆-alkoxy is optionally substituted with one or more halogen.

15. The compound according to any one of claims 1 to 14, wherein R²⁵ is hydrogen.

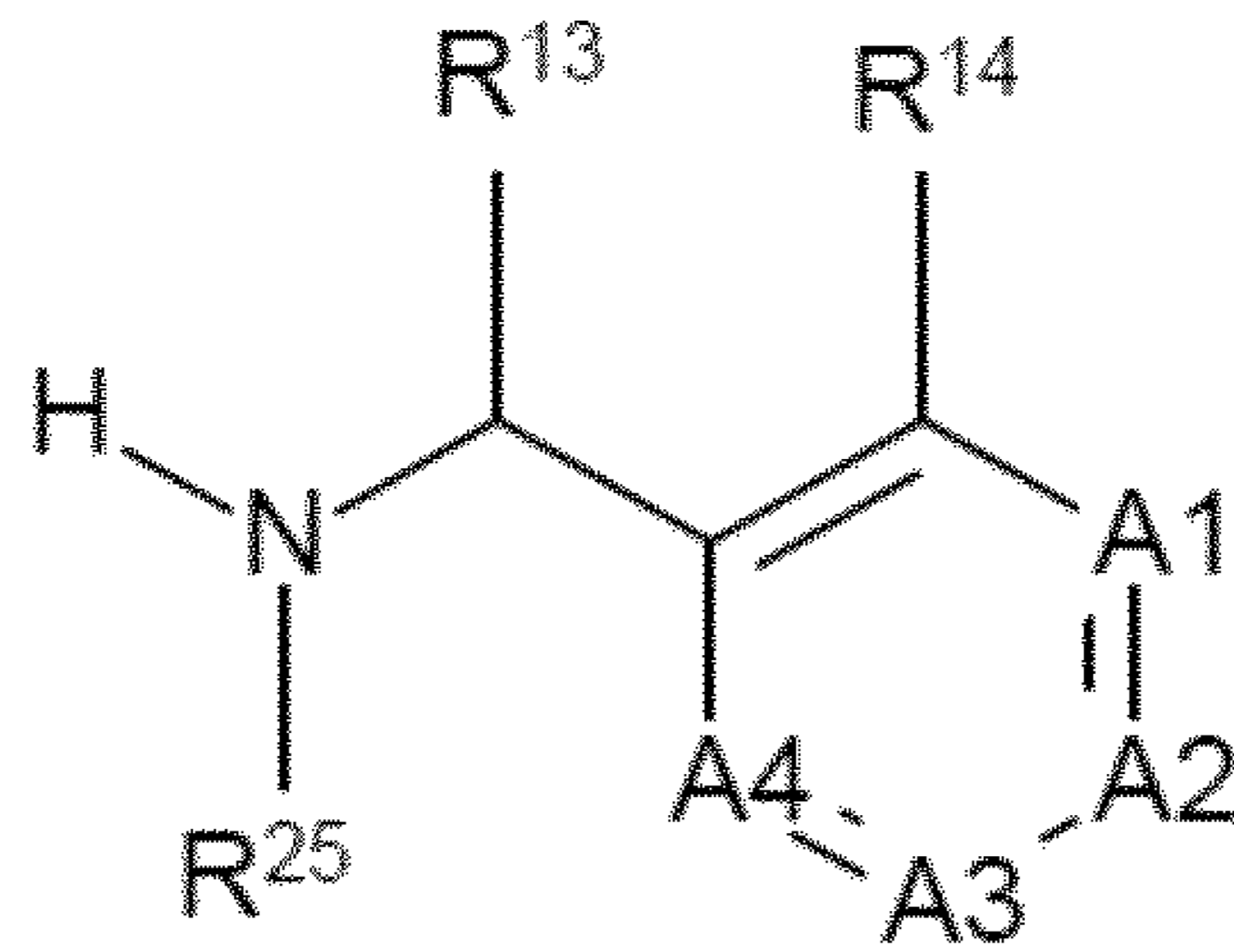
16. Process for preparing the compound according to Formula (I) comprising the step of

reacting a compound of Formula (A)



Formula (A)

with a compound of Formula (B)



Formula (B)

wherein R^1 , R^7 , R^{13} , R^{14} , A1, A2, A3, A4, R^{19} and R^{25} are defined as in any one of claims 1 to 15,

5 to obtain the compound according to Formula (I).

17. Veterinary composition comprising

- compound according to Formula (I) according to any one of claims 1 to 15, and
- one or more physiologically acceptable excipient(s).

18. Compound according to Formula (I) according to any one of claims 1 to 15 or veterinary
10 composition according to claim 17 for use as a medicament.

19. Compound according to Formula (I) according to any one of claims 1 to 15 or veterinary composition according to claim 17 for use in the treatment of disorders/diseases caused by helminths.

20. Compound according to Formula (I) according to any one of claims 1 to 15 or veterinary
15 composition according to claim 17 for use according to claim 19 wherein the disease is the heartworm disease.

21. Method of treating a disease caused by helminths which comprises administering to an animal, in particular a dog, a therapeutically effective amount of a compound according to Formula (I) according to any one of claims 1 to 15 or veterinary composition according to claim 17.

20 22. Method of treating a disease according to claim 21 wherein the disease is the heartworm disease.