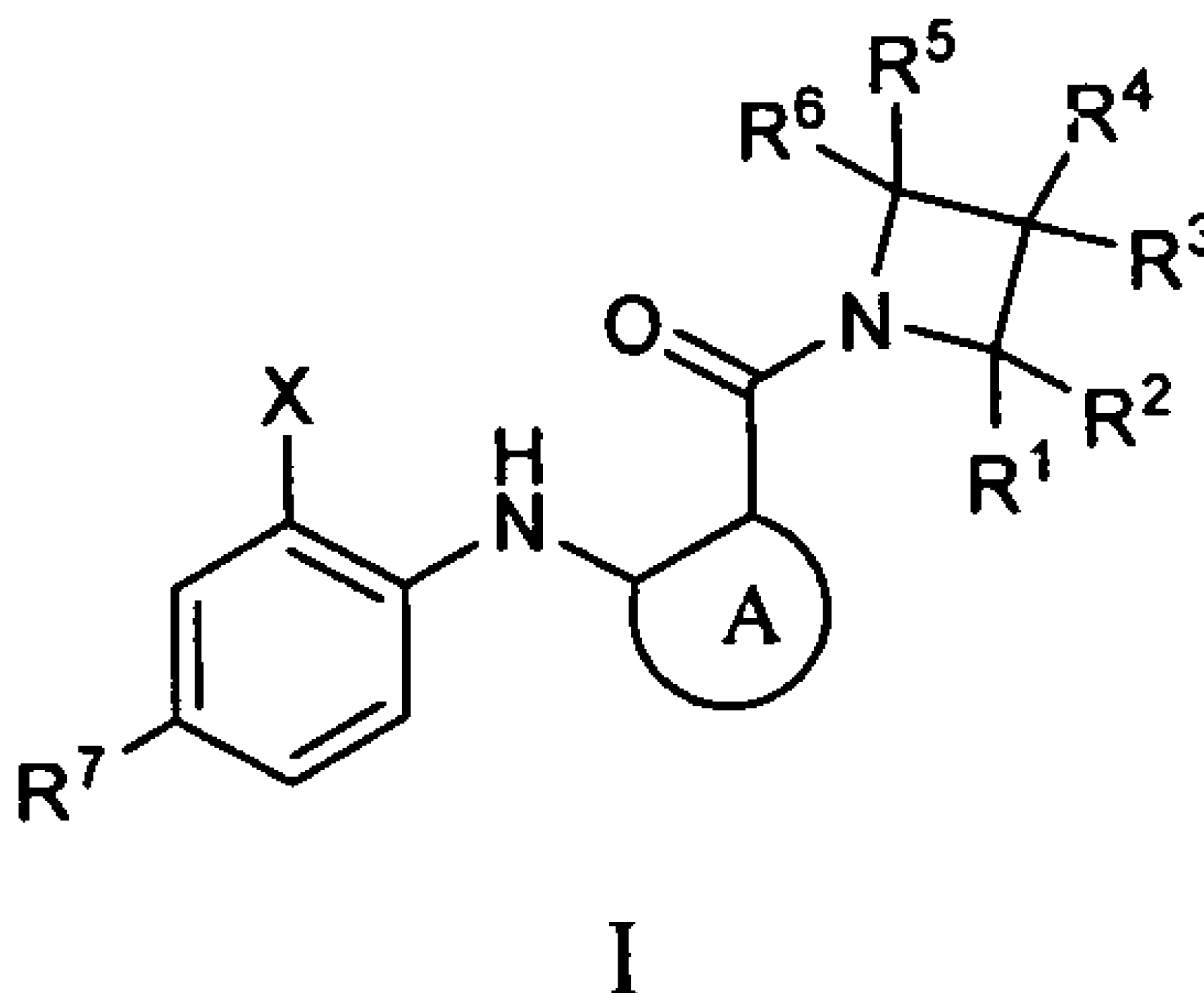




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(54) Titre : PROCÉDES D'UTILISATION D'INHIBITEURS DE MEK
(54) Title: METHODS OF USING MEK INHIBITORS



(57) Abrégé/Abstract:

The present invention provides methods of treating cancer by administering a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments.

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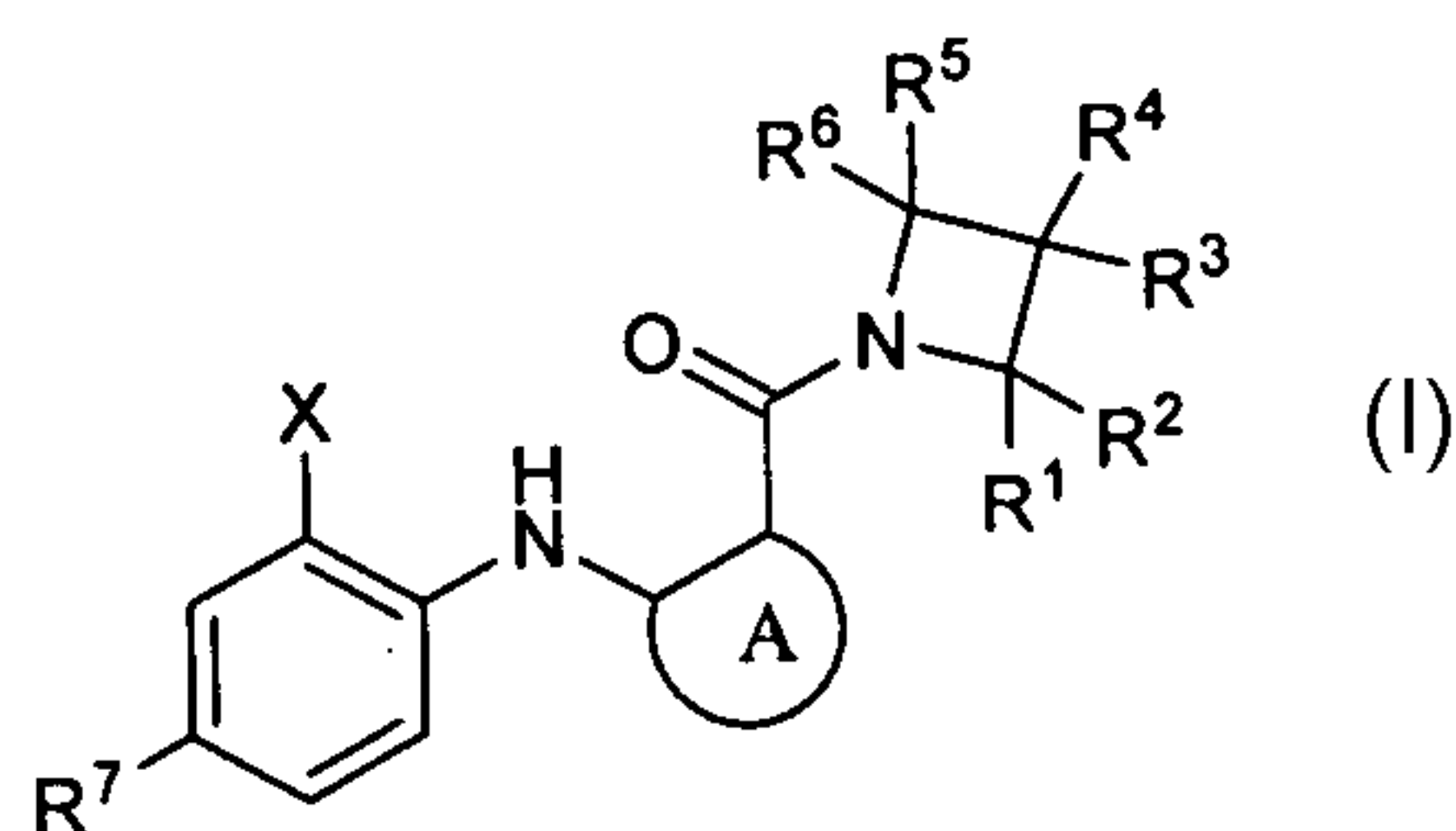
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(54) Title: METHODS OF USING MEK INHIBITORS



(57) Abstract: The present invention provides methods of treating cancer by administering a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, in combination with other cancer treatments.

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METHODS OF USING MEK INHIBITORS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] This invention relates to methods of treating cancer with a compound that inhibits protein kinase enzymatic activity and the resultant modulation of cellular activities (such as proliferation, differentiation, programmed cell death, migration, chemoinvasion and metabolism) in combination with anticancer agents.

State of the Art

[0002] Improvements in the specificity of agents used to treat various disease states such as cancer, metabolic, and inflammatory diseases is of considerable interest because of the therapeutic benefits which would be realized if the side effects associated with the administration of these agents could be reduced. Traditionally, dramatic improvements in the treatment of cancer are associated with identification of therapeutic agents acting through novel mechanisms.

[0003] Protein kinases are enzymes that catalyze the phosphorylation of proteins at the hydroxy groups of tyrosine, serine and threonine residues of proteins. The kinase complement of the human genome contains 518 putative protein kinase genes (Manning et al, Science, (2002), 298, 1912). The consequences of this activity include effects on cell differentiation, proliferation, transcription, translation, metabolism, cell cycle progression, apoptosis, metabolism, cytoskeletal rearrangement and movement; *i.e.*, protein kinases mediate the majority of signal transduction in eukaryotic cells. Furthermore, abnormal protein kinase activity has been related to a host of disorders, ranging from relatively non-life threatening diseases such as psoriasis to cancer. Chromosomal mapping has revealed that over 200 kinases map to disease loci, including cancer, inflammatory and metabolic disease.

[0004] Tyrosine kinases can be categorized as receptor type or non-receptor type. Receptor-type tyrosine kinases have an extracellular, a transmembrane, and an intracellular portion, while non-receptor type tyrosine kinases are wholly intracellular.

[0005] Receptor-type tyrosine kinases are comprised of a large number of transmembrane receptors with diverse biological activity. In fact, about 20 different subfamilies of receptor-type tyrosine kinases have been identified. One tyrosine kinase subfamily, designated the HER subfamily, is comprised of EGFR (HER1),

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HER2, HER3, and HER4. Ligands of this subfamily of receptors identified so far include epithelial growth factor, TGF- α , amphiregulin, HB-EGF, betacellulin and heregulin. Another subfamily of these receptor-type tyrosine kinases is the insulin subfamily, which includes INS-R, IGF-IR, and IR-R. The PDGF subfamily includes the PDGF- α and - β receptors, CSFIR, c-kit and FLK-II. Then there is the FLK family, which is comprised of the kinase insert domain receptor (KDR), fetal liver kinase-1 (FLK-1), fetal liver kinase-4 (FLK-4) and the fms-like tyrosine kinase-1 (Flt-1). The PDGF and FLK families are usually considered together due to the similarities of the two groups. For a detailed discussion of the receptor-type tyrosine kinases, see Plowman et al. (1994) DN&P 7(6): 334-339.

[0006] The non-receptor type of tyrosine kinases is also comprised of numerous subfamilies, including Src, Frk, Btk, Csk, Abl, Syk/Zap70, Fes/Fps, Fak, Jak, and Ack. Each of these subfamilies is further sub-divided into varying receptors. For example, the Src subfamily is one of the largest and includes Src, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr, and Yrk. The Src subfamily of enzymes has been linked to oncogenesis. For a more detailed discussion of the non-receptor type of tyrosine kinases, see Bolen (1993) Oncogene, 8:2025-2031.

[0007] Serine-threonine kinases play critical roles in intracellular signal transduction and include multiple families, such as STE, CKI, AGC, CAMK, and CMGC. Important subfamilies include, the MAP kinases, p38, JNK and ERK, which modulate signal transduction resulting from such diverse stimuli as mitogenic, stress, proinflammatory and antiapoptotic pathways. Members of the MAP kinase subfamily have been targeted for therapeutic intervention, including p38a, JNK isozymes and Raf.

[0008] Since protein kinases and their ligands play critical roles in various cellular activities, deregulation of protein kinase enzymatic activity can lead to altered cellular properties, such as uncontrolled cell growth associated with cancer. In addition to oncological indications, altered kinase signaling is implicated in numerous other pathological diseases, such as immunological disorders, metabolic and cardiovascular diseases, inflammatory diseases, and degenerative diseases. Therefore, both receptor and non-receptor protein kinases are attractive targets for small molecule drug discovery.

[0009] One particularly attractive goal for therapeutic use of kinase modulation relates to oncological indications. For example, modulation of protein kinase activity for the treatment of cancer has been demonstrated successfully with the FDA approval of Gleevec® (imatinib mesylate, produced by Novartis Pharmaceutical Corporation of East Hanover, NJ) for the treatment of Chronic Myeloid Leukemia (CML) and gastrointestinal stroma cancers. Gleevec is a selective Abl kinase inhibitor.

[0010] Modulation (particularly inhibition) of cell proliferation and angiogenesis, two key cellular processes needed for tumor growth and survival (Matter A. *Drug Disc Technol* 2001 6, 1005-1024), is an attractive goal for development of small-molecule drugs. Anti-angiogenic therapy represents a potentially important approach for the treatment of solid tumors and other diseases associated with dysregulated vascularization, including ischemic coronary artery disease, diabetic retinopathy, psoriasis and rheumatoid arthritis. As well, cell antiproliferative agents are desirable to slow or stop the growth of tumors.

[0011] One particularly attractive target for small-molecule modulation, with respect to antiangiogenic and antiproliferative activity is MEK. Inhibition of MEK1 (MAPK/ERK Kinase) is a promising strategy to control the growth of tumors that are dependent on aberrant ERK/MAPK pathway signaling (Solit et al., 2006; Wellbrock et al., 2004). The MEK-ERK signal transduction cascade is a conserved pathway which regulates cell growth, proliferation, differentiation, and apoptosis in response to growth factors, cytokines, and hormones. This pathway operates downstream of Ras which is often upregulated or mutated in human tumors. It has been demonstrated that MEK is a critical effector of Ras function. The ERK/MAPK pathway is upregulated in 30% of all tumors and oncogenic activating mutations in K-Ras and B-Raf have been identified in 22% and 18% of all cancers respectively (Allen et al., 2003; Bamford S, 2004; Davies et al., 2002; Malumbres and Barbacid, 2003). A large portion of human cancers, including 66% (B-Raf) of malignant melanomas, 60% (K-Ras) and 4% (B-Raf) of pancreatic cancers, 50% of colorectal cancers (colon, in particular, K-Ras: 30%, B-Raf: 15%), 20% (K-Ras) of lung cancers, 27% (B-Raf) papillary and anaplastic thyroid cancer, and 10-20% (B-Raf) of endometriod ovarian cancers, harbor activating Ras and Raf mutations. Other cancers that may be treatable by inhibiting the ERK/MAPK pathway include kidney cancer (Rika Hoshino, et. al. *Oncogene* 21 January 1999, Volume 18, Number 3, Pages 813-822), breast cancer (Santen RJ, et. al. *Steroid Biochem Mol Biol* 2002, 80239), multiple myeloma Hu L

et. al. *Blood* **2003**, 101, 3126), ovarian cancer Nicosia SV et. al. *Hematol Oncol Clin North Am* **2003**, 17 927), and AML (Milella M et. al. *Curr Pharm Des* **2005**, 11, 2779).

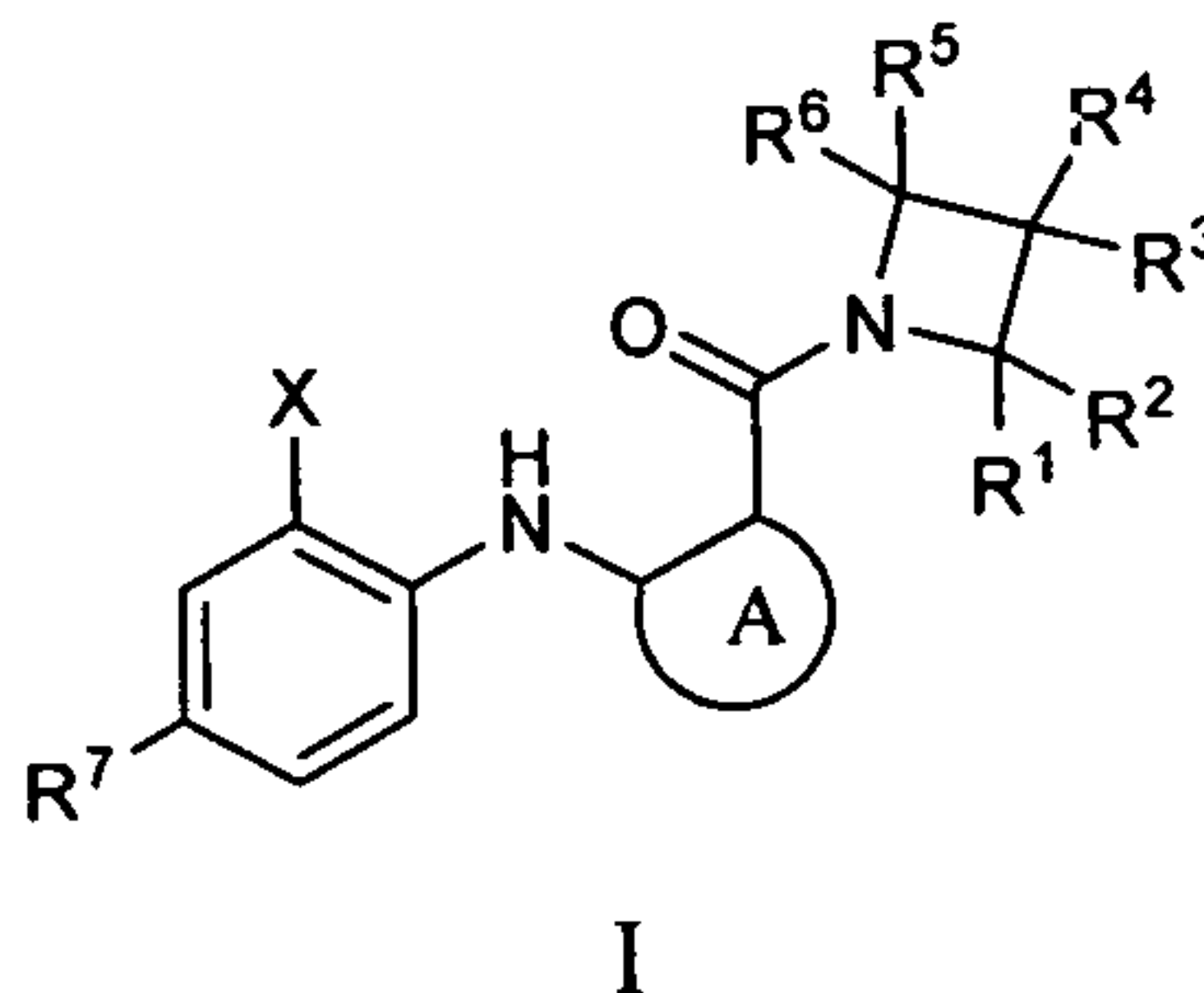
[0012] It has been shown that inhibition of the ERK pathway, and in particular inhibition of MEK kinase activity, results in anti-metastatic and anti-angiogenic effects largely due to a reduction of cell-cell contact and motility as well as downregulation of vascular endothelial growth factor (VEGF) expression. Furthermore, expression of dominant negative MEK, or ERK reduced the transforming ability of mutant Ras as seen in cell culture and in primary and metastatic growth of human tumor xenografts *in vivo*. Therefore, the MEK-ERK signal transduction pathway is an appropriate pathway to target for therapeutic intervention.

[0013] It is well established that combining treatments with different mechanisms of action often leads to enhanced anti-tumor activity as compared to single treatments administered alone. This is true for combinations of chemotherapies (e.g. Kyrgiou M. et. al. *J Natl Cancer Inst* **2006**, 98, 1655) and combinations of antibodies and chemotherapy (e.g. Pasetto LM et. al. *Anticancer Res* **2006**, 26, 3973).

SUMMARY OF THE INVENTION

[0014] The compositions of the invention are used to treat diseases associated with abnormal and or unregulated cellular activities. Disease states which can be treated by the methods and compositions provided herein include cancer. The invention is directed to methods of treating these diseases by administering a Compound of Formula I in combination with one or more treatment(s).

[0015] One aspect of the Invention is directed to a method of treating cancer which method comprises administering to a patient a therapeutically effective amount of a compound of Formula I:



or a pharmaceutically acceptable salt or solvate, thereof; or administering a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula I and a pharmaceutically acceptable carrier, excipient, or diluent in combination with one or more treatment(s) selected from surgery, one or more chemotherapeutic agent(s), one or more of the hormone therapy(s), one or more of the antibody(s), hypothermia therapy, radioactive iodine therapy, and radiation wherein the Compound of Formula I is that where A, X, R¹, R², R³, R⁴, R⁵, R⁶, and R⁷ are as defined in Group A, Group B, Group C, or Group D:

Group A:

A is arylene optionally substituted with one, two, three or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶ where R¹⁰, R¹², R¹⁴ and R¹⁶ are independently hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkoxy, hydroxy, alkoxy, amino, alkylamino, dialkylamino, haloalkyl, -NHS(O)₂R⁸, -CN, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'} and -NR⁸C(O)R^{8'};

X is alkyl, halo, haloalkyl, or haloalkoxy;

R¹, R², R³, R⁴, R⁵ and R⁶ are independently hydrogen, halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, -CH₂N(R²⁵)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂)), -CH₂NR²⁵C(=NH)(N(R^{25a})(CN)), -CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; or one of R¹ and R² together with the carbon to which they are attached, R³ and R⁴ together with the carbon to which they are attached, and R⁵ and R⁶ together with the carbon to which they are attached form C(O) or C(=NOH);

m is 0, 1, or 2;

R⁷ is hydrogen, halo or alkyl;

R^8 , $R^{8'}$ and $R^{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl; where the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, alkoxycarbonyl, alkenyloxycarbonyl, optionally substituted cycloalkyl, optionally substituted cycloalkyloxycarbonyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted aryloxycarbonyl, optionally substituted arylalkyl, optionally substituted arylalkyloxy, optionally substituted arylalkyloxycarbonyl, nitro, cyano, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{34}SO_2R^{34a}$ (where R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl), $-SO_2NR^{35}R^{35a}$ (where R^{35} is hydrogen or alkyl and R^{35a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl), $-NR^{32}C(O)R^{32a}$ (where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), and $-C(O)NR^{33}R^{33a}$ (where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl);

R^9 is alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl; where the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, or five groups selected from halo, hydroxy, alkyl, haloalkyl, haloalkoxy, amino, alkylamino, and dialkylamino;

R^{25} and R^{25b} are independently hydrogen, alkyl, alkenyl, optionally substituted cycloalkyl, or optionally substituted aryl; and

R^{25a} is hydrogen, alkyl, or alkenyl;

Group B:

A is heteroarylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , R^{16} and R^{19} where R^{10} , R^{12} , R^{14} and R^{16} are independently hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkoxy, hydroxy, alkoxy, cyano,

amino, alkylamino, dialkylamino, haloalkyl, alkylsulfonylamino, alkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, alkenyloxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, or alkylcarbonylamino; where R^{19} is hydrogen, alkyl, or alkenyl; and where each alkyl and alkenyl, either alone or as part of another group within R^{10} , R^{12} , R^{14} , R^{16} , and R^{19} is independently optionally substituted with halo, hydroxy, or alkoxy;

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

m is 1 or 2;

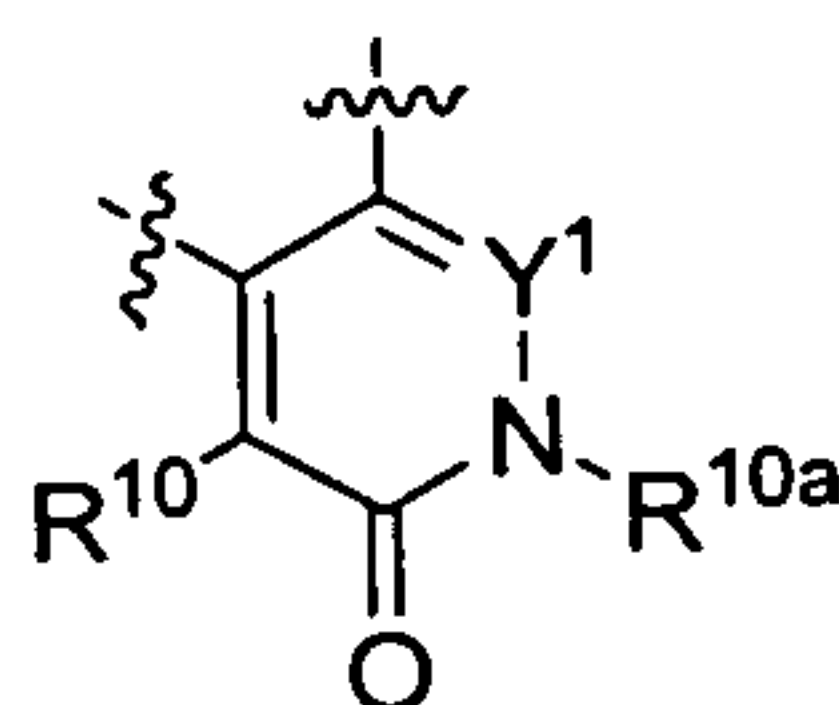
R^7 is hydrogen, halo or alkyl; and

R^8 , $R^{8'}$ and $R^{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, haloalkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, where the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where

n is 0, 1, or 2 and R³¹ is optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), -NR³⁶S(O)₂R^{36a} (where R³⁶ is hydrogen, alkyl, or alkenyl and R^{36a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), -S(O)₂NR³⁷R^{37a} (where R³⁷ is hydrogen, alkyl, or alkenyl and R^{37a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted aryloxy, optionally substituted arylalkyloxy, optionally substituted heteroaryl, -NHC(O)R³² (where R³² is alkyl, alkenyl, alkoxy, or cycloalkyl) and -NR³⁰R^{30'} (where R³⁰ and R^{30'} are independently hydrogen, alkyl, or hydroxyalkyl), and -C(O)NHR³³ (where R³³ is alkyl, alkenyl, alkynyl, or cycloalkyl);

Group C:

A is



(a)

where R¹⁰ is hydrogen, alkyl, alkenyl, alkynyl, halo, haloalkoxy, hydroxy, alkoxy, amino, alkylamino, dialkylamino, haloalkyl, -NHS(O)₂R⁸, -CN, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'} and -NR⁸C(O)R^{8'};

R^{10a} is hydrogen, alkyl, or alkenyl;

$$Y^1 \text{ is } =CH- \text{ or } =N-;$$

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1, R^2, R^3, R^4, R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl,

alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

m is 1 or 2;

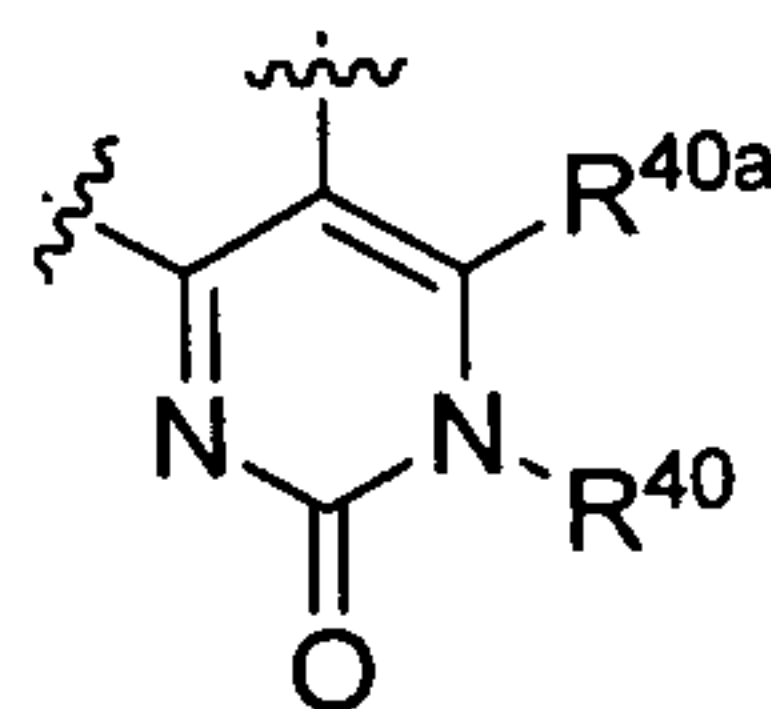
R^7 is hydrogen, halo or alkyl; and

R^8 , $R^{8'}$ and $R^{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, haloalkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, where the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{36}S(O)_2R^{36a}$ (where R^{36} is hydrogen, alkyl, or alkenyl and R^{36a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-S(O)_2NR^{37}R^{37a}$ (where R^{37} is hydrogen, alkyl, or alkenyl and R^{37a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted aryloxy, optionally substituted arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (where R^{32} is alkyl, alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently

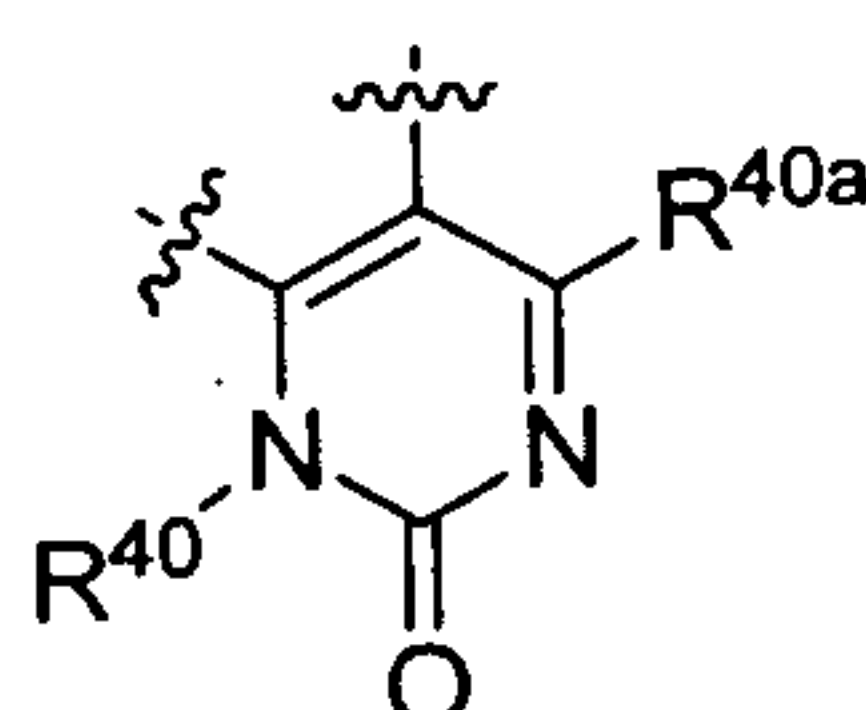
hydrogen, alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (where R^{33} is alkyl, alkenyl, alkynyl, or cycloalkyl); or

Group D:

A is



(b) or



(c)

R^{40} and R^{40a} are independently hydrogen or alkyl;

X is alkyl, halo, haloalkyl, or haloalkoxy;

R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl, where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; or one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

m is 1 or 2;

R^7 is hydrogen, halo or alkyl; and

R^8 , $R^{8'}$ and $R^{8''}$ are independently selected from hydrogen, hydroxy, optionally substituted alkoxy, alkyl, haloalkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl, where the alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from alkyl, halo, hydroxy, hydroxyalkyl, optionally substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and R^{31} is optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{36}S(O)_2R^{36a}$ (where R^{36} is hydrogen, alkyl, or alkenyl and R^{36a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-S(O)_2NR^{37}R^{37a}$ (where R^{37} is hydrogen, alkyl, or alkenyl and R^{37a} is alkyl, alkenyl, optionally substituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted aryloxy, optionally substituted arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (where R^{32} is alkyl, alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (where R^{33} is alkyl, alkenyl, alkynyl, or cycloalkyl).

DETAILED DESCRIPTION OF THE INVENTION

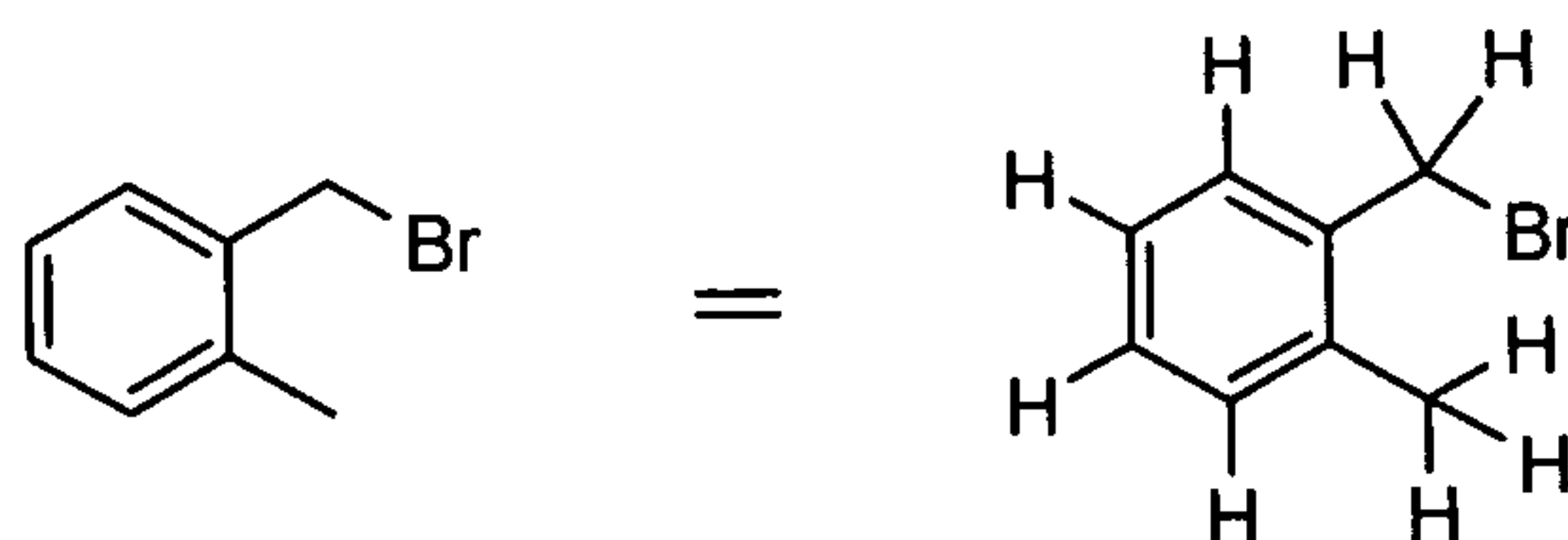
Definitions for the Mek Compound

[0016] The following terms have the indicated meanings throughout:

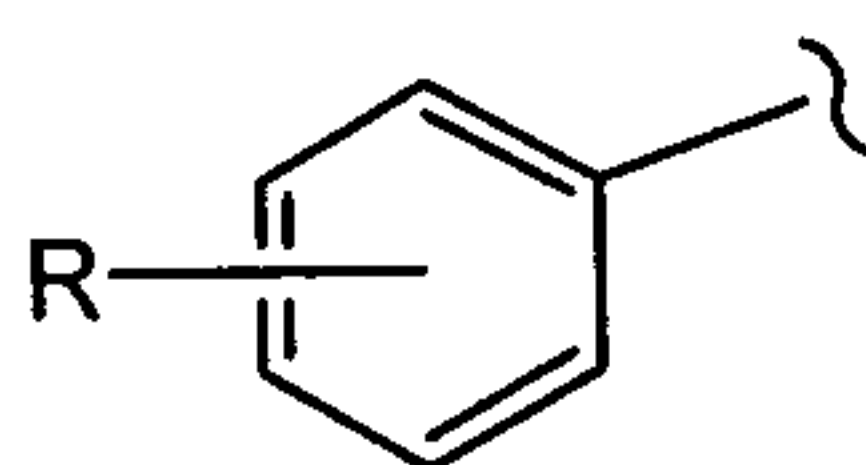
[0017] The symbol “-” means a single bond, “=” means a double bond, “≡” means a triple bond, and “---” means a single bond and optionally a double bond. When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four.

[0018] When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four. For example, in the structure on the left-hand side of the schematic

below there are nine hydrogens implied. The nine hydrogens are depicted in the right-hand structure. Sometimes a particular atom in a structure is described in textual formula as having a hydrogen or hydrogens as substitution (expressly defined hydrogen), for example, $-\text{CH}_2\text{CH}_2-$. It is understood by one of ordinary skill in the art that the aforementioned descriptive techniques are common in the chemical arts to provide brevity and simplicity to description of otherwise complex structures.

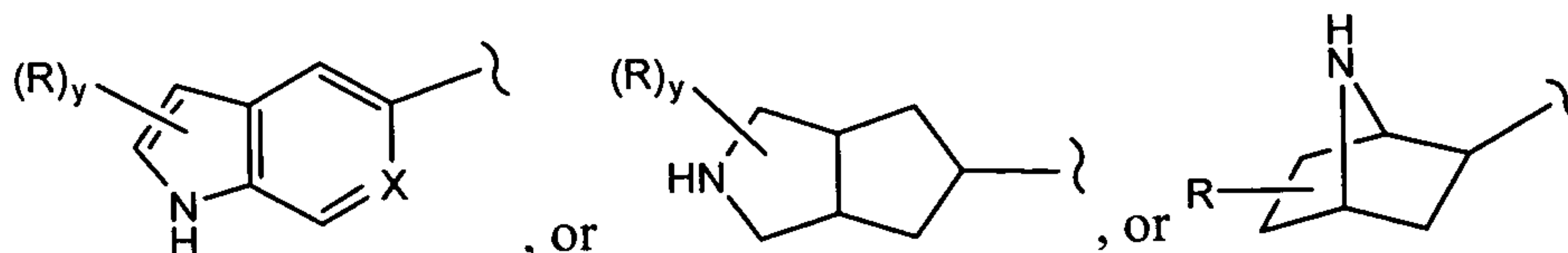


[0019] If a group “R” is depicted as “floating” on a ring system, as for example in the formula:



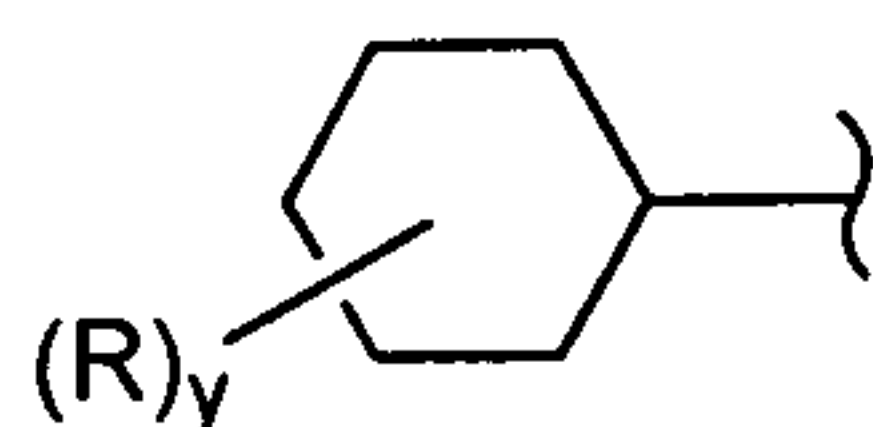
then, unless otherwise defined, a substituent “R” may reside on any atom of the ring system, assuming replacement of a depicted, implied, or expressly defined hydrogen from one of the ring atoms, so long as a stable structure is formed.

[0020] If a group “R” is depicted as floating on a fused ring system, as for example in the formulae:

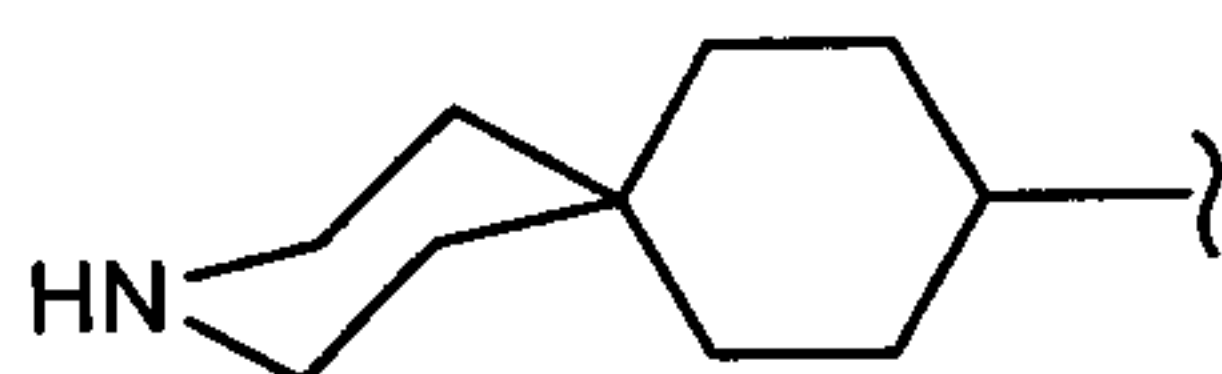


then, unless otherwise defined, a substituent “R” may reside on any atom of the fused ring system, assuming replacement of a depicted hydrogen (for example the $-\text{NH}-$ in the formula above), implied hydrogen (for example as in the formula above, where the hydrogens are not shown but understood to be present), or expressly defined hydrogen (for example where in the formula above, “X” equals $=\text{CH}-$) from one of the ring atoms, so long as a stable structure is formed. In the example depicted, the “R” group may reside on either the 5-membered or the 6-membered ring of the fused ring system. In the formula depicted above, when y is 2 for example, then the two “R’s” may reside on any two atoms of the ring system, again assuming each replaces a depicted, implied, or expressly defined hydrogen on the ring.

[0021] When a group “R” is depicted as existing on a ring system containing saturated carbons, as for example in the formula:



where, in this example, “y” can be more than one, assuming each replaces a currently depicted, implied, or expressly defined hydrogen on the ring; then, unless otherwise defined, where the resulting structure is stable, two “R’s” may reside on the same carbon. A simple example is when R is a methyl group; there can exist a geminal dimethyl on a carbon of the depicted ring (an “annular” carbon). In another example, two R’s on the same carbon, including that carbon, may form a ring, thus creating a spirocyclic ring (a “spirocyclyl” group) structure with the depicted ring as for example in the formula:



[0022] “Acyl” means a $-C(O)R$ radical where R is optionally substituted alkyl, optionally substituted alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, or heterocycloalkylalkyl, as defined herein, e.g., acetyl, benzoyl, trifluoromethylcarbonyl, or 2-methoxyethylcarbonyl, and the like.

[0023] “Acylamino” means a $-NRR'$ group where R is acyl, as defined herein, and R' is hydrogen or alkyl.

[0024] “Administration” and variants thereof (e.g., “administering” a compound) in reference to a compound of the invention means introducing the compound or a prodrug of the compound into the system of the animal in need of treatment. When a compound of the invention or prodrug thereof is provided in combination with one or more other active agents (e.g., surgery, radiation, and chemotherapy, etc.), “administration” and its variants are each understood to include concurrent and sequential introduction of the compound or prodrug thereof and other agents.

[0025] “Alkenyl” means a means a linear monovalent hydrocarbon radical of one to six carbon atoms or a branched monovalent hydrocarbon radical of three to 6 carbon atoms which radical contains at least one double bond, e.g., ethenyl, propenyl, 1-but-3-enyl, 1-pent-3-enyl, 1-hex-5-enyl and the like.

[0026] "Alkenylcarbonyl" means a $-C(O)R$ group where R is alkenyl, as defined herein.

[0027] "Alkenyloxycarbonyl" means a $-C(O)OR$ group where R is alkenyl, as defined herein.

[0028] "Alkoxy" means an $-OR$ group where R is alkyl group as defined herein. Examples include methoxy, ethoxy, propoxy, isopropoxy, and the like. Lower-alkoxy refers to groups containing one to six carbons.

[0029] "Alkoxyalkyl" means an alkyl group, as defined herein, substituted with at least one, preferably one, two, or three, alkoxy groups as defined herein. Representative examples include methoxymethyl and the like.

[0030] "Alkoxycarbonyl" means a $-C(O)OR$ group where R is alkyl as defined herein.

[0031] "Alkoxycarbonylamino" means a $-NR'R''$ group where R' is hydrogen, alkyl, hydroxy, or alkoxy and R'' is alkoxycarbonyl, as defined herein.

[0032] "Alkyl" means a linear saturated monovalent hydrocarbon radical of one to eight carbon atoms or a branched saturated monovalent hydrocarbon radical of three to eight carbon atoms, e.g., methyl, ethyl, propyl, 2-propyl, butyl (including all isomeric forms), or pentyl (including all isomeric forms), and the like.

[0033] "Alkylamino" means a $-NHR$ radical where R is alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., methylamino, ethylamino, *n*-propylamino, *iso*-propylamino, *n*-butylamino, *iso*-butylamino, *tert*-butylamino, or methylamino-N-oxide, and the like.

[0034] "Alkylaminoalkyl" means an alkyl group substituted with one or two alkylamino groups, as defined herein.

[0035] "Alkylaminocarbonyl" means a $-C(O)R$ group where R is alkylamino, as defined herein.

[0036] "Alkylcarbonyl" means a $-C(O)R$ group where R is alkyl, as defined herein.

[0037] "Alkylcarbonylamino" means a $-NRR'$ group where R is hydrogen or alkyl as defined herein and R' is alkylcarbonyl, as defined herein.

[0038] "Alkylcarbonyloxy" means an $-OC(O)R$ group where R is alkyl, as defined herein.

[0039] "Alkylsulfonylamino" means a $-NRS(O)_2R'$ group where R is hydrogen or alkyl as defined herein, and R' is alkyl, as defined herein.

[0040] "Alkynyl" means a straight or branched hydrocarbon radical having from 2 to 8 carbon atoms and at least one triple bond and includes ethynyl, propynyl, butynyl, pentyn-2-yl and the like.

[0041] "Aminoalkyl" means an alkyl group substituted with at least one amino group and in another embodiment, one, two or three amino groups.

[0042] "Aminocarbonyl" means a $-C(O)NH_2$ group.

[0043] "Aryl" means a monovalent six- to fourteen-membered, mono- or bi-carbocyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the bicyclic ring is aromatic. Unless stated otherwise, the valency of the group may be located on any atom of any ring within the radical, valency rules permitting. Representative examples include phenyl, naphthyl, and indanyl, and the like.

[0044] "Arylene" means a divalent six- to fourteen-membered, mono- or bi-carbocyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the bicyclic ring is aromatic. Representative examples include phenylene, naphthylene, and indanylene, and the like.

[0045] "Arylalkyl" means an alkyl group, as defined herein, substituted with one or two aryl groups, as defined herein. Examples include benzyl, phenethyl, and the like.

[0046] "Carboxy ester" means a $-C(O)OR$ group where R is lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, aryl or arylalkyl, each of which is defined herein. Representative examples include methoxycarbonyl, ethoxycarbonyl, and benzyloxycarbonyl, and the like.

[0047] "Cycloalkyl" means a monocyclic or fused bicyclic, saturated or partially unsaturated (but not aromatic), monovalent hydrocarbon radical of three to ten carbon ring atoms. Fused bicyclic hydrocarbon radical includes bridged ring systems. Unless stated otherwise, the valency of the group may be located on any atom of any ring within the radical, valency rules permitting. One or two ring carbon atoms may be replaced by a $-C(O)-$, $-C(S)-$, or $-C(=NH)-$ group. The term cycloalkyl includes, but is not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexyl, or cyclohex-3-enyl, and the like.

[0048] "Dialkylamino" means a $-NRR'$ radical where R and R' are alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., dimethylamino, diethylamino, *N,N*-methylpropylamino or *N,N*-methylethylamino, and the like.

[0049] “Dialkylaminoalkyl” means an alkyl group substituted with one or two dialkylamino groups, as defined herein.

[0050] “Dialkylaminocarbonyl” means a -C(O)R group where R is dialkylamino, as defined herein.

[0051] “Fused-polycyclic” or “fused ring system” means a polycyclic ring system that contains fused rings and, unless otherwise indicated, can contain bridged rings; that is, where two rings have more than one shared atom in their ring structures. In this application, fused-polycyclics and fused ring systems are not necessarily all aromatic ring systems. Typically, but not necessarily, fused-polycyclics share a vicinal set of atoms, for example naphthalene or 1,2,3,4-tetrahydro-naphthalene. A spiro ring system is not a fused-polycyclic by this definition, but fused polycyclic ring systems of the invention may themselves have spiro rings attached thereto via a single ring atom of the fused-polycyclic. In some examples, as appreciated by one of ordinary skill in the art, two adjacent groups on an aromatic system may be fused together to form a ring structure. The fused ring structure may contain heteroatoms and may be optionally substituted with one or more groups. It should additionally be noted that saturated carbons of such fused groups (*i.e.* saturated ring structures) can contain two substitution groups.

[0052] “Haloalkoxy” means an -OR' group where R' is haloalkyl as defined herein, e.g., trifluoromethoxy or 2,2,2-trifluoroethoxy, and the like.

[0053] “Halogen” or “halo” means fluoro, chloro, bromo and iodo.

[0054] “Haloalkyl” means an alkyl group, as defined herein, that is substituted with one or more halogens, preferably one to five halo atoms. Representative examples include trifluoromethyl, difluoromethyl, 1-chloro-2-fluoro-ethyl, and the like.

[0055] “Heteroaryl” means a monocyclic, fused bicyclic, or fused tricyclic, monovalent radical of 5 to 14 ring atoms containing one or more, preferably one, two, three, or four ring heteroatoms independently selected from -O-, -S(O)_n- (n is 0, 1, or 2), -N-, -N(R^x)-, and the remaining ring atoms being carbon, wherein the ring comprising a monocyclic radical is aromatic and wherein at least one of the fused rings comprising a bicyclic or tricyclic radical is aromatic. One or two ring carbon atoms of any nonaromatic rings comprising a bicyclic or tricyclic radical may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. R^x is hydrogen, alkyl, hydroxy, alkoxy, acyl, or alkylsulfonyl. Unless stated otherwise, the valency may be located on

any atom of any ring of the heteroaryl group, valency rules permitting. In particular, when the point of valency is located on the nitrogen, R^x is absent. The term heteroaryl includes, but is not limited to, 1,2,4-triazolyl, 1,3,5-triazolyl, phthalimidyl, pyridinyl, pyrrolyl, imidazolyl, thienyl, furanyl, indolyl, 2,3-dihydro-1*H*-indolyl (including, for example, 2,3-dihydro-1*H*-indol-2-yl or 2,3-dihydro-1*H*-indol-5-yl, and the like), isoindolyl, indolinyl, isoindolinyl, benzimidazolyl, benzodioxol-4-yl, benzofuranyl, cinnolinyl, indolizinyl, naphthyridin-3-yl, phthalazin-3-yl, phthalazin-4-yl, pteridinyl, purinyl, quinazolinyl, quinoxalinyl, tetrazoyl, pyrazolyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isooxazolyl, oxadiazolyl, benzoxazolyl, quinolinyl, isoquinolinyl, tetrahydroisoquinolinyl (including, for example, tetrahydroisoquinolin-4-yl or tetrahydroisoquinolin-6-yl, and the like), pyrrolo[3,2-*c*]pyridinyl (including, for example, pyrrolo[3,2-*c*]pyridin-2-yl or pyrrolo[3,2-*c*]pyridin-7-yl, and the like), benzopyranyl, thiazolyl, isothiazolyl, thiadiazolyl, benzothiazolyl, benzothienyl, and the derivatives thereof, or N-oxide or a protected derivative thereof.

[0056] “Heteroarylene” means a monocyclic, fused bicyclic, or fused tricyclic, divalent radical of 5 to 14 ring atoms containing one or more, preferably one, two, three, or four ring heteroatoms independently selected from -O-, -S(O)_{*n*}- (*n* is 0, 1, or 2), -N-, -N(R^{19})-, and the remaining ring atoms being carbon, wherein the ring comprising a monocyclic radical is aromatic and wherein at least one of the fused rings comprising a bicyclic or tricyclic radical is aromatic. One or two ring carbon atoms of any nonaromatic rings comprising a bicyclic or tricyclic radical may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. R^{19} is hydrogen, alkyl, or alkenyl. Unless stated otherwise, the valencies may be located on any atom of any ring of the heteroarylene group, valency rules permitting. In particular, when the point of valency is located on the nitrogen, R^x is absent. The term heteroaryl includes, but is not limited to, thien-diyl, benzo[*d*]isoxazol-diyl, benzo[*d*]isothiazol-diyl, 1*H*-indazol-diyl (optionally substituted at the N1 position with R^{19}), benzo[*d*]oxazol-diyl, benzo[*d*]thiazol-diyl, 1*H*-benzo[*d*]imidazol-diyl (optionally substituted at the N1 position with R^{19}), 1*H*-benzo[*d*][1,2,3]triazol-diyl (optionally substituted at the N1 position with R^{19}), imidazo[1,2-*a*]pyridin-diyl, cinnolin-diyl, quinolin-diyl, pyridin-diyl, 1-oxido-pyridin-diyl, [1,2,4]triazolo[4,3-*a*]pyridin-diyl, and 2,3-dihydroimidazo[1,2-*a*]pyridin-diyl, and the like.

[0057] “Heterocycloalkyl” means a saturated or partially unsaturated (but not aromatic) monovalent monocyclic group of 3 to 8 ring atoms or a saturated or partially unsaturated (but not aromatic) monovalent fused bicyclic group of 5 to 12 ring atoms in which one or more (and in another embodiment, one, two, three, or four) ring heteroatoms independently selected from O, S(O)_n (n is 0, 1, or 2), N, N(R^y) (where R^y is hydrogen, alkyl, hydroxy, alkoxy, acyl, or alkylsulfonyl), the remaining ring atoms being carbon. One or two ring carbon atoms may be replaced by a -C(O)-, -C(S)-, or -C(=NH)- group. Fused bicyclic radical includes bridged ring systems. Unless otherwise stated, the valency of the group may be located on any atom of any ring within the radical, valency rules permitting. When the point of valency is located on a nitrogen atom, R^y is absent. The term heterocycloalkyl includes, but is not limited to, azetidiny, pyrrolidiny, 2-oxopyrrolidiny, 2,5-dihydro-1*H*-pyrrolyl, piperidiny, 4-piperidonyl, morpholiny, piperaziny, 2-oxopiperaziny, tetrahydropyrany, 2-oxopiperidiny, thiomorpholiny, thiamorpholiny, perhydroazepiny, pyrazolidiny, imidazolinyl, imidazolidiny, dihydropyridiny, tetrahydropyridiny, oxazolinyl, oxazolidiny, isoxazolidiny, thiazolinyl, thiazolidiny, quinuclidiny, isothiazolidiny, octahydroindolyl, octahydroisoindolyl, decahydroisoquinolyl, tetrahydrofuryl, and tetrahydropyrany, and the derivatives thereof and N-oxide or a protected derivative thereof.

[0058] “Hydroxyalkyl” means an alkyl, as defined herein, substituted with at least one, preferably one, two, or three, hydroxy group(s), provided that if two hydroxy groups are present they are not both on the same carbon atom. Representative examples include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 1-(hydroxymethyl)-2-hydroxyethyl, 2,3-dihydroxybutyl, 3,4-dihydroxybutyl and 2-(hydroxymethyl)-3-hydroxypropyl, preferably 2-hydroxyethyl, 2,3-dihydroxypropyl, and 1-(hydroxymethyl)-2-hydroxyethyl, and the like.

[0059] “Hydroxyamino” means a -NH(OH) group.

[0060] “Optional” or “optionally” means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. One of ordinary skill in the art would understand that with respect to any molecule described as containing one or more optional substituents, only sterically practical and/or

synthetically feasible compounds are meant to be included. "Optionally substituted" refers to all subsequent modifiers in a term. So, for example, in the term "optionally substituted arylC₁₋₈ alkyl," both the "C₁₋₈ alkyl" portion and the "aryl" portion of the molecule may or may not be substituted. A list of exemplary optional substitutions is presented below in the definition of "substituted."

[0061] "Optionally substituted alkoxy" means an -OR radical where R is optionally substituted alkyl as defined herein. Representative examples include -OCH₂CH₂OCH₃, -OCH₂CH₂OH, -OCH₂CH(NH₂)CH₃, and the like.

[0062] "Optionally substituted alkyl" means an alkyl radical, as defined herein, optionally substituted with one or more group(s) (and in another embodiment one, two, three, four, or five groups) independently selected from alkylcarbonyl, alkenylcarbonyl, cycloalkylcarbonyl, alkylcarbonyloxy, alkenylcarbonyloxy, amino, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, cyano, cyanoalkylaminocarbonyl, alkoxy, alkenyloxy, halo, hydroxy, hydroxyalkoxy, carboxy, alkylcarbonylamino, alkylcarbonyloxy, -S(O)₀₋₂-alkyl, -S(O)₀₋₂-alkenyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, -NR^cS(O)₂-alkyl (where R^c is hydrogen, alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxy, alkoxy, alkenyloxy, or cyanoalkyl), alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylaminoalkyloxy, dialkylaminoalkyloxy, alkoxycarbonyl, alkenyloxycarbonyl, alkoxycarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkoxyalkyloxy, and -C(O)NR^aR^b (where R^a and R^b are independently hydrogen, alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxy, alkoxy, alkenyloxy, or cyanoalkyl).

[0063] "Optionally substituted aryl" means an aryl group, as defined herein, which is optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -C(O)NR'R'' (where R' is hydrogen or alkyl and R'' is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), -NR'C(O)R'' (where R' is hydrogen or alkyl and R'' is alkyl, aryl, heteroaryl, or heterocycloalkyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

[0064] “Optionally substituted arylalkyl means an alkyl group substituted with one or two optionally substituted aryl group(s) as defined herein.

[0065] “Optionally substituted arylalkyloxy” means an -OR group where R is optionally substituted arylalkyl, as defined herein.

[0066] “Optionally substituted arylalkyloxycarbonyl” means a -C(O)R group where R is optionally substituted arylalkyloxy, as defined herein.

[0067] “Optionally substituted aryloxy” means an -OR group where R is optionally substituted aryl, as defined herein.

[0068] “Optionally substituted aryloxycarbonyl” means a -C(O)R group where R is optionally substituted aryloxy as defined herein.

[0069] “Optionally substituted cycloalkyl” means a cycloalkyl radical, as defined herein, that is optionally substituted with one, two, three, or four groups independently selected from alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkoxy, oxo, hydroxy, cyano, nitro, amino, mono(C₁-C₆)alkylamino, dialkylamino, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, carboxy ester, cycloalkyl, hydroxyalkyl, -C(O)NR'R" (where R' is hydrogen, alkyl, hydroxy, or alkoxy and R" is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, heteroaryl, or heterocycloalkyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heterocyclyl).

[0070] “Optionally substituted cycloalkyloxycarbonyl” means a -C(O)OR group where R is optionally substituted cycloalkyl as defined herein.

[0071] “Optionally substituted heteroaryl” means a heteroaryl group, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, alkyl, alkenyl, alkynyl, alkoxy, hydroxy, oxo (valency rules permitting), carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, heteroaryl, optionally substituted aryl, -C(O)NR'R" (where R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, heteroaryl, or heterocycloalkyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

[0072] “Optionally substituted heterocycloalkyl” means a heterocycloalkyl ring, as defined herein, optionally substituted with one, two, three, four, or five groups

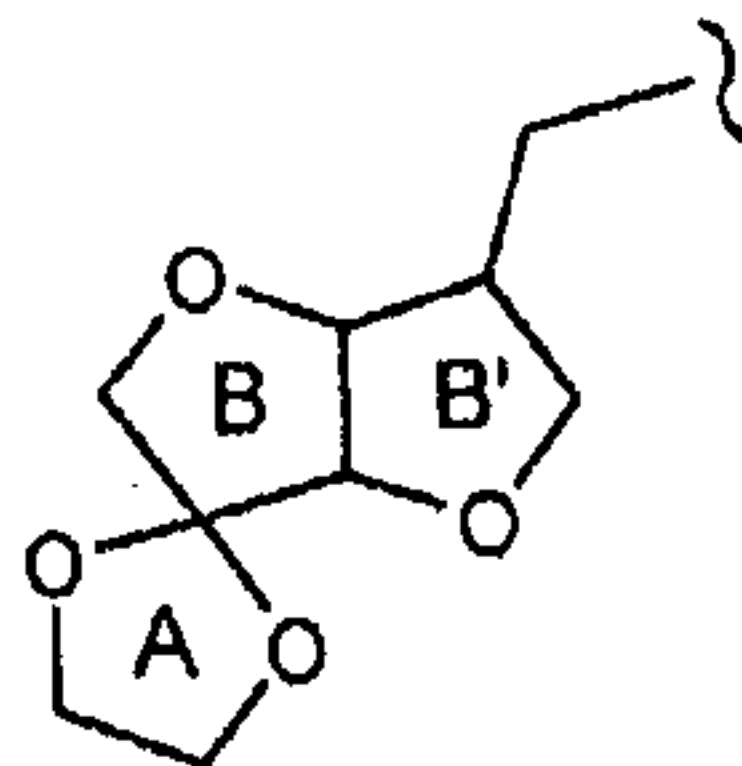
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selected from halo, haloalkyl, haloalkoxy, hydroxy, oxo, alkyl, alkenyl, alkynyl, alkoxy, optionally substituted cycloalkyl, heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, alkoxycarbonyl, aryloxy carbonyl, arylalkyloxycarbonyl, cycloalkyloxycarbonyl, cycloalkylalkyloxycarbonyl, $-C(O)NR'R''$ (where R' is hydrogen or alkyl and R'' is hydrogen, alkyl, aryl, heteroaryl, or heterocycloalkyl), $-NR'C(O)R''$ (where R' is hydrogen or alkyl and R'' is alkyl, aryl, heteroaryl, or heterocycloalkyl), amino, alkylamino, dialkylamino, and $-NHS(O)_2R'$ (where R' is alkyl, aryl, or heteroaryl).

[0073] "Saturated bridged ring system" refers to a bicyclic or polycyclic ring system that is not aromatic. Such a system may contain isolated or conjugated unsaturation, but not aromatic or heteroaromatic rings in its core structure (but may have aromatic substitution thereon). For example, hexahydro-furo[3,2-b]furan, 2,3,3a,4,7,7a-hexahydro-1H-indene, 7-aza-bicyclo[2.2.1]heptane, and 1,2,3,4,4a,5,8,8a-octahydro-naphthalene are all included in the class "saturated bridged ring system."

[0074] "Spiro", "Spirocyclyl" or "spiro ring" refers to a ring originating from a particular annular carbon of another ring. For example, as depicted below, a ring atom of a saturated bridged ring system (rings B and B'), but not a bridgehead atom, can be a shared atom between the saturated bridged ring system and a spirocyclyl (ring A) attached thereto.



[0075] "Yield" for each of the reactions described herein is expressed as a percentage of the theoretical yield.

Definitions for the Compound of formula 100

[0076] The terms used to describe the scope of formula 100 are defined in WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004).

For example "optionally substituted alkyl" for formula 100 has the meaning given in WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004). Whenever a compound of formula 100 is described in this application, whether by structure or by use of the term "formula 100," the terms used

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to describe that compound are defined by WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004).

Definitions for the Compound of formula 101

[0077] The terms used to describe the scope of formula 101 are defined in WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789).

For example "optionally substituted heterocyclyl" for formula 101 has the meaning given in WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789). Whenever a compound of formula 101 is described in this application, whether by structure or by use of the term "formula 101," the terms used to describe that compound are defined by WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789).

Definitions for the Compound of formula A-B-C

[0078] The terms used to describe the scope of formula A-B-C are defined in WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336).

For example "optionally substituted heterocyclyl" for formula A-B-C has the meaning given in WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336). Whenever a compound of formula A-B-C is described in this application, whether by structure or by use of the term "formula A-B-C," the terms used to describe that compound are defined by WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336).

Definitions for the Compound of formula 103

[0079] The terms used to describe the scope of formula 103 are defined in WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140).

For example "optionally substituted heterocyclyl" for formula 103 has the meaning given in WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140). Whenever a compound of formula 103 is described in this application, whether by structure or by use of the term "formula 103," the terms used to describe that compound are defined by WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140).

Definitions for the Compound of formula 105

[0080] The terms used to describe the scope of formula 105 are defined in WO 2006/074057 (US Nat'l Stage Application Serial No. 11/722,719).

For example "optionally substituted heterocyclyl" for formula 105 has the meaning given in WO 2006/074057 (US Nat'l Stage Application

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Serial No. 11/722,719). Whenever a compound of formula 105 is described in this application, whether by structure or by use of the term "formula 105," the terms used to describe that compound are defined by WO 2006/074057 (US Nat'l Stage Application Serial No. 11/722,719).

Definitions for the Compound of formula 107

[0081] The terms used to describe the scope of formula 107 are defined in WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555).

For example "optionally substituted aryl" for formula 107 has the meaning given in WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555). Whenever a compound of formula 107 is described in this application, whether by structure or by use of the term "formula 107," the terms used to describe that compound are defined by WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555).

Definitions for the Compound of formula 108

[0082] The terms used to describe the scope of formula 108 are defined in WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173).

For example "optionally substituted aryl" for formula 108 has the meaning given in WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173). Whenever a compound of formula 108 is described in this application, whether by structure or by use of the term "formula 108," the terms used to describe that compound are defined by WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173).

Definitions for the Compound of formula 109

[0083] The terms used to describe the scope of formula 109 are defined in WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291).

For example "optionally substituted aryl" for formula 109 has the meaning given in WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291). Whenever a compound of formula 109 is described in this application, whether by structure or by use of the term "formula 109," the terms used to describe that compound are defined by WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291).

Other Definitions

[0084] “AKT inhibitor” includes, for example, LY294002, PKC412, and compounds described in WO 2006/071819 and WO05/117909.

[0085] “Alkylating agent(s)” includes, for example, one or more of the following: Chlorambucil, Chlormethine, Cyclophosphamide, Ifosfamide, Melphalan, Carmustine, Streptozocin, Fotemustine, Lomustine, Streptozocin, Carboplatin, Cisplatin, Oxaliplatin, BBR3464, Busulfan, Dacarbazine, Mechlorethamine, Procarbazine, Temozolomide, ThioTEPA, and Uramustine.

[0086] “Antibody(s)” includes, for example, one or more of the following: IGF1R antibody (including, for example, α IGF-1R A12 MoAb, 19D12, h7C10 and CP-751871), Alemtuzumab, Bevacizumab (Avastin®), Cetuximab (Erbix®), Gemtuzumab, Gemtuzumab ozogamicin, Ibritumomab (tiuxetan), Panitumumab, Rituximab, Tositumomab, and Trastuzumab (Herceptin®).

[0087] “Antimetabolite(s)” include, for example, methotrexate, Pemetrexed, Raltitrexed, Cladribine, Clofarabine, Fludarabine, Mercaptopurine, Thioguanine, Capecitabine, Cytarabine, fluorouracil (administered with or without leucovorin or folinic acid), and Gemcitabine.

[0088] “Antimicrotubule agent(s)” includes, for example, Vincristine, Vinblastine, Vinorelbine, Vinflunine, and Vindesine.

[0089] “Aromatase inhibitor(s)” includes, for example, one or more of the following: Aminoglutethimide, Anastrozole (Arimidex®), Letrozole (Femara®), Exemestane (Aromasin®), and Formestane (Lentaron®).

[0090] “Cancer” refers to cellular-proliferative disease states, including but not limited to: Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney

(adenocarcinoma, Wilm's tumor [nephroblastoma], lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochondroma (osteochondrogenous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma [pinealoma], glioblastoma multiforme, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma [serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma], granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia [acute and chronic], acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma [malignant lymphoma]; Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; Adrenal Glands: neuroblastoma; and breast cancer. Thus, the term "cancerous cell" as provided herein, includes a cell afflicted by any one of the above-identified conditions.

[0091] "cMET inhibitor" includes, for example, compounds described in WO06/108059, WO 2006/014325, and WO 2005/030140.

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[0092] "EGFR inhibitor" includes, for example, one or more of the following: Lapatinib (Tykerb®), gefitinib (Iressa®), erlotinib (Tarceva®), Zactima (ZD6474), AEE788 and HKI-272, EKB-569, CI1033, and compounds described in WO 2004/006846 and WO 2004/050681.

[0093] "ErbB2 inhibitor" includes, for example, Lapatinib (GW572016), and PKI-166.

[0094] "Hormone therapy" or "hormonal therapy" includes, for example, treatment with one or more of the following: steroids (e.g. dexamethasone), finasteride, tamoxifen, and an aromatase inhibitor.

[0095] "HSP90 inhibitor(s)" includes, for example, 17-AAG, 17-DMAG, Geldanamycin, 5-(2,4-dihydroxy-5-isopropylphenyl)-*N*-ethyl-4-(4-(morpholinomethyl)phenyl)isoxazole-3-carboxamide [NVP-AUY922 (VER 52296)], 6-chloro-9-((4-methoxy-3,5-dimethylpyridin-2-yl)methyl)-9*H*-purin-2-amine (CNF2024, also named BIIB021), compounds disclosed in WO2004072051, compounds disclosed in WO2005028434, compounds disclosed in WO2007035620 and compounds disclosed in WO2006091963.

[0096] "Hypothermia therapy" is a type of treatment in which body tissue is exposed to high temperatures to damage and kill cancer cells or to make cancer cells more sensitive to the effects of radiation and certain anticancer drugs.

[0097] "IGF1R inhibitor(s)" include, for example, Tyrphostin AG 1024 and compounds described in WO06/074057.

[0098] "Kinase-dependent diseases or conditions" refer to pathologic conditions that depend on the activity of one or more protein kinases. Kinases either directly or indirectly participate in the signal transduction pathways of a variety of cellular activities including proliferation, adhesion, migration, differentiation and invasion. Diseases associated with kinase activities include tumor growth, the pathologic neovascularization that supports solid tumor growth, and associated with other diseases where excessive local vascularization is involved such as ocular diseases (diabetic retinopathy, age-related macular degeneration, and the like) and inflammation (psoriasis, rheumatoid arthritis, and the like).

[0099] While not wishing to be bound to theory, phosphatases can also play a role in "kinase-dependent diseases or conditions" as cognates of kinases; that is, kinases

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phosphorylate and phosphatases dephosphorylate, for example protein substrates. Therefore compounds of the invention, while modulating kinase activity as described herein, may also modulate, either directly or indirectly, phosphatase activity. This additional modulation, if present, may be synergistic (or not) to activity of compounds of the invention toward a related or otherwise interdependent kinase or kinase family. In any case, as stated previously, the compounds of the invention are useful for treating diseases characterized in part by abnormal levels of cell proliferation (*i.e.* tumor growth), programmed cell death (apoptosis), cell migration and invasion and angiogenesis associated with tumor growth.

[00100] "Metabolite" refers to the break-down or end product of a compound or its salt produced by metabolism or biotransformation in the animal or human body; for example, biotransformation to a more polar molecule such as by oxidation, reduction, or hydrolysis, or to a conjugate (see Goodman and Gilman, "The Pharmacological Basis of Therapeutics" 8^{sup}.th Ed., Pergamon Press, Gilman et al. (eds), 1990 for a discussion of biotransformation). As used herein, the metabolite of a compound of the invention or its salt may be the biologically active form of the compound in the body. In one example, a prodrug may be used such that the biologically active form, a metabolite, is released *in vivo*. In another example, a biologically active metabolite is discovered serendipitously, that is, no prodrug design *per se* was undertaken. An assay for activity of a metabolite of a compound of the present invention is known to one of skill in the art in light of the present disclosure.

[00101] "Patient" for the purposes of the present invention includes humans and other animals, particularly mammals, and other organisms. Thus the methods are applicable to both human therapy and veterinary applications. In an embodiment the patient is a mammal, and in another embodiment the patient is human.

[00102] A "pharmaceutically acceptable salt" of a compound means a salt that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. It is understood that the pharmaceutically acceptable salts are non-toxic. Additional information on suitable pharmaceutically acceptable salts can be found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985 or S. M.

Berge, et al., "Pharmaceutical Salts," J. Pharm. Sci., 1977;66:1-19.

[00103] Examples of pharmaceutically acceptable acid addition salts include those formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; as well as organic acids such as acetic acid, trifluoroacetic acid, propionic acid, hexanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, 3-(4-hydroxybenzoyl)benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethanedisulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, glucoheptonic acid, 4,4'-methylenebis-(3-hydroxy-2-ene-1-carboxylic acid), 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid, p-toluenesulfonic acid, and salicylic acid and the like.

[00104] Examples of a pharmaceutically acceptable base addition salts include those formed when an acidic proton present in the parent compound is replaced by a metal ion, such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Preferable salts are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins. Examples of organic bases include isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglucamine, theobromine, purines, piperazine, piperidine, N-ethylpiperidine, tromethamine, N-methylglucamine, polyamine resins, and the like. Exemplary organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline, and caffeine.

[00105] "Platin(s)," and "platin-containing agent(s)" include, for example, cisplatin, carboplatin, and oxaliplatin.

[00106] "Prodrug" refers to compounds that are transformed (typically rapidly) *in vivo* to yield the parent compound of the above formulae, for example, by hydrolysis

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in blood. Common examples include, but are not limited to, ester and amide forms of a compound having an active form bearing a carboxylic acid moiety. Examples of pharmaceutically acceptable esters of the compounds of this invention include, but are not limited to, alkyl esters (for example with between about one and about six carbons) the alkyl group is a straight or branched chain. Acceptable esters also include cycloalkyl esters and arylalkyl esters such as, but not limited to benzyl. Examples of pharmaceutically acceptable amides of the compounds of this invention include, but are not limited to, primary amides, and secondary and tertiary alkyl amides (for example with between about one and about six carbons). Amides and esters of the compounds of the present invention may be prepared according to conventional methods. A thorough discussion of prodrugs 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 Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987.

[00107] "Raf inhibitor(s)" include, for example, sorafenib and compounds described in WO 2005/112932.

[00108] "Rapamycin analogue(s)" include for example, CCI-779, AP23573, RAD001, TAF93, and compounds described in WO 2004/101583 and US 7,160,867.

[00109] "Receptor Tyrosine Kinase inhibitor(s)" includes, for example, inhibitors of AKT, EGFR, ErbB2, IGF1R, Met, Raf, and VEGFR2. Examples of receptor tyrosine kinase inhibitors can be found in WO 2006/108059 (US Nat'l Stage Application Serial No. 11/910,720), WO 2006/074057 (US Nat'l Stage Application Serial No. 11/722,719), WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291), WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140), WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173), WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336), WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555), WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789), and WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004).

In particular, the applications cited in this paragraph are incorporated for the purpose of providing specific examples and generic embodiments (and the definitions associated with the terms used in the embodiments) of compounds

that are useful in the practice of the invention. These references also describe in vitro assays useful in the practice of this invention.

[00110] “Taxane(s)” includes, for example, one or more of the following: Paclitaxel (Taxol[®]) and Docetaxel (Taxotere[®]).

[00111] “Therapeutically effective amount” is an amount of a compound of the invention, that when administered to a patient, ameliorates a symptom of the disease. The amount of a compound of the invention which constitutes a “therapeutically effective amount” will vary depending on the compound, the disease state and its severity, the age of the patient to be treated, and the like. The therapeutically effective amount can be determined routinely by one of ordinary skill in the art having regard to their knowledge and to this disclosure.

[00112] “Topoisomerase inhibitor” includes, for example, one or more of the following: amsacrine, camptothecin, etoposide, etoposide phosphate, exatecan, irinotecan, lurtotecan, and teniposide, and topotecan.

[00113] “Treating” or “treatment” of a disease, disorder, or syndrome, as used herein, includes (i) preventing the disease, disorder, or syndrome from occurring in a human, i.e. causing the clinical symptoms of the disease, disorder, or syndrome not to develop in an animal that may be exposed to or predisposed to the disease, disorder, or syndrome but does not yet experience or display symptoms of the disease, disorder, or syndrome; (ii) inhibiting the disease, disorder, or syndrome, *i.e.*, arresting its development; and (iii) relieving the disease, disorder, or syndrome, *i.e.*, causing regression of the disease, disorder, or syndrome. As is known in the art, adjustments for systemic versus localized delivery, age, body weight, general health, sex, diet, time of administration, drug interaction and the severity of the condition may be necessary, and will be ascertainable with routine experimentation by one of ordinary skill in the art.

[00114] “SRC and/or ABL kinase inhibitor(s)” includes, for example, dasatinib, imatinib (Gleevec[®]), and compounds described in WO 2006/074057.

[00115] “VEGFR inhibitor” includes, for example, one or more of the following: ZD6474 (Zactima), sorafenib, Angiozyme, AZD2171, SU5416, PTK787, AEE788, sunitinib (SUTENT), and compounds described in WO 2004/050681 and WO 2004/006846.

Embodiments of the Invention

[00116] In one embodiment, the cancer is mediated, at least in part, by inhibiting MEK.

[00117] In another embodiment, the cancer is selected from melanoma, colon cancer, rectal cancer, pancreatic cancer, breast cancer, non-small cell lung cancer, small cell lung cancer, papillary thyroid cancer, anaplastic thyroid cancer, endometrial cancer, and ovarian cancer.

[00118] In another embodiment, one or more of the treatment(s) is one or more chemotherapeutic agent(s).

[00119] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from a taxane(s), a platin(s), a topoisomerase inhibitor(s), an alkylating agent(s), an antimetabolite(s), an antimicrotubule agent(s), and a bcr-abl inhibitor(s). In another embodiment, one or more of the chemotherapeutic agent(s) is an antimicrotubule agent(s) selected from Vincristine, Vinblastine, Vinorelbine, and Vindesine.

[00120] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from rapamycin, carboplatin, cisplatin, oxaliplatin, gemcitabine, dacarbazine, topotecan, and irinotecan.

[00121] In another embodiment, one or more of the chemotherapeutic agent(s) is an AKT inhibitor. In another embodiment, the AKT inhibitor is selected from a compound in Table 2a and Table 2b.

[00122] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from a compound in Table 2a and Table 2b.

[00123] In another embodiment, one or more of the chemotherapeutic agent(s) is a cMET inhibitor. In another embodiment, the cMET inhibitor is selected from a compound in Table 3a, Table 3b, and Table 3c.

[00124] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from a compound in Table 3a, Table 3b, and Table 3c.

[00125] In another embodiment, one or more of the chemotherapeutic agent(s) is an EGFR inhibitor. In another embodiment, the EGFR inhibitor is selected from Lapatinib (Tykerb®), gefitinib (Iressa®), erlotinib (Tarceva®), Zactima (ZD6474), AEE788, HKI-272, EKB-569, CI1033, and a compound selected from Table 4 and

Table 7. In another embodiment, the EGFR inhibitor is selected from Table 4 and Table 7.

[00126] In another embodiment, one or more of the chemotherapeutic agent(s) is a compound selected from Table 4 and Table 7.

[00127] In another embodiment, one or more of the chemotherapeutic agent(s) is an ErbB2 inhibitor. In another embodiment, the chemotherapeutic agent(s) is selected from lapatinib, EKB-569, HKI272, and CI1033.

[00128] In another embodiment, one or more of the chemotherapeutic agent(s) is an HSP90 inhibitor. In another embodiment, the HSP90 inhibitor is 17-AAG, 17-DMAG, Geldanamycin, and CNF2024.

[00129] In another embodiment, one or more of the chemotherapeutic agent(s) is an IGF1R inhibitor. In another embodiment, the IGF1R inhibitor is selected from a compound in Table 5a and Table 5b.

[00130] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from a compound in Table 5a and Table 5b.

[00131] In another embodiment, one or more of the chemotherapeutic agent(s) is an Raf inhibitor. In another embodiment, the Raf inhibitor is selected from sorafenib and a compound in Table 6.

[00132] In another embodiment, one or more of the chemotherapeutic agent(s) is a VEGFR inhibitor. In another embodiment, the VEGFR inhibitor is selected from a compound in Table 4 and Table 7.

[00133] In another embodiment, one or more of the chemotherapeutic agent(s) is selected from rapamycin, a rapamycin analogue, PI103, SF1126, and BEZ235. In another embodiment, one or more of the chemotherapeutic agent(s) is selected from rapamycin, CCI-779, AP23573, RAD001, TAFA93, PI103, SF1126, and BEZ235. In another embodiment, one or more of the chemotherapeutic agent(s) is selected from rapamycin, CCI-779, AP23573, RAD001, PI103, and SF1126. In another embodiment, one or more of the chemotherapeutic agent(s) is rapamycin. In another embodiment, one or more of the chemotherapeutic agent(s) is a rapamycin analogue.

[00134] In another embodiment, one or more of the chemotherapeutic agent(s) is 2-methyl-2-(4-(3-methyl-2-oxo-8-(quinolin-3-yl)-2,3-dihydro-1*H*-imidazo[4,5-*c*]quinolin-1-yl)phenyl)propanenitrile.

[00135] In another embodiment, one or more of the treatment(s) is selected from radiation and hypothermia therapy. In another embodiment, one or more of the treatment(s) is radiation.

[00136] In another embodiment, one or more of the treatment(s) is one or more antibody(s). In another embodiment, one or more of the antibody(s) is selected from IGF1R antibody (including, for example, α IGF-1R A12 MoAb, 19D12, h7C10 and CP-751871), Alemtuzumab, Bevacizumab (Avastin®), Cetuximab (Erbix®), Gemtuzumab, Gemtuzumab ozogamicin, Ibritumomab (tiuxetan), Panitumumab, Rituximab, Tositumomab, and Trastuzumab (Herceptin®).

[00137] In another embodiment, one or more of the treatment(s) is surgery.

[00138] In another embodiment, one or more of the treatment(s) is one or more hormone therapy(s). In another embodiment, one or more of the hormone therapy(s) is selected from tamoxifen and an aromatase inhibitor.

[00139] In another embodiment, one or more of the chemotherapeutic agent(s) is gemcitabine.

[00140] In another embodiment, one or more of the chemotherapeutic agent(s) is Imatinib (i.e. Gleevec®).

[00141] In another embodiment, the cancer is primary or relapsed CML and/or acute myelogenous leukemia (AML) and one or more of the treatment(s) is selected from one or more of the chemotherapeutic agent(s) and one or more antibody(s). In another embodiment one or more of the chemotherapeutic agent(s) is selected from Imatinib (i.e. Gleevec®) and PKC412; in another embodiment, one or more of the chemotherapeutic agent(s) is Imatinib (i.e. Gleevec®). In another embodiment one or more of the antibody(s) is selected from α IGF-1R A12 MoAb and trastuzumab.

[00142] In another embodiment, the cancer is prostate cancer and one or more of the treatment(s) is selected from one or more antibody(s). In another embodiment one or more of the antibody(s) is α IGF-1R A12 MoAb.

[00143] In another embodiment, the cancer is malignant melanoma and one or more of the treatment(s) is selected from surgery and one or more chemotherapeutic agent(s). In another embodiment, one or more of the chemotherapeutic agent(s) is selected from an alkylating agent(s), a taxane(s), a platin(s), and a Raf inhibitor(s). In another embodiment, one or more chemotherapeutic agent(s) is selected from sorafenib, Paclitaxel (Taxol®), Docetaxel (Taxotere®), dacarbazine, rapamycin, imatinib mesylate (Gleevec®), sorafenib, and carboplatin.

[00144] In another embodiment, the cancer is colon or rectal cancer and one or more of the treatment(s) is selected from surgery, radiation, one or more chemotherapeutic agent(s), and one or more antibody(s). In another embodiment, one or more of the chemotherapeutic agent(s) is selected from cisplatin, oxaliplatin, carboplatin, 5-fluorouracil, Capecitabine (Xeloda), Irinotecan (Camptosar), FOLFOX (Folinic acid, 5-FU, Oxaliplatin), and leucovorin. In another embodiment one or more of the antibody(s) is selected from bevacizumab and cetuximab.

[00145] In another embodiment, the cancer is pancreatic cancer and one or more of the treatment(s) is selected from surgery, radiation, and one or more chemotherapeutic agent(s). In another embodiment, one or more of the chemotherapeutic agent(s) is selected from erlotinib (Tarceva®), gemcitabine, 5-fluorouracil, leucovorin, cisplatin, oxaliplatin, carboplatin, gemcitabine, irinotecan, paclitaxel, capecitabine, and streptozocin.

[00146] In another embodiment, the cancer is breast cancer and one or more of the treatment(s) is selected from surgery, radiation, one or more chemotherapeutic agent(s), one or more hormone therapy(s), and one or more antibody(s). In another embodiment one or more of the chemotherapeutic agent(s) is selected from lapatinib (Tykerb®), Paclitaxel (Taxol®), docetaxel, capecitabine, Cyclophosphamide (Cytosan), methotrexate, fluorouracil, doxorubicin, epirubicin, gemcitabine, carboplatin (Paraplatin), cisplatin (Platinol), vinorelbine (Navelbine), capecitabine (Xeloda), pegylated liposomal doxorubicin (Doxil), and albumin-bound paclitaxel (Abraxane). In another embodiment one or more of the antibody(s) is selected from α IGF-1R A12 MoAb, bevacizumab (Avastin), and trastuzumab. In another embodiment, one or more of the hormone therapy(s) is selected from tamoxifen, Toremifene (Fareston), Fulvestrant (Faslodex), Megestrol acetate (Megace), ovarian ablation, and an aromatase inhibitor(s); in another embodiment, one or more of the aromatase inhibitor(s) is selected from etozole (Femara), anastrozole (Arimidex), and exemestane (Aromasin).

[00147] In another embodiment, the cancer is non-small cell lung cancer and one or more of the treatment(s) is selected from surgery, radiation, one or more antibody(s), and one or more chemotherapeutic agent(s). In another embodiment, the chemotherapeutic agent(s) is selected from cisplatin, oxaliplatin, carboplatin, Zactima (ZD6474), Paclitaxel, Docetaxel (Taxotere®), Gemcitabine (Gemzar®), Vinorelbine,

Irinotecan, Etoposide, Vinblastine, Erlotinib (Tarceva®), and Pemetrexed. In another embodiment, one or more of the antibody(s) is Bevacizumab.

[00148] In another embodiment, the cancer is small cell lung cancer and one or more of the treatment(s) is selected from surgery, radiation, and one or more chemotherapy agent(s). In another embodiment, one or more of the chemotherapy agent(s) is selected from cisplatin, oxaliplatin, carboplatin, etoposide, irinotecan, fosfamide, paclitaxel, docetaxel, gemcitabine, Topotecan, cyclophosphamide/doxorubicin/vincristine (CAV), methotrexate, and vinorelbine.

[00149] In another embodiment, the cancer is papillary or anaplastic thyroid cancer, and one or more of the treatment(s) is selected from surgery, radiation, radioactive iodine therapy, one or more hormone therapy(s), and one or more chemotherapeutic agent(s). In another embodiment, one or more of the chemotherapeutic agent(s) is selected from thyroid hormone pills, Doxorubicin and a platin(s).

[00150] In another embodiment, the cancer is endometrial cancer and one or more of the treatment(s) is selected from surgery, radiation, hormone therapy, and one or more chemotherapeutic agent(s). In another embodiment, one or more of the chemotherapeutic agent(s) is selected from paclitaxel, doxorubicin, and cisplatin. In another embodiment, one or more of the hormone therapy is selected from medroxyprogesterone acetate, megestrol acetate, and Tamoxifen.

[00151] In another embodiment, the cancer is ovarian cancer and one or more of the treatment(s) is selected from surgery, radiation, and one or more chemotherapeutic agent(s). In another embodiment, one or more of the chemotherapeutic agent(s) is selected from a platin(s) compound (such as cisplatin, oxaliplatin and carboplatin), a taxane (such as paclitaxel or docetaxel), topotecan, anthracyclines (such as doxorubicin (Adriamycin) and liposomal doxorubicin (Doxil)), gemcitabine, cyclophosphamide, vinorelbine (Navelbine), hexamethylmelamine, ifosfamide, and etoposide.

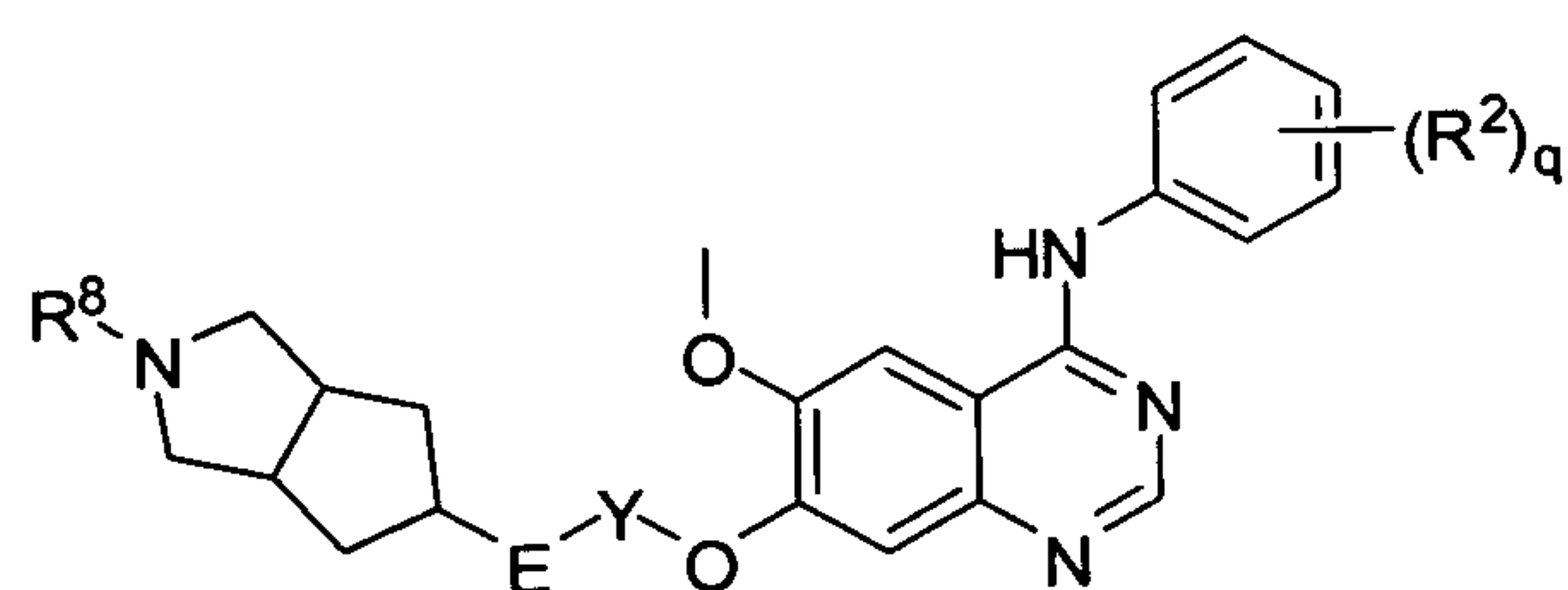
[00152] In another embodiment, one or more of the treatment(s) is selected from one or more chemotherapeutic agent(s), radiation, hypothermia therapy, one or more antibody(s), and surgery. In another embodiment, one or more of the chemotherapeutic agent(s) is selected from an EGFR inhibitor, isotretinoin, a platin (e.g., cisplatin, oxaliplatin, and carboplatin), epirubicin, bleomycin, doxorubicin, cyclophosphamide, a taxane (e.g. docetaxel (Taxotere®)), and fluorouracil [5-FU]. In

another embodiment, one or more of the chemotherapeutic agent(s) is selected from cisplatin, carboplatin, and docetaxel. In another embodiment, one or more of the antibody(s) is cetuximab (Erbitux®).

[00153] In another embodiment one or more of the treatment(s) is selected from radiation and surgery.

[00154] In another embodiment of the invention, one or more of the treatments is selected from rapamycin, CCI-779, AP23573, RAD001, carboplatin, cisplatin, oxaliplatin, gemcitabine, dacarbazine, topotecan, irinotecan, sorafenib, paclitaxel, docetaxel, Lapatinib (Tykerb®), gefitinib (Iressa®), erlotinib (Tarceva®), Zactima (ZD6474), 5-fluorouracil, Capecitabine (Xeloda), FOLFOX (Folinic acid, 5-FU, Oxaliplatin), streptozocin, Cyclophosphamide (Cytosan), methotrexate, doxorubicin, epirubicin, vinorelbine (Navelbine), pegylated liposomal doxorubicin (Doxil), and albumin-bound paclitaxel (Abraxane), Etoposide, Vinblastine, Pemetrexed, leucovorin, fosfamide, cyclophosphamide/doxorubicin/vincristine (CAV), thyroid hormone pills, hexamethylmelamine, ifosfamide, Imatinib (i.e. Gleevec®), ^aIGF-1R A12 MoAb, IGF-1R 19D12, IGF-1R h7C10, IGF-1R CP-751871, Alemtuzumab, Bevacizumab (Avastin®), Cetuximab (Erbitux®), Gemtuzumab, Gemtuzumab ozogamicin, Ibritumomab (tiuxetan), Panitumumab, Rituximab, Tositumomab, Trastuzumab (Herceptin®), tamoxifen, Toremifene (Fareston), Fulvestrant (Faslodex), Megestrol acetate (Megace), ovarian ablation, medroxyprogesterone acetate, megestrol acetate, and an aromatase inhibitor.

[00155] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula **100**:



100

where q is 1, 2, or 3; E is -NR⁹-, -O-, or absent and Y is -CH₂CH₂-, -CH₂-, or absent provided that when E is -NR⁹- or -O-, then Y is -CH₂CH₂-; R² is selected from halogen, trihalomethyl, -CN, -NO₂, -OR³, and optionally substituted lower alkyl; R⁸ is selected from -H, optionally substituted lower alkyl, -CO₂R³, -C(O)N(R³)R⁴, -SO₂R⁴, and -C(O)R³; or a single geometric isomer, stereoisomer, racemate, enantiomer, or

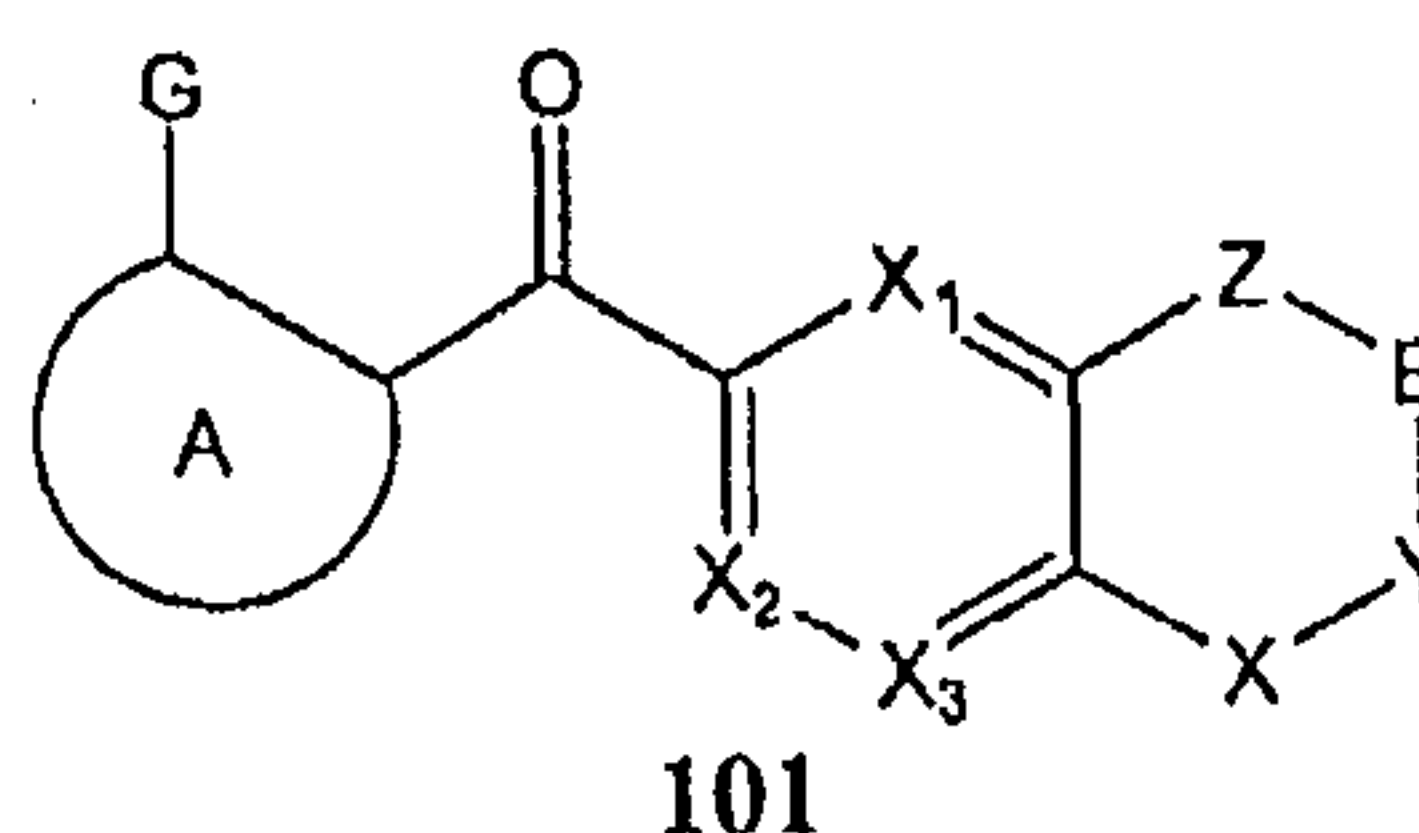
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diastereomer, thereof and optionally as a pharmaceutically acceptable salt or hydrate thereof. The terms used to describe the scope of formula 100 are defined in WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004).

For example "optionally substituted alkyl" for formula 100 has the meaning given in WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004). Whenever a compound of formula 100 is described in this application, whether by structure or by use of the term "formula 100," the terms used to describe that compound are defined by WO 2004/006846 (US Nat'l Stage Application Serial No. 10/522,004).

[00156] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula 101:



or a pharmaceutically acceptable salt, hydrate or solvate thereof, where

A is a three- to seven-membered alicyclic, a five- to six-membered ortho-arylene or a five- to six-membered ortho-heteroarylene containing between one and three heteroatoms, either of the aforementioned optionally substituted with up to four R; each R is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, -OC(O)R³, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆alkyl;

optionally two of R, together with the atoms to which they are attached, form a first ring system fused with A, said first ring system substituted with zero to three of R¹;

X₁, X₂ and X₃ are independently selected from -CR¹= or -N=;

each R¹ is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, -OC(O)R³, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆alkyl;

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Z and X are each independently selected from $-C(R^2)=$, $-N=$, $-N(R^2)-$, $-S(O)_{0-2}-$, and $-O-$;

E and Y are each independently selected from absent, $-C(R^2)(R^2)-$, $-C(=O)-$, $-C(R^2)=$ and $-N=$, but E and Y are not both absent, and E and Y are not both $-N=$ when both Z and X are $-N=$;

each R^2 is independently selected from R^3 , $-N(R^3)(R^3)$, $-C(O)N(R^3)R^3$, $-N(R^3)CO_2R^3$, $-N(R^3)C(O)N(R^3)R^3$, and $-N(R^3)C(O)R^3$;

each R^3 is independently selected from $-H$, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} alicyclic, optionally substituted aryl, optionally substituted aryl C_{1-3} alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C_{1-3} alkyl;

optionally two of R^3 , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl, said optionally substituted five- to seven-membered heterocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P; and

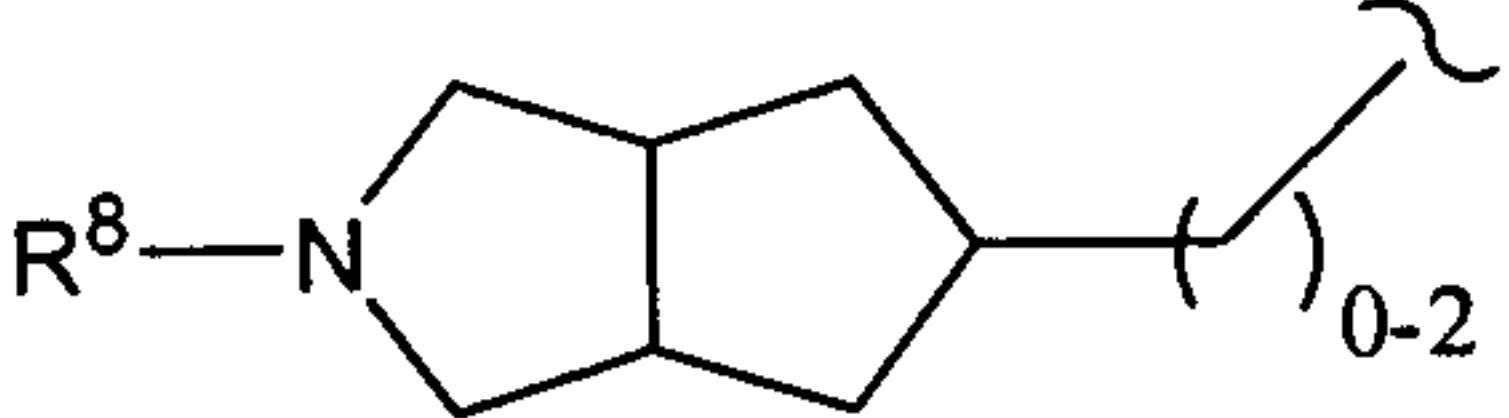
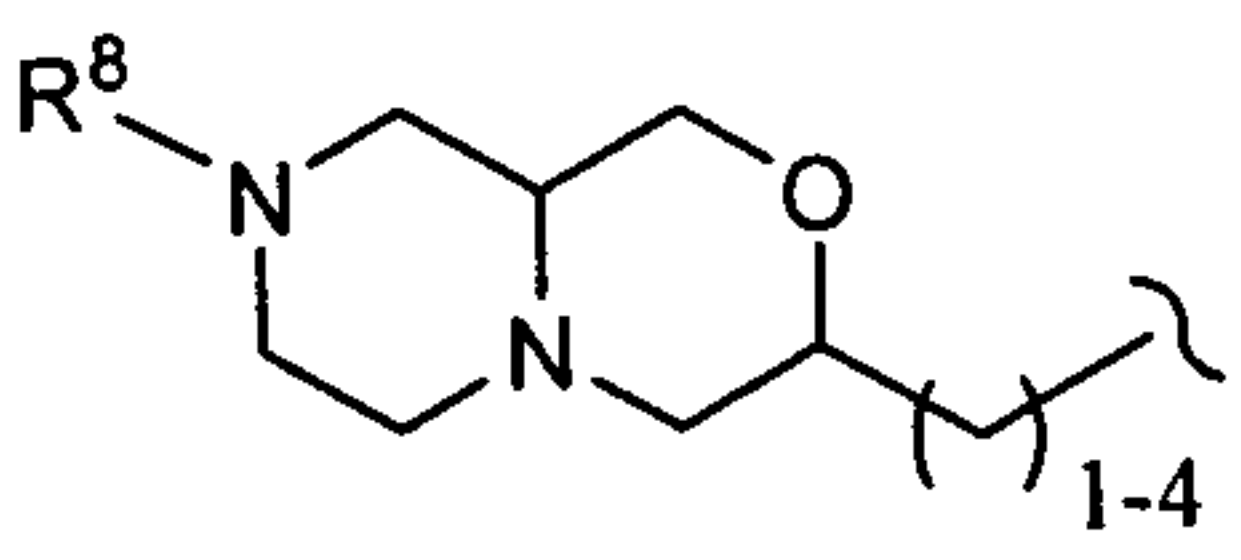
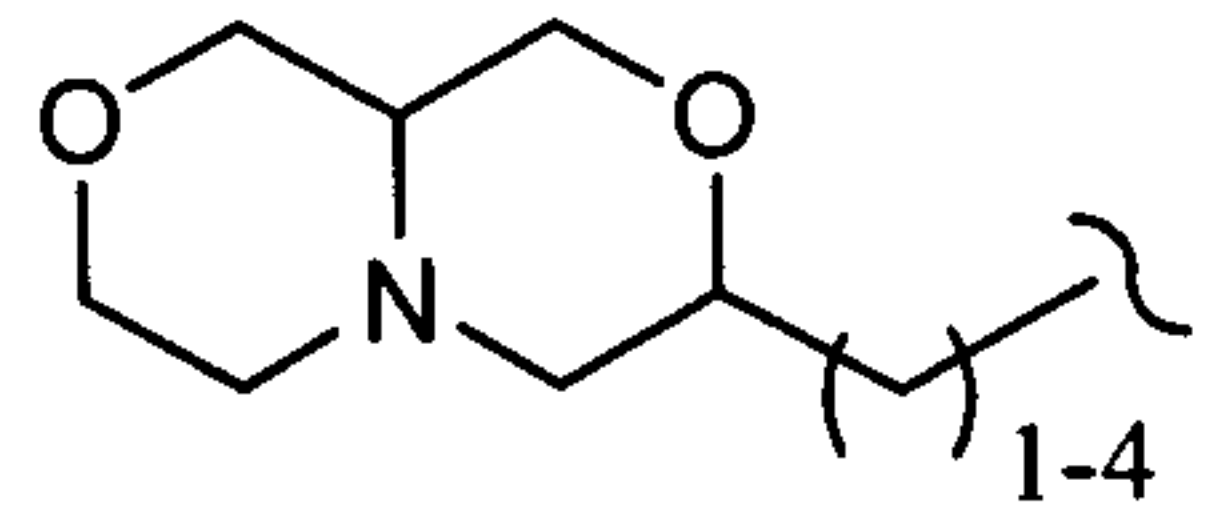
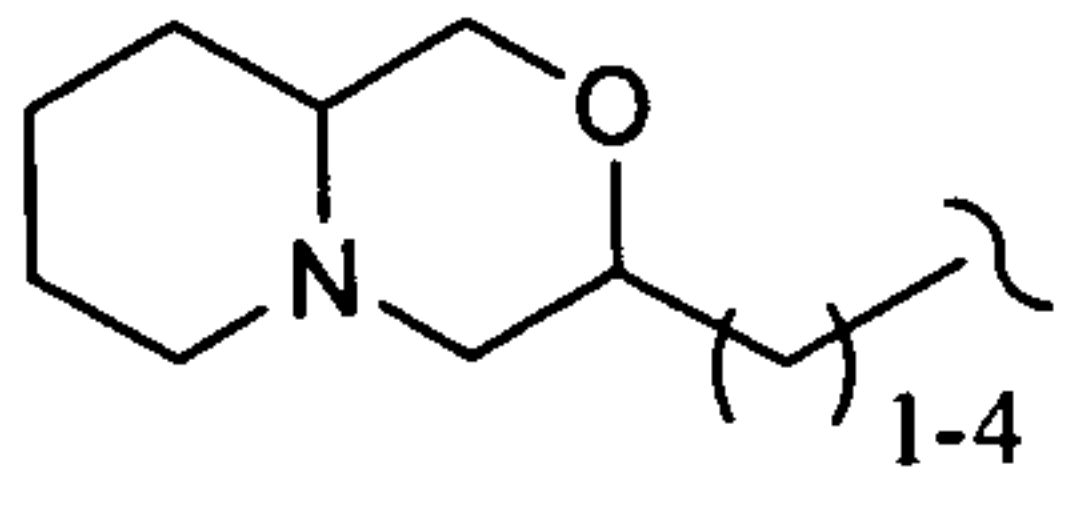
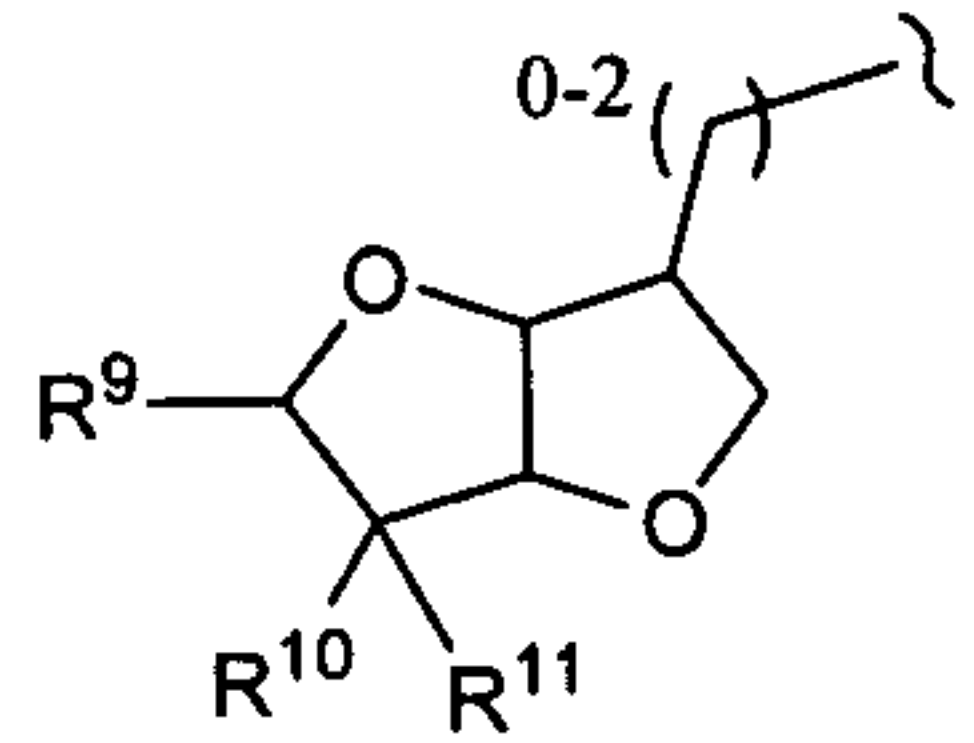
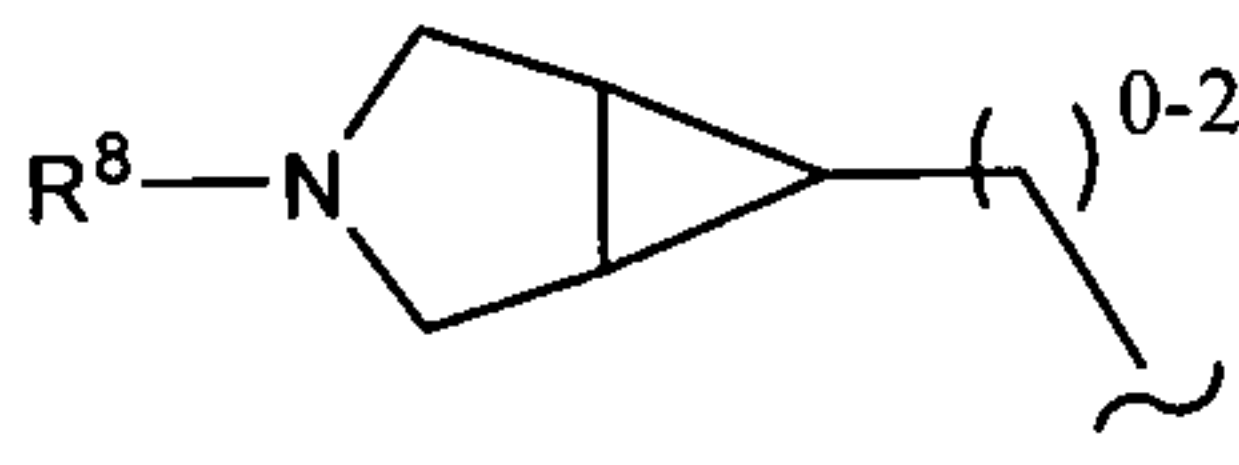
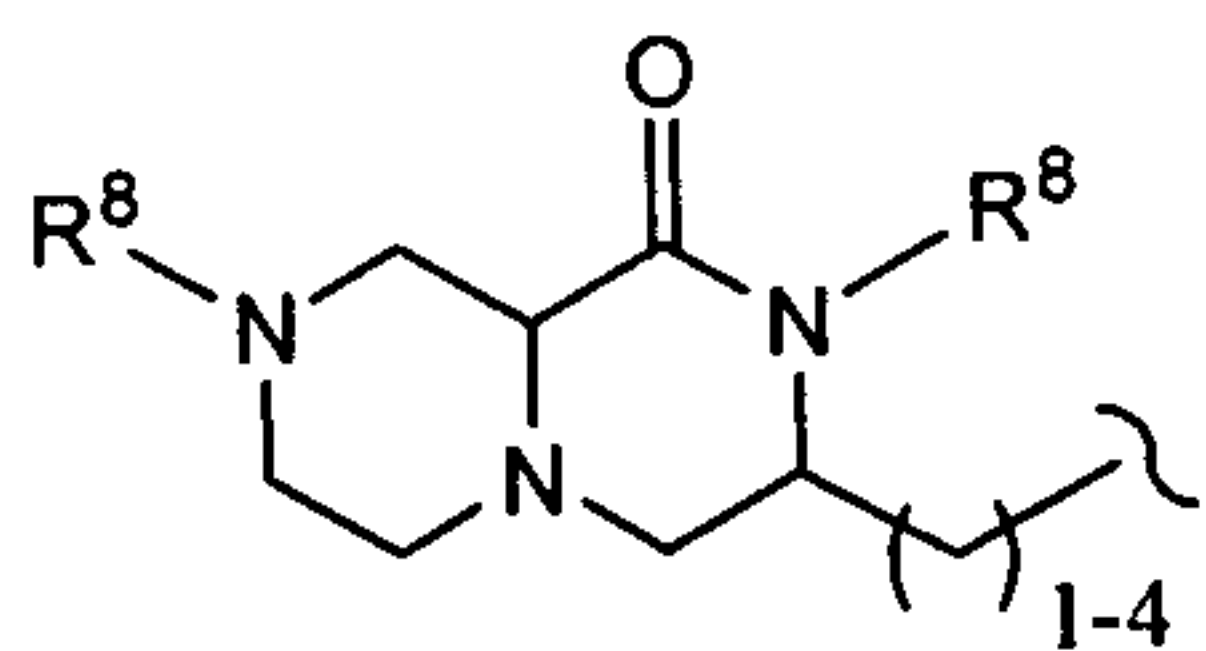
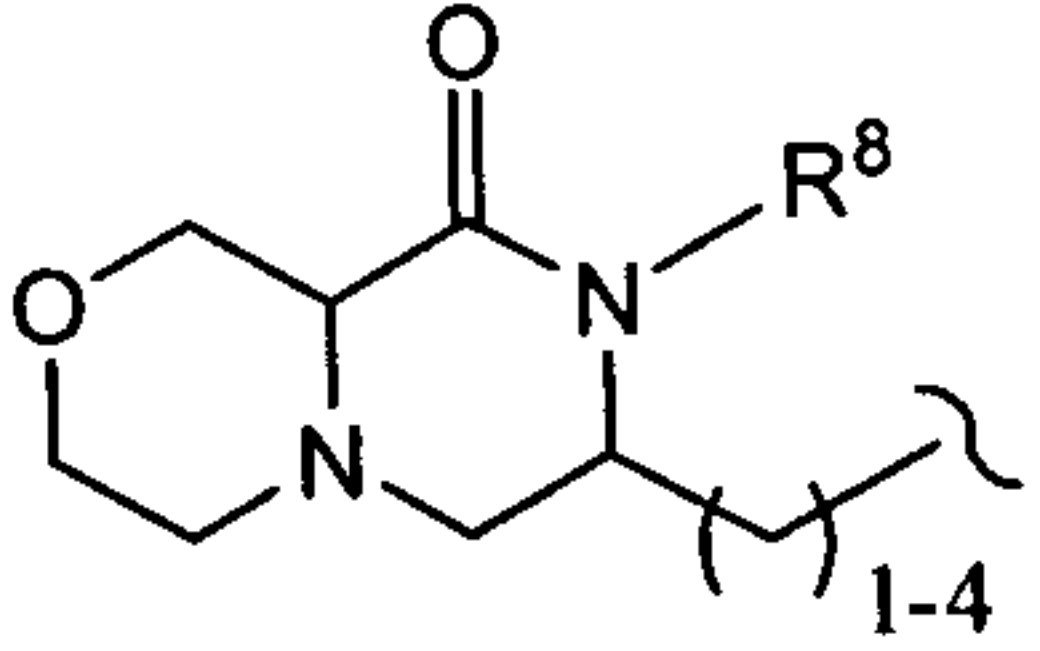
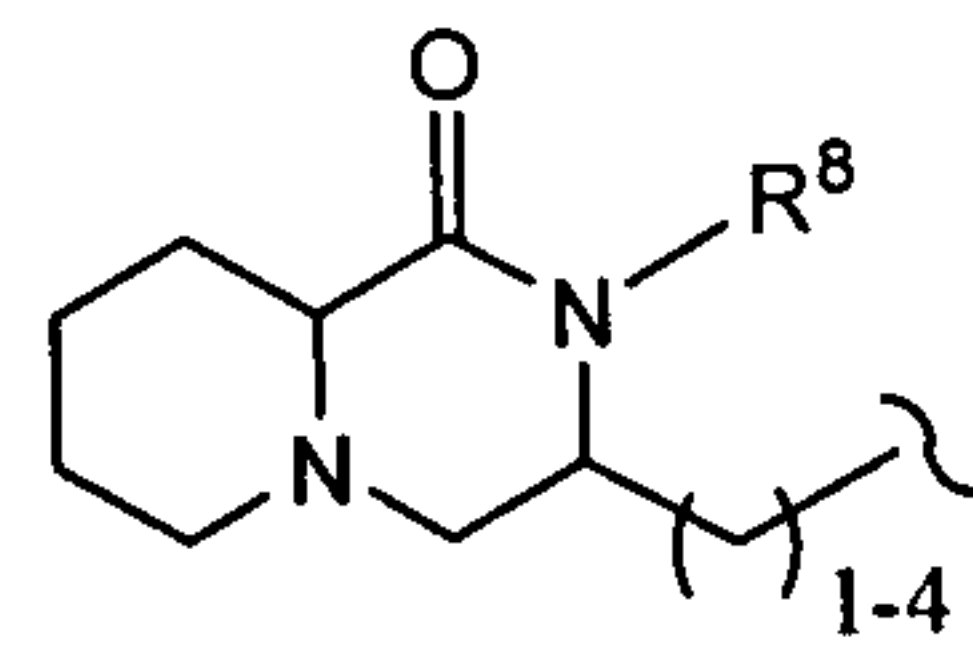
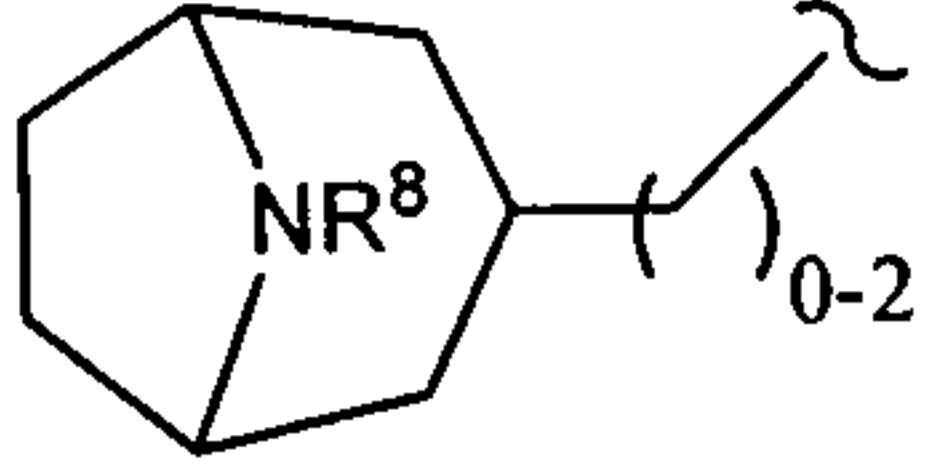
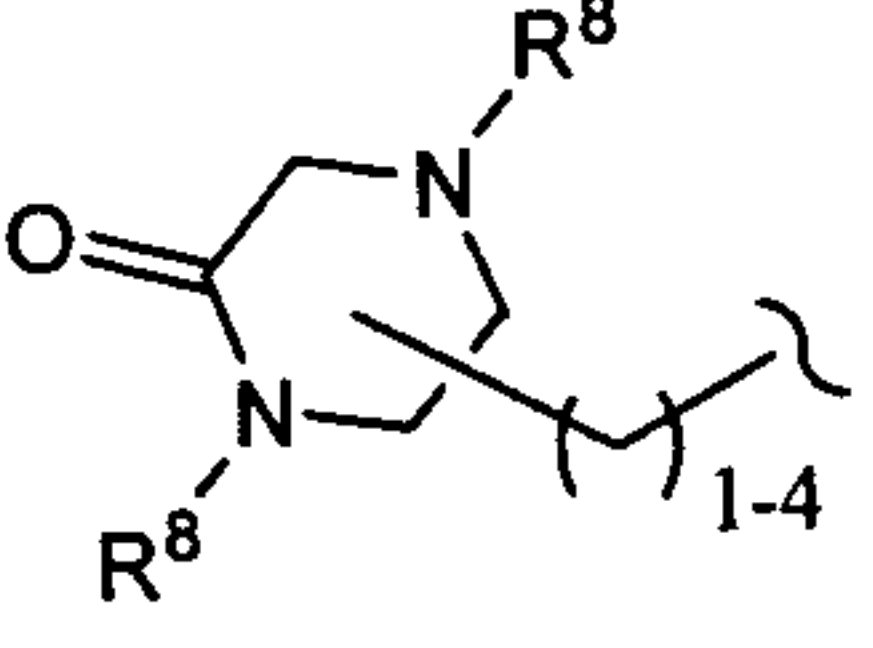
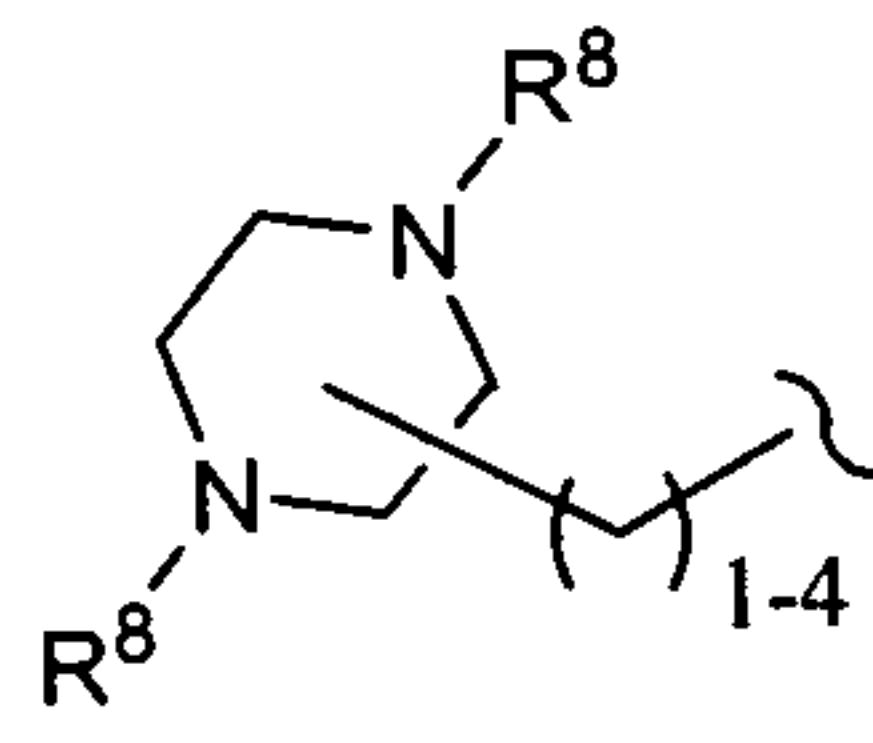
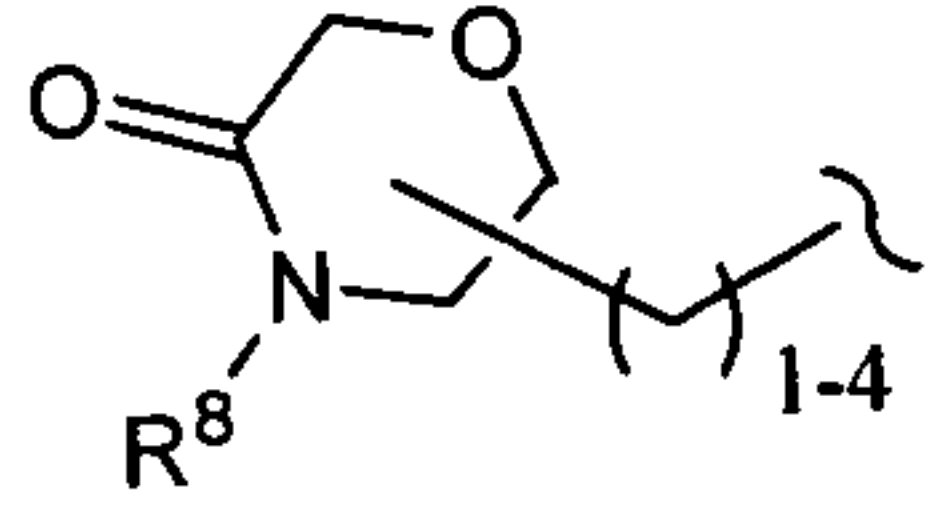
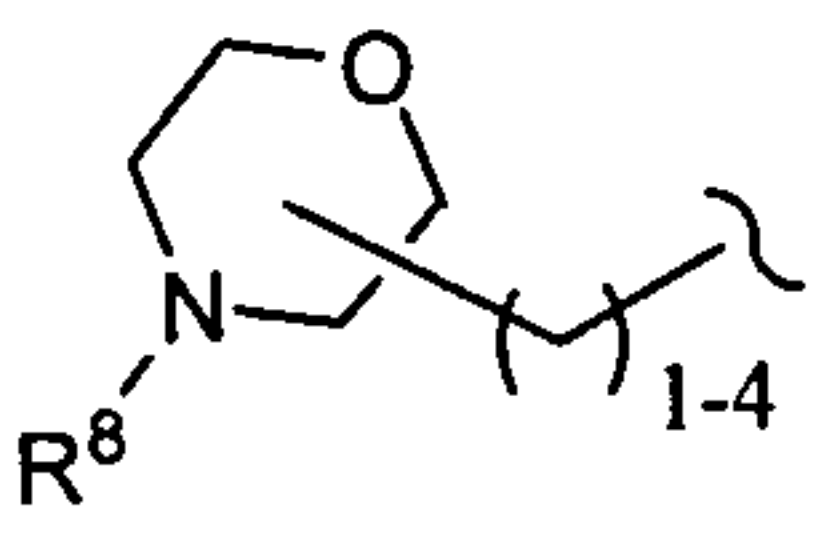
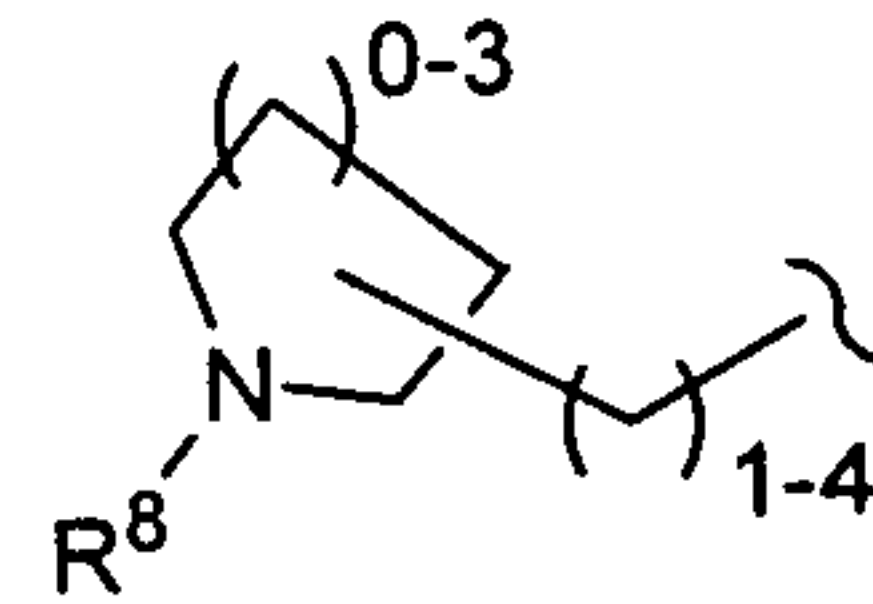
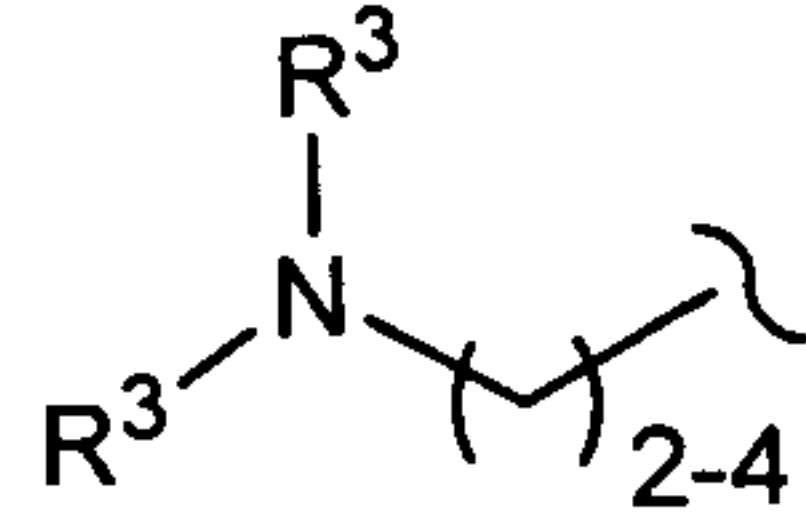
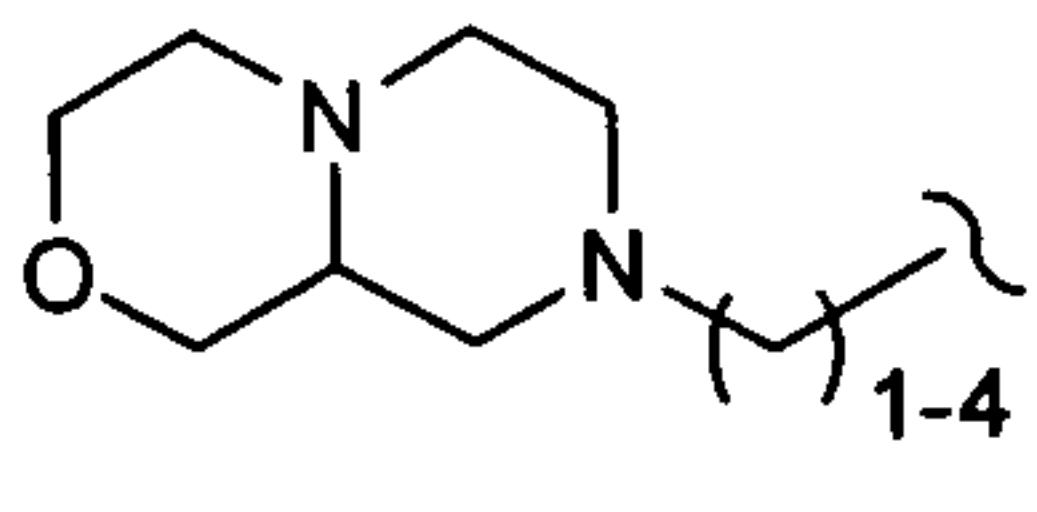
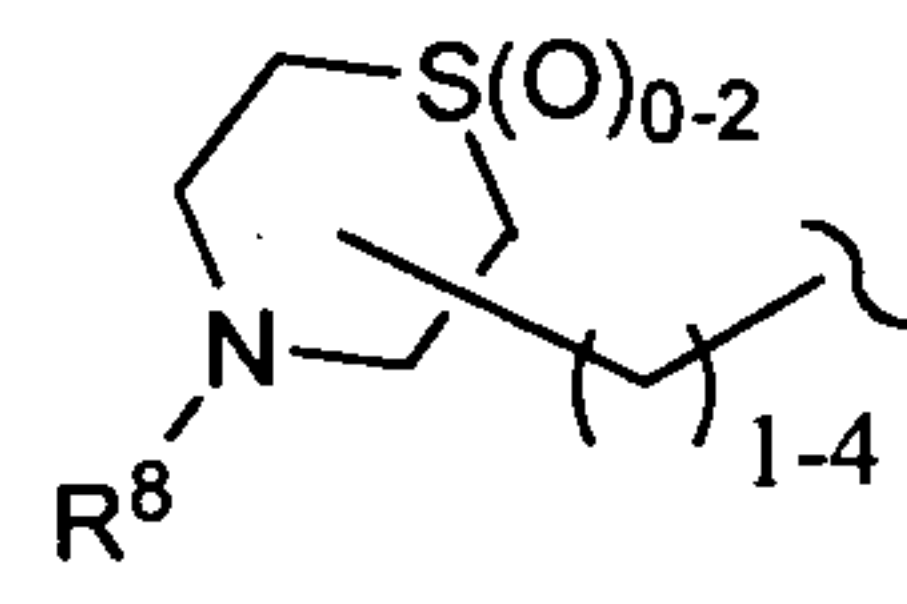
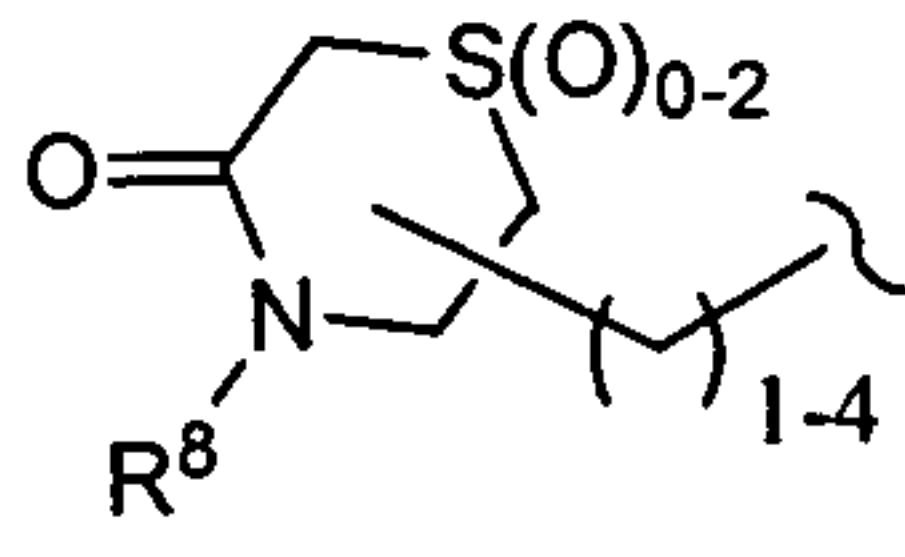
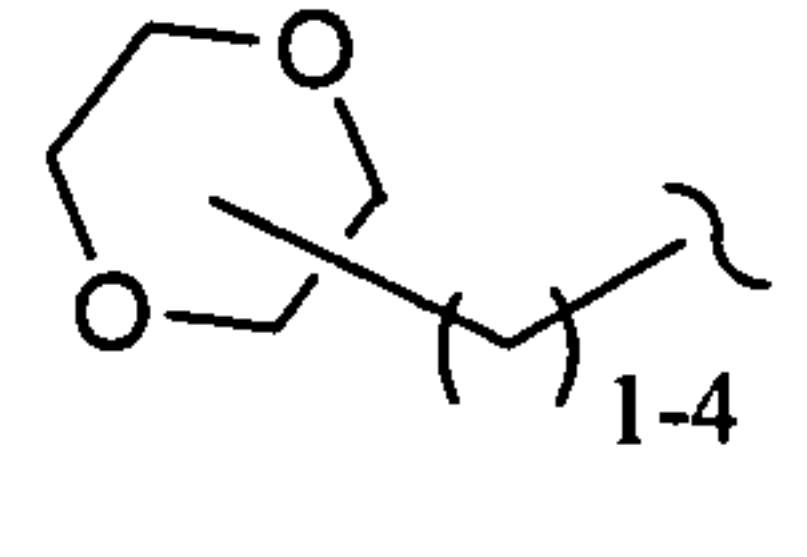
G is selected from $-CO_2R^3$, $-C(O)R^3$, $-C(O)N(R^3)R^3$, $-C(O)(NR^3)$, $-C(O)NR^3[C(R^3)_2]_{0-1}R^3$, $-C(O)NR^3O[C(R^3)_2]_{0-1}R^3$, $-N(R^3)CO_2R^3$, $-N(R^3)C(O)N(R^3)R^3$, $-N(R^3)C(O)R^3$, $-N(R^3)R^3$, $-S(O)_{0-2}R^3$, $-SO_2N(R^3)R^3$, optionally substituted aryl C_{0-3} alkyl, and optionally substituted heterocyclyl C_{0-3} alkyl;

with the proviso, however, that the compound is not 2-[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-6-yl)carbonyl]-N-(2-furanylmethyl)-benzamide, N-cyclopropyl-2-[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-6-yl)carbonyl]-benzamide, or 2-[(3,4-dihydro-3-oxo-2H-1,4-benzoxazin-6-yl)carbonyl]-N-(phenylmethyl)-benzamide.

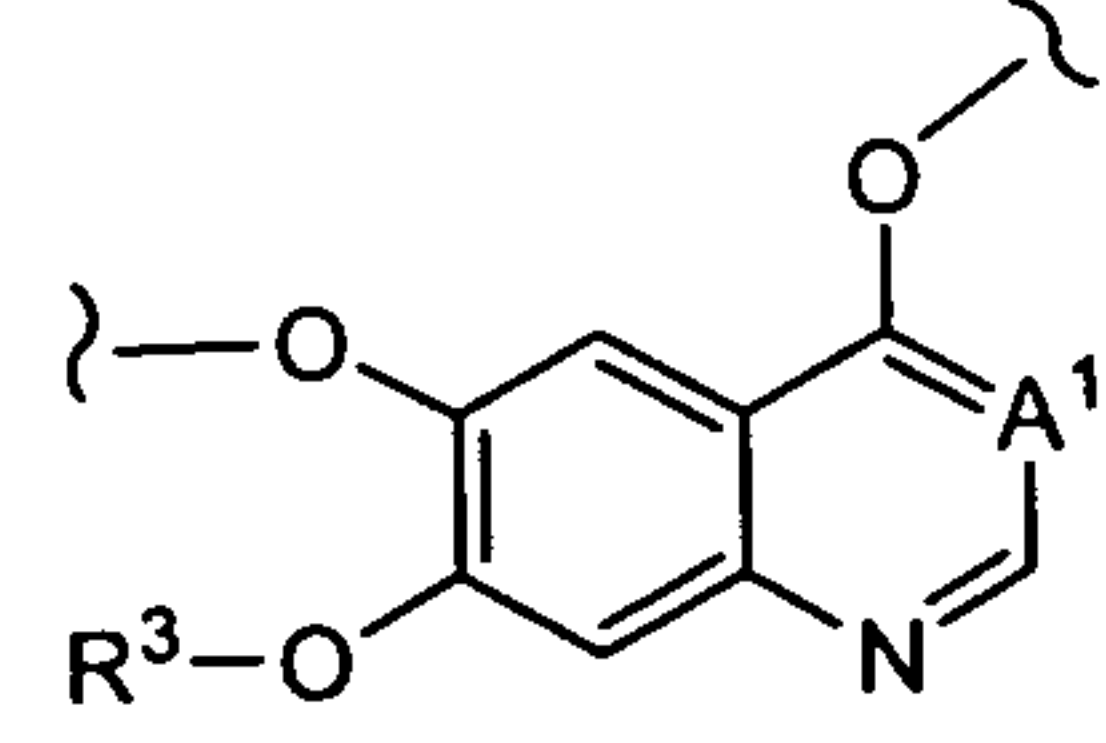
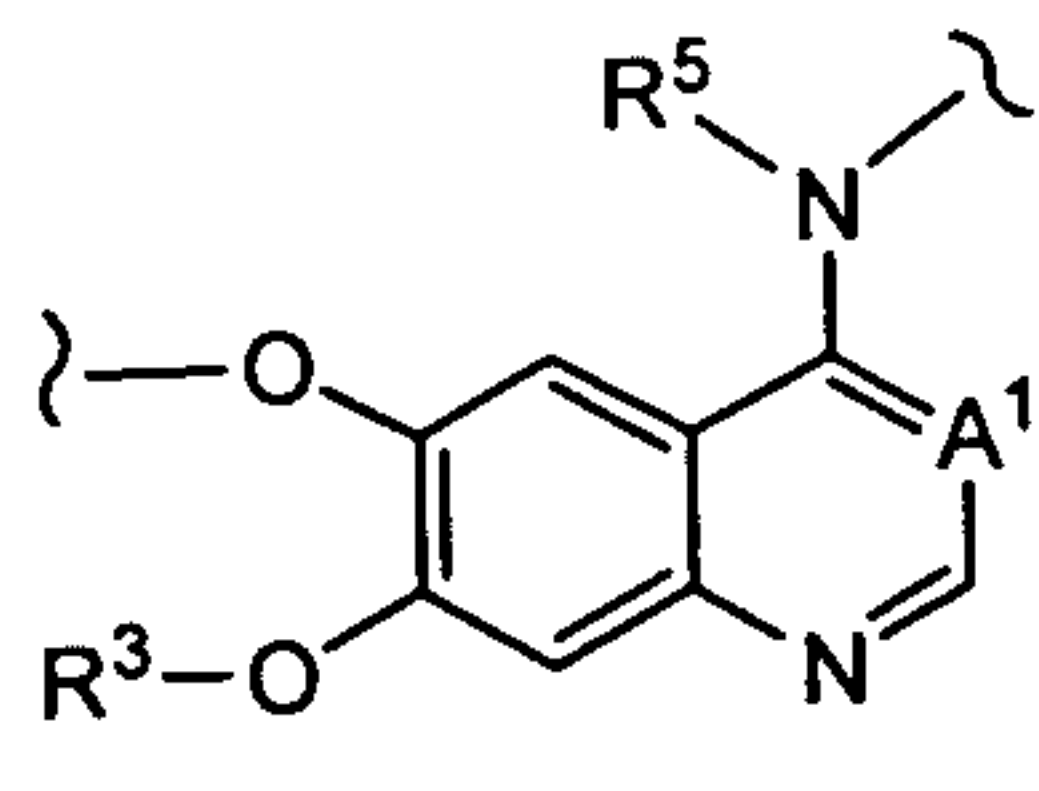
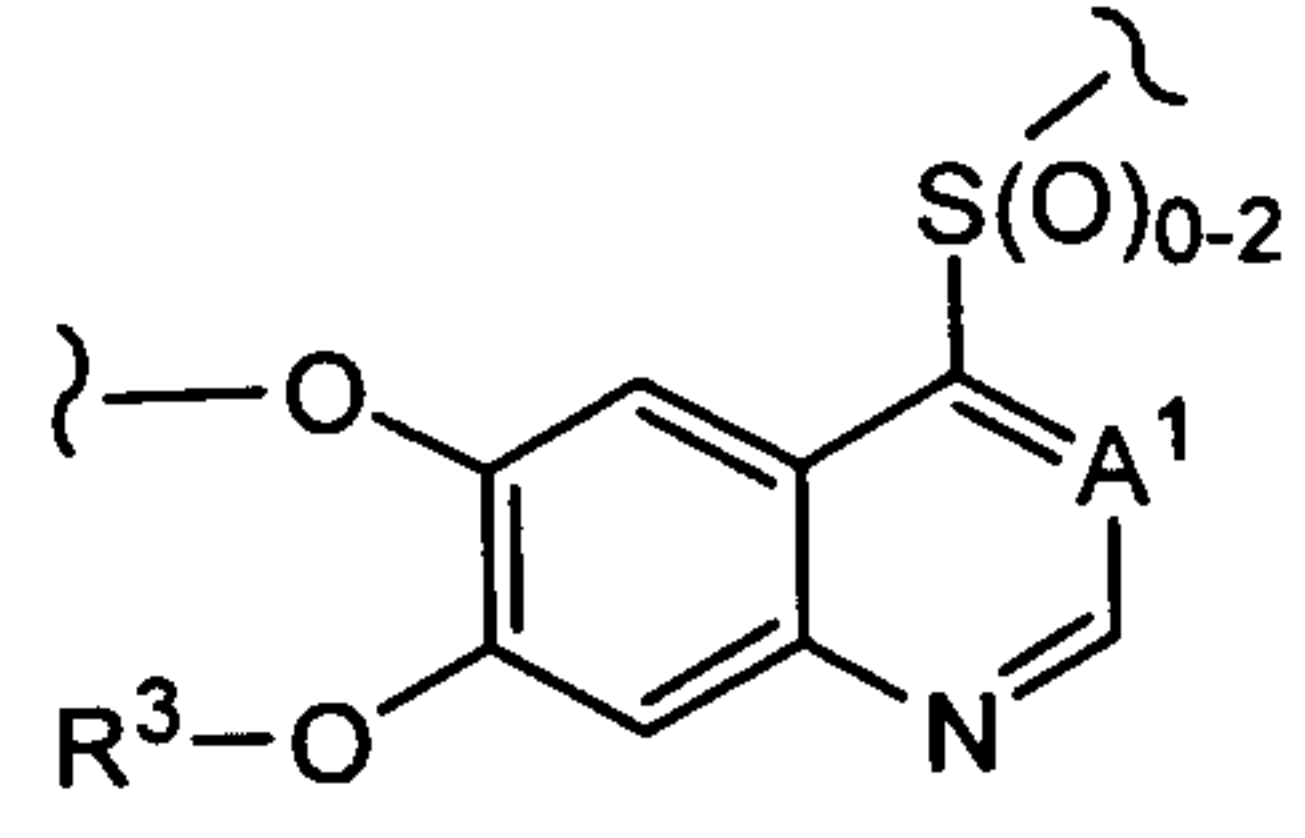
The terms used to describe the scope of formula 101 are defined in WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789).

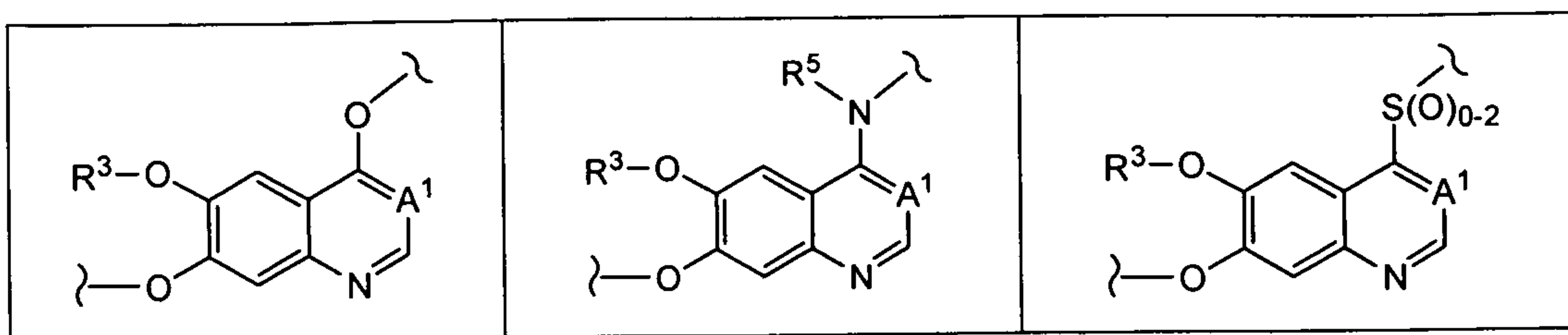
For example "optionally substituted heterocyclyl" for formula 101 has the meaning given in WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789). Whenever a compound of formula 101 is described in this application, whether by structure or by use of the term "formula 101," the terms used to describe that compound are defined by WO 2005/112932 (US Nat'l Stage Application Serial No. 11/568,789).

[00157] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula A-B-C or a pharmaceutically acceptable salt or hydrate thereof, wherein, A is selected from:

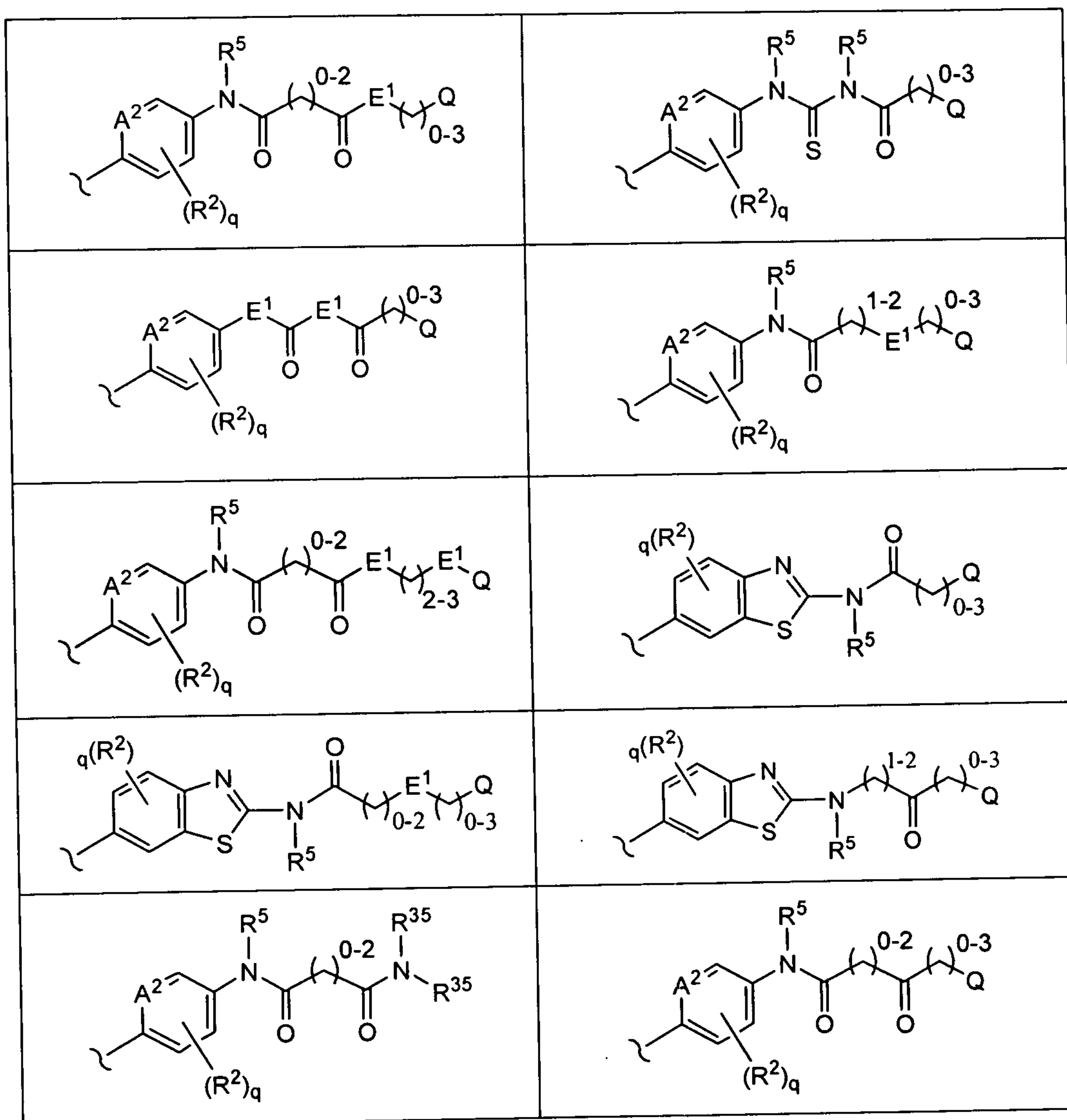
$-R^3$		
		
		
		
		
		
		

B is selected from:

		
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and, C is selected from:



wherein R^2 is selected from -H, halogen, trihalomethyl, -CN, -NH₂, -NO₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted lower alkyl;

q is 0 to 2;

each R^3 is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted arylalkyl, and optionally substituted heteroarylalkyl;

two R^3 , together with the nitrogen to which they are attached, form a four- to seven-membered heteroalicyclic, said four- to seven-membered heteroalicyclic optionally containing one additional heteroatom; when one said additional heteroatom is a nitrogen, then said nitrogen is optionally substituted with a group selected from -H, trihalomethyl, $-SO_2R^5$, $-SO_2NR^5R^5$, $-CO_2R^5$, $-C(O)NR^5R^5$, $-C(O)R^5$, and optionally substituted lower alkyl;

each R^{35} is independently selected from -H, $-C(=O)R^3$, $-C(=O)OR^3$, $-C(=O)SR^3$, $-SO_2R^3$, $-C(=O)N(R^3)R^3$, and optionally substituted lower alkyl;

two R^{35} , together with the nitrogen to which they are attached, can combine to form a heteroalicyclic optionally substituted with between one and four of R^{60} , said heteroalicyclic may have an additional annular heteroatom, and said heteroalicyclic may have an aryl fused thereto, said aryl optionally substituted with an additional one to four of R^{60} ;

A^1 is selected from $=N-$, $=C(H)-$, and $=C(CN)-$;

A^2 is either $=N-$ or $=C(H)-$;

R^5 is -H or optionally substituted lower alkyl;

R^8 is selected from R^3 , $-SO_2NR^3R^3$, $-CO_2R^3$, $-C(O)NR^3R^3$, $-SO_2R^3$, and $-C(O)R^3$;

R^9 , R^{10} , and R^{11} are each independently selected from -H, and $-OR^{12}$; or

R^9 is selected from -H, and $-OR^{12}$, and R^{10} and R^{11} , when taken together, are either an optionally substituted alkylidene or an oxo; and

R^{12} is selected from -H, $-C(O)R^3$, optionally substituted lower alkylidyne, optionally substituted lower arylalkylidyne, optionally substituted lower heterocyclalkylidyne, optionally substituted lower alkylidene, optionally substituted lower alkylidenearyl, optionally substituted lower alkylideneheterocycl, optionally substituted lower alkyl, optionally substituted lower alkylaryl, optionally substituted aryl, optionally substituted lower heterocyclalkyl, and optionally substituted heterocycl;

or two R^{12} 's, when taken together, form 1) a corresponding spirocyclic ketal when said two R^{12} 's stem from R^{10} and R^{11} , or 2) a corresponding cyclic ketal when said two R^{12} 's stem from R^9 and one of R^{10} and R^{11} ;

E^1 is selected from -O-, $-CH_2-$, $-N(R^5)-$, and $-S(O)_{0-2}-$;

Q is a five- to ten-membered ring system, optionally substituted with between zero and four of R^{20} ;

R^{20} is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted lower alkyl;

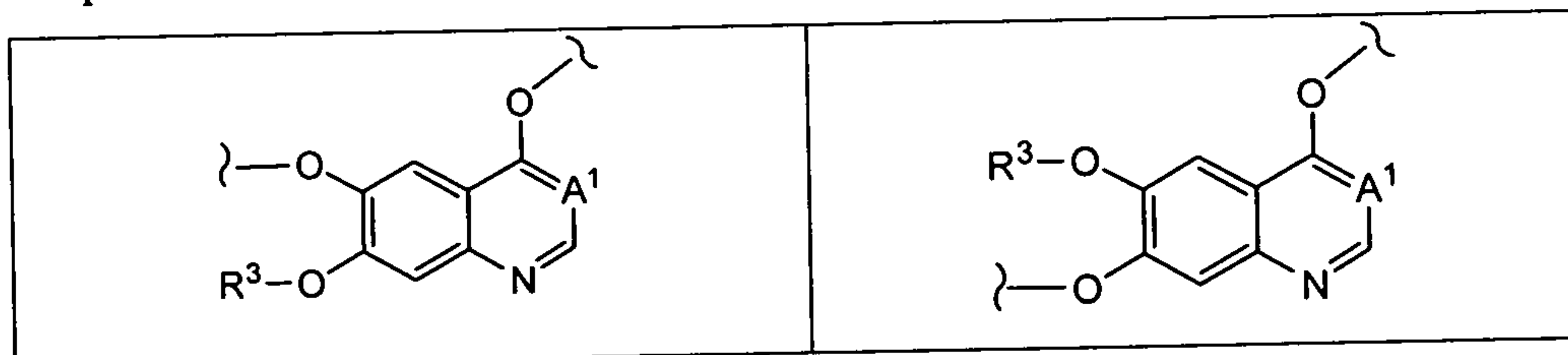
R^{60} is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heteroarylalkyl, and optionally substituted arylalkyl;

two of R^{60} , when attached to a non-aromatic carbon, can be oxo;

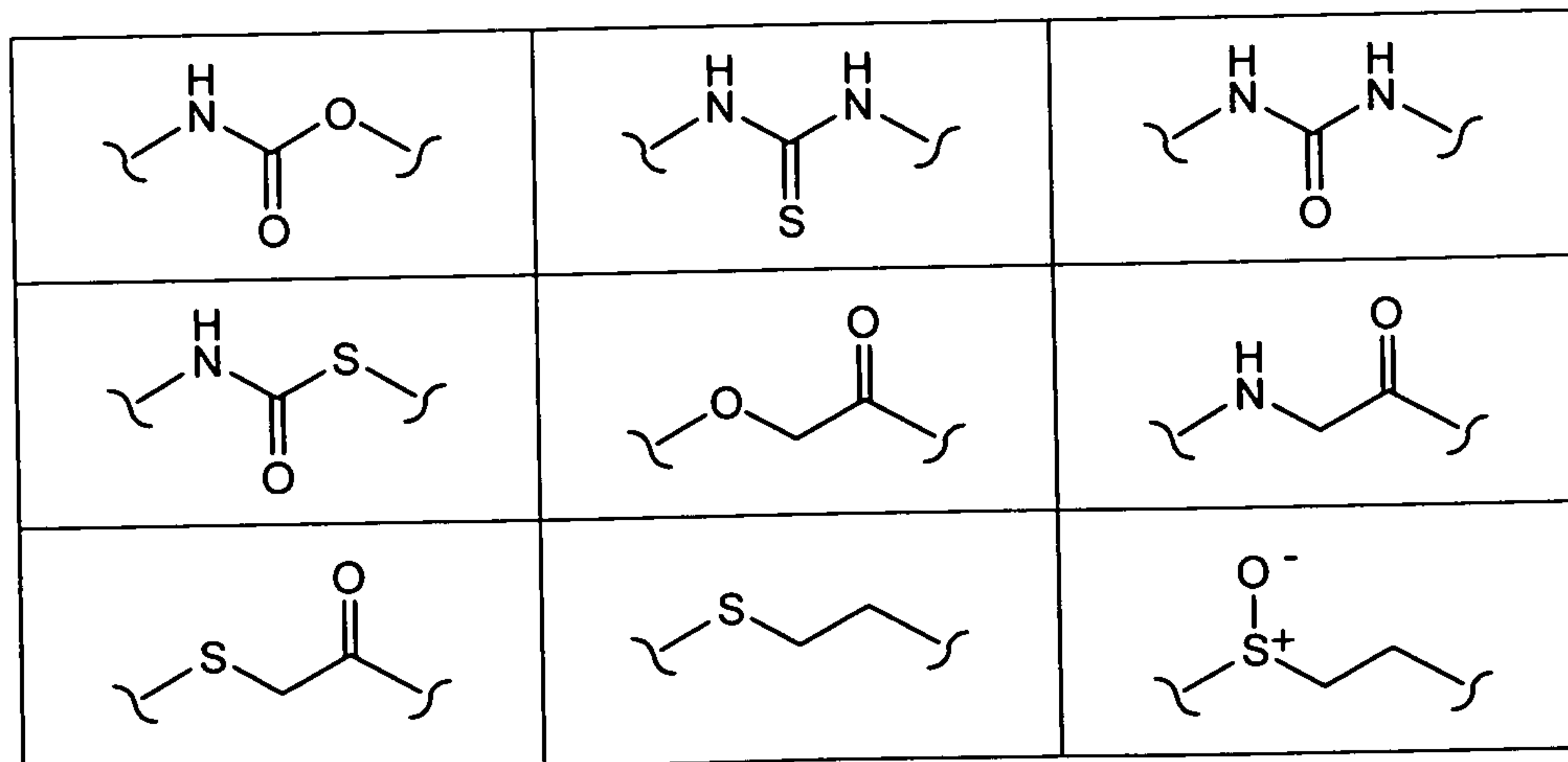
each methylene in any of the above formulae is independently optionally substituted with R^{25} ;

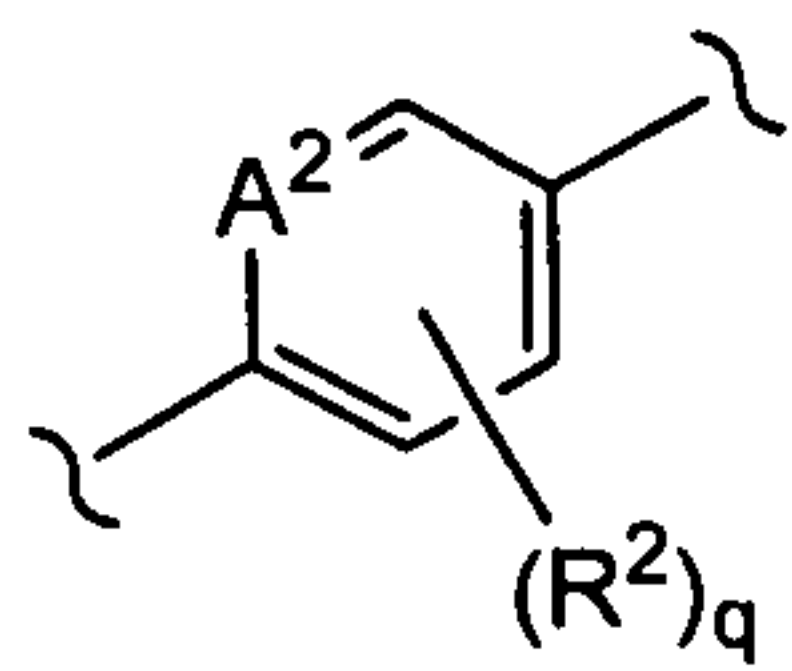
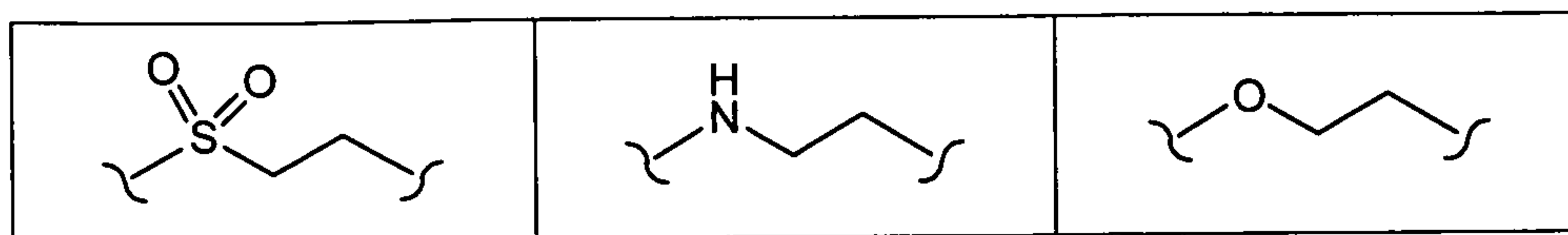
each R^{25} is independently selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted arylalkyl, heteroarylalkyl, and optionally substituted lower alkyl; two of R^{25} , together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic, two of R^{25} on a single carbon can be oxo;

with the proviso that when B is selected from:

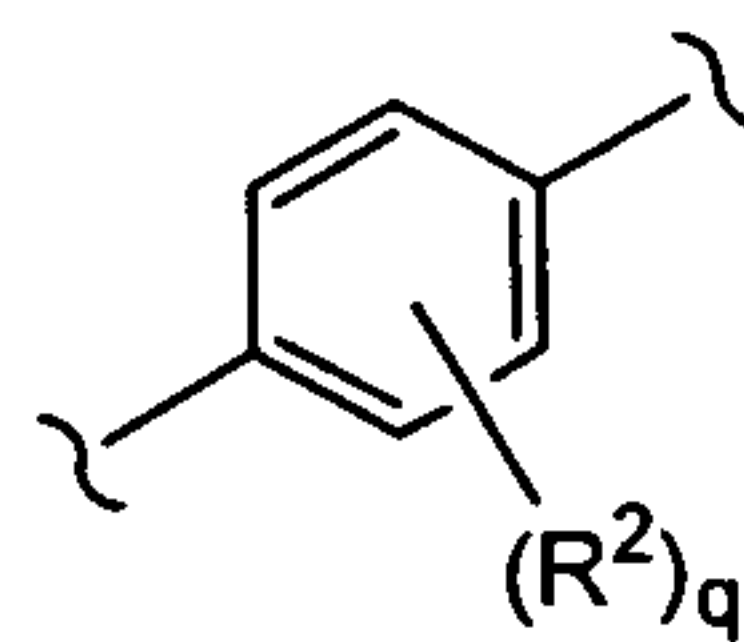
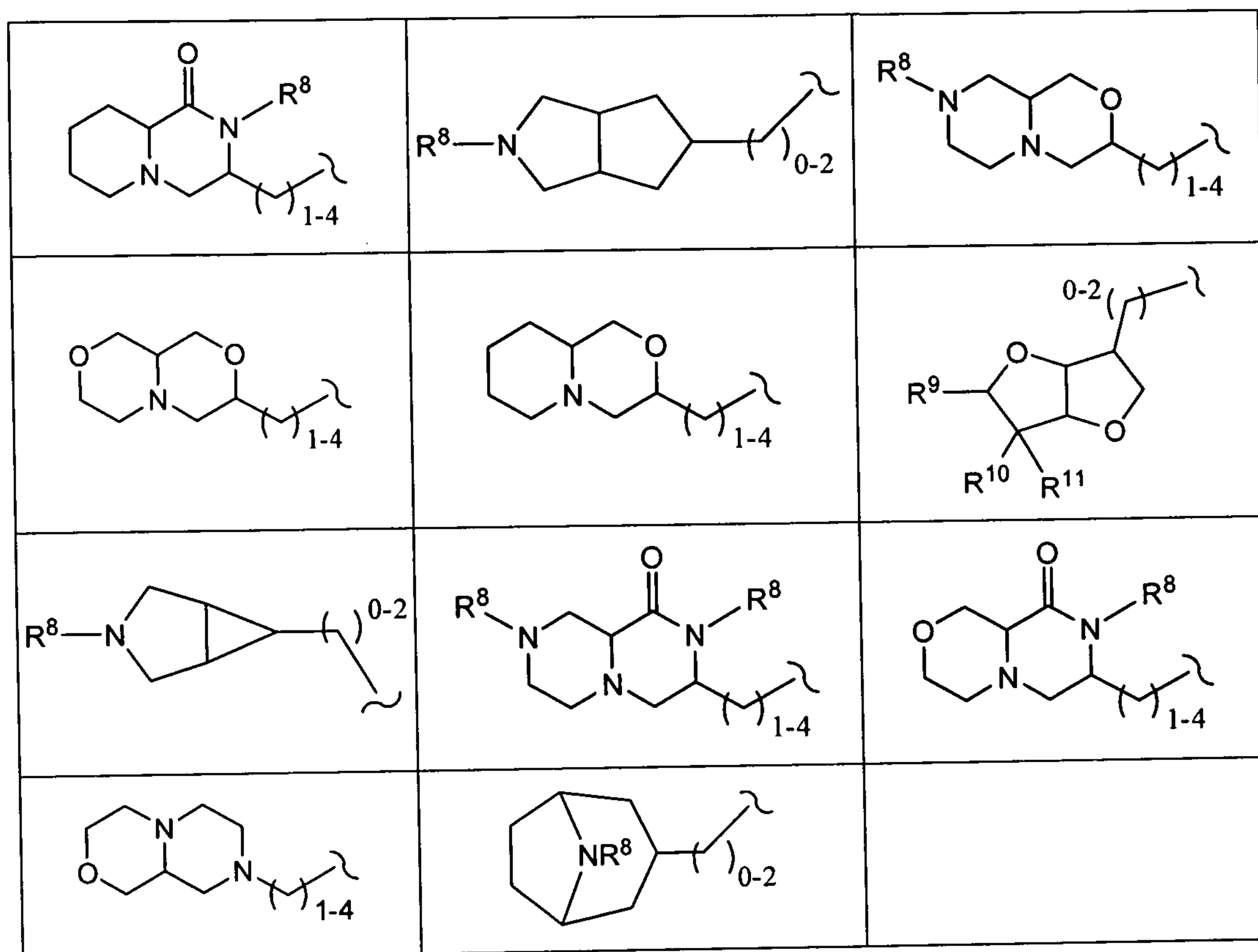


and C contains $(R^2)_q$, and the remaining portion of C contains one of:

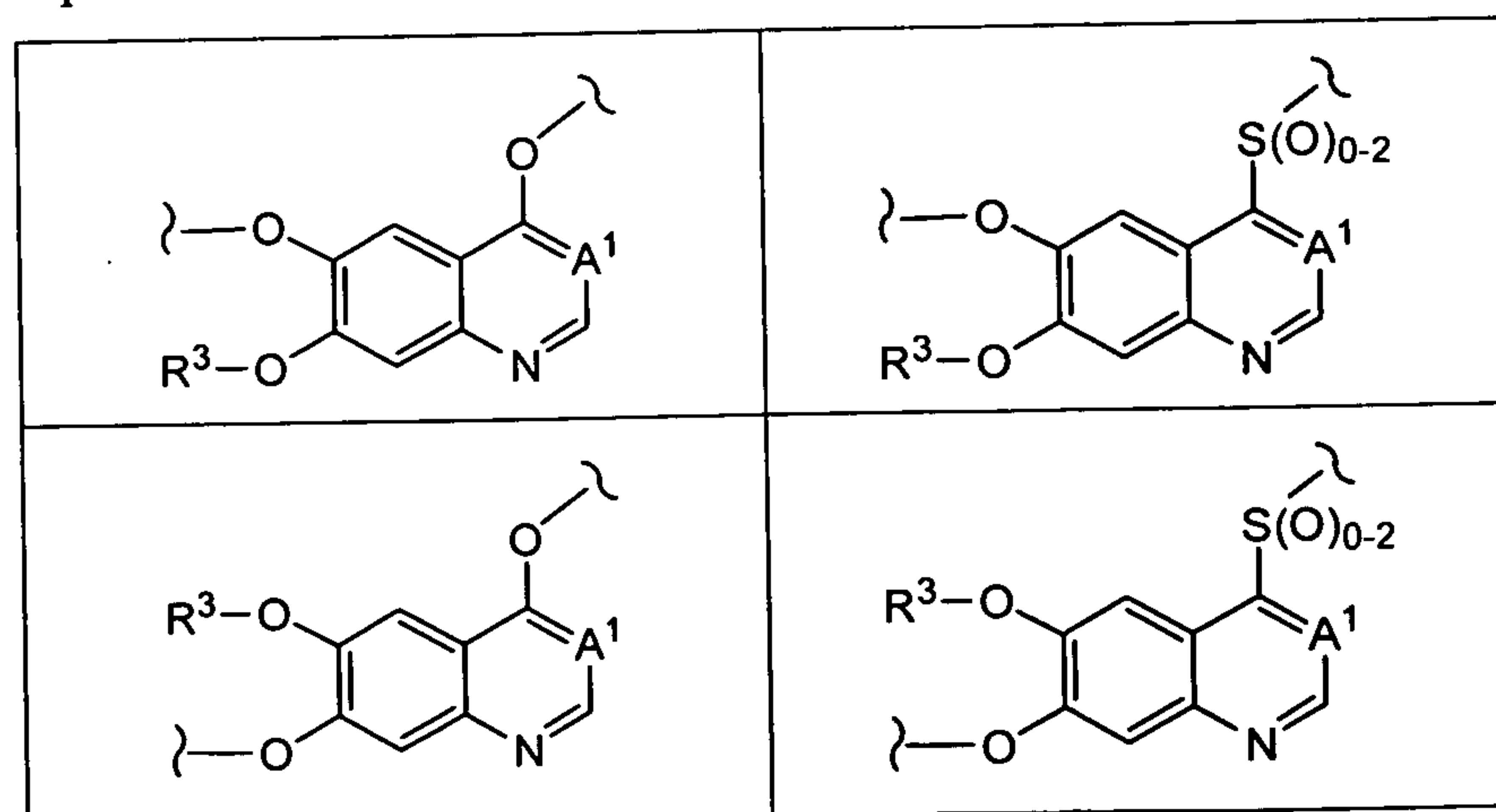




directly attached to $(R^2)_q$, then A must be one of:

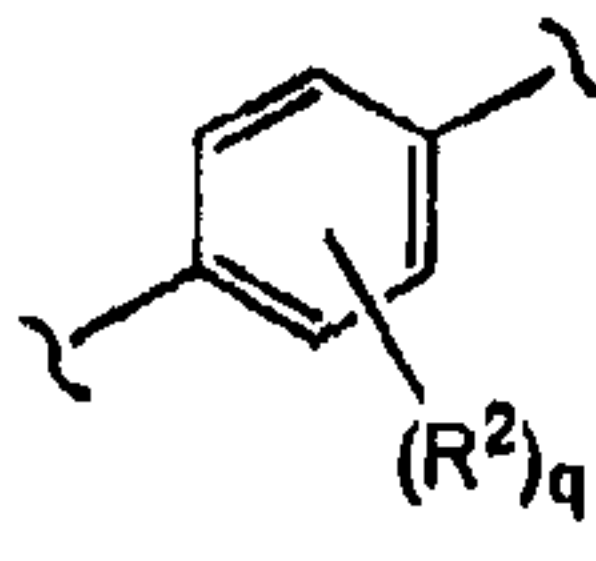


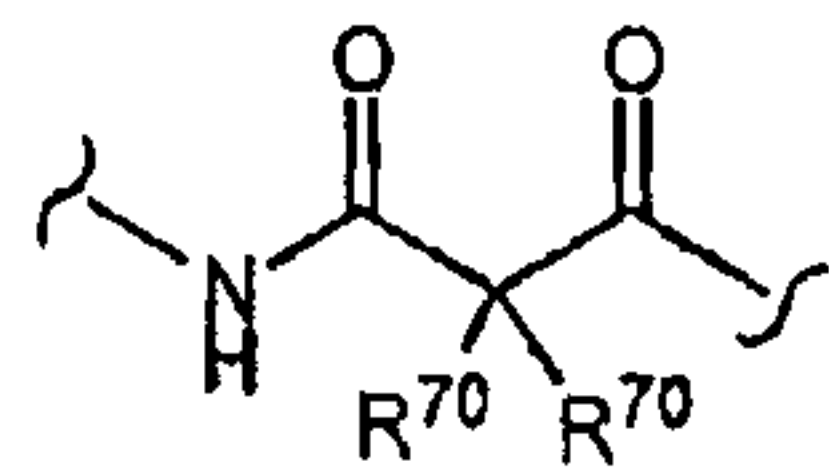
and with the proviso that when C contains $(R^2)_q$, and B is selected from:



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then the portion of C directly attached to  cannot contain

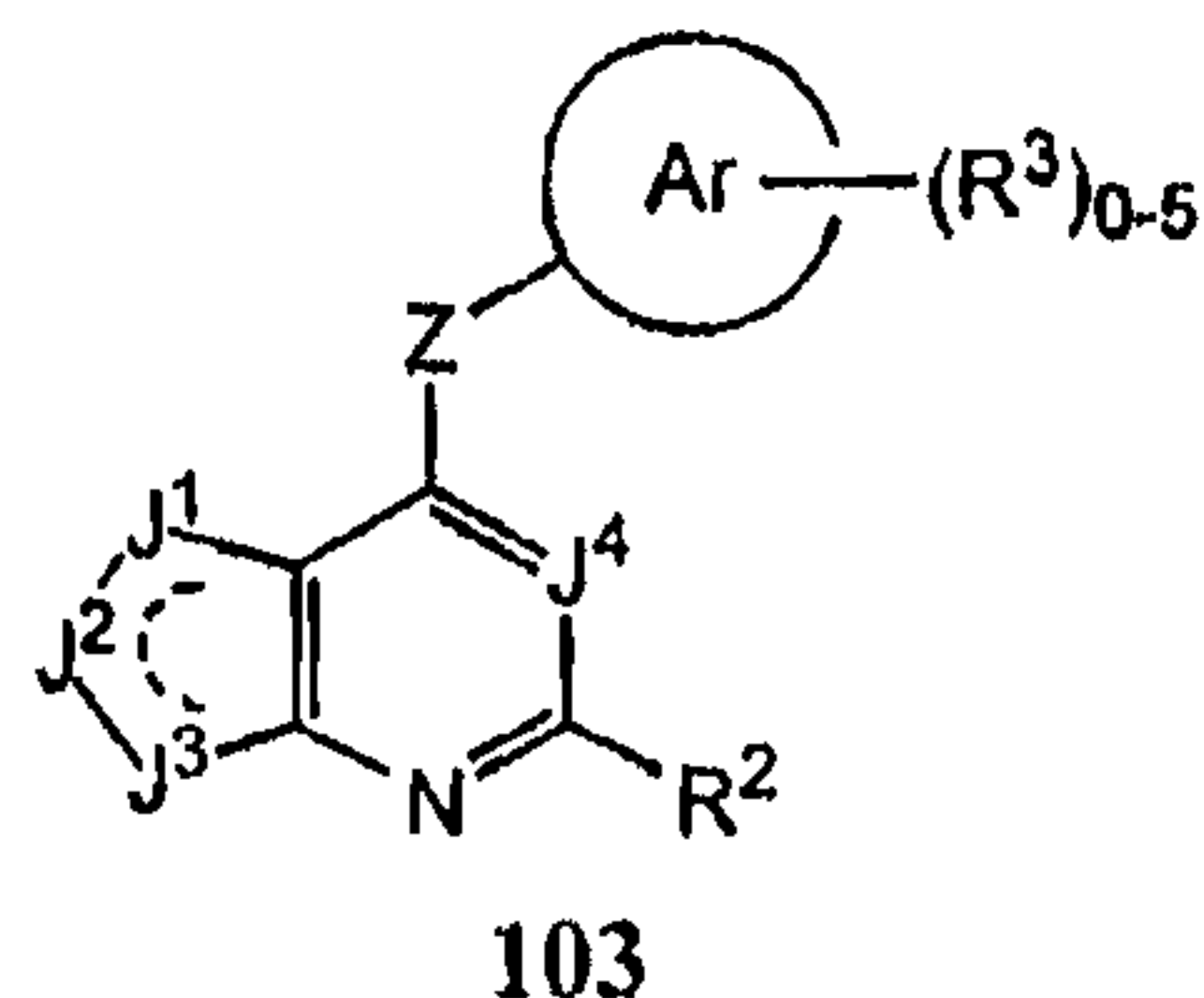


, when R^{70} is selected from -H, C_{1-4} alkyl, and C_{1-4} alkoxyl.

The terms used to describe the scope of formula A-B-C are defined in WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336).

For example "optionally substituted heterocyclyl" for formula A-B-C has the meaning given in WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336). Whenever a compound of formula A-B-C is described in this application, whether by structure or by use of the term "formula A-B-C," the terms used to describe that compound are defined by WO 2005/030140 (US Nat'l Stage Application Serial No. 10/573,336).

[00158] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula 103:



or a pharmaceutically acceptable salt or hydrate hereof, wherein,

each of J^1 , J^2 , and J^3 is independently selected from =N-, =C(R^1)-, -N(R^1)-, -O- and -S(O)₀₋₂-;

each R^1 is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -OR²⁰, -N(R^{20})R²⁰, -S(O)₀₋₂R²⁰, -SO₂N(R^{20})R²⁰, -CO₂R²⁰, -C(O)N(R^{20})R²⁰, -N(R^{20})SO₂R²⁰, -N(R^{20})C(O)R²⁰, -NCO₂R²⁰, -C(O)R²⁰; optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted aryl C_{1-6} alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl C_{1-6} alkyl and -D-R⁵⁰;
 R^2 is selected from -H, halogen, -OR²⁰, -S(O)₀₋₂R²⁰, -NO₂, -N(R^{20})R²⁰, and optionally substituted C_{1-6} alkyl;

J^4 is selected from =N-, =C(H)-, and =C(CN)-;

Ar is either a five- or six-membered arylene or a five- or six-membered heteroarylene containing between one and three heteroatoms;

each R^3 is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -OR²⁰, -N(R²⁰)R²⁰, -S(O)₀₋₂R²⁰, -SO₂N(R²⁰)R²⁰, -CO₂R²⁰, -C(O)N(R²⁰)R²⁰, -N(R²⁰)SO₂R²⁰, -N(R²⁰)C(O)R²⁰, -NCO₂R²⁰, -C(O)R²⁰, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl C₁₋₆alkyl and a group -B-L-T, wherein

B is selected from absent, -N(R¹³)-, -N(SO₂R¹³)-, -O-, -S(O)₀₋₂-, and -C(=O)-;

L is selected from absent, -C(=S)N(R¹³)-, -C(=NR¹⁴)N(R¹³)-, -SO₂N(R¹³)-, -SO₂-, -C(=O)N(R¹³)-, -N(R¹³)-, -C(=O)C₁₋₂alkylN(R¹³)-, -N(R¹³)C₁₋₂alkylC(=O)-, -C(=O)C₀₋₁alkylC(=O)N(R¹³)-, -C₀₋₄alkylene-, -C(=O)C₀₋₁alkylC(=O)OR³-, -C(=NR¹⁴)C₀₋₁alkylC(=O)-, -C(=O)-, -C(=O)C₀₋₁alkylC(=O)-, and an optionally substituted four to six-membered heterocyclyl containing between one and three annular heteroatoms including at least one nitrogen; and

T is selected from -H, -R¹³, -C₀₋₄alkyl, -C₀₋₄alkylQ, -OC₀₋₄alkylQ, -C₀₋₄alkylOQ, -N(R¹³)C₀₋₄alkylQ, -SO₂C₀₋₄alkylQ, -C(=O)C₀₋₄alkylQ, -C₀₋₄alkylN(R¹³)Q, and -C(=O)N(R¹³)C₀₋₄alkylQ,

wherein each of the aforementioned alkyls and alkylenes of -B-L-T is optionally substituted with one or two of R⁶⁰;

Z is selected from -S(O)₀₋₂-, -O-, and -NR⁴-;

R⁴ is either -H or optionally substituted C₁₋₆alkyl;

each D is independently selected from -O-, -S(O)₀₋₂-, and -NR⁵-;

each R⁵ is independently -H or optionally substituted C₁₋₆alkyl;

each R¹³ is independently selected from -H, -C(=O)R²⁰, -C(=O)OR²⁰, -C(=O)SR²⁰, -SO₂R²⁰, -C(=O)N(R²⁰)R²⁰, and optionally substituted C₁₋₄alkyl;

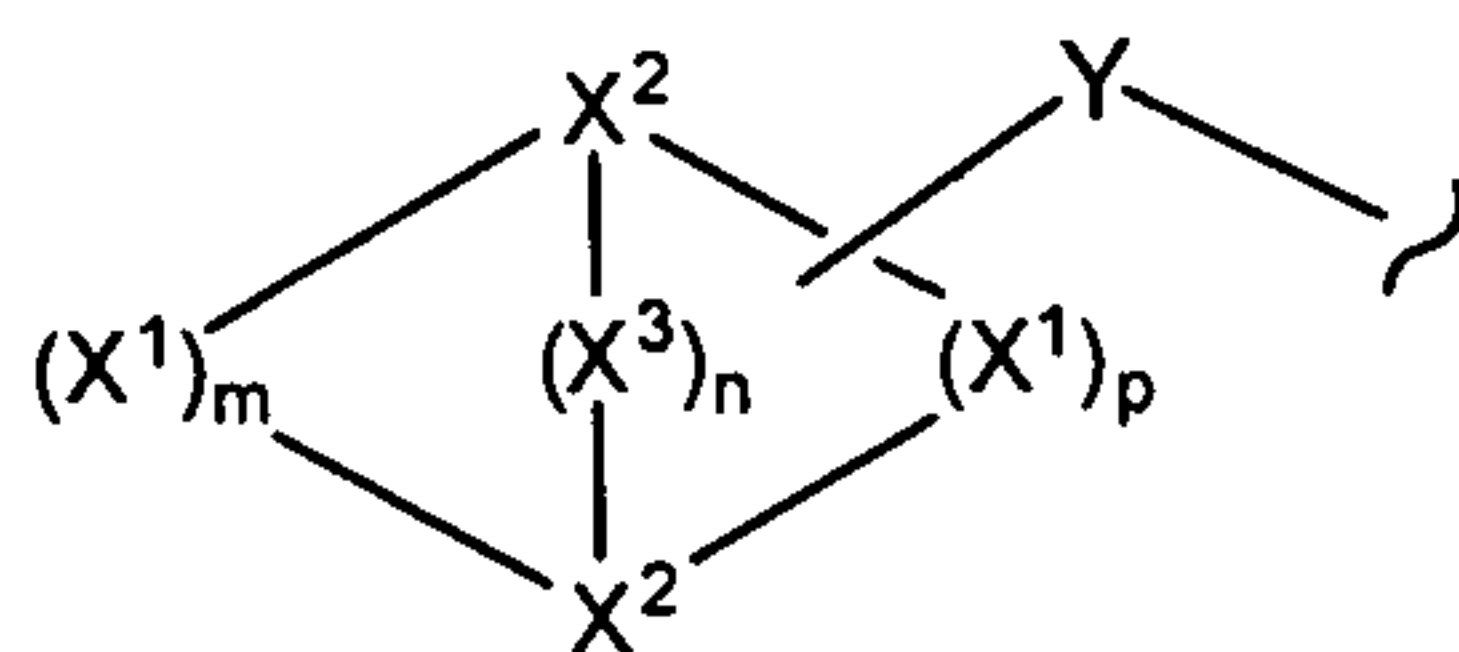
two of R¹³, together with the atom or atoms to which they are attached, can combine to form a heteroalicyclic optionally substituted with between one and four of R⁶⁰, said heteroalicyclic can comprise up to four annular heteroatoms, and said heteroalicyclic can comprise an aryl or heteroaryl fused thereto, in which case said aryl or heteroaryl is optionally substituted with an additional one to four of R⁶⁰;

each R¹⁴ is independently selected from -H, -NO₂, -N(R²⁰)R²⁰, -CN, -OR²⁰, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋

₆alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl C₁₋₆alkyl;

Q is a five- to ten-membered annular system, optionally substituted with between zero and four of R²⁰;

each R⁵⁰ is independently either R²⁰, or according to formula 120;



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wherein X¹, X², and optionally X³, represent the atoms of a saturated bridged ring system, said saturated bridged ring system comprising up to four annular heteroatoms represented by any of X¹, X², and X³; wherein,

each X¹ is independently selected from -C(R⁶)R⁷-, -O-, -S(O)₀₋₂-, and -NR⁸-;

each X² is independently an optionally substituted bridgehead methine or a bridgehead nitrogen;

each X³ is independently selected from -C(R⁶)R⁷-, -O-, -S(O)₀₋₂-, and -NR⁸-;

Y is either:

an optionally substituted lower alkylene linker, between D and either 1) any annular atom of the saturated bridged ring system, except X² when X² is a bridgehead nitrogen, or 2) any heteroatom, represented by any of R⁶ or R⁷; provided there are at least two carbon atoms between D and any annular heteroatom of the saturated bridged ring system or any heteroatom represented by any of R⁶ or R⁷;

or Y is absent, when Y is absent, said saturated bridged ring system, is directly attached to D via an annular carbon of said saturated bridged ring system, unless D is -SO₂-, in which case said saturated bridged ring system, is directly attached to D via an any annular atom of said saturated bridged ring system;

m and p are each independently one to four;

n is zero to two, when n equals zero there is a single bond between the two bridgehead X²'s;

R⁶ and R⁷ are each independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -OR²⁰, -N(R²⁰)R²⁰, -S(O)₀₋₂R²⁰, -SO₂N(R²⁰)R²⁰, -CO₂R²⁰, -C(O)N(R²⁰)R²⁰, -N(R²⁰)SO₂R²⁰, -N(R²⁰)C(O)R²⁰, -NCO₂R²⁰, -C(O)R²⁰, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl,

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- optionally substituted heterocyclyl, optionally substituted heterocyclyl C₁₋₆alkyl, and a bond to either Y or D; or
- R⁶ and R⁷, when taken together are oxo; or
- R⁶ and R⁷, when taken together with a common carbon to which they are attached, form a optionally substituted three- to seven-membered spirocyclyl, said optionally substituted three- to seven-membered spirocyclyl optionally containing at least one additional annular heteroatom selected from N, O, S, and P;
- each R⁸ is independently selected from -R²⁰, Y, -SO₂N(R²⁰)R²⁰, -CO₂R²⁰, -C(O)N(R²⁰)R²⁰, -SO₂R²⁰, and -C(O)R²⁰;
- each R²⁰ is independently selected from -H, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆alkyl; or two of R²⁰, when taken together with a common nitrogen to which they are attached, can form an optionally substituted five- to seven-membered heterocyclyl, said optionally substituted five- to seven-membered heterocyclyl optionally containing at least one additional annular heteroatom selected from N, O, S, and P;
- each R⁶⁰ is independantly selected from -H, halogen, trihalomethyl, -CN, -NO₂, -OR²⁰, -N(R²⁰)R²⁰, -S(O)₀₋₂R²⁰, -SO₂N(R²⁰)R²⁰, -CO₂R²⁰, -C(O)N(R²⁰)R²⁰, -N(R²⁰)SO₂R²⁰, -N(R²⁰)C(O)R²⁰, -N(R²⁰)CO₂R²⁰, -C(O)R²⁰, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl C₁₋₆alkyl;
- two of R⁶⁰, when taken together with a common carbon to which they are attached, can form an optionally substituted three- to seven-membered alicyclic or heteroalicyclic; and
- two of R⁶⁰, when taken together can be oxo.

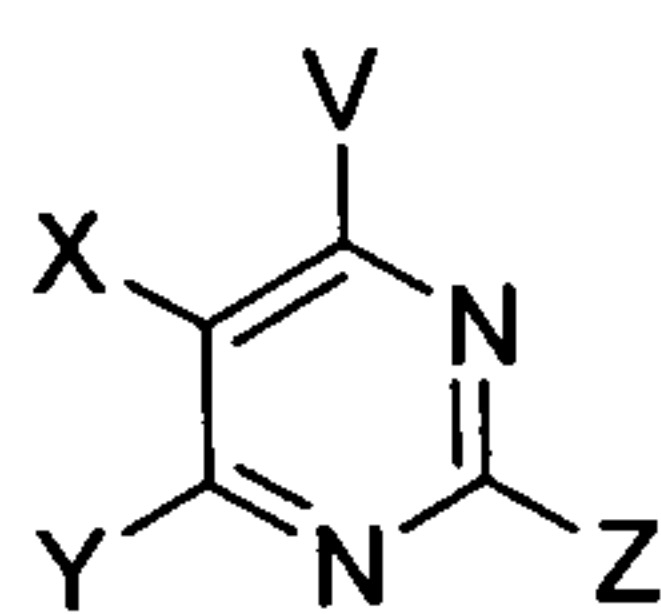
The terms used to describe the scope of formula 103 are defined in WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140).

For example "optionally substituted heterocyclyl" for formula 103 has the meaning given in WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140). Whenever a compound of formula 103 is described in this application, whether by structure or by use of the term "formula 103," the terms used to describe that compound are defined by WO 2006/014325 (US Nat'l Stage Application Serial No. 11/571,140).

[00159] In another embodiment, one or more of the chemotherapeutic agent(s) is *N*-[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]-*N'*-[2-(4-fluorophenyl)ethyl]ethanediamide or pharmaceutically acceptable salt or hydrate thereof.

[00160] In another embodiment, the cMet inhibitor is *N*-[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]-*N'*-[2-(4-fluorophenyl)ethyl]ethanediamide or a pharmaceutically acceptable salt or hydrate thereof.

[00161] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula **105**:



105

or a pharmaceutically acceptable salt or hydrate thereof, wherein,

V is NR_1R_{1a} , or $\text{O}-\text{R}_1$, wherein

R_1 is H, CN, halo, $-\text{NR}_{13}\text{R}_{14}$, $\text{C}(\text{O})\text{NR}_{13}\text{R}_{14}$, $\text{C}_1\text{-C}_6$ alkyl, $-\text{C}(\text{O})\text{-C}_1\text{-C}_6$ alkyl, $-\text{C}_0\text{-C}_6$ alkyl- R_{20} , wherein R_{20} is aryl, heteroaryl, heterocyclyl, or a 5-12 membered fused bicyclic or tricyclic saturated, partially saturated, or unsaturated ring system containing 0-4 ring atoms selected from N, O, and S, wherein aryl, heteroaryl, $\text{C}_3\text{-C}_7$ heterocyclyl, or the 5-12 membered ring system are optionally substituted with one, two, or three groups independently selected from $\text{C}_1\text{-C}_6$ alkyl, and $-\text{C}_0\text{-C}_6$ alkyl- R_{21} ;

R_{1a} is H or $\text{C}_1\text{-C}_6$ alkyl; or

when V is NR_1R_{1a} , R_1 and R_{1a} together with the nitrogen to which they are attached form a 4-7 membered heterocyclyl or heteroaryl group containing, in addition to the nitrogen, up to two additional heteroatoms independently selected from O, N, and S, and wherein each heterocyclyl or heteroaryl group is optionally substituted with one or two of $\text{C}_1\text{-C}_6$ alkyl, $-\text{NR}_{13}\text{R}_{14}$ or $\text{C}_3\text{-C}_7$ cycloalkyl;

X is H, halo, $\text{C}_1\text{-C}_6$ alkyl, NO_2 , mono-, di-, or tri-halo substituted methyl, $\text{NR}_{13}\text{R}_{14}$, $\text{C}(\text{O})\text{O}-\text{C}_1\text{-C}_6$ alkyl, or $\text{N}(\text{R}_{13})\text{-C}(\text{O})\text{-C}_1\text{-C}_6$ alkyl;

Y is H, halo, OH, C₁-C₆ alkyl, C₀-C₆ alkyl-NR₁₅R₁₆, NR₁₅R₁₆, C₁-C₆ alkoxy, -N(R₁₃)-(CH₂)_n-NR₁₅R₁₆, -C(O)O-C₁-C₆ alkyl, -O-(CH₂)_n-NR₁₅R₁₆, -C(O)-C₁-C₆ alkyl, -C₀-C₆-alkyl-R₂₁, -O-R₂₁, -C(O)-R₂₁, -O-(CH₂)_n-R₂₁, -C(O)-NR₁₃R₁₄, -C(O)-N(R₁₃)-aryl, -C(O)-N(R₁₃)-(CH₂)_n-NR₁₅R₁₆, -C(O)-N(R₁₃)-(CH₂)_n-aryl, -C(O)-N(R₁₃)-(CH₂)_n-heterocyclyl;

or X and Y together with the atoms to which they are attached form a 4-7 membered heterocyclyl or heteroaryl group containing one or two heteroatoms independently selected from O, N, and S, wherein the heterocyclyl or heteroaryl group is optionally substituted with one or two moieties independently selected from halo, C₁-C₆ alkyl, aryl-C₁-C₆ alkyl-, aryl-(CH₂)_n-O-(CH₂)_n-aryl-, arylOH, C₃-C₇ cycloalkyl, heterocyclyl, -aryl-N(R₁₃)C(O)-C₃-C₇ cycloalkyl-C(O)-N(R₁₄)-aryl, or a group of the formula -L-M-Q, wherein

L is a bond or C₃-C₇ cycloalkyl,

M is C₁-C₆ alkyl, C₂-C₆ alkenyl, or C₂-C₆ alkynyl,

Q is NR₁₃R₁₄, N(R₁₃)C(O)-C₁-C₆ alkyl, heterocyclyl, or a saturated fused bicyclic ring containing one or two heteroatoms independently selected from O, N, and S,

wherein each aryl, heteroaryl, or heterocyclyl substituent on the group formed by X and Y is optionally further substituted with one or two moieties independently selected from halo, C(O)O-(CH₂)_n-phenyl, and C(O)-C₁-C₆ alkyl;

Z is H, NR₂R₃, -S-R_{2a}, or -O-R_{2a}, wherein

R₂ is -C₁-C₆ alkyl, -C₁-C₆ alkyl-NR₁₃R₁₄, -C(O)-aryl, -C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-(C₃-C₇-cycloalkyl), -C₀-C₆-alkyl-heterocyclyl, or -C₀-C₆ alkyl-5-12 membered fused bicyclic or tricyclic saturated, partially saturated, or unsaturated ring system containing 0-4 ring atoms selected from N, O, and S, wherein each alkyl is optionally substituted with phenyl, and each aryl, heteroaryl, C₃-C₇ cycloalkyl, heterocyclyl, or 5-12

membered ring system is optionally substituted with one, two, or three groups independently selected from halo, mono-, di-, or tri-halo substituted methyl or methoxy, CN, NO₂, NR₁₃R₁₄, C(O)O-C₁-C₆ alkyl, N(R₁₃)C(O)-C₁-C₆ alkyl, -SO₂NR₁₃R₁₄, -O-C(O)-NR₁₃R₁₄, -C₀-C₆ alkyl-C(O)NR₁₅R₁₆, C₁-C₆ alkoxy, C₁-C₆

thioalkoxy, $-O-(CH_2)_n-NR_{15}R_{16}$, $-C_1-C_6$ alkyl- $NR_{13}R_{14}$, $-N(R_{13})-C(O)-C_1-C_6$ alkyl, $-N(R_{13})-C(O)-aryl$, $-C_0-C_6$ alkyl- $C(O)-N(R_{13})-(CH_2)_n-NR_{15}R_{16}$, $-C_0-C_6$ alkyl- $C(O)-N(R_{13})-(CH_2)_n-aryl$, $-O-(CH_2)_n-C(O)-N(R_{13})-(CH_2)_n-NR_{15}R_{16}$, $-O-(CH_2)_n-C(O)-NR_{15}R_{16}$, $-C_0-C_6$ alkyl- $C(O)-N(R_{13})-(CH_2)_n-O-C_1-C_6$ alkyl, $-C_0-C_6$ alkyl- $N(R_{13})-C(O)O-C_1-C_6$ alkyl, $-C_0-C_6$ alkyl- $C(O)-heterocyclyl$, $-C_0-C_6$ alkyl- $C(O)-heteroaryl$, $-C_0-C_6$ alkyl- $C(O)-aryl$, $-C_0-C_6$ -alkyl- R_{21} , aryloxy, $-O-(CH_2)_n-R_{21}$, $-SO_2$ -heterocyclyl, $N(R_{13})-C(O)-C_3-C_7$ -cycloalkyl, $-C_0-C_6$ alkyl $C(O)O-R_{21}$, C_3-C_7 -cycloalkyl, $-C_0-C_6$ alkyl R_{21} , $-SC_1-C_6$ alkyl or C_1-C_6 alkyl optionally substituted with halo or cyano, wherein each aryl, heteroaryl, cycloalkyl, or heterocyclyl

substituent is further optionally substituted with 1-3 groups independently selected from halo, CF_3 , C_1-C_6 alkyl, C_1-C_6 haloalkoxy, $NR_{13}R_{14}$ and C_1-C_6 alkoxy;

R_3 is H or C_1-C_6 alkyl;

or R_2 and R_3 together with the nitrogen to which they are attached form a 4-7 membered heterocyclyl or heteroaryl group containing up to three heteroatoms independently selected from O, N, and S, and wherein the heterocyclyl or heteroaryl group is optionally substituted with one or two of halo or C_1-C_6 alkyl;

R_{2a} is aryl or C_0-C_6 alkyl-heteroaryl, wherein the aryl and heteroaryl are optionally substituted with aryl, $-N(R_{13})-C(O)-C_3-C_7$ cycloalkyl or $-C(O)NR_{13}R_{14}$;

R_{13} and R_{14} are independently H or C_1-C_6 alkyl;

R_{15} and R_{16} are independently H, C_1-C_6 alkyl, heteroaryl, or heterocyclyl, or R_{15} and R_{16} together with the nitrogen to which they are attached form a 4-7 membered heterocyclyl or heteroaryl group wherein one or two ring carbons are each optionally replaced with a heteroatom independently selected from O, N, and S, and wherein each heterocyclyl or heteroaryl group is optionally substituted with one or two moieties independently selected from halo, C_1-C_6 alkyl, or $-C(O)O-C_1-C_6$ alkyl;

R_{21} is heterocyclyl, aryl, heteroaryl, or C_3-C_7 cycloalkyl, and wherein alkyl, aryl, heteroaryl, C_3-C_7 cycloalkyl, and heterocyclyl are optionally substituted with

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one or two moieties independently selected from halo, $-\text{S}(\text{O})_2-\text{C}_0-\text{C}_1$ alkyl, $-\text{C}(\text{O})-\text{C}_0-\text{C}_1$ alkyl, $-\text{C}(\text{O})-\text{H}$, $-\text{C}_0-\text{C}_1$ alkyl-aryl, C_1-C_6 alkyl, $\text{NR}_{13}\text{R}_{14}$, and heterocyclyl;

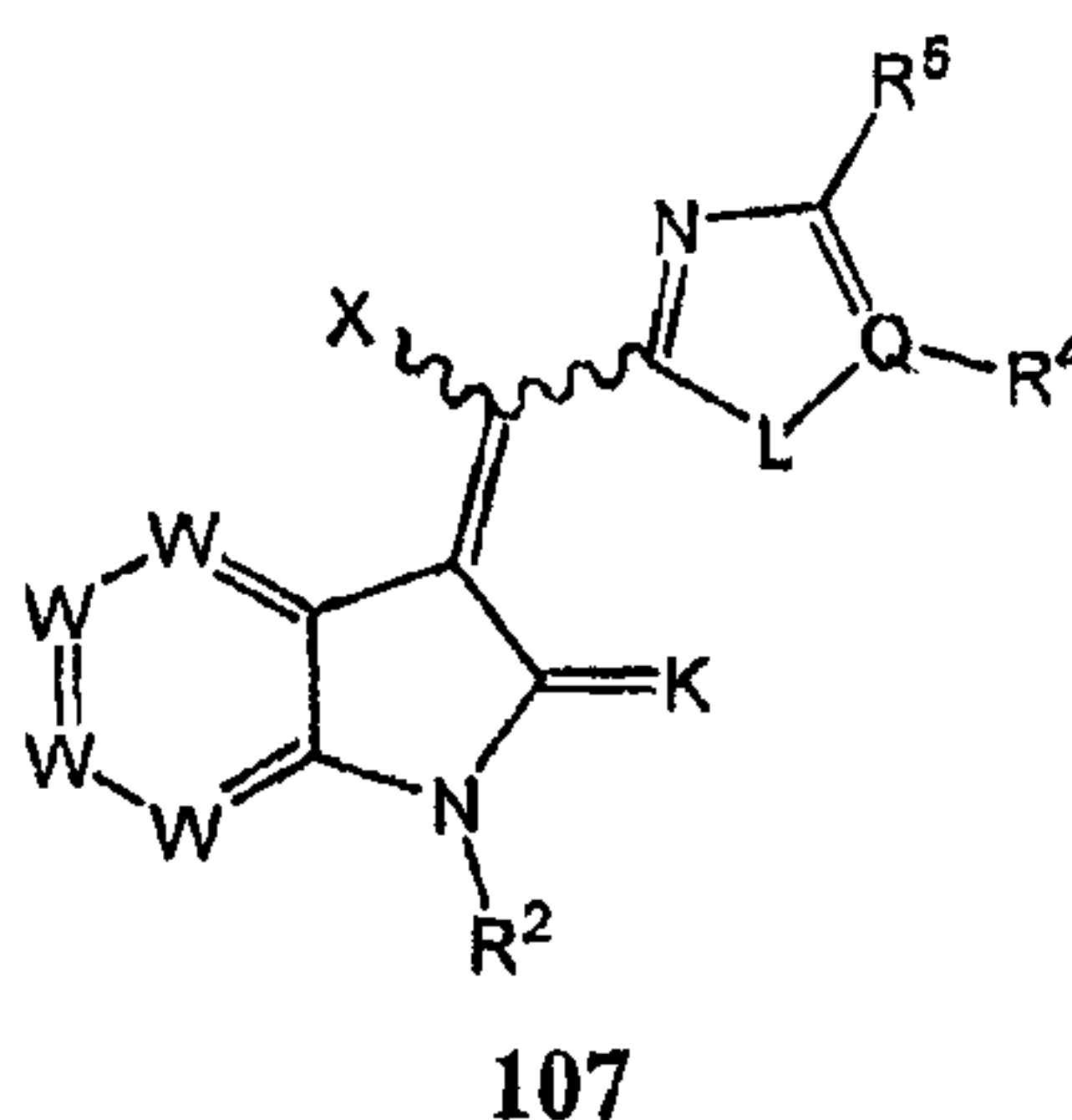
n is 0-6;

provided that when V is NH_2 , X , Y and Z are not simultaneously H .

The terms used to describe the scope of formula 105 are defined in WO 2006/074057 (US Nat'l Stage Application Serial No. 11/722,719).

For example "optionally substituted heterocyclyl" for formula 105 has the meaning given in WO 2006/074057 (US Nat'l Stage Application Serial No. 11/722,719). Whenever a compound of formula 105 is described in this application, whether by structure or by use of the term "formula 105," the terms used to describe that compound are defined by WO 2006/074057 (US Nat'l Stage Application Serial No. 11/722,719).

[00162] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula 107:



or a pharmaceutically acceptable salt or hydrate thereof, wherein,

each W is independently N or CR^1 ;

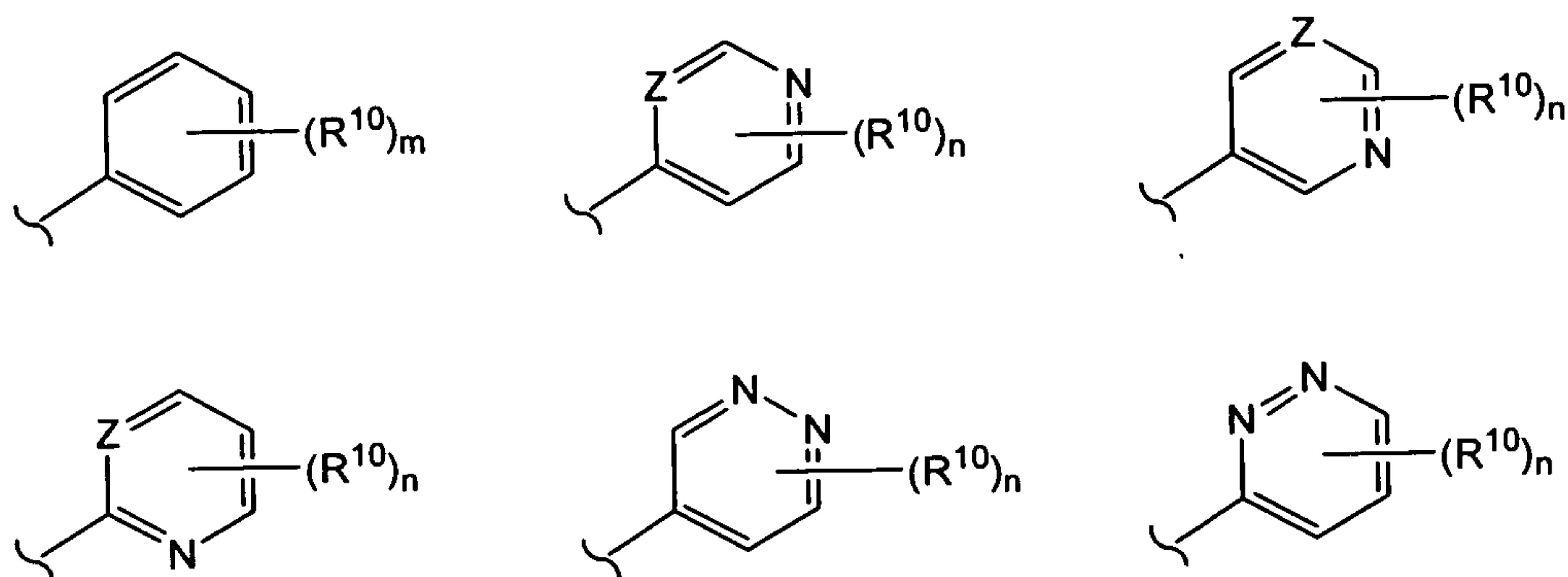
each R^1 is independently selected from $-\text{H}$, halogen, trihaloalkyl, $-\text{CN}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{OR}^6$, $-\text{N}=\text{CNR}^6\text{R}^7$, $-\text{N}(\text{R}^6)\text{C}(=\text{NR}^8)\text{NR}^6\text{R}^7$, $-\text{SR}^6$, $-\text{S}(\text{O})_{1-2}\text{R}^6$, $-\text{SO}_2\text{NR}^6\text{R}^7$, $-\text{CO}_2\text{R}^6$, $-\text{C}(\text{O})\text{NR}^6\text{R}^7$, $-\text{C}(\text{O})\text{N}(\text{OR}^6)\text{R}^7$, $-\text{C}(=\text{NR}^8)\text{NR}^6\text{R}^7$, $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^7$, $-\text{NC}(\text{O})\text{R}^6$, $-\text{NCO}_2\text{R}^6$, $-\text{C}(\text{O})\text{R}^7$, $-\text{R}^7$, and $-\text{A}-\text{R}^7$; provided at least one of R^1 is $-\text{A}-\text{R}^7$, wherein, only for said at least one $-\text{A}-\text{R}^7$, R^7 must be an optionally substituted heteroalicyclic ring, and any nitrogen of said optionally substituted heteroalicyclic ring cannot be directly bound to A ;

A is O , $\text{S}(\text{O})_{0-2}$, and NR^6 ;

L is O , $\text{S}(\text{O})_{0-2}$, or NR^3 ;

Q is C or N , when Q is N , then R^4 does not exist;

- R^2 and R^3 are each independently -H or $-R^7$;
- R^4 and R^5 are each independently selected from -H, $-OR^6$, $-NR^6R^7$, $-S(O)_{0-2}R^6$, $-SO_2NR^6R^7$, $-CO_2R^6$, $-C(O)NR^6R^7$, $-N(R^6)SO_2R^6$, $-NC(O)R^6$, $-NCO_2R^6$, $-C(O)R^7$, $-CN$, $-NO_2$, $-NH_2$, halogen, trihalomethyl, and $-R^7$; or
- R^4 and R^5 , when taken together, form a five or six-membered aromatic ring system containing between zero and two nitrogens, said five or six-membered aromatic ring system optionally substituted with between zero and four of R^{15} ;
- R^6 is selected from -H, optionally substituted C_{1-8} alkyl, optionally substituted aryl C_{1-8} alkyl, optionally substituted heterocyclyl C_{1-8} alkyl, optionally substituted aryl, and optionally substituted heterocyclyl;
- R^7 is selected from -H, optionally substituted C_{1-8} alkyl, optionally substituted aryl C_{1-8} alkyl, optionally substituted heterocyclyl C_{1-8} alkyl, optionally substituted aryl, and optionally substituted heterocyclyl; provided that there are at least two carbons between any heteroatom of R^7 and A or either nitrogen to which R^2 or R^3 are attached; or
- R^6 and R^7 , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclic ring, said optionally substituted five- to seven-membered heterocyclic ring optionally containing at least one additional heteroatom selected from nitrogen, oxygen, sulfur, and phosphorus;
- R^8 is -H, $-NO_2$, $-CN$, $-OR^6$, and optionally substituted C_{1-8} alkyl;
- X is selected from one of the following six formulae:



wherein m is zero to five, n is zero to three, and Z is N or CR^{10} ;

- R^{10} is selected from -H, halogen, trihalomethyl, $-NH_2$, $-NO_2$, $-OR^6$, $-N=CNR^6R^7$, $-NR^6R^7$, $-N(R^6)C(=NR^8)NR^6R^7$, $-SR^6$, $-S(O)_{1-2}R^6$, $-SO_2NR^6R^7$, $-CO_2R^6$, $-C(O)NR^6R^7$, $-C(O)N(OR^6)R^7$, $-C(=NR^8)NR^6R^7$, $-N(R^6)SO_2R^6$, $-NC(O)R^6$, $-NCO_2R^6$, $-C(O)R^7$, and R^7 ;

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K is O, S, or NR¹¹;

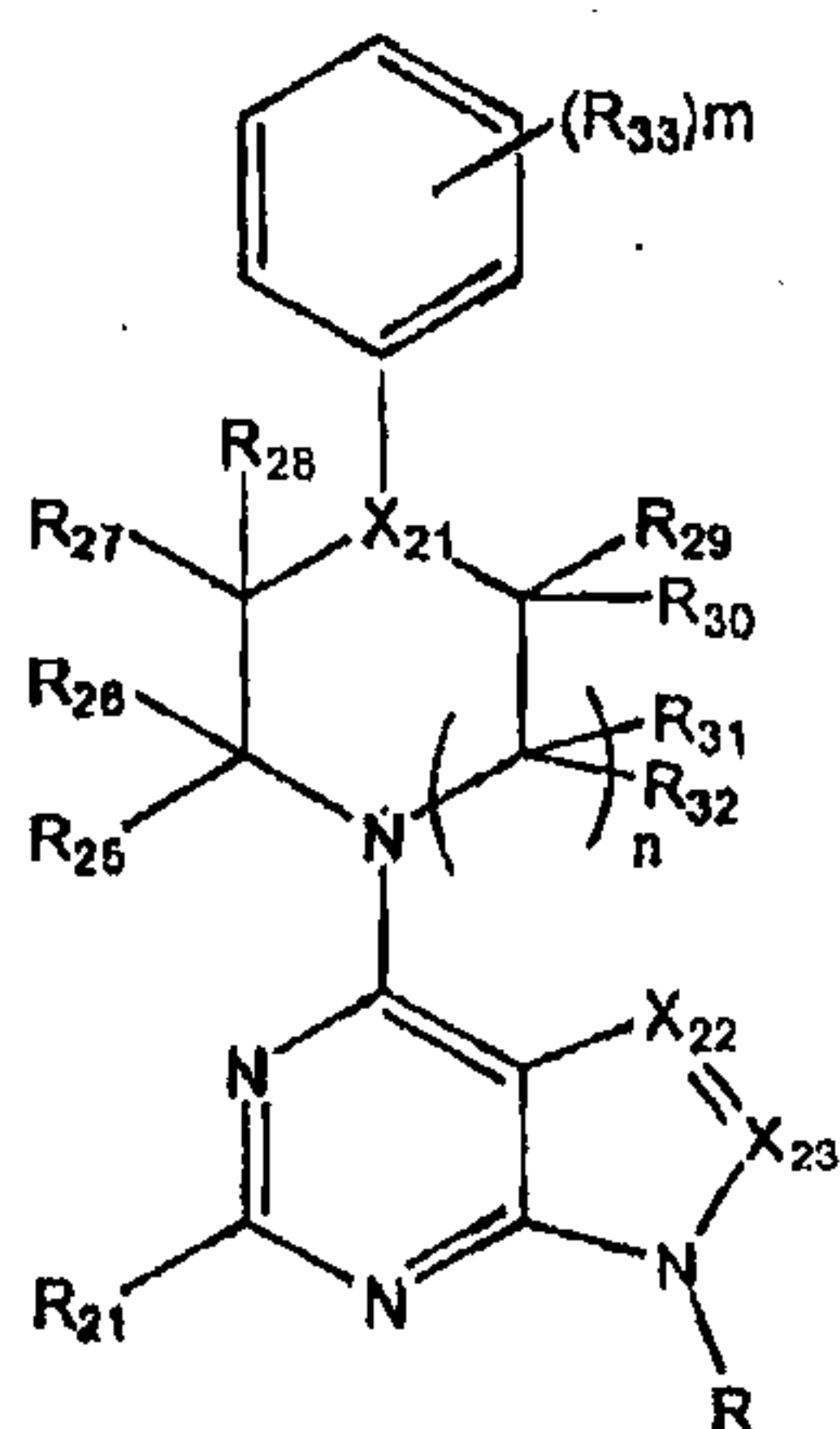
R¹¹ is selected from cyano, -NO₂, -OR⁶, -S(O)₁₋₂R⁶, -SO₂NR⁶R⁷, -CO₂R⁶, -C(O)NR⁶R⁷, -C(O)N(OR⁶)R⁷, -C(O)R⁷, and R⁶; and

each R¹⁵ is independently selected from -H, halogen, -NH₂, -NO₂, -OR⁶, -N=CNR⁶R⁷, -NR⁶R⁷, -N(R⁶)C(=NR⁸)NR⁶R⁷, -SR⁶, -S(O)₁₋₂R⁶, -SO₂NR⁶R⁷, -CO₂R⁶, -C(O)NR⁶R⁷, -C(O)N(OR⁶)R⁷, -C(=NR⁸)NR⁶R⁷, -N(R⁶)SO₂R⁶, -NC(O)R⁶, -NCO₂R⁶, -C(O)R⁷, and R⁷.

The terms used to describe the scope of formula 107 are defined in WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555).

For example "optionally substituted aryl" for formula 107 has the meaning given in WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555). Whenever a compound of formula 107 is described in this application, whether by structure or by use of the term "formula 107," the terms used to describe that compound are defined by WO 2004/050681 (US Nat'l Stage Application Serial No. 10/533,555).

[00163] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula 108:



108

or a pharmaceutically acceptable salt or hydrate thereof, wherein,

X₂₁ is N or CR₂₂;

X₂₂ is N or CR₂₃;

X₂₃ is N or CR₂₄, but when X₂₂ is N then X₂₃ is CR₂₄;

each of R₂₁, R₂₂, R₂₃, R₂₄, R₂₅, R₂₆, R₂₇, R₂₈, R₂₉ and R₃₀, and each R₃₁, R₃₂ and R₃₃ is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NR₃₅R_{35a},

-S(O)₀₋₂R₃₅, -SO₂NR₃₅R_{35a}, -CO₂R₃₅, -C(O)NR₃₅R_{35a}, -N(R₃₅)SO₂R₃₅,
 -N(R₃₅)C(O)R₃₅, -N(R₃₅)CO₂R₃₅, -OR₃₅, -C(O)R₃₅, optionally substituted lower
 alkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally
 substituted heterocyclalkyl, and optionally substituted arylalkyl;

R is selected from -H, halogen, trihalomethyl, -S(O)₀₋₂R₃₅, -SO₂NR₃₅R_{35a}, -CO₂R₃₅,
 -C(O)NR₃₅R_{35a}, -OR₃₅, -C(O)R₃₅, optionally substituted lower alkyl, optionally
 substituted aryl, optionally substituted heterocyclyl, optionally substituted
 heterocyclalkyl, and optionally substituted arylalkyl; or

two of R₂₅, R₂₆, R₂₇, R₂₈, R₂₉, R₃₀, R₃₁ or R₃₂, together with the atom or respective
 atoms to which they are attached, combine to form an optionally substituted
 spirocyclic ring system, optionally substituted fused ring system, and optionally
 substituted saturated bridged ring system;

each of R₃₅ and R_{35a} is independently selected from -H, optionally substituted lower
 alkyl, optionally substituted lower alkoxy, optionally substituted aryl,
 optionally substituted lower arylalkyl, optionally substituted lower aryl alkoxy,
 optionally substituted heterocyclyl, and optionally substituted lower
 heterocyclalkyl; or

R₃₅ and R_{35a}, together with the atom or respective atoms to which they are attached,
 combine to form an optionally substituted five- to seven-membered heterocyclyl;
 and

m is an integer from 0 to 5;

n is an integer from 1 to 2; and

with the provisos that when X₂₂ is CR₂₃ and X₂₃ is N then R is not optionally
 substituted aryl, aralkyl or heteroaryl, and that when X₂₂ is N and X₂₃ is CR₂₄ then
 R is not optional substituted aryl or heteroaryl and R₂₁ is not -NR₃₅R_{35a}, and that
 when X₂₂ is CR₂₃ and X₂₃ is CR₂₄ then R₂₁ is not optionally substituted aryl;

and that compounds 4-(4-(2-fluorophenyl)piperazin-1-yl)-1*H*-pyrazolo[3,4-
 d]pyrimidine, 4-(4-(3-chlorophenyl)piperazin-1-yl)-1*H*-pyrazolo[3,4-
 d]pyrimidine, 6-(4-(2-nitro-4-(trifluoromethyl)phenyl)piperazin-1-yl)-7*H*-purine,
 6-(4-(4-fluorophenyl)piperazin-1-yl)-7*H*-purine, 6-(4-(2,5-
 dimethylphenyl)piperazin-1-yl)-7*H*-purine, 6-(4-(3,4-dichlorophenyl)piperazin-1-
 yl)-7*H*-purine, 6-(4-(2-fluorophenyl)piperazin-1-yl)-7*H*-purine, 6-(4-(3-
 chlorophenyl)piperazin-1-yl)-7*H*-purine, 6-(4-(4-methoxyphenyl)piperazin-1-yl)-
 7*H*-purine, 6-(4-(4-nitrophenyl)piperazin-1-yl)-7*H*-purine, 6-(4-phenylpiperazin-

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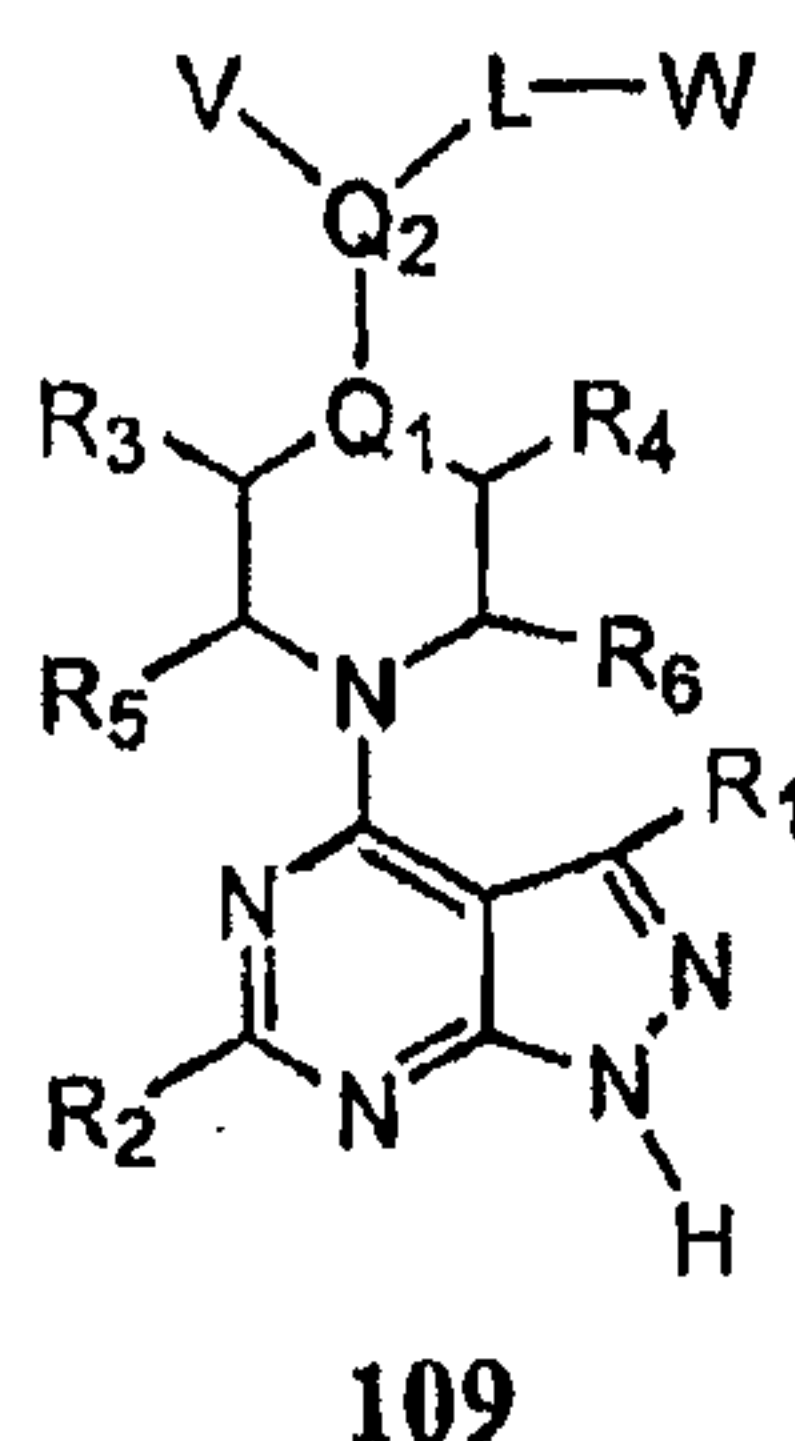
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1-yl)-7*H*-purine, 4-(4-phenylpiperazin-1-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine, 4-phenyl-1-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)piperidin-4-ol, 6-(4-(2-methoxyphenyl)piperazin-1-yl)-7*H*-purine, 6-(4-(2-chlorophenyl)piperazin-1-yl)-7*H*-purine, 6-(4-*o*-tolylpiperazin-1-yl)-7*H*-purine, 6-(4-(3-(trifluoromethyl)phenyl)piperazin-1-yl)-7*H*-purine, 6-(4-(2-methoxyphenyl)piperazin-1-yl)-7*H*-purine are not included in Formula I.

The terms used to describe the scope of formula 108 are defined in WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173).

For example "optionally substituted aryl" for formula 108 has the meaning given in WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173). Whenever a compound of formula 108 is described in this application, whether by structure or by use of the term "formula 108," the terms used to describe that compound are defined by WO 2005/117909 (US Nat'l Stage Application Serial No. 11/568,173).

[00164] In another embodiment, one or more of the chemotherapeutic agent(s) is of formula 109:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

R_1 is H, halo, cyano, aryl, heteroaryl, C_{1-4} alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl, wherein the aryl, heteroaryl, alkyl, alkenyl and alkynyl are optionally substituted with one or two groups independently selected from CO_2R_{10} , $CONR_{10}R_{11}$, OR_{10} , and $NR_{10}R_{11}$;

R_2 is H, NH_2 , SH, OH, or C_1-C_2 alkyl;

R_3 , R_4 , R_5 , and R_6 are each independently H, oxo, CO_2R_{10} , $CONR_{10}R_{11}$, C_{1-4} alkyl, C_1-C_6 alkoxy, or C_1-C_6 alkoxy- C_1-C_4 alkyl, wherein the C_1-C_4 alkyl, C_1-C_6 alkoxy and C_1-C_6 alkoxy- C_1-C_4 alkyl in each group are independently optionally substituted with

1 or 2 substituents independently selected from CO_2R_{10} , $\text{CONR}_{10}\text{R}_{11}$, OR_{10} , and $\text{NR}_{10}\text{R}_{11}$, or

R_3 and R_5 together with the carbons to which they are attached form a $\text{C}_3\text{-C}_7$ carbocyclic ring, wherein the ring is optionally substituted with H, halo, cyano, nitro, or amino,

R_4 and R_6 together with the carbons to which they are attached form a $\text{C}_3\text{-C}_7$ carbocyclic ring, wherein the ring is optionally substituted with H, halo, cyano, nitro, or amino

R_3 and R_6 together with the carbons to which they are attached form a bridged $\text{C}_5\text{-C}_7$ carbocyclic ring, wherein the ring is optionally substituted with H, halo, cyano, nitro, or amino, or

R_4 and R_5 together with the carbons to which they are attached form a bridged $\text{C}_5\text{-C}_7$ carbocyclic ring, wherein the ring is optionally substituted with H, halo, cyano, nitro, or amino;

L is C_{0-4} alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $-\text{N}(\text{R}_{12})-$, $-\text{C}(\text{O})\text{N}(\text{R}_{12})-$, $-\text{N}(\text{R}_{12})\text{C}(\text{O})-$, $-\text{C}(\text{O})-$, $-\text{O}(\text{CH}_2)_n-$, or $-(\text{CH}_2)_n\text{-O}-$, wherein n is 1-4;

Q_1 is N or CR_{13} , wherein R_{13} is H or $\text{C}(\text{O})\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$;

Q_2 is a bond, CR_{14} , O or N, wherein R_{14} is H, OH, C_{1-4} alkyl, C_{1-4} alkoxy, $\text{NR}_{15}\text{R}_{15}$, wherein R_{15} is H or C_{1-4} alkyl, or Q_2 and V together form $\text{C}(=\text{O})$;

when Q_2 is a bond,

V is absent and R_{13} is not H;

when Q_1 is CR_{13} and Q_2 is CH,

V is H, OH, NH_2 , C_{1-6} alkoxy, $\text{NR}_{10}\text{R}_{11}$, $\text{O}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $\text{O}(\text{CH}_2)_n$ attached to a C or N of a 4-7 membered heterocyclyl, $\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$,

$\text{NR}_{12}\text{C}(\text{O})\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $\text{NR}_{12}\text{C}(\text{O})(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$,

$(\text{CH}_2)_m\text{O}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $(\text{CH}_2)_m\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$,

$(\text{CH}_2)_m\text{CHR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, C_{1-4} alkyl optionally substituted with OH or $\text{NR}_{10}\text{R}_{11}$, or

V is a 4-7 membered unsaturated cyclic containing 1-3 atom of O or N, or

V is a bicyclic solublizing group;

when Q_1 is N and Q_2 is CH, or when Q_1 is CR_{13} and Q_2 is O or N,

V is H, $(\text{CH}_2)_m\text{O}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $(\text{CH}_2)_m\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$,

$(\text{CH}_2)_m\text{CHR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $\text{C}(\text{O})\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $\text{C}(\text{O})$

$(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $\text{C}(\text{O})\text{O}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$, $\text{C}(\text{O})\text{C}(\text{O})\text{NR}_{12}(\text{CH}_2)_n\text{NR}_{10}\text{R}_{11}$,

SO₂(CH₂)_nNR₁₀R₁₁, C(O)-C₂-C₆ alkenyl, or C₁₋₄ alkyl optionally substituted with OH or NR₁₀R₁₁, or

V is a 4-7 membered saturated or unsaturated cyclic or heterocyclic containing 1-3 atoms of O or N, optionally substituted with 1 or 2 C₁-C₃ alkoxy groups or

V is a "bicyclic solublizing group";

m is 1-3,

n is 1-4,

W is C₁-C₆ alkyl, NR₁₀R₁₁, or W is

aryl, C₃-C₇ cycloalkyl, heterocyclyl, heteroaryl, or 5-12 membered fused bicyclic or tricyclic saturated, partially saturated, or unsaturated ring system containing 0-4 ring atoms selected from N, O, and S, wherein each aryl, cycloalkyl, heterocyclyl, heteroaryl, and fused bicyclic or tricyclic ring system is optionally substituted with 1, 2, or 3 substituents independently selected from halo, CN, NO₂, CF₃, OH, NR₁₀R₁₁, C₁-C₆ alkoxy, C₁-C₆ alkyl, NO₂, C(O)OC₁-C₆ alkyl, C(O)NR₁₂-C₁-C₆ alkoxy, C(O)NR₁₂-heterocyclyl, aryl, O-aryl, O-CH₂-aryl, N-aryl, wherein each aryl substituent is optionally further substituted with halo, or

V, Q₂, L, and W together form an aryl ring, heteroaryl ring, C₃-C₇ cycloalkyl ring, heterocyclyl ring, or a 5-12 membered fused bicyclic or tricyclic saturated, partially saturated or unsaturated ring system containing 0-4 ring atoms selected from N, O, and S, wherein each ring or ring system is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO₂, CF₃, OH, NR₁₀R₁₁, C₁-C₆ alkoxy, C₁-C₆ alkyl, NO₂, C(O)OC₁-C₆ alkyl, C(O)NR₁₂-C₁-C₆ alkoxy, C(O)NR₁₂-heterocyclyl, aryl, O-aryl, NH-aryl, wherein each aryl substituent is optionally further substituted with halo; and

R₁₀, R₁₁ and R₁₂ are each independently H or C₁₋₆ alkyl which is optionally substituted with aryl or heteroaryl,

provided the compound is not a compound selected from:

4-(4-(2-fluorophenyl)piperazin-1-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidine;
4-(4-(3-chlorophenyl)piperazin-1-yl)-1*H*-pyrazolo[3,4-*d*]pyrimidine;
ethyl 4-(1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)piperazine-1-carboxylate;
tert-butyl 4-(1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)piperazine-1-carboxylate; and
N-(4-phenoxyphenyl)-4-(1*H*-pyrazolo[3,4-*d*]pyrimidin-4-yl)piperazine-1-carboxamide.

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The terms used to describe the scope of formula 109 are defined in WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291).

For example "optionally substituted aryl" for formula 109 has the meaning given in WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291). Whenever a compound of formula 109 is described in this application, whether by structure or by use of the term "formula 109," the terms used to describe that compound are defined by WO 2006/071819 (US Nat'l Stage Application Serial No. 11/722,291).

[00165] For each of the foregoing embodiments, the Compound of Formula I can be selected from any of the following embodiments, including from the Representative Compounds in Table 1.

[00166] In another embodiment of the Invention, the Compound of Formula I is that where R^7 is halo and all other groups are as defined in the Summary of the Invention for Group A, Group B, Group C, or Group D. In another embodiment, R^7 is iodo or bromo. In another embodiment, R^7 is iodo. In another embodiment, the compound is that where R^7 is iodo or bromo and all other groups are as defined in the Summary of the Invention for Group A.

[00167] In another embodiment of the Invention, the Compound of Formula I is that where X is halo and all other groups are as defined in the Summary of the Invention for Group A, Group B, Group C, or Group D. In another embodiment, X is fluoro or chloro. In another embodiment, X is fluoro. In another embodiment, the compound is that where X is fluoro or chloro and all other groups are as defined in the Summary of the Invention for Group A.

[00168] In another embodiment of the Invention, the Compound of Formula I is that where R^7 and X are halo and all other groups are as defined in the Summary of the Invention for Group A, Group B, Group C, or Group D. More specifically, R^7 is iodo and X is fluoro. In another embodiment, the compound is that where R^7 is iodo and X is fluoro and all other groups are as defined in the Summary of the Invention for Group A.

[00169] In another embodiment of the Invention, the Compound of Formula I is that where R^1 , R^2 , R^5 , and R^6 are hydrogen and all other groups are as defined in the Summary of the Invention for Group A, Group B, Group C, or Group D. In another embodiment, R^1 , R^2 , R^5 , and R^6 are hydrogen and all other groups are as defined in the Summary of the Invention for Group A.

[00170] In another embodiment of the Invention, the compound of Formula I is selected from Group A where all groups are as defined in the Summary of the Invention.

[00171] In another embodiment of the invention (A1), the Compound of Formula I is that where X and R⁷ are halo and all other groups are as defined in the Summary of the Invention for a compound of Group A.

[00172] In another embodiment (A2), the compound of Formula I is selected from Group A where R¹⁰ and R¹² are independently hydrogen or halo. In another embodiment, R¹⁰ and R¹² are independently hydrogen or fluoro. In another embodiment, R¹⁰ is 3-fluoro and R¹² is hydrogen. In another embodiment, R¹⁰ and R¹² are fluoro, in another embodiment, 3-fluoro and 4-fluoro, 4-fluoro and 5-fluoro, or 4-fluoro and 6-fluoro.

[00173] In another embodiment of the invention (A3), the compound of Formula I is that where R¹, R², R⁵ and R⁶ are hydrogen and all other groups are as defined in the Summary of the Invention for Group A.

[00174] In another embodiment (A4), the compound of Formula I is selected from Group A where X, R⁷, and A are as defined in the Summary of the Invention; and one of R¹, R², R³, R⁴, R⁵, and R⁶ is halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, -CH₂N(R²⁵)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂)), -CH₂NR²⁵C(=NH)(N(R^{25a})(CN)), -CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; and the others of R¹, R², R³, R⁴, R⁵, and R⁶ are as defined in the Summary of the Invention; or

one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached forms $C(O)$ or $C(=NOH)$; and the others of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are as defined in the Summary of the Invention.

[00175] In another embodiment of the Invention (A5), the compound of Formula I is selected from Group A where X , R^7 , and A are as defined in the Summary of the Invention; and

R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the Summary of the Invention; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and

R^1 , R^2 , R^5 and R^6 are as defined in the Summary of the Invention.

[00176] In another embodiment of embodiment A5, the Compound of Formula I is that where R^1 , R^2 , R^5 and R^6 are hydrogen.

[00177] In another embodiment of the Invention (A6), the compound of Formula I is selected from Group A where X , R^7 , and A are as defined in the Summary of the Invention; and

R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$,

-CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂),
 -CH₂NR²⁵C(=NH)(N(R^{25a})(CN), -CH₂NR²⁵C(=NH)(R²⁵),
 -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl,
 heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl,
 heteroaryl, and heterocycloalkyl are independently optionally substituted with
 one, two, three, four, five, six or seven groups independently selected from
 halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally
 substituted heterocycloalkyl, optionally substituted aryl, optionally substituted
 arylalkyl, optionally substituted heteroaryl, optionally substituted
 heteroarylalkyl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -
 C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'};
 or

R³ and R⁴ together with the carbon to which they are attached form C(O) or
 C(=NOH);

R¹, R², R⁵ and R⁶ are as defined in the Summary of the Invention.

[00178] In another embodiment of embodiment A, the Compound of Formula I is
 that where R¹, R², R⁵ and R⁶ are hydrogen.

[00179] In another embodiment of the Invention (A7), the compound of Formula I
 is selected from Group A where X and R⁷ are halo; A is phenylene optionally
 substituted with R¹⁰ and R¹² where R¹⁰ and R¹² are independently hydrogen or halo;
 R¹, R², R⁵ and R⁶ are hydrogen;

R³ is hydrogen and R⁴ is -NR⁸R^{8'} (where R⁸ is hydrogen, hydroxy, alkyl, alkoxy, aryl,
 cycloalkyl, heteroaryl, or heterocycloalkyl and R^{8'} is hydroxy, alkoxy, aryl,
 cycloalkyl, heteroaryl, or heterocycloalkyl), -NHS(O)₂R⁸, -CN, -S(O)_mR⁸,
 -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'},
 -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, alkenyl, and alkynyl; where
 the alkenyl and alkynyl are optionally substituted with one, two, three, four,
 five, six or seven groups independently selected from halo, alkyl, haloalkyl,
 nitro, optionally substituted cycloalkyl, optionally substituted
 heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl,
 optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸,
 -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -
 NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; or

R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

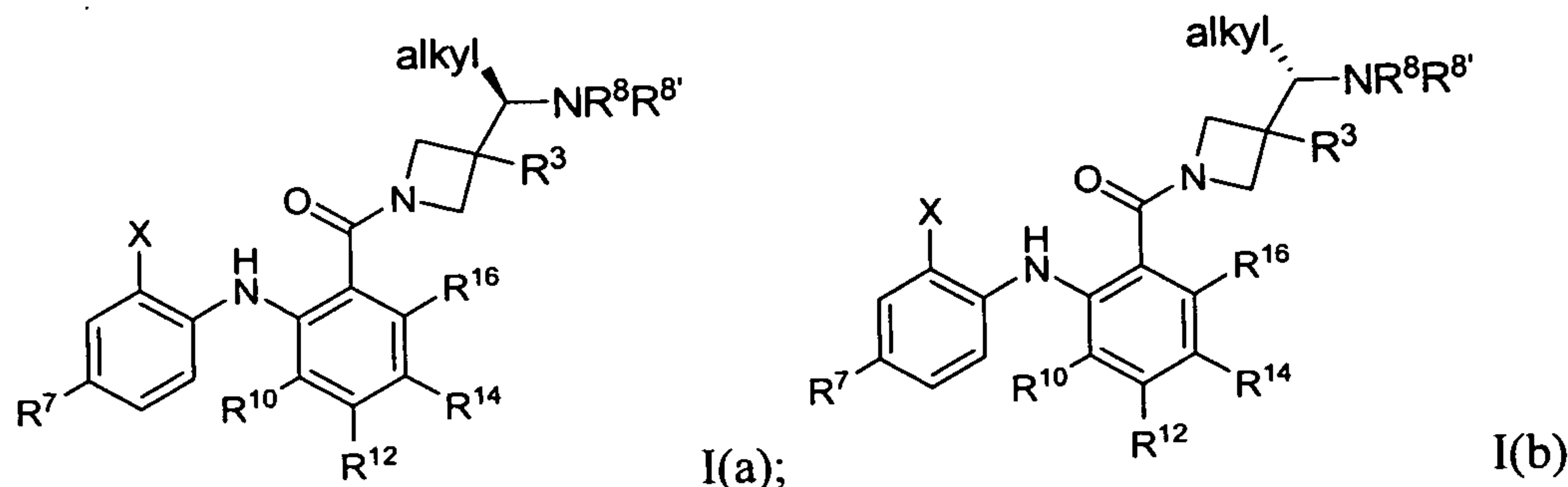
m , $R^{8''}$, and R^9 are as defined in the Summary of the Invention for a compound of Group A; and unless otherwise specified in this embodiment, R^8 and $R^{8'}$ are as defined in the Summary of the Invention for a compound of Group A.

[00180] In another embodiment of the Invention (A8), the compound of Formula I is selected from Group A where R^3 is hydrogen, halo, hydroxy, alkoxy, or amino. In another embodiment, R^3 is hydrogen, fluoro, hydroxy, methoxy, or amino. In another embodiment, R^3 is hydrogen or hydroxy. In another embodiment, R^3 is hydroxy.

[00181] In another embodiment of embodiment A8, the Compound of Formula I is that where X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12} where R^{10} and R^{12} are independently hydrogen or halo; R^1 , R^2 , R^5 and R^6 are hydrogen; and R^4 , is as defined in the Summary of the Invention for a compound of Group A.

[00182] Another embodiment of the Invention (A9) is that where the compound of Formula I is selected from Group A where R^1 , R^2 , R^5 and R^6 are hydrogen; R^3 is hydrogen, halo, hydroxy, alkoxy, or amino; and R^4 is heterocycloalkyl, heteroaryl, or alkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ and all other groups are as defined in the Summary of the Invention for a compound of Group A.

[00183] In another embodiment of embodiment A9, the Compound of Formula I is that where R^4 is alkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ and all other groups are as defined in the Summary of the Invention for a compound of Group A. In another embodiment, the compound is of Formula I(a) or I(b):



where R^3 is as defined in A9; X , R^7 , R^8 , $R^{8'}$, R^{10} , R^{12} , R^{14} , and R^{16} are as defined in the Summary of the Invention for a compound of Group A.

[00184] In another embodiment of embodiment A9, the Compound of Formula I is that where R^4 is heterocycloalkyl.

[00185] In another embodiment of embodiment A9, the compound of Formula I is that where X and R⁷ are halo; A is phenylene optionally substituted with R¹⁰ and R¹² where R¹⁰ and R¹² are independently hydrogen or halo; R³ is hydroxy; and R⁴ is alkyl substituted with -NR⁸R^{8'} or R⁴ is heterocycloalkyl optionally substituted with one, two, or three groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR⁸R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; and where m, R³, R⁸, R^{8'}, R^{8''}, and R⁹ are as defined in the Summary of the Invention for a compound of Group A.

[00186] In another embodiment of the Invention (A10), the compound of Formula I is selected from Group A where

R⁴ is

- a) hydrogen;
- b) -CH₂N(R²⁵)(NR^{25a}R^{25b});
- c) -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b});
- d) -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂));
- e) -CH₂NR²⁵C(=NH)(N(R^{25a})(CN));
- f) -CH₂NR²⁵C(=NH)(R²⁵);
- g) -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂);
- h) alkyl;
- i) alkyl substituted with one or two -OR⁸ where R⁸ is hydrogen, aryl, or alkyl where the alkyl is substituted with one or two hydroxy;
- j) alkyl substituted with one, two, or three halo;
- k) alkyl substituted with nitro;
- l) alkyl substituted with -S(O)_mR⁹ (where m is 0 and R⁹ is aryl);
- m) alkyl substituted with optionally substituted heterocycloalkyl;
- n) alkenyl;
- o) -NR⁸R^{8'} (where R⁸ and R^{8'} are independently hydrogen; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with one or two -NR³⁰R^{30'} where R³⁰ and R^{30'} are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with optionally substituted heteroaryl; or alkyl substituted with optionally substituted cycloalkyl);

- p) $-C(O)NR^8R^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; hydroxy; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; or optionally substituted alkoxy);
- q) $-NR^8C(O)OR^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl);
- r) alkyl substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen, alkyl, alkenyl, alkynyl, or alkyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; hydroxy; alkoxy; alkyl; alkenyl; alkynyl; optionally substituted alkoxy; alkyl substituted with one or two hydroxy; alkyl substituted with one or two alkoxy; alkyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with one or two hydroxy and one or two $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with one, two, three, four, or five halo; alkyl substituted with optionally substituted cycloalkyl; alkyl substituted with optionally substituted aryl; alkyl substituted with one or two hydroxy and one optionally substituted aryl; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with optionally substituted heteroaryl; heteroaryl; aryl; aryl substituted with one or two hydroxy; aryl substituted with one or two alkoxy; aryl substituted with one or two halo; aryl substituted with one or two $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl; aryl substituted with $-NR^{34}SO_2R^{34a}$ where R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl; cycloalkyl; cycloalkyl substituted with one or two hydroxy; cycloalkyl substituted with one or two hydroxy and one or two hydroxyalkyl; cycloalkyl substituted with one or two alkoxy; cycloalkyl substituted with carboxy; cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; alkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; cycloalkyl substituted with optionally substituted cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted with alkyl; heterocycloalkyl substituted with alkoxycarbonyl; heterocycloalkyl substituted with optionally substituted arylalkyl; heterocycloalkyl substituted

- with one or two hydroxy; heterocycloalkyl substituted with one or two alkoxy; heterocycloalkyl substituted with one or two hydroxyalkyl; heterocycloalkyl substituted with one or two hydroxy, one or two alkoxy, and one or two hydroxyalkyl; alkyl substituted with optionally substituted aryloxy; alkyl substituted with $-S(O)_nR^{31}$ where n is 0 and R^{31} is alkyl; alkyl substituted with carboxy; alkyl substituted with alkoxycarbonyl; or alkyl substituted with $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl);
- s) $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; alkyl; alkyl substituted with one or two hydroxy; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, hydroxyalkyl, or alkenyl);
- t) cycloalkyl;
- u) cycloalkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;
- v) heterocycloalkyl;
- w) heterocycloalkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;
- x) heterocycloalkyl substituted with one or two alkyl;
- y) heterocycloalkyl substituted with $-C(O)OR^8$ where R^8 is alkyl or alkenyl;
- z) alkyl substituted with $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl and $R^{8'}$ is alkyl; alkenyl; or alkyl substituted with alkoxy, aryl, and one, two, or three halo);
- aa) heteroaryl;
- bb) heteroaryl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl; alkyl substituted with optionally substituted heteroaryl;
- cc) alkyl substituted with $-NR^8S(O)_2R^9$ where R^8 is hydrogen, alkyl, or alkenyl and R^9 is alkyl or alkenyl;
- dd) alkyl substituted with $-NR^8C(O)OR^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;
- ee) alkyl substituted with one aryl and one $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl; or

ff) alkyl substituted with one or two $-OR^8$ (where R^8 is hydrogen) and one or two $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl.

[00187] In another embodiment, R^4 is hydrogen, $-CH_2N(H)(NHCH_3)$, $-CH_2NHC(=NH)(NH_2)$, $-CH_2NHC(=NH)(NHNO_2)$, $-CH_2NHC(=NH)(NHCN)$, $-CH_2NHC(=NH)(phenyl)$, $-CH_2NHC(NH_2)=CH(NO_2)$, methyl, ethyl, hydroxymethyl, 2,3-dihydroxypropyl, 3-hydroxy-2-methyl-prop-2-yl, *N*-(1-methoxy-prop-2-yl)-aminomethyl, *N*-(ethoxypropyl)-aminomethyl, *N*-(ethoxyethyl)-aminomethyl, *N*-(2,2-dimethoxyethyl)-aminomethyl, *N*-(methoxyethyl)-aminomethyl, *N*-(isopropoxyethyl)-aminomethyl, trifluoromethyl, 1-nitro-ethyl, 1-methyl-1-nitro-ethyl, 1-nitro-propyl, 3-methyl-1-nitro-butyl, phenylthiomethyl, allyl, ethenyl, 2-methylthio-ethylaminomethyl, 3-methylthio-propylaminomethyl, *N*-(*tert*-butoxycarbonylaminopropyl)-aminomethyl, *N*-(1-carboxyethyl)-aminomethyl, *N*-(1*R*-carboxyethyl)-aminomethyl, *N*-(1*S*-carboxyethyl)-aminomethyl, *N*-(1-methoxycarbonyl-ethyl)-aminomethyl, $-NH_2$, $-NH(CH_2)_3CH_3$, $-NHCH_3$, $-NH(CH_2CH_3)$, $-NHCH_2CH(CH_3)_2$, $-NHCH_2CH_2OH$, $-NHCH_2CH_2CH_2NH_2$, $-N(CH_3)CH_2CH_2(heteroaryl)$, $-NHCH_2(cycloalkyl)$, $-C(O)NH_2$, $-C(O)NHOH$, $-C(O)NH(OCH_2CH(OH)CH_2OH)$, $-C(O)NH(CH_2)_3CH_3$, $-C(O)NHCH_2CH=CH_2$, $-C(O)NHCH_2CH_3$, $-C(O)NHCH_2CH_2OH$, $-C(O)NHCH_2CH(OH)CH_2OH$, $-C(O)NHCH_2CH_2CH(OH)CH_2OH$, $-C(O)NHCH_2CH_2(piperidin-1-yl)$, $-C(O)NH(phenyl)$, $-C(O)NHCH_2CH_2N(CH_2CH_3)_2$, $-NHC(O)OC(CH_3)_3$, $-NHC(O)OCH_3$, azetidinylmethyl, pyrrolidinylmethyl, 3-hydroxy-pyrrolidinylmethyl, 2-(methoxymethyl)-pyrrolidinylmethyl, 2*S*-(methoxymethyl)-pyrrolidinylmethyl, 2*R*-(methoxymethyl)-pyrrolidinylmethyl, morpholinylmethyl, hydroxypiperidinylmethyl, 4-alkyl-piperazinylmethyl, 4-alkyl-homopiperazinylmethyl, 4-(heterocycloalkyl)-piperidinylmethyl, 4-(dialkylaminoalkyl)-piperazinylmethyl, *N*-hydroxyaminomethyl, *N*-methoxyaminomethyl, *N*-ethoxyaminomethyl, *N*-ethylaminomethyl, 1-(*N*-ethyl-amino)-ethyl, *N,N*-diethylaminomethyl, *N,N*-dimethylaminomethyl, aminomethyl, 1-amino-ethyl, 1*R*-amino-ethyl, 1*S*-amino-ethyl, 1-(methylamino)-ethyl, 1-(*N,N*-dimethylamino)-ethyl, 1-amino-1-methyl-ethyl, 1-aminopropyl, 1*S*-aminopropyl, 1*R*-aminopropyl, *N*-(*n*-propyl)-aminomethyl, *N*-(isopropyl)-aminomethyl, 2-(*N*-isopropylamino)-ethyl, 3-(*N*-isopropylamino)-2-methyl-prop-2-yl, 1-(*N*-ethyl-amino)-propyl, 1-(*N,N*-diethyl-amino)-propyl, 1-aminobutyl, 1-amino-isobutyl, *N*-(2-aminoethyl)-aminomethyl, *N*-(*n*-butyl)-aminomethyl, *N*-isobutylaminomethyl, *tert*-butylaminomethyl, 1-(*tert*-butylamino)-ethyl,

sec-butylaminomethyl, *N*-(2-methyl-but-3-yl)-aminomethyl, *N*-(3,3-dimethyl-butyl)-aminomethyl, *N*-(3-methylbut-3-yl)-aminomethyl, *N*-(2-methylbutyl)-aminomethyl, *N*-(pent-3-yl)-aminomethyl, *n*-pentylaminomethyl, isopentylaminomethyl, *sec*-pentylaminomethyl, neopentylaminomethyl, *N*-(2,2,4-trimethyl-pent-4-yl)-aminomethyl, *N*-(2-ethyl-butyl)-aminomethyl, *N*-allyl-aminomethyl, 3-methyl-but-1-yn-3-ylaminomethyl, *N*-(2,3-dihydroxypropyloxy)-aminomethyl, *N*-cyclopropylaminomethyl, *N*-cyclobutylaminomethyl, *N*-cyclopentylaminomethyl, *N*-cyclopenten-4-ylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1(*R,S*)-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(3,4-dihydroxy-cyclopentyl)-aminomethyl, *N*-(1-hydroxymethyl-cyclopent-1-yl)-aminomethyl, *N*-(2,3-dihydroxy-4-hydroxymethyl-cyclopentyl)-aminomethyl, *N*-(1(*R,S*)-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1-carboxy-cyclopentyl)-aminomethyl, *N*-cyclohexylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(*cis*-4-hydroxy-cyclohexyl)-aminomethyl, *N*-(*trans*-4-hydroxy-cyclohexyl)-aminomethyl, 1-[*N*-(*cis*-4-hydroxy-cyclohexyl)-amino]-ethyl, 1-[*N*-(*trans*-4-hydroxy-cyclohexyl)-amino]-ethyl, *N*-(1(*R*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1(*S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1-hydroxymethyl-cyclohexyl)-aminomethyl, *N*-(2-cyclohexyl-cyclohexyl)-aminomethyl, *N*-{(2*R*,3*S*,4*R*,6*R*)-2-(hydroxymethyl)-3,4-dihydroxy-6-methoxy-tetrahydro-2*H*-pyran-5-yl}-aminomethyl, *N*-(cycloheptyl)-aminomethyl, *N*-(cyclooctyl)-aminomethyl, [(1*r*,3*r*,5*R*,7*R*)-tricyclo[3.3.1.1^{3,7}]dec-2-ylamino]methyl, *N*-[1-(cyclopropylaminocarbonyl)-cyclopentyl]-aminomethyl, -CH₂NHC(CH₃)₂C(O)NH(cyclohexyl), -CH₂NHC(CH₃)₂C(O)NH(CH₂CH₃), *N*-(1-benzyloxy-cyclopent-2-yl)-aminomethyl, *N*-(cyclopropylmethyl)-aminomethyl, *N*-(cyclohexylmethyl)-aminomethyl, *N*-(1-cyclohexylethyl)-aminomethyl, *N*-(imidazolyl)-aminomethyl, *N*-(1,3,5-triazinyl)-aminomethyl, *N*-(5-hydroxy-pyrazol-3-yl)-aminomethyl, *N*-(5-methyl-pyrazol-3-yl)-aminomethyl, *N*-(benzimidazolyl)-aminomethyl, *N*-(pyrimidin-2-yl)-aminomethyl, *N*-(pyridin-2-yl)-aminomethyl, *N*-(pyridin-3-yl)-aminomethyl, *N*-(pyridin-4-yl)-aminomethyl, *N*-indan-1-yl-aminomethyl, *N*-indan-2-yl-aminomethyl, phenylaminomethyl, *N*-(2-hydroxyphenyl)-aminomethyl, *N*-(3-hydroxyphenyl)-aminomethyl, *N*-(4-

hydroxyphenyl)-aminomethyl, *N*-(2-methoxyphenyl)-aminomethyl, *N*-(3-methoxyphenyl)-aminomethyl, *N*-(4-methoxyphenyl)-aminomethyl, *N*-(2-fluorophenyl)-aminomethyl, *N*-(3-fluorophenyl)-aminomethyl, *N*-(4-fluorophenyl)-aminomethyl, *N*-(2-chlorophenyl)-aminomethyl, *N*-(3-chlorophenyl)-aminomethyl, *N*-(4-chlorophenyl)-aminomethyl, *N*-(3-methylcarbonylamino-phenyl)-aminomethyl, *N*-(4-methylcarbonylamino-phenyl)-aminomethyl, *N*-(2-aminophenyl)-aminomethyl, *N*-(3-aminophenyl)-aminomethyl, *N*-(4-aminophenyl)-aminomethyl, *N*-(2-methylsulfonylamino-phenyl)-aminomethyl, *N*-(3-methylsulfonylamino-phenyl)-aminomethyl, *N*-(4-methylsulfonylamino-phenyl)-aminomethyl, *N*-(2-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(3-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(benzyl)-aminomethyl, *N*-(2-hydroxyphenylmethyl)-aminomethyl, *N*-(3-hydroxyphenylmethyl)-aminomethyl, *N*-(4-hydroxyphenylmethyl)-aminomethyl, *N*-(2-(*N*-methylpiperazin-1-yl)-phenylmethyl)-aminomethyl, *N*-(4-alkyl-phenethyl)-aminomethyl, *N*-(1-hydroxy-3-phenyl-prop-2-yl)-aminomethyl, *N*-(pyrrolidin-2-ylmethyl)-aminomethyl, *N*-(*N*-alkyl-pyrrolidinylmethyl)-aminomethyl, *N*-(*N*-alkyl-pyrrolidinylethyl)-aminomethyl, *N*-(pyrrolidinylpropyl)-aminomethyl, *N*-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-aminomethyl, *N*-(tetrahydrofuranylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyran-4-ylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyranylethyl)-aminomethyl, *N*-(piperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-*tert*-butoxycarbonylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-4-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-5-ylmethyl)-aminomethyl, *N*-[2-(imidazol-4-yl)-ethyl]-aminomethyl, *N*-[3-(imidazolyl)-propyl]-aminomethyl, *N*-(pyridin-3-ylethyl)-aminomethyl, *N*-(pyridin-4-ylethyl)-aminomethyl, *N*-(thien-2-ylethyl)-aminomethyl, *N*-(furan-2-ylethyl)-aminomethyl, *N*-(5-methyl-1,3,4-oxadiazol-2-ylmethyl)-aminomethyl, *N*-(2-indolin-3-ylethyl)-aminomethyl, 2-(*N,N*-dimethylamino)-ethylaminomethyl, 2-(*N,N*-dimethylamino)-1-methyl-ethylaminomethyl, 3-aminopropylaminomethyl, 3-(*N,N*-dimethylamino)-propylaminomethyl, 3-(*N,N*-diethylamino)-propylaminomethyl, *N*-(*N,N*-diisopropylaminoethyl)-aminomethyl, *N*-(*N,N*-dimethylaminobutyl)-aminomethyl, *N*-(3-hydroxypropyl)-aminomethyl, *N*-(2-hydroxypropyl)-aminomethyl, *N*-(1,2-dihydroxypropyl)-aminomethyl, *N*-(1-amino-2-hydroxy-prop-3-yl)-aminomethyl, *N*-(*N*-ethoxycarbonyl-piperidin-4-yl)-aminomethyl, *N*-(*N*-benzylpiperidin-4-yl)-aminomethyl, *N*-(homopiperidin-3-yl)-aminomethyl, *N*-(*N*-benzylpyrrolidin-3-yl)-aminomethyl, *N*-(*N*-ethylpiperidin-3-yl)aminomethyl,

2,2,2-trifluoroethylaminomethyl, 3,3,3-trifluoropropylaminomethyl, 2,2,3,3,3-pentafluoropropylaminomethyl, $-\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $-\text{CH}_2\text{N}(\text{CH}_3)(\text{CH}_2\text{CH}_2\text{OH})$, $-\text{CH}_2\text{NH}(\text{CH}_2\text{CH}_2\text{OH})$, $-\text{CH}_2\text{NH}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH})$, $-\text{CH}_2\text{N}(\text{CH}_3)(N\text{-methyl-pyrrolidin-3-yl})$, $-\text{CH}_2\text{NH}(\text{C}(\text{CH}_3)_2\text{CH}_2\text{OH})$, $-\text{NHC}(\text{O})\text{CH}(\text{CH}_3)_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{NH}(\text{CH}_3)$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $-\text{NHC}(\text{O})\text{CH}_2\text{NH}_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $-\text{NHC}(\text{O})\text{CH}_2(4\text{-alkyl-piperazinyl})$, $-\text{NHC}(\text{O})\text{CH}_2(\text{piperidinyl})$, $N\text{-(phenyloxyethyl)-aminomethyl}$, cyclopentyl, 1-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, *cis*-2-amino-cyclopentyl, *trans*-2-amino-cyclopentyl, (*cis,trans*)-2-hydroxy-cyclohexyl, *cis*-2-hydroxy-cyclohexyl, *trans*-2-hydroxy-cyclohexyl, (*cis,trans*)-2-amino-cyclohexyl, *cis*-2-amino-cyclohexyl, *trans*-2-amino-cyclohexyl, azetidin-3-yl, pyrrolidinyl, $N\text{-alkyl-pyrrolidinyl}$, 3-(dialkylamino)-pyrrolidinyl, piperidinyl, 2-methyl-piperidin-6-yl, $N\text{-tert-butoxycarbonylpiperidin-2-yl}$, piperazinyl, $-\text{CH}_2\text{NHC}(\text{O})\text{CH}_3$, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{O})\text{CH}_3$, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{O})\text{C}(\text{OCH}_3)(\text{CF}_3)\text{phenyl}$, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, imidazol-1-yl, imidazol-2-yl, imidazol-4-yl, imidazol-5-yl, $N\text{-methyl-imidazol-2-yl}$, 5-methyl-imidazol-2-yl, 1,2,4-triazol-3-yl, thiazol-2-yl, 2-aminopyrimidin-3-yl, pyridinyl, benzimidazolyl, imidazol-1-ylmethyl, imidazol-2-ylmethyl, triazolylmethyl, (5-amino-3-methylpyrazol-1-yl)-methyl, phenoxymethyl, methylsulfonylaminomethyl, 1-(methoxycarbonylamino)-ethyl, 1-amino-1-phenylmethyl, or 1-amino-3-hydroxy-propyl.

[00188] In another embodiment of embodiment A10, the Compound of Formula I is that where X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12} where R^{10} and R^{12} are independently hydrogen or halo; R^1 , R^2 , R^5 and R^6 are hydrogen; and R^3 is hydrogen, halo, hydroxy, alkoxy, or amino.

[00189] In another embodiment of embodiment A10, the Compound of Formula I is that where R^3 is hydrogen and R^4 is

- a) hydrogen;
- b) $-\text{NR}^8\text{R}^{8'}$ (where R^8 and $\text{R}^{8'}$ are independently hydrogen; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with one or two $-\text{NR}^{30}\text{R}^{30'}$ where R^{30} and $\text{R}^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with optionally substituted heteroaryl; or alkyl substituted with optionally substituted cycloalkyl);

- c) $-\text{C}(\text{O})\text{NR}^8\text{R}^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl; and $\text{R}^{8'}$ is hydrogen; hydroxy; alkyl; alkenyl; alkyl substituted with one or two hydroxy; alkyl substituted with heterocycloalkyl; alkyl substituted with $-\text{NR}^{30}\text{R}^{30'}$ where R^{30} and $\text{R}^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; or optionally substituted alkoxy);
- d) $-\text{NR}^8\text{C}(\text{O})\text{OR}^{8'}$ (where R^8 and $\text{R}^{8'}$ are independently hydrogen, alkyl, or alkenyl);
- e) $-\text{NR}^8\text{C}(\text{O})\text{R}^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl; and $\text{R}^{8'}$ is hydrogen; alkyl; alkyl substituted with one or two hydroxy; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with $-\text{NR}^{30}\text{R}^{30'}$ where R^{30} and $\text{R}^{30'}$ are independently hydrogen, alkyl, hydroxyalkyl, or alkenyl);
- f) alkyl;
- g) alkyl substituted with one or two $-\text{OR}^8$ (where R^8 is hydrogen);
- h) alkyl substituted with $-\text{NR}^8\text{R}^{8'}$ (where R^8 is hydrogen, alkyl, alkenyl, alkynyl, or alkyl substituted with one or two hydroxy; and $\text{R}^{8'}$ is hydrogen; alkyl; alkenyl; alkynyl; alkyl substituted with one or two hydroxy; heterocycloalkyl substituted with alkyl; or alkyl substituted with $-\text{NR}^{30}\text{R}^{30'}$ where R^{30} and $\text{R}^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl);
- i) heterocycloalkyl; or
- j) heterocycloalkyl substituted with $-\text{NR}^8\text{R}^{8'}$ (where R^8 and $\text{R}^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[00190] In another embodiment, R^3 is hydrogen and R^4 is hydrogen, hydroxymethyl, $-\text{NH}_2$, $-\text{NH}(\text{CH}_2)_3\text{CH}_3$, $-\text{NHCH}_3$, $-\text{NH}(\text{CH}_2\text{CH}_3)$, $-\text{NHCH}_2\text{CH}(\text{CH}_3)_2$, $-\text{NHCH}_2\text{CH}_2\text{OH}$, $-\text{NHCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$, $-\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2(\text{pyridin-2-yl})$, $-\text{NHCH}_2(\text{cyclopropyl})$, $-\text{NHCH}_2(\text{cyclopentyl})$, $-\text{NHCH}_2(\text{cyclohexyl})$, $-\text{C}(\text{O})\text{NHOH}$, $-\text{C}(\text{O})\text{NH}(\text{OCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH})$, $-\text{C}(\text{O})\text{NH}(\text{CH}_2)_3\text{CH}_3$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}=\text{CH}_2$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}_3$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}_2\text{OH}$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}_2(\text{piperidin-1-yl})$, $-\text{C}(\text{O})\text{NH}(\text{phenyl})$, $-\text{C}(\text{O})\text{NHCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$, *N*-(isopropyl)-aminomethyl, *N,N*-dimethylaminomethyl, *N*-(2-aminoethyl)-aminomethyl, $-\text{NHC}(\text{O})\text{OC}(\text{CH}_3)_3$, $-\text{NHC}(\text{O})\text{OCH}_3$, $-\text{NHC}(\text{O})\text{CH}(\text{CH}_3)_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{NH}_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{N}(\text{CH}_2\text{CH}_3)_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{NH}(\text{CH}_3)$, $-\text{NHC}(\text{O})\text{H}$, $-\text{NHC}(\text{O})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $-\text{NHC}(\text{O})\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $-\text{NHC}(\text{O})\text{CH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $-\text{NHC}(\text{O})\text{CH}_2(4\text{-alkyl-piperazinyl})$, $-\text{NHC}(\text{O})\text{CH}_2(\text{piperidinyl})$, pyrrolidinyl,

3-(dialkylamino)-pyrrolidinyl, piperidinyl, 2-methyl-piperidin-6-yl, *N*-methylpiperidin-2-yl, or piperazin-2-yl.

[00191] In another embodiment of embodiment A10, the Compound of Formula I is that where R^3 is alkoxy and R^4 is alkyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl). In another embodiment, R^3 is methoxy and R^4 is alkyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[00192] In another embodiment of embodiment A10, the Compound of Formula I is that where R^3 is halo and R^4 is alkyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl). In another embodiment, R^3 is fluoro and R^4 is alkyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[00193] In another embodiment of embodiment A10, the Compound of Formula I is that where R^3 is amino and R^4 is alkyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl).

[00194] In another embodiment of embodiment A10, the Compound of Formula I is that where R^3 is hydroxy and R^4 is

- a) hydrogen;
- b) $-\text{CH}_2\text{N}(\text{R}^{25})(\text{NR}^{25a}\text{R}^{25b})$;
- c) $-\text{CH}_2\text{NR}^{25}\text{C}(=\text{NH})(\text{NR}^{25a}\text{R}^{25b})$;
- d) $-\text{CH}_2\text{NR}^{25}\text{C}(=\text{NH})(\text{N}(\text{R}^{25a})(\text{NO}_2))$;
- e) $-\text{CH}_2\text{NR}^{25}\text{C}(=\text{NH})(\text{N}(\text{R}^{25a})(\text{CN}))$;
- f) $-\text{CH}_2\text{NR}^{25}\text{C}(=\text{NH})(\text{R}^{25})$;
- g) $-\text{CH}_2\text{NR}^{25}\text{C}(\text{NR}^{25a}\text{R}^{25b})=\text{CH}(\text{NO}_2)$;
- h) alkyl;
- i) alkenyl;
- j) alkyl substituted with one or two $-\text{OR}^8$ where R^8 is hydrogen, aryl, or alkyl where the alkyl is substituted with one or two hydroxy;
- k) alkyl substituted with one, two, or three halo;
- l) alkyl substituted with nitro;
- m) alkyl substituted with $-\text{S}(\text{O})_m\text{R}^9$ (where m is 0 and R^9 is aryl);
- n) alkyl substituted with optionally substituted heterocycloalkyl;
- o) alkyl substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen, alkyl, alkenyl, alkynyl, or alkyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; hydroxy;

alkoxy; alkyl; alkenyl; alkynyl; optionally substituted alkoxy; alkyl substituted with one or two hydroxy; alkyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; alkyl substituted with one or two hydroxy and one or two $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; heterocycloalkyl substituted with alkyl, alkoxycarbonyl, or optionally substituted arylalkyl; alkyl substituted with one, two, three, four, or five halo; alkyl substituted with optionally substituted cycloalkyl; alkyl substituted with optionally substituted aryl; alkyl substituted with one or two hydroxy and one optionally substituted aryl; alkyl substituted with optionally substituted heterocycloalkyl; alkyl substituted with optionally substituted heteroaryl; heteroaryl; aryl; aryl substituted with one or two hydroxy; aryl substituted with one or two alkoxy; aryl substituted with one or two halo; aryl substituted with one or two $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl; aryl substituted with $-NR^{34}SO_2R^{34a}$ where R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl; cycloalkyl; cycloalkyl substituted with one or two hydroxy; cycloalkyl substituted with one or two hydroxy and one or two hydroxyalkyl; cycloalkyl substituted with one or two alkoxy; cycloalkyl substituted with carboxy; cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; cycloalkyl substituted with optionally substituted cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted with one or two hydroxy; heterocycloalkyl substituted with one or two alkoxy; heterocycloalkyl substituted with one or two hydroxyalkyl; heterocycloalkyl substituted with one or two hydroxy, one or two alkoxy, and one or two hydroxyalkyl; alkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl; alkyl substituted with optionally substituted aryloxy; alkyl substituted with $-S(O)_nR^{31}$ where n is 0 and R^{31} is alkyl; alkyl substituted with carboxy; alkyl substituted with alkoxycarbonyl; or alkyl substituted with $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl);

p) heterocycloalkyl;

- q) $-C(O)NR^8R^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl; and $R^{8'}$ is hydrogen; alkyl; alkyl; alkenyl; or substituted with one or two hydroxy;);
- r) alkyl substituted with $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, alkyl, or alkenyl and $R^{8'}$ is alkyl; alkenyl; or alkyl substituted with alkoxy, aryl, and one, two, or three halo);
- s) cycloalkyl;
- t) cycloalkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;
- u) cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl;
- v) heterocycloalkyl;
- w) heterocycloalkyl substituted with one or two alkyl;
- x) heterocycloalkyl substituted with $-C(O)OR^8$ where R^8 is alkyl or alkenyl;
- y) heteroaryl;
- z) heteroaryl optionally substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;
- aa) alkyl substituted with optionally substituted heteroaryl;
- bb) alkyl substituted with $-NR^8S(O)_2R^9$ where R^8 is hydrogen, alkyl, or alkenyl and R^9 is alkyl or alkenyl;
- cc) alkyl substituted with $-NR^8C(O)OR^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl;
- dd) alkyl substituted with one aryl and one $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl; or
- ee) alkyl substituted with one or two $-OR^8$ (where R^8 is hydrogen) and one or two $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, alkyl, or alkenyl.

[00195] In another embodiment, R^3 is hydroxy and R^4 is hydrogen, $-CH_2N(H)(NHCH_3)$, $-CH_2NHC(=NH)(NH_2)$, $-CH_2NHC(=NH)(NHNO_2)$, $-CH_2NHC(=NH)(NHCN)$, $-CH_2NHC(=NH)(phenyl)$, $-CH_2NHC(NH_2)=CH(NO_2)$, methyl, ethyl, hydroxymethyl, 2,3-dihydroxypropyl, 3-hydroxy-2-methyl-prop-2-yl, *N*-(1-methoxy-prop-2-yl)-aminomethyl, *N*-(ethoxypropyl)-aminomethyl, *N*-(ethoxyethyl)-aminomethyl, *N*-(2,2-dimethoxyethyl)-aminomethyl, *N*-(methoxyethyl)-aminomethyl, *N*-(isopropoxyethyl)-aminomethyl, trifluoromethyl, 1-nitro-ethyl, 1-methyl-1-nitro-ethyl, 1-nitro-propyl, 3-methyl-1-nitro-butyl, phenylthiomethyl, allyl, ethenyl, 2-methylthio-ethylaminomethyl, 3-methylthio-

propylaminomethyl, *N*-(*tert*-butoxycarbonylaminopropyl)-aminomethyl, *N*-(1-carboxyethyl)-aminomethyl, *N*-(1*R*-carboxyethyl)-aminomethyl, *N*-(1*S*-carboxyethyl)-aminomethyl, *N*-(1-methoxycarbonylethyl)-aminomethyl, azetidinylmethyl, pyrrolidinylmethyl, 3-hydroxy-pyrrolidinylmethyl, 2-(methoxymethyl)-pyrrolidinylmethyl, 2*S*-(methoxymethyl)-pyrrolidinylmethyl, 2*R*-(methoxymethyl)-pyrrolidinylmethyl, morpholinylmethyl, 4-hydroxypiperidinylmethyl, 4-methyl-piperazinylmethyl, 4-methyl-homopiperazinylmethyl, 4-(piperidinyl)-piperidinylmethyl, 4-[2-(*N,N*-diethylamino)-ethyl]-piperazinylmethyl, *N*-hydroxyaminomethyl, *N*-methoxyaminomethyl, *N*-ethoxyaminomethyl, *N*-ethylaminomethyl, 1-(*N*-ethyl-amino)-ethyl, *N,N*-diethylaminomethyl, *N,N*-dimethylaminomethyl, aminomethyl, 1-amino-ethyl, 1*R*-amino-ethyl, 1*S*-amino-ethyl, 1-(methylamino)-ethyl, 1-(*N,N*-dimethylamino)-ethyl, 1-amino-1-methyl-ethyl, 1-aminopropyl, 1*S*-aminopropyl, 1*R*-aminopropyl, *N*-(*n*-propyl)-aminomethyl, *N*-(isopropyl)-aminomethyl, 2-(*N*-isopropylamino)-ethyl, 3-(*N*-isopropylamino)-2-methyl-prop-2-yl, 1-(*N*-ethyl-amino)-propyl, 1-(*N,N*-diethyl-amino)-propyl, 1-aminobutyl, 1-amino-isobutyl, *N*-(*n*-butyl)-aminomethyl, *N*-isobutylaminomethyl, *tert*-butylaminomethyl, 1-(*tert*-butylamino)-ethyl, *sec*-butylaminomethyl, *N*-(2-methyl-but-3-yl)-aminomethyl, *N*-(3,3-dimethyl-butyl)-aminomethyl, *N*-(3-methylbut-3-yl)-aminomethyl, *N*-(2-methylbutyl)-aminomethyl, *N*-(pent-3-yl)-aminomethyl, *n*-pentylaminomethyl, isopentylaminomethyl, *sec*-pentylaminomethyl, neopentylaminomethyl, *N*-(2,2,4-trimethyl-pent-4-yl)-aminomethyl, *N*-(2-ethyl-butyl)-aminomethyl, *N*-allyl-aminomethyl, 3-methyl-but-1-yn-3-ylaminomethyl, *N*-(2,3-dihydroxypropyloxy)-aminomethyl, *N*-cyclopropylaminomethyl, *N*-cyclopentylaminomethyl, *N*-cyclopenten-4-ylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-cyclopent-2-yl)-aminomethyl, *N*-(1(*R,S*)-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-hydroxy-1-methyl-cyclopent-2-yl)-aminomethyl, *N*-(3,4-dihydroxy-cyclopentyl)-aminomethyl, *N*-(1-hydroxymethyl-cyclopent-1-yl)-aminomethyl, *N*-(2,3-dihydroxy-4-hydroxymethyl-cyclopentyl)-aminomethyl, *N*-(1(*R,S*)-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*S*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1*R*-methoxy-cyclopent-2-yl)-aminomethyl, *N*-(1-carboxy-cyclopentyl)-aminomethyl, *N*-cyclohexylaminomethyl, *N*-(1(*R,S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(1(*R*)-hydroxy-cyclohex-2-yl)-aminomethyl,

N-(1(*S*)-hydroxy-cyclohex-2-yl)-aminomethyl, *N*-(*cis*-4-hydroxy-cyclohexyl)-aminomethyl, *N*-(*trans*-4-hydroxy-cyclohexyl)-aminomethyl, 1-[*N*-(*cis*-4-hydroxy-cyclohexyl)-amino]-ethyl, 1-[*N*-(*trans*-4-hydroxy-cyclohexyl)-amino]-ethyl, *N*-(1-hydroxymethyl-cyclohexyl)-aminomethyl, *N*-(2-cyclohexyl-cyclohexyl)-aminomethyl, *N*-{(2*R*,3*S*,4*R*,6*R*)-2-(hydroxymethyl)-3,4-dihydroxy-6-methoxy-tetrahydro-2*H*-pyran-5-yl}-aminomethyl, *N*-(cycloheptyl)-aminomethyl, *N*-(cyclooctyl)-aminomethyl, [(1*r*,3*r*,5*R*,7*R*)-tricyclo[3.3.1.1^{3,7}]dec-2-ylamino]methyl, *N*-(1-benzyloxy-cyclopent-2-yl)-aminomethyl, *N*-[1-(cyclopropylaminocarbonyl)-cyclopentyl]-aminomethyl, -CH₂NHC(CH₃)₂C(O)NH(cyclohexyl), -CH₂NHC(CH₃)₂C(O)NH(CH₂CH₃), *N*-(cyclopropylmethyl)-aminomethyl, *N*-(cyclohexylmethyl)-aminomethyl, *N*-(1-cyclohexylethyl)-aminomethyl, *N*-(imidazolyl)-aminomethyl, *N*-(1,3,5-triazinyl)-aminomethyl, *N*-(5-hydroxy-pyrazol-3-yl)-aminomethyl, *N*-(5-methyl-pyrazol-3-yl)-aminomethyl, *N*-(benzimidazolyl)-aminomethyl, *N*-(pyrimidin-2-yl)-aminomethyl, *N*-(pyridin-2-yl)-aminomethyl, *N*-(pyridin-3-yl)-aminomethyl, *N*-(pyridin-4-yl)-aminomethyl, *N*-indan-1-yl-aminomethyl, *N*-indan-2-yl-aminomethyl, phenylaminomethyl, *N*-(2-hydroxyphenyl)-aminomethyl, *N*-(3-hydroxyphenyl)-aminomethyl, *N*-(4-hydroxyphenyl)-aminomethyl, *N*-(2-methoxyphenyl)-aminomethyl, *N*-(3-methoxyphenyl)-aminomethyl, *N*-(4-methoxyphenyl)-aminomethyl, *N*-(2-fluorophenyl)-aminomethyl, *N*-(3-fluorophenyl)-aminomethyl, *N*-(4-fluorophenyl)-aminomethyl, *N*-(2-chlorophenyl)-aminomethyl, *N*-(3-chlorophenyl)-aminomethyl, *N*-(4-chlorophenyl)-aminomethyl, *N*-(3-methylcarbonylamino-phenyl)-aminomethyl, *N*-(4-methylcarbonylamino-phenyl)-aminomethyl, *N*-(2-aminophenyl)-aminomethyl, *N*-(3-aminophenyl)-aminomethyl, *N*-(4-aminophenyl)-aminomethyl, *N*-(2-methylsulfonylamino-phenyl)-aminomethyl, *N*-(3-methylsulfonylamino-phenyl)-aminomethyl, *N*-(4-methylsulfonylamino-phenyl)-aminomethyl, *N*-(2-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(3-fluoro-4-hydroxy-phenyl)-aminomethyl, *N*-(benzyl)-aminomethyl, *N*-(2-hydroxyphenylmethyl)-aminomethyl, *N*-(3-hydroxyphenylmethyl)-aminomethyl, *N*-(4-hydroxyphenylmethyl)-aminomethyl, *N*-(2-(*N*-methylpiperazin-1-yl)-phenylmethyl)-aminomethyl, *N*-(4-methyl-phenethyl)-aminomethyl, *N*-(1-hydroxy-3-phenyl-prop-2-yl)-aminomethyl, *N*-(pyrrolidin-2-ylmethyl)-aminomethyl, *N*-(*N*-ethyl-pyrrolidinylmethyl)-aminomethyl, *N*-(*N*-methyl-pyrrolidin-2-ylethyl)-aminomethyl, *N*-(pyrrolidinylpropyl)-aminomethyl, *N*-(1,1-dimethyl-2-pyrrolidin-1-yl-ethyl)-aminomethyl, *N*-(tetrahydrofuranylmethyl)-

aminomethyl, *N*-(tetrahydro-2*H*-pyran-4-ylmethyl)-aminomethyl, *N*-(tetrahydro-2*H*-pyranylethyl)-aminomethyl, *N*-(piperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-*tert*-butoxycarbonylpiperidin-4-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-5-ylmethyl)-aminomethyl, *N*-(*N*-methylimidazol-4-ylmethyl)-aminomethyl, *N*-[2-(imidazol-4-yl)-ethyl]-aminomethyl, *N*-[3-(imidazolyl)-propyl]-aminomethyl, *N*-(pyridin-3-ylethyl)-aminomethyl, *N*-(pyridin-4-ylethyl)-aminomethyl, *N*-(thien-2-ylethyl)-aminomethyl, *N*-(furan-2-ylethyl)-aminomethyl, *N*-(5-methyl-1,3,4-oxadiazol-2-ylmethyl)-aminomethyl, *N*-(2-indolin-3-ylethyl)-aminomethyl, 2-(*N,N*-dimethylamino)-ethylaminomethyl, 2-(*N,N*-dimethylamino)-1-methyl-ethylaminomethyl, 3-aminopropylaminomethyl, 3-(*N,N*-dimethylamino)-propylaminomethyl, 3-(*N,N*-diethylamino)-propylaminomethyl, *N*-(*N,N*-diisopropylaminoethyl)-aminomethyl, *N*-(*N,N*-dimethylaminobutyl)-aminomethyl, 3-hydroxypropylaminomethyl, *N*-(1,2-dihydroxypropyl)-aminomethyl, *N*-(1-amino-2-hydroxy-prop-3-yl)-aminomethyl, *N*-(*N*-ethoxycarbonyl-piperidin-4-yl)-aminomethyl, *N*-(*N*-benzylpiperidin-4-yl)-aminomethyl, *N*-(homopiperidin-3-yl)-aminomethyl, *N*-(*N*-benzylpyrrolidin-3-yl)-aminomethyl, *N*-(*N*-ethylpiperidin-3-yl)aminomethyl, 2,2,2-trifluoroethylaminomethyl, 3,3,3-trifluoropropylaminomethyl, 2,2,3,3,3-pentafluoropropylaminomethyl, -CH₂N(CH₂CH₂OH)₂, -CH₂N(CH₃)(CH₂CH₂OH), -CH₂NH(CH₂CH₂OH), -CH₂NH(CH₂CH₂CH₂CH₂OH), -CH₂NH(C(CH₃)₂CH₂OH), -CH₂N(CH₃)(*N*-methyl-pyrrolidin-3-yl), -C(O)NH₂, -C(O)NHCH₂CH=CH₂, -C(O)NHCH₂CH(OH)CH₂OH, *N*-(phenyloxyethyl)-aminomethyl, -CH₂NHC(O)CH₃, -CH(CH₃)NHC(O)CH₃, -CH(CH₃)NHC(O)C(OCH₃)(CF₃)phenyl, cyclopentyl, 1-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, (*cis,trans*)-2-amino-cyclopentyl, *cis*-2-amino-cyclopentyl, *trans*-2-amino-cyclopentyl, (*cis,trans*)-2-hydroxy-cyclohexyl, *cis*-2-hydroxy-cyclohexyl, *trans*-2-hydroxy-cyclohexyl, (*cis,trans*)-2-amino-cyclohexyl, *cis*-2-amino-cyclohexyl, *trans*-2-amino-cyclohexyl, azetidin-3-yl, pyrrolidinyl, *N*-methyl-pyrrolidin-2-yl, *N*-ethyl-pyrrolidin-2-yl, 3-(dimethylamino)-pyrrolidinyl, piperidinyl, 2-methyl-piperidin-6-yl, *N*-methylpiperidin-2-yl, *N*-*tert*-butoxycarbonylpiperidin-2-yl, piperazin-2-yl, pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl, imidazol-1-yl, imidazol-2-yl, imidazol-4-yl, imidazol-5-yl, *N*-methyl-imidazol-2-yl, 5-methyl-imidazol-2-yl, 1,2,4-triazol-3-yl, thiazol-2-yl, 2-aminopyrimidin-3-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, benzimidazolyl, imidazol-1-ylmethyl, imidazol-2-ylmethyl, triazol-1-ylmethyl, (5-amino-3-methyl-pyrazol-3-yl)-methyl,

phenoxymethyl, 2-hydroxyethyloxymethyl, methylsulfonylaminomethyl, 1-(methoxycarbonylamino)-ethyl, 1-amino-1-phenyl-methyl, or 1-amino-3-hydroxy-propyl.

[00196] Another embodiment of the Invention (A11) is that where the compound of Formula I is selected from Group A where R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$. In another embodiment, X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12} where R^{10} and R^{12} are independently hydrogen or halo; R^1 , R^2 , R^5 and R^6 are hydrogen; and R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$.

[00197] Another embodiment of the Invention (A12) is that where the compound of Formula I is selected from Group A where X and R^7 are halo; A is phenylene optionally substituted with R^{10} and R^{12} where R^{10} and R^{12} are independently hydrogen or halo; and R^1 , R^2 , R^4 , R^5 and R^6 are hydrogen.

[00198] Another embodiment of the Invention (A13) is that where the compound of Formula I is selected from Group A where A is phenylene.

[00199] Another embodiment of the Invention (A14) is that where the compound of Formula I is selected from Group A where R^1 is hydrogen and R^2 is alkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ and all other groups are as defined in the Summary of the Invention for a compound of Group A.

[00200] Another embodiment of the Invention (A15) is that where the compound of Formula I is selected from Group A where A is phenylene; R^7 is iodo or bromo; X is fluoro or chloro; and R^1 , R^2 , R^5 , and R^6 are hydrogen; and R^{10} , R^{12} , R^{14} , and R^{16} are independently hydrogen or fluoro. In another embodiment, R^{10} is 3-fluoro and R^{12} , R^{14} , and R^{16} are hydrogen or halo; R^{10} is 3-fluoro, R^{12} is 4-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 5-fluoro, and R^{14} and R^{16} are hydrogen; R^{10} is 4-fluoro, R^{12} is 6-fluoro, and R^{14} and R^{16} are hydrogen; or R^{12} is 4-fluoro and R^{10} , R^{14} , and R^{16} are hydrogen.

[00201] In another embodiment of the invention is a compound of Formula selected from Group A where R^3 is hydroxy and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^3 is hydroxy and R^4 is heterocycloalkyl or alkyl, where the alkyl is optionally substituted

with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with groups independently selected from hydroxy and alkyl).

[00202] In another embodiment of the Invention (B1) the compound of Formula I is selected from Group B where all groups are as defined in the Summary of the Invention.

[00203] In another embodiment of the invention (B2), the Compound of Formula I is that where X and R^7 are halo; and all other groups are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, X is fluoro or chloro and R^7 is iodo or bromo.

[00204] In another embodiment of the invention (B3), the compound of Formula I is selected from Group B where R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$ and R^4 is as defined in the Summary of the Invention; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and all other groups are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R^1 , R^2 , R^5 and R^6 are hydrogen; and X and R^7 are halo.

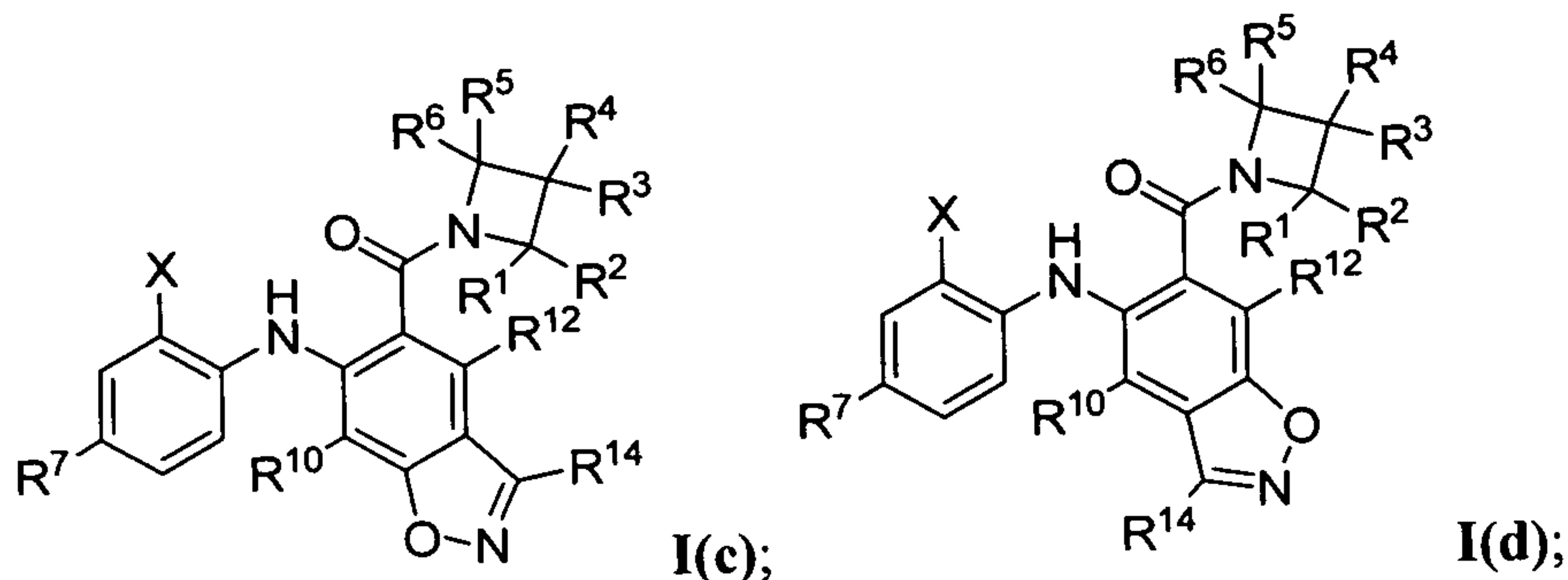
[00205] In another embodiment of the invention (B4), the compound of Formula I is selected from Group B where R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$,

-CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R¹, R², R⁵ and R⁶ are hydrogen; and X and R⁷ are halo.

[00206] In another embodiment of the invention (B5), the Compound of Formula I is that where A is heteroarylene selected from thien-diyl, benzo[d]isoxazol-diyl, benzo[d]isothiazol-diyl, 1*H*-indazol-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is as defined in the Summary of the Invention for a compound of Group B), benzo[d]oxazol-diyl, benzo[d]thiazol-diyl, 1*H*-benzo[d]imidazol-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is as defined in the Summary of the Invention for a compound of Group B), 1*H*-benzo[d][1,2,3]triazol-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is as defined in the Summary of the Invention for a compound of Group B), imidazo[1,2-*a*]pyridin-diyl, cinnolin-diyl, quinolin-diyl, pyridin-diyl, 1-oxido-pyridin-diyl, [1,2,4]triazolo[4,3-*a*]pyridin-diyl, and 2,3-dihydroimidazo[1,2-*a*]pyridin-diyl; and A is further optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶ where R¹⁰, R¹², R¹⁴, and R¹⁶ and all other groups are as defined in the Summary of the Invention for a compound of Group B. In another embodiment A is selected from thien-3,4-diyl, benzo[d]isoxazol-5,6-diyl, benzo[d]isothiazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is alkyl or alkenyl), benzo[d]oxazol-5,6-diyl, benzo[d]thiazol-5,6-diyl, 1*H*-benzo[d]imidazol-5,6-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is alkyl or alkenyl), 1*H*-benzo[d][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-5,6-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, 1-oxido-pyridin-3,4-diyl, [1,2,4]triazolo[4,3-*a*]pyridin-6,7-diyl, and 2,3-dihydroimidazo[1,2-*a*]pyridin-6,7-diyl.

[00207] In another embodiment of the Invention (B6), the compound of Formula I is selected from Group B where A is thien-diyl and X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, and R¹² are as defined in the Summary of the Invention for a compound of Group B. In another embodiment A is thien-3,4-diyl; R¹⁰ and R¹² are hydrogen; X and R⁷ are halo; and R¹, R², R⁵, and R⁶ are hydrogen. In another embodiment, X is fluoro or chloro; R⁷ is iodo or bromo; R³ is hydrogen or hydroxy; and R⁴ is -NR⁸R^{8'} (where R⁸ and R^{8'} are independently hydrogen or alkyl), heterocycloalkyl, heteroaryl (optionally substituted with alkyl), or alkyl where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl).

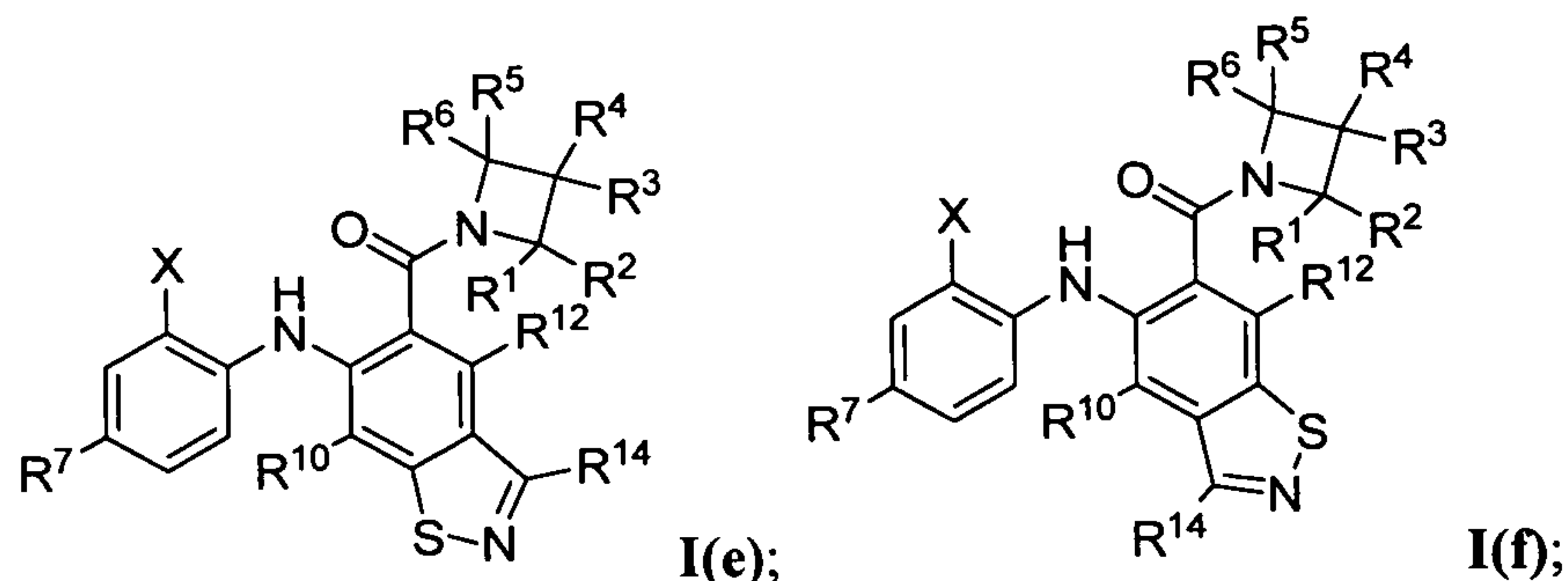
[00208] In another embodiment (B7), the compound of Formula I is more specifically according to Formula I(c) or I(d)



where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹² and R¹⁴ are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R³ and R⁴ are as defined in the Summary of the Invention for Group B; and R¹⁰, R¹², and R¹⁴ are independently hydrogen, halo, or alkyl. In another embodiment, X is fluoro or chloro and R⁷ is iodo or bromo; R¹⁰ is hydrogen or halo, in another embodiment hydrogen or fluoro; R¹² is hydrogen; R¹⁴ is hydrogen or alkyl; and R³ is hydroxy. In another embodiment, R⁴ is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R⁴ is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-

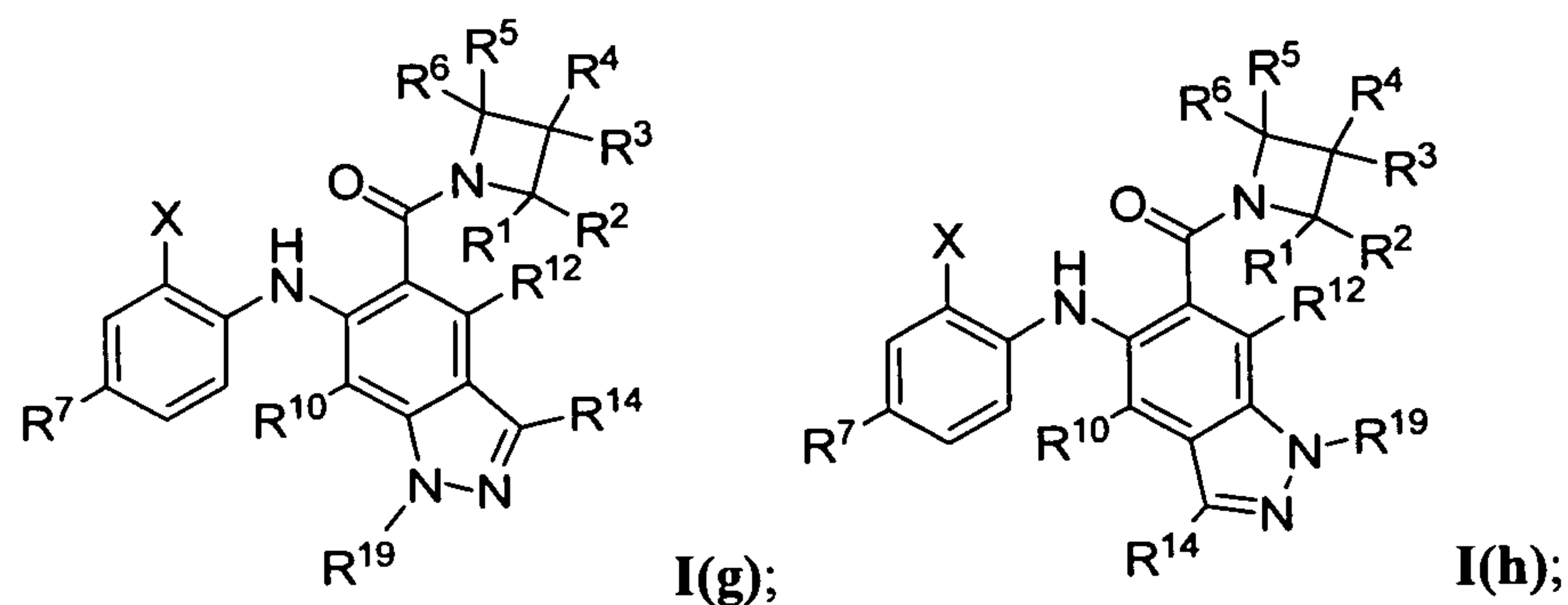
ethyl, 1(*R,S*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-*cis*-dihydroxy-cyclopentylamino)-ethyl.

[00209] In another embodiment of the Invention (B8), the compound of Formula I is more specifically according to Formula I(e) or I(f):



where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹² and R¹⁴ are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R³ and R⁴ are as defined in the Summary of the Invention for Group B; and R¹⁰, R¹², and R¹⁴ are independently hydrogen, halo, or alkyl. In another embodiment, X is fluoro or chloro and R⁷ is iodo or bromo; R¹⁰ is hydrogen or halo, in another embodiment hydrogen or fluoro; R¹² and R¹⁴ are hydrogen; R³ is hydroxy; and R⁴ is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00210] In another embodiment of the Invention (B9), the compound of Formula I is in another embodiment according to Formula I(g) or I(h):



where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹², R¹⁴, and R¹⁹ are as defined in the Summary of the Invention for a compound of Group B.

[00211] In another embodiment of embodiment B9, the compound of Formula I is more specifically according to Formula I(g) or I(h) where

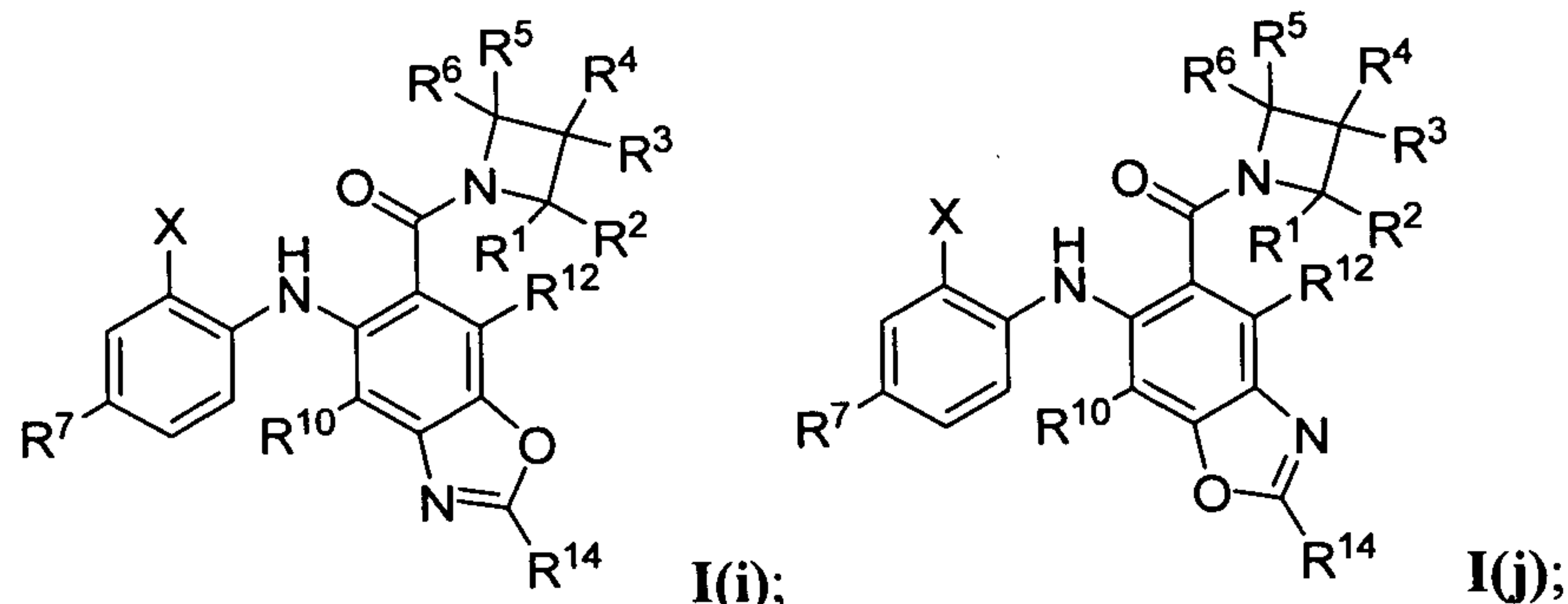
R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, cycloalkyl, heteroaryl, or heterocycloalkyl; where the cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the Summary of the Invention; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and

all other groups are as defined in the Summary of the Invention for a compound of Group B.

[00212] In another embodiment of embodiment B9, the compound of Formula I is more specifically according to Formula I(g) or I(h) where R^3 is hydroxy and all other groups are as defined in the Summary of the Invention for a compound of Group B.

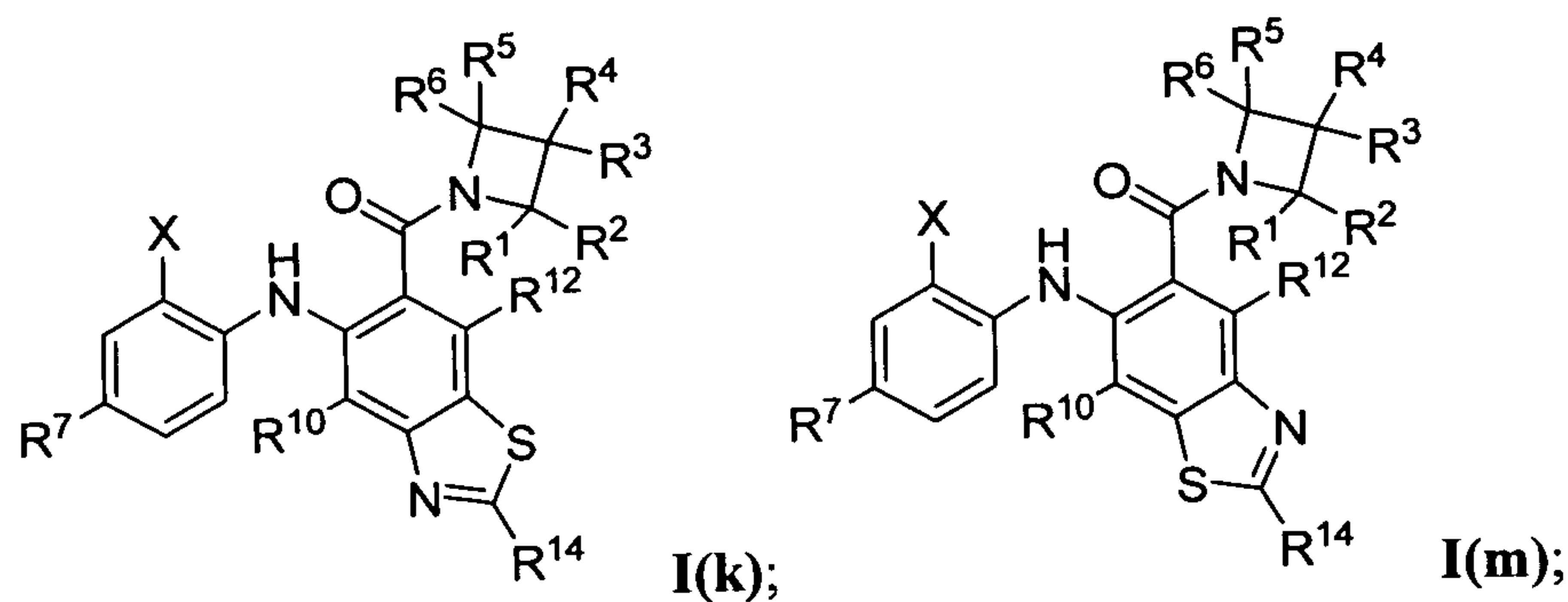
[00213] In another embodiment of embodiment B9, the compound of Formula I is more specifically according to Formula I(g) or I(h) where R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the Summary of the Invention for Group B; R^{10} , R^{12} , and R^{14} are independently hydrogen, halo, or alkyl; and R^{19} is hydrogen or methyl. In another embodiment, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, in another embodiment hydrogen or fluoro; R^{12} and R^{14} are hydrogen; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00214] In another embodiment of the Invention (B10), the compound of Formula I is more specifically according to Formula I(i) or I(j):



where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹² and R¹⁴ are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R³ and R⁴ are as defined in the Summary of the Invention for Group B; and R¹⁰, R¹², and R¹⁴ are independently hydrogen, halo, or alkyl. In another embodiment, X is fluoro or chloro and R⁷ is iodo or bromo; R¹⁰ is hydrogen or halo, in another embodiment hydrogen or fluoro; R¹² and R¹⁴ are hydrogen; R³ is hydroxy; and R⁴ is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

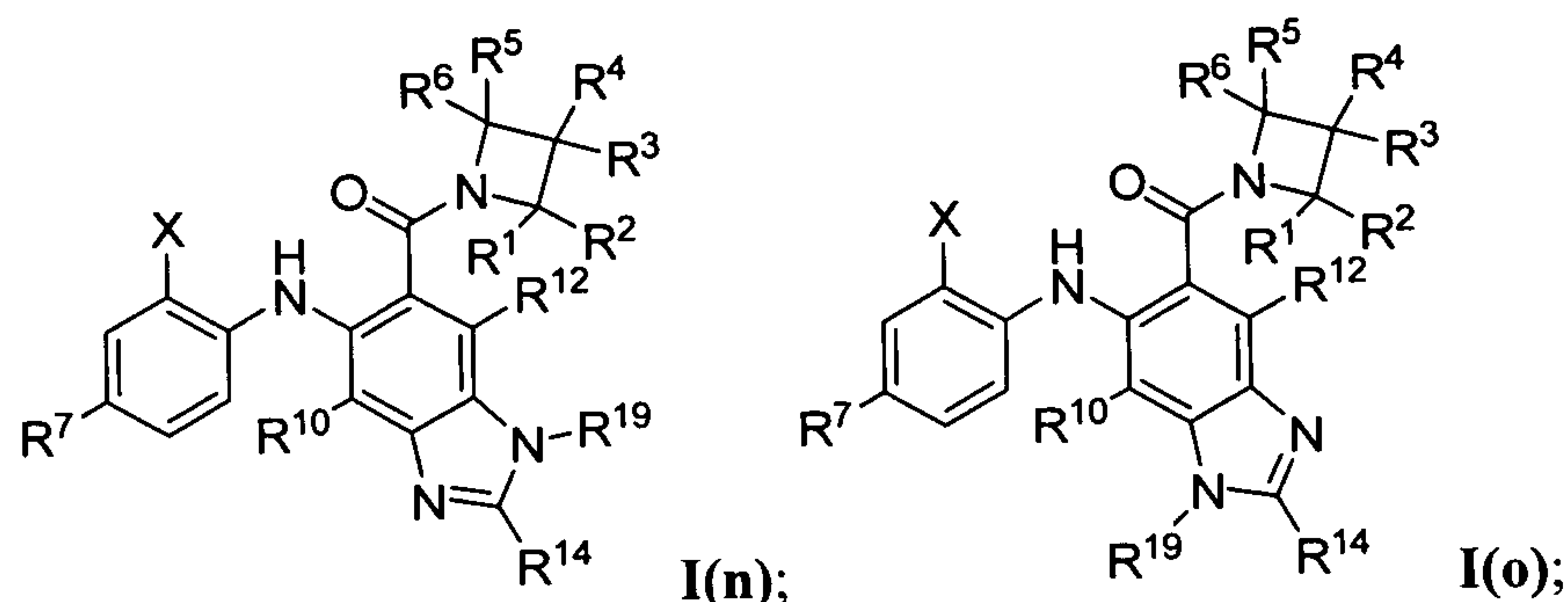
[00215] In another embodiment of the Invention (B11), the compound of Formula I is more specifically according to Formula I(k) or I(m):



where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹² and R¹⁴ are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R³ and R⁴ are as defined in the Summary of the Invention for Group B; and R¹⁰, R¹², and R¹⁴ are independently hydrogen, halo, or alkyl. In another embodiment, X is fluoro or chloro and R⁷ is iodo or bromo; R¹⁰ is hydrogen or halo, in another embodiment hydrogen or fluoro; R¹² and R¹⁴ are

hydrogen; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00216] In another embodiment of the Invention (B12), the compound of Formula I is more specifically according to Formula I(n) or I(o):



where X, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{12} , R^{14} , and R^{19} are as defined in the Summary of the Invention for a compound of Group B.

[00217] In another embodiment of embodiment B12, the compound of Formula I is more specifically according to Formula I(n) or I(o) where R^7 is halo or alkyl; and all other groups are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R^7 is iodo or bromo.

[00218] In another embodiment of embodiment B12, the compound of Formula I is more specifically according to Formula I(n) or I(o) where X is halo, haloalkyl, or haloalkoxy; and all other groups are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, X is halo. In another embodiment X is fluoro or chloro.

[00219] In another embodiment of embodiment B12, the compound of Formula I is more specifically according to Formula I(n) or I(o) where

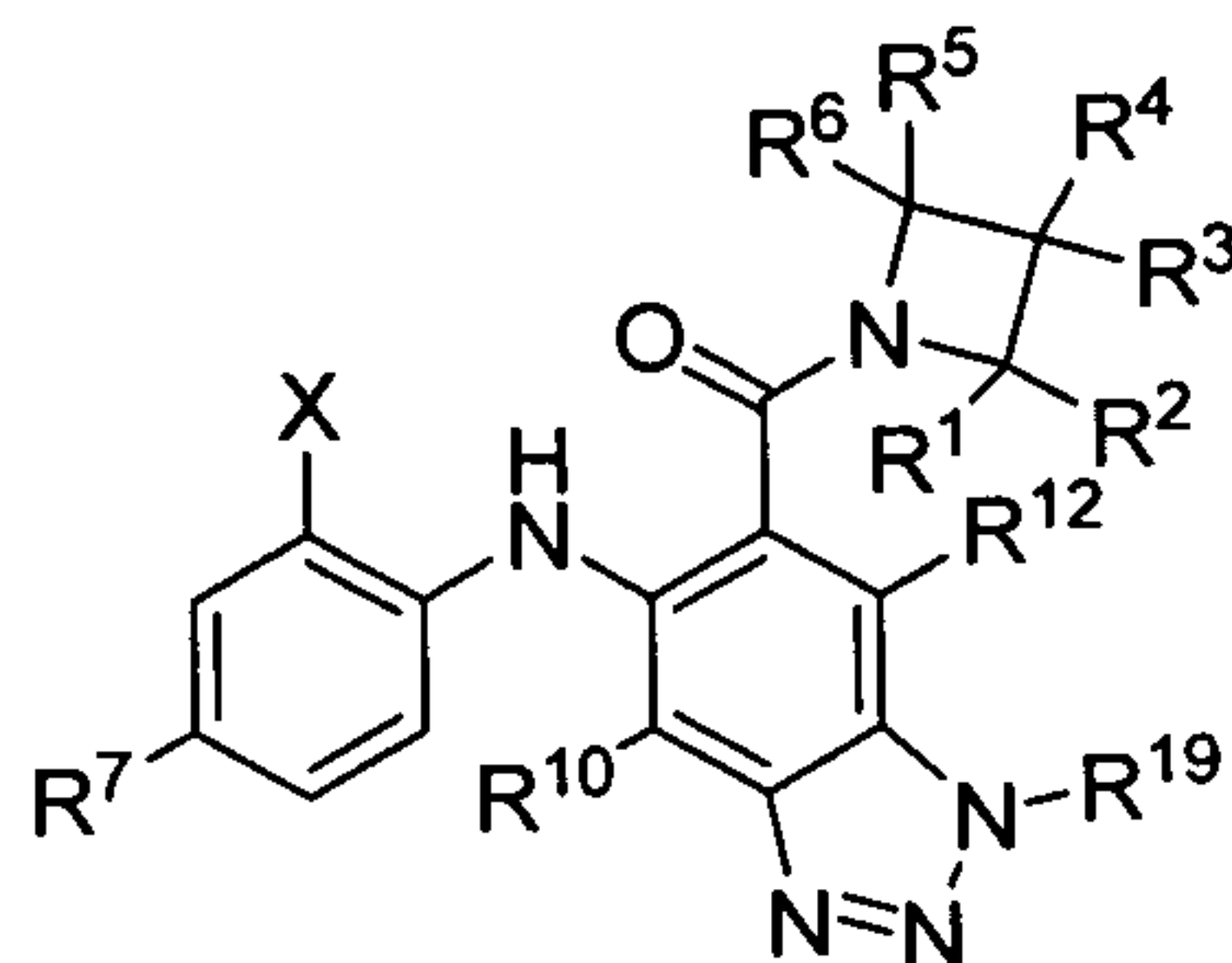
R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl,

heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; and R^4 is as defined in the Summary of the Invention; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and

unless otherwise indicated, R^8 and $R^{8'}$ are as defined in the Summary of the Invention; and all other groups are as defined in the Summary of the Invention for a compound of Group B.

[00220] In another embodiment of embodiment B12, the compound of Formula I is more specifically according to Formula I(n) or I(o) where R^{19} is alkyl; R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the Summary of the Invention for Group B; and R^{10} , R^{12} , and R^{14} are independently hydrogen or halo. In another embodiment, R^{19} is methyl; X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or fluoro; R^{12} and R^{14} are hydrogen; and R^3 is hydroxy. In another embodiment, R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

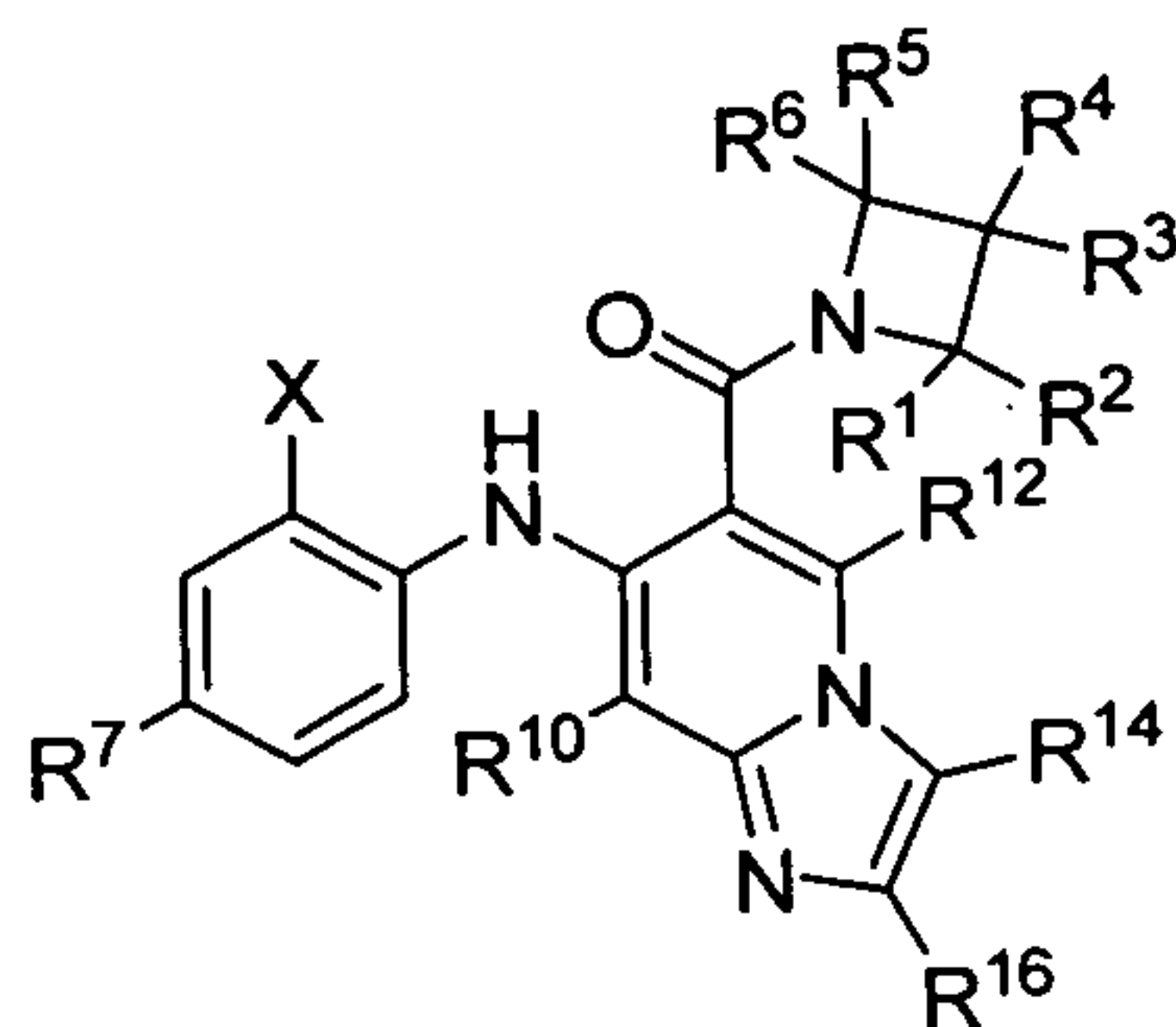
[00221] In another embodiment of the Invention (B13), the compound of Formula I is more specifically according to Formula I(p):



I(p)

where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹², and R¹⁹ are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R³ and R⁴ are as defined in the Summary of the Invention for Group B; and R¹⁰ and R¹² are independently hydrogen, halo, or alkyl. In another embodiment, X is fluoro or chloro; R⁷ is iodo or bromo; R¹⁰ is hydrogen or halo, in another embodiment hydrogen or fluoro; R¹² is hydrogen; R¹⁹ is hydrogen or alkyl, in another embodiment hydrogen or methyl; R³ is hydroxy. In another embodiment, R⁴ is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R⁴ is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00222] In another embodiment of the Invention (B14), the compound of Formula I is more specifically according to Formula I(q):



I(q)

where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹², R¹⁴, and R¹⁶ are as defined in the Summary of the Invention for a compound of Group B.

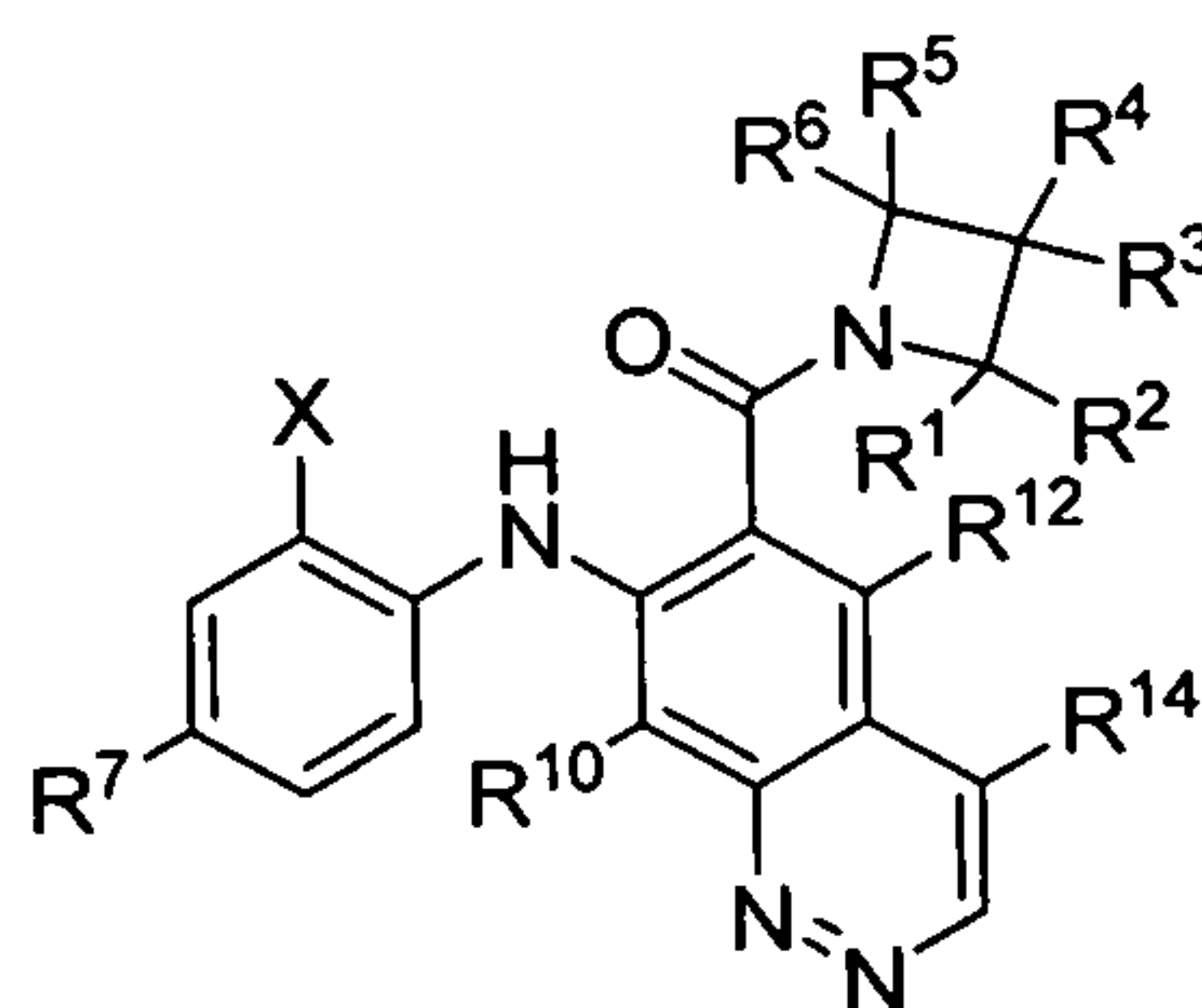
[00223] In another embodiment of embodiment B14, the compound of Formula I is more specifically according to Formula I(q) where

R³ is halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, -CH₂N(R²⁵)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂)), -CH₂NR²⁵C(=NH)(N(R^{25a})(CN)), -CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; and R⁴ is as defined in the Summary of the Invention; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and

all other groups are as defined in the Summary of the Invention for a compound of Group B.

[00224] In another embodiment of embodiment B14, the compound of Formula I is more specifically according to Formula I(q) where R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the Summary of the Invention for Group B; and R^{10} , R^{12} , R^{14} , and R^{16} are independently hydrogen or halo. In another embodiment, R^{10} is halo and R^{12} , R^{14} , and R^{16} are hydrogen. In another embodiment, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is chloro; and R^3 is hydroxy. In another embodiment, R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00225] In another embodiment of the Invention (B15), the compound of Formula I is more specifically according to Formula I(r):

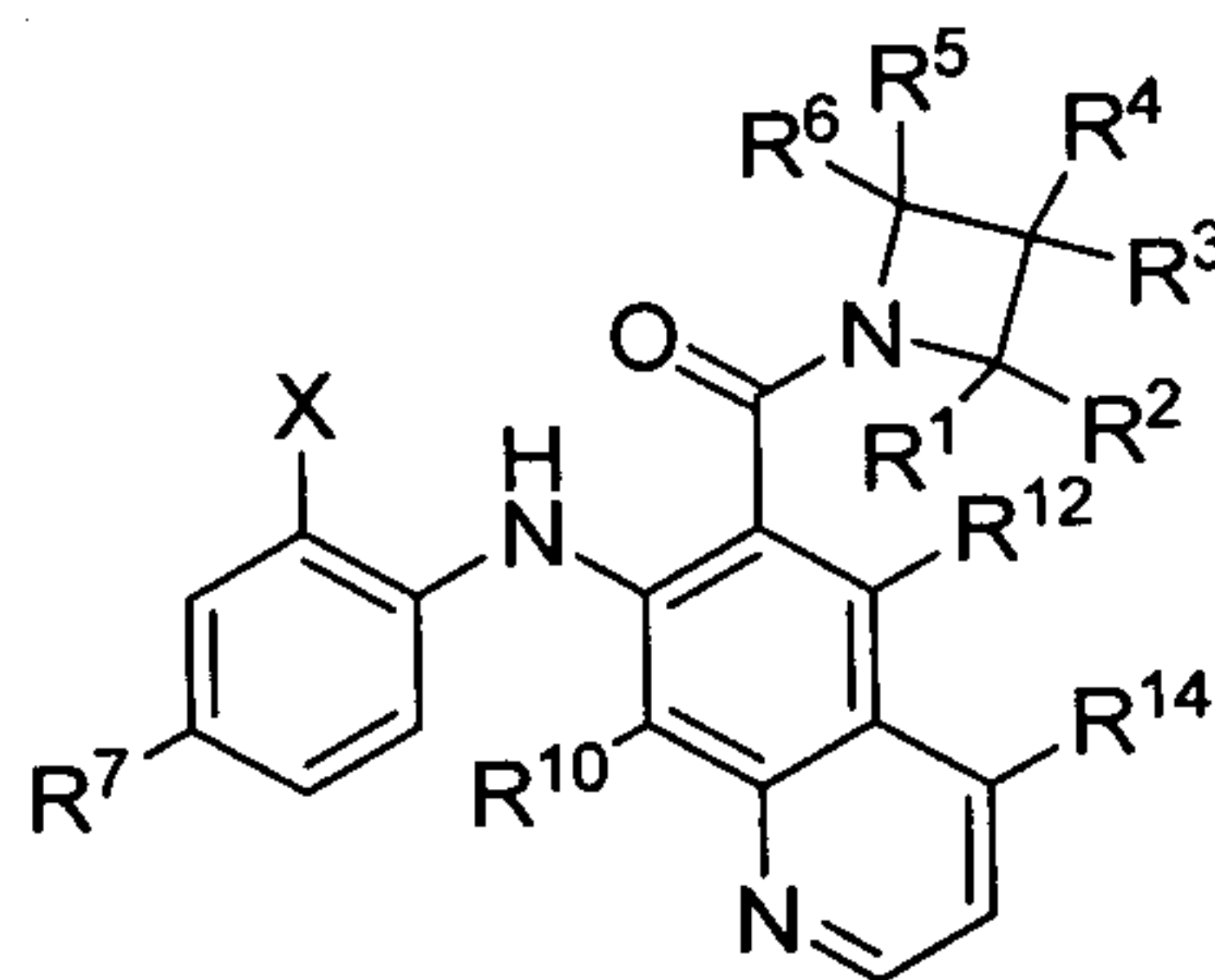


I(r)

where X, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{12} and R^{14} are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the Summary of the Invention for Group B; R^{10} and R^{12} are independently hydrogen, halo, or alkyl; and R^{14} is hydrogen, halo, alkyl, or amino. In another embodiment, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is hydrogen or halo, in another embodiment hydrogen or fluoro; R^{12} is hydrogen; R^{14} is hydrogen, alkyl, or amino, in another embodiment hydrogen, methyl, or amino; R^3 is hydroxy. In another embodiment, R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl

where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

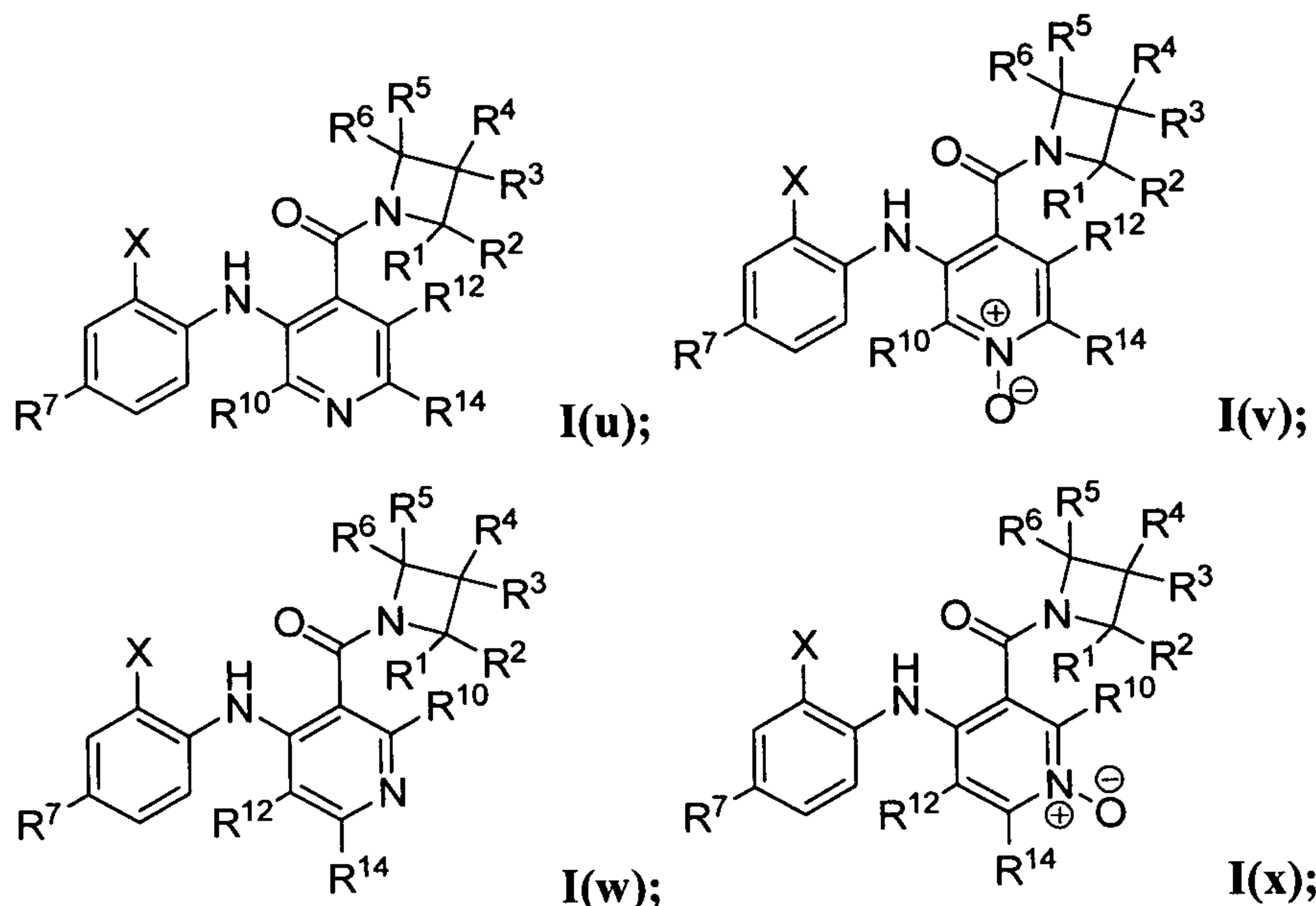
[00226] In another embodiment of the Invention (B16), the compound of Formula I is more specifically according to Formula I(s):



I(s)

where X , R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^{10} , R^{12} and R^{14} are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the Summary of the Invention for Group B; and R^{10} and R^{12} are independently hydrogen, halo, or alkyl; and R^{14} is hydrogen, halo, alkyl, or amino. In another embodiment, X is fluoro or chloro and R^7 is iodo or bromo; R^{10} is hydrogen or halo, in another embodiment hydrogen or fluoro; R^{12} is hydrogen; R^{14} is hydrogen, methyl, or amino; R^3 is hydroxy; and R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00227] In another embodiment of the Invention (B18), the compound of Formula I is more specifically according to Formula I(u), I(v), I(w), or I(x):



where X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, R¹² and R¹⁴ are as defined in the Summary of the Invention for a compound of Group B.

[00228] In another embodiment of embodiment B18, the compound of Formula I is more specifically according to Formula I(u), I(v), I(w), or I(x) where R³ is halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, -CH₂N(R²⁵)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂)), -CH₂NR²⁵C(=NH)(N(R^{25a})(CN)), -CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; and R⁴ is as defined in the Summary of the Invention for a compound of Group B; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the Summary of the Invention for a compound of Group B.

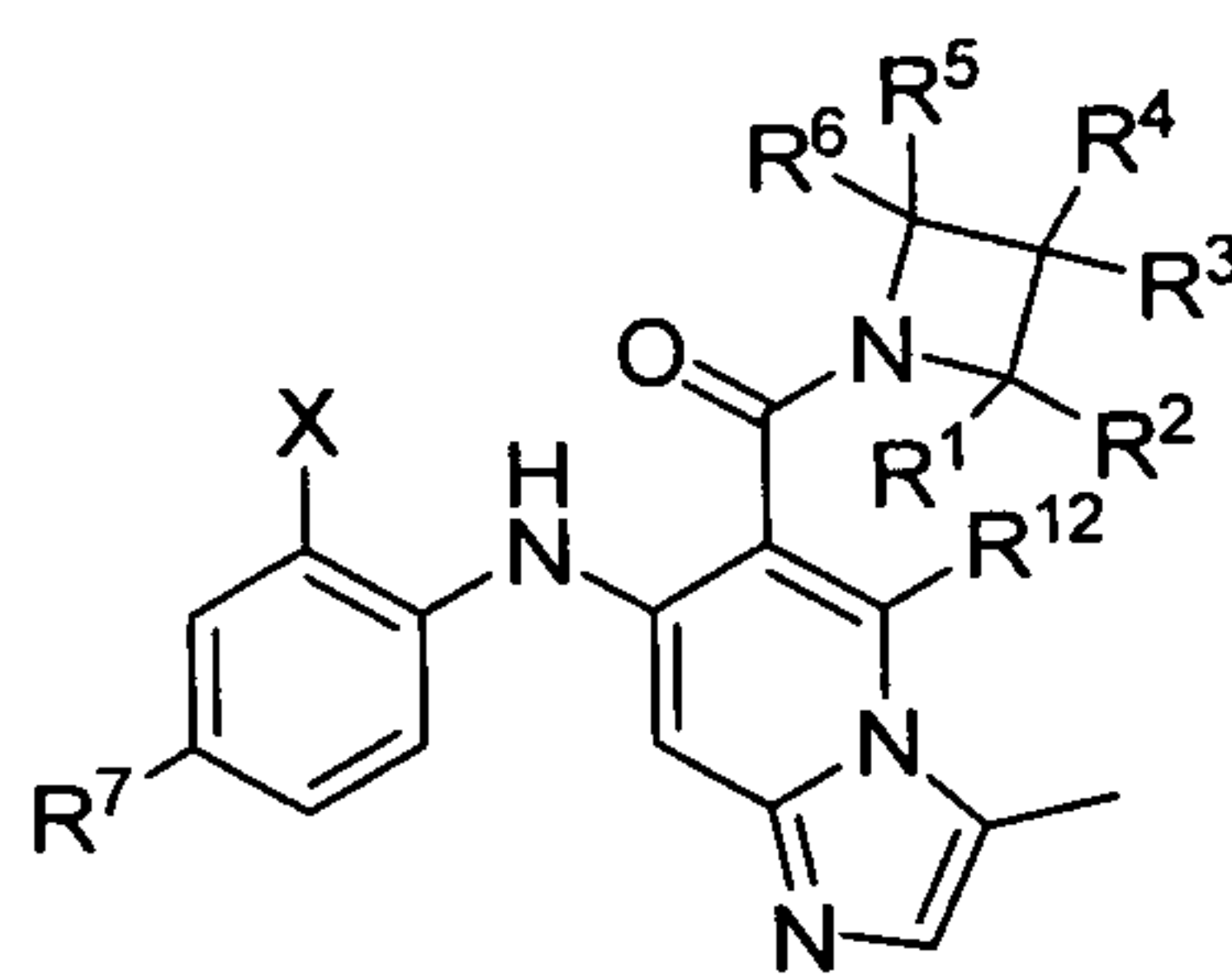
[00229] In another embodiment of embodiment B18, the compound of Formula I is more specifically according to Formula I(t), I(u), I(v), or I(w) where R^3 and R^4 are independently halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^{8'}$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and all other groups are as defined in the Summary of the Invention for a compound of Group B.

[00230] In another embodiment of embodiment B18, the compound of Formula I is more specifically according to Formula I(u), I(v), I(w), or I(x) where R^4 is heterocycloalkyl, heteroaryl (optionally substituted with alkyl), or alkyl where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). In another embodiment, R^4 is piperidinyl, pyrrolidinyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-propyl.

[00231] In another embodiment of embodiment B18, the compound of Formula I is more specifically according to Formula I(u), I(v), I(w), or I(x) where R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; R^3 and R^4 are as defined in the Summary of the Invention for Group B; and R^{10} , R^{12} , and R^{14} are independently hydrogen, halo, or alkyl. In another embodiment, X is fluoro or chloro; R^7 is iodo or bromo; R^{10} is

hydrogen or halo, in another embodiment hydrogen or fluoro; R^{12} and R^{14} are hydrogen; and R^3 is hydroxy. In another embodiment R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00232] In another embodiment of the Invention (B19), the compound of Formula I is more specifically according to Formula I(cc)

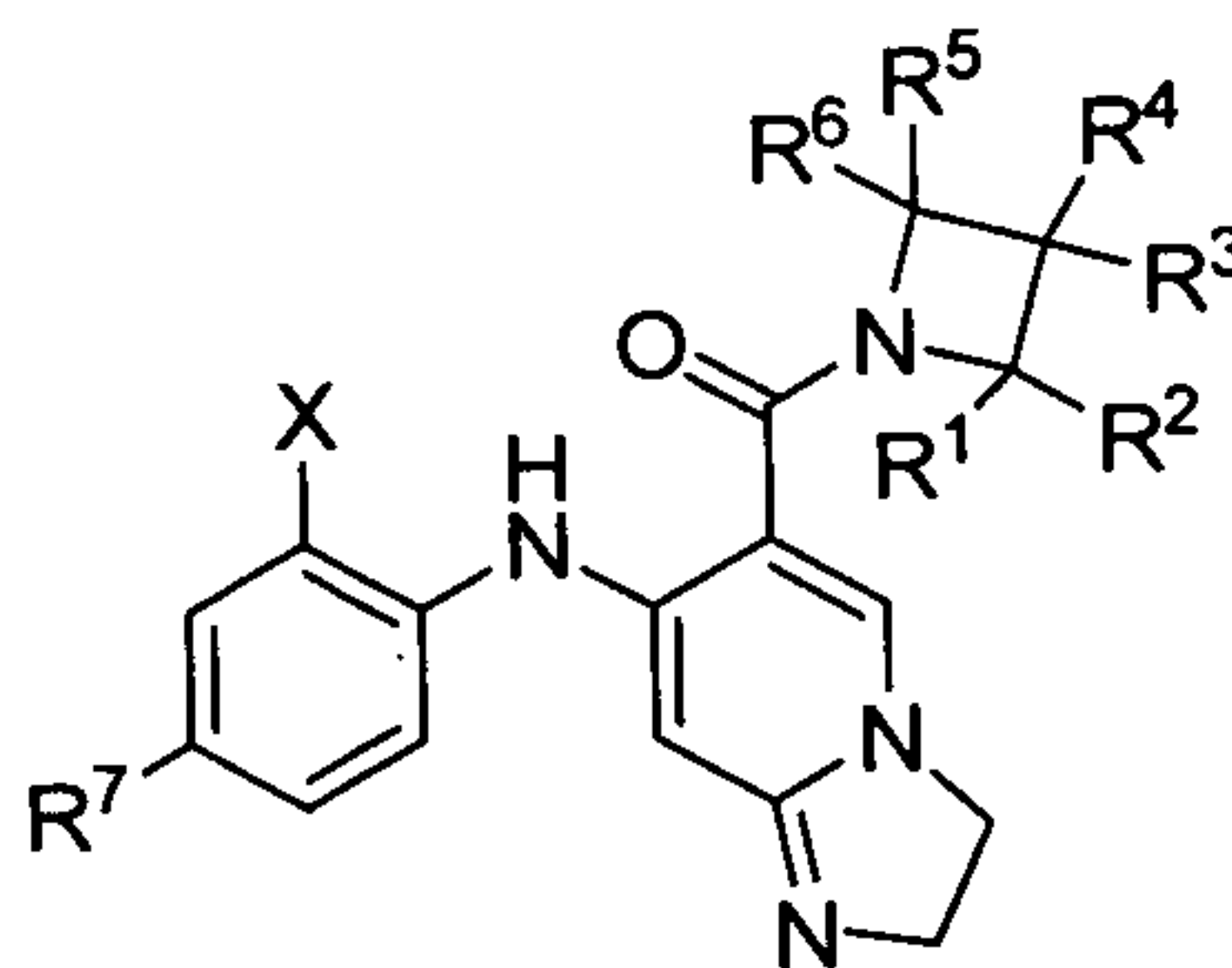


I(cc)

where X, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , and R^7 are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R^1 , R^2 , R^5 , and R^6 are hydrogen; and X and R^7 are halo. In another embodiment, X is fluoro or chloro; and R^3 is hydrogen or hydroxy; R^7 is iodo or bromo. In another embodiment, R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00233] In an embodiment (B19a) of embodiment B19, the compound of Formula I is that where R^4 is heterocycloalkyl or alkyl where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). In another embodiment, R^4 is piperidinyl, pyrrolidinyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00234] In another embodiment of the Invention (B20), the compound of Formula I is more specifically according to Formula I(dd)



I(dd)

where X, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , and R^7 are as defined in the Summary of the Invention for a compound of Group B. In another embodiment, R^1 , R^2 , R^5 , and R^6 are hydrogen; and X and R^7 are halo. In another embodiment, X is fluoro or chloro; and R^3 is hydrogen or hydroxy; R^7 is iodo or bromo. In another embodiment, R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl,

1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00235] In an embodiment (B20a) of embodiment B20, the compound of Formula I is that where R^4 is heterocycloalkyl or alkyl where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). In another embodiment, R^4 is piperidinyl, pyrrolidinyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00236] In one embodiment of the Invention (C1), the compound of Formula I is selected from Group C where all groups are as defined in the Summary of the Invention.

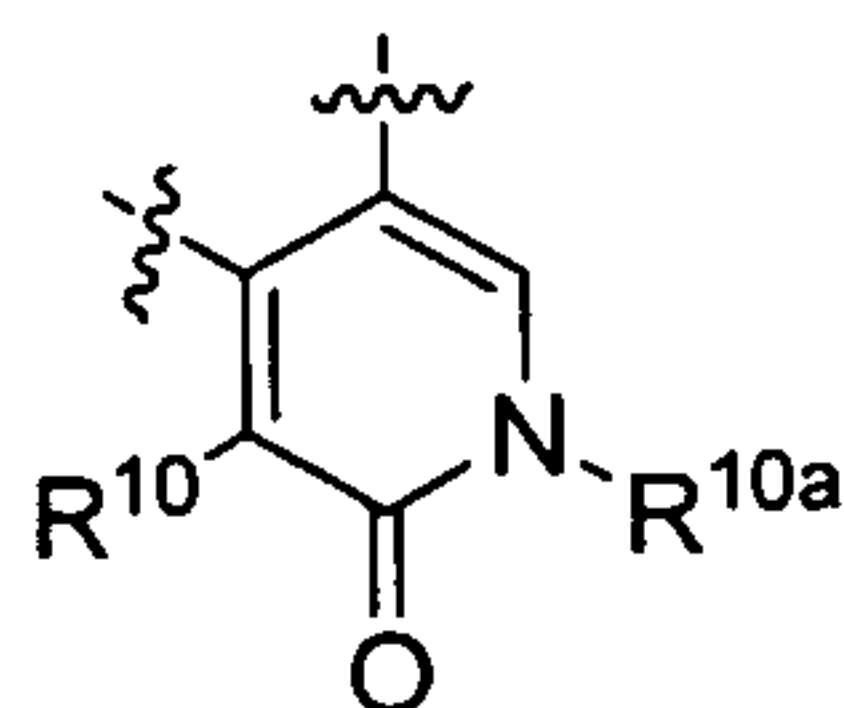
[00237] In another embodiment of the invention (C2), the compound of Formula I is that where X and R^7 are halo; and all other groups are as defined for a compound selected from Group C.

[00238] In another embodiment of the invention (C3), the compound of Formula I is selected from Group C where R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or

heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^8$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^8$, $-NR^8C(O)NR^8R^8$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; and R^4 is as defined in the Summary of the Invention; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and all other groups are as defined in the Summary of the Invention for a compound of Group C. In another embodiment, R^1 , R^2 , R^5 and R^6 are hydrogen; and X and R^7 are halo.

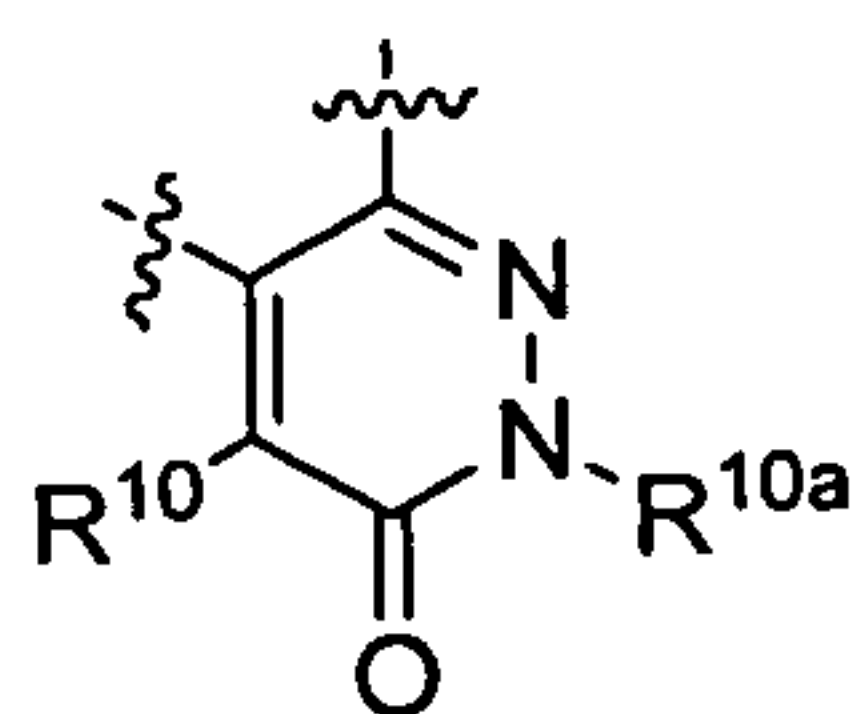
[00239] In another embodiment of the invention (C4), the compound of Formula I is selected from Group C where R^3 and R^4 are independently halo, nitro, $-NR^8R^8$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^8$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^8$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^8$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, $-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$, $-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^8$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^8$, $-NR^8C(O)NR^8R^8$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and all other groups are as defined in the Summary of the Invention for a compound of Group C. In another embodiment, R^1 , R^2 , R^5 and R^6 are hydrogen; and X and R^7 are halo.

[00240] In another embodiment of the invention (C5), the compound of Formula I is that where A is



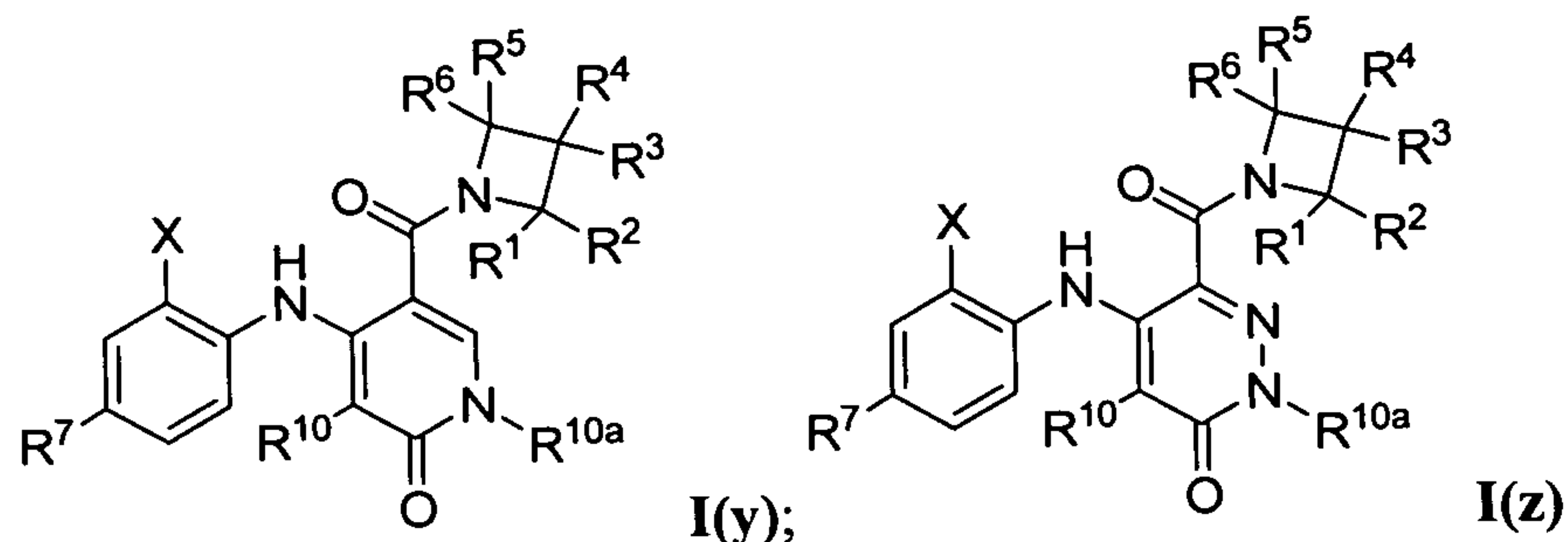
and X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, and R^{10a} are as defined in the Summary of the invention for a compound of Group C. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R¹⁰ is hydrogen or halo; and R^{10a} is alkyl. In another embodiment, X is fluoro or chloro; R³ is hydroxy; R⁷ is iodo or bromo; R¹⁰ is hydrogen or fluoro; and R^{10a} is methyl. In another embodiment, R⁴ is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R⁴ is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00241] In another embodiment of the invention (C6), the compound of Formula I is that where A is



and X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, and R^{10a} are as defined in the Summary of the invention for a compound of Group C. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R¹⁰ is hydrogen or halo; and R^{10a} is alkyl. In another

[00242] In another embodiment of the Invention (C7), the compound of Formula I is more specifically of Formula I(y) or I(z):



where R¹, R², R⁵, and R⁶ are hydrogen; X and R⁷ are halo; R³, R⁴, R¹⁰, R^{10a}, and Y¹ are as defined in the Summary of the Invention for a compound of Group C. In another embodiment, X is fluoro or chloro; R⁷ is iodo or bromo; R¹⁰ is hydrogen, halo, or alkyl, in another embodiment hydrogen or halo; and R^{10a} is alkyl, in another embodiment methyl. In another embodiment R¹⁰ is hydrogen or fluoro; R³ is hydroxy; and R⁴ is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or alkyl and R^{8'} is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl.

[00243] In one embodiment of the Invention (D), the compound of Formula I is selected from Group D where all groups are as defined in the Summary of the Invention.

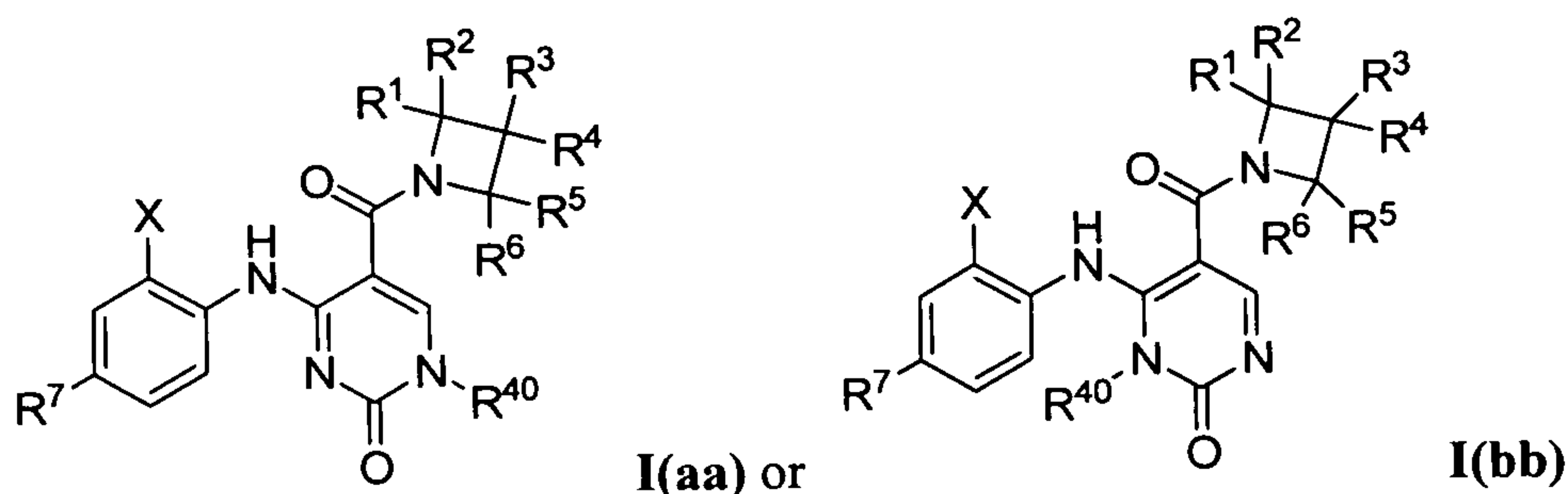
[00244] In another embodiment of the invention (D1), the compound of Formula I is that where X and R⁷ are halo; and all other groups are as defined for a compound selected from Group D.

[00245] In another embodiment of the invention (D2), the compound of Formula I is selected from Group D where R³ is halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, -CH₂N(R²⁵)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂)), -CH₂NR²⁵C(=NH)(N(R^{25a})(CN)), -CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; and R⁴ is as defined in the Summary of the Invention; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in the Summary of the Invention for a compound of Group C. In another embodiment, R¹, R², R⁵ and R⁶ are hydrogen; and X and R⁷ are halo.

[00246] In another embodiment of the invention (D3), the compound of Formula I is selected from Group D where R³ and R⁴ are independently halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, -CH₂N(R²⁵)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(NR^{25a}R^{25b}), -CH₂NR²⁵C(=NH)(N(R^{25a})(NO₂)), -CH₂NR²⁵C(=NH)(N(R^{25a})(CN)), -CH₂NR²⁵C(=NH)(R²⁵), -CH₂NR²⁵C(NR^{25a}R^{25b})=CH(NO₂), alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo,

alkyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-OR^8$, $-NR^8R^8$, $-NR^8S(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^8$, $-NR^8C(O)NR^8R^8$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; or R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and all other groups are as defined in the Summary of the Invention for a compound of Group C. In another embodiment, R^1 , R^2 , R^5 and R^6 are hydrogen; and X and R^7 are halo.

[00247] In another embodiment of the invention (D4), the compound of Formula I is that where A is



where R^{40} is hydrogen or methyl (in another embodiment, R^{40} is hydrogen) and all other groups are as defined in the Summary of the Invention. In another embodiment, R^1 , R^2 , R^5 , and R^6 are hydrogen; X and R^7 are halo; and R^{40} is hydrogen or methyl. In another embodiment, X is fluoro or chloro; and R^3 is hydrogen or hydroxy; R^7 is iodo or bromo. In another embodiment, R^4 is heterocycloalkyl, alkyl, or heteroaryl, where the alkyl is optionally substituted with $-NR^8R^8$ (where R^8 is hydrogen or alkyl and R^8 is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl) and the heteroaryl is optionally substituted with alkyl. In another embodiment, R^4 is piperidinyl, pyrrolidinyl, benzimidazolyl, *N*-methyl-benzimidazolyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00248] In an embodiment (D4a) of the invention of D4, the compound of Formula I is that where R^4 is heterocycloalkyl or alkyl where the alkyl is optionally substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen or alkyl and $R^{8'}$ is hydrogen, alkyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl). In another embodiment, R^4 is piperidinyl, pyrrolidinyl, methylaminomethyl, 1(*R,S*)-amino-ethyl, 1(*R*)-amino-ethyl, 1(*S*)-amino-ethyl, 1(*R,S*)-(methylamino)-ethyl, 1(*R*)-(methylamino)-ethyl, 1(*S*)-(methylamino)-ethyl, 1(*R,S*)-(dimethylamino)-ethyl, 1(*R*)-(dimethylamino)-ethyl, 1(*S*)-(dimethylamino)-ethyl, 1(*R,S*)-amino-propyl, 1(*R*)-amino-propyl, 1(*S*)-amino-propyl, 1(*R,S*)-(methylamino)-propyl, 1(*R*)-(methylamino)-propyl, 1(*S*)-(methylamino)-propyl, 1(*R,S*)-(dimethylamino)-propyl, 1(*R*)-(dimethylamino)-propyl, 1(*S*)-(dimethylamino)-propyl, 1(*R,S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, 1(*R*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl, or 1(*S*)-(3,4-cis-dihydroxy-cyclopentylamino)-ethyl.

[00249] Another embodiment of the Invention (E) is directed to a Compound of Formula I selected from Group A, Group B, and Group C where

Group A

A is phenylene optionally substituted with one or two groups selected from R^{10} , R^{12} , R^{14} , and R^{16} where R^{10} , R^{12} , R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1 , R^2 , R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, $-NR^8R^{8'}$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^{8'}$, $-NR^8C(O)R^{8'}$,

$-CH_2N(R^{25})(NR^{25a}R^{25b})$, $-CH_2NR^{25}C(=NH)(NR^{25a}R^{25b})$,

$-CH_2NR^{25}C(=NH)(N(R^{25a})(NO_2))$, $-CH_2NR^{25}C(=NH)(N(R^{25a})(CN))$,

$-CH_2NR^{25}C(=NH)(R^{25})$, $-CH_2NR^{25}C(NR^{25a}R^{25b})=CH(NO_2)$, alkyl, alkenyl,

cycloalkyl, heterocycloalkyl, or heteroaryl; where the R^4 alkyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$,

$-NR^8C(O)R^{8'}$, $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^{8'}$, and aryl; where the R^4 cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and

$-NR^8R^{8'}$; where the R^4 heterocycloalkyl is optionally substituted with one or two groups independently selected from alkyl and $-C(O)OR^{8'}$; and where the

R^4 heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

m is 0;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, alkyl, alkenyl, alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

where the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (where n is 0 and R^{31} is alkyl), carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl); or where the alkyl is optionally substituted with one, two, three, four, or five halo;

where the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and alkyl;

where the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from alkyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

where the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (where R^{32} is hydrogen or alkyl and R^{32a} is alkyl, alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (where R^{34} is hydrogen or alkyl and R^{34a} is alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

where the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, $-C(O)NR^{33}R^{33a}$ (where R^{33} is hydrogen or alkyl and R^{33a} is alkyl, alkenyl, alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and

R^9 is alkyl or aryl;

Group B

A is thien-3,4-diyl, benzo[*d*]isoxazol-5,6-diyl, 1*H*-indazol-5,6-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is alkyl or alkenyl), benzo[*d*]oxazol-5,6-diyl, benzo[*d*]thiazol-5,6-diyl, 1*H*-benzo[*d*]imidazol-5,6-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is alkyl or alkenyl), 1*H*-benzo[*d*][1,2,3]triazol-5,6-diyl (optionally substituted at the N1 position with R¹⁹ where R¹⁹ is alkyl or alkenyl), imidazo[1,2-*a*]pyridin-6,7-diyl, cinnolin-6,7-diyl, quinolin-6,7-diyl, pyridin-3,4-diyl, or 1-oxido-pyridin-3,4-diyl; where A is optionally substituted with one, two, or three groups independently selected from R¹⁰, R¹², R¹⁴, R¹⁶ and R¹⁹ where R¹⁰, R¹², R¹⁴ and R¹⁶ are independently hydrogen, alkyl, halo, or amino; and R¹⁹ is hydrogen or alkyl;

X is halo;

R¹, R², R⁵ and R⁶ are hydrogen;

R³ is hydrogen or hydroxy;

R⁴ is -NR⁸R^{8'}, heterocycloalkyl, heteroaryl, or alkyl; where the alkyl is optionally substituted with -NR⁸R^{8'} and where the heteroaryl is optionally substituted with alkyl;

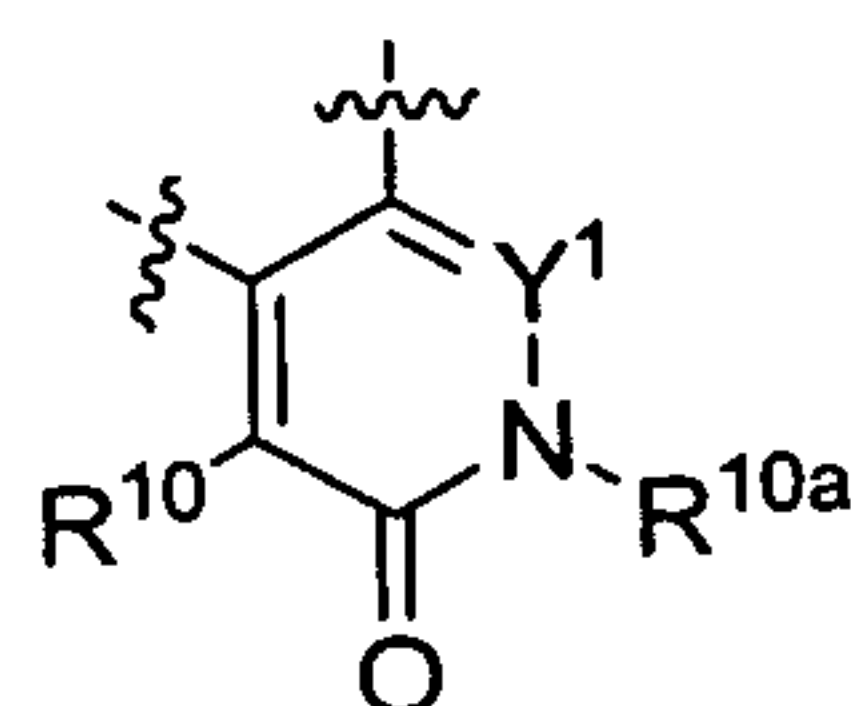
R⁷ is halo;

R⁸ is hydrogen or alkyl; and

R^{8'} is hydrogen, alkyl, or cycloalkyl; where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl;

Group C

A is



(a)

where R¹⁰ is hydrogen or halo;

R^{10a} is hydrogen or alkyl;

Y¹ is =CH- or =N-;

X is halo;

R¹, R², R⁵ and R⁶ are hydrogen;

R³ is hydrogen or hydroxy;

R^4 is $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or alkyl; where the alkyl is optionally substituted with $-NR^8R^{8'}$ and where the heteroaryl is optionally substituted with alkyl;

R^7 is halo;

R^8 is hydrogen or alkyl; and

$R^{8'}$ is hydrogen, alkyl, or cycloalkyl; where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and alkyl.

Representative MEK Compounds

[00250] Representative compounds of Formula I are depicted below. The examples are merely illustrative and do not limit the scope of the invention in any way. Compounds of the invention are named according to systematic application of the nomenclature rules agreed upon by the International Union of Pure and Applied Chemistry (IUPAC), International Union of Biochemistry and Molecular Biology (IUBMB), and the Chemical Abstracts Service (CAS). Names were generated using ACD/Labs naming software 8.00 release, product version 8.08.

Table 1. Representative MEK Inhibitors

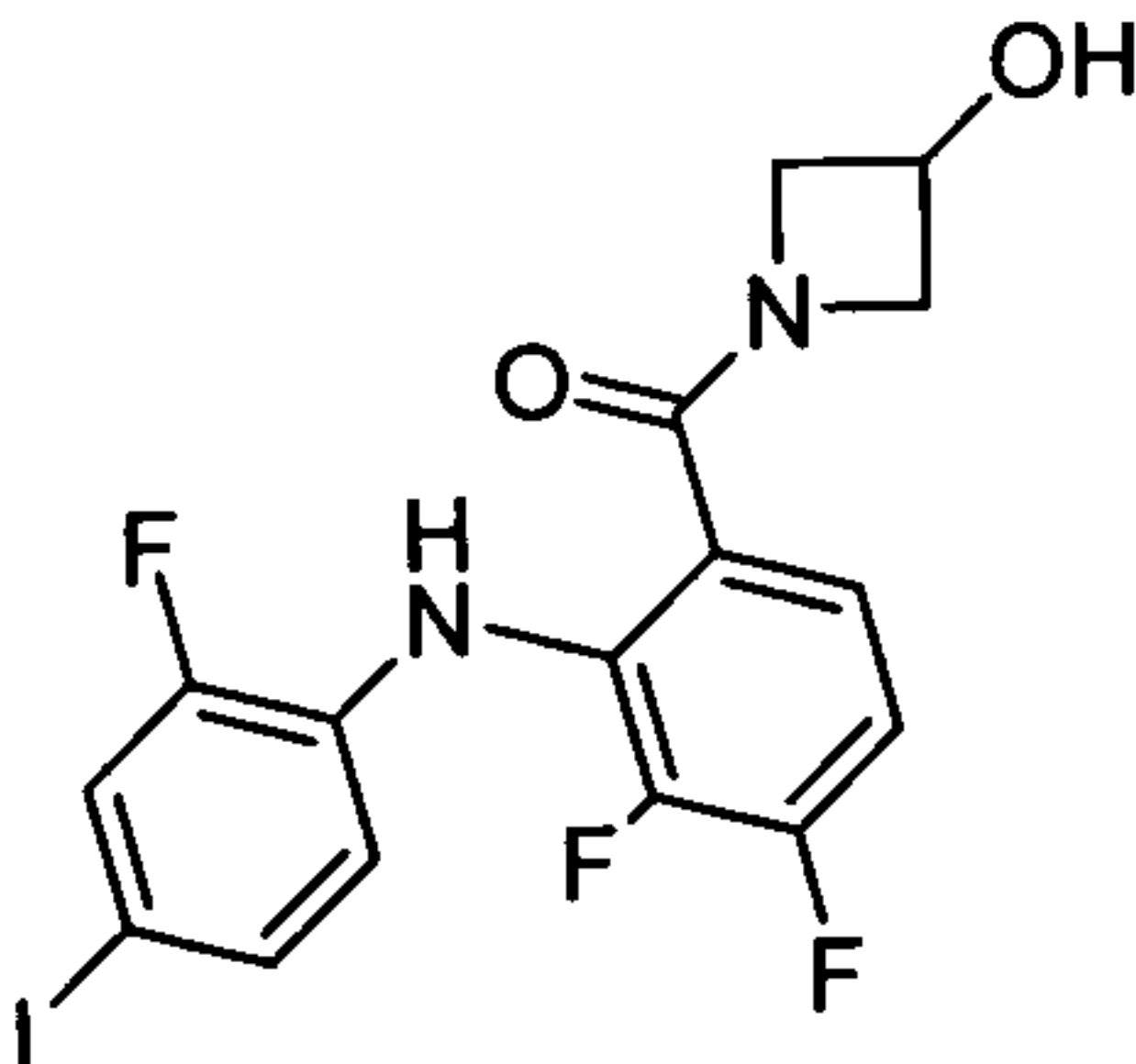
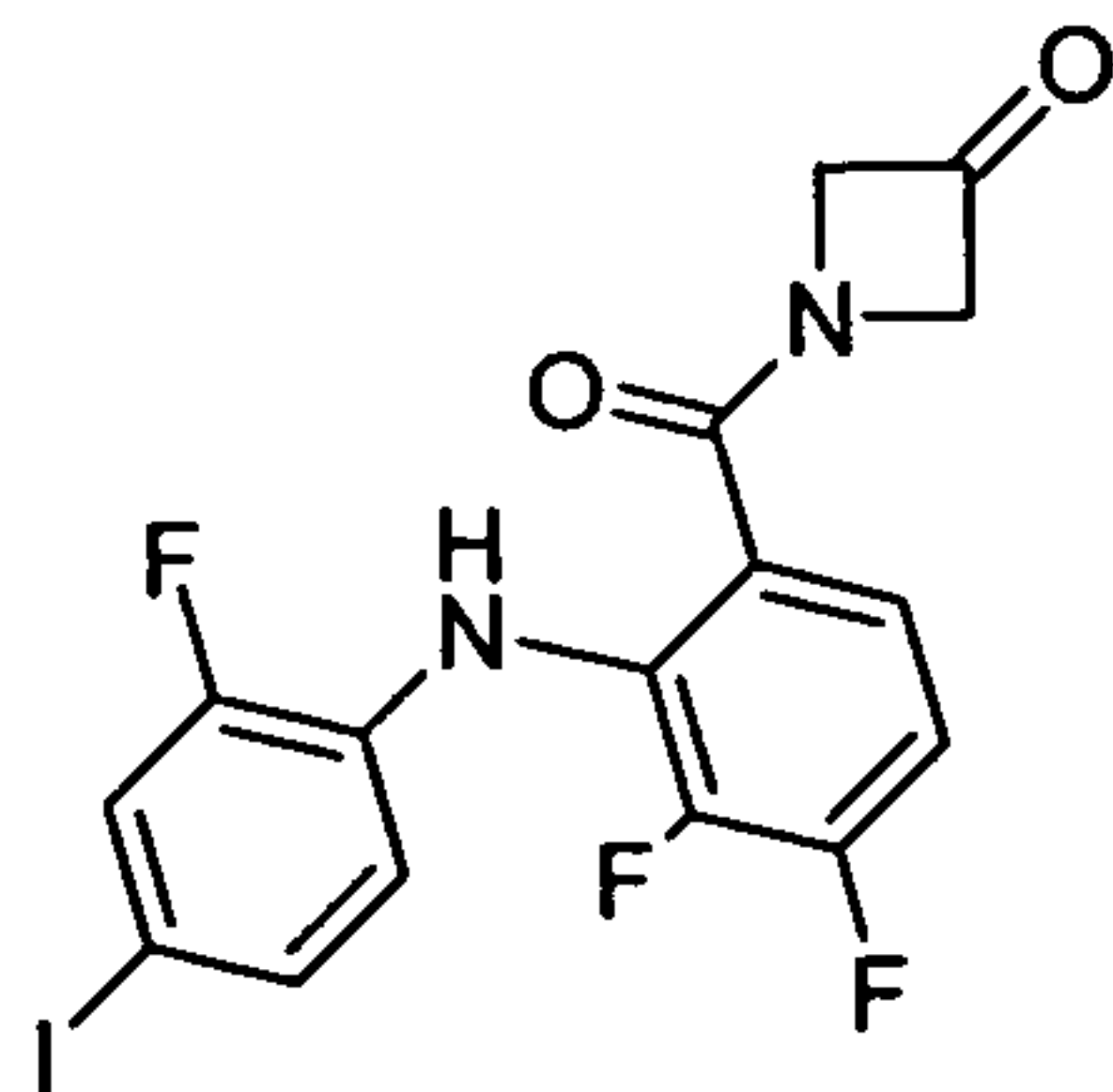
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
1		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)azetidin-3-ol
2		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-carbonyl)azetidin-3-one

Table 1. Representative MEK Inhibitors

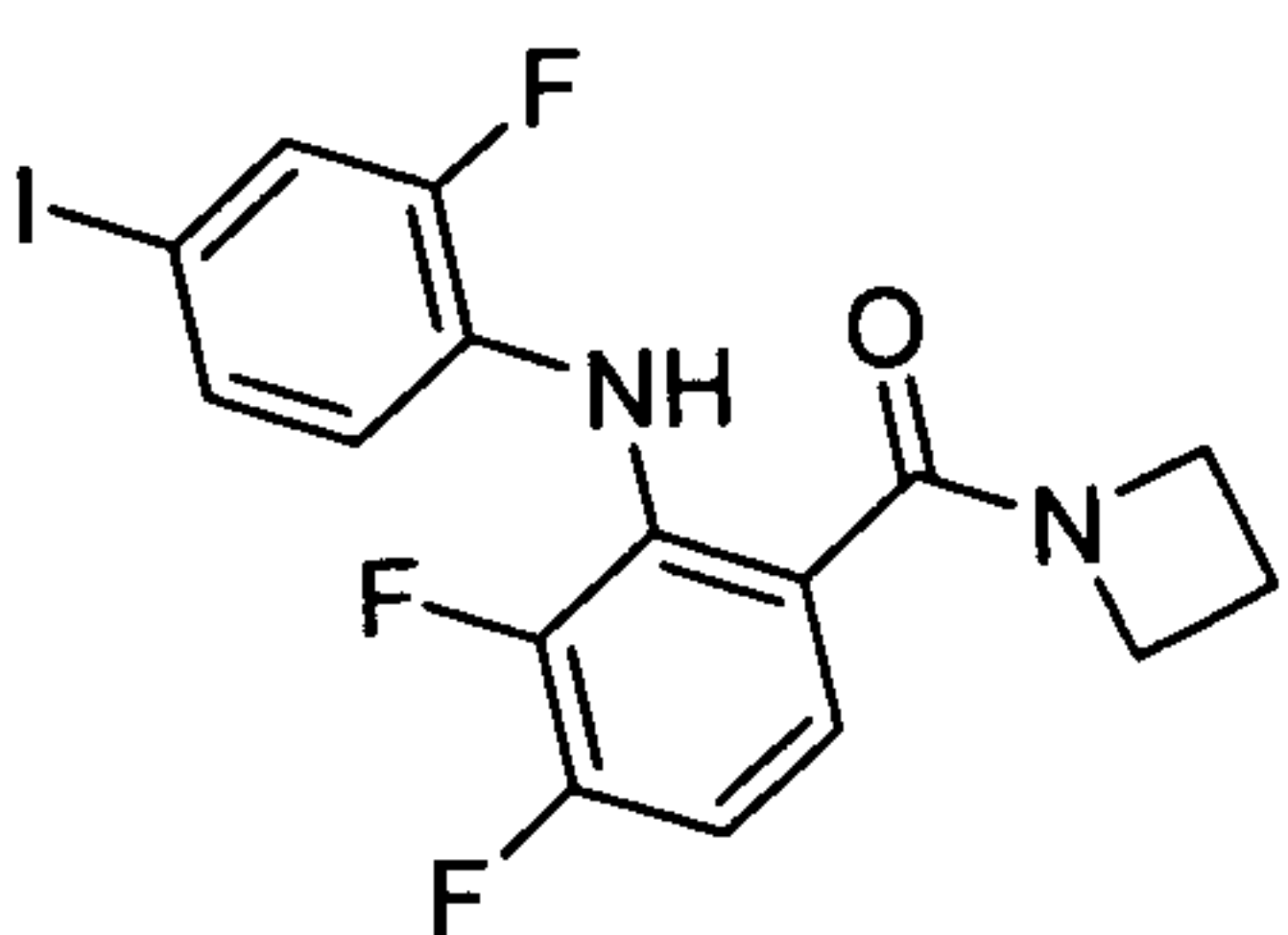
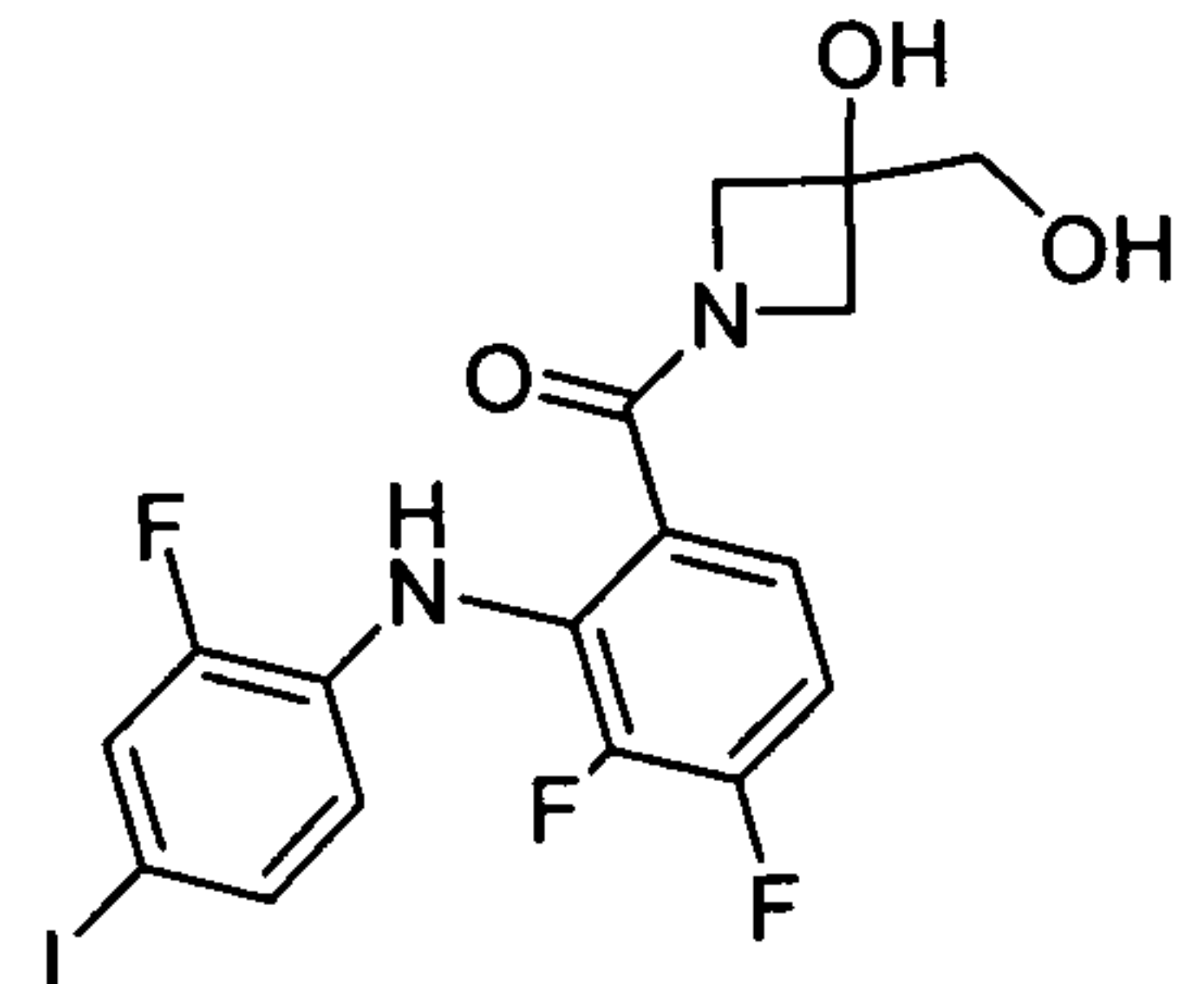
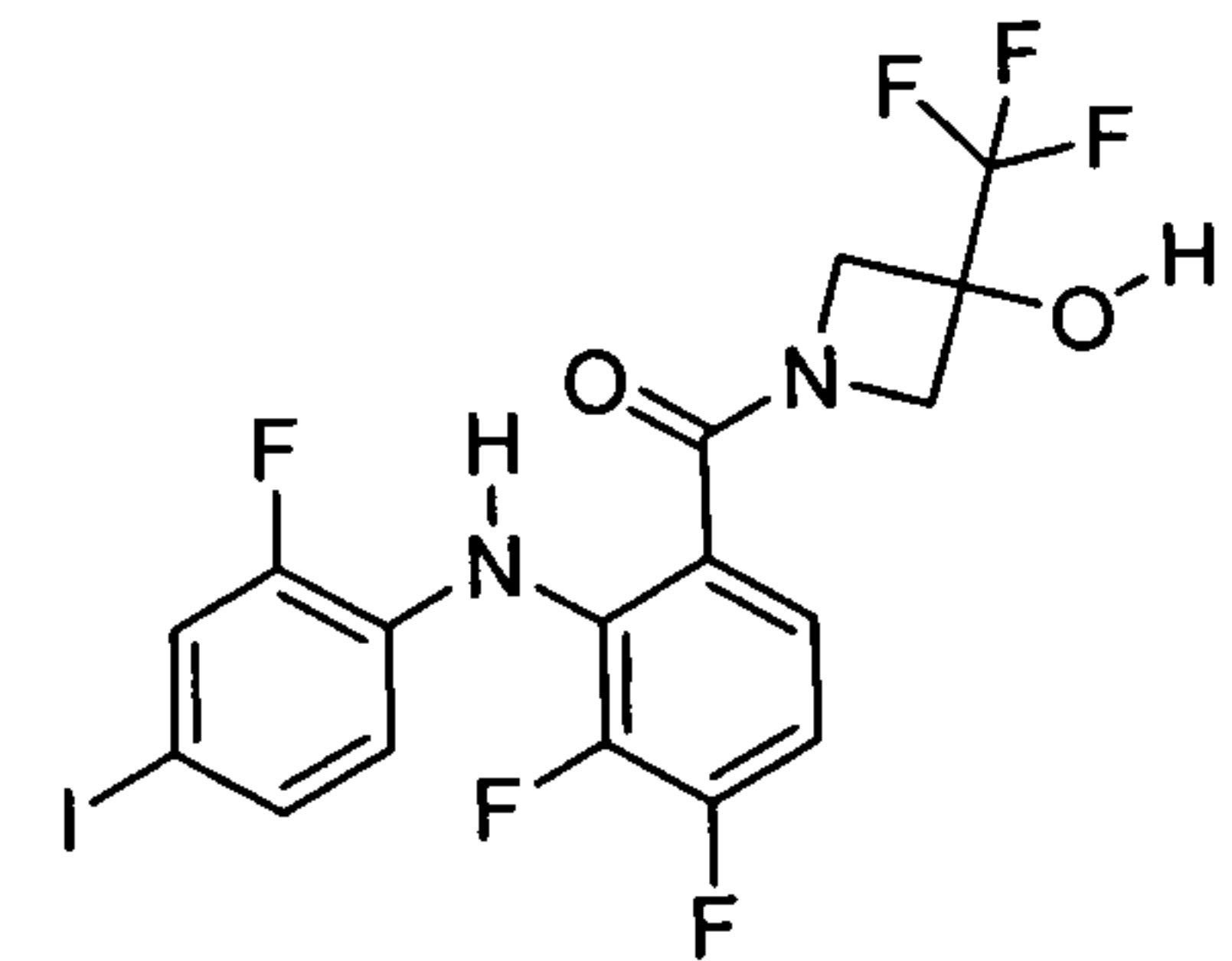
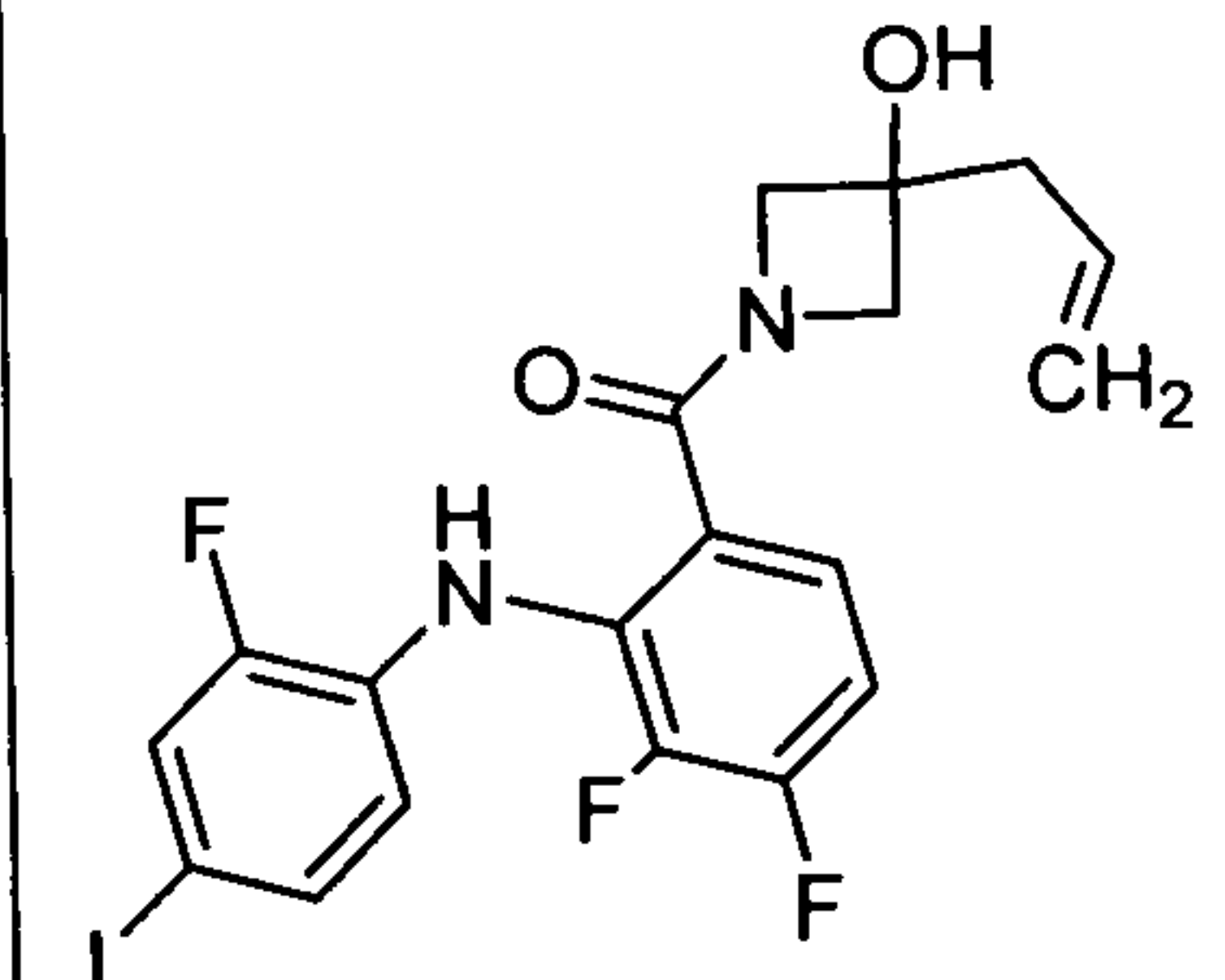
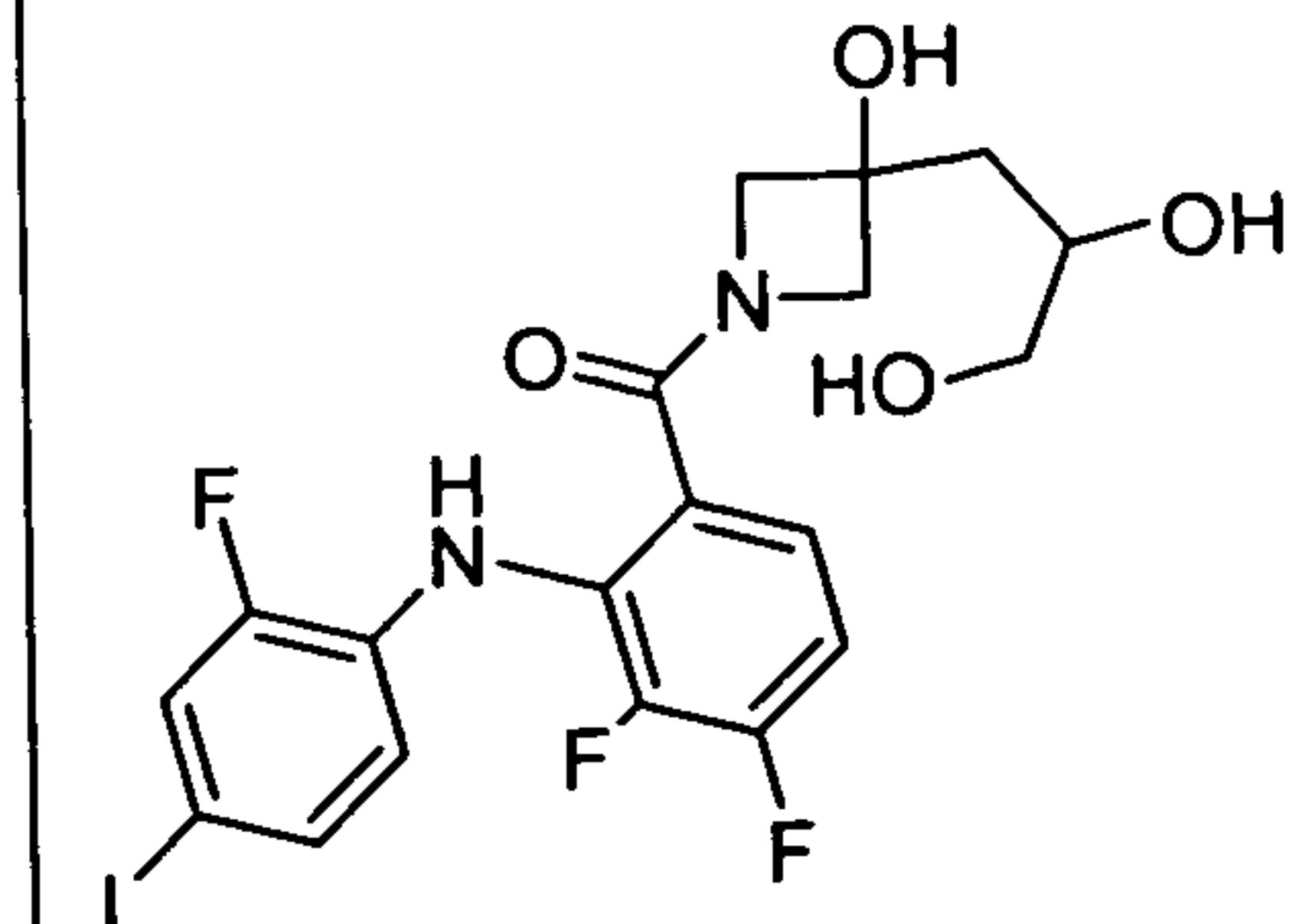
Cmpd No.	Structure	Name
3		6-(azetidin-1-ylcarbonyl)-2,3-difluoro-N-(2-fluoro-4-iodophenyl)aniline
4		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol
5		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol
6		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-prop-2-en-1-ylazetidin-3-ol
7		3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]propane-1,2-diol

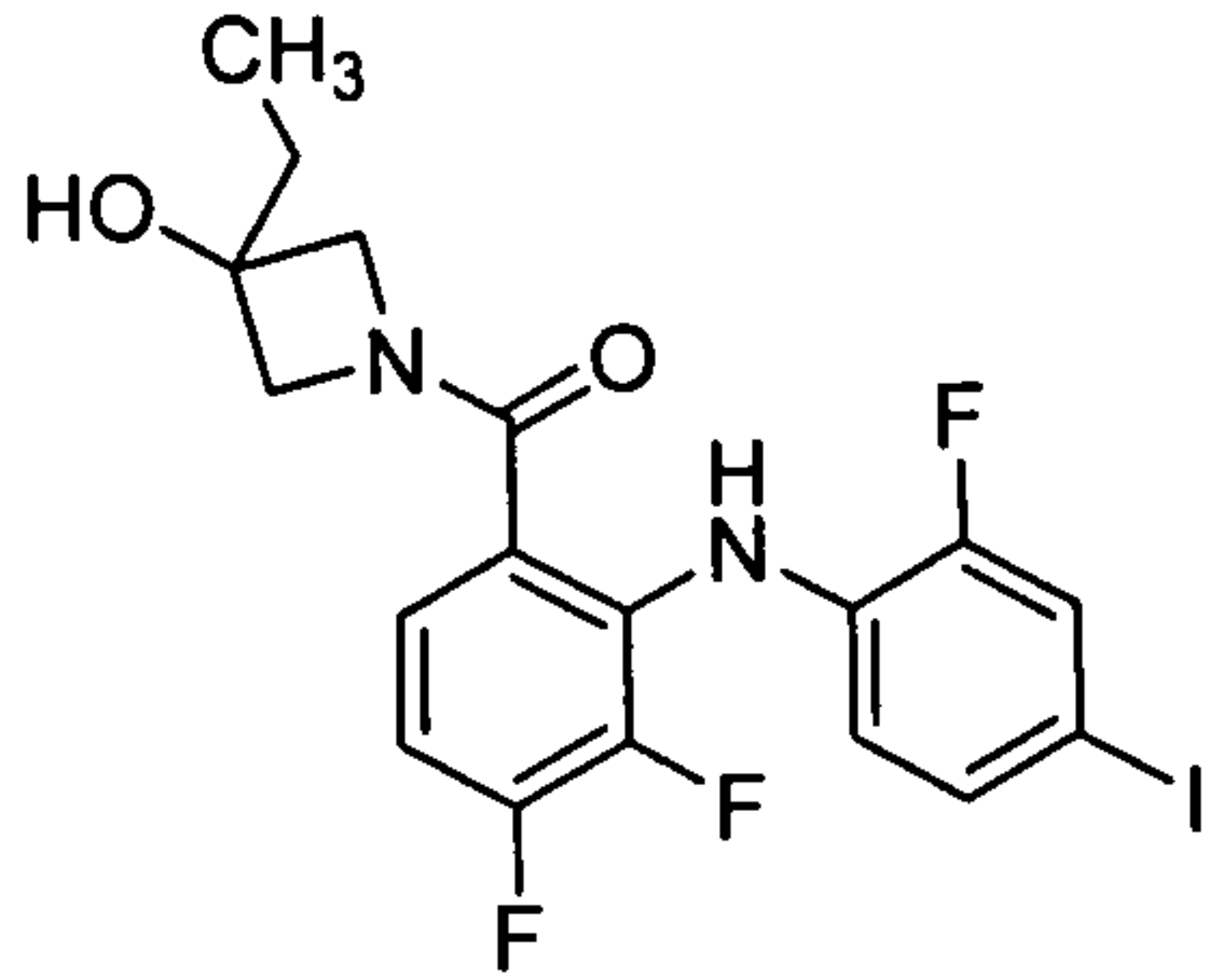
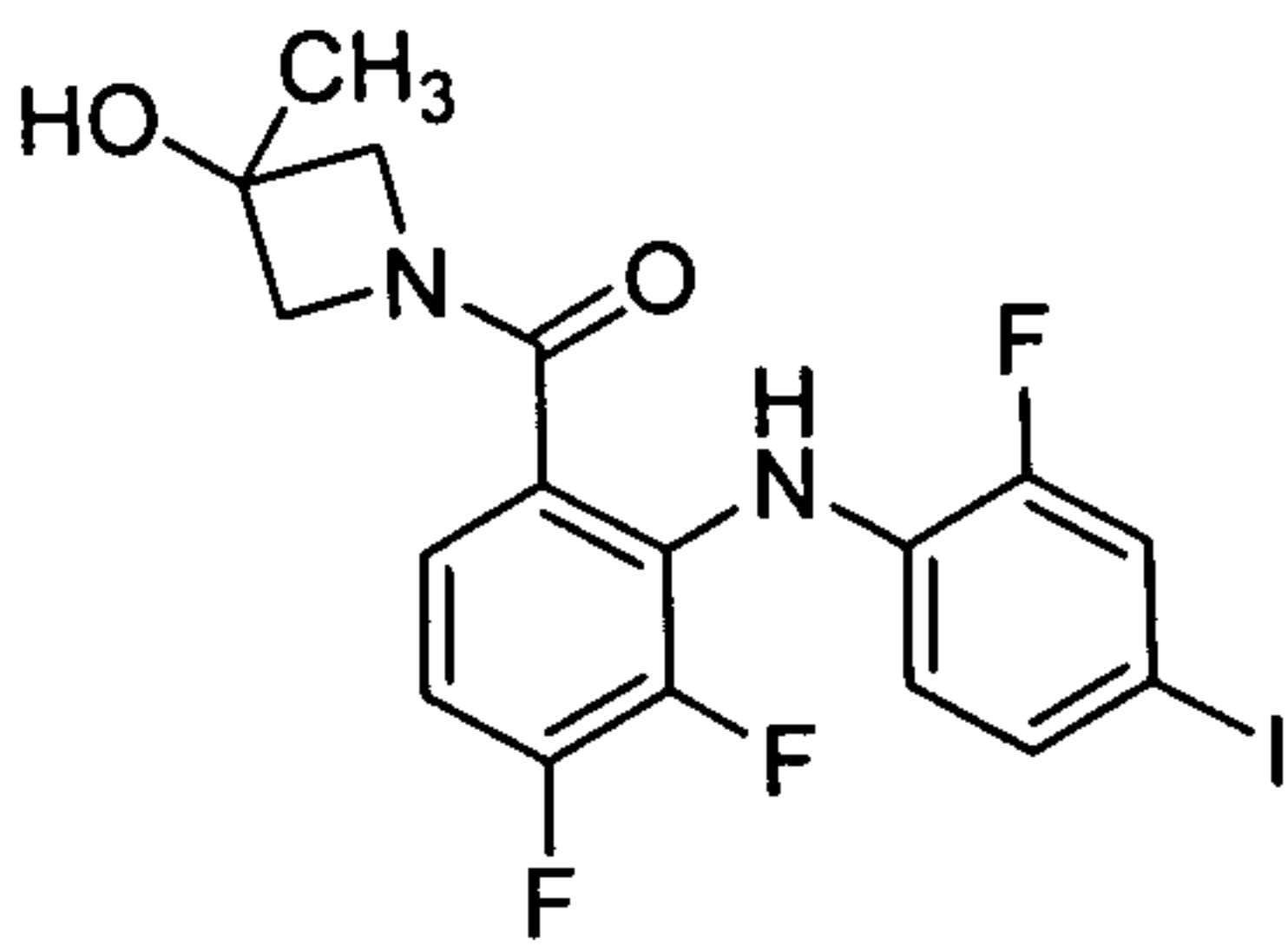
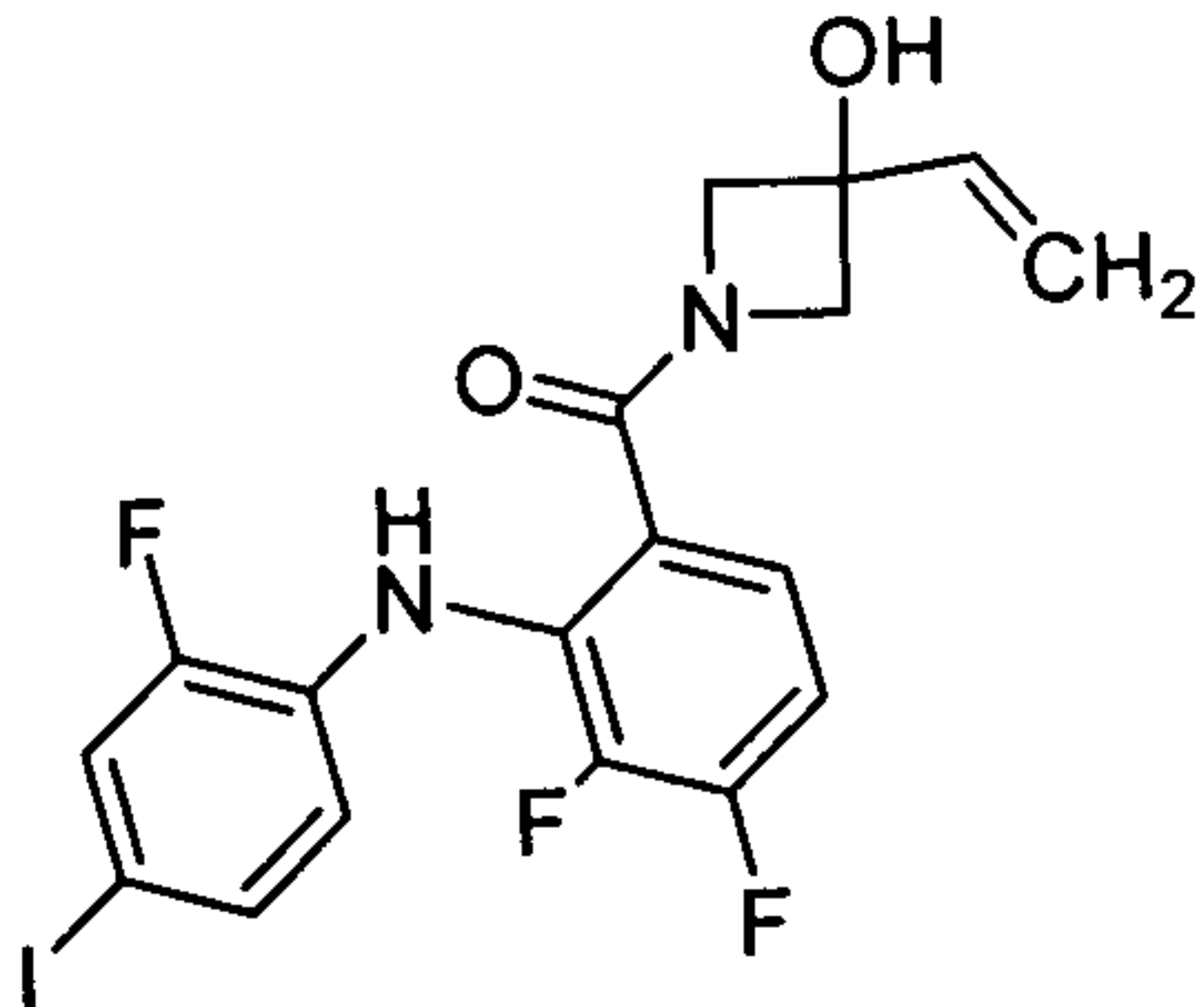
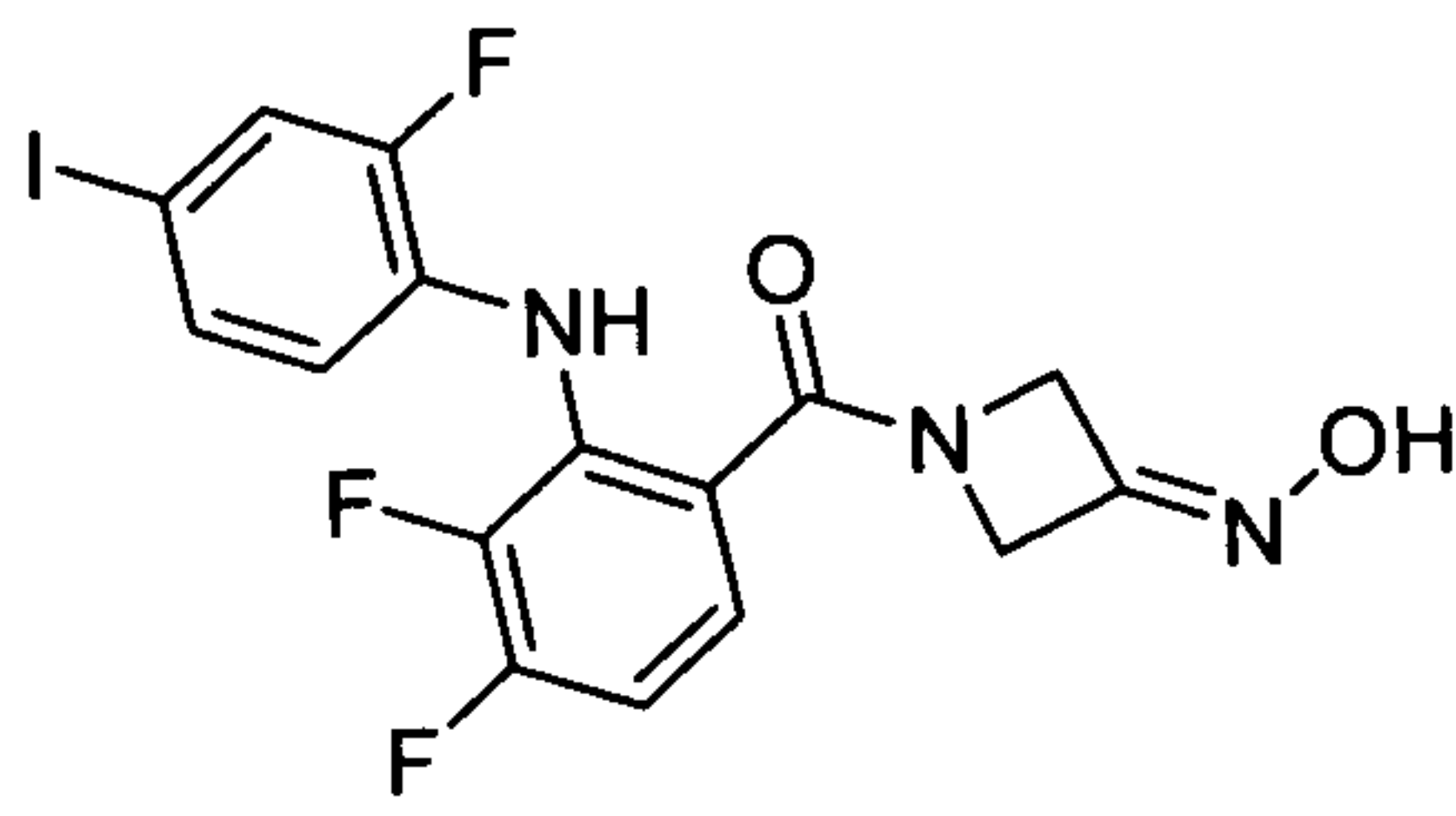
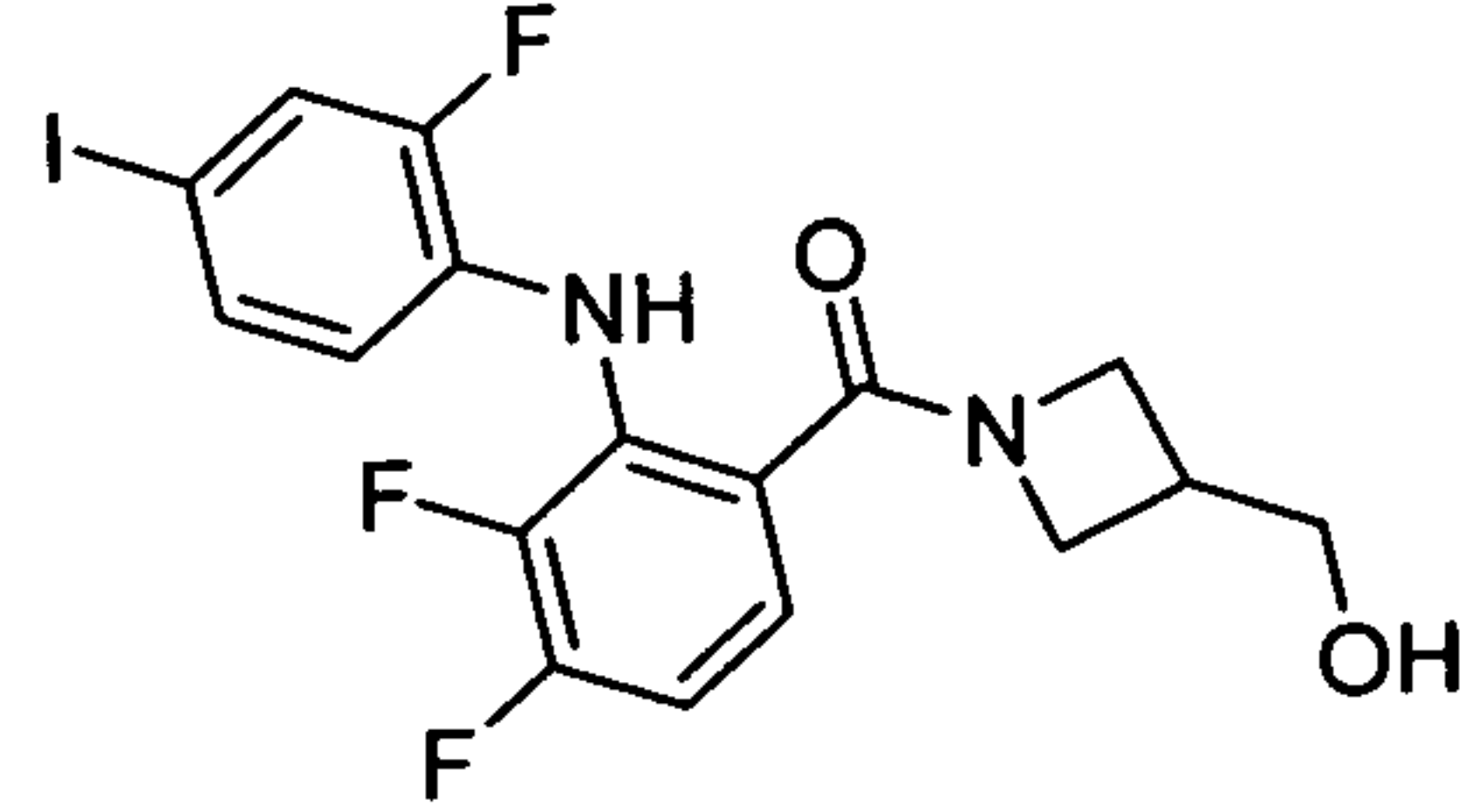
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
8		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethylazetidin-3-ol
9		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-methylazetidin-3-ol
10		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethenylazetidin-3-ol
11		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime
12		[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol

Table 1. Representative MEK Inhibitors

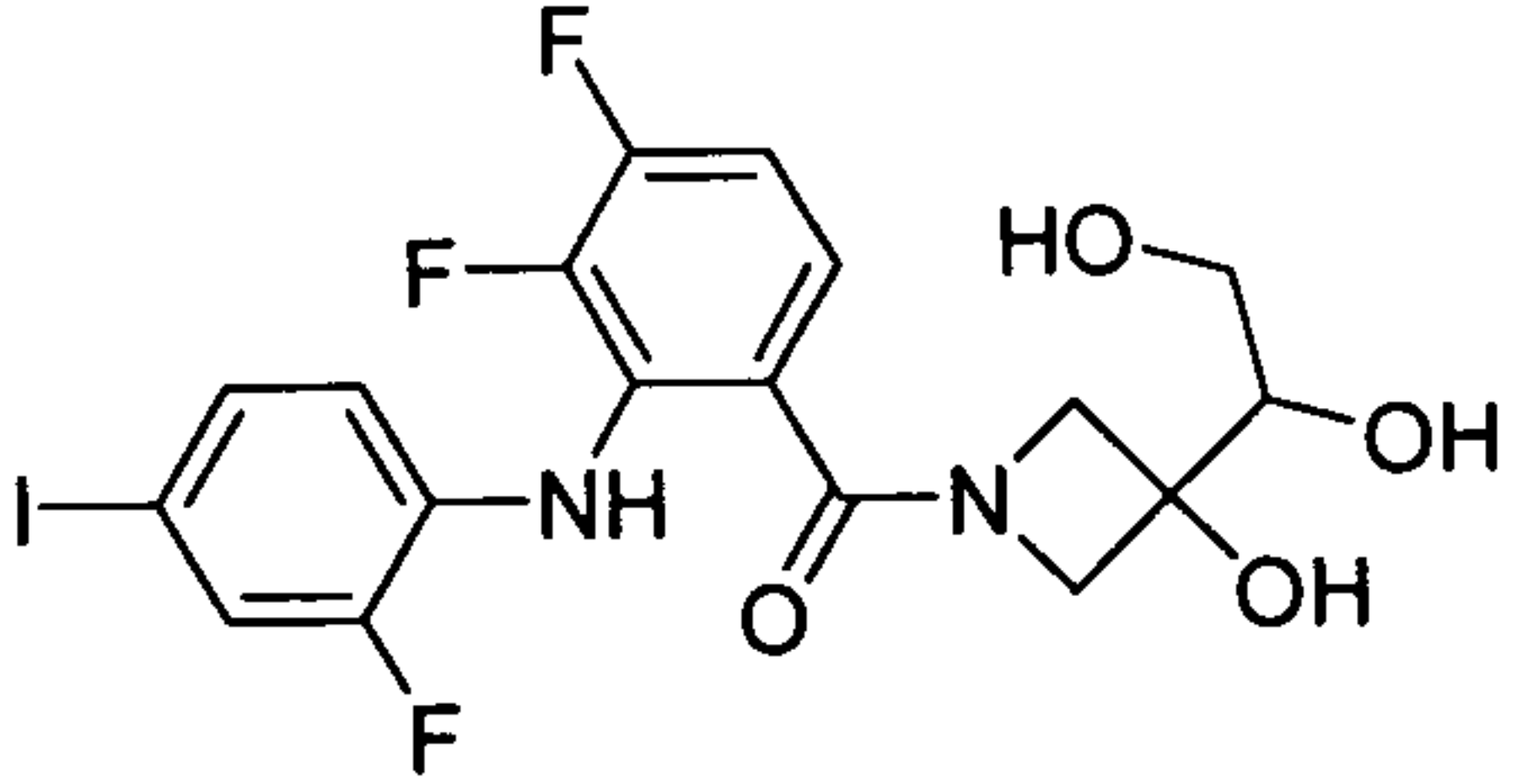
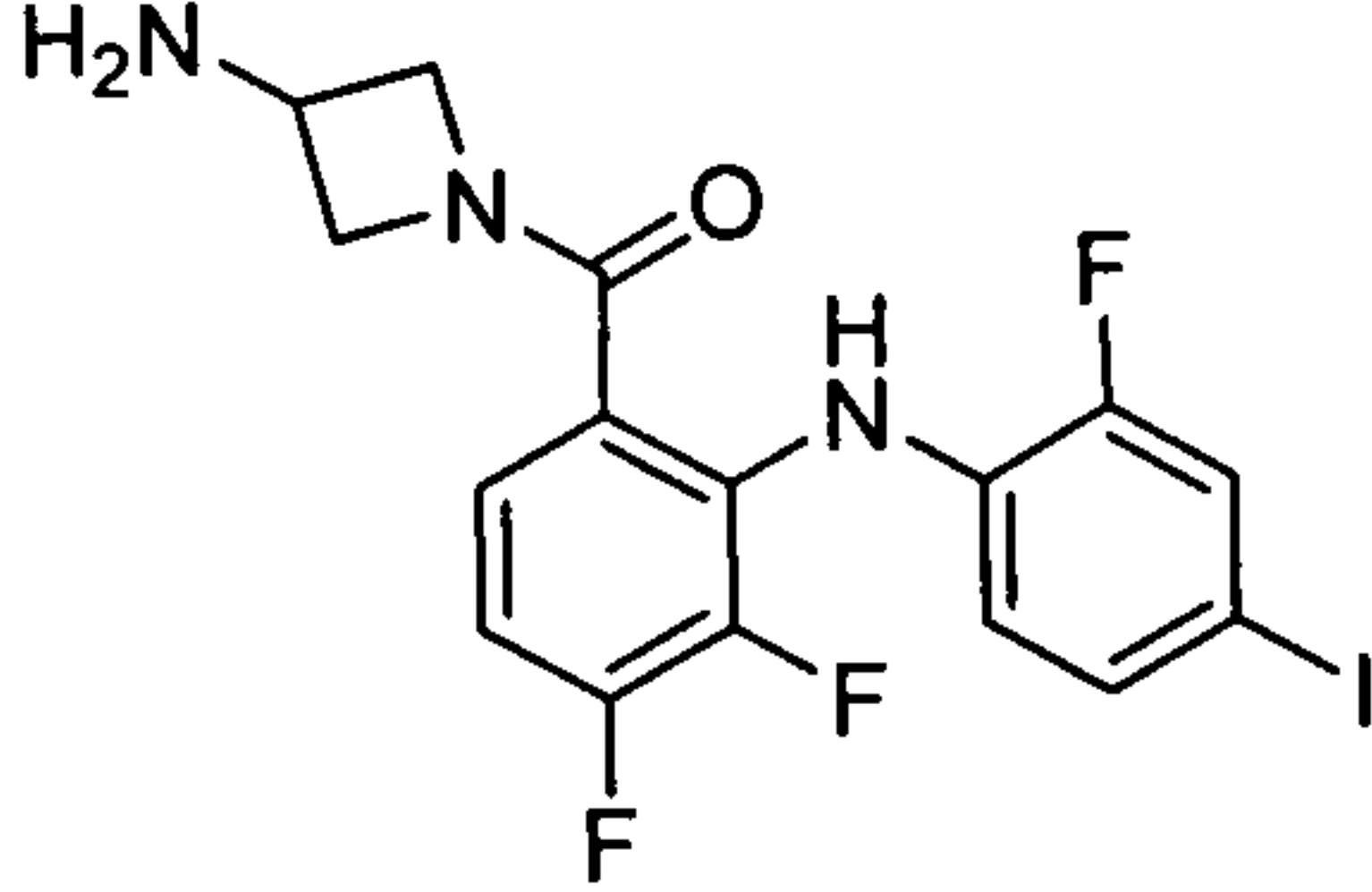
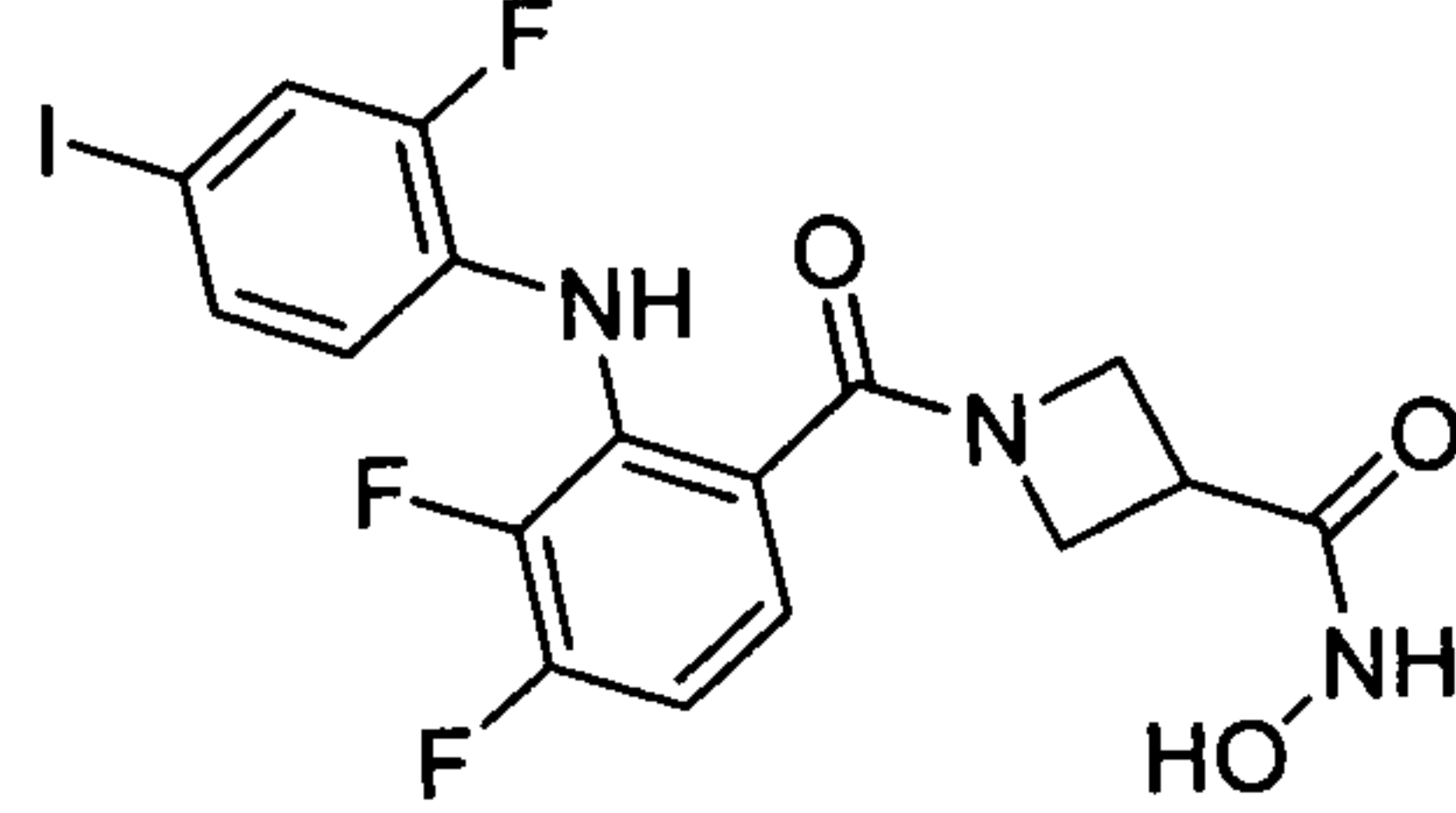
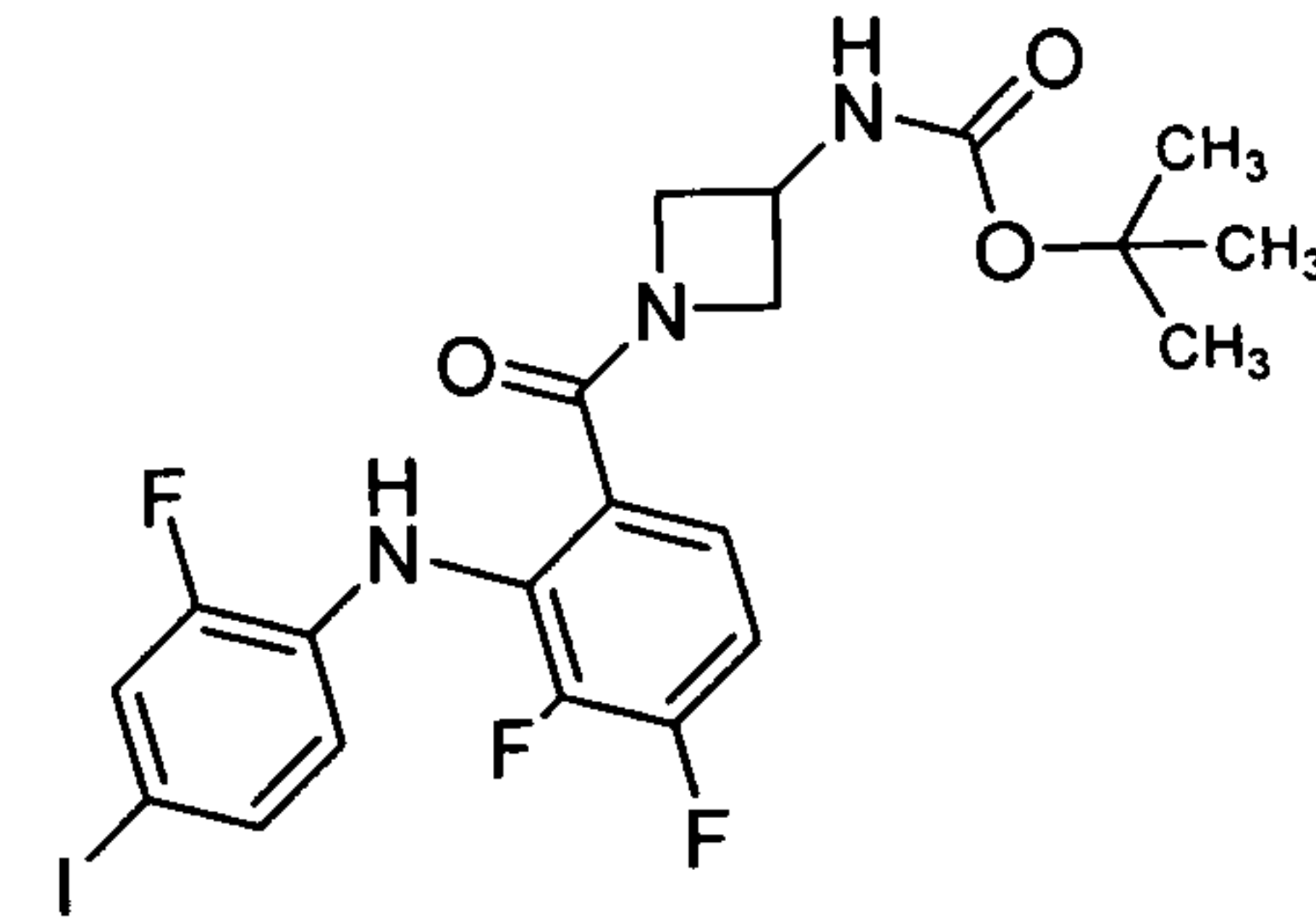
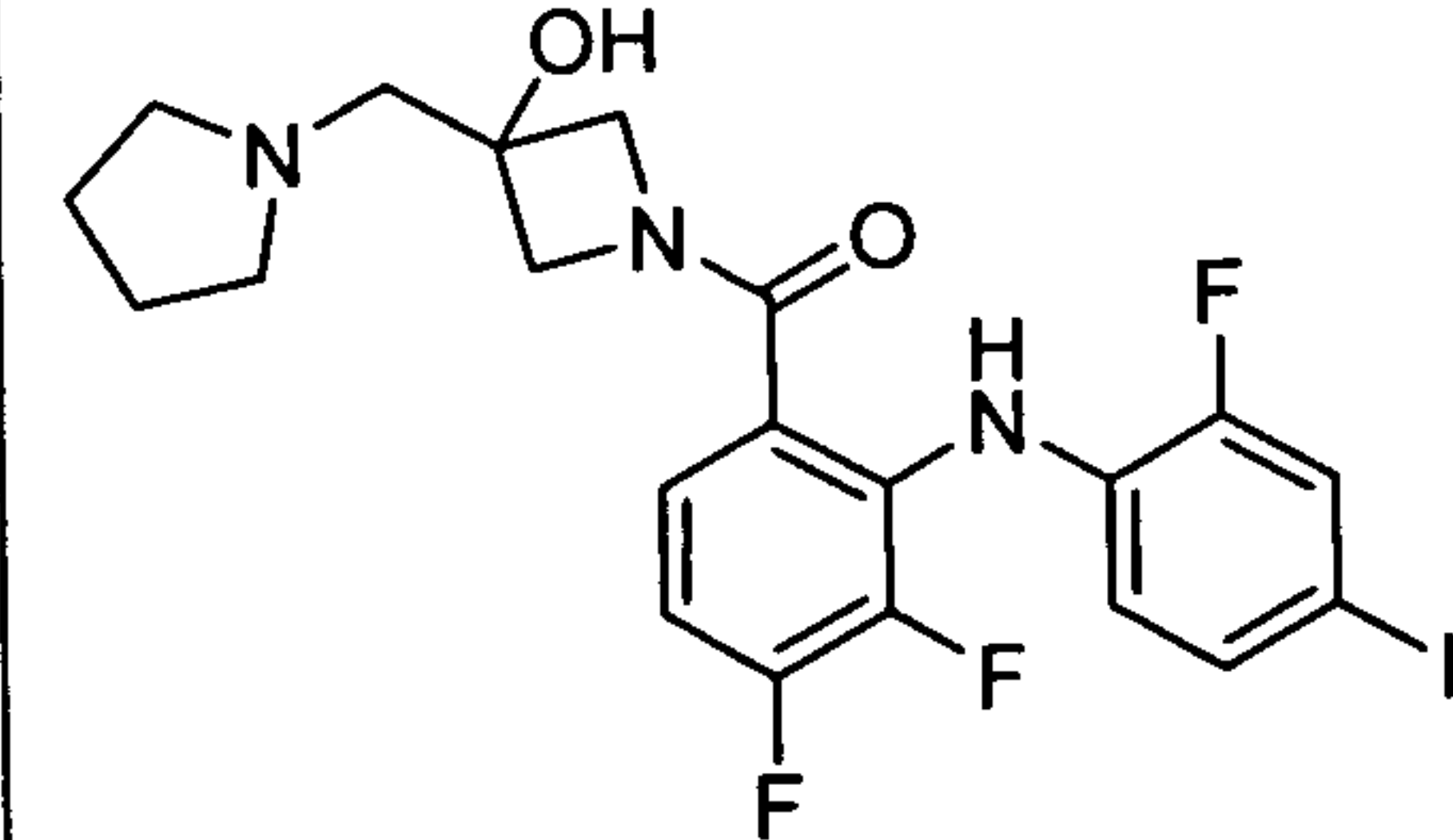
Cmpd No.	Structure	Name
13		1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethane-1,2-diol
14		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
15		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-hydroxyazetidine-3-carboxamide
16		1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate
17		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(pyrrolidin-1-ylmethyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

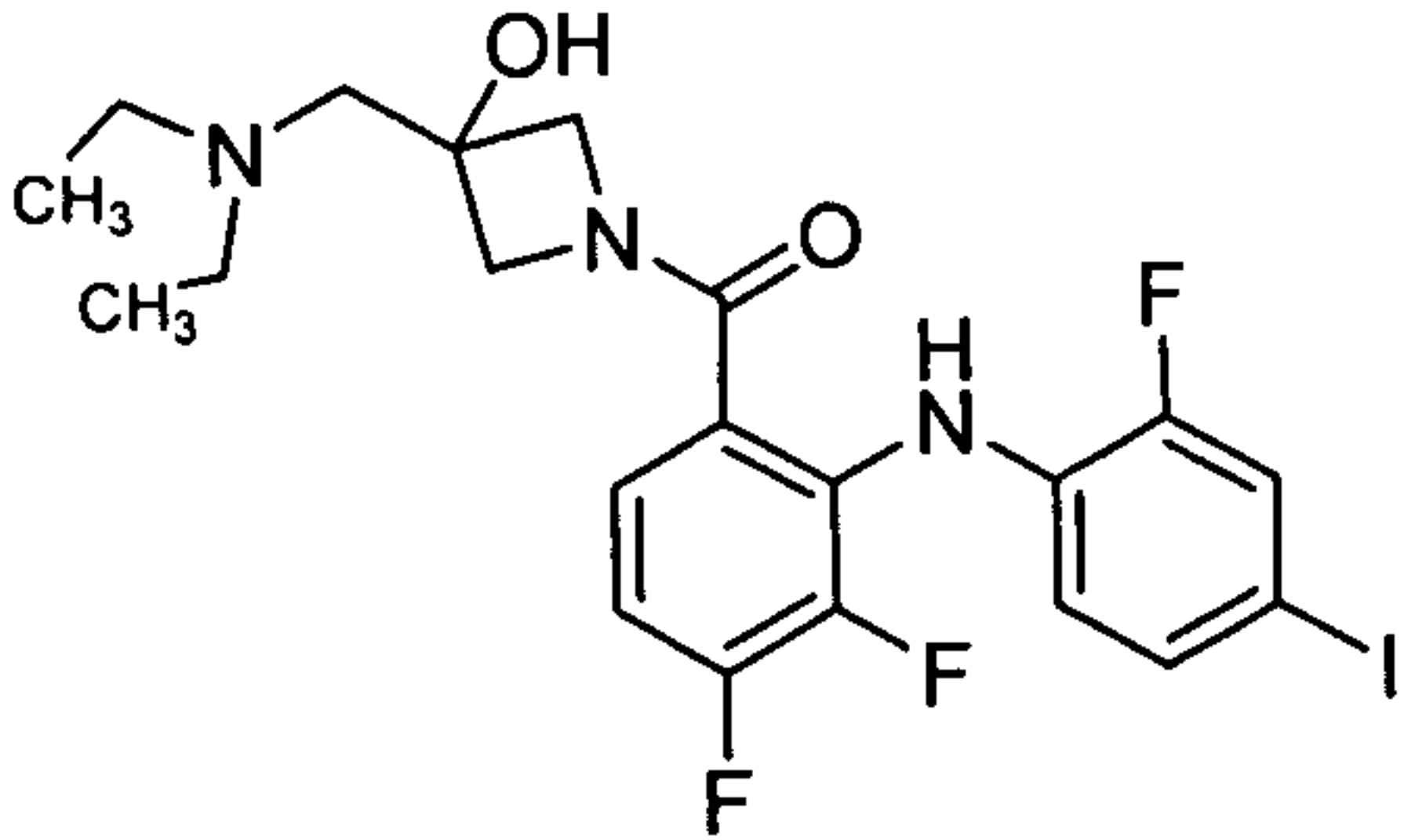
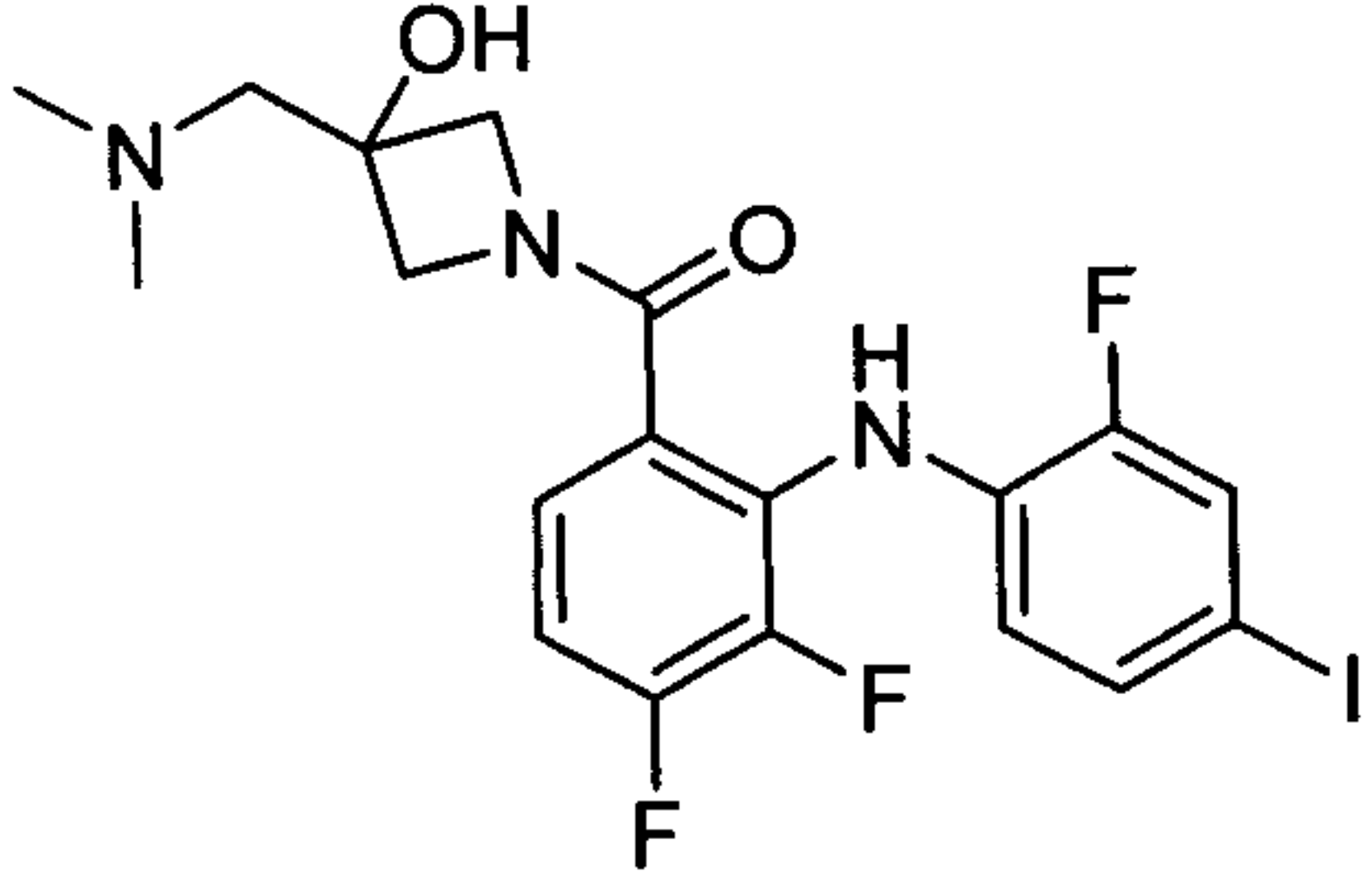
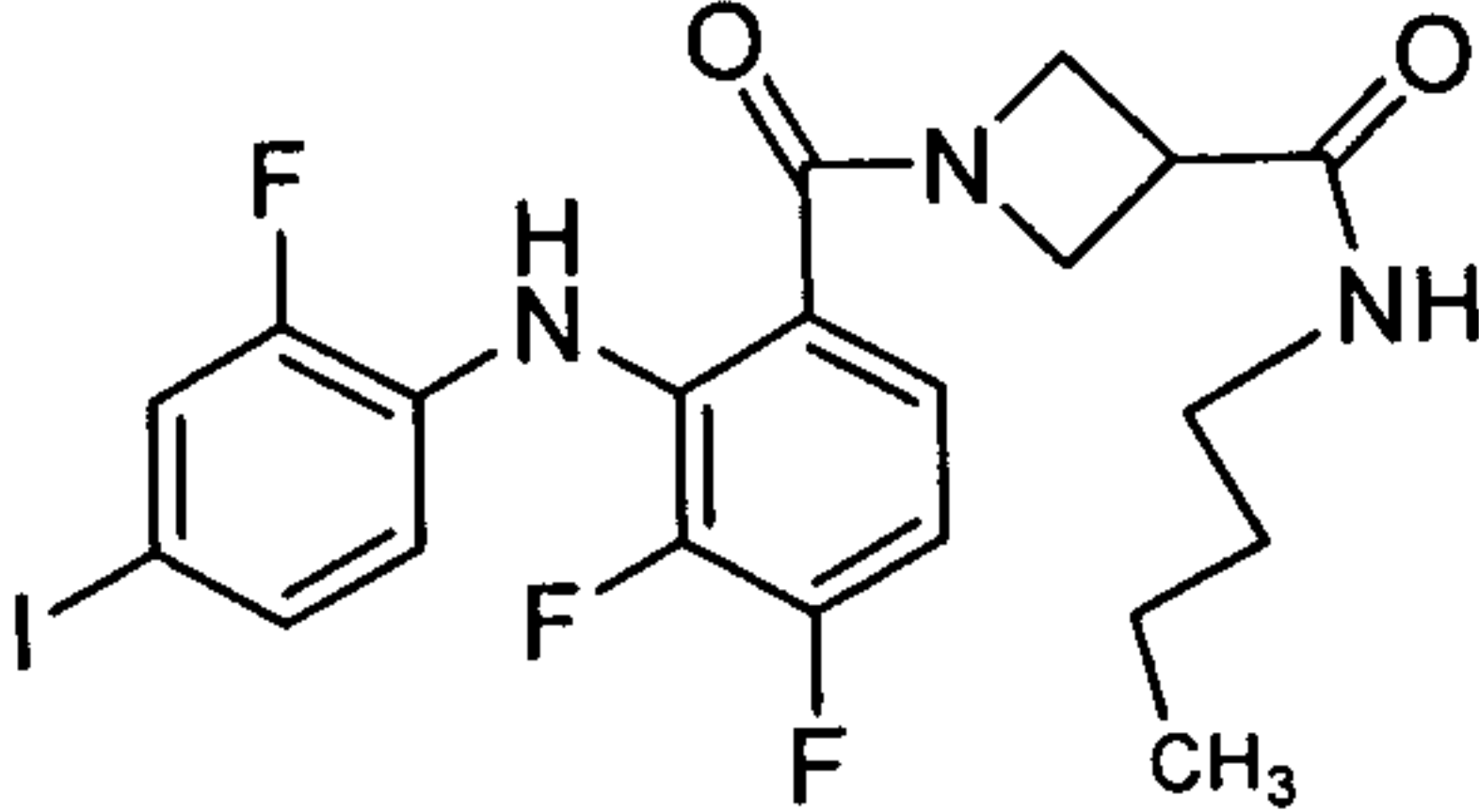
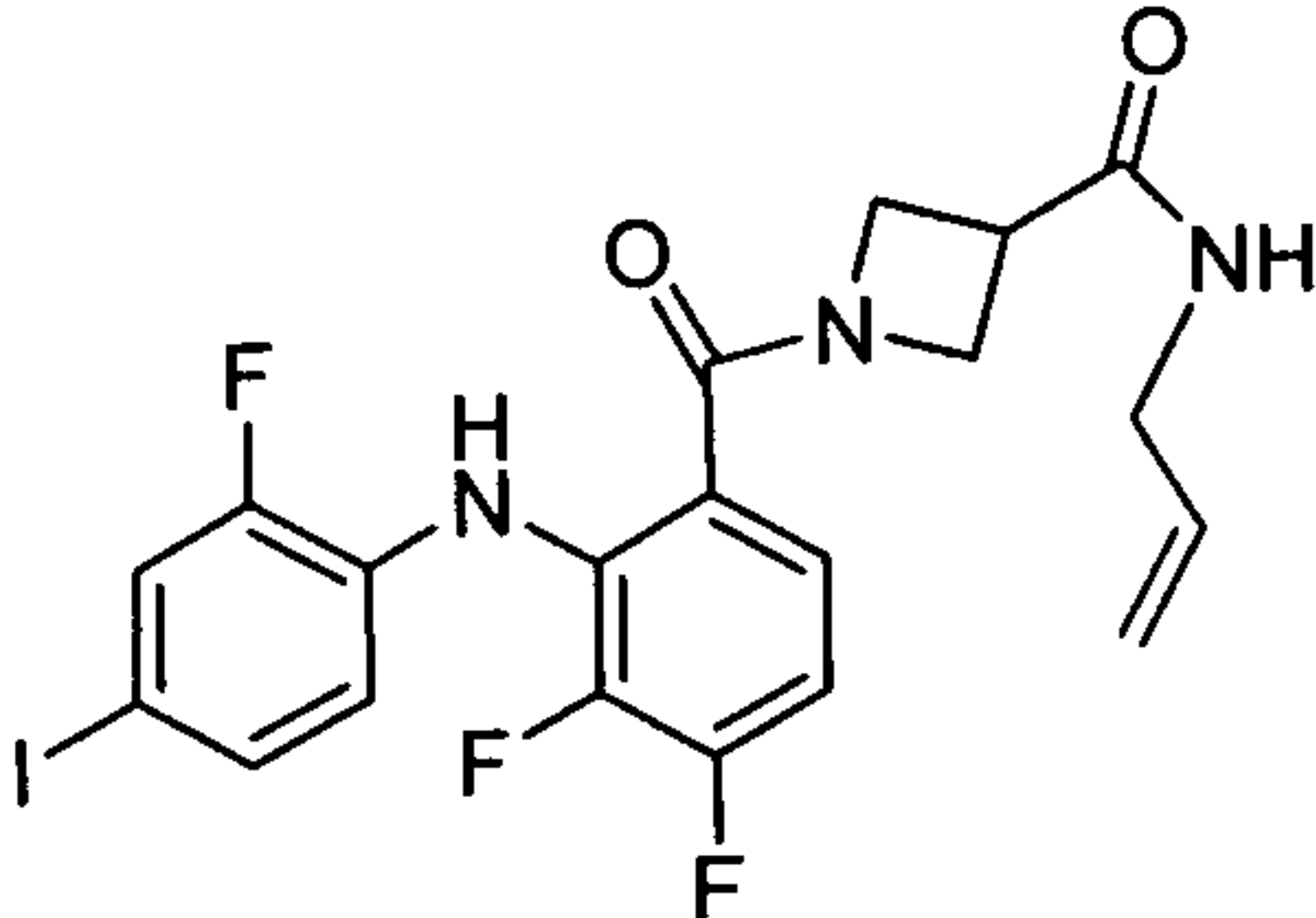
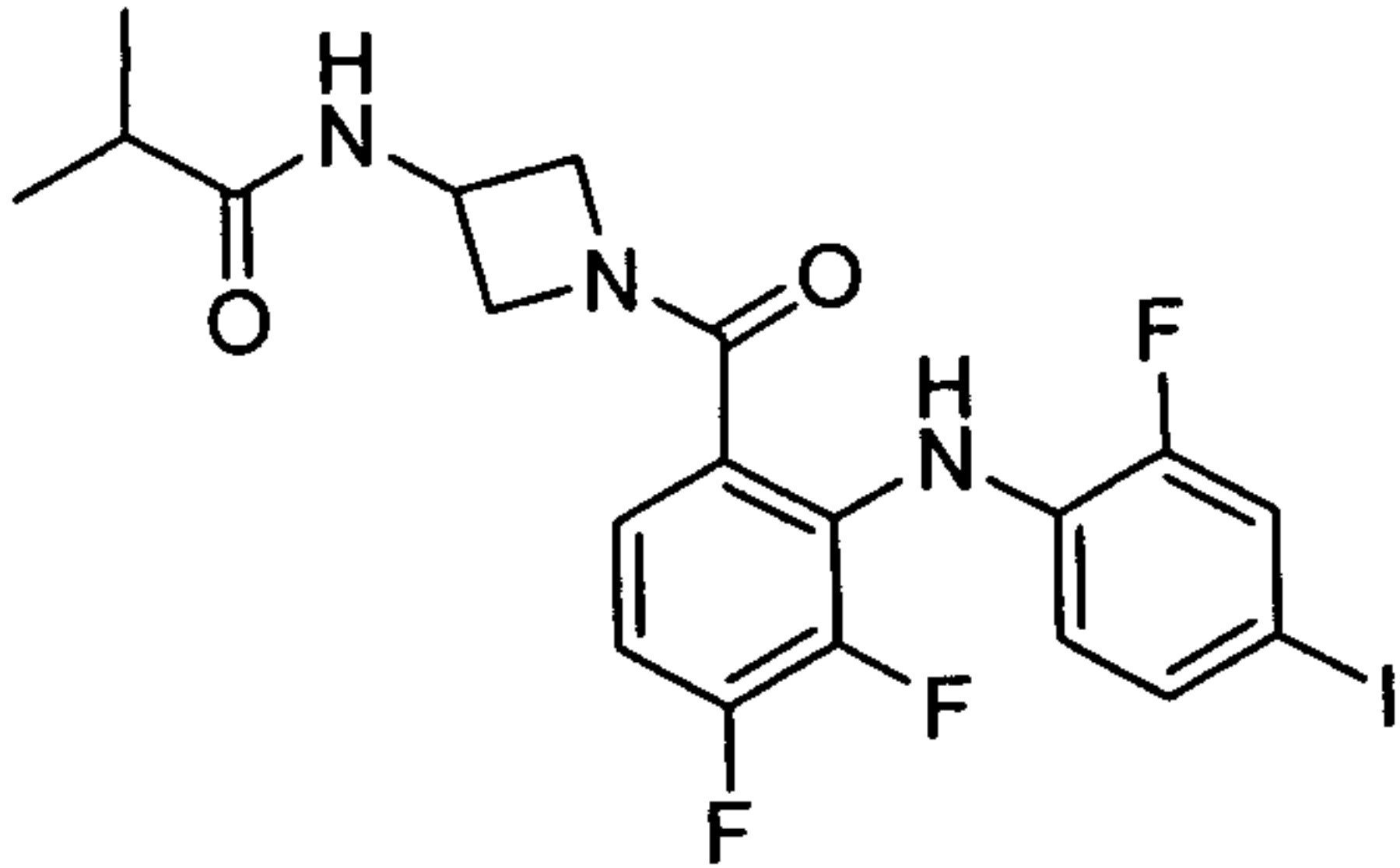
Cmpd No.	Structure	Name
18		3-[(diethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
19		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(dimethylamino)methyl]azetidin-3-ol
20		N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide
21		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-prop-2-en-1-ylazetidine-3-carboxamide
22		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-methylpropanamide

Table 1. Representative MEK Inhibitors

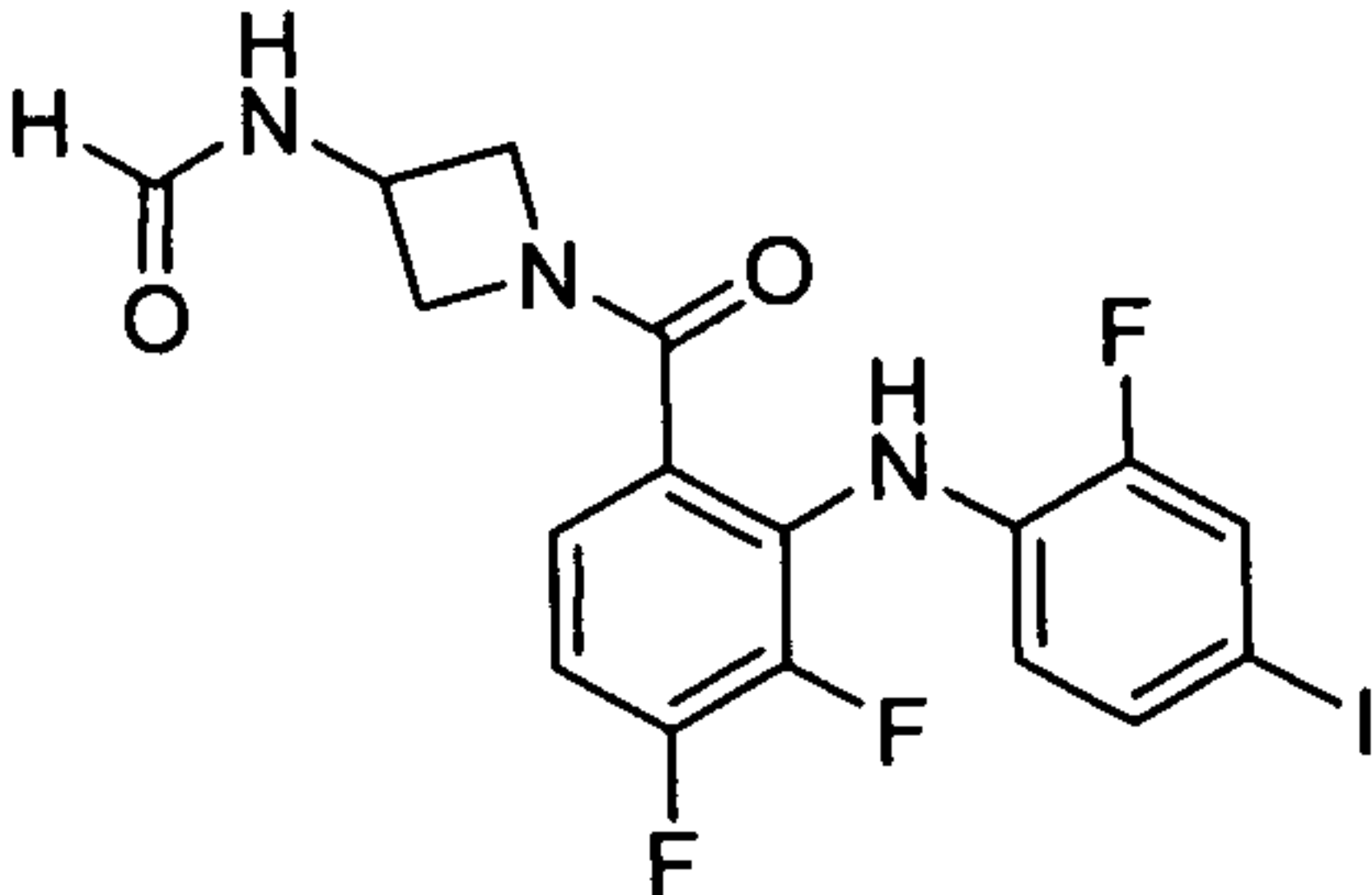
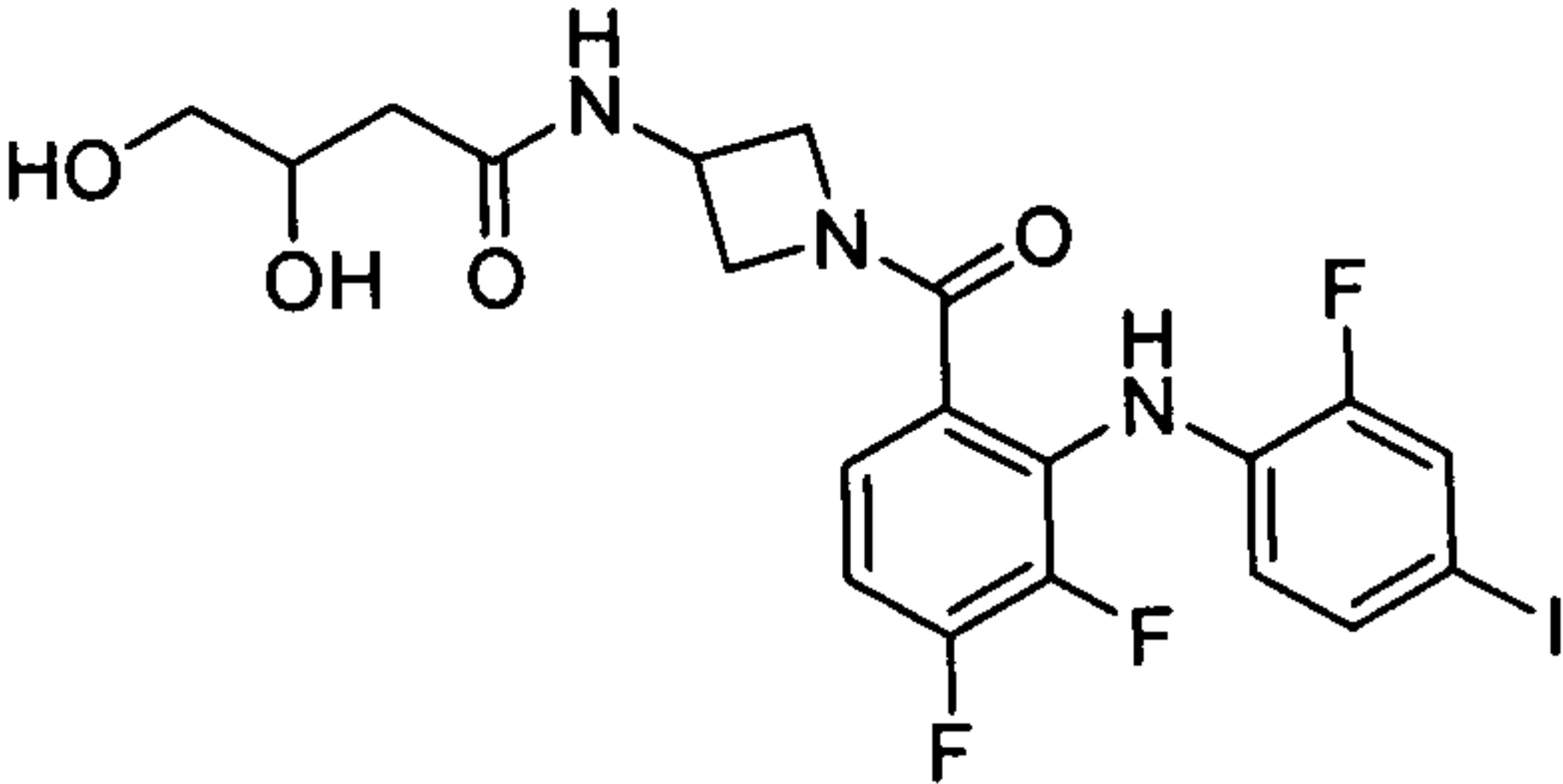
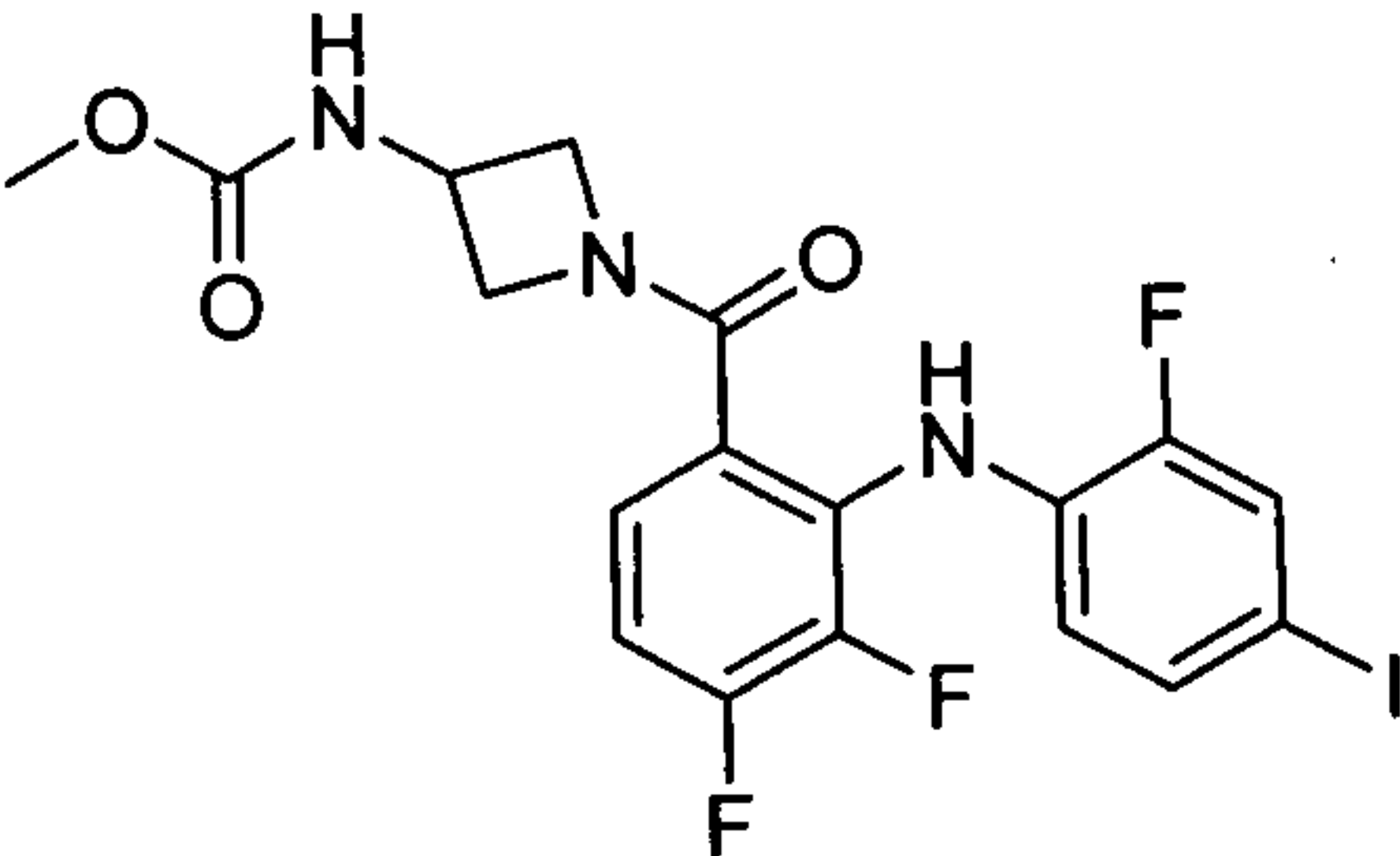
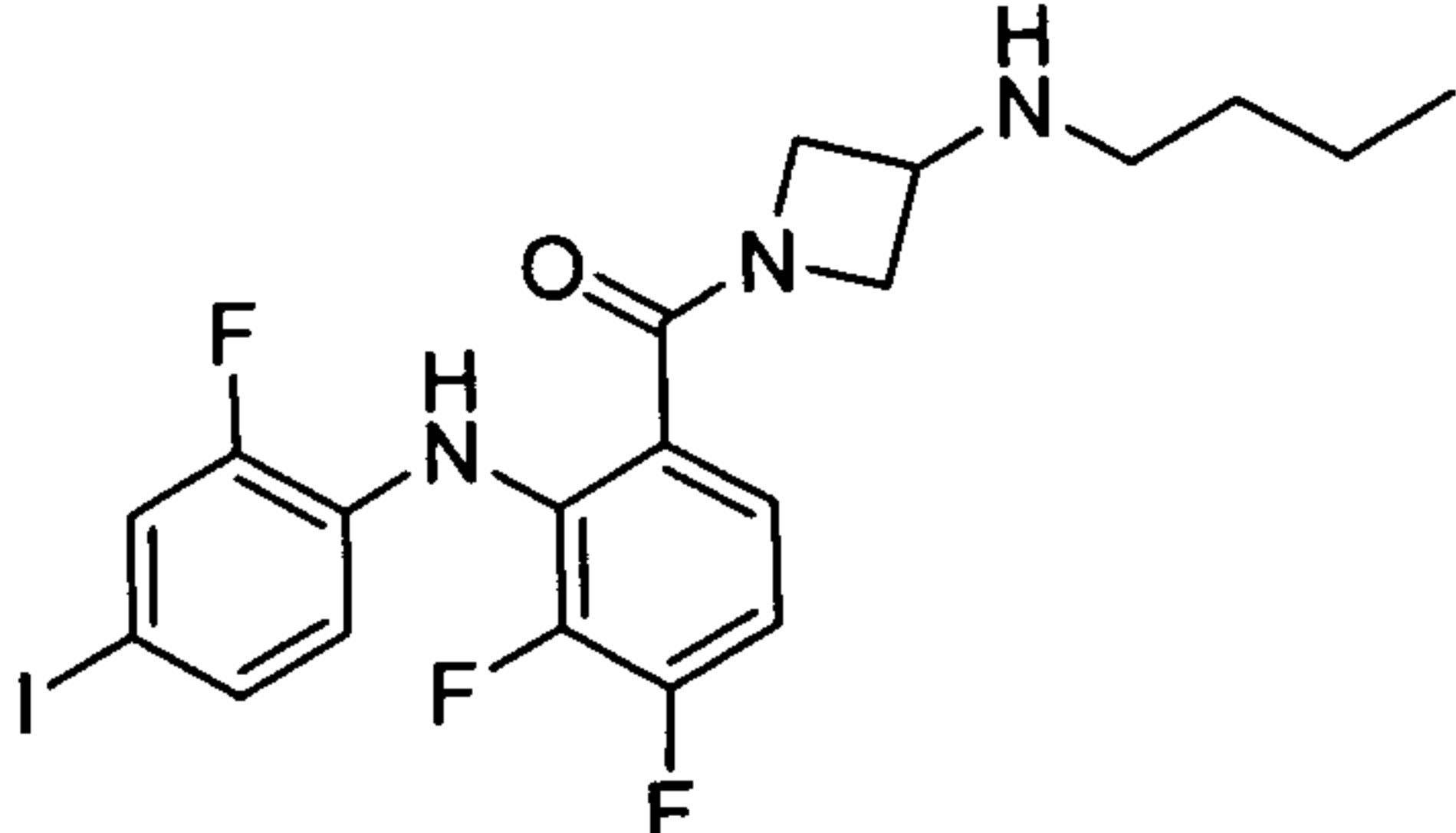
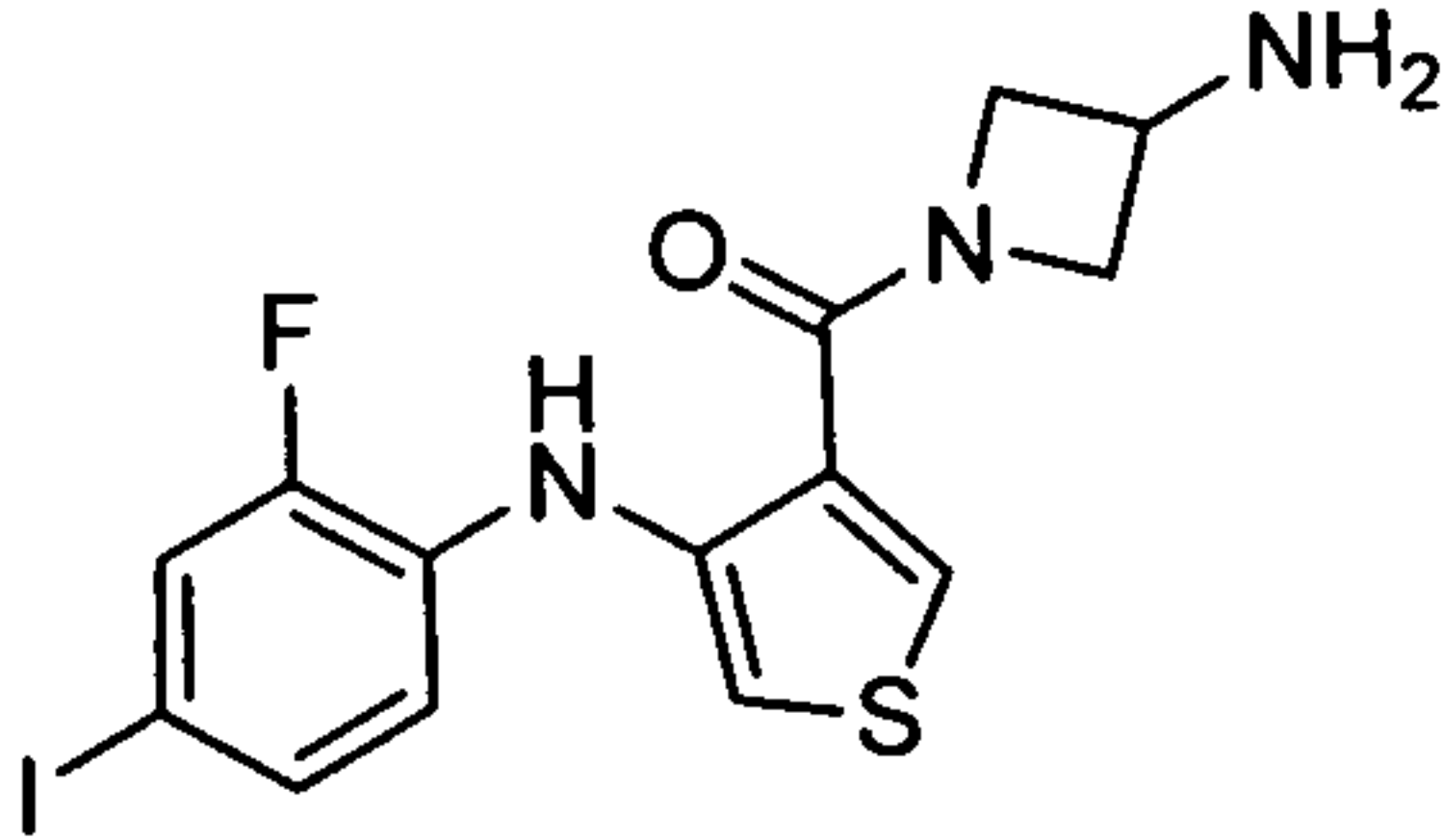
Cmpd No.	Structure	Name
23		<i>N</i> -[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]formamide
24		<i>N</i> -[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-3,4-dihydroxybutanamide
25		methyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate
26		<i>N</i> -butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
27		1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-amine

Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
28		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
29		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2 <i>R</i>)-piperidin-2-yl]azetidin-3-ol
30		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyrrolidin-2-ylazetidin-3-ol
31		(<i>R</i>)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyrrolidin-2-ylazetidin-3-ol
32		(<i>S</i>)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyrrolidin-2-ylazetidin-3-ol

Table 1. Representative MEK Inhibitors

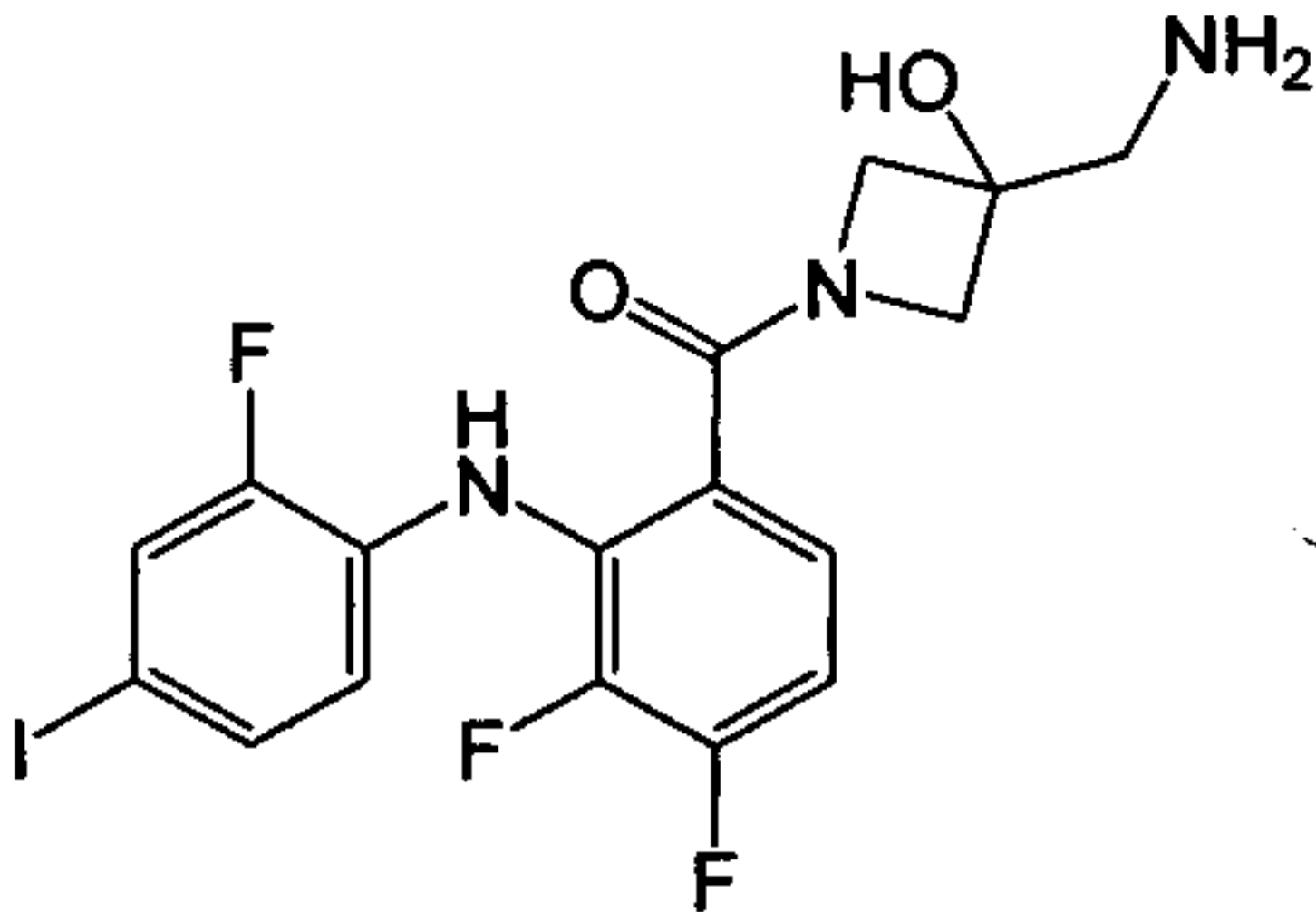
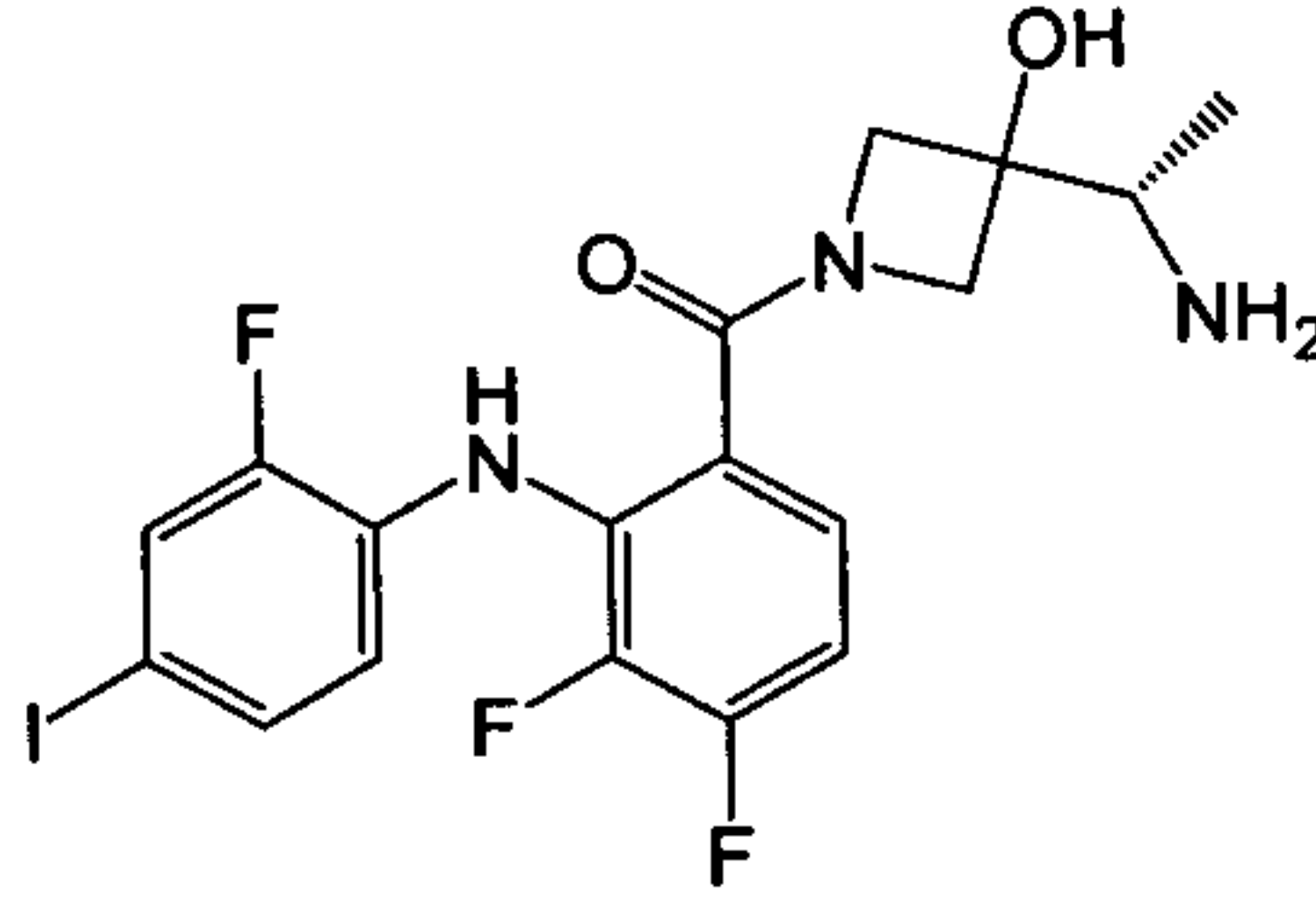
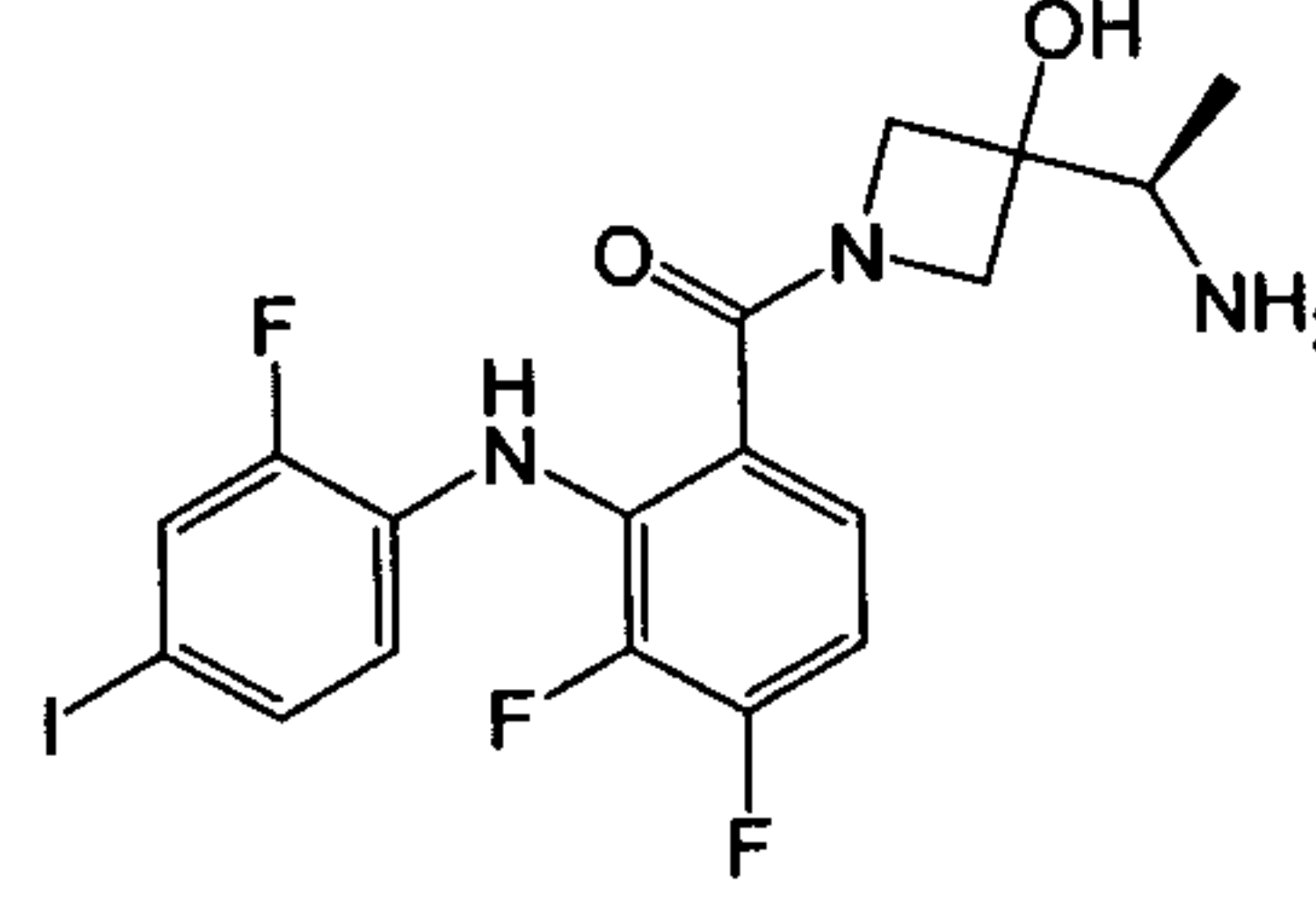
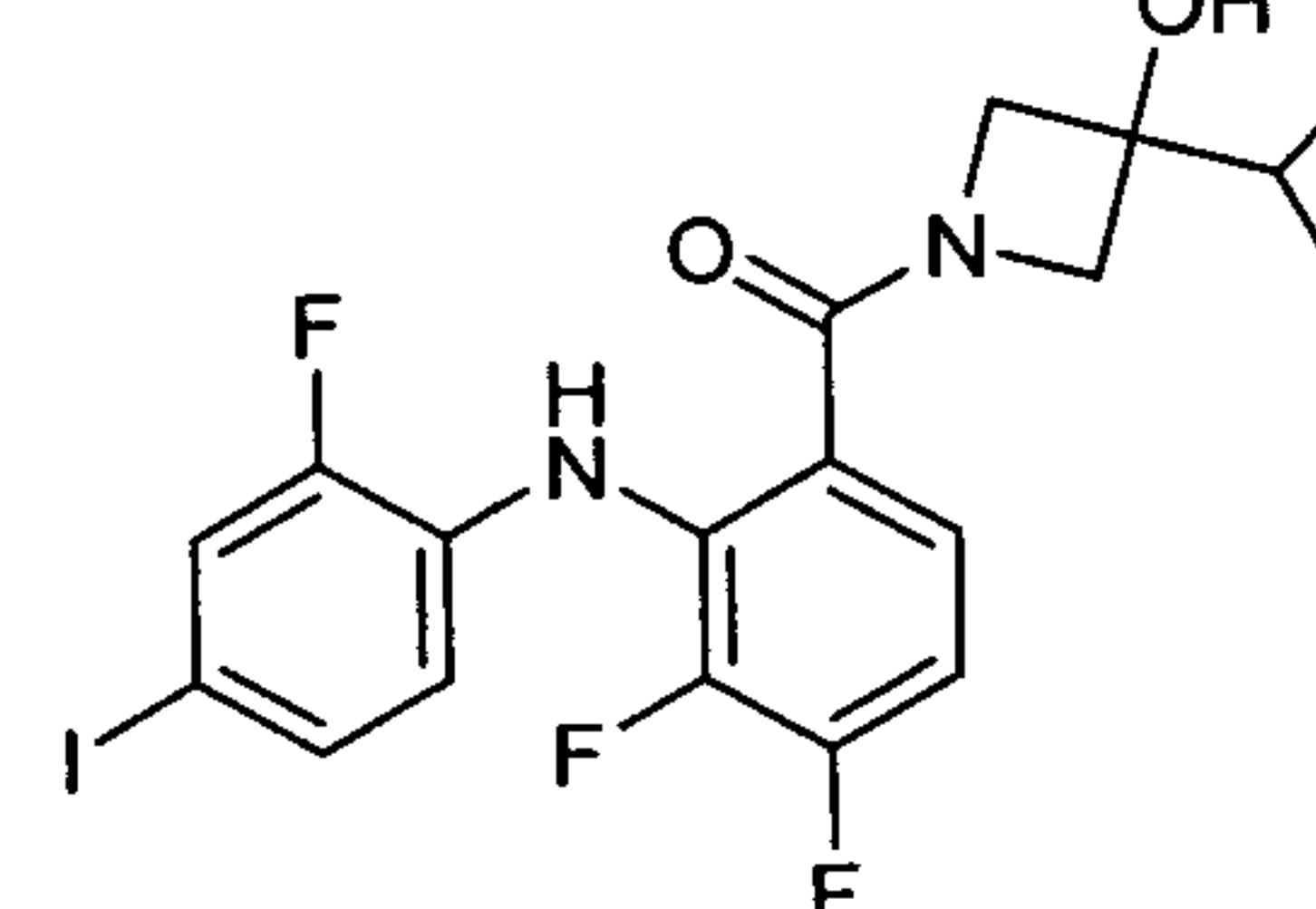
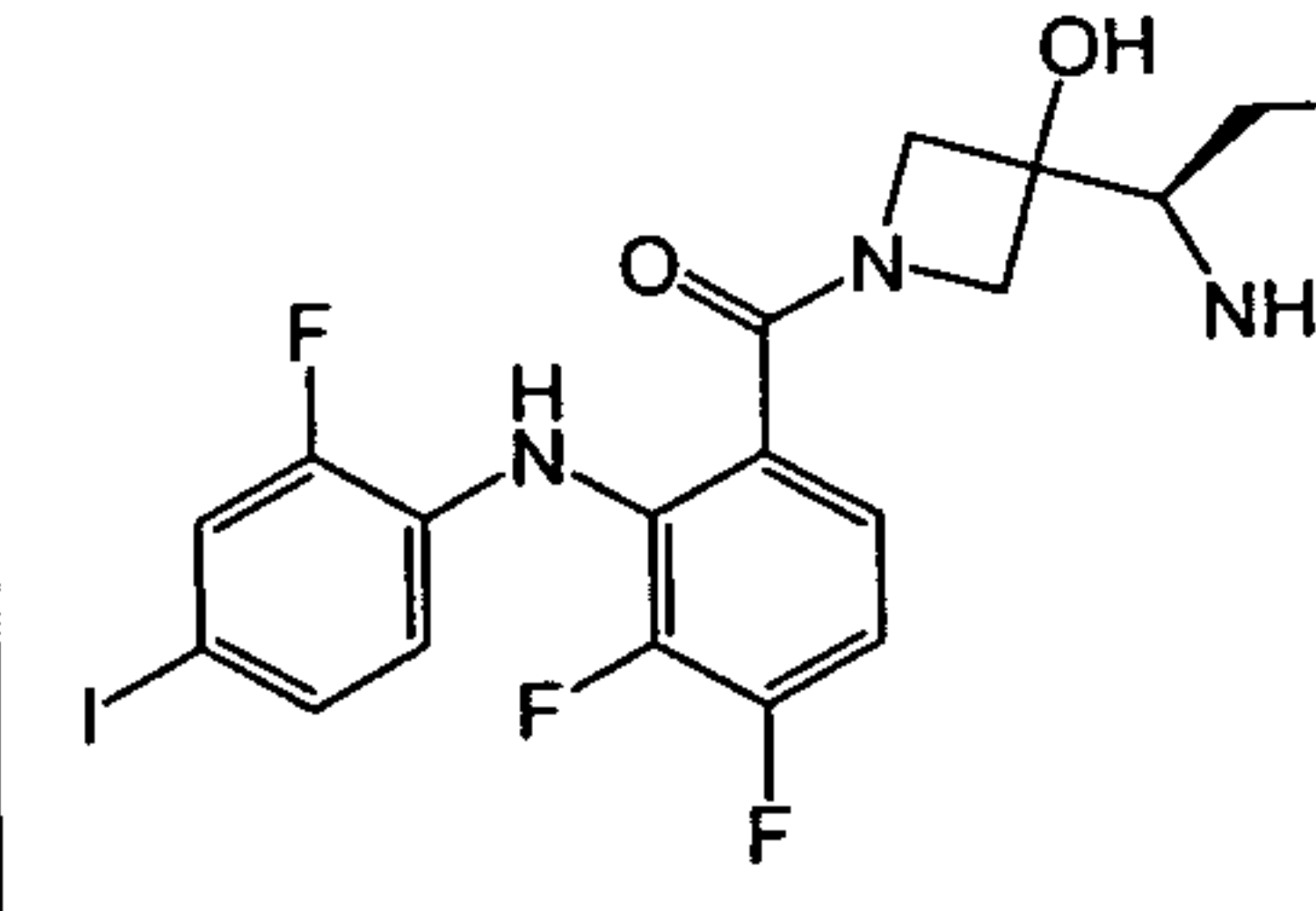
Cmpd No.	Structure	Name
33		3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
34		3-[(1S)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
35		3-[(1R)-1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
36		(3-(1-aminopropyl)-3-hydroxyazetidin-1-yl)(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)methanone
37		(R)-(3-(1-aminopropyl)-3-hydroxyazetidin-1-yl)(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)methanone
38		(S)-(3-(1-aminopropyl)-3-hydroxyazetidin-1-yl)(3,4-difluoro-

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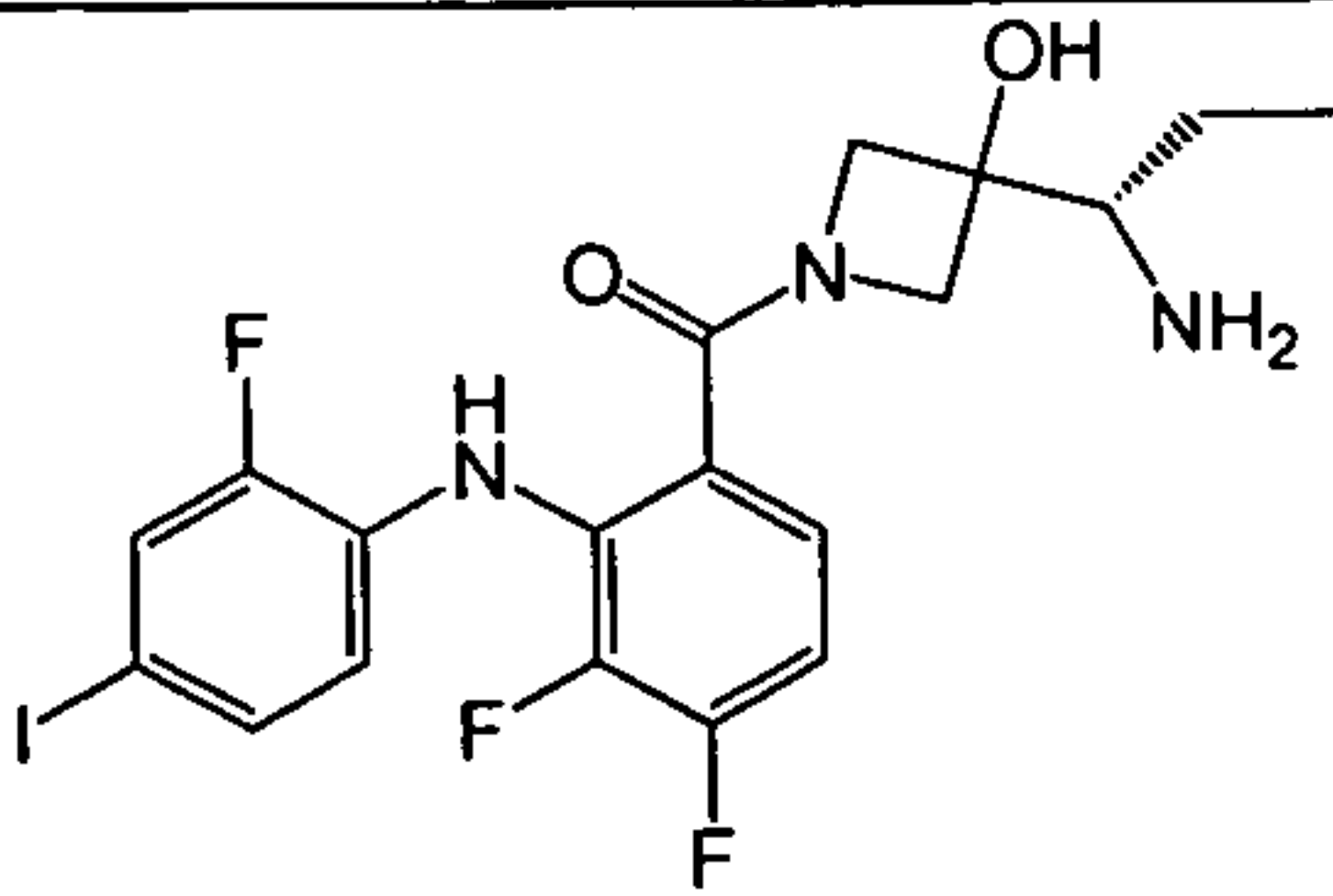
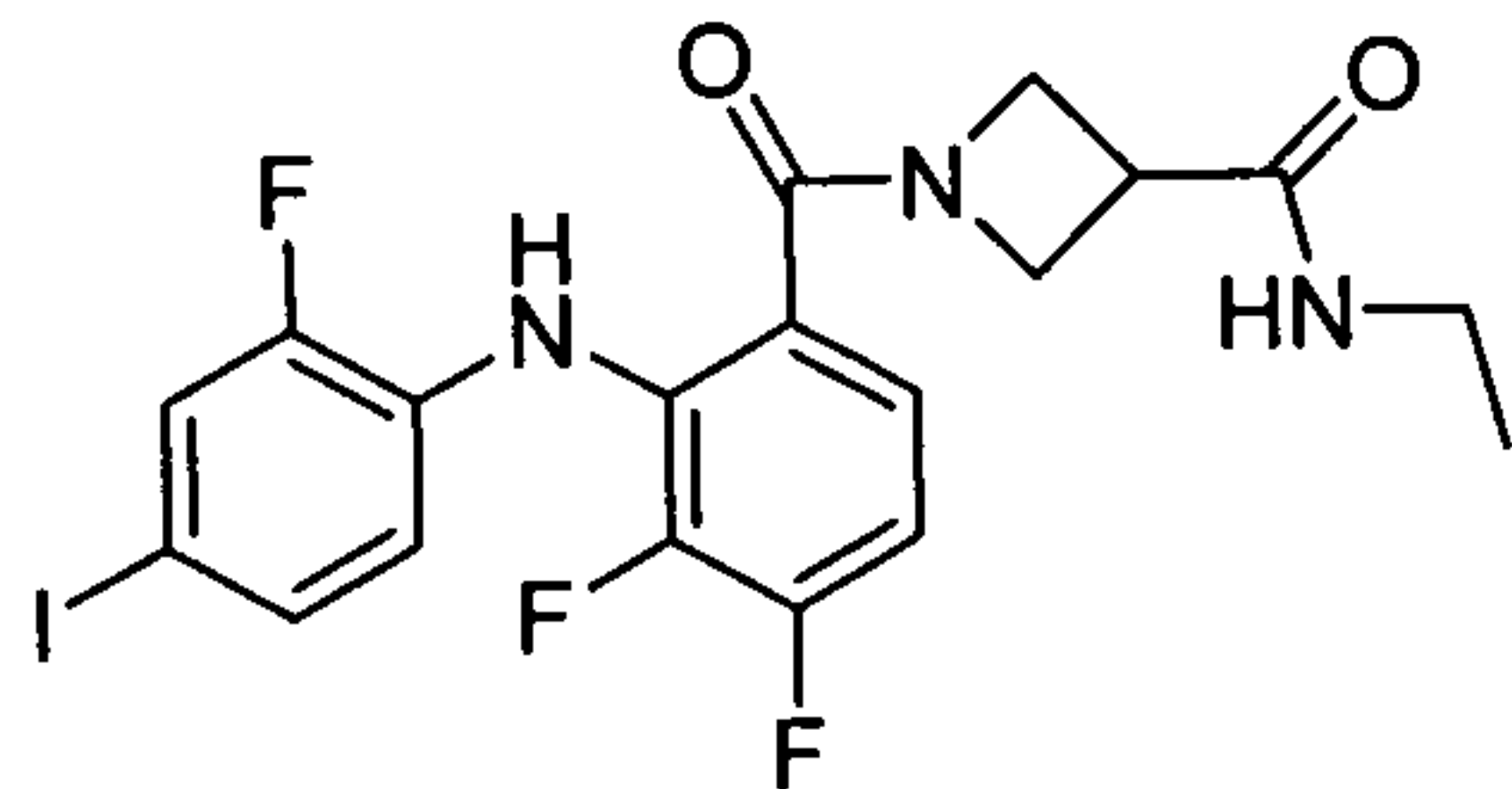
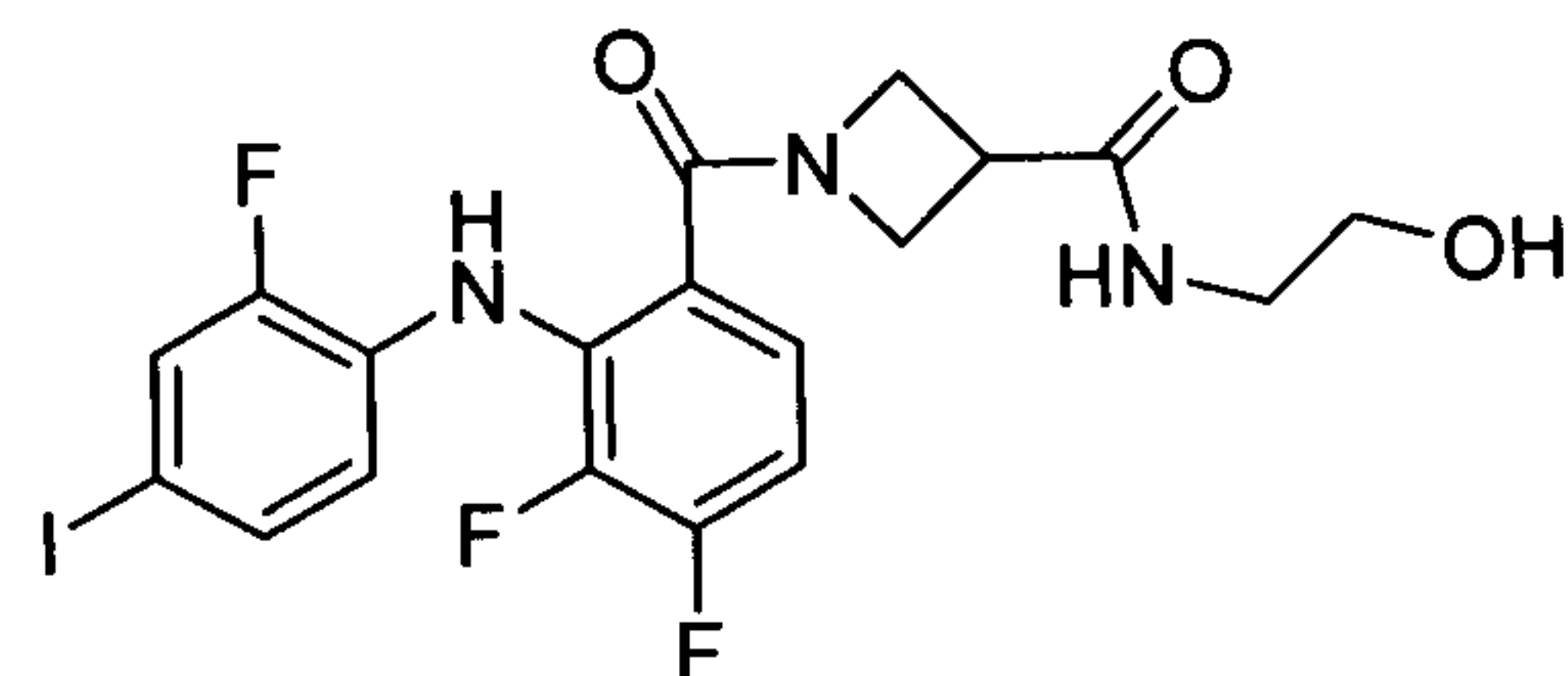
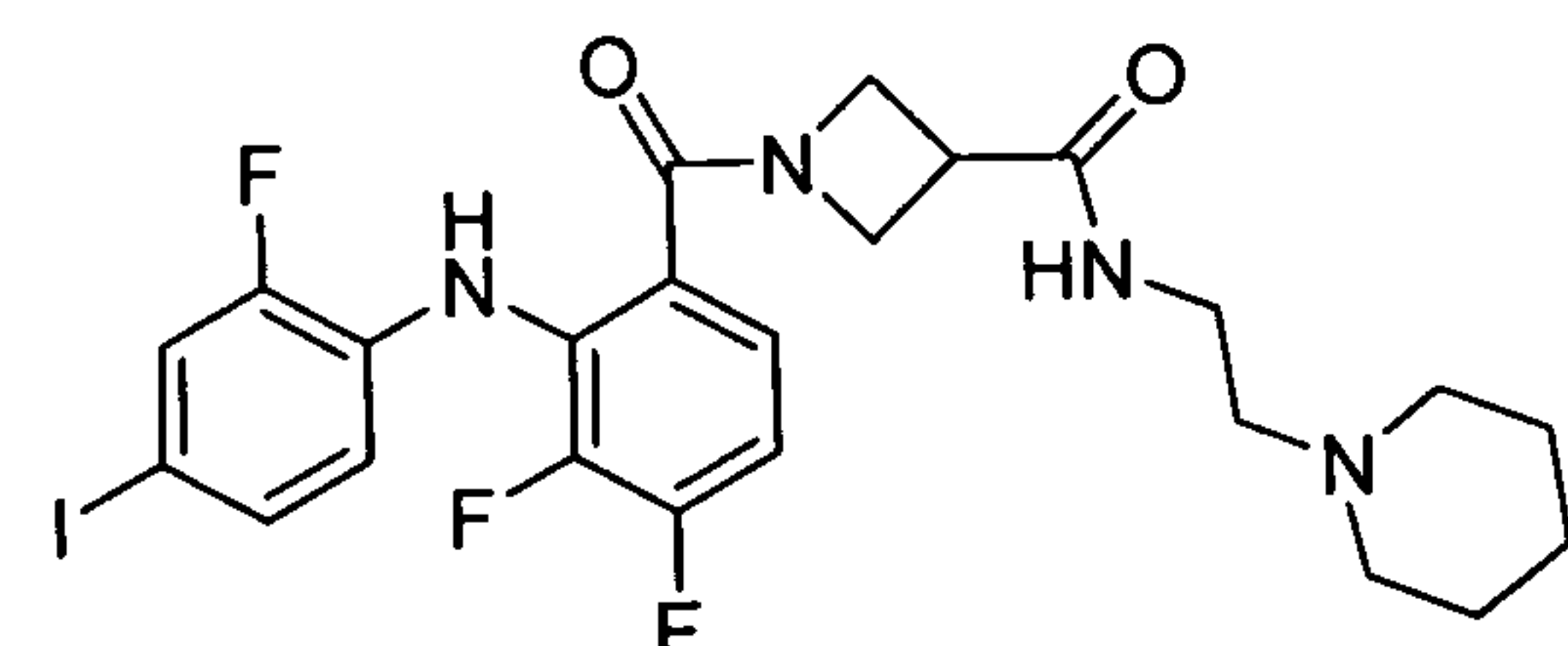
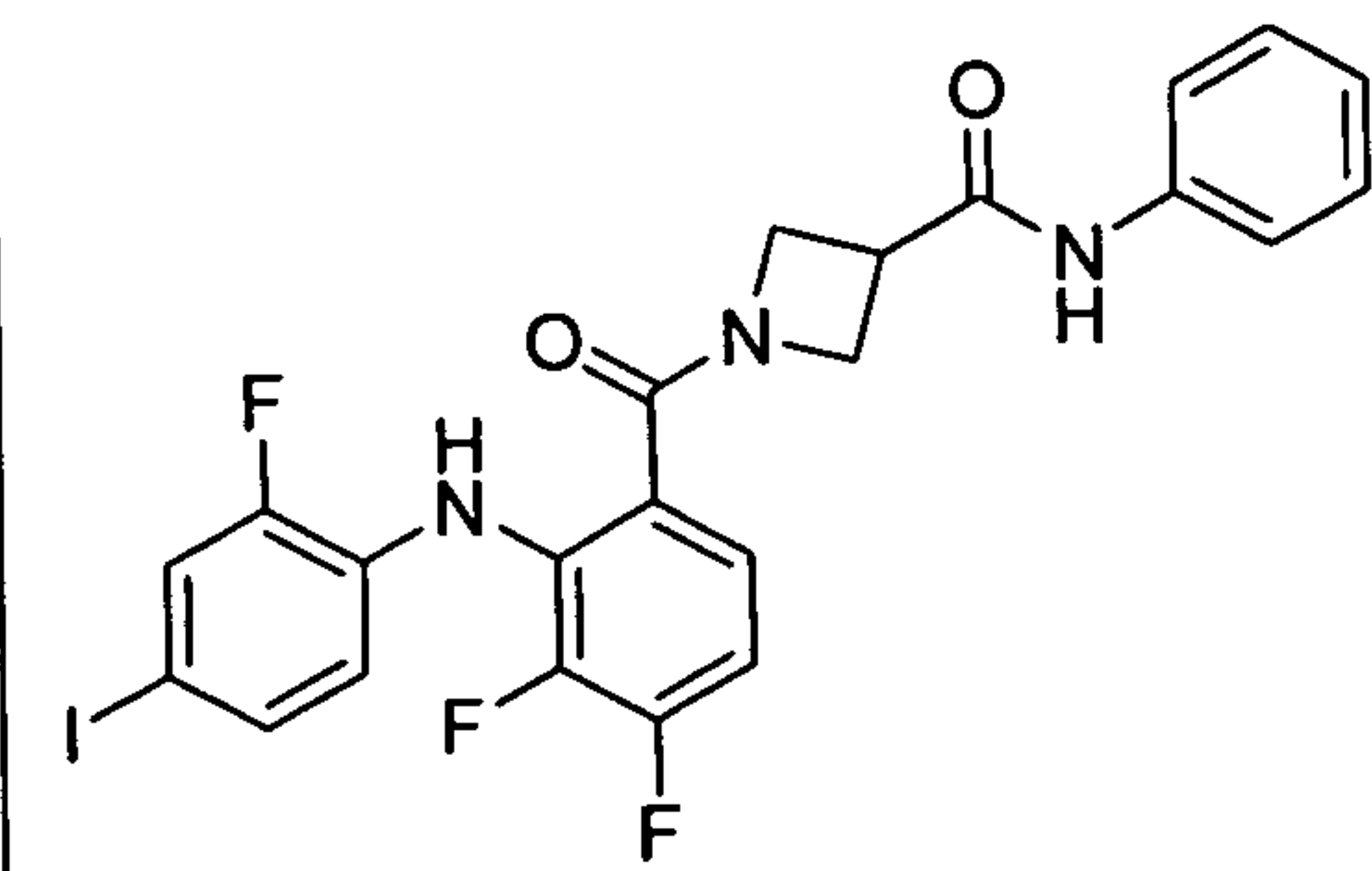
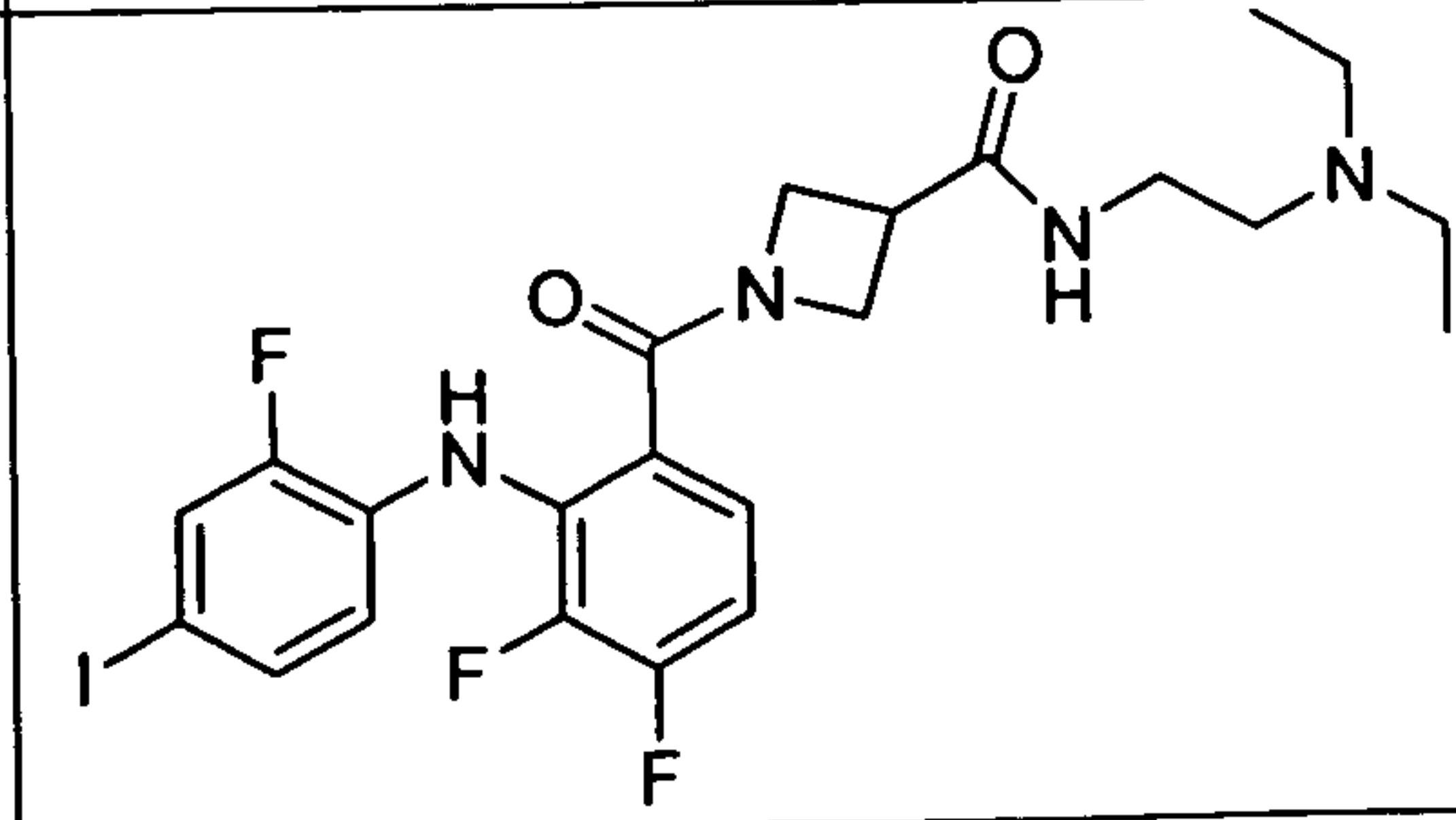
Cmpd No.	Structure	Name
		2-(2-fluoro-4-iodophenylamino)phenyl)methanone
39		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-ethylazetidine-3-carboxamide
40		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-(2-hydroxyethyl)azetidine-3-carboxamide
41		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-(2-piperidin-1-ylethyl)azetidine-3-carboxamide
42		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-phenylazetidine-3-carboxamide
43		N-[2-(diethylamino)ethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide

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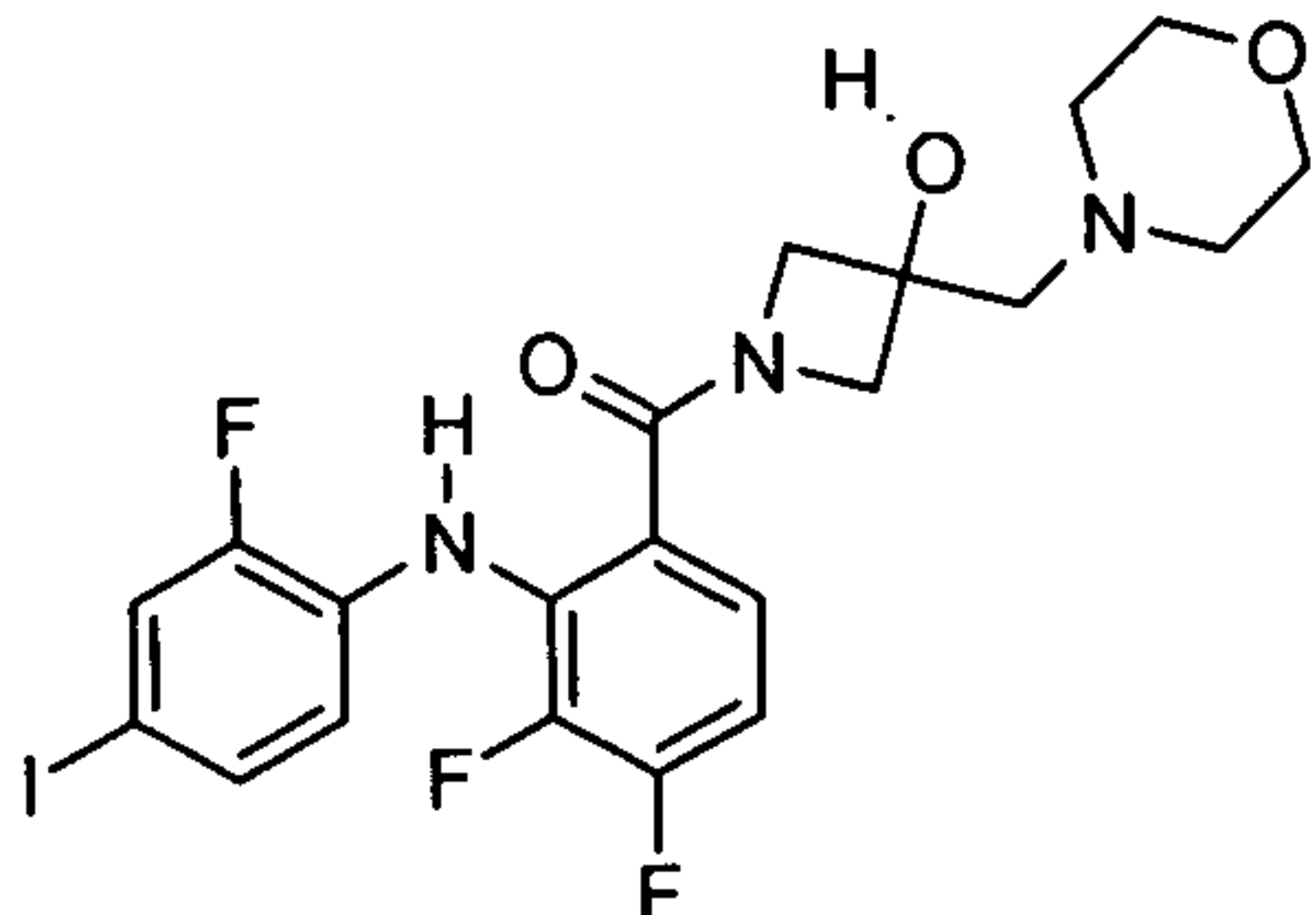
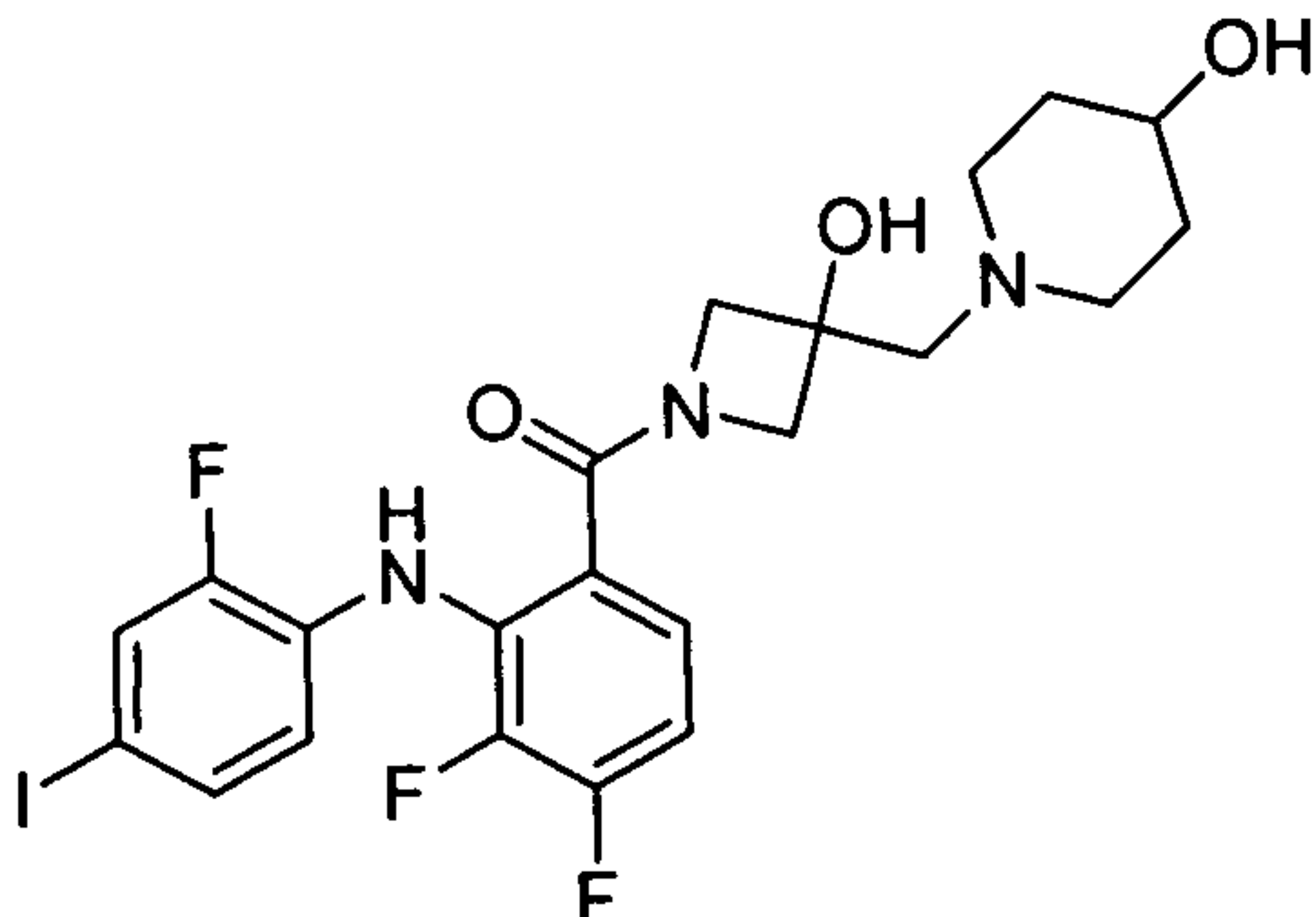
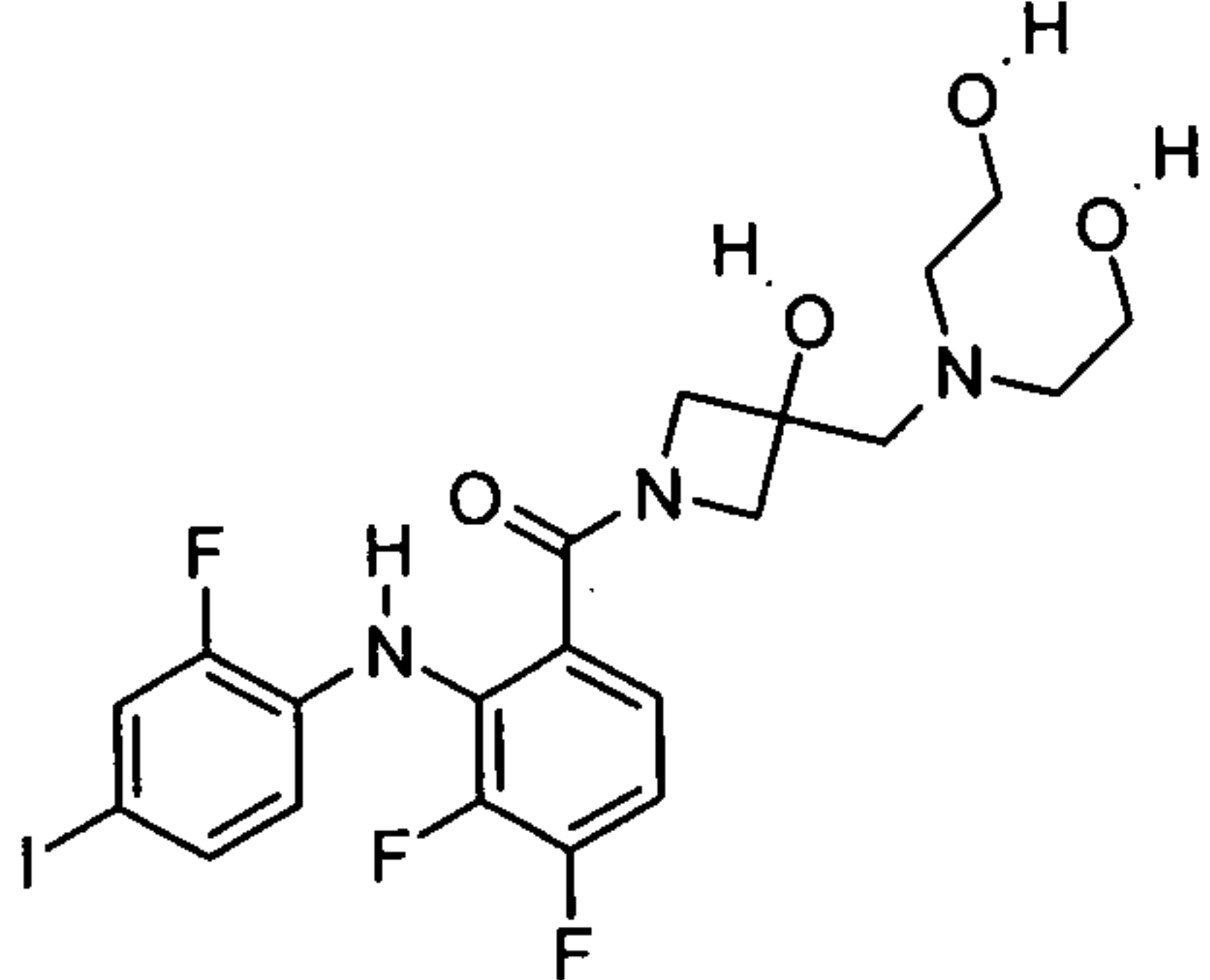
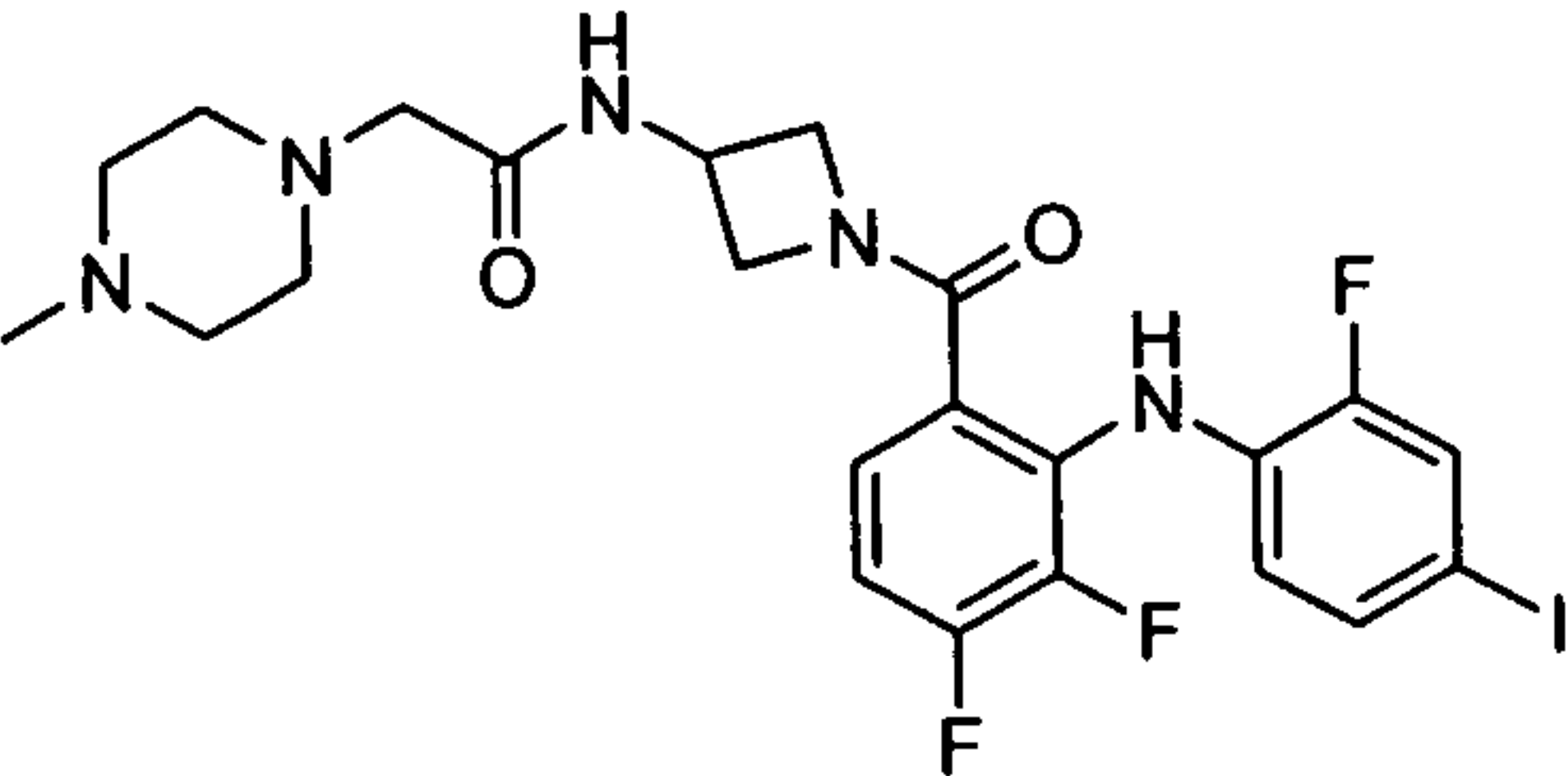
Cmpd No.	Structure	Name
44		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(morpholin-4-ylmethyl)azetidin-3-ol
45		1-{{1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl}methyl}piperidin-4-ol
46		3-{[bis(2-hydroxyethyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
47		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-(4-methylpiperazin-1-yl)acetamide

Table 1. Representative MEK Inhibitors

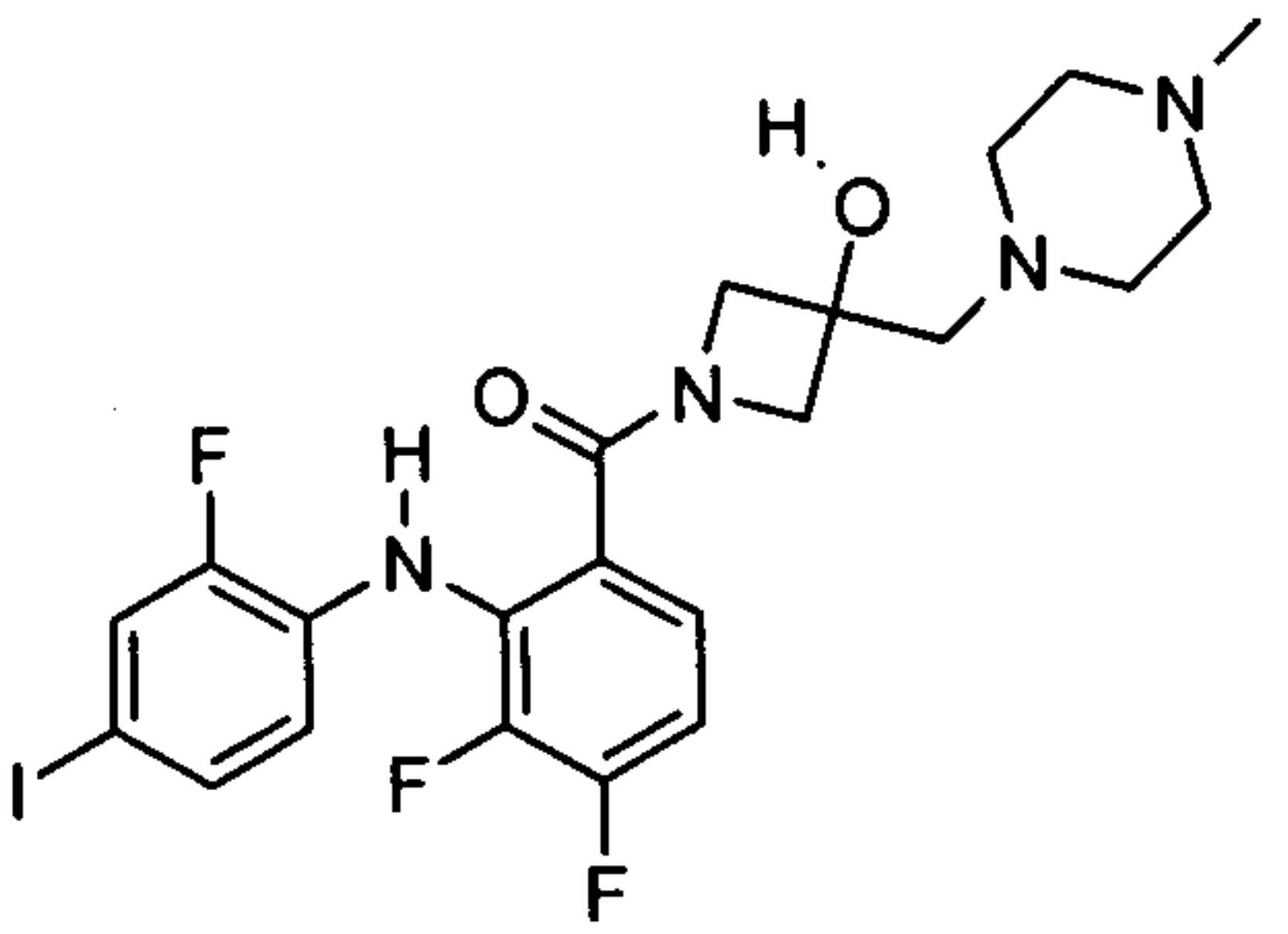
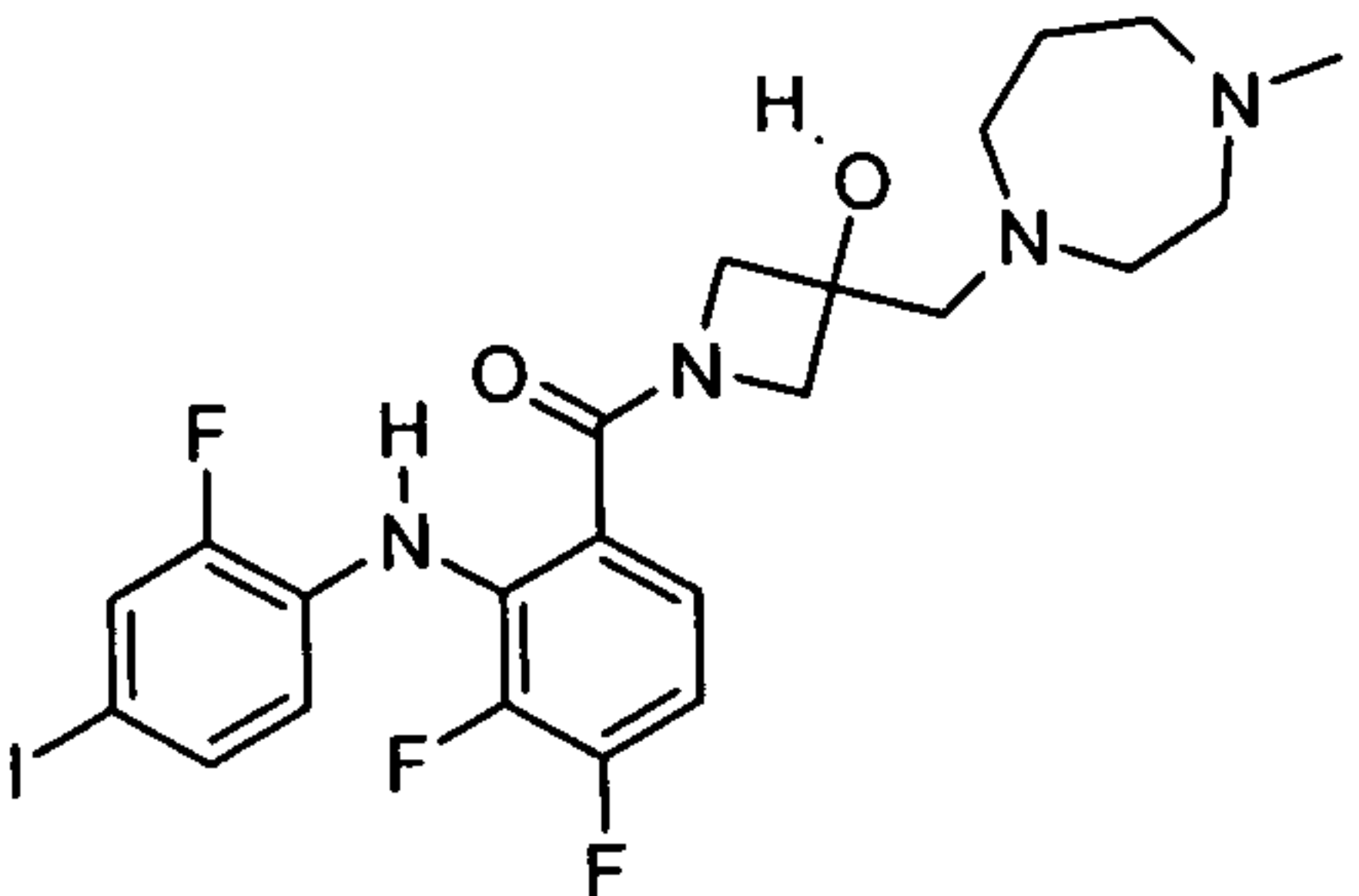
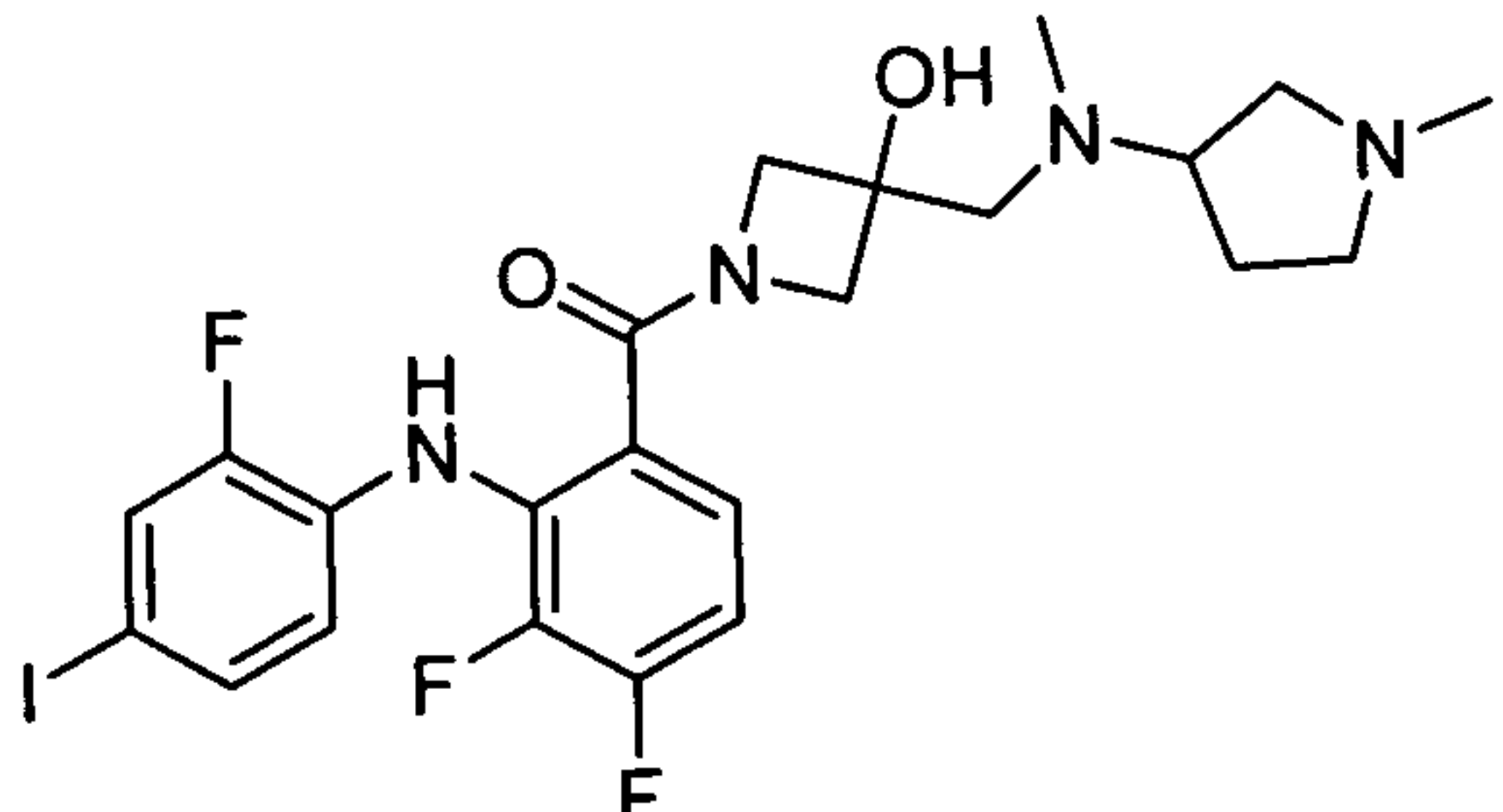
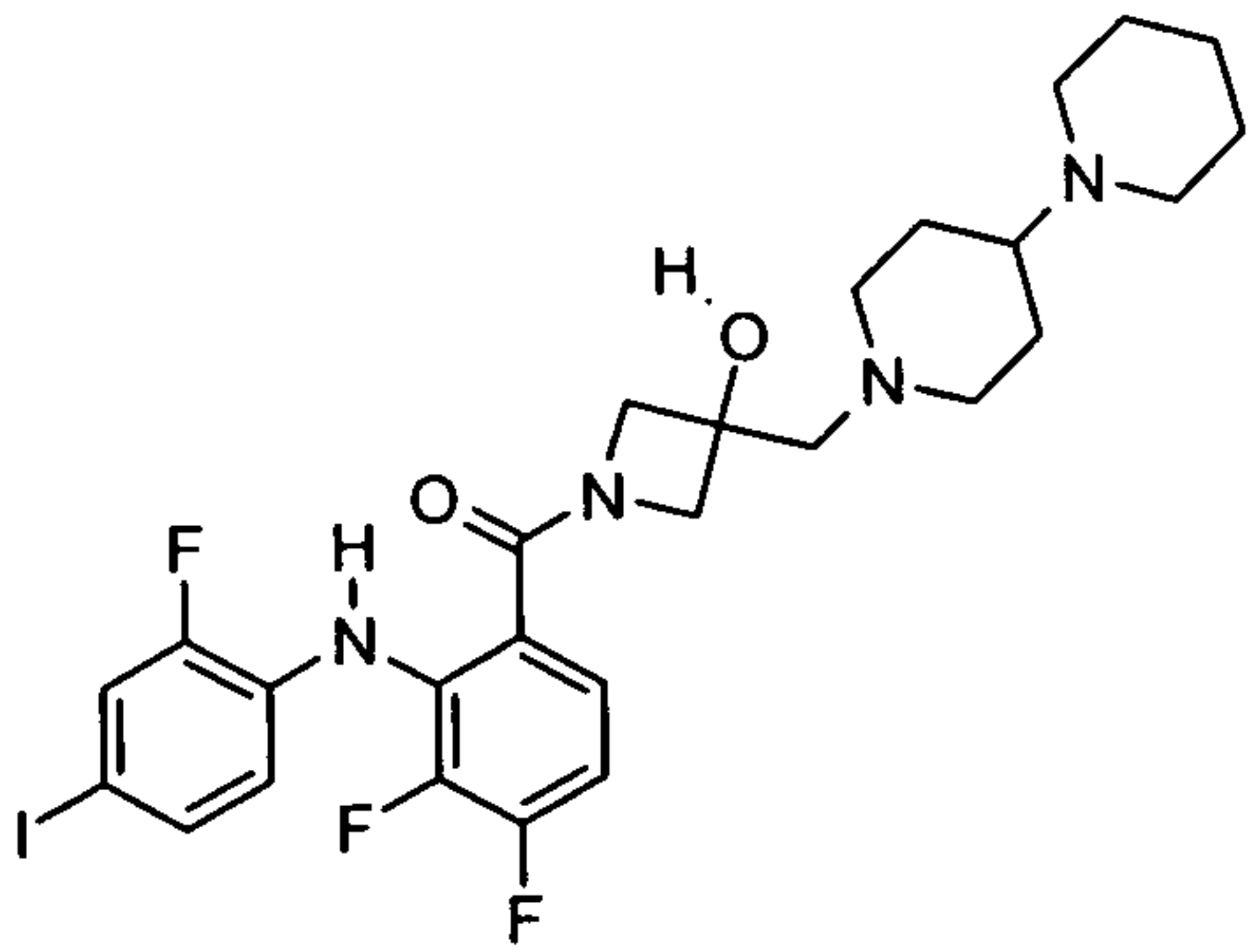
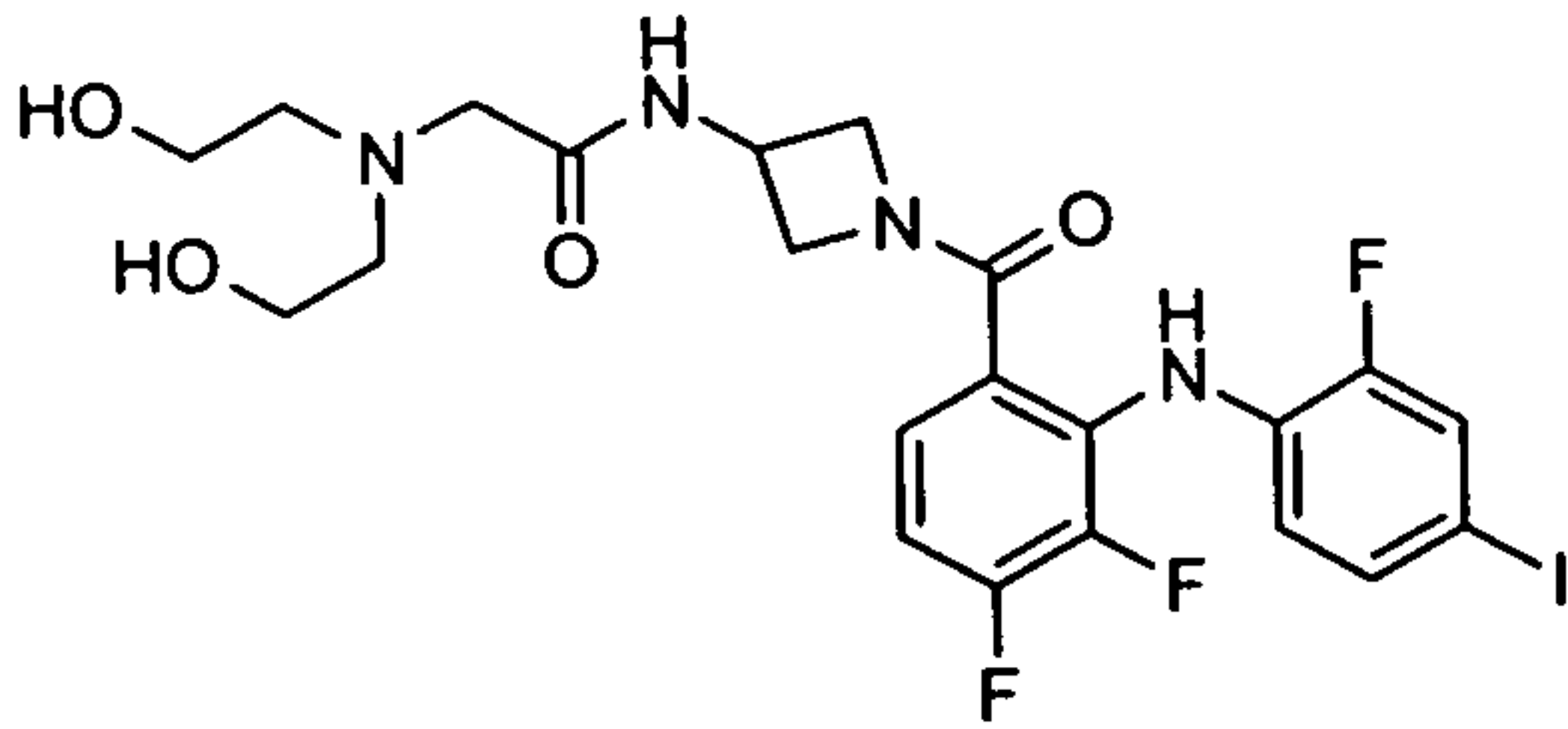
Cmpd No.	Structure	Name
48		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methylpiperazin-1-yl)methyl]azetidin-3-ol
49		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(4-methyl-1,4-diazepan-1-yl)methyl]azetidin-3-ol
50		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}azetidin-3-ol
51		3-(1,4'-bipiperidin-1'-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
52		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N,N-bis(2-hydroxyethyl)glycinamide

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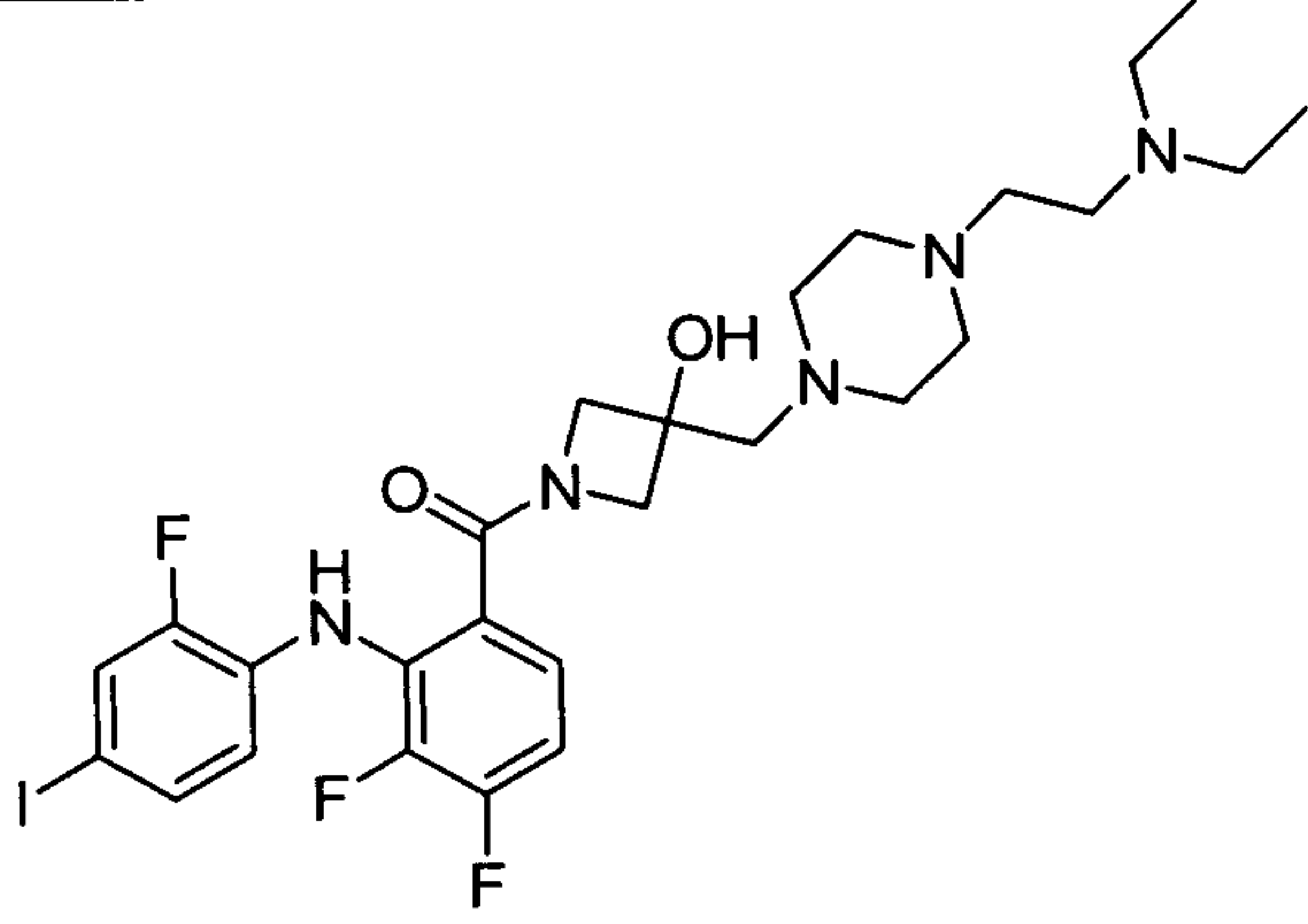
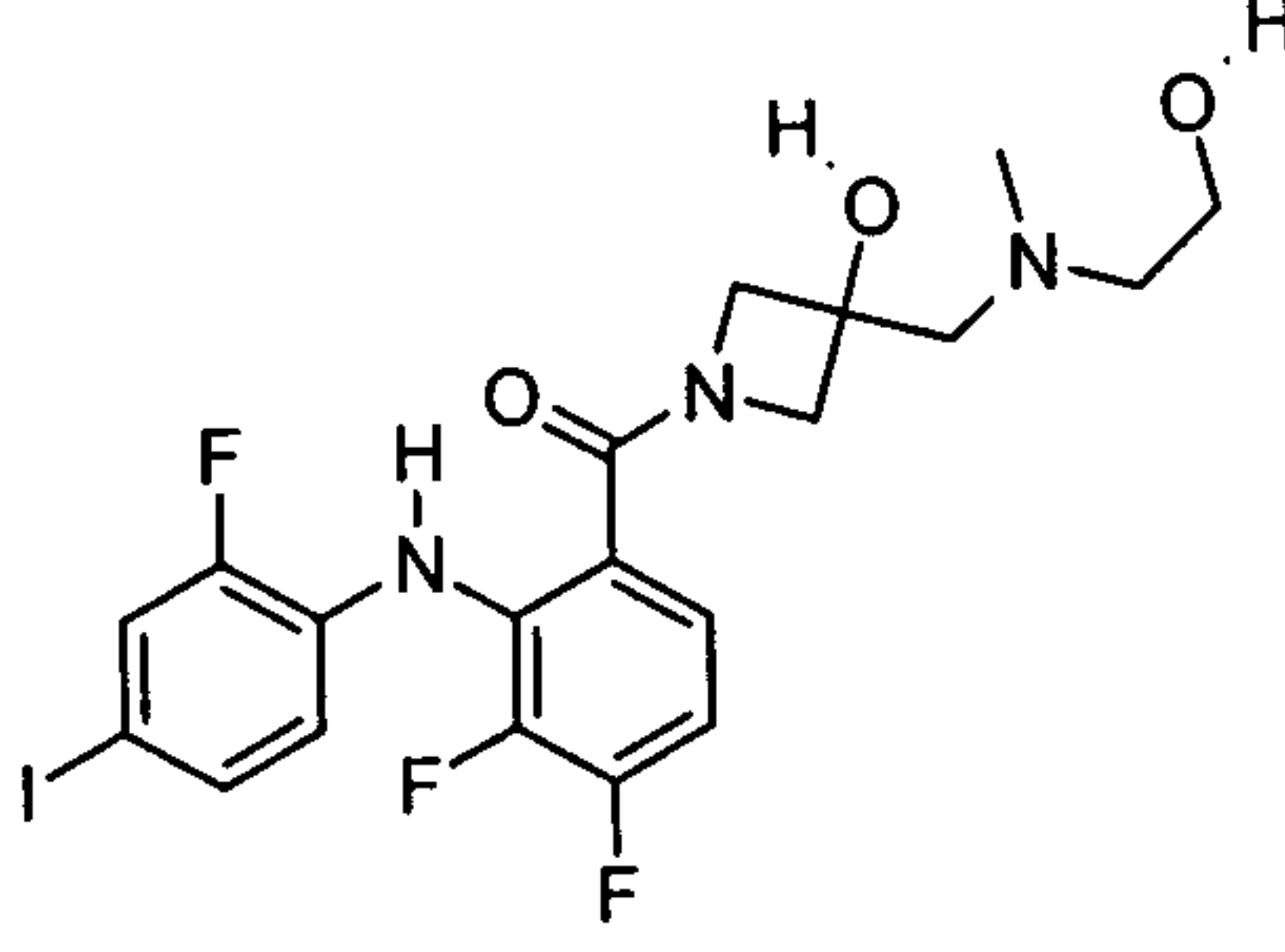
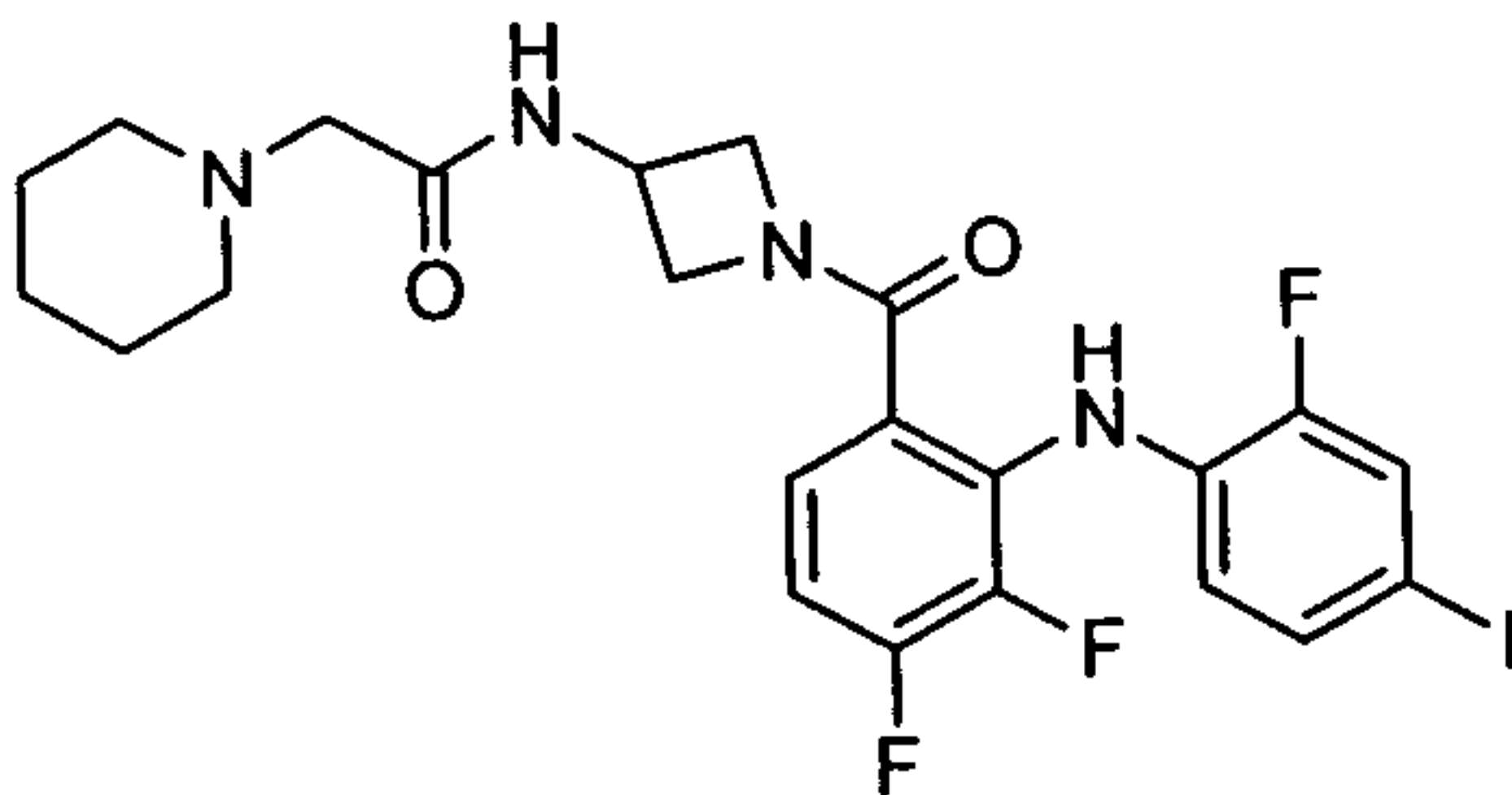
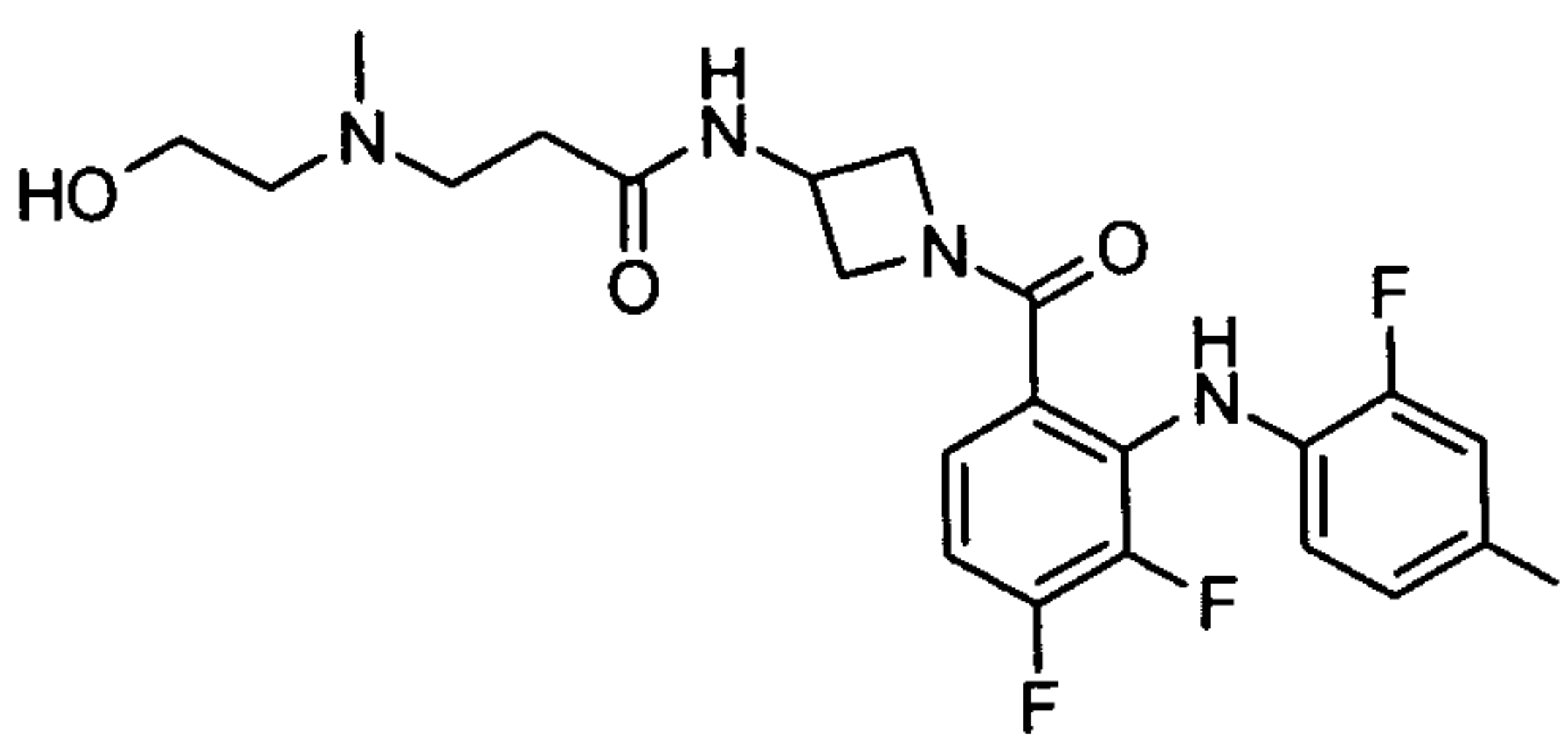
Cmpd No.	Structure	Name
53		3-({4-[2-(diethylamino)ethyl]piperazin-1-yl}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
54		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-hydroxyethyl)(methylamino)methyl]azetidin-3-ol
55		<i>N</i> -[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-piperidin-1-ylacetamide
56		<i>N</i> -[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]- <i>N</i> 3-(2-hydroxyethyl)- <i>N</i> 3-methyl-beta-alaninamide

Table 1. Representative MEK Inhibitors

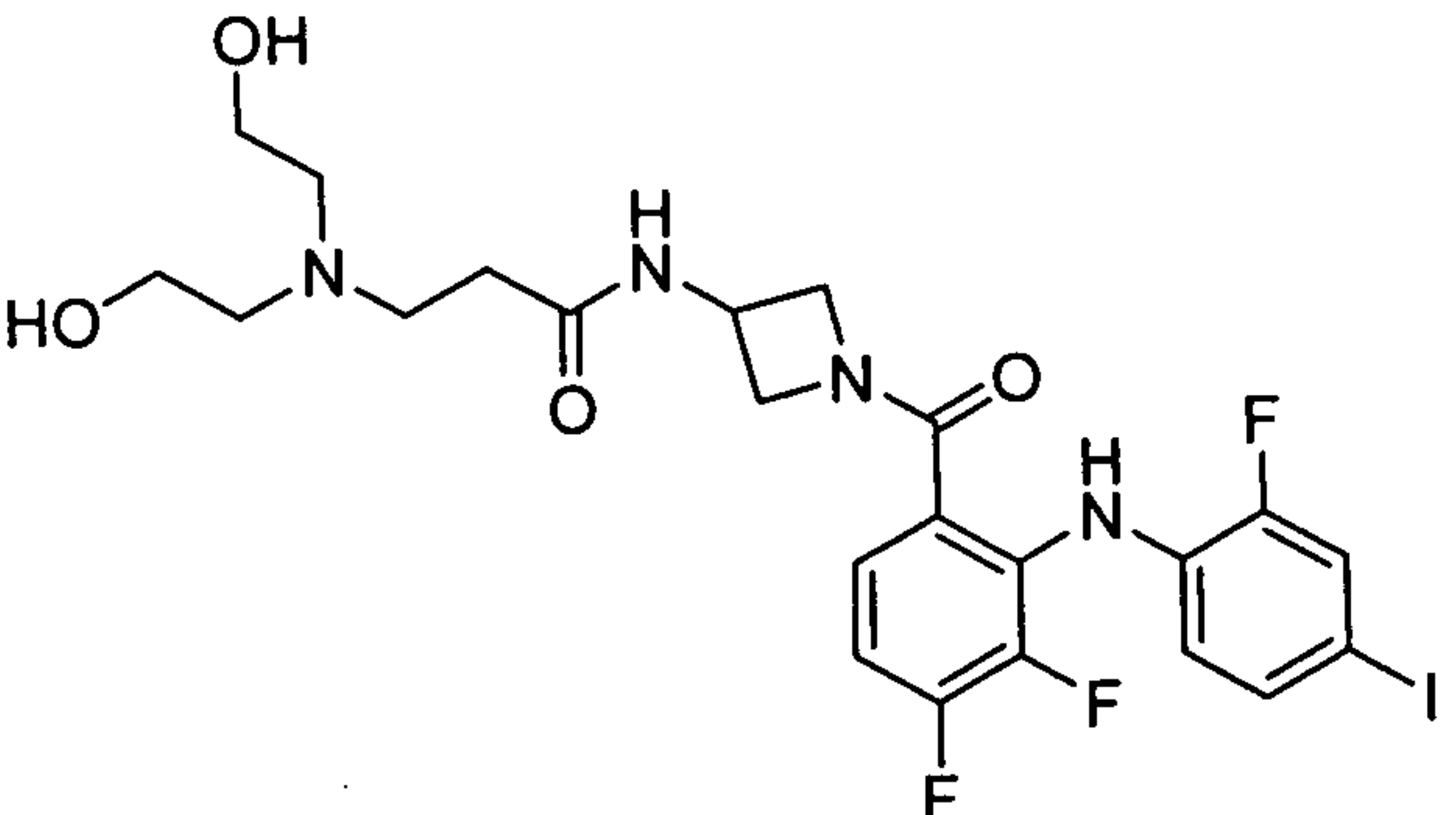
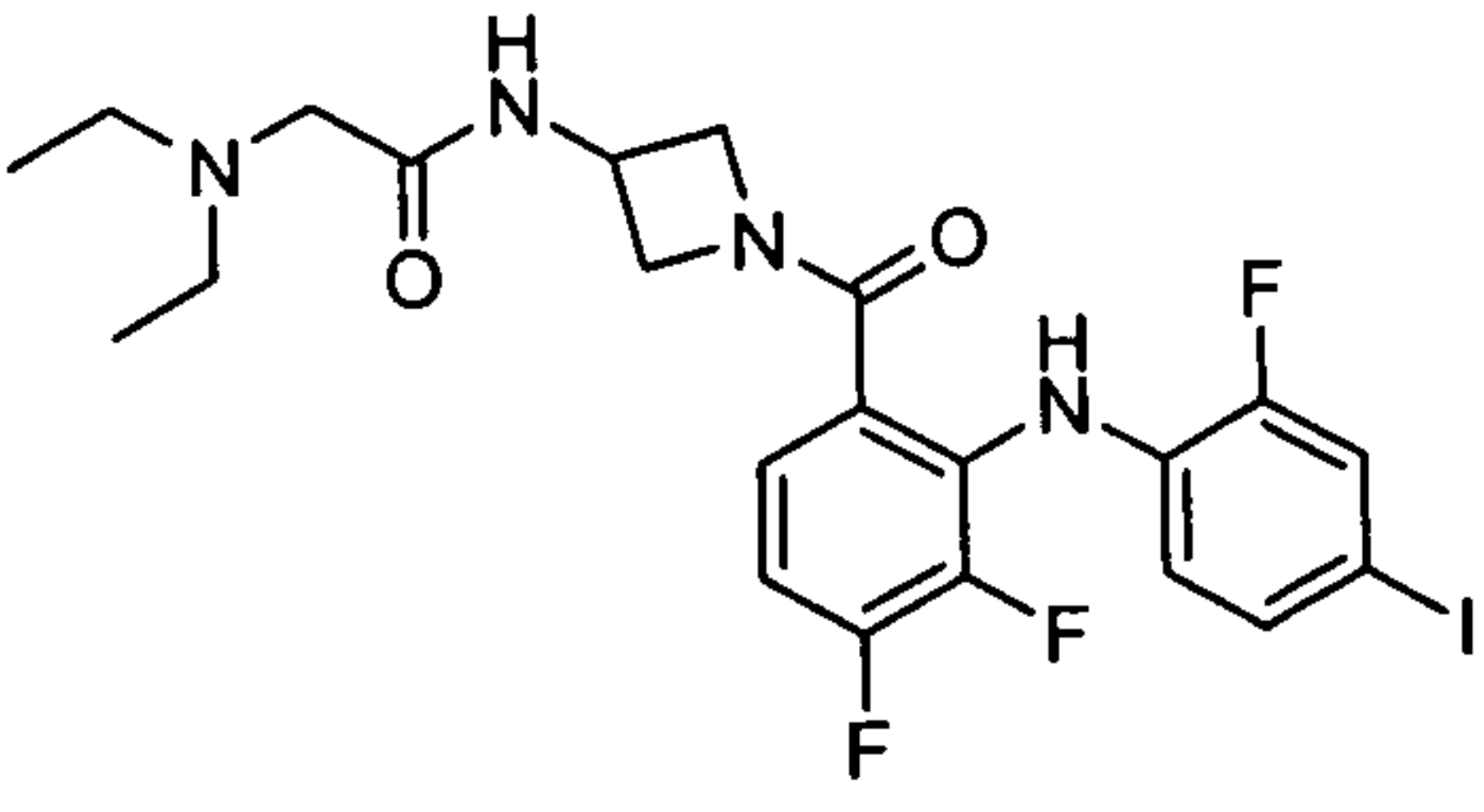
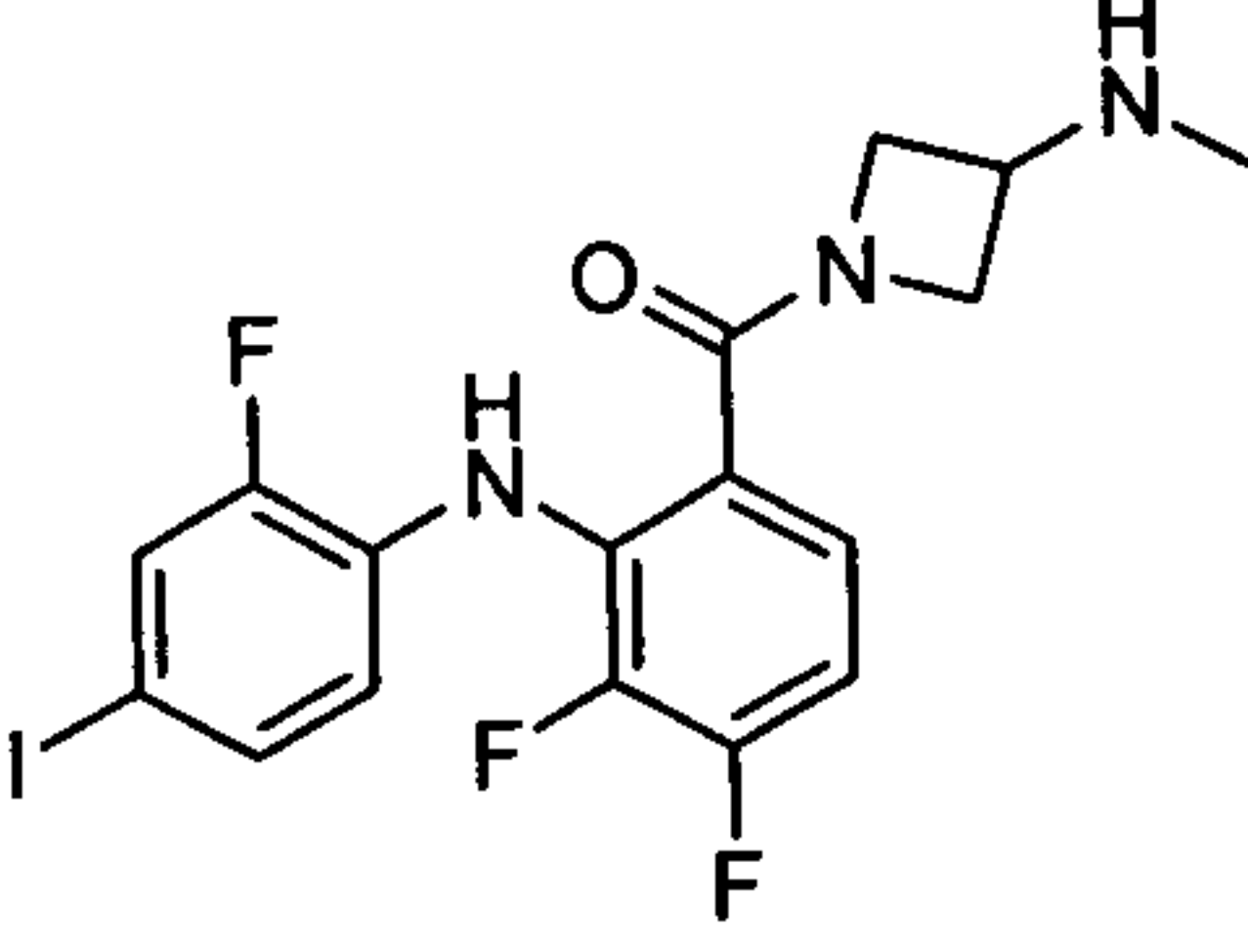
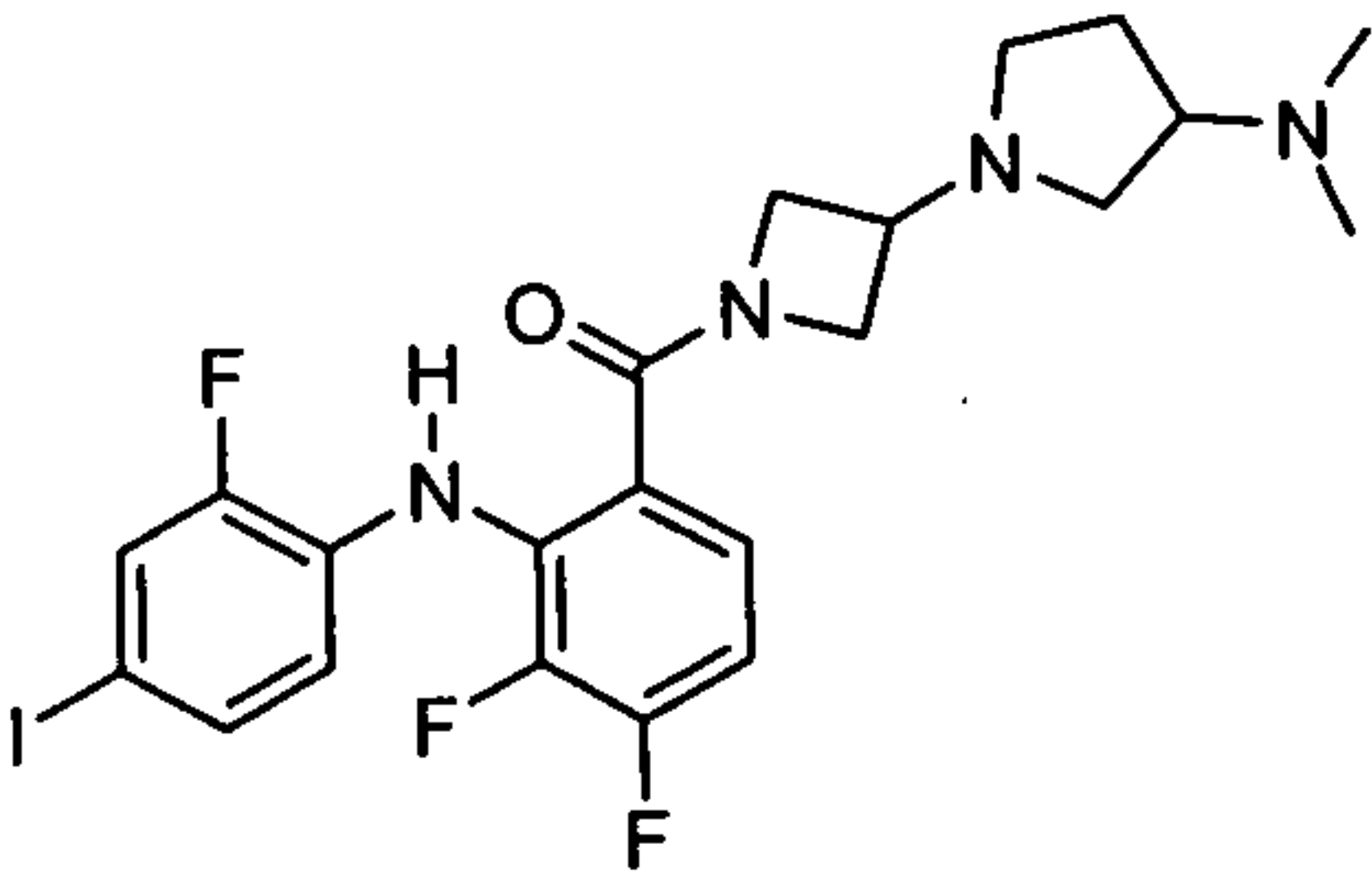
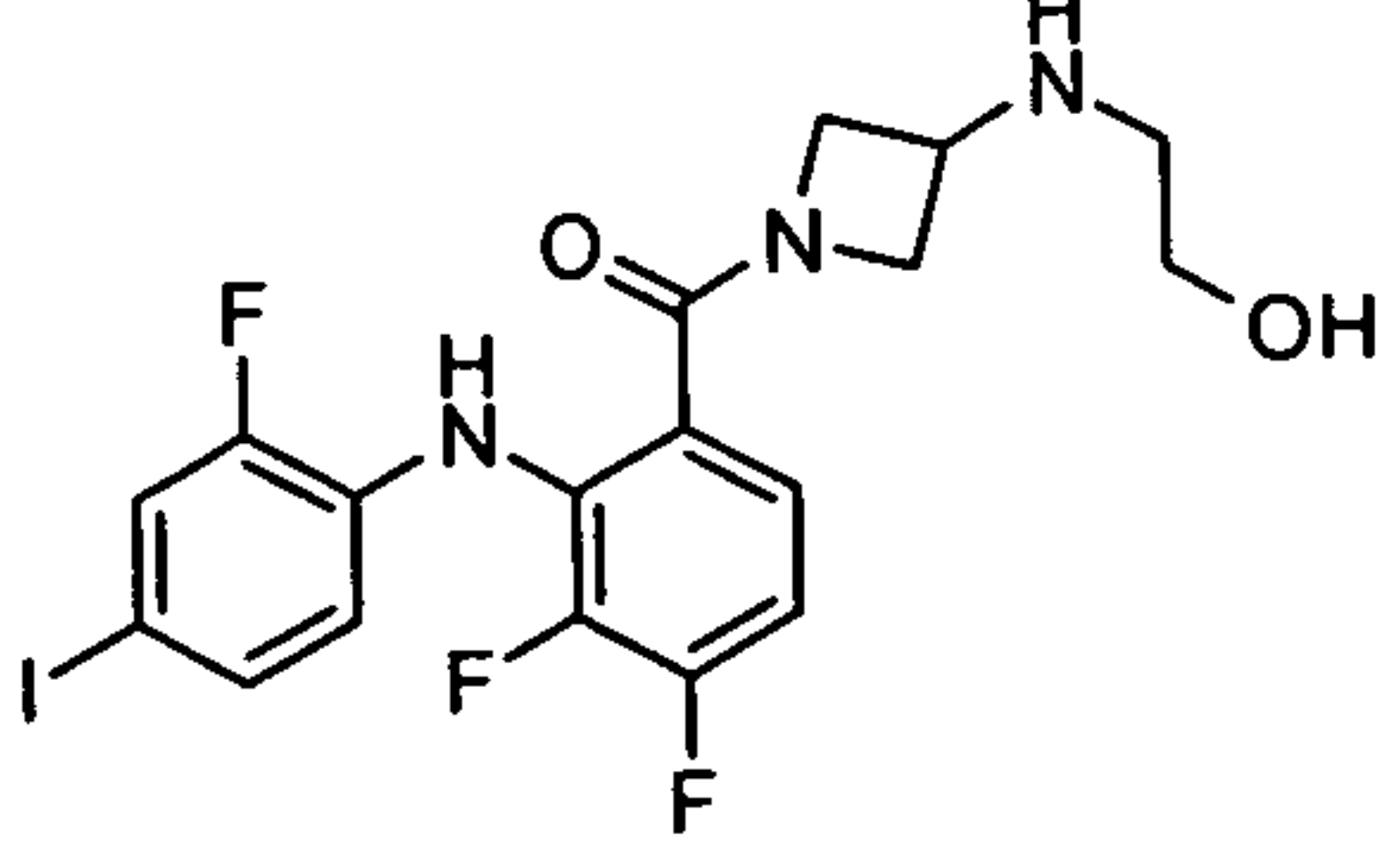
Cmpd No.	Structure	Name
57		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N3,N3-bis(2-hydroxyethyl)-beta-alaninamide
58		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N2,N2-diethylglycinamide
59		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-methylazetidin-3-amine
60		1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N,N-dimethylpyrrolidin-3-amine
61		2-{{1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl}amino}ethanol

Table 1. Representative MEK Inhibitors

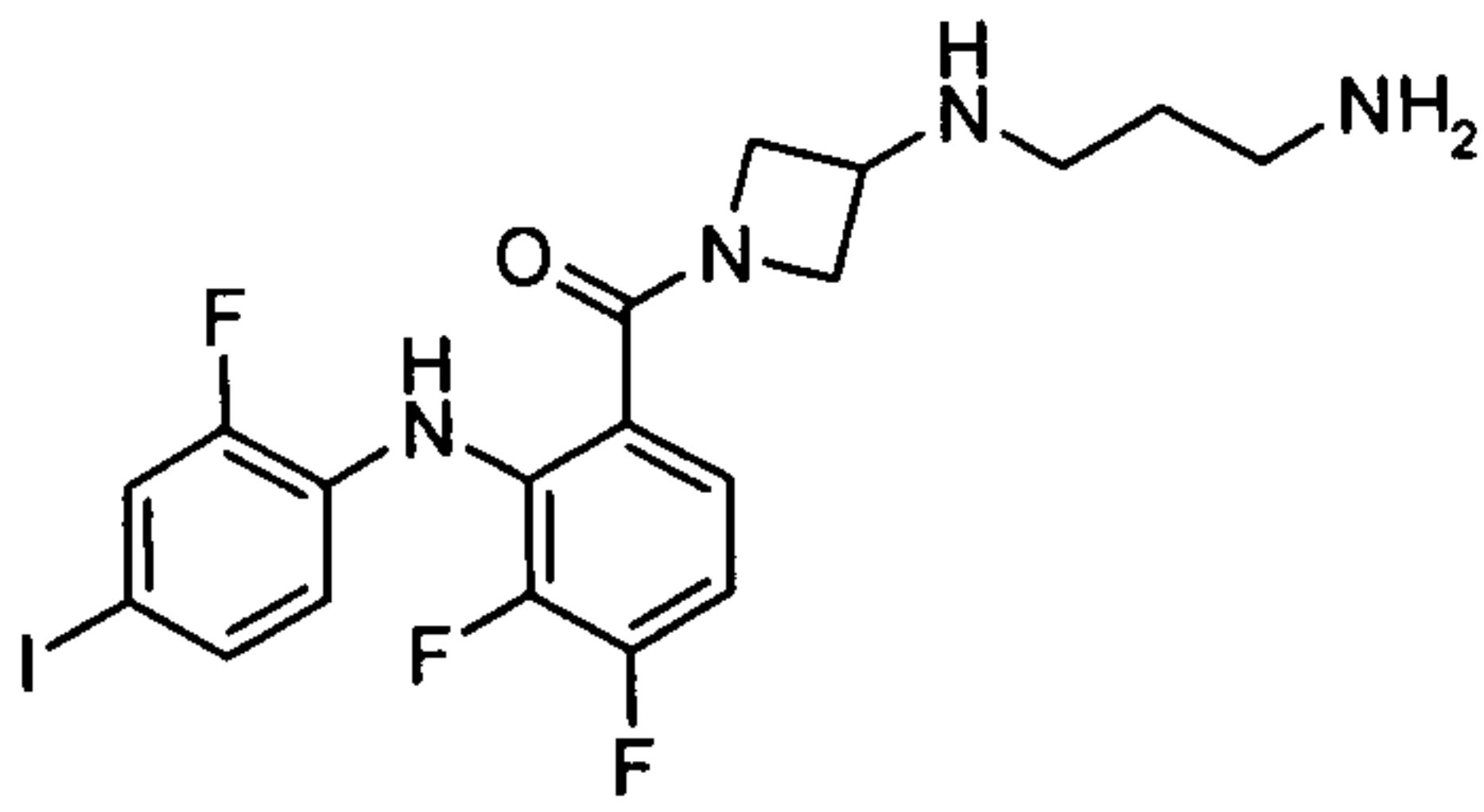
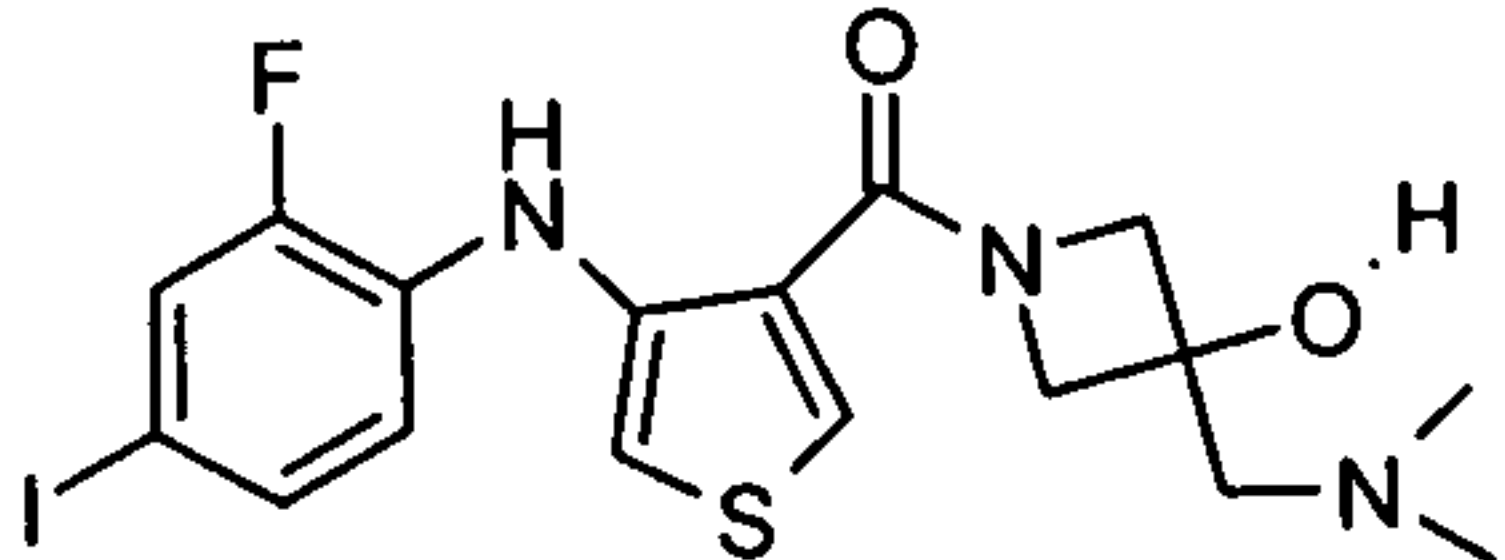
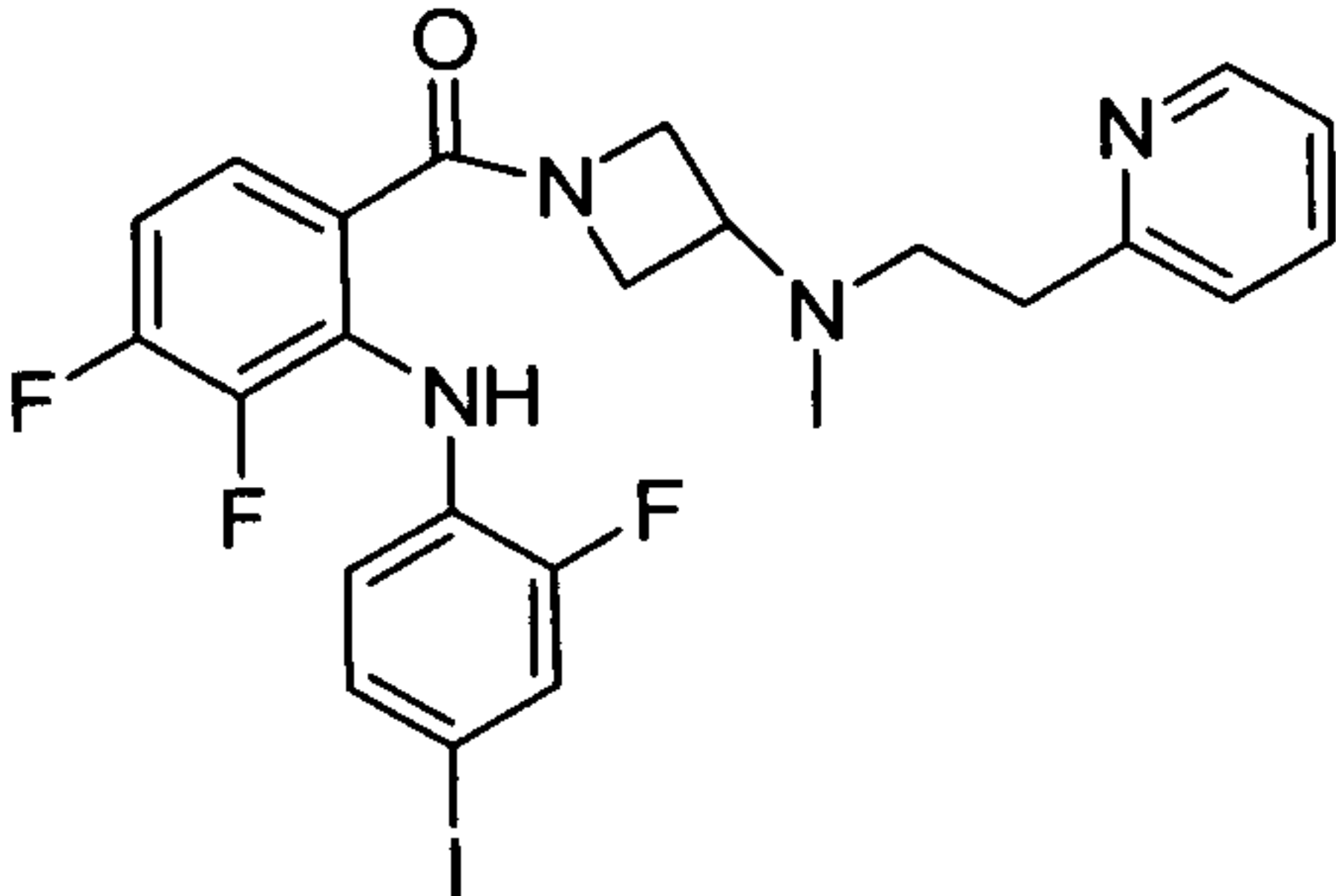
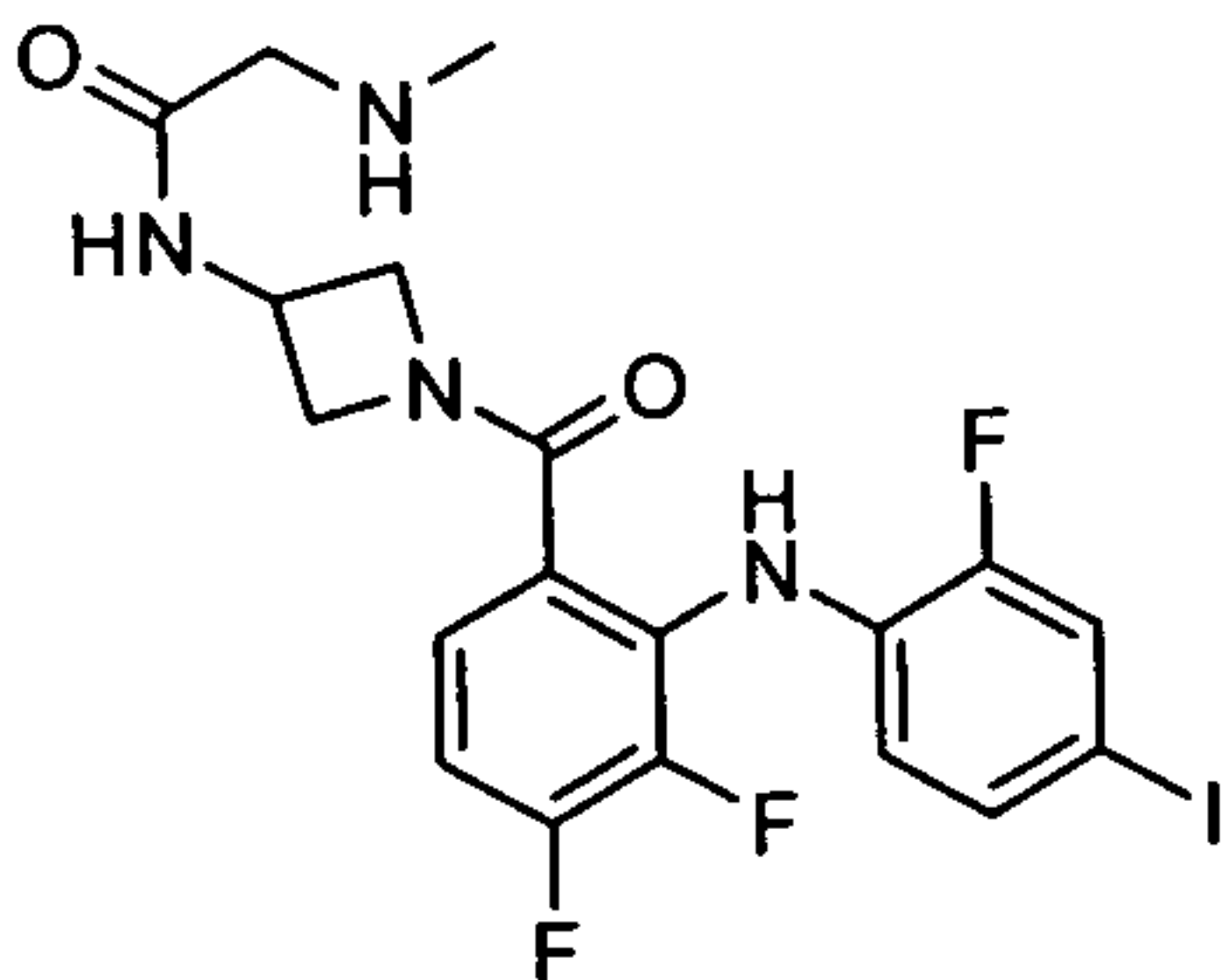
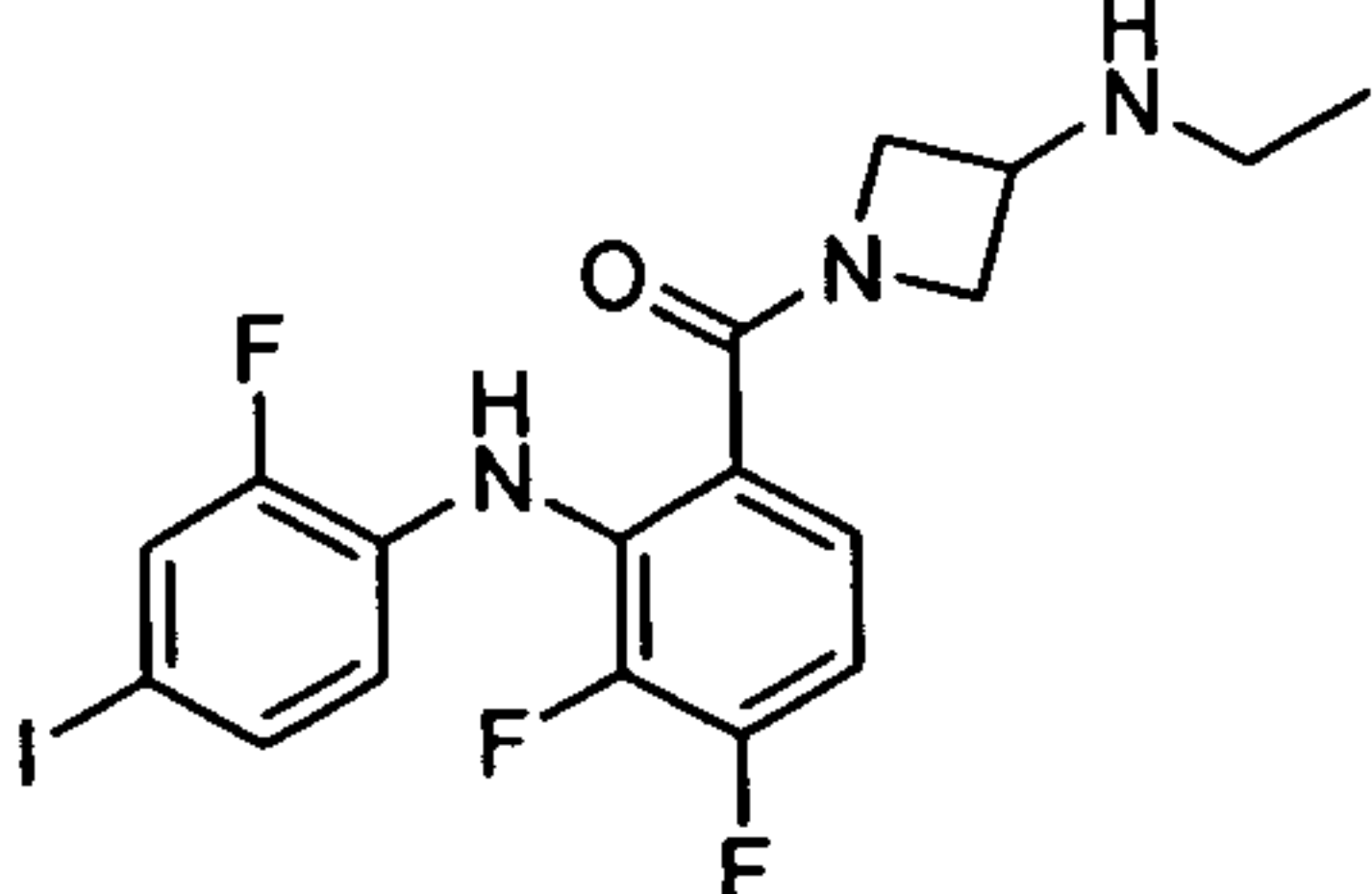
Cmpd No.	Structure	Name
62		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]propane-1,3-diamine
63		3-[(dimethylamino)methyl]-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol
64		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-methyl-N-(2-pyridin-2-ylethyl)azetidin-3-amine
65		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-N2-methylglycinamide
66		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-ethylazetidin-3-amine

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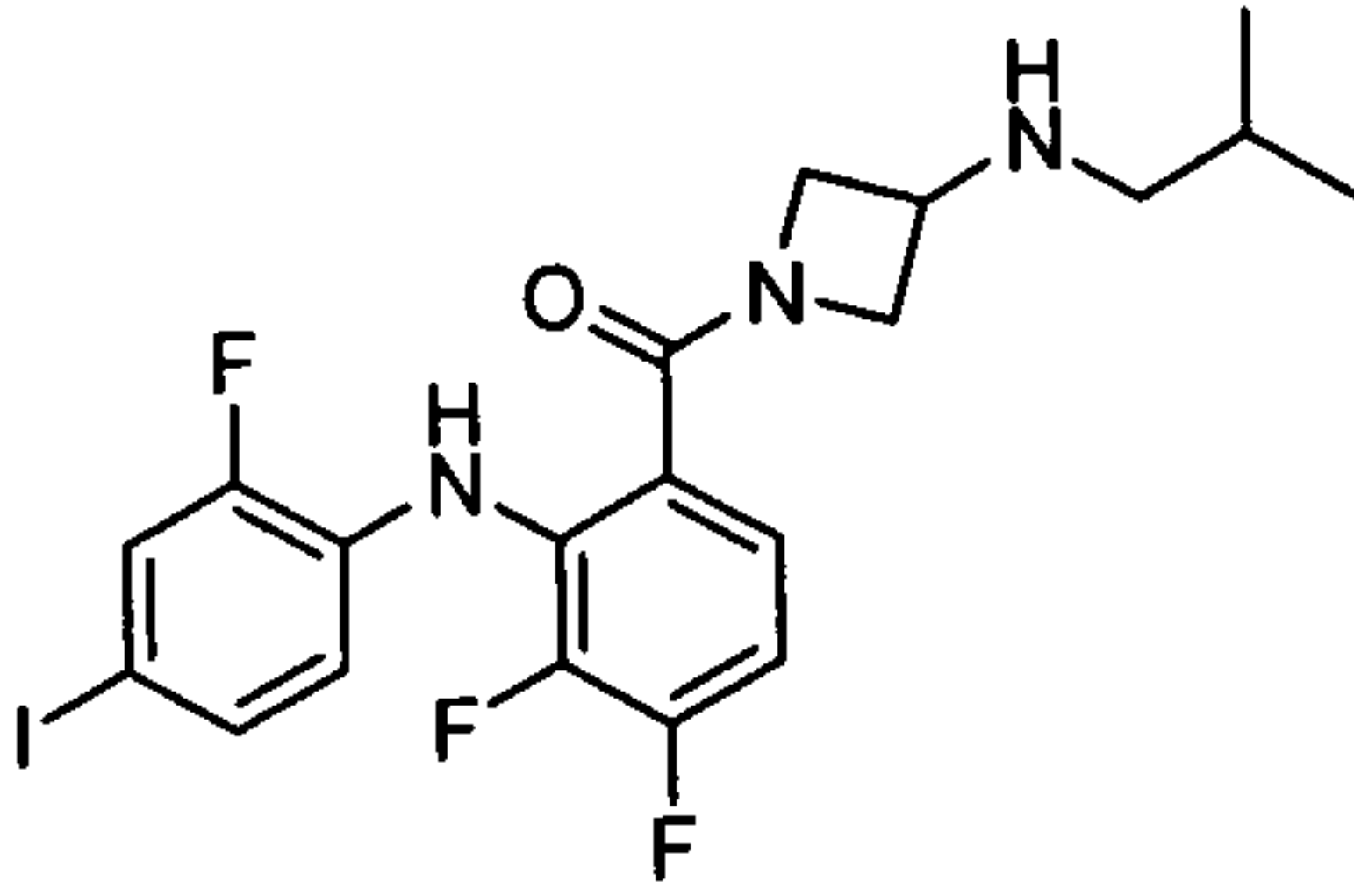
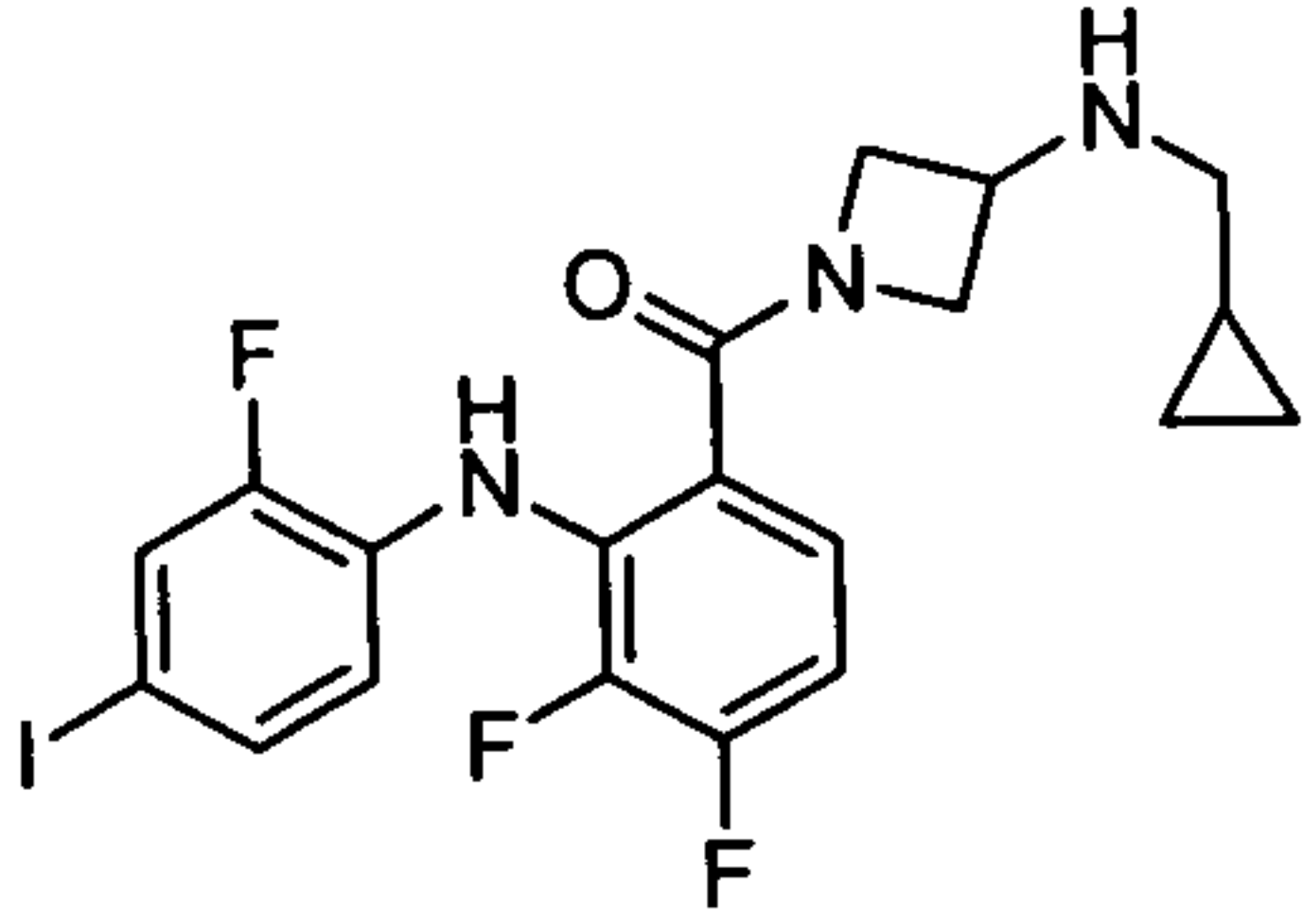
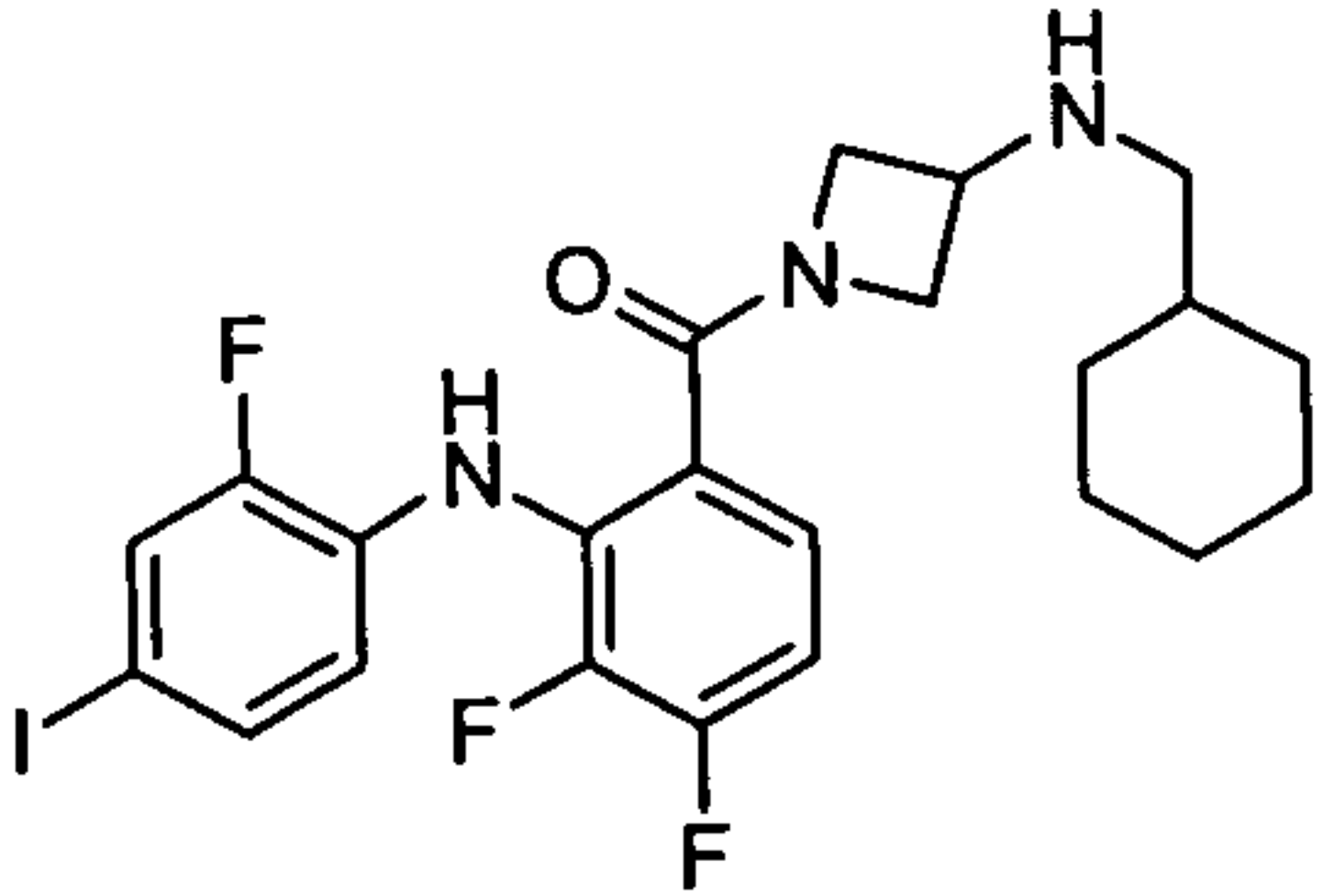
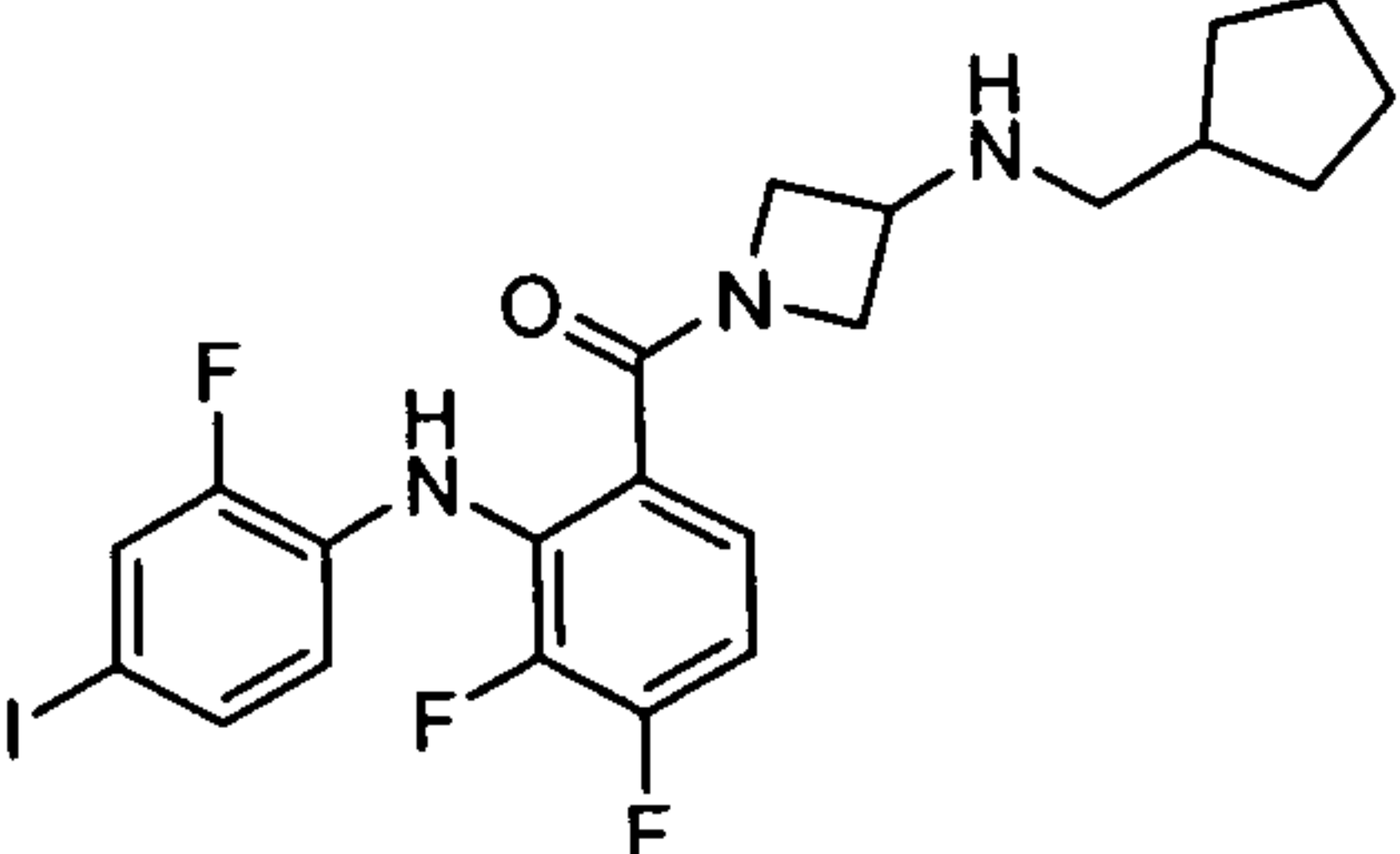
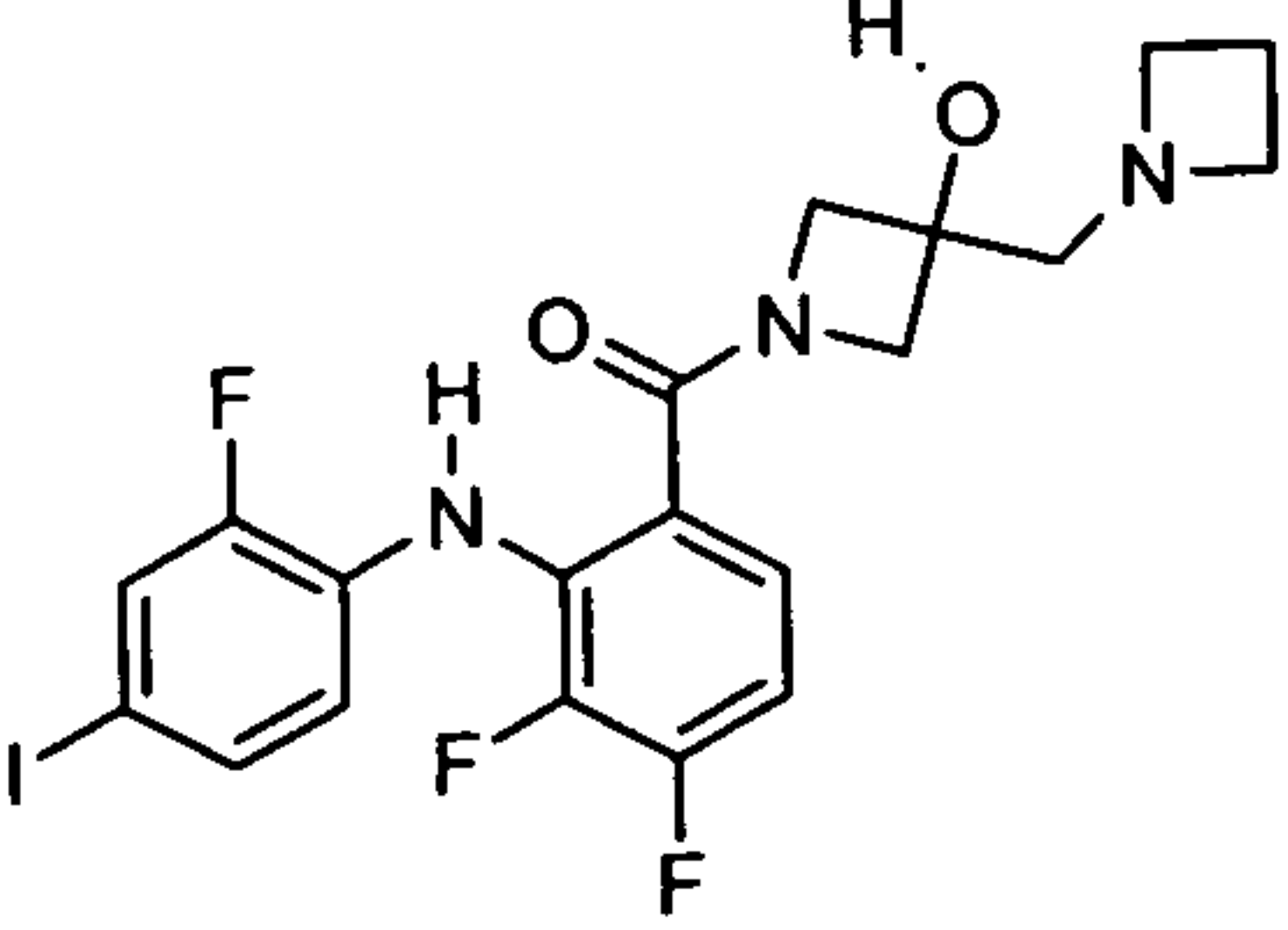
Cmpd No.	Structure	Name
67		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-(2-methylpropyl)azetidin-3-amine
68		N-(cyclopropylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
69		N-(cyclohexylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
70		N-(cyclopentylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
71		3-(azetidin-1-ylmethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

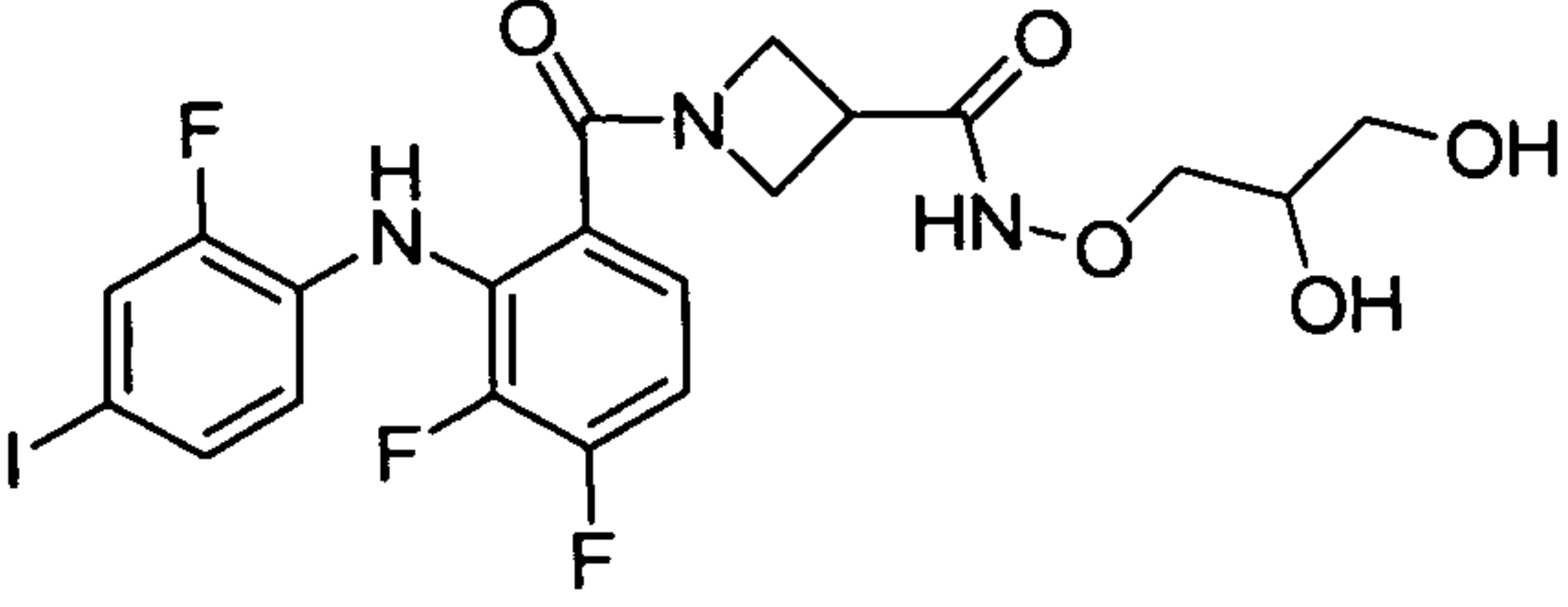
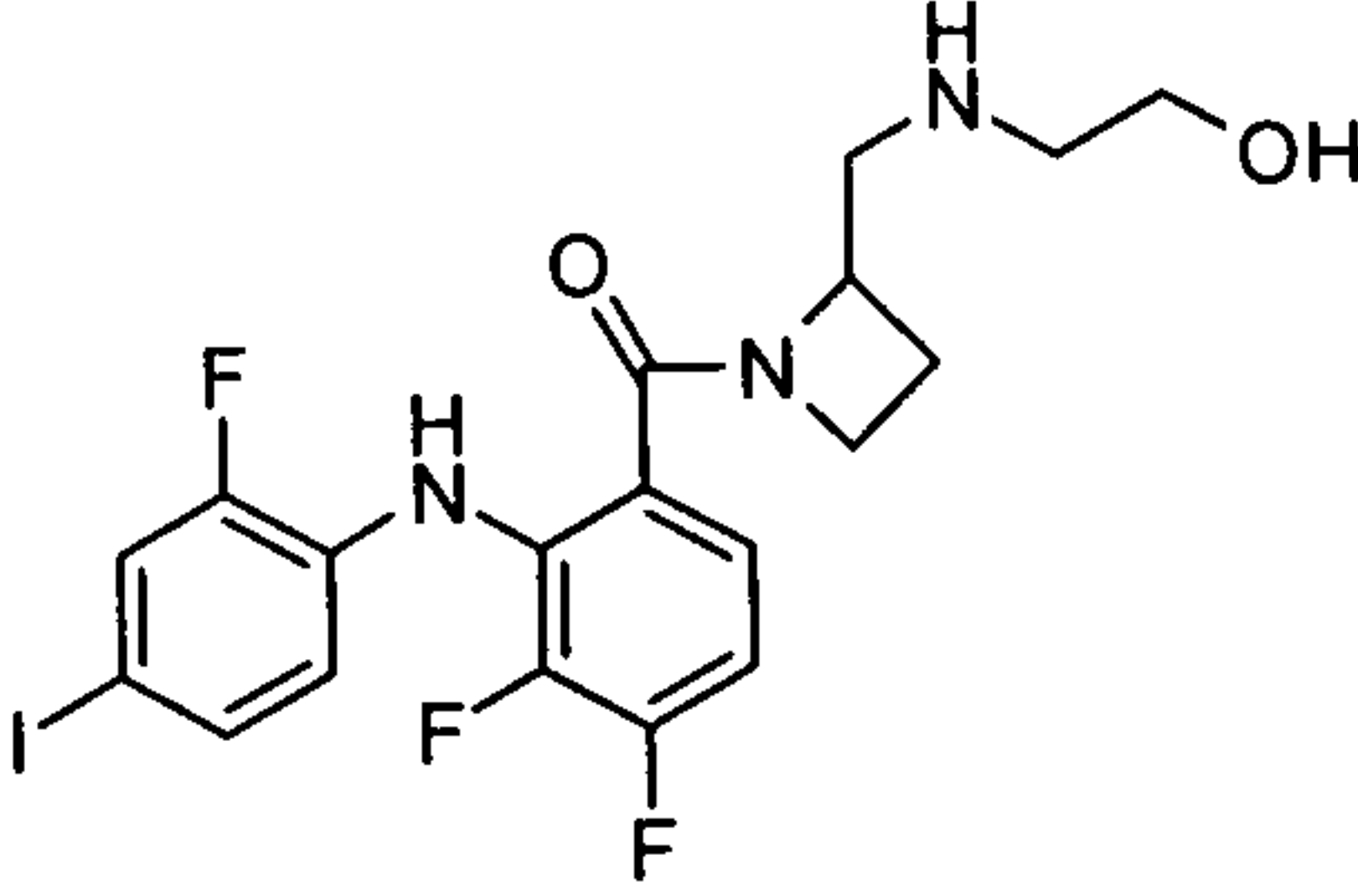
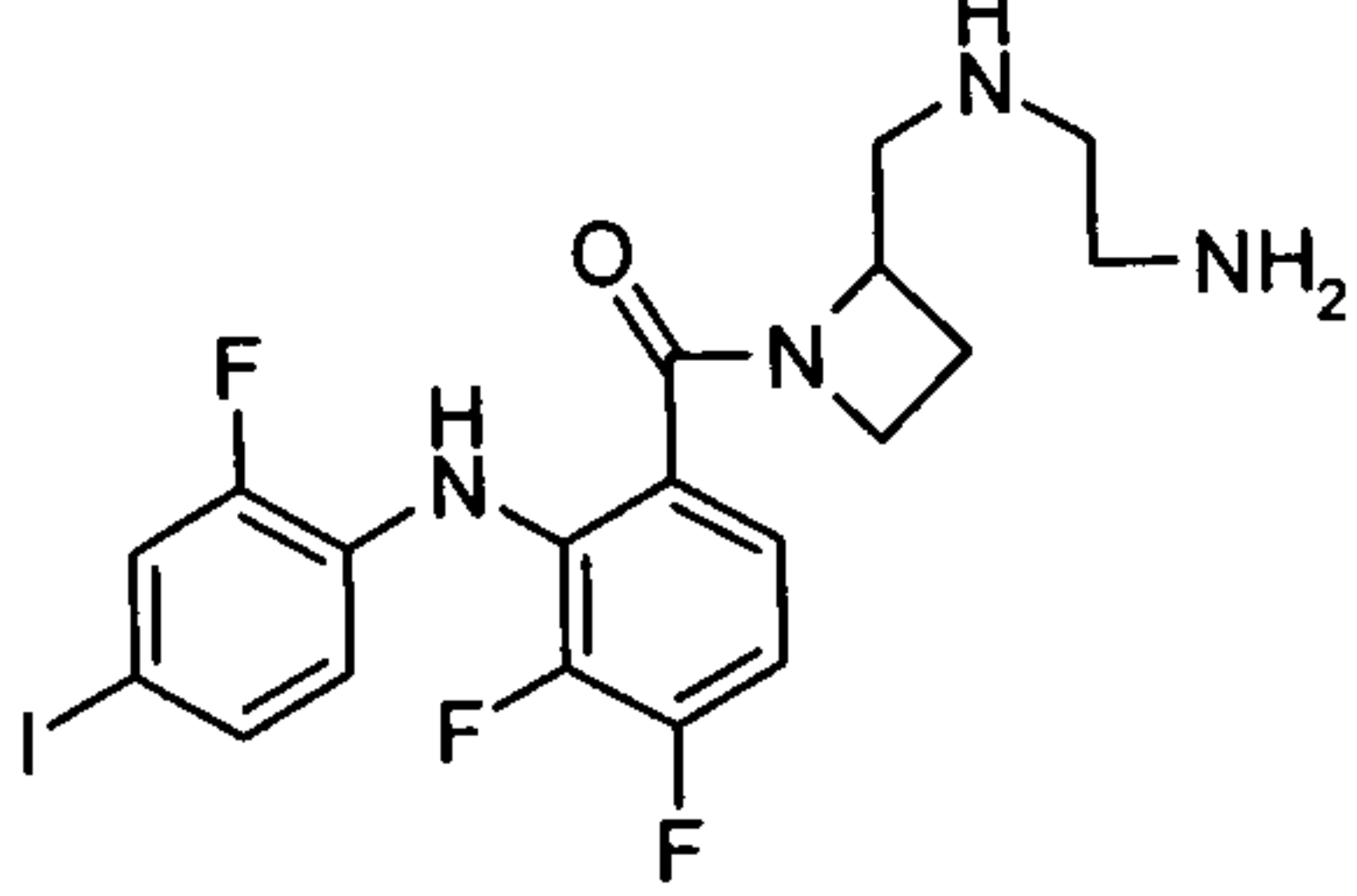
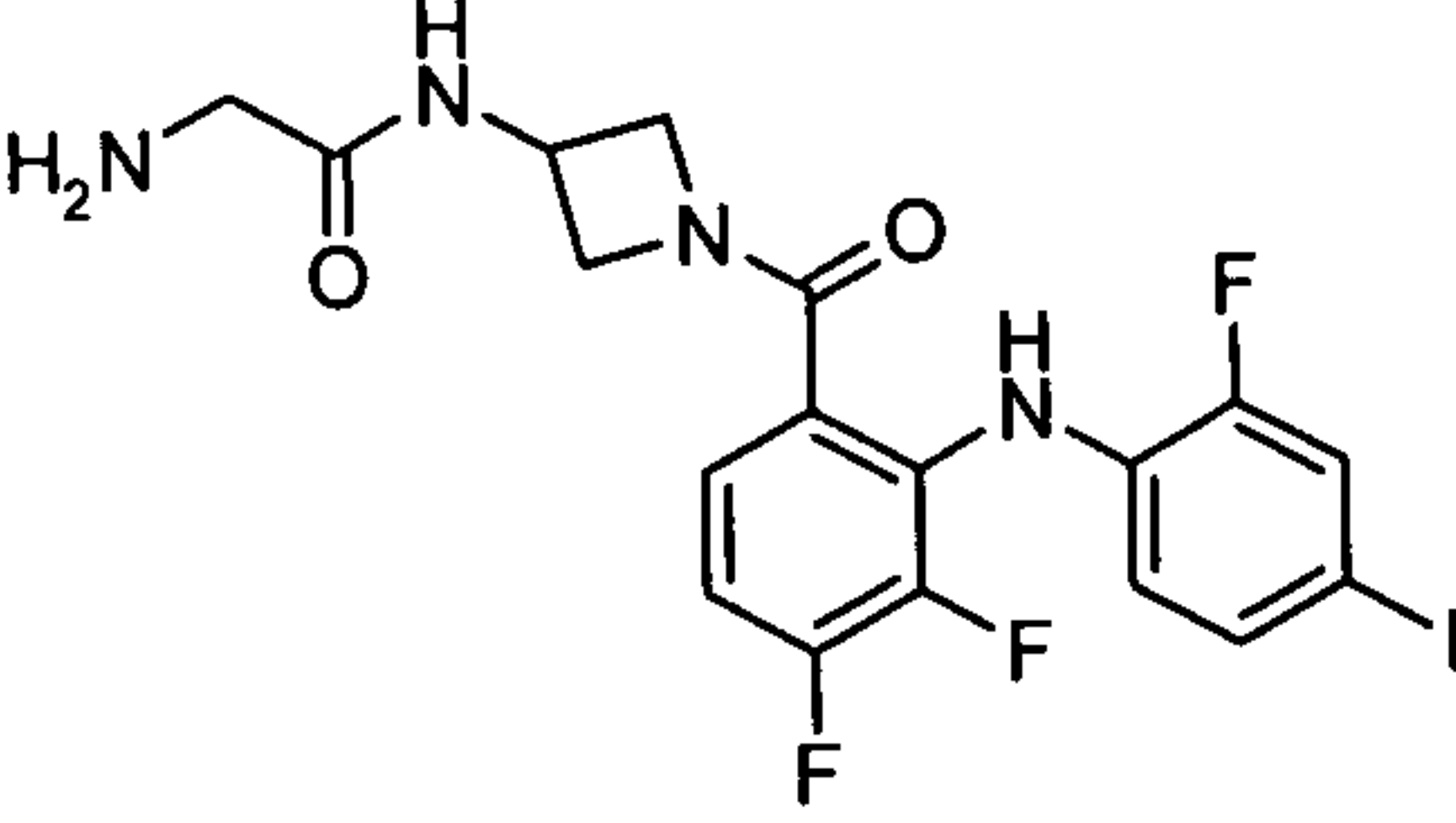
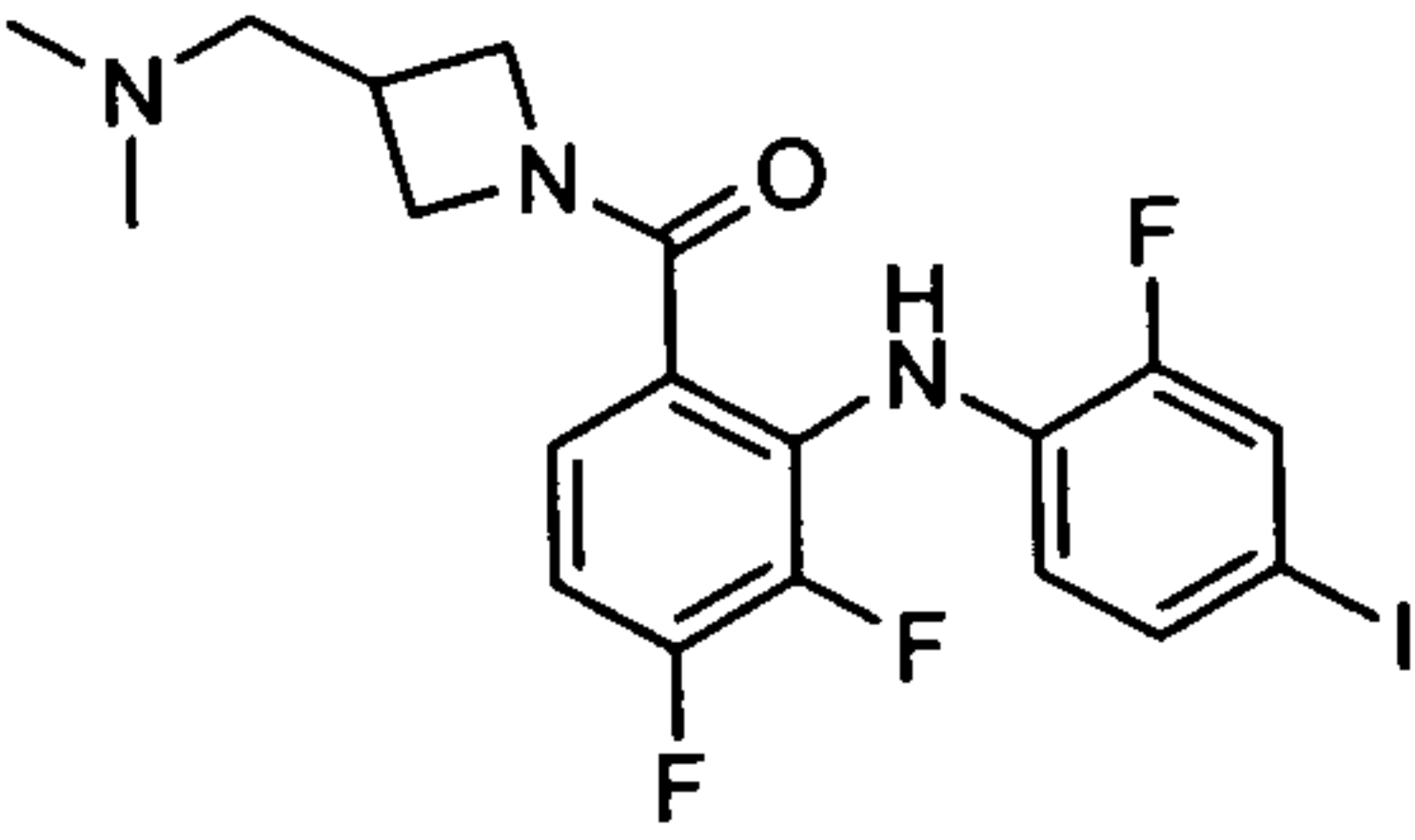
Cmpd No.	Structure	Name
72		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-[(2,3-dihydroxypropyl)oxy]azetidine-3-carboxamide
73		2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}amino)ethanol
74		N-{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methyl}ethane-1,2-diamine
75		N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]glycinamide
76		6-({3-[(dimethylamino)methyl]azetidin-1-yl}carbonyl)-2,3-difluoro-N-(2-fluoro-4-iodophenyl)aniline

Table 1. Representative MEK Inhibitors

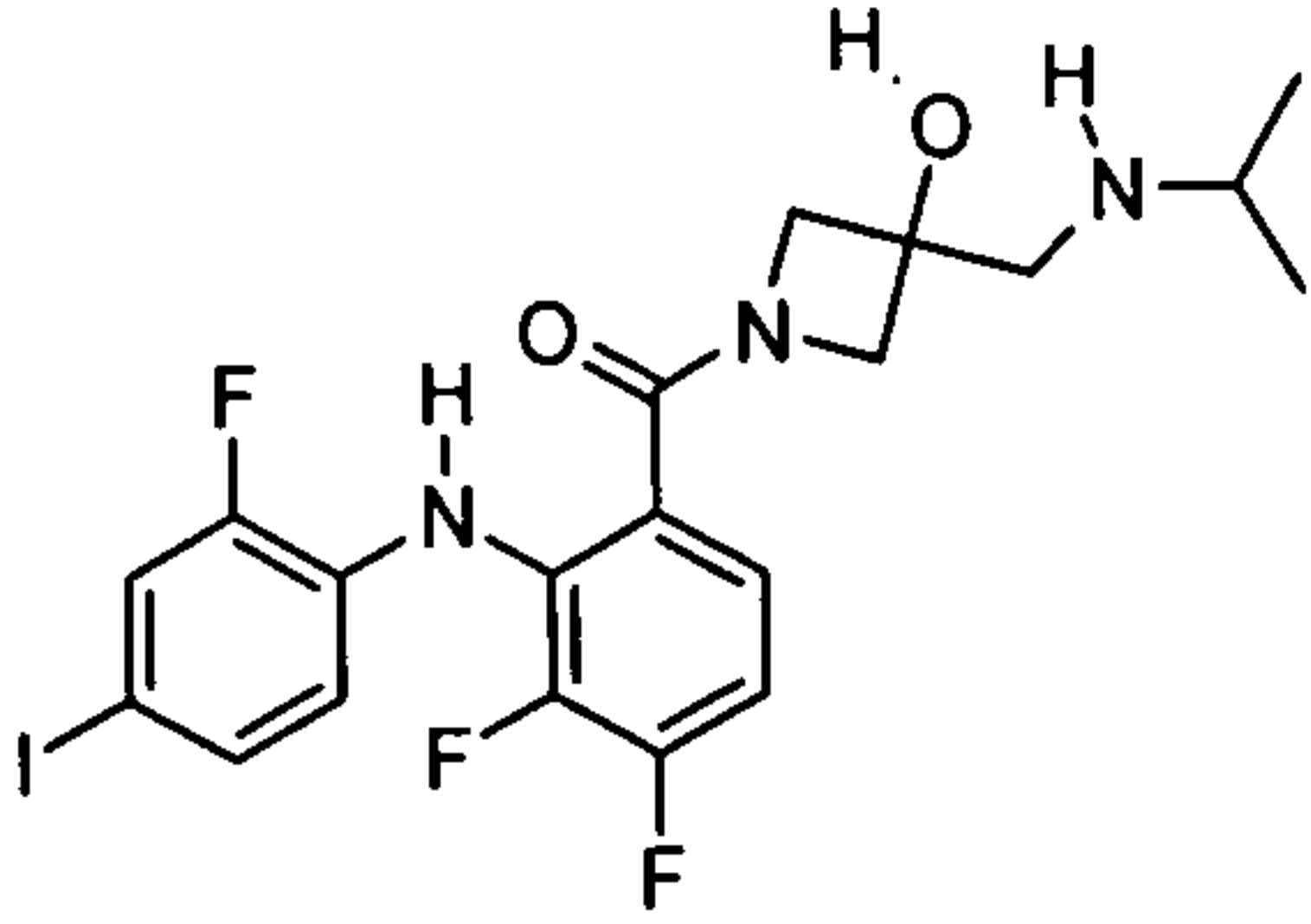
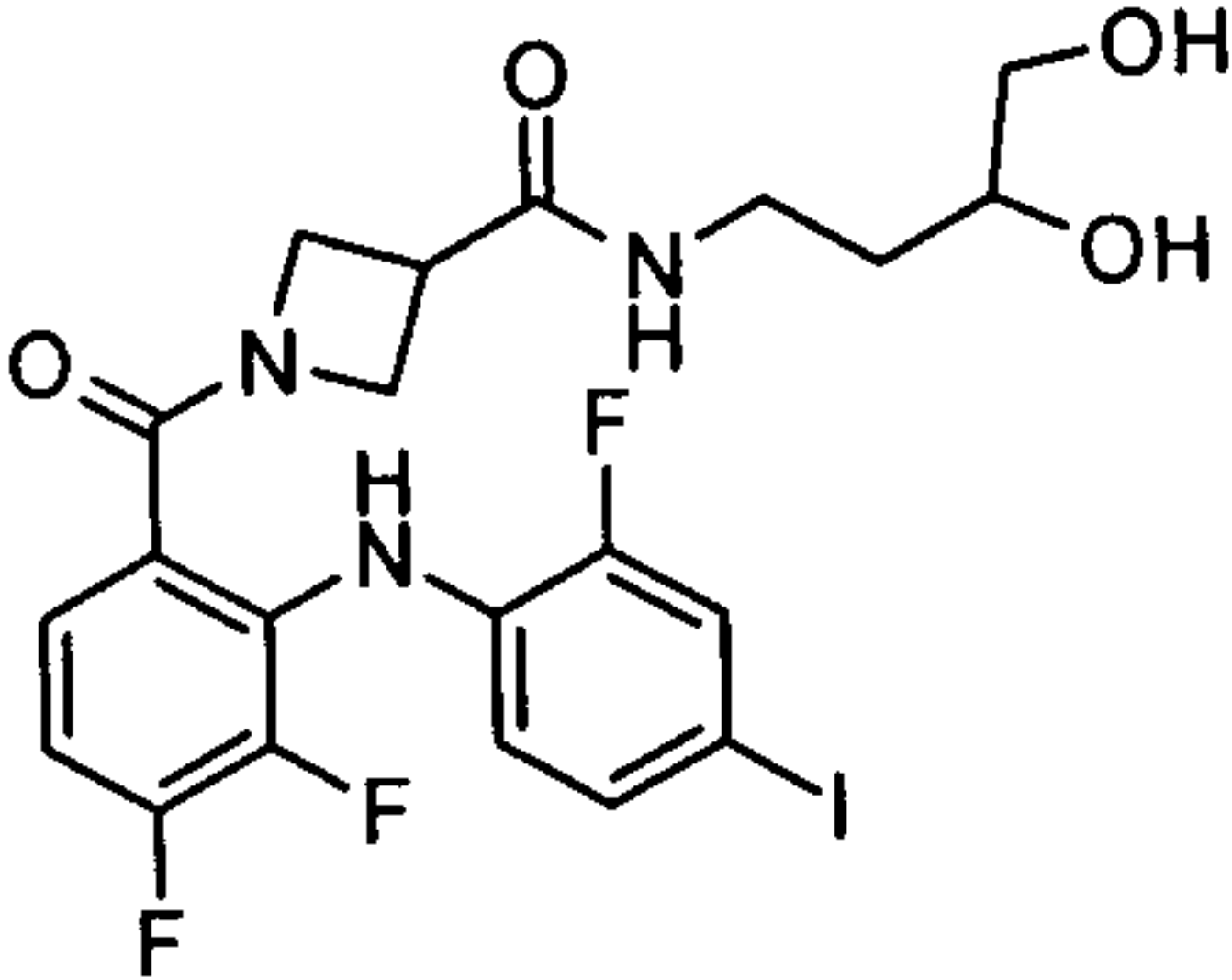
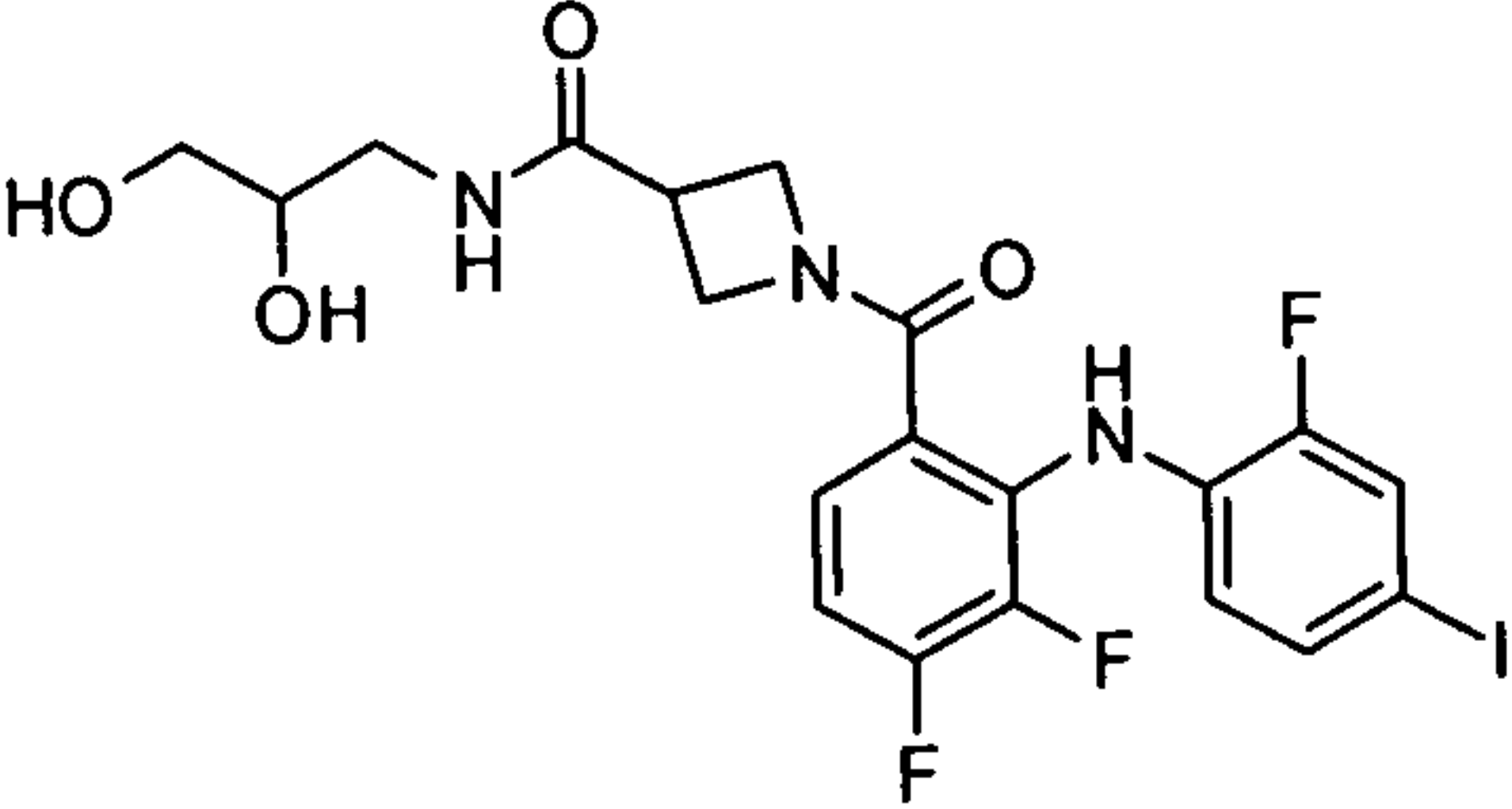
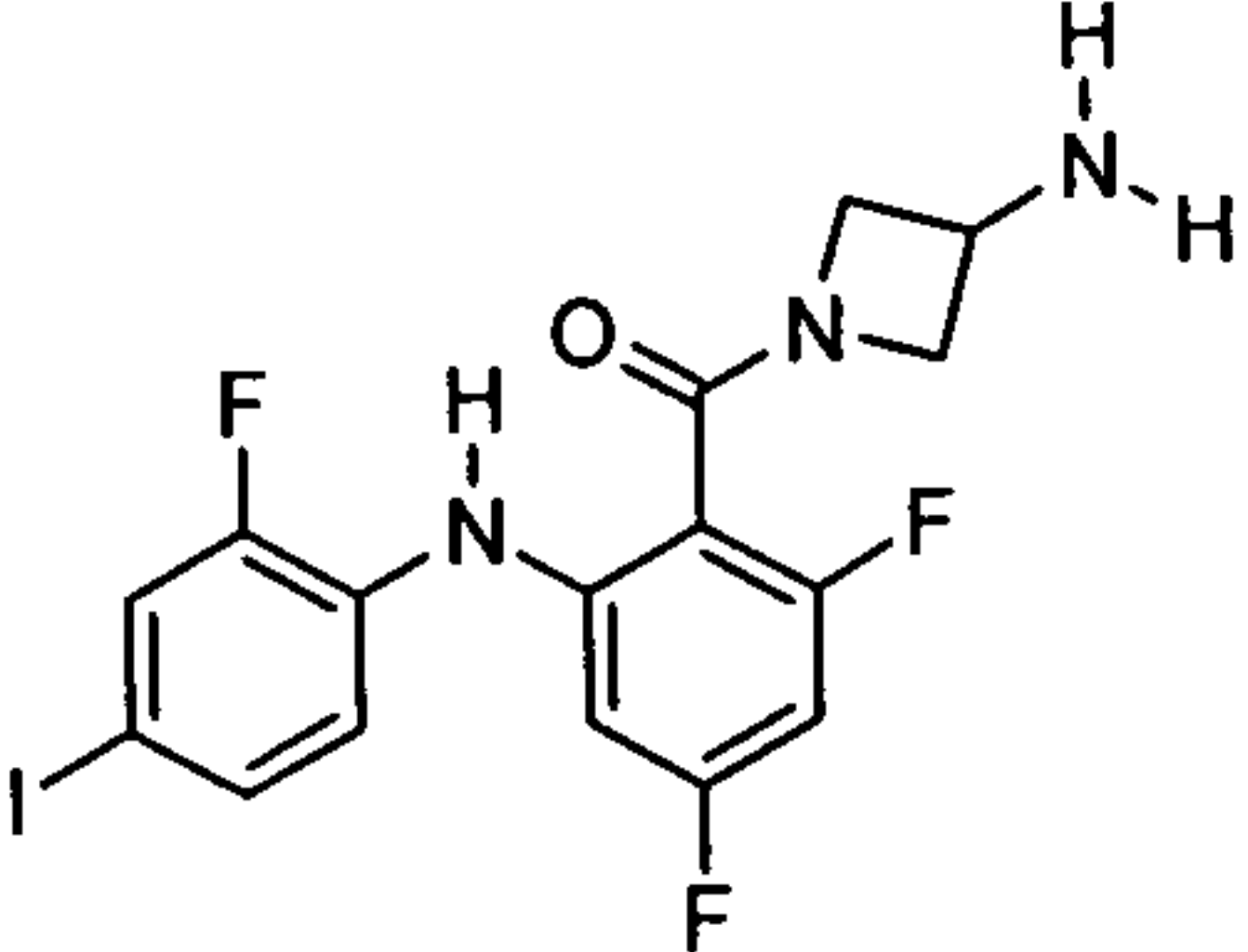
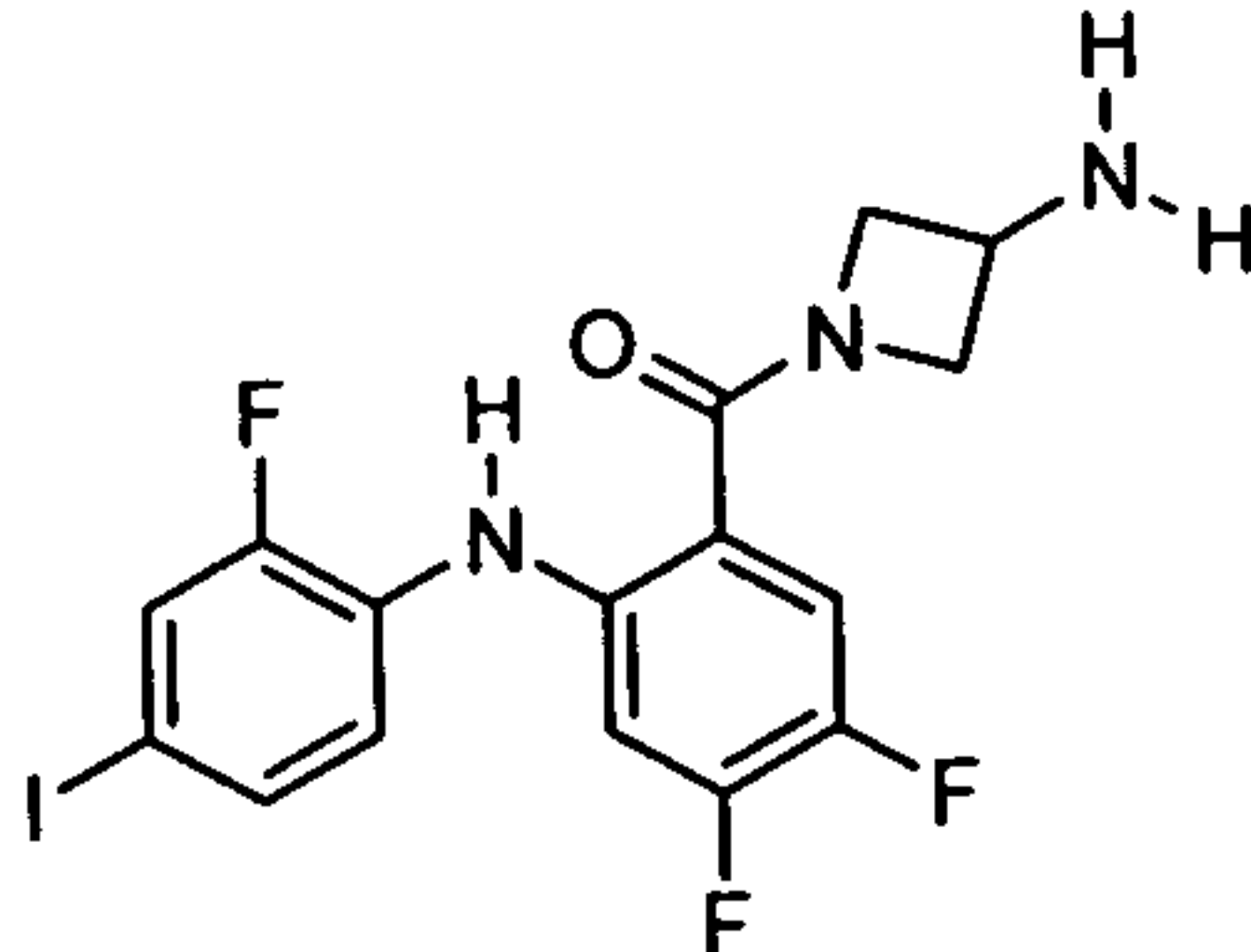
Cmpd No.	Structure	Name
77		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(1-methylethyl)amino}methyl}azetidin-3-ol
78		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-(3,4-dihydroxybutyl)azetidine-3-carboxamide
79		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-(2,3-dihydroxypropyl)azetidine-3-carboxamide
80		1-({2,4-difluoro-6-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine
81		1-({4,5-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine

Table 1. Representative MEK Inhibitors

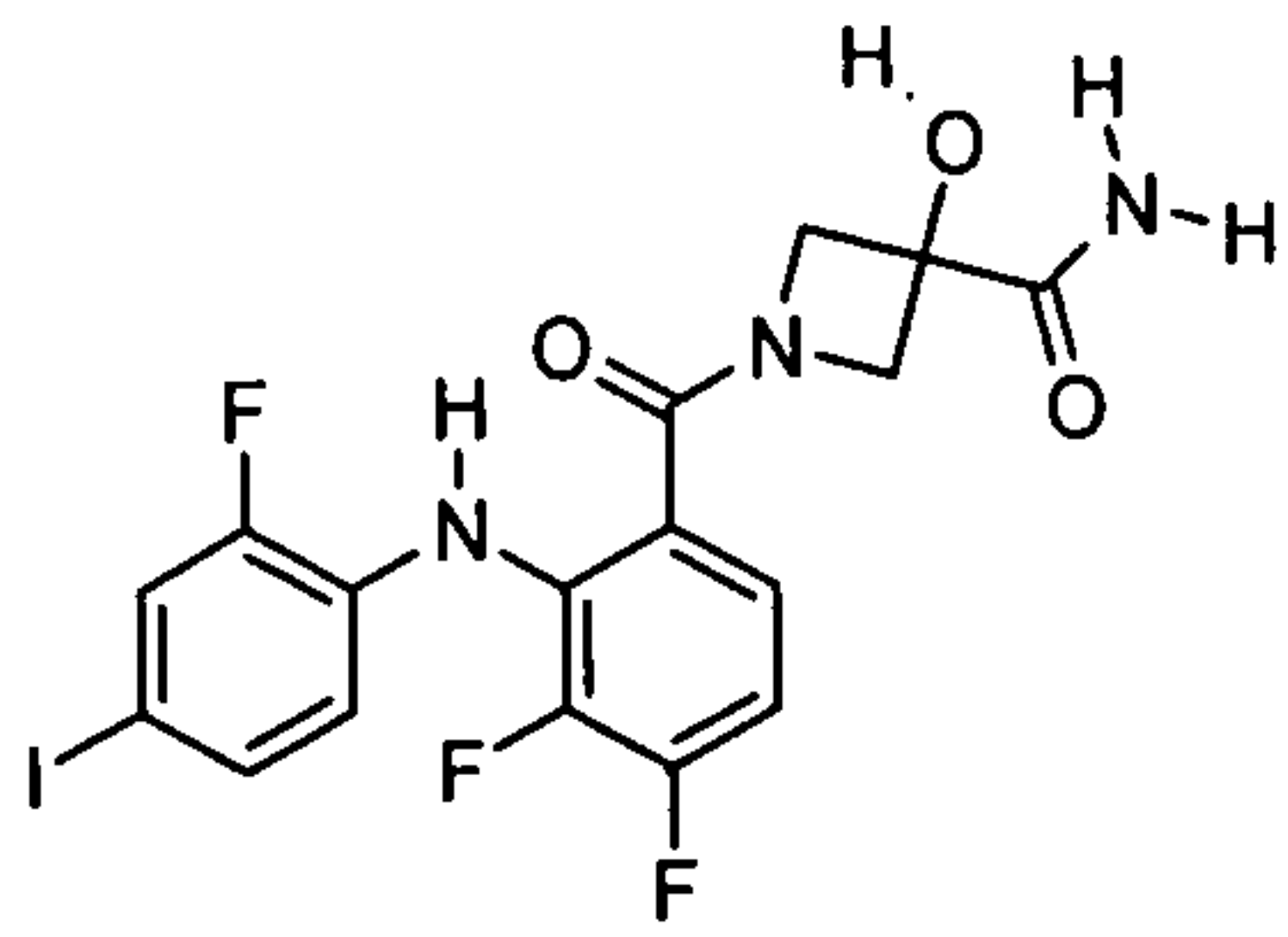
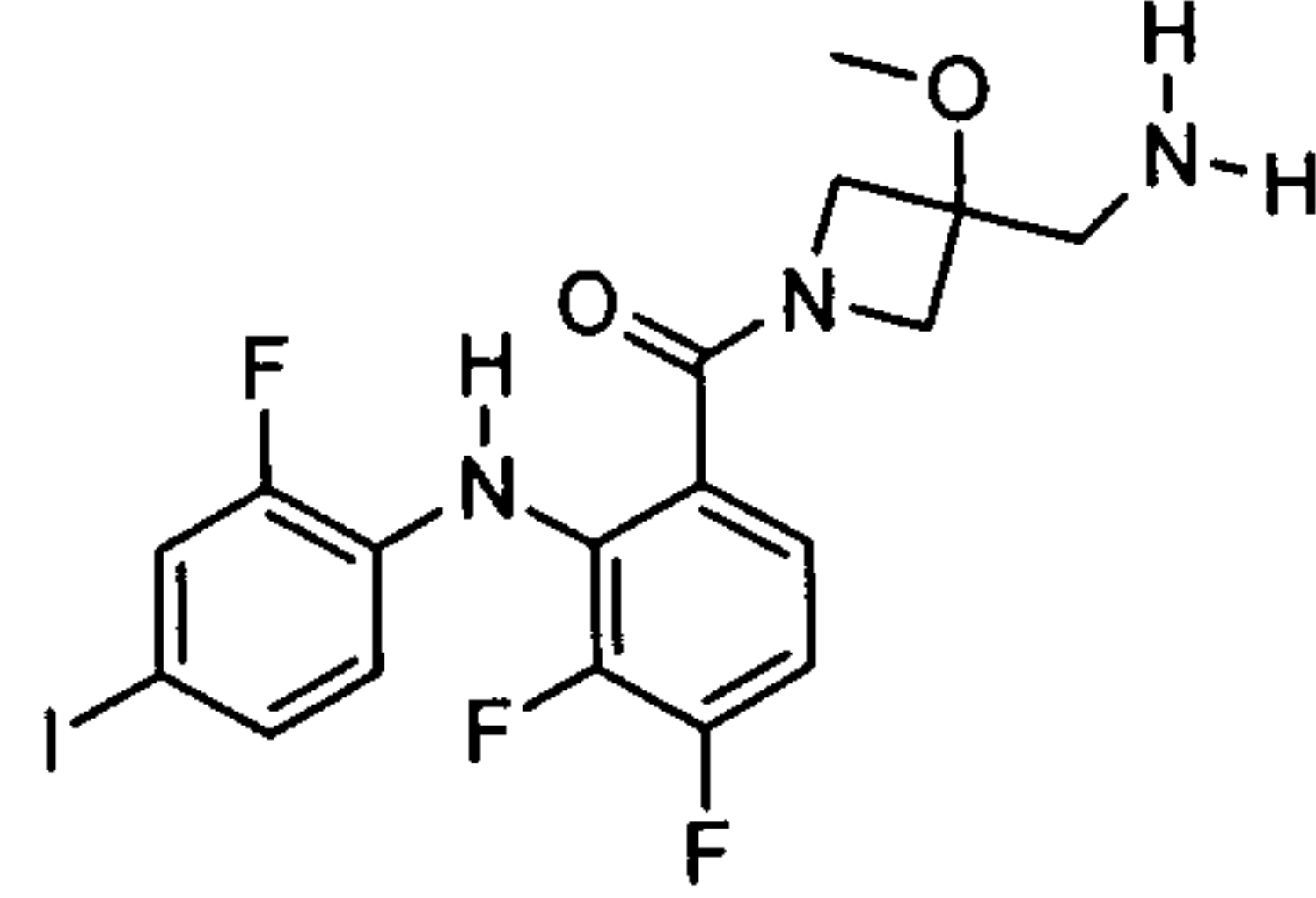
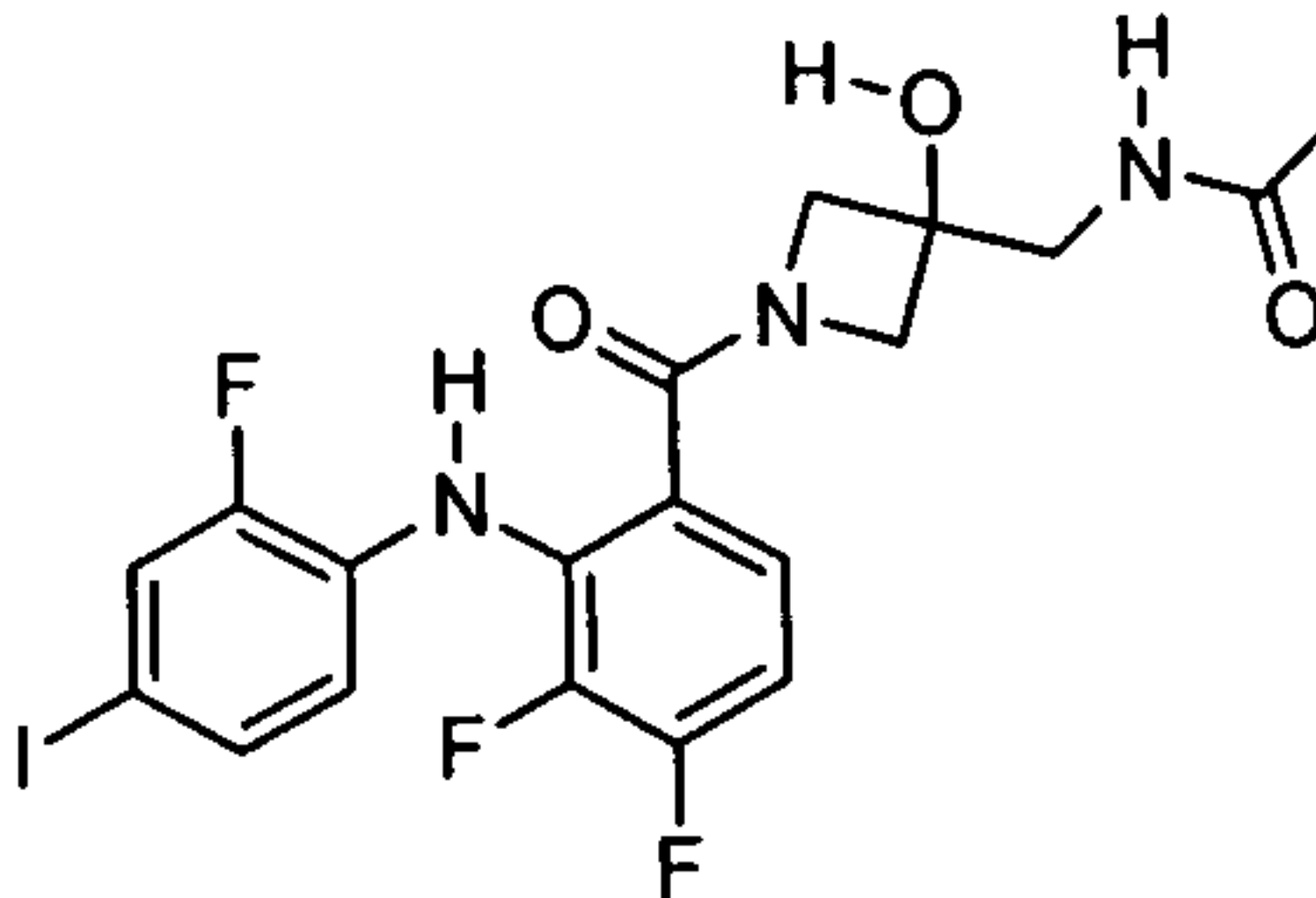
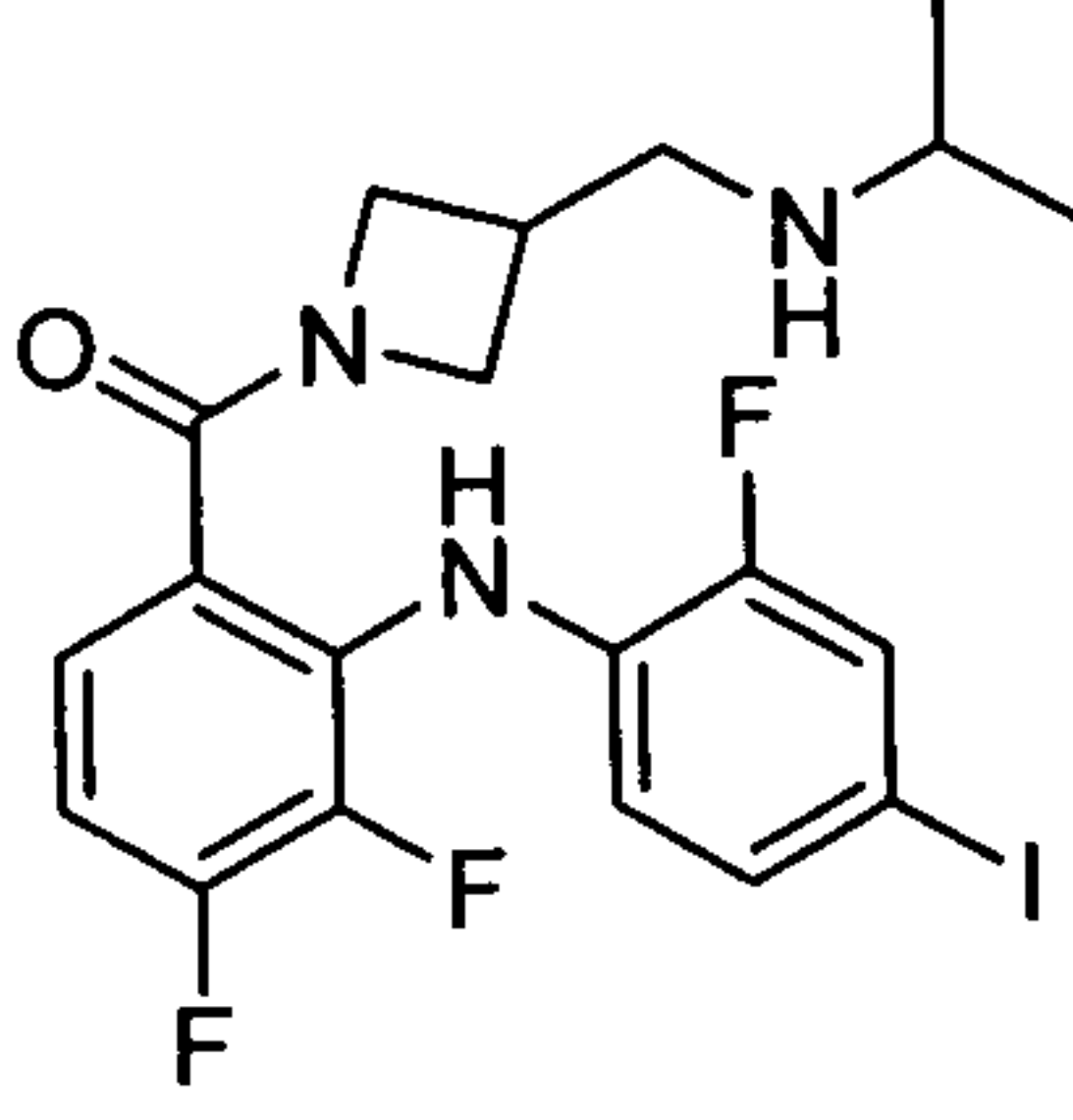
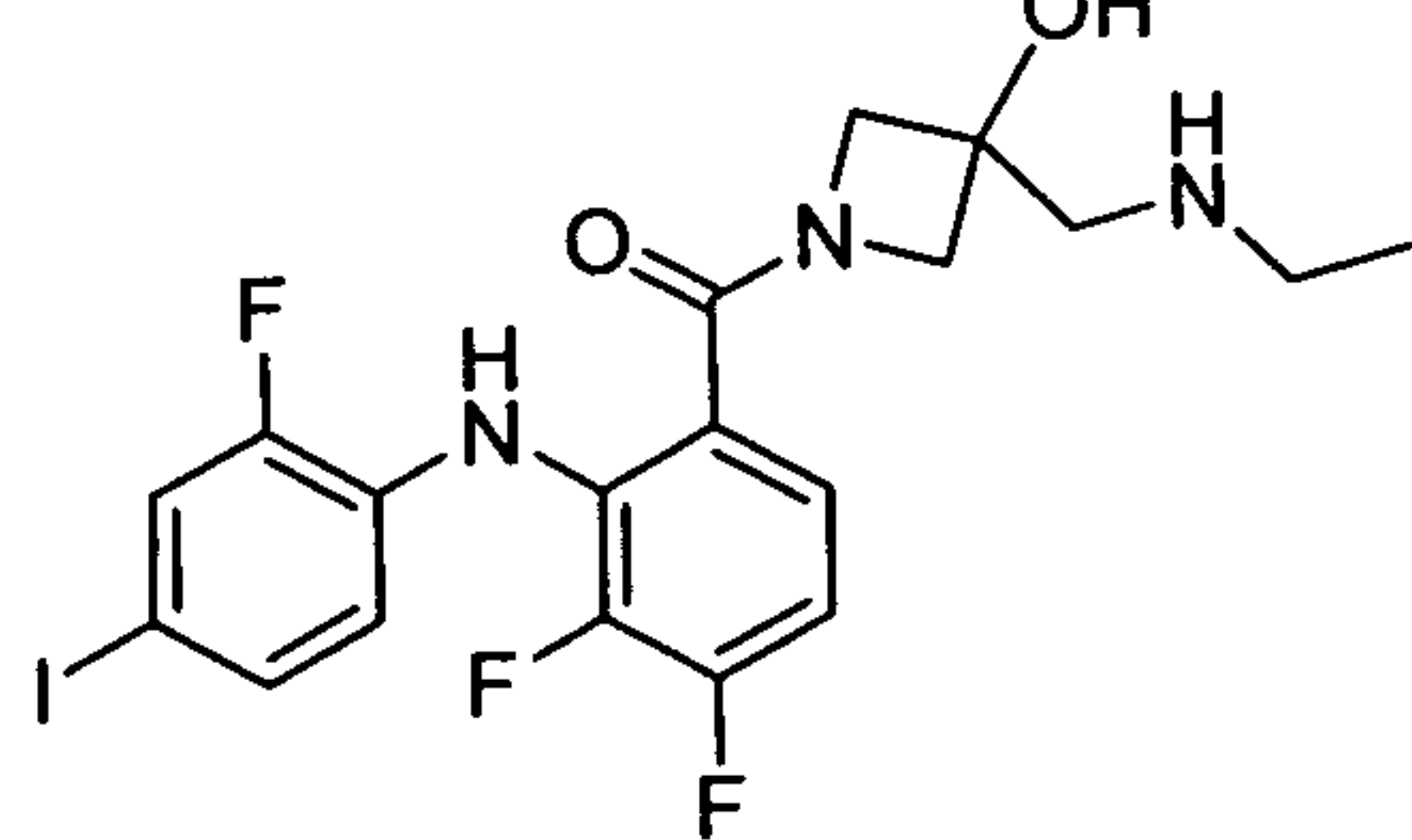
Cmpd No.	Structure	Name
82		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidine-3-carboxamide
83		6-{{3-(aminomethyl)-3-(methoxy)azetidin-1-yl}carbonyl}-2,3-difluoro-N-(2-fluoro-4-iodophenyl)aniline
84		N-{{1-([3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl]carbonyl)-3-hydroxyazetidin-3-yl}methyl}acetamide
85		2,3-difluoro-N-(2-fluoro-4-iodophenyl)-6-{{3-[[1-(1-methylethyl)amino]methyl]azetidin-1-yl}carbonyl}aniline
86		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(ethylamino)methyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

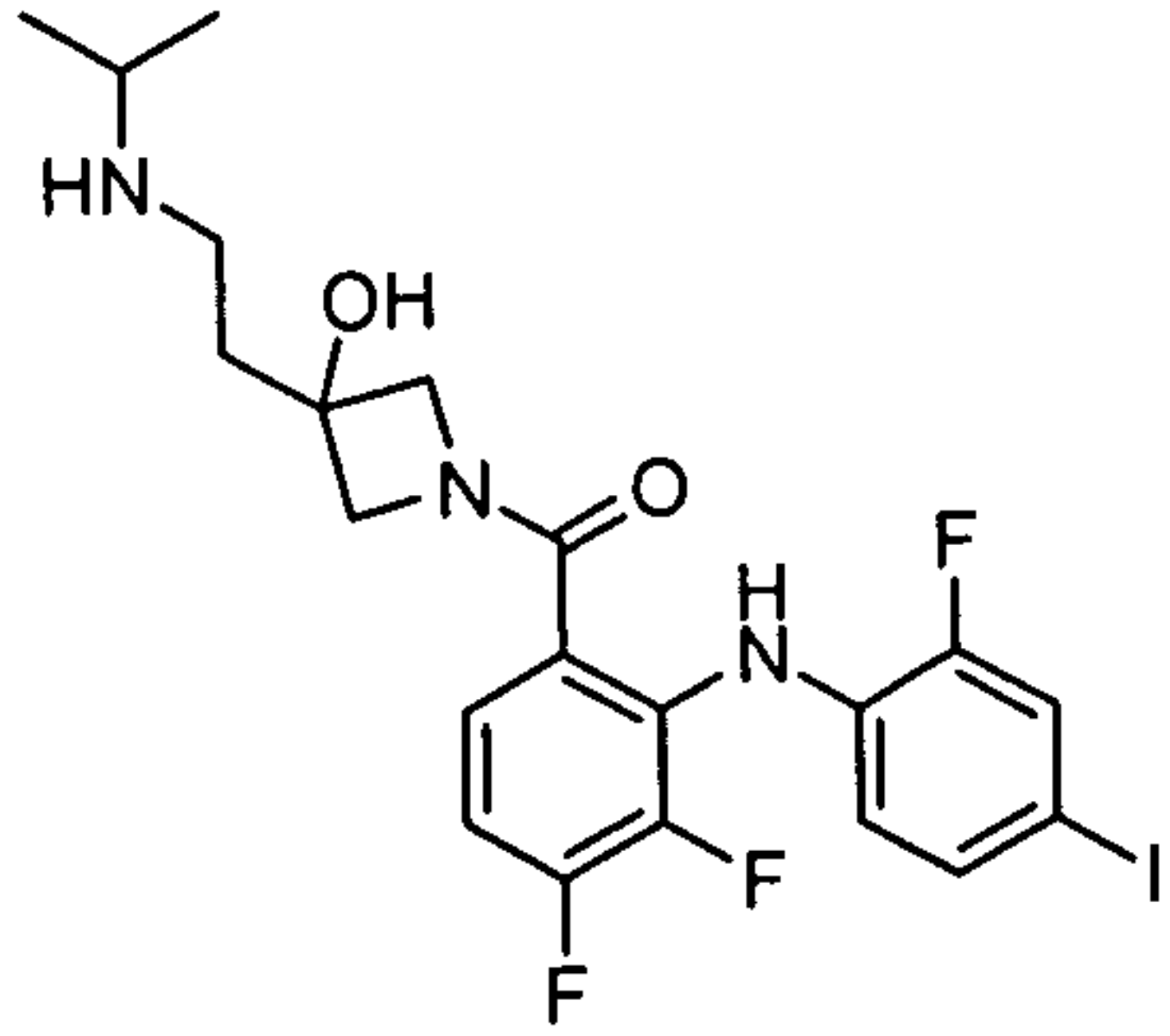
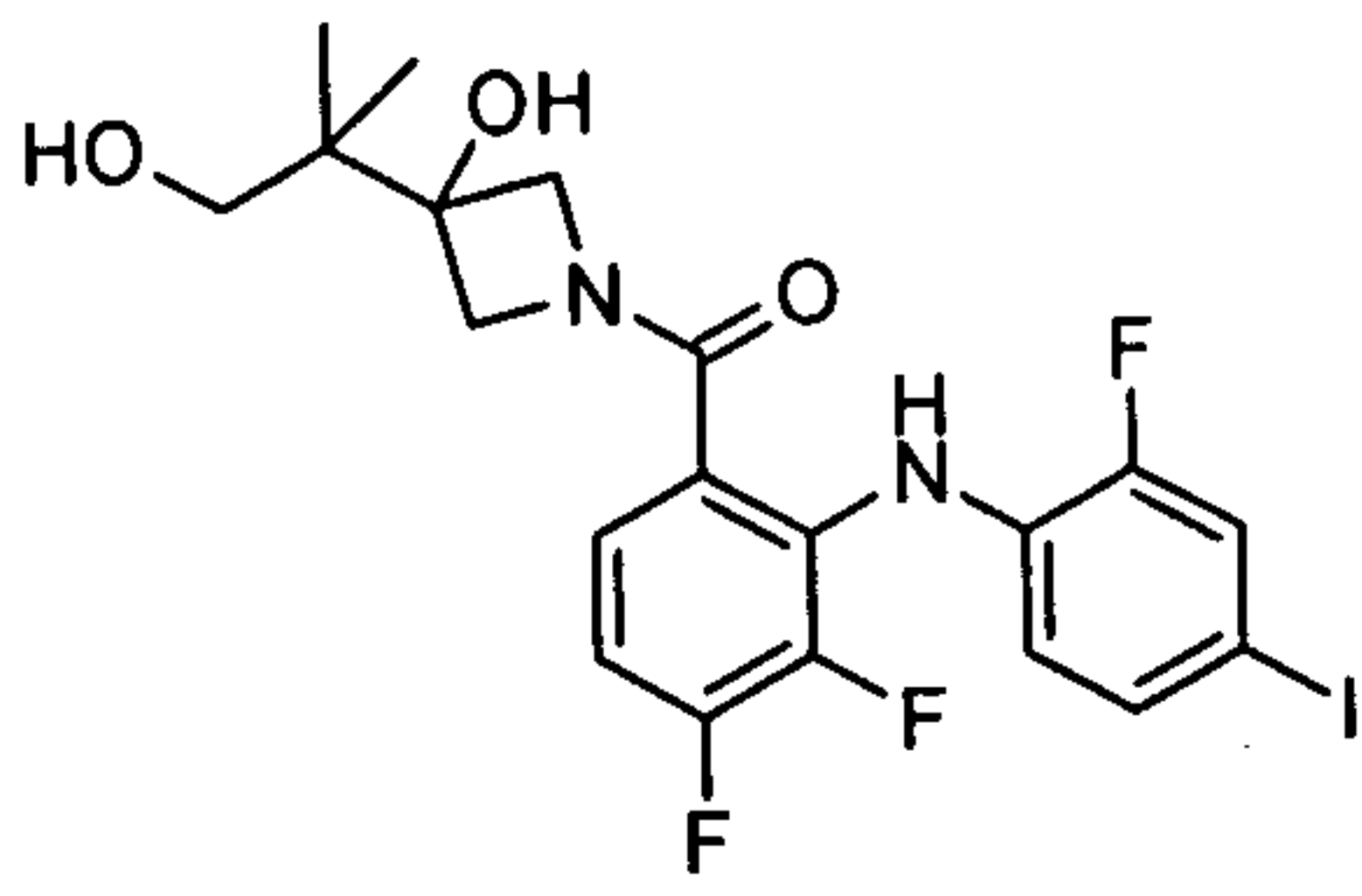
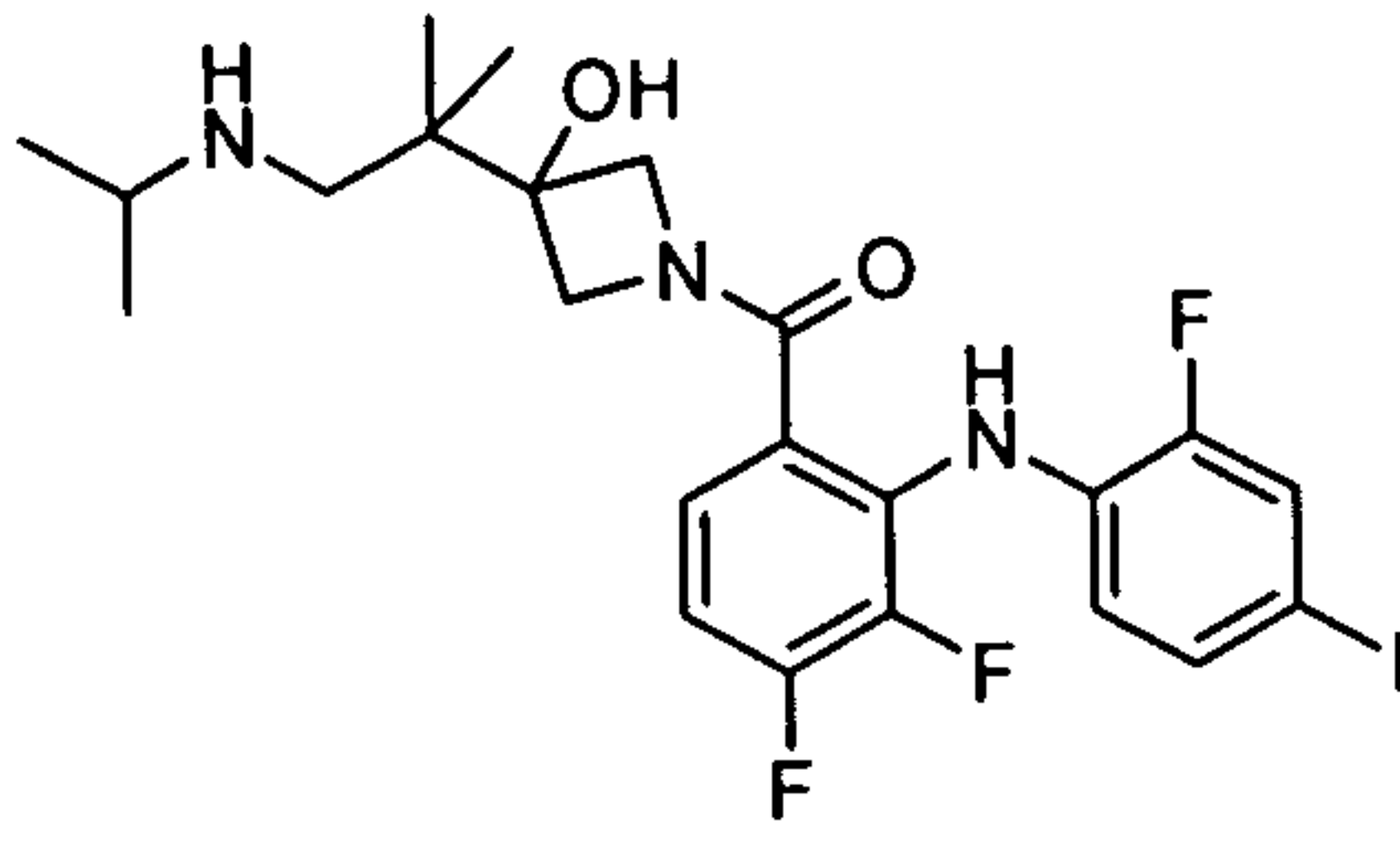
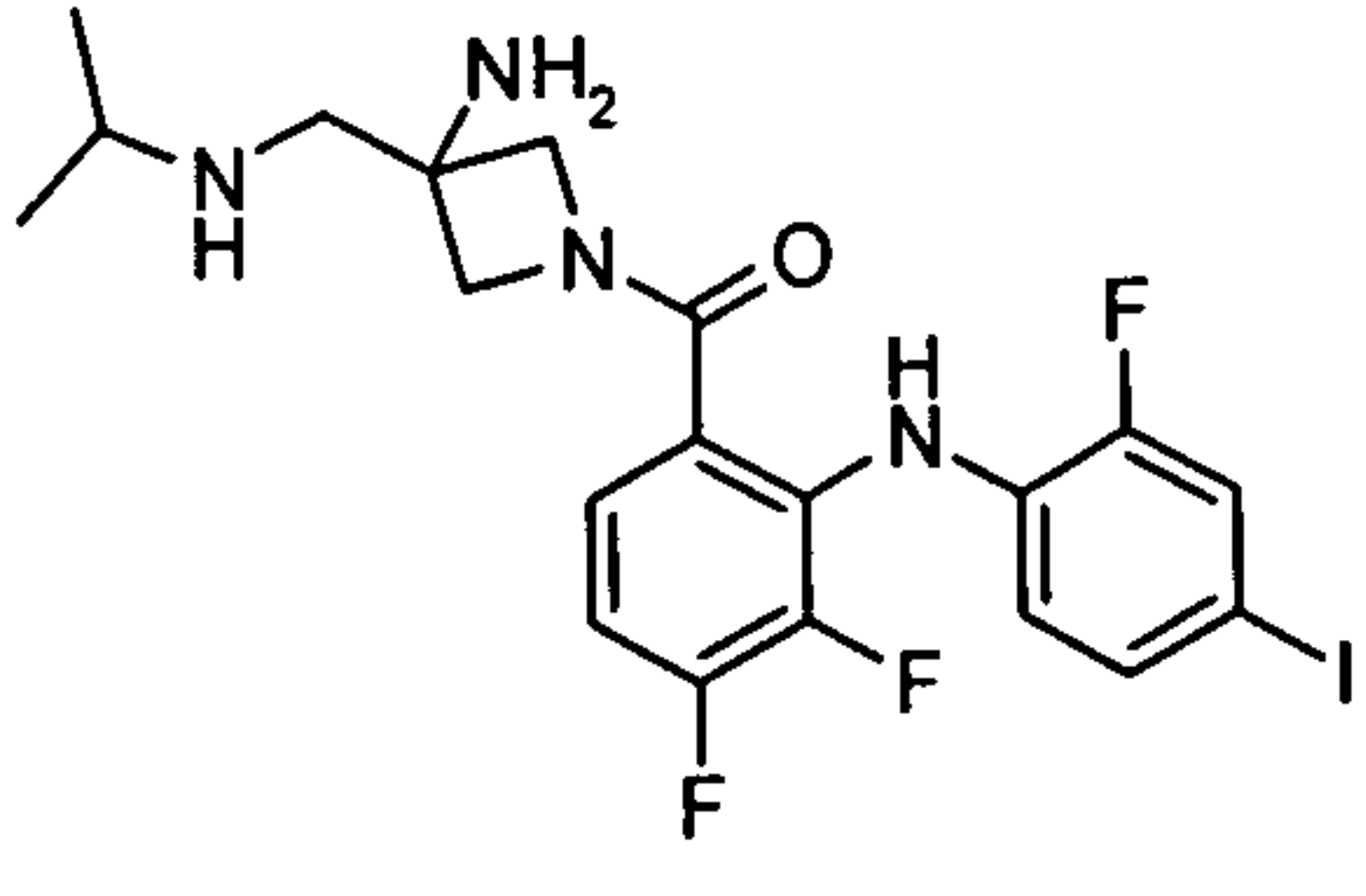
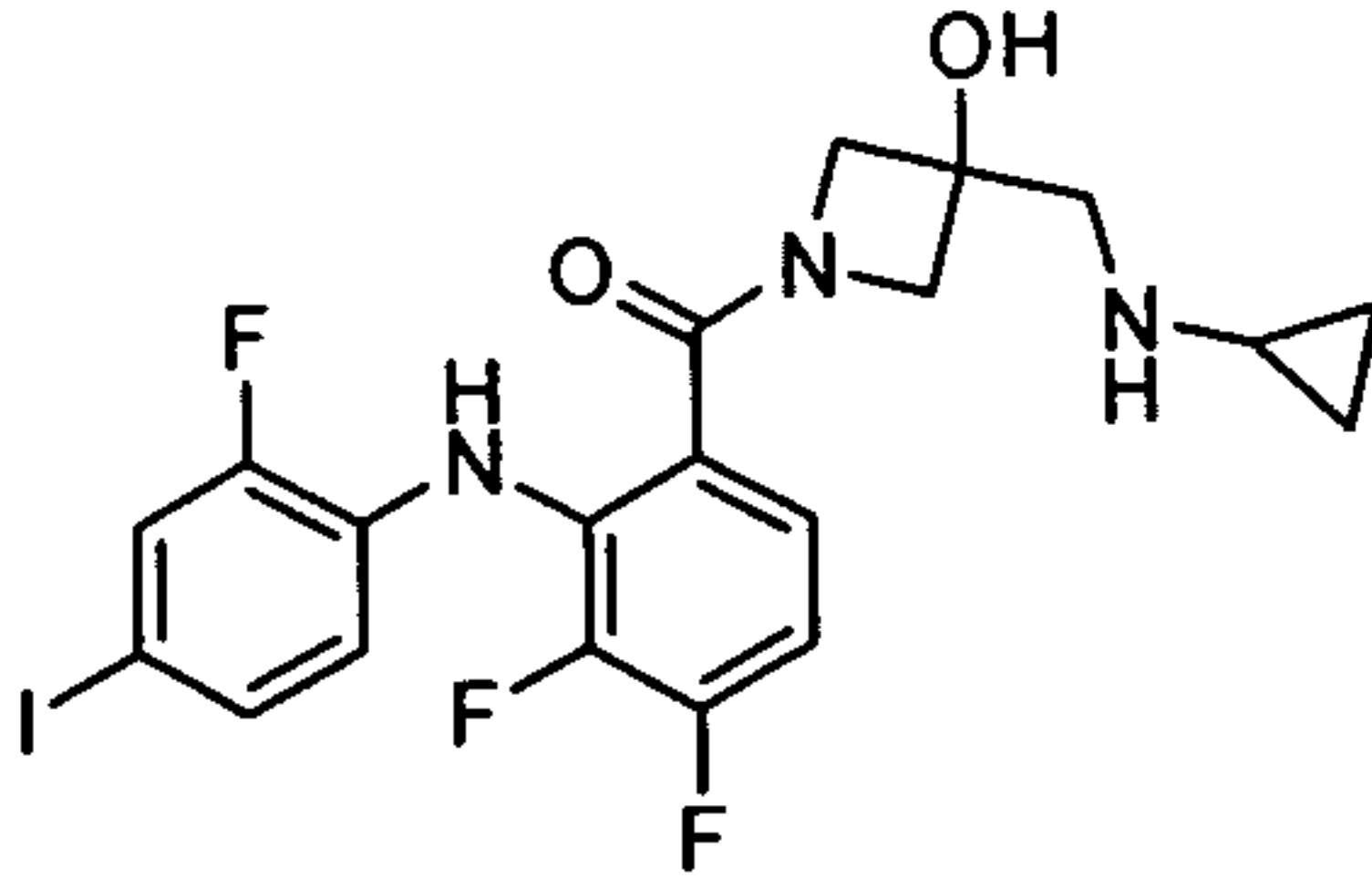
Cmpd No.	Structure	Name
87		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{2-[(1-methylethyl)amino]ethyl}azetidin-3-ol
88		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(2-hydroxy-1,1-dimethylethyl)azetidin-3-ol
89		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1,1-dimethyl-2-[(1-methylethyl)amino]ethyl}azetidin-3-ol
90		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[1-methylethyl)amino]methyl}azetidin-3-amine
91		3-[(cyclopropylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

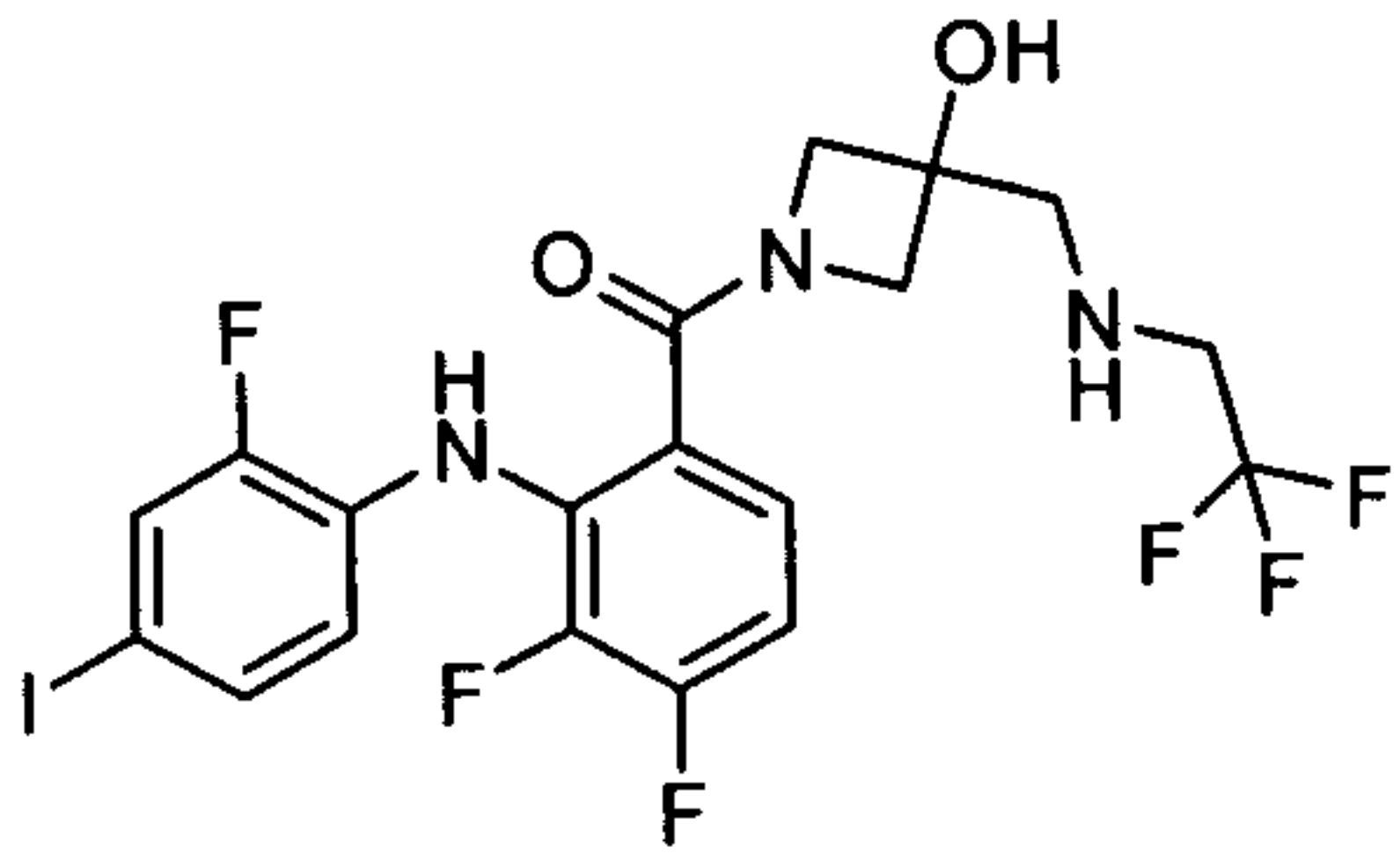
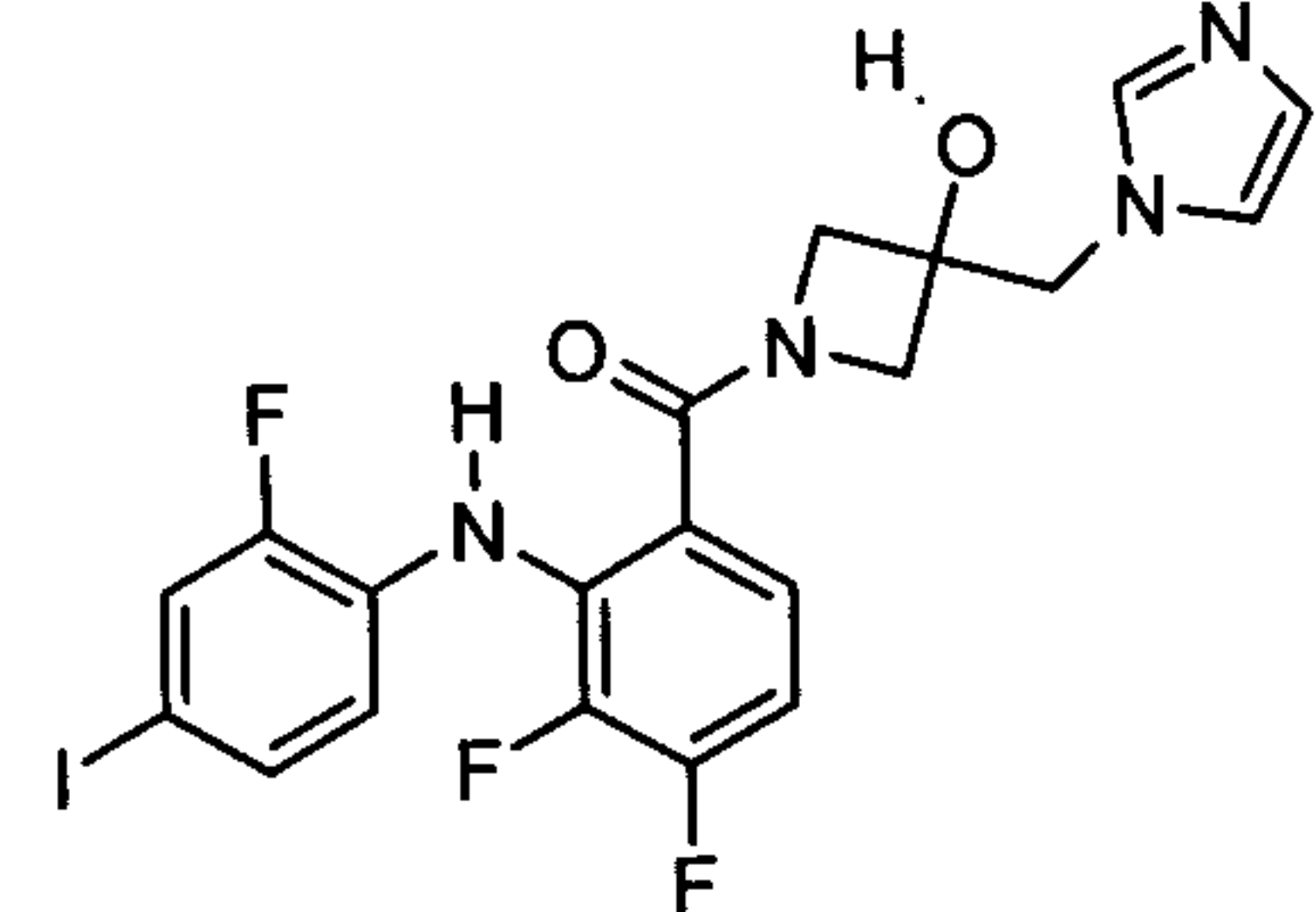
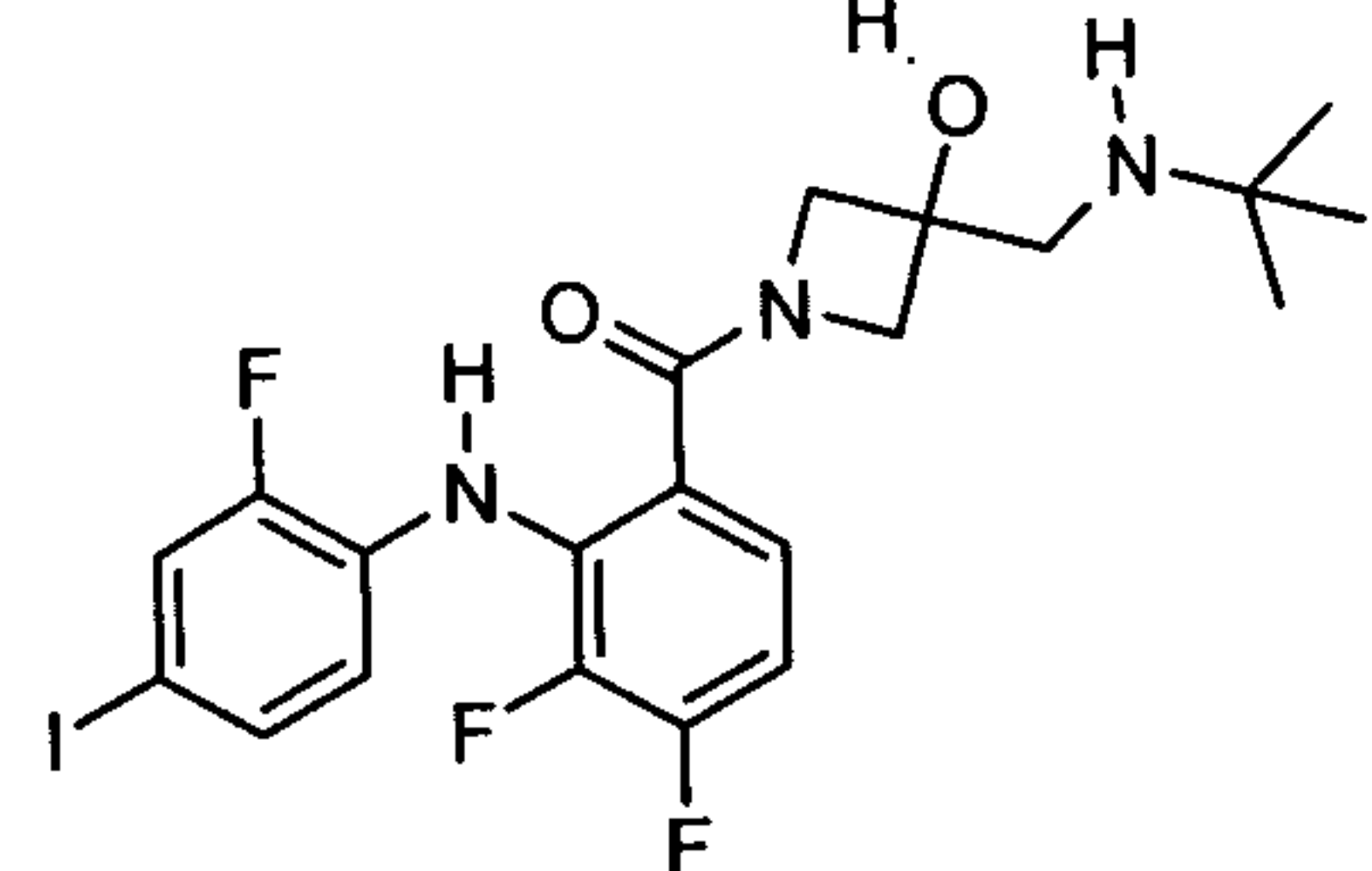
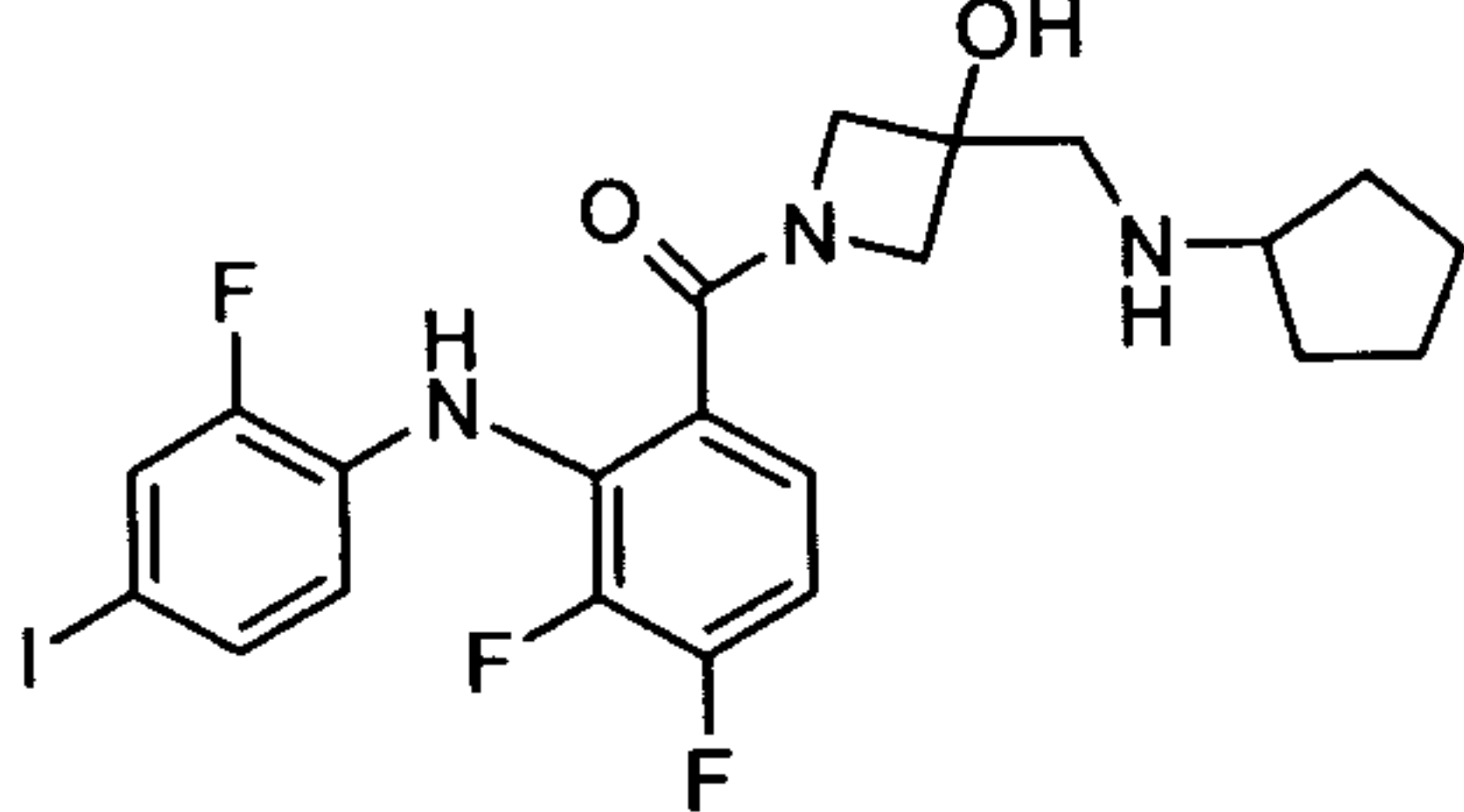
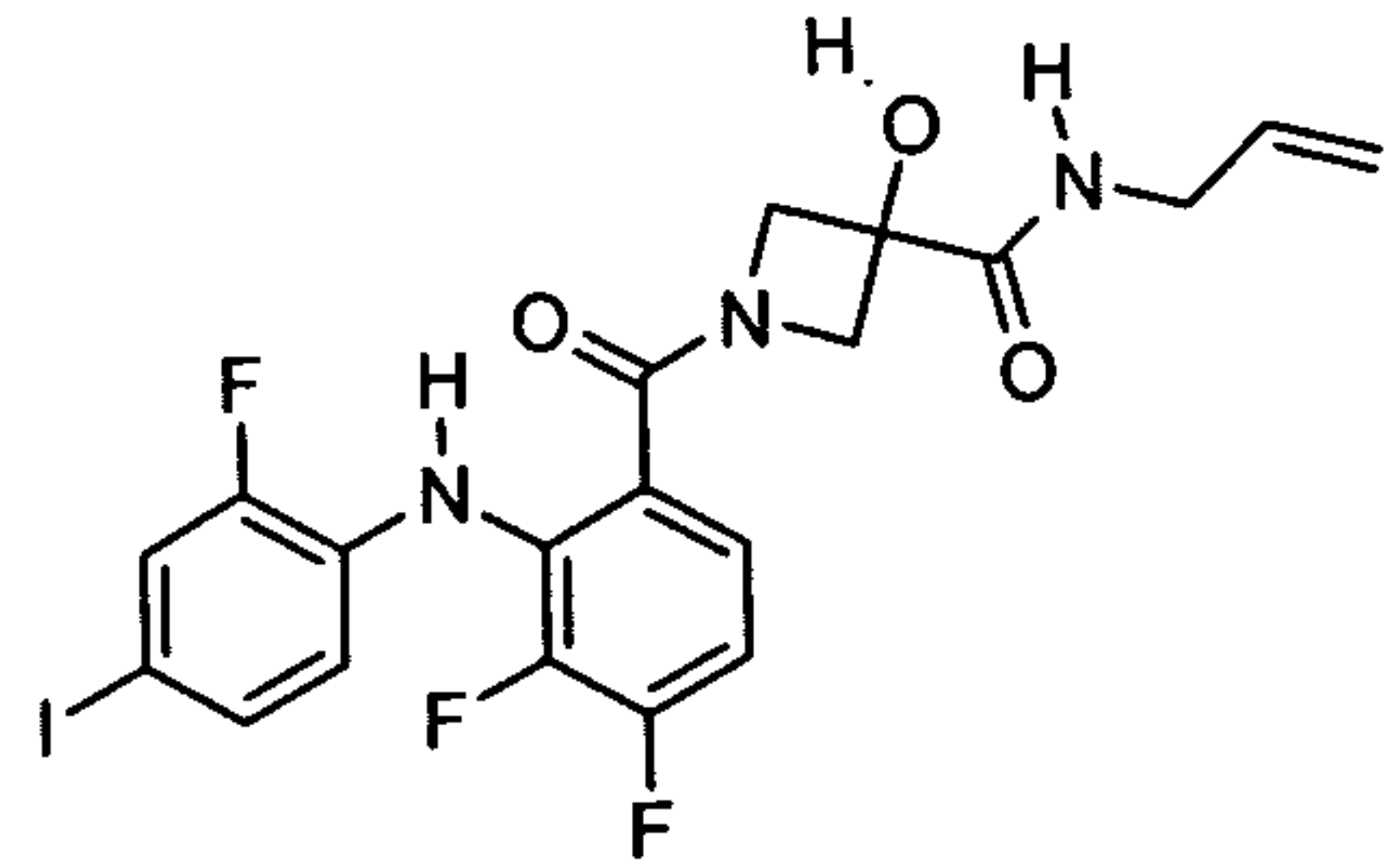
Cmpd No.	Structure	Name
92		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(2,2,2-trifluoroethyl)amino}methyl}azetidin-3-ol
93		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1H-imidazol-1-ylmethyl)azetidin-3-ol
94		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(1,1-dimethylethyl)amino}methyl}azetidin-3-ol
95		3-[(cyclopentylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
96		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxy-N-prop-2-en-1-ylazetidine-3-carboxamide

Table 1. Representative MEK Inhibitors

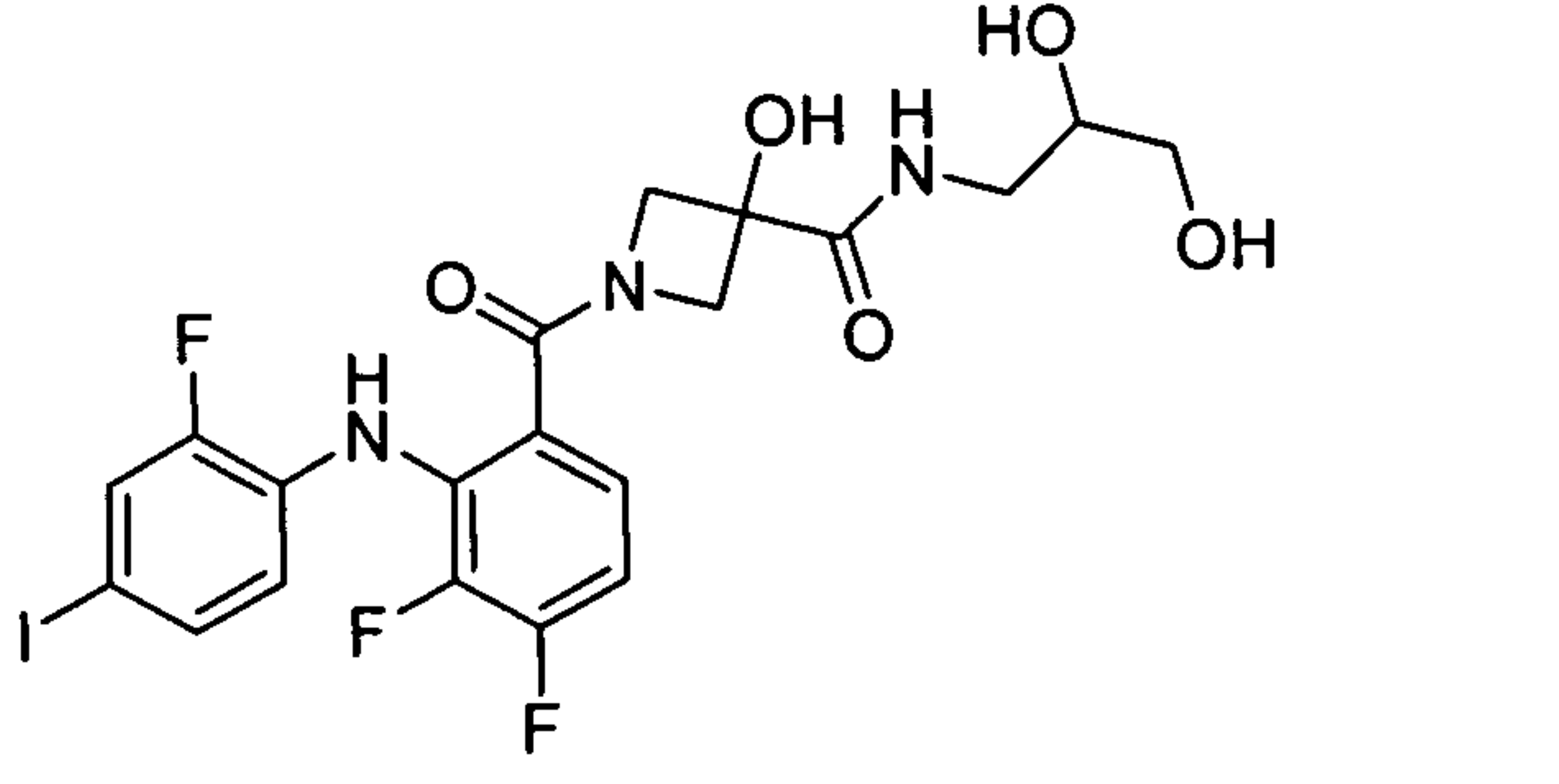
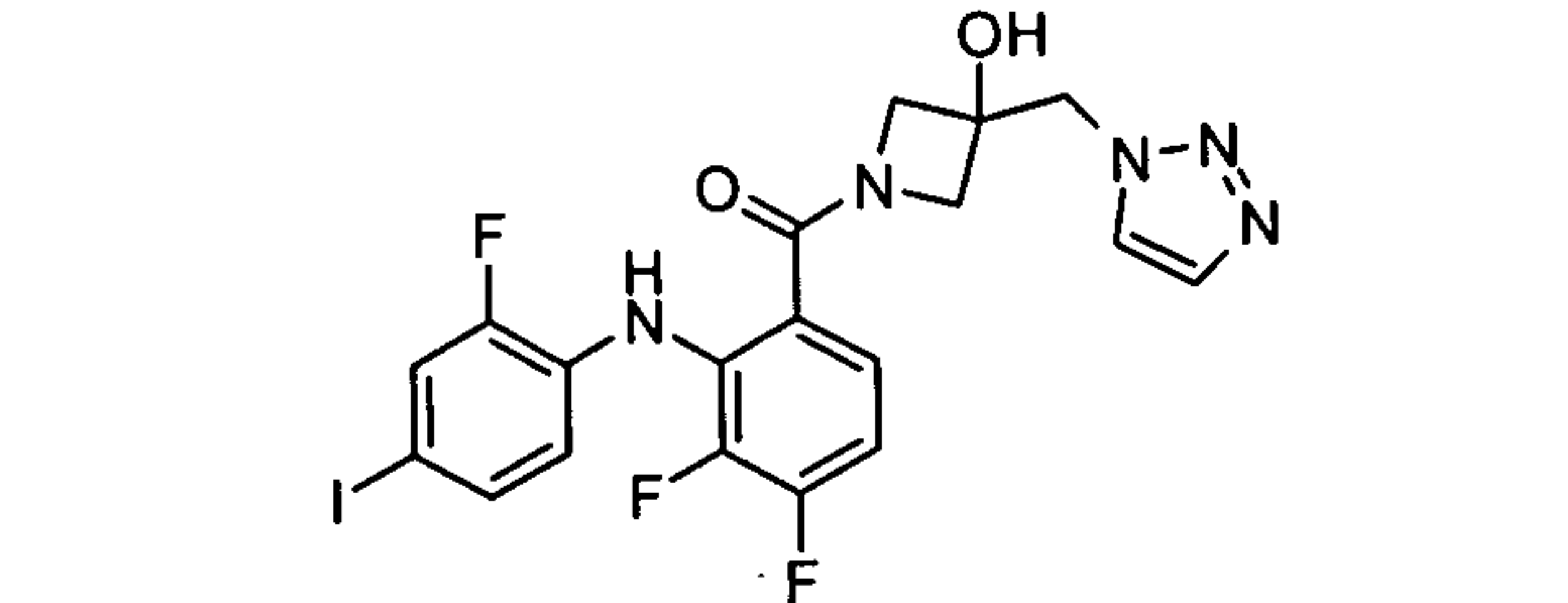
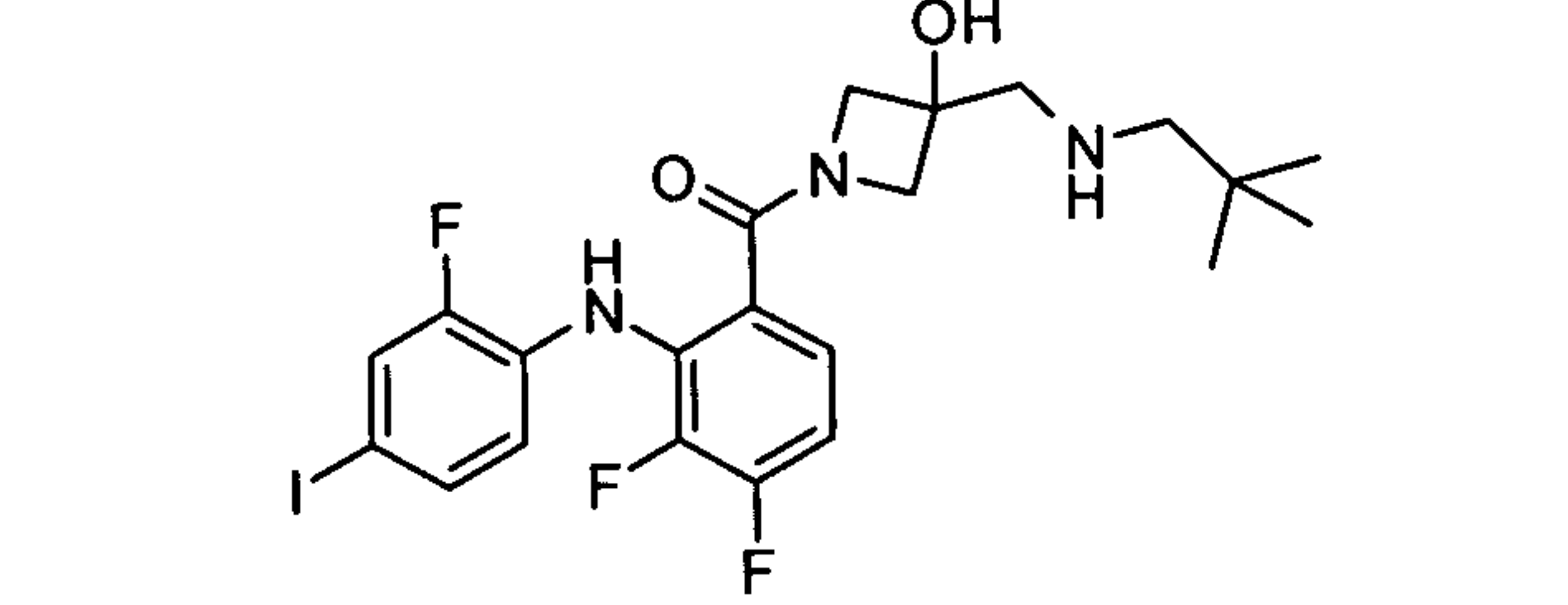
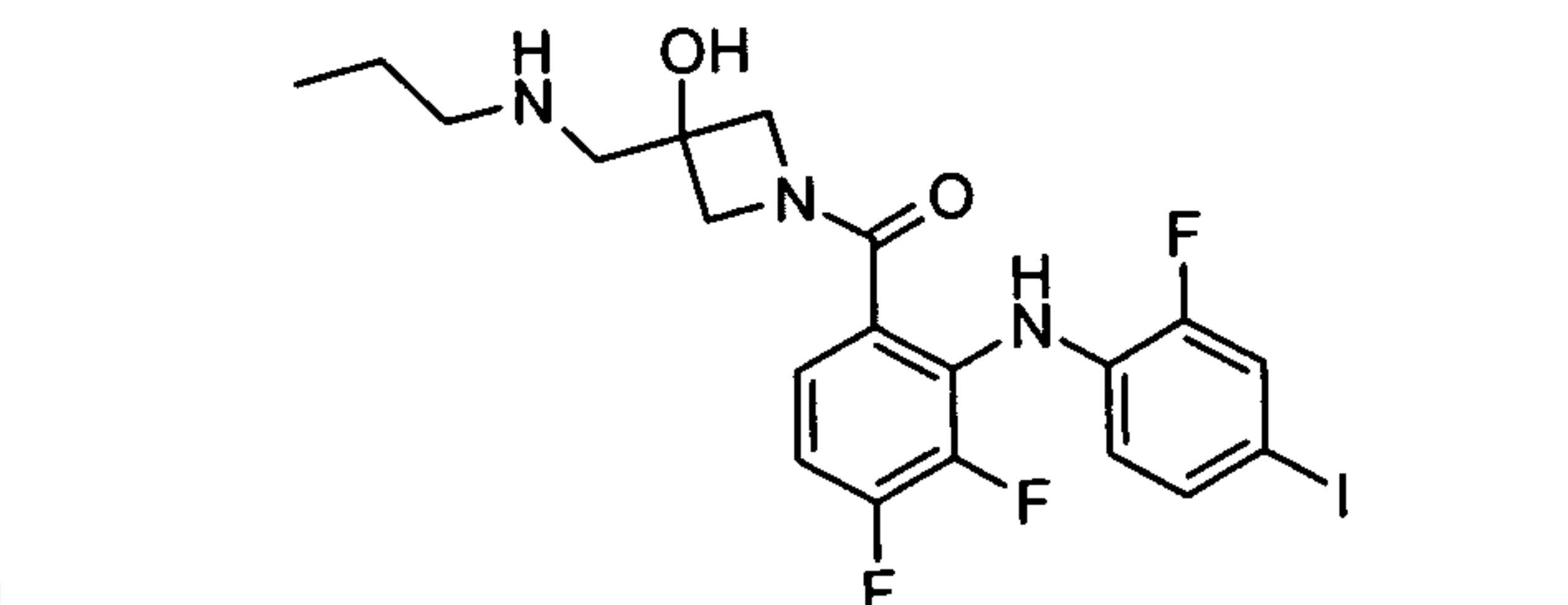
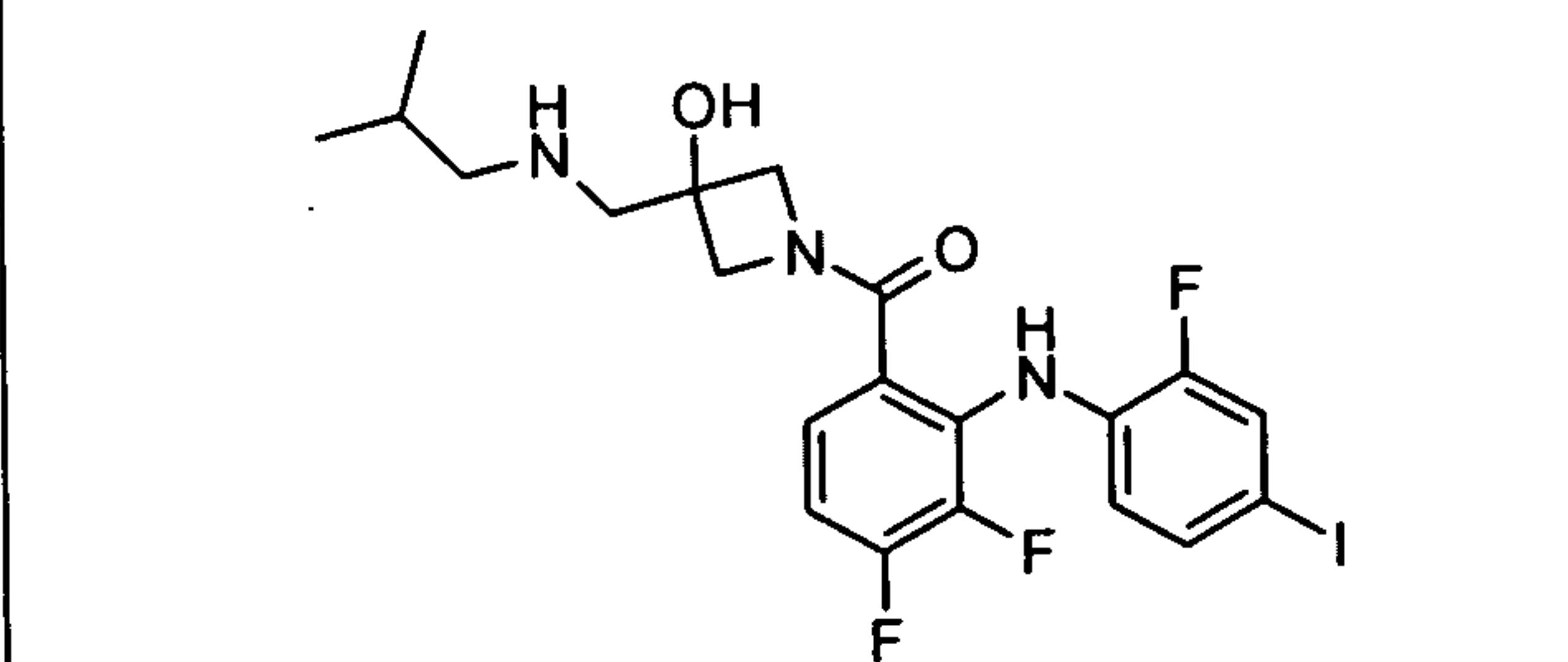
Cmpd No.	Structure	Name
97		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-N-(2,3-dihydroxypropyl)-3-hydroxyazetidine-3-carboxamide
98		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1H-1,2,3-triazol-1-ylmethyl)azetidin-3-ol
99		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2,2-dimethylpropyl)amino]methyl}azetidin-3-ol
100		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(propylamino)methyl]azetidin-3-ol
101		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-methylpropyl)amino]methyl}azetidin-3-ol

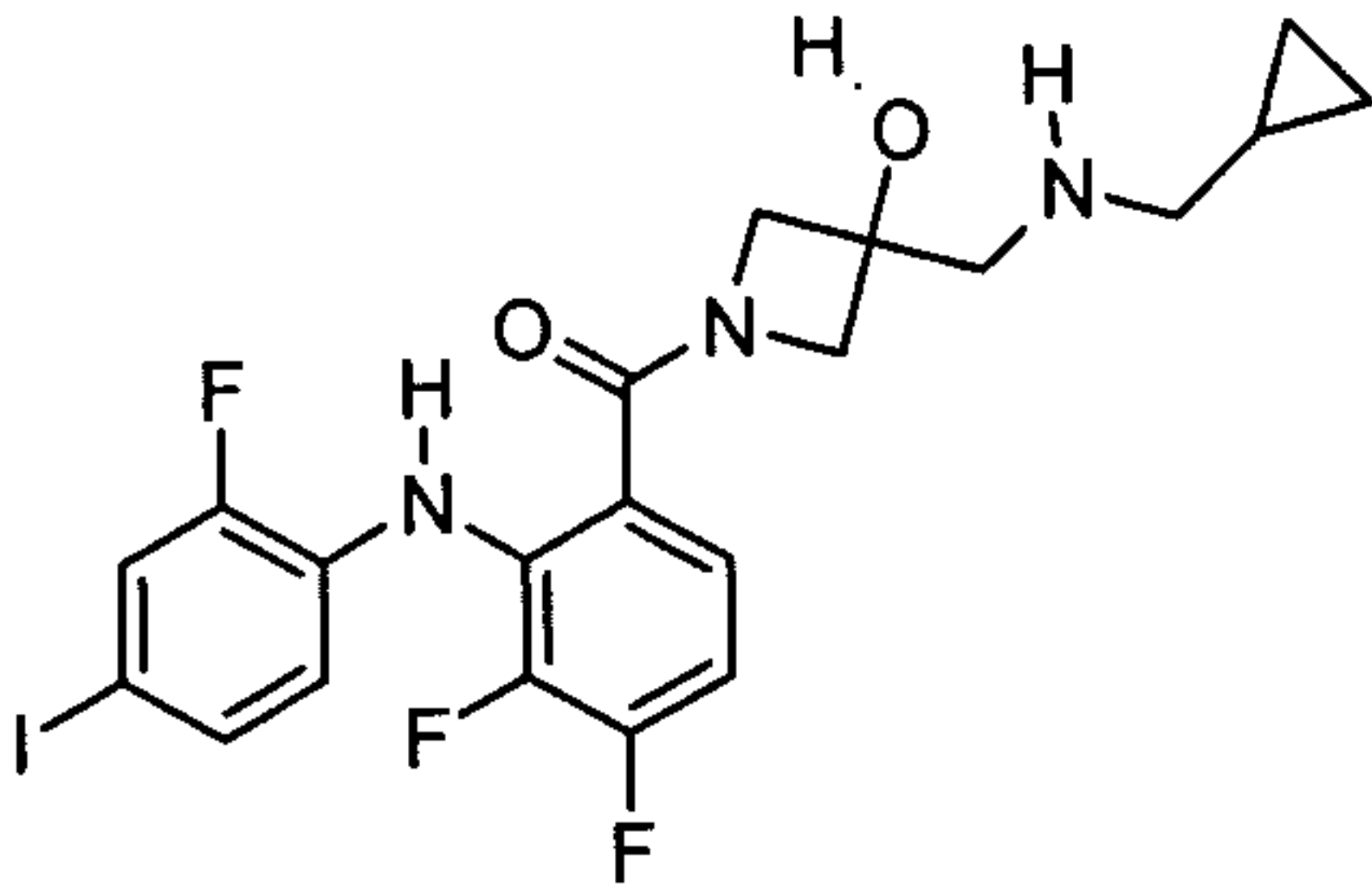
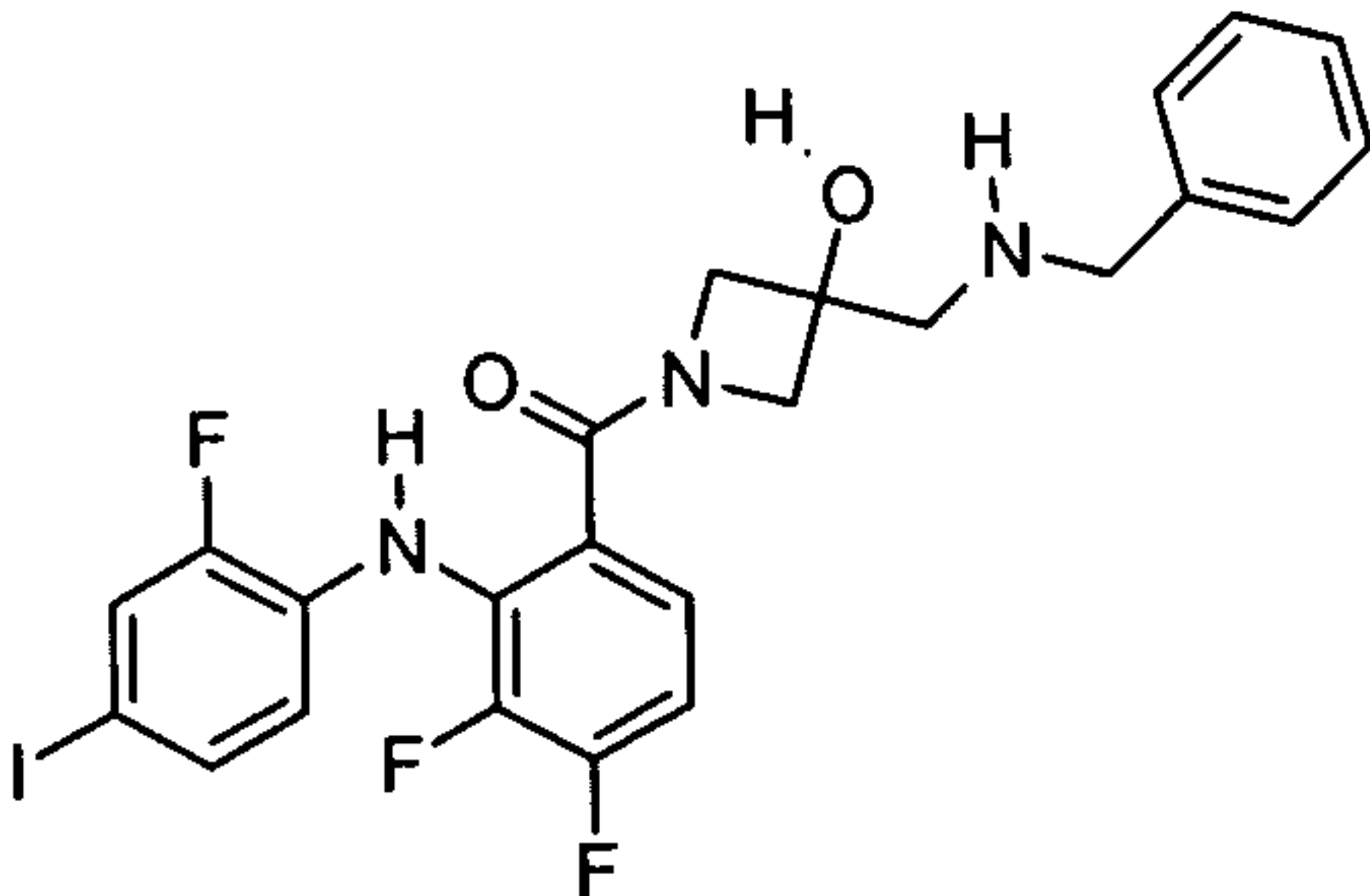
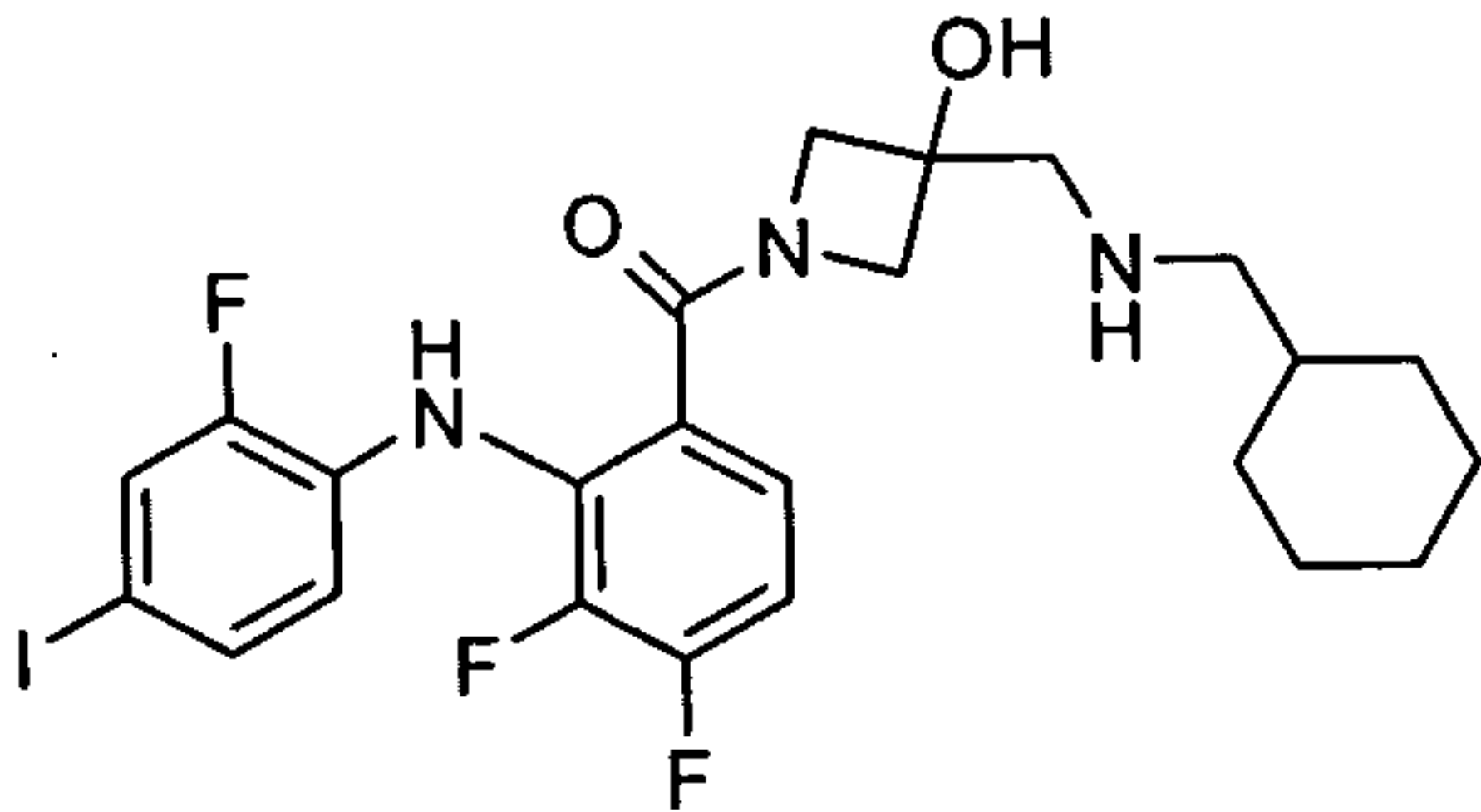
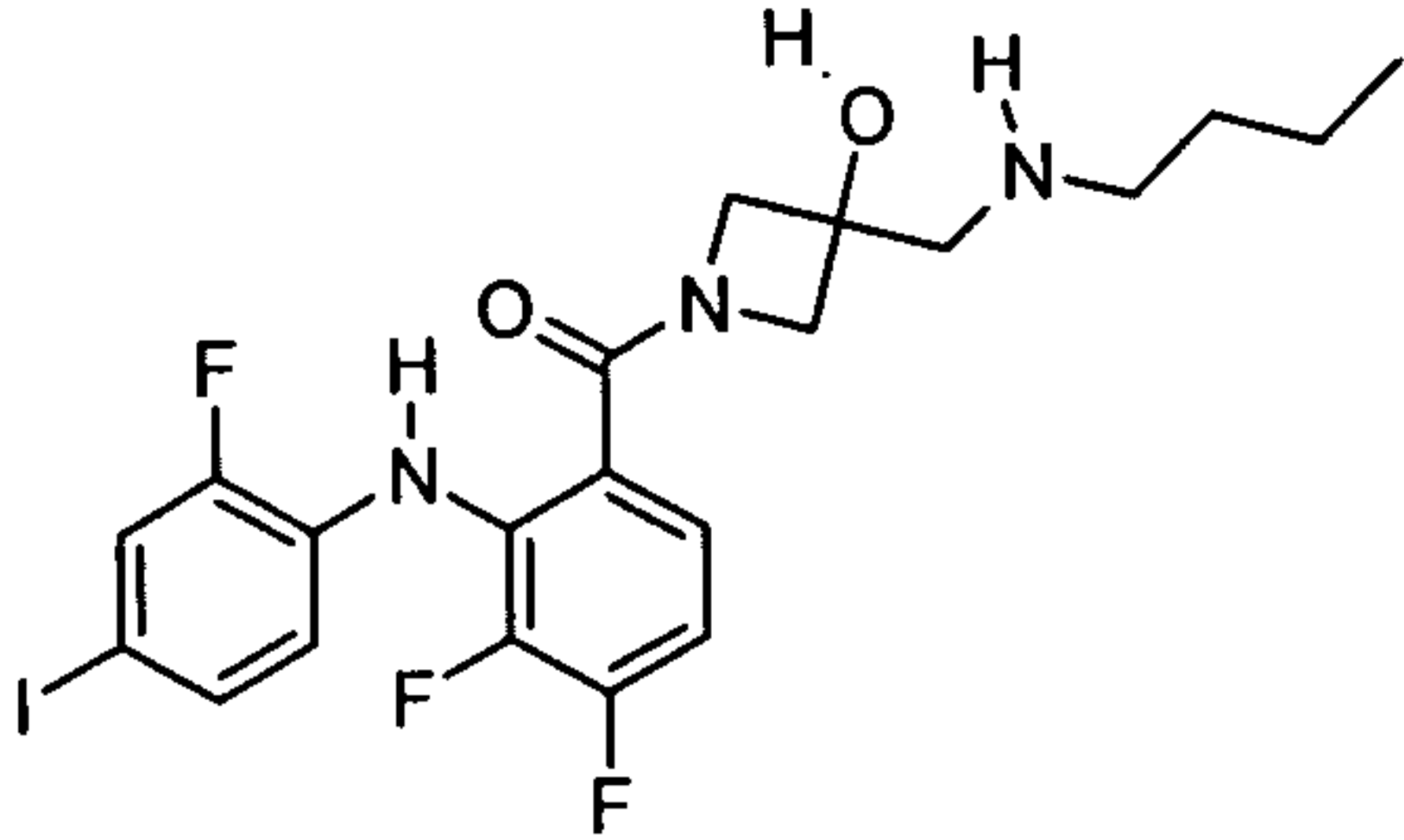
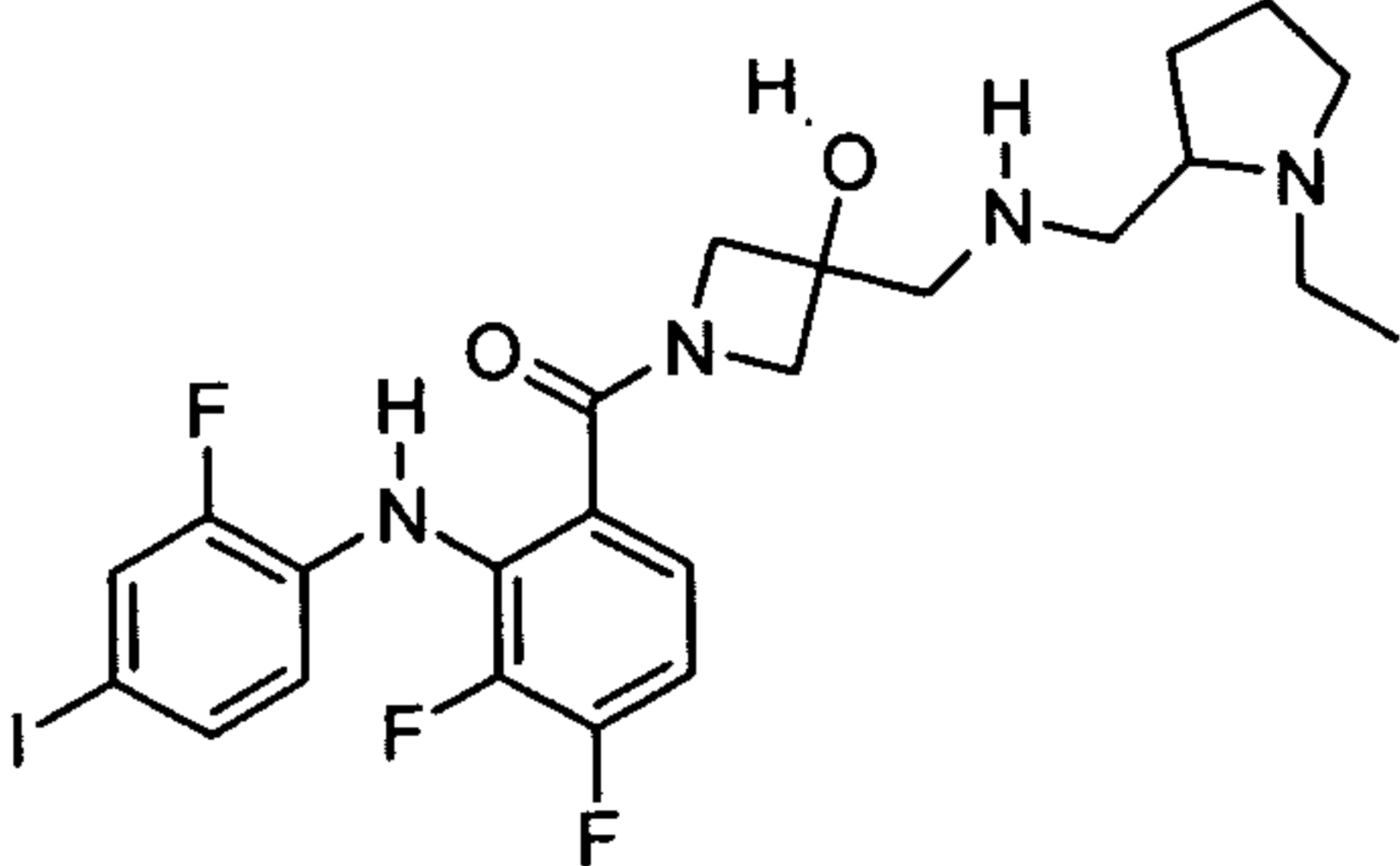
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
102		3-(((cyclopropylmethyl)amino)methyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol
103		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((phenylmethyl)amino)methyl)azetidin-3-ol
104		3-(((cyclohexylmethyl)amino)methyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol
105		3-((butylamino)methyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol
106		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1-ethylpyrrolidin-2-yl)methyl)amino)methyl)azetidin-3-ol

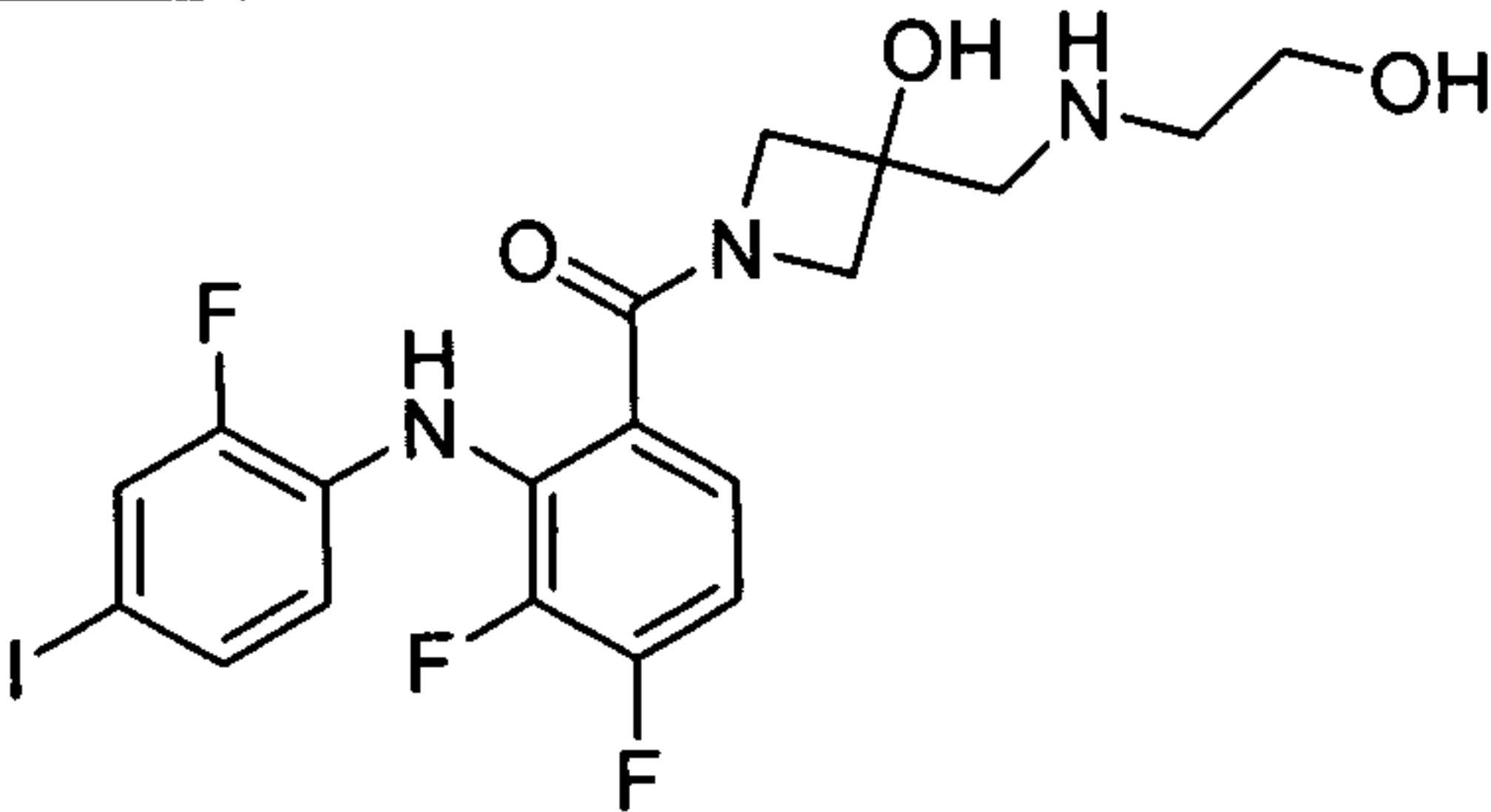
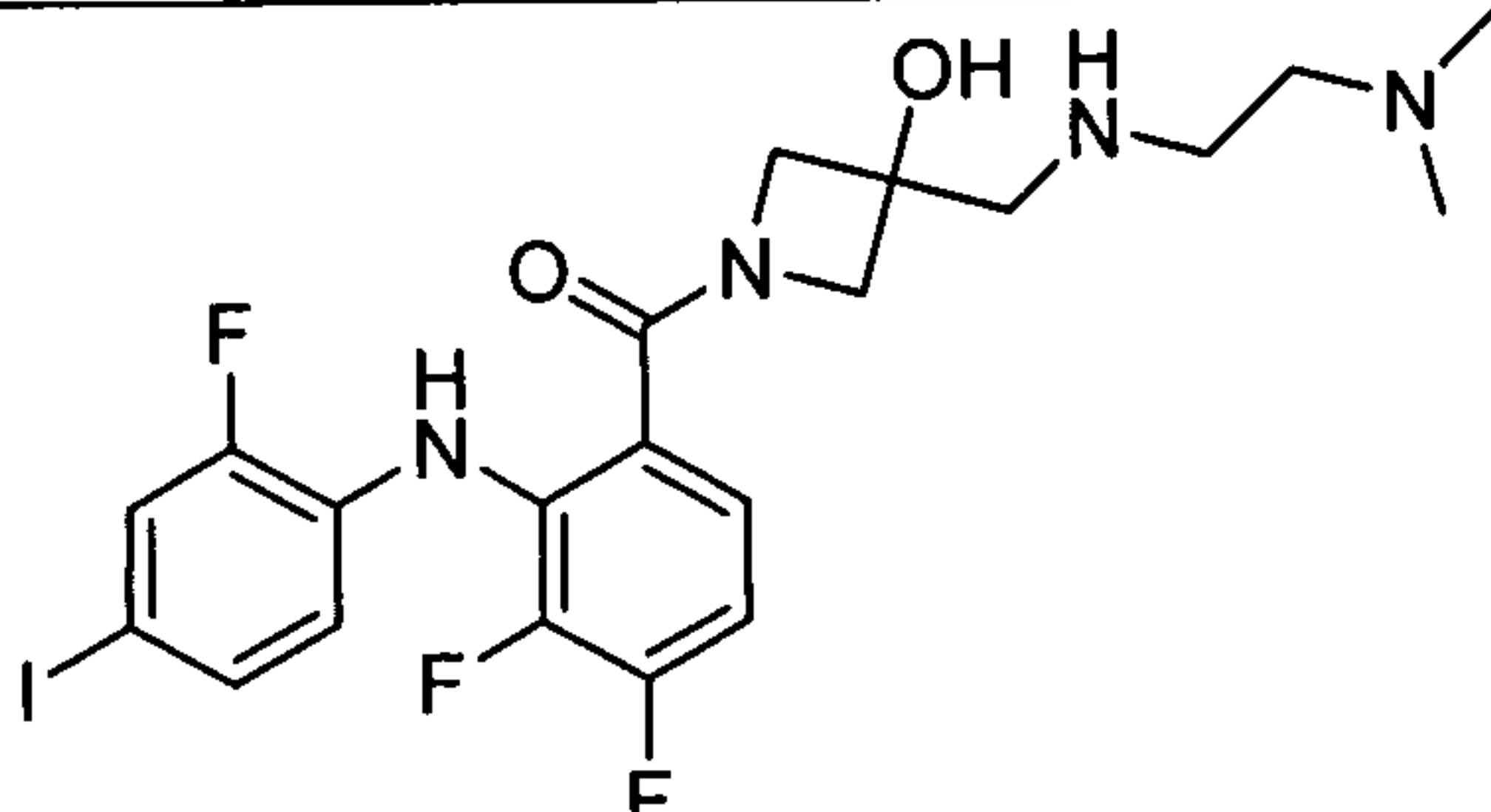
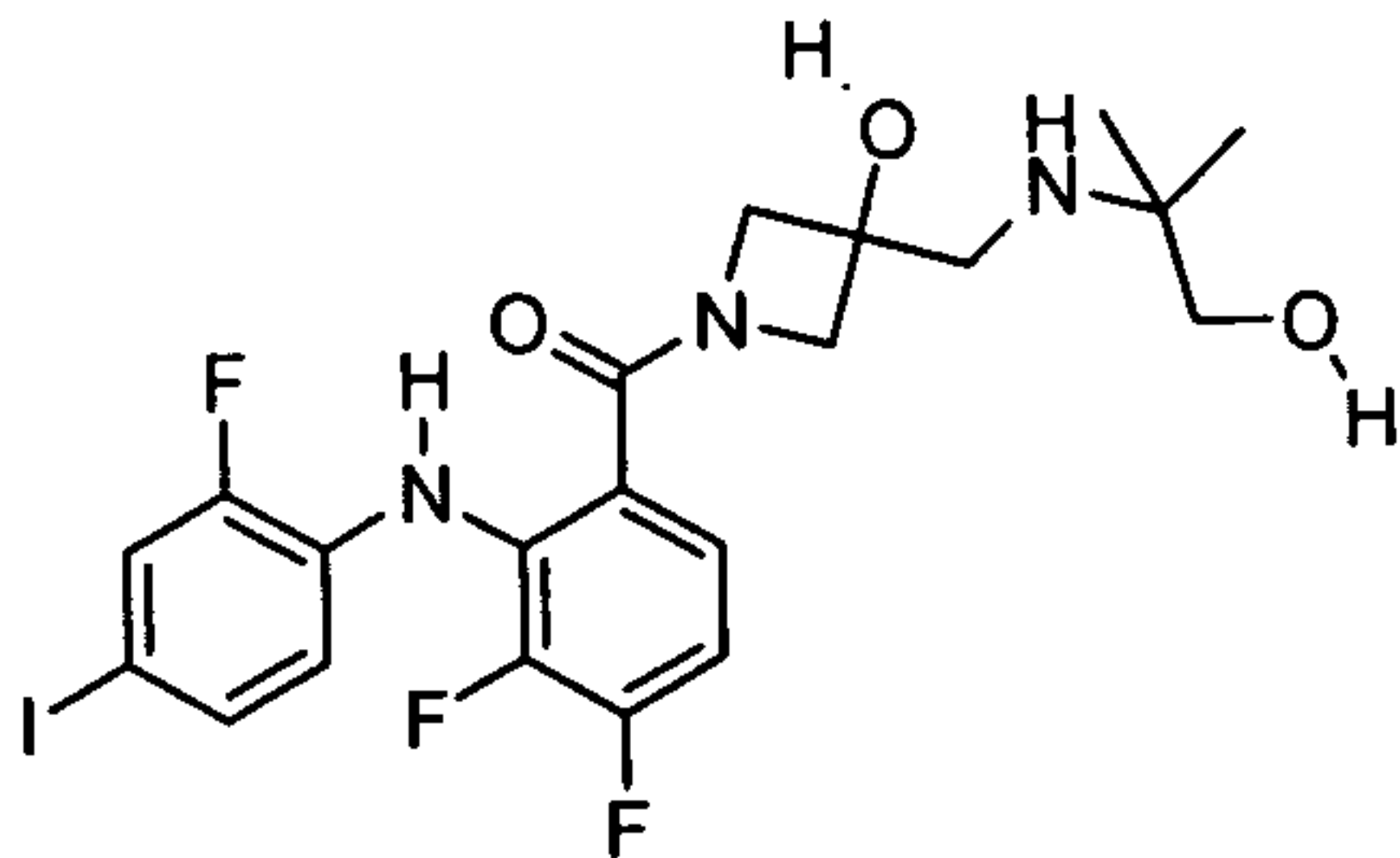
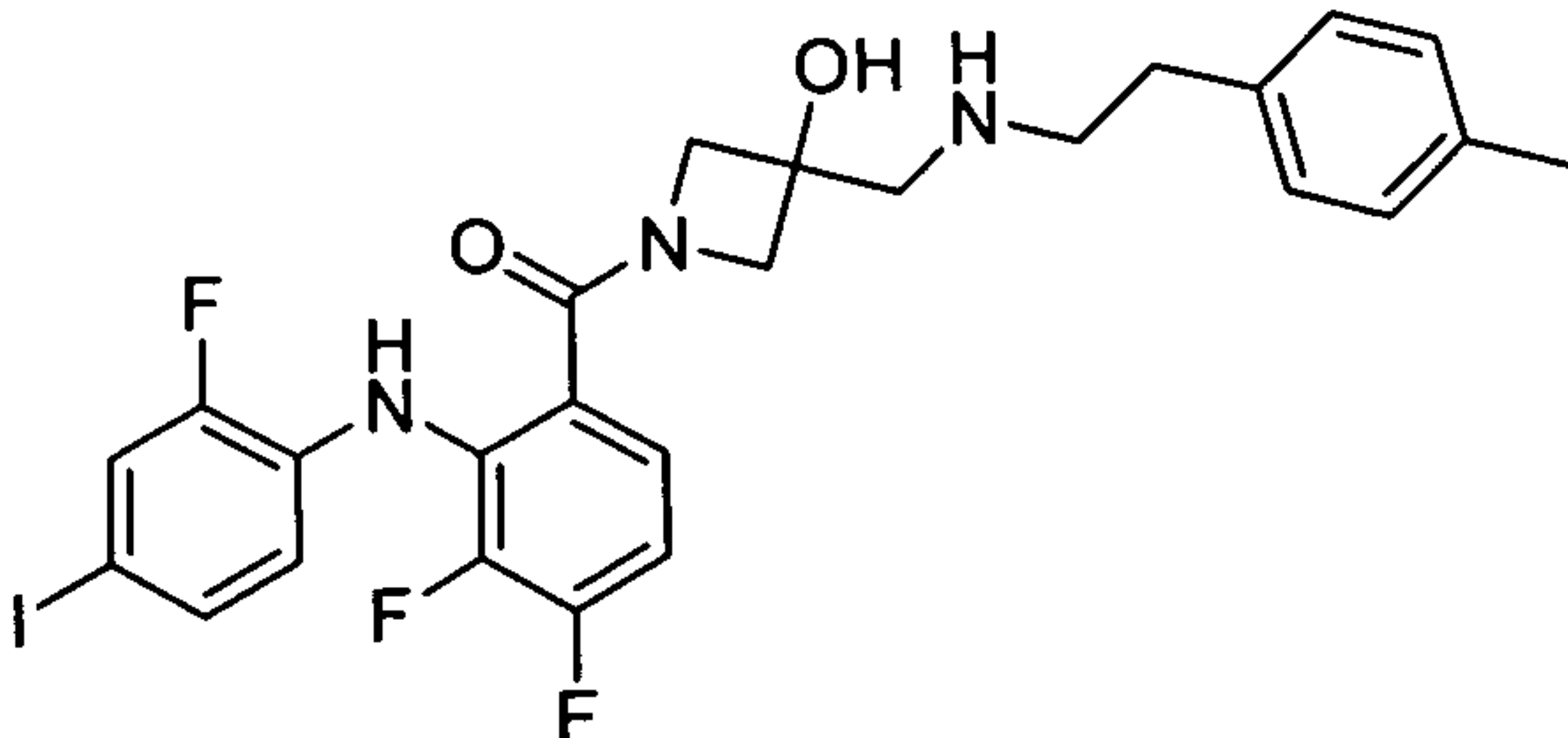
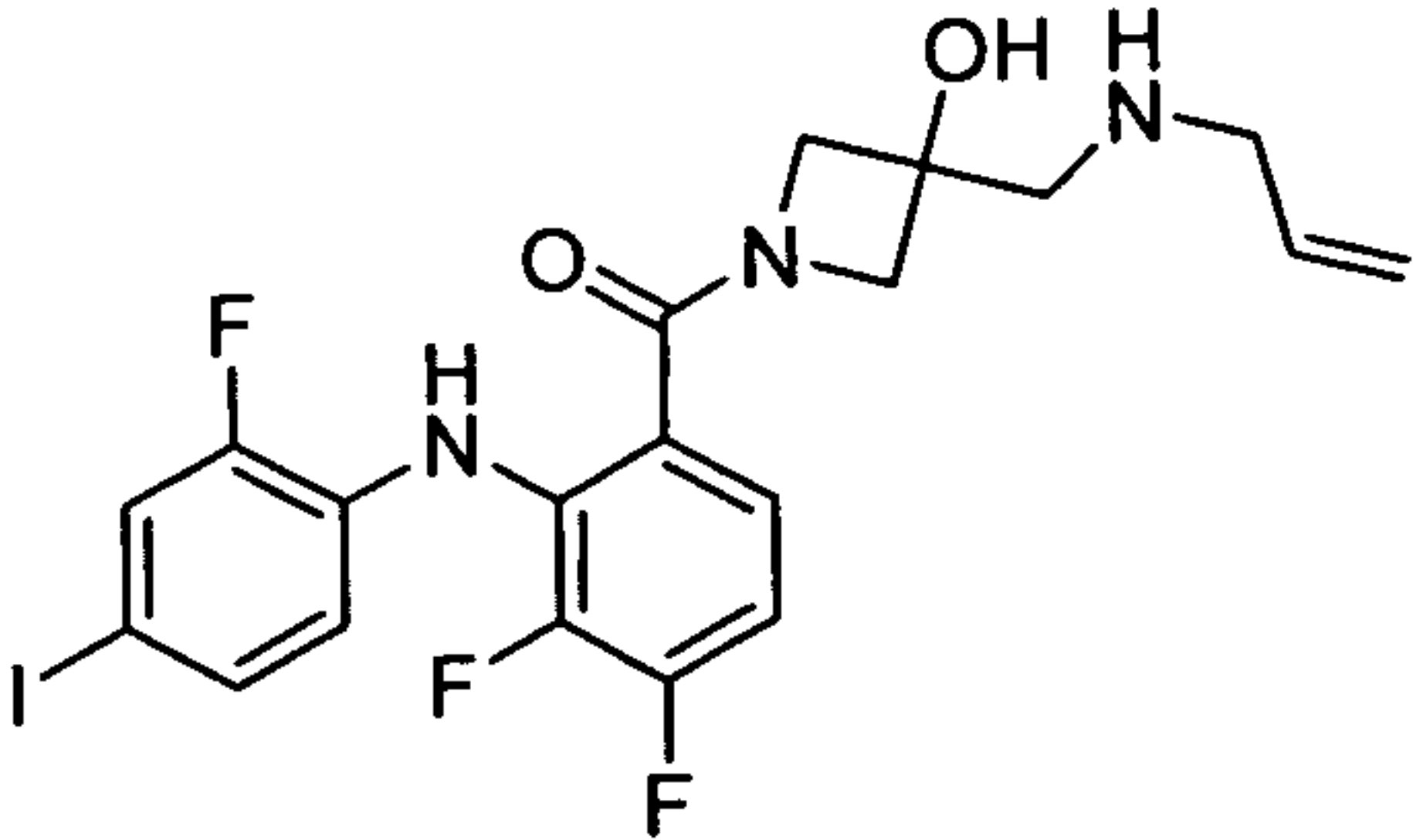
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
107		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[2-(hydroxyethyl)amino]methyl}azetidin-3-ol
108		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)ethyl]amino}methyl)azetidin-3-ol
109		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[2-(hydroxy-1,1-dimethylethyl)amino]methyl}azetidin-3-ol
110		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(4-methylphenyl)ethyl]amino}methyl)azetidin-3-ol
111		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(prop-2-en-1-ylamino)methyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
112		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((2-(1-methylpyrrolidin-2-yl)ethyl)amino)methyl)azetidin-3-ol
113		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((2,3-dihydro-1H-inden-2-ylamino)methyl)azetidin-3-ol
114		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((tetrahydrofuran-2-ylmethyl)amino)methyl)azetidin-3-ol
115		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((2-(tetrahydro-2H-pyran-4-yl)ethyl)amino)methyl)azetidin-3-ol
116		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1S,2S)-2-hydroxycyclopentyl)amino)methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

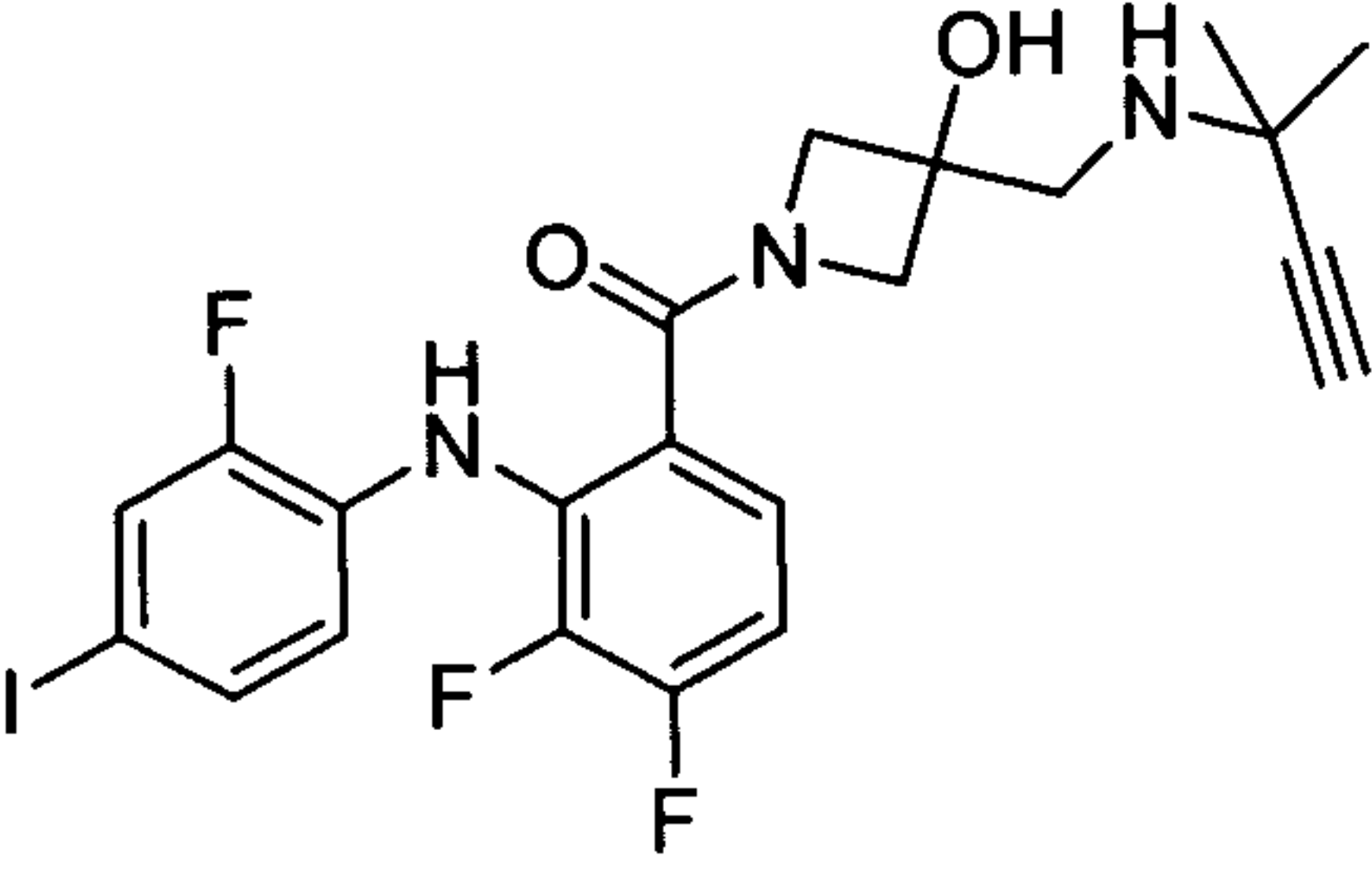
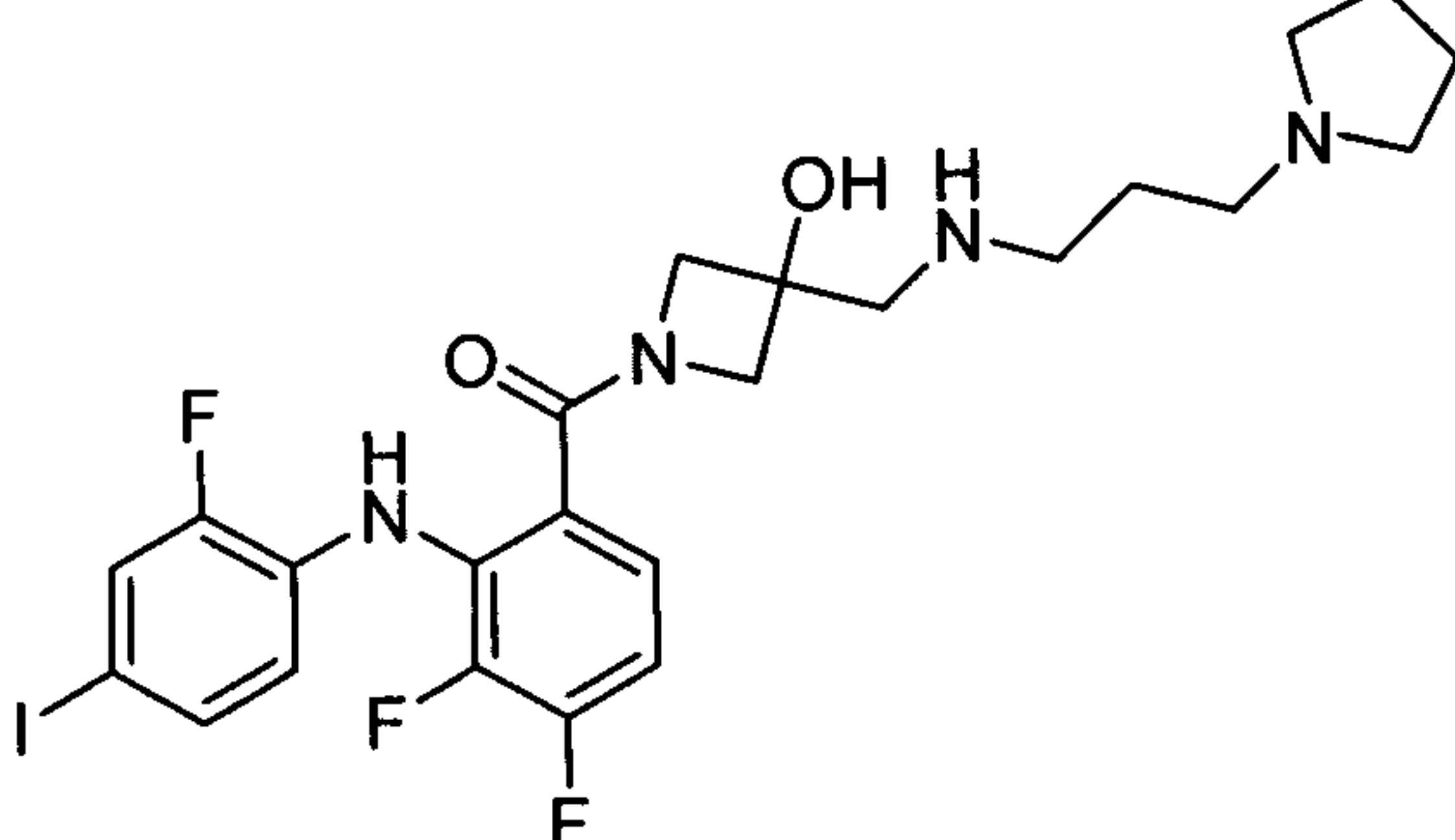
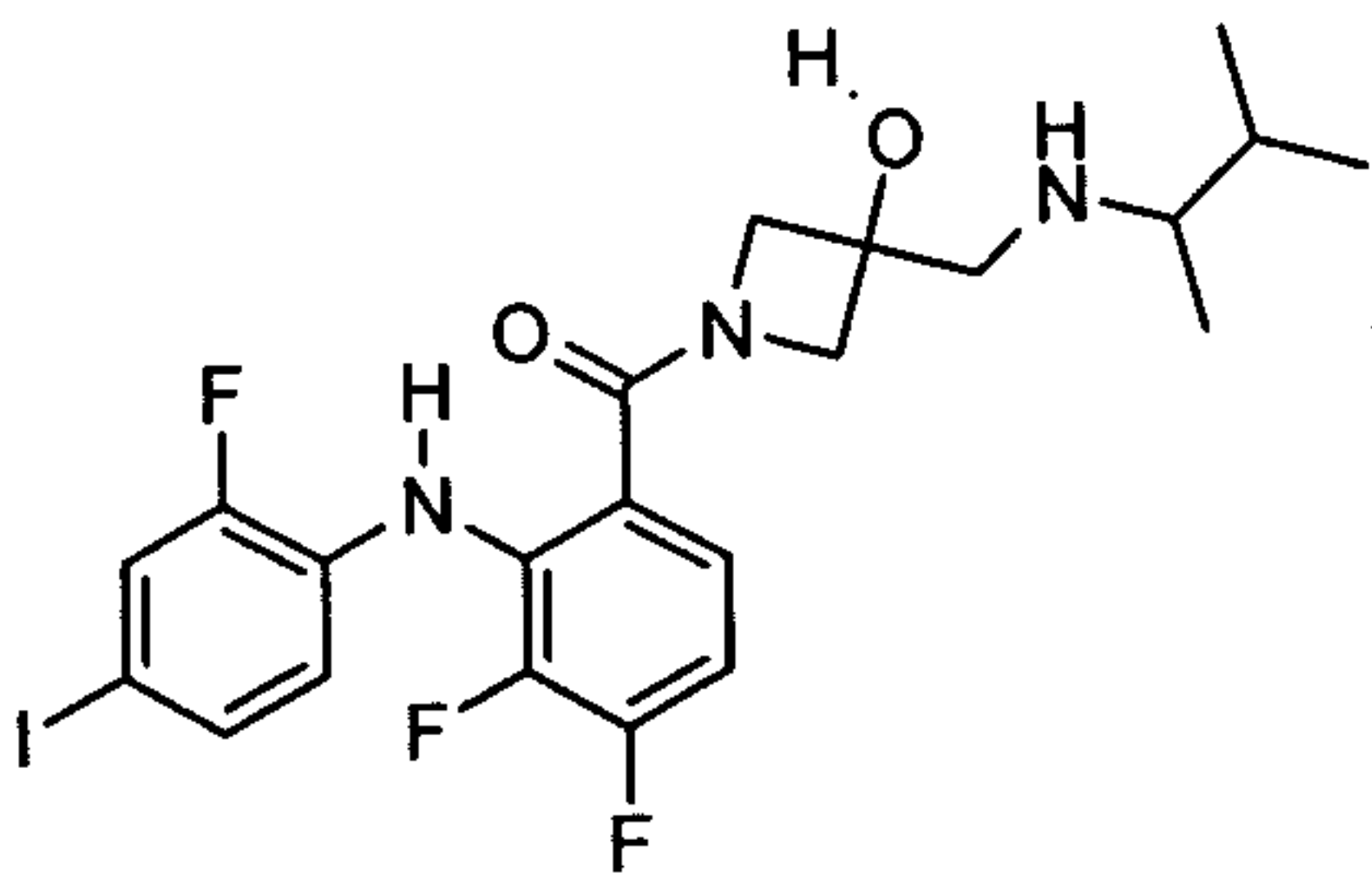
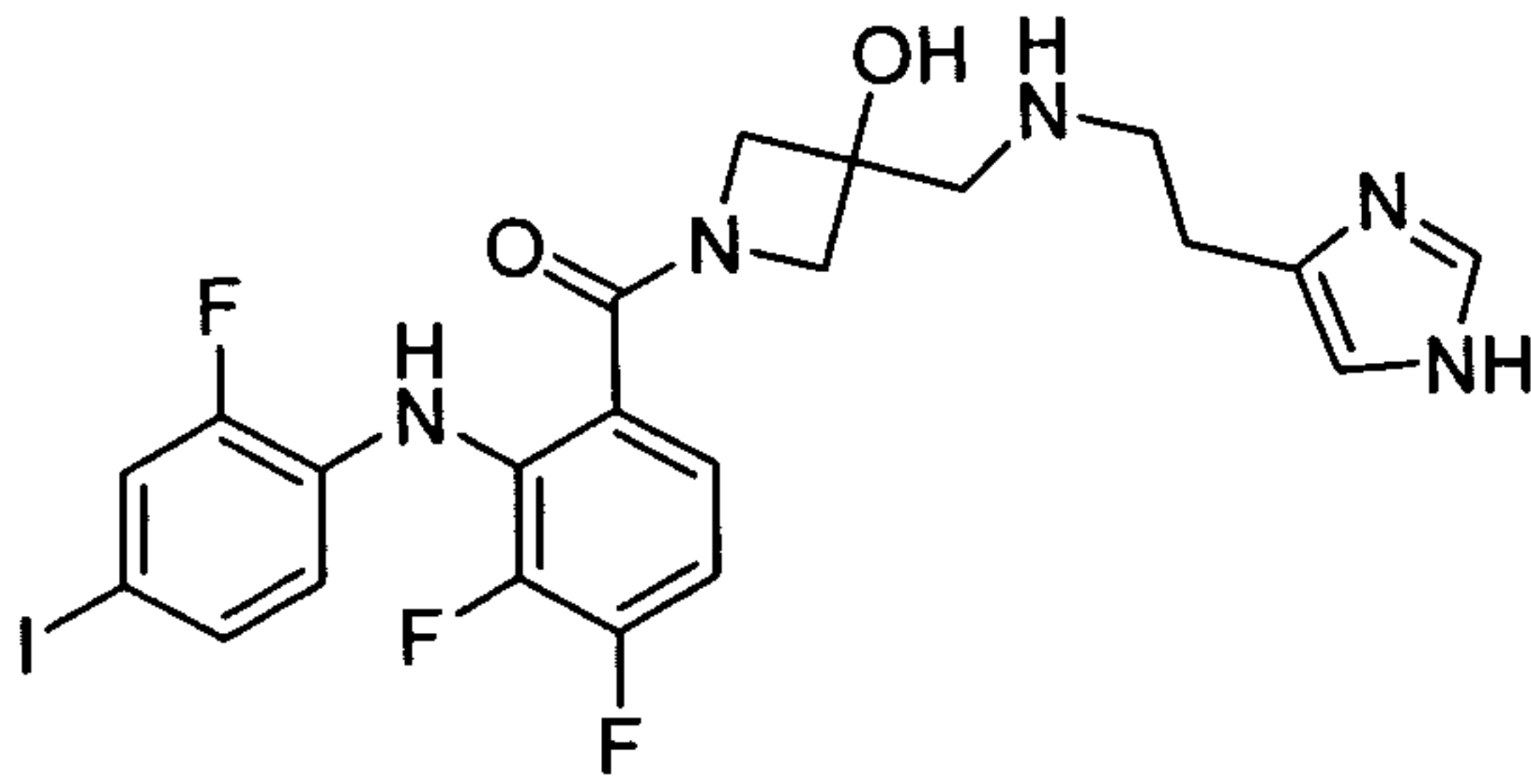
Cmpd No.	Structure	Name
117		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1,1-dimethylprop-2-yn-1-yl)amino)methyl)azetidin-3-ol
118		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((3-pyrrolidin-1-yl)propyl)amino)methyl)azetidin-3-ol
119		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1,2-dimethylpropyl)amino)methyl)azetidin-3-ol
120		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((2-(1H-imidazol-4-yl)ethyl)amino)methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

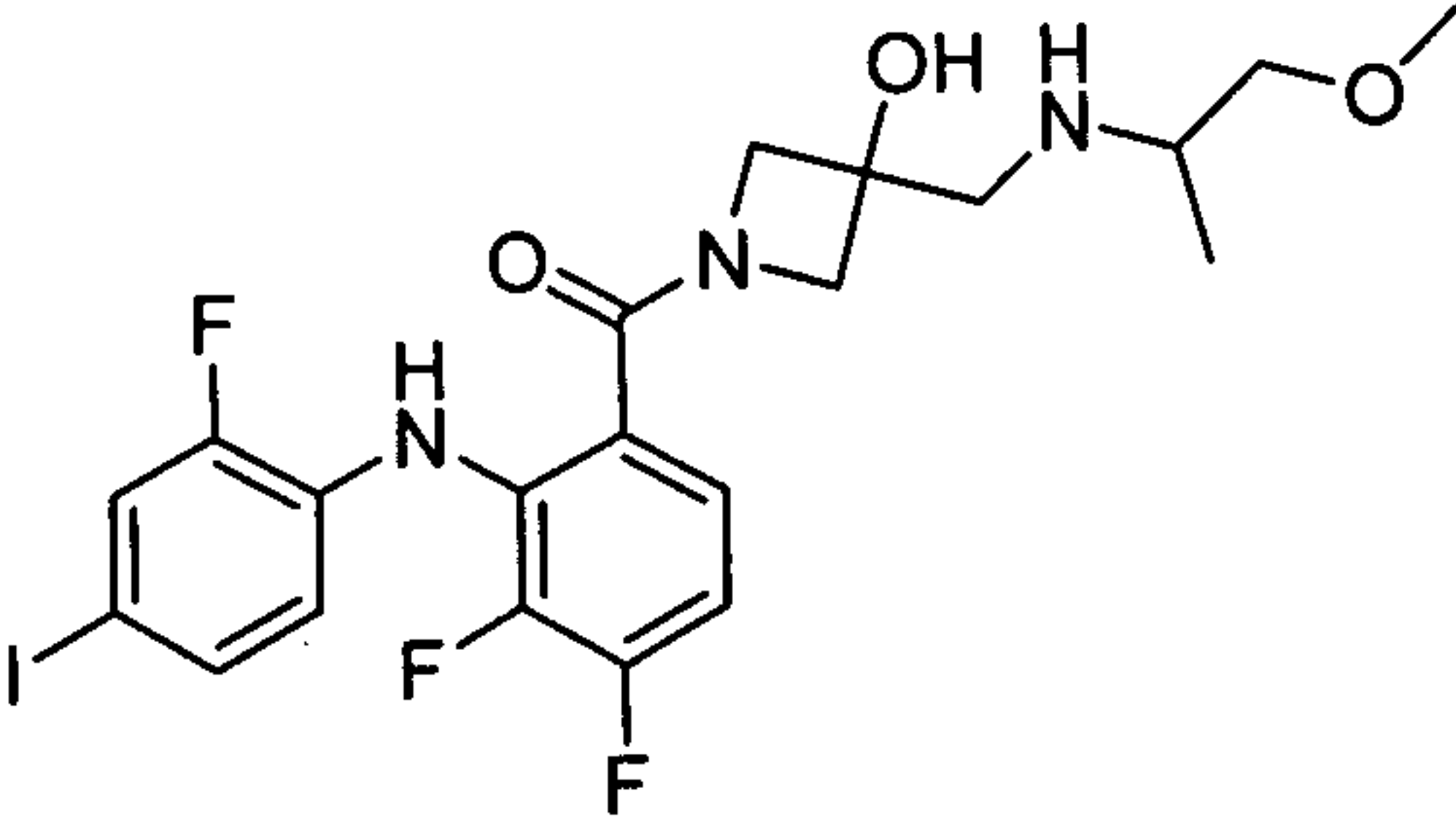
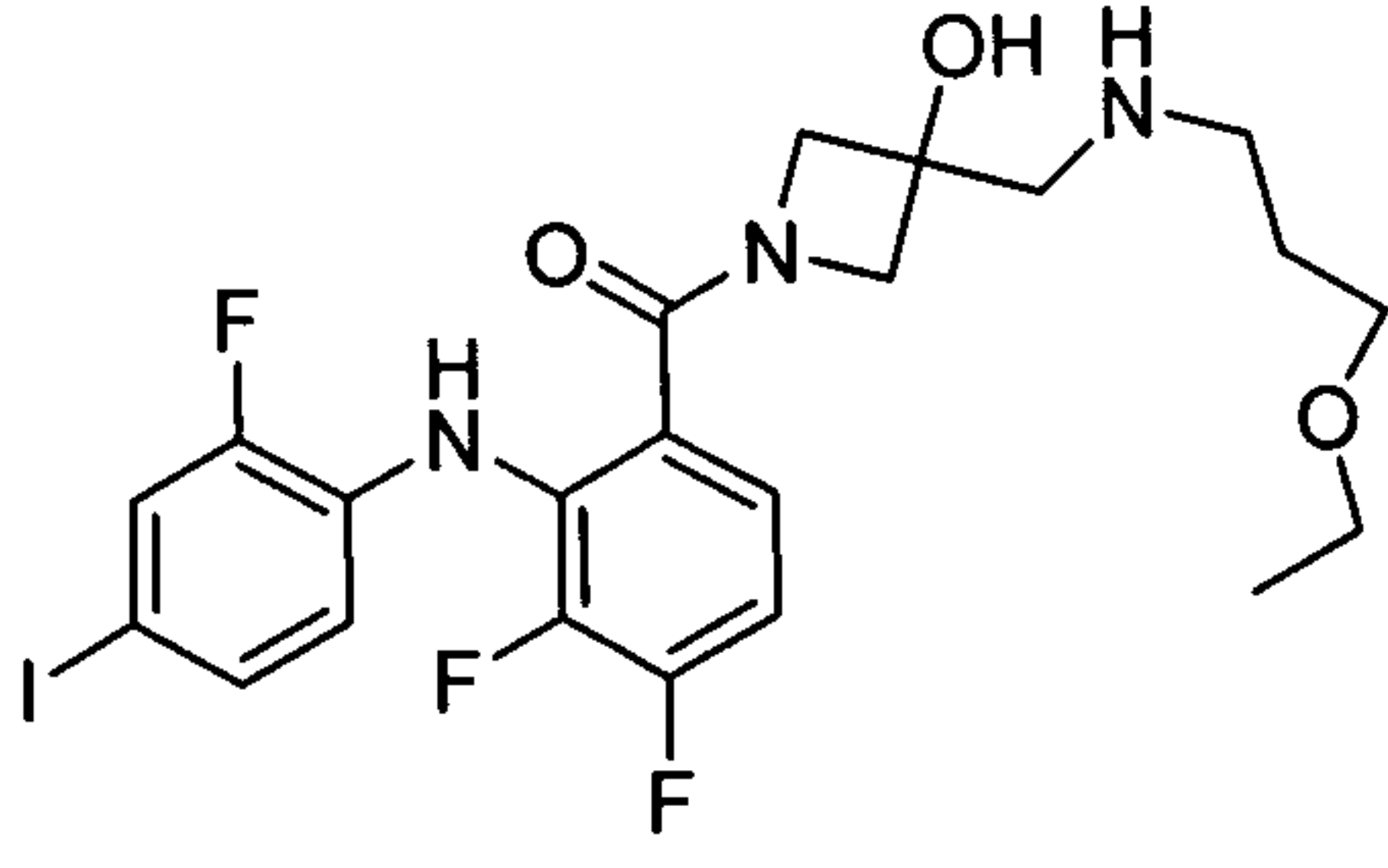
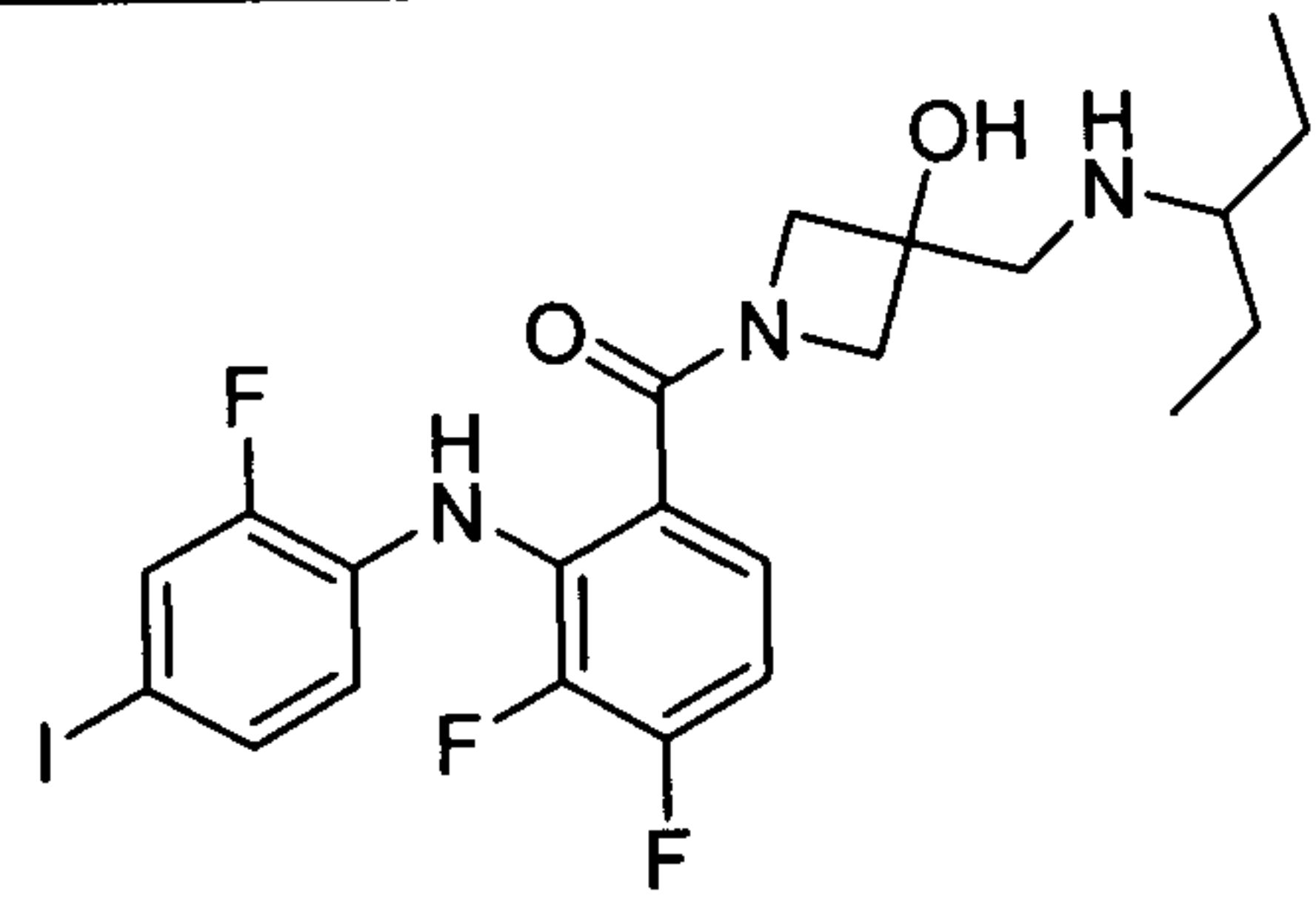
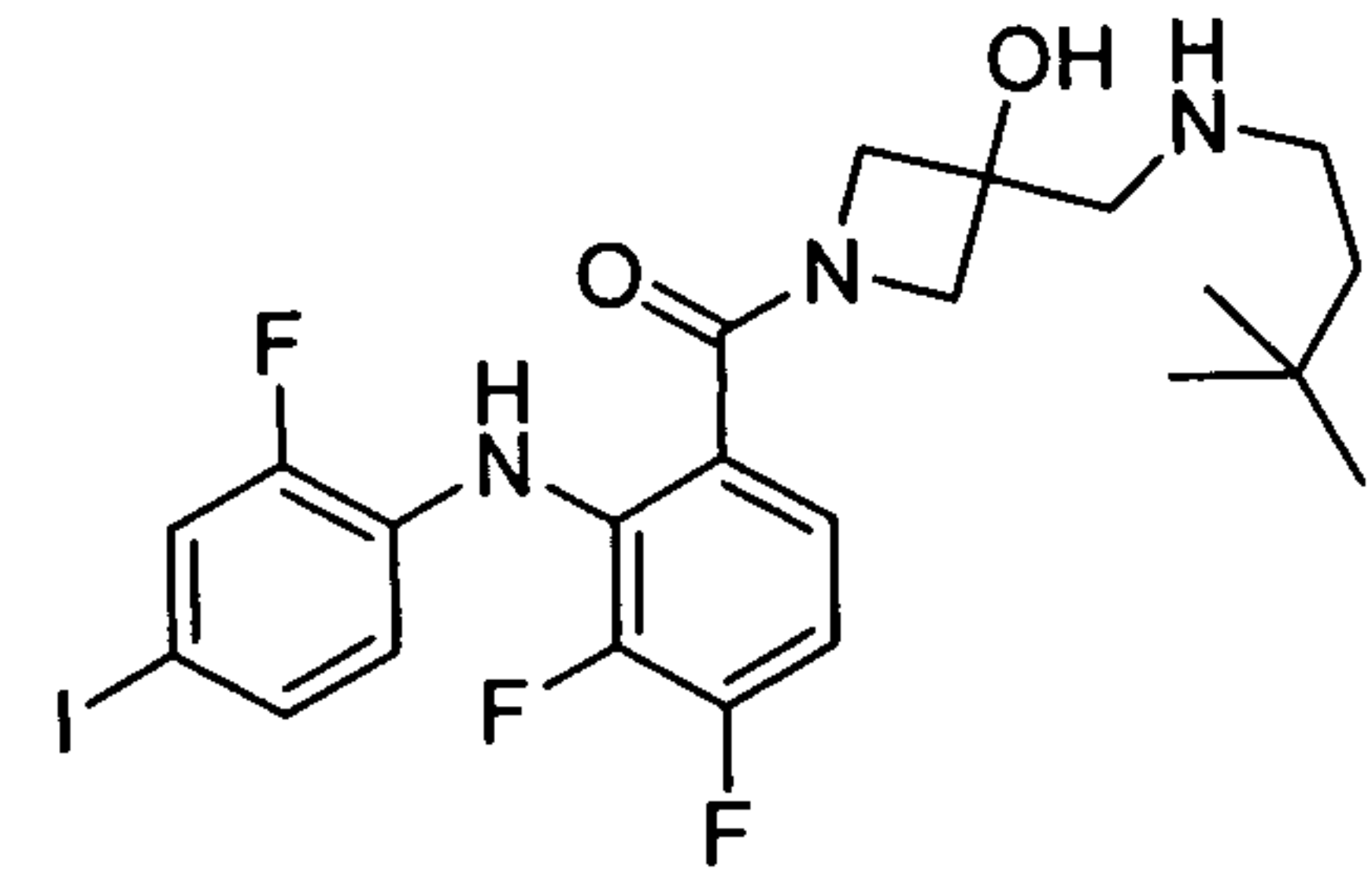
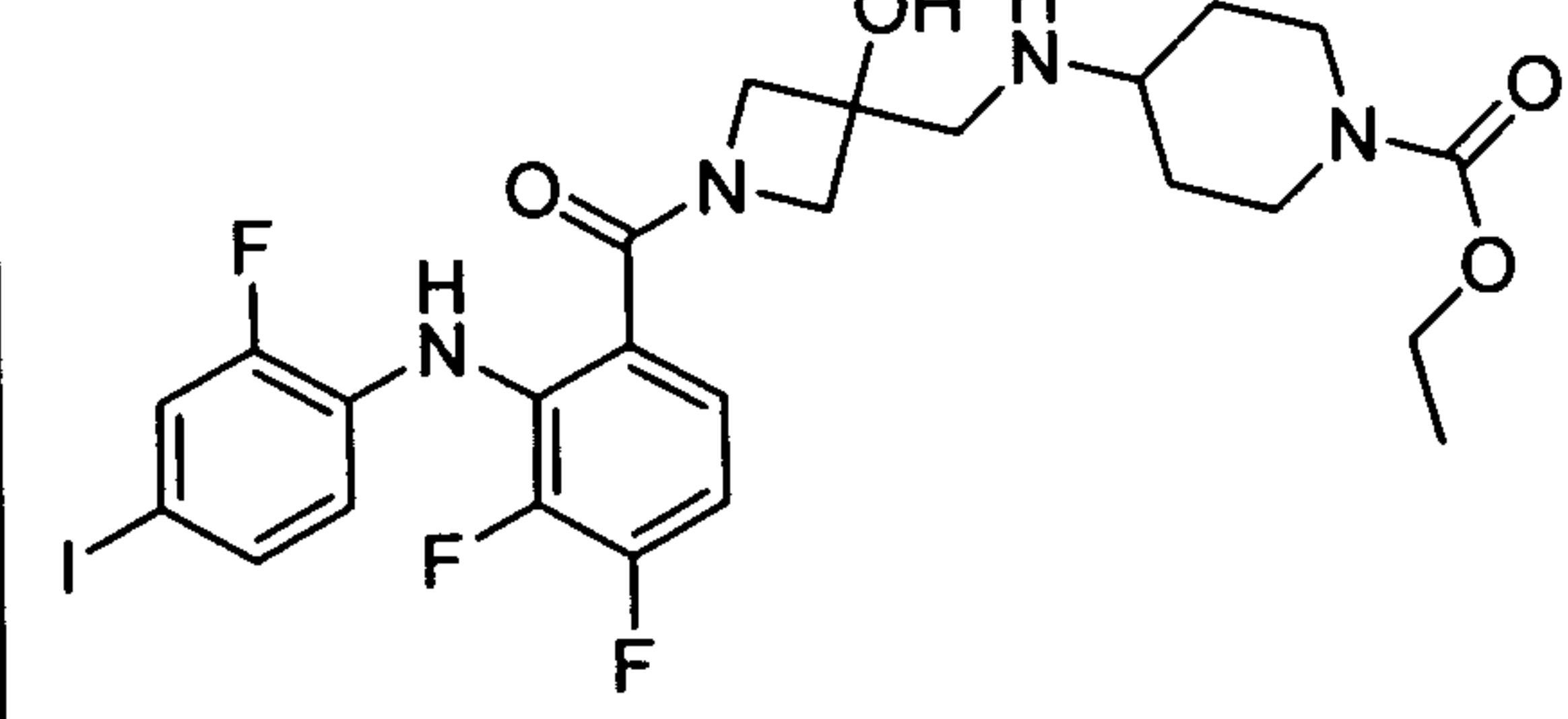
Cmpd No.	Structure	Name
121		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((1-methyl-2-(methyloxy)ethyl)amino)methylazetidin-3-ol
122		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((3-(ethyloxy)propyl)amino)methylazetidin-3-ol
123		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((1-ethylpropyl)amino)methylazetidin-3-ol
124		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((3,3-dimethylbutyl)amino)methylazetidin-3-ol
125		ethyl 4-((1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-hydroxyazetidin-3-yl)methyl)amino)piperidine-1-carboxylate

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
126		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(3-methylbutyl)amino}methyl}azetidin-3-ol
127		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[2-(ethyloxy)ethyl]amino}methyl}azetidin-3-ol
128		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[3-(dimethylamino)propyl]amino}methyl}azetidin-3-ol
129		3-[(cyclobutylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
130		3-{{[3-(diethylamino)propyl]amino}methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

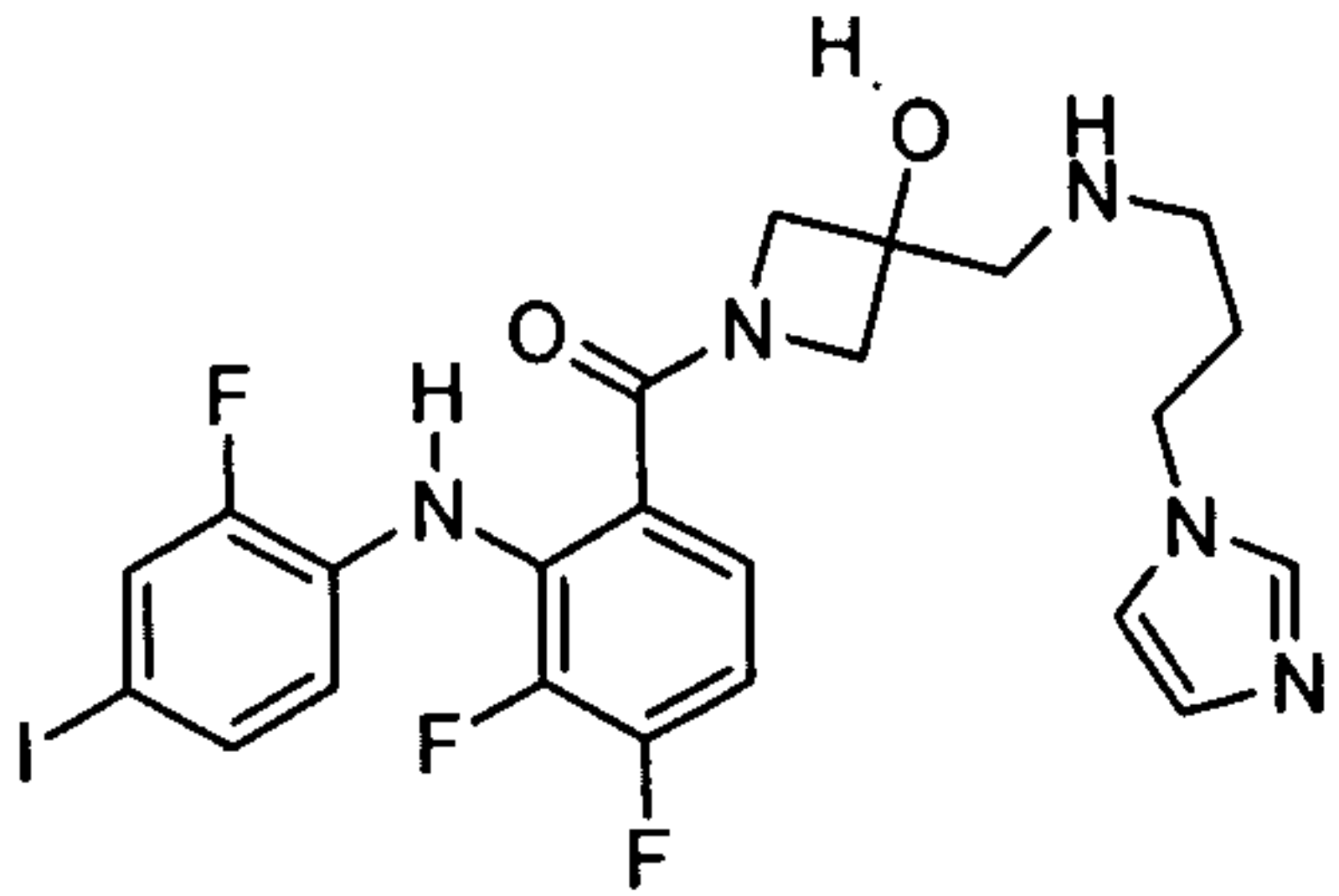
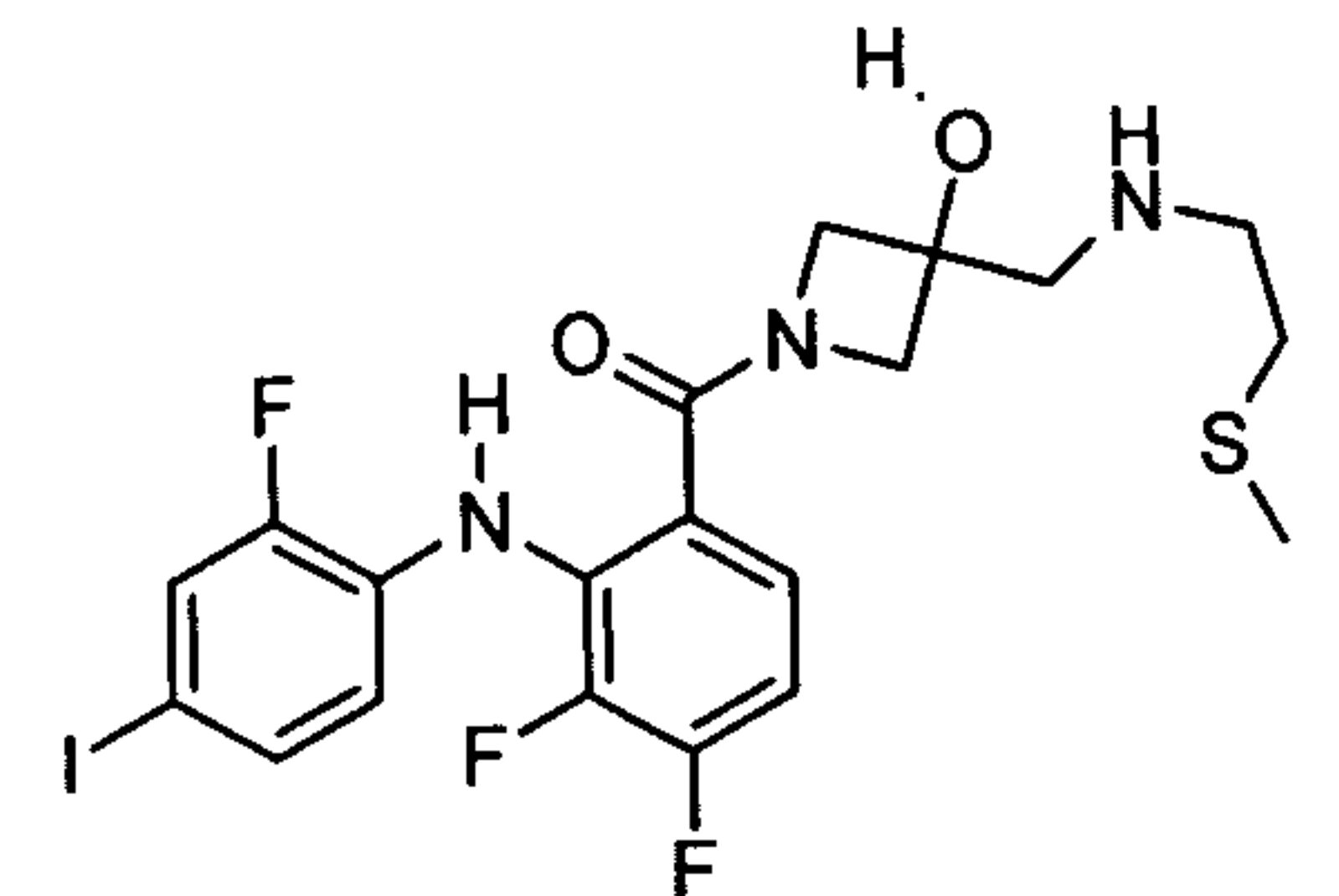
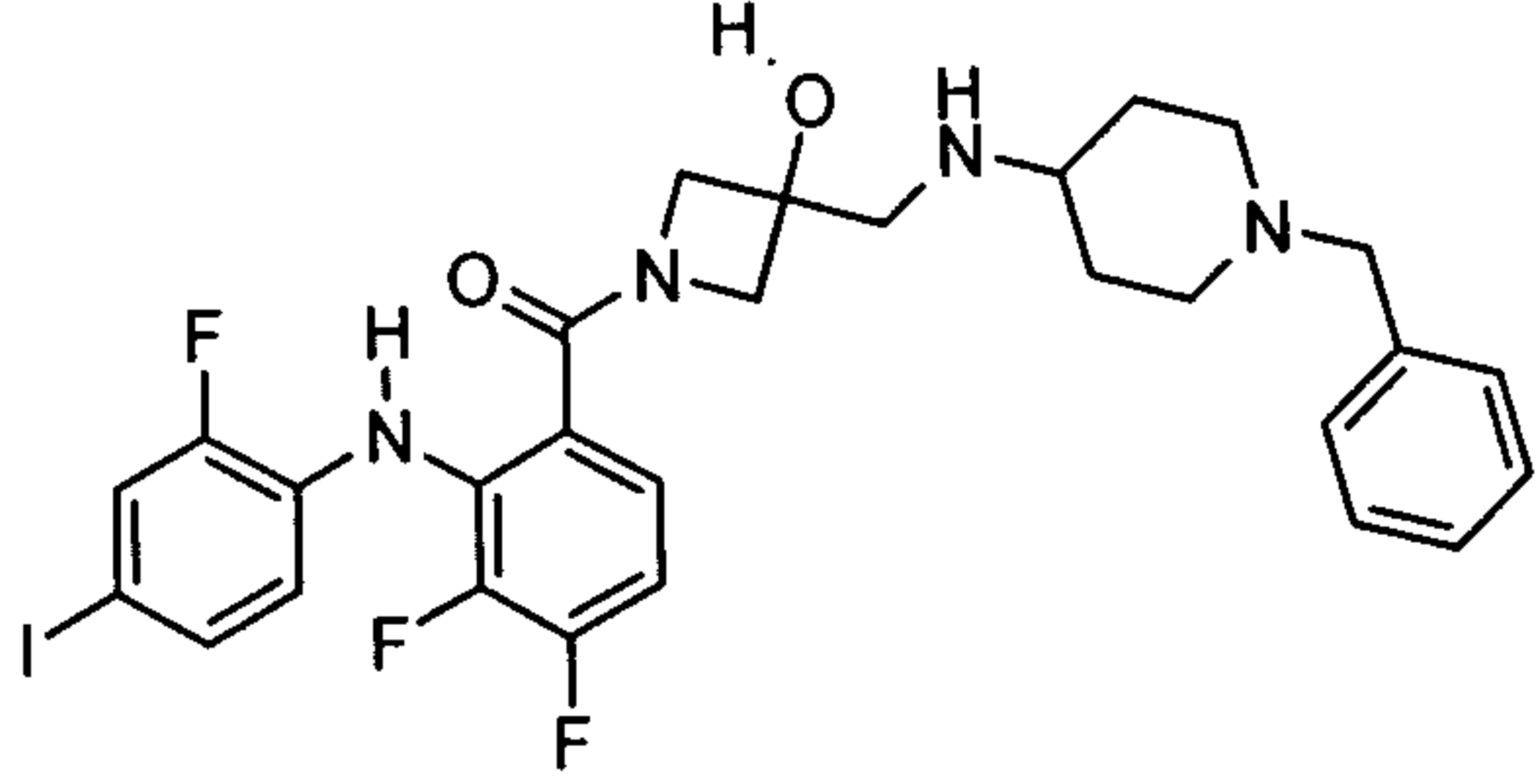
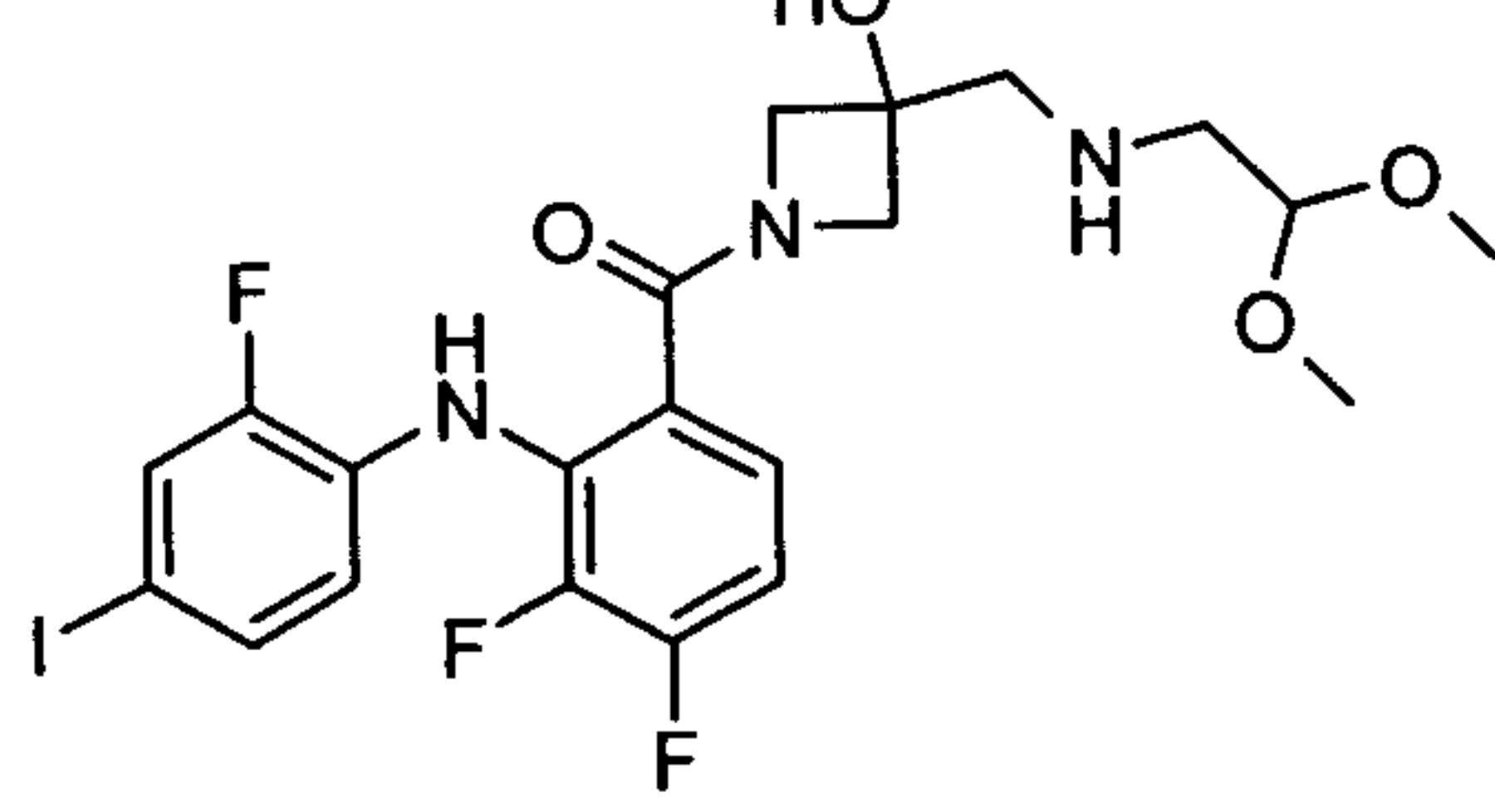
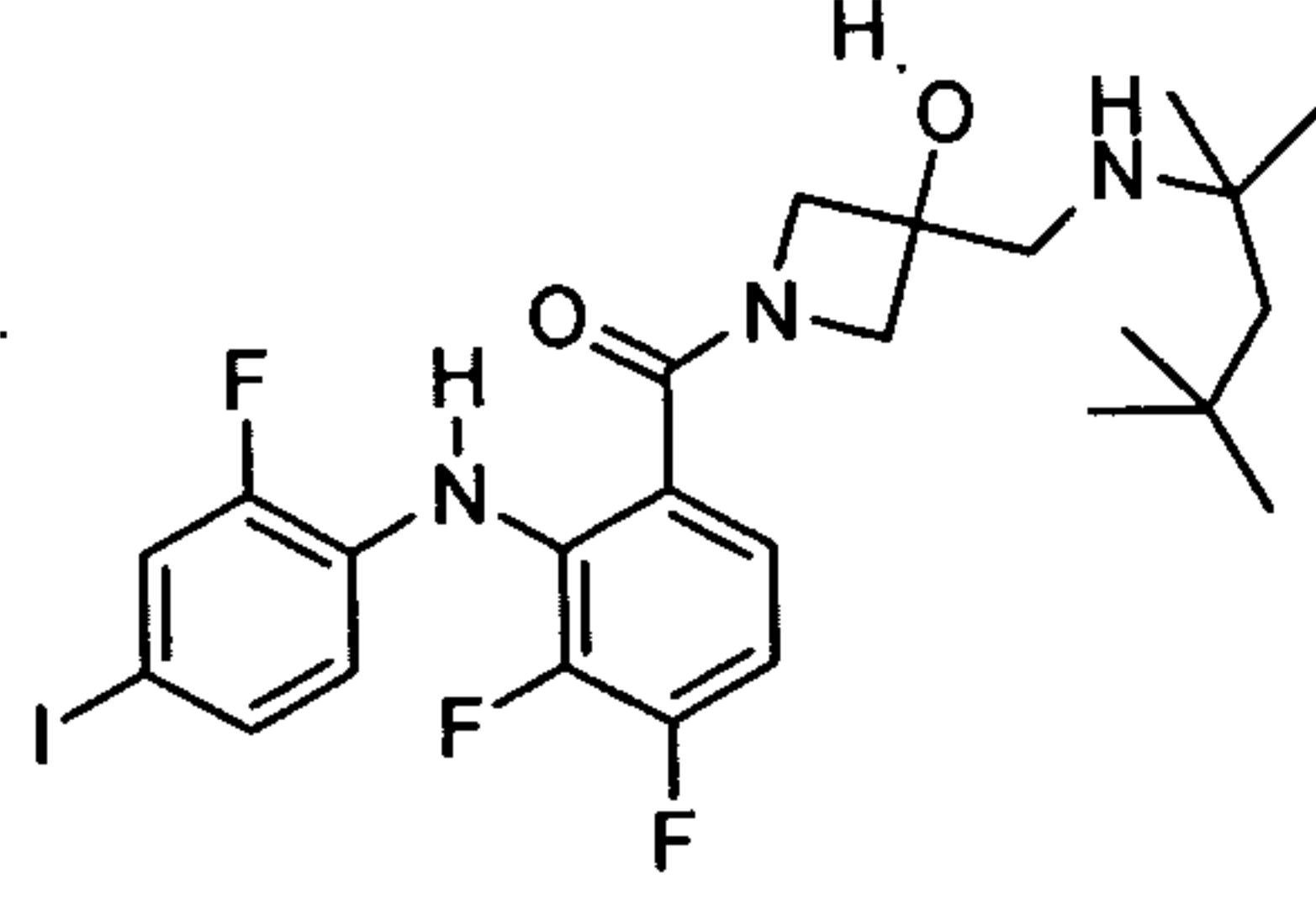
Cmpd No.	Structure	Name
131		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(1 <i>H</i> -imidazol-1-yl)propyl]amino}methyl)azetidin-3-ol
132		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(methylthio)ethyl]amino}methyl)azetidin-3-ol
133		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(phenylmethyl)piperidin-4-yl]amino}methyl)azetidin-3-ol
134		3-({[2,2-bis(methoxy)ethyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
135		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1,1,3,3-tetramethylbutyl)amino]methyl}azetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
136		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1,1-dimethylpropyl)amino)methyl)azetidin-3-ol
137		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((2,3-dihydro-1H-inden-1-ylamino)methyl)azetidin-3-ol
138		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((2-((phenylmethyl)oxy)cyclopentyl)amino)methyl)azetidin-3-ol
139		3-(((3-amino-2-hydroxypropyl)amino)methyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol
140		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((2-hydroxy-1-(phenylmethyl)ethyl)amino)methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

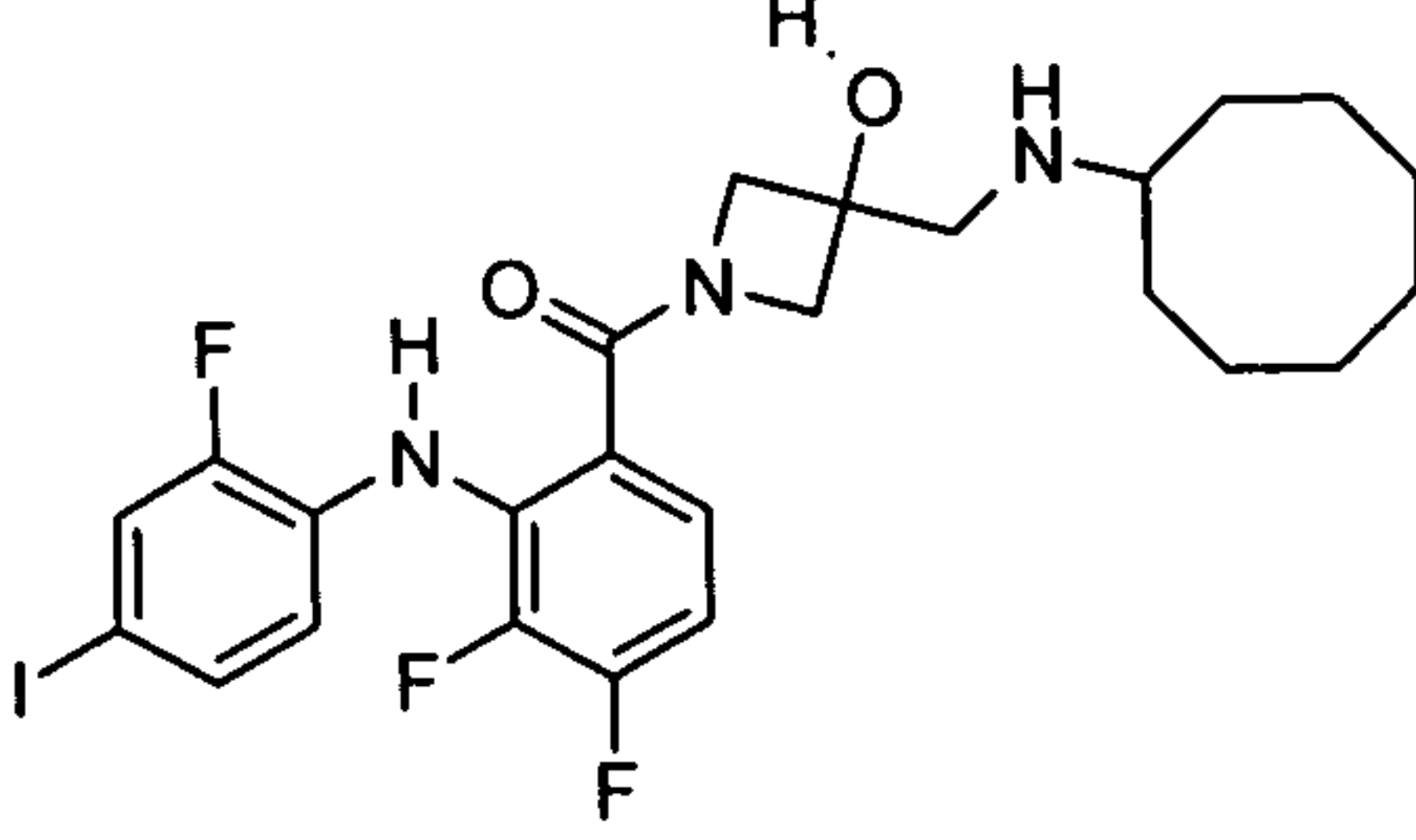
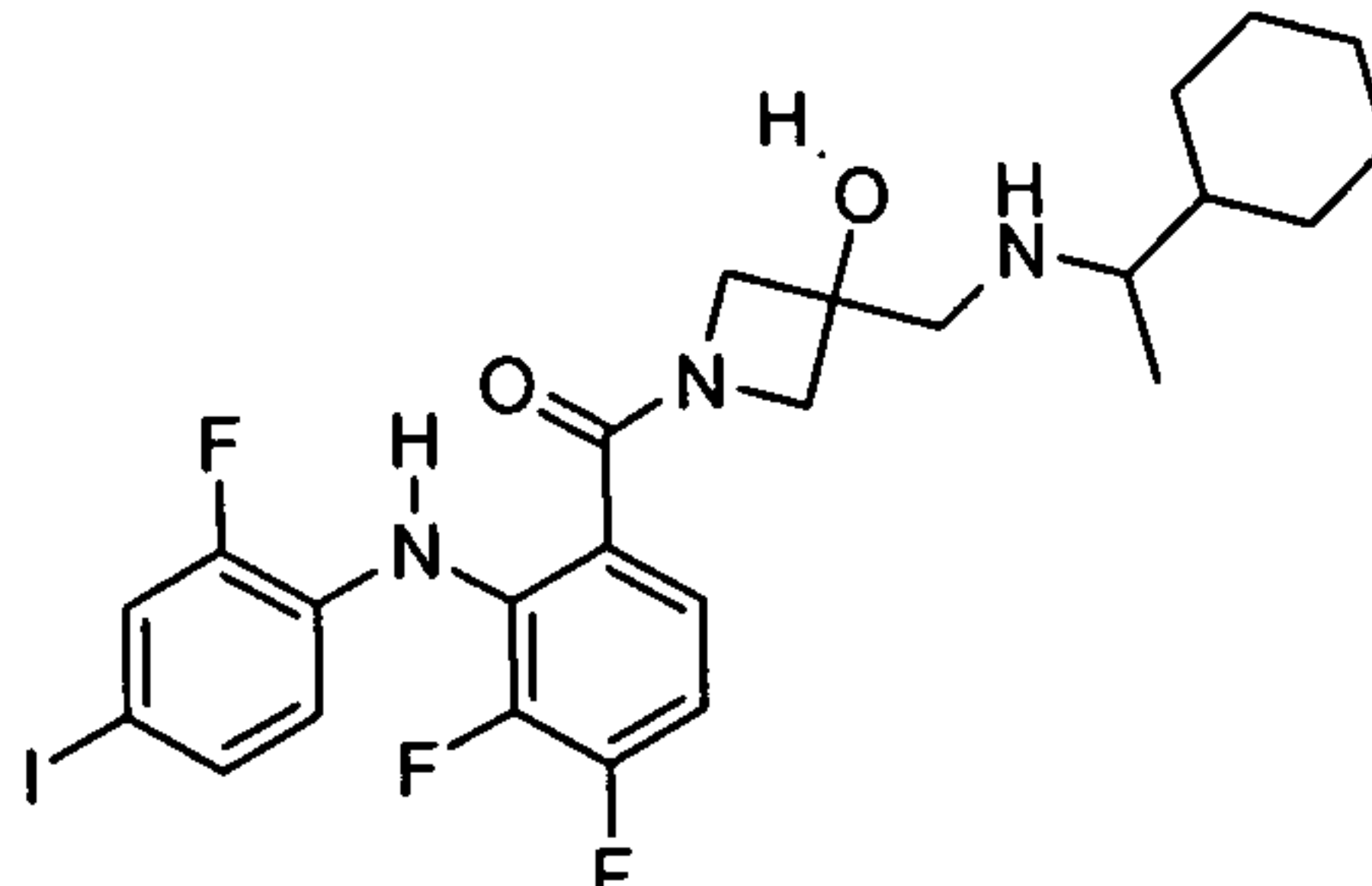
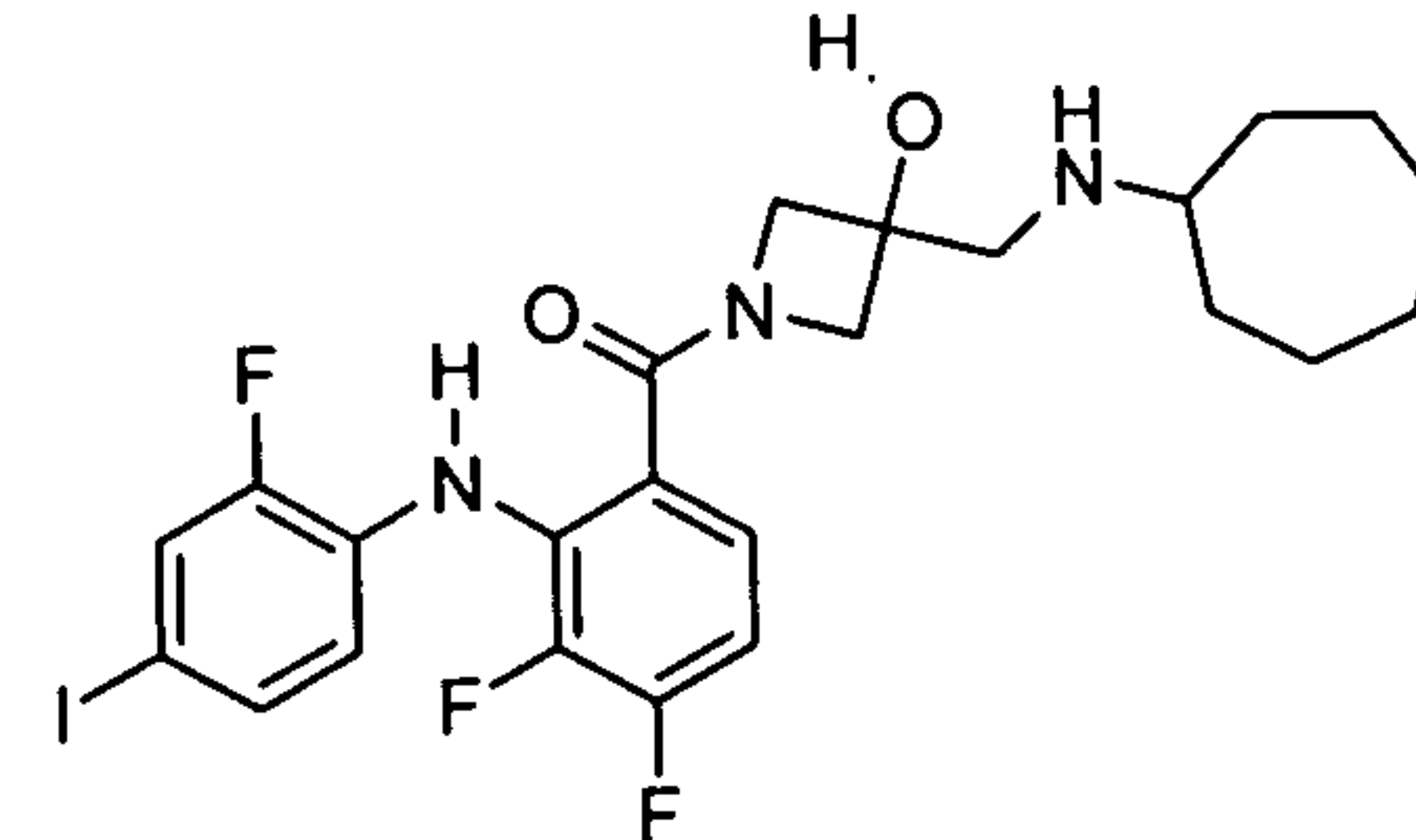
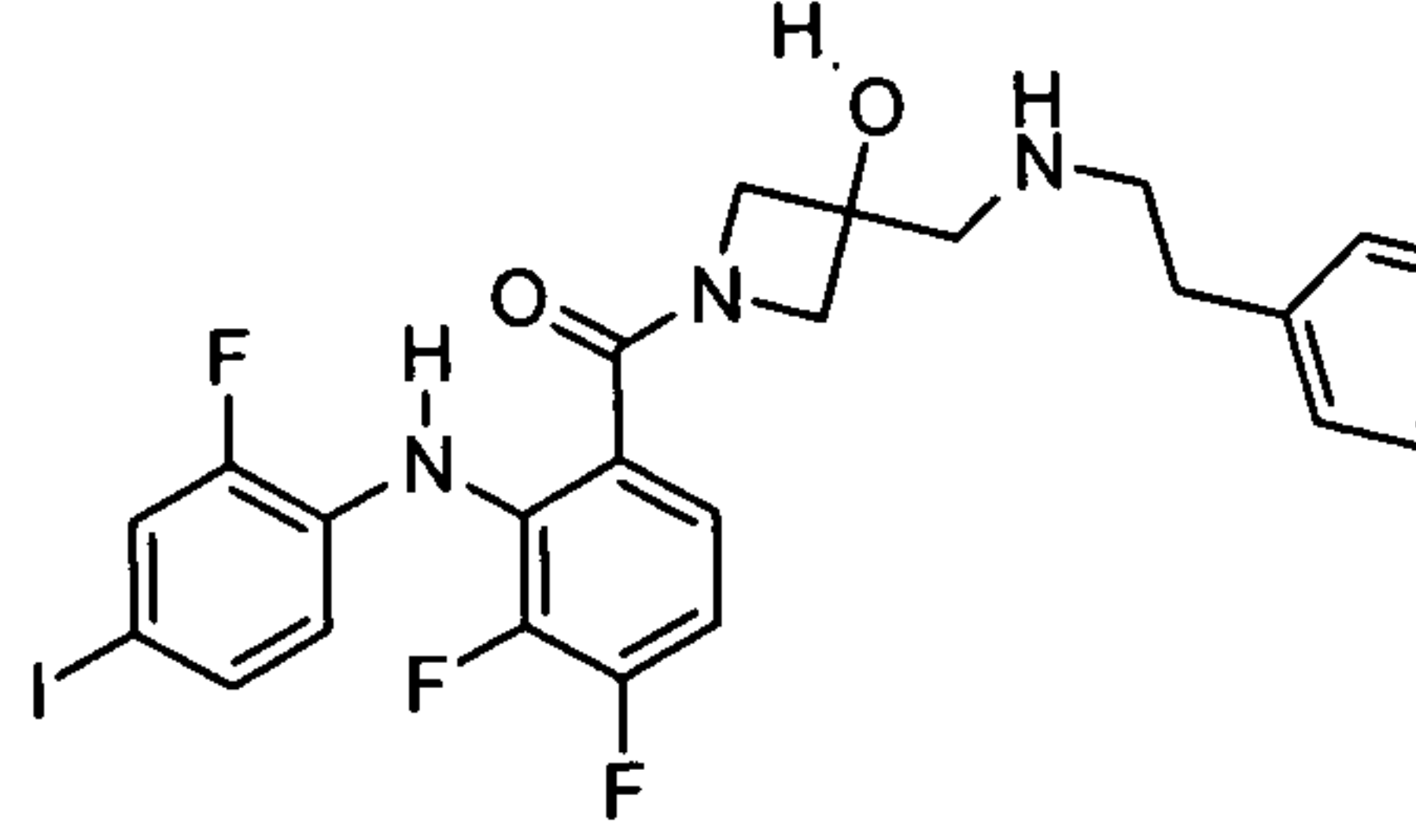
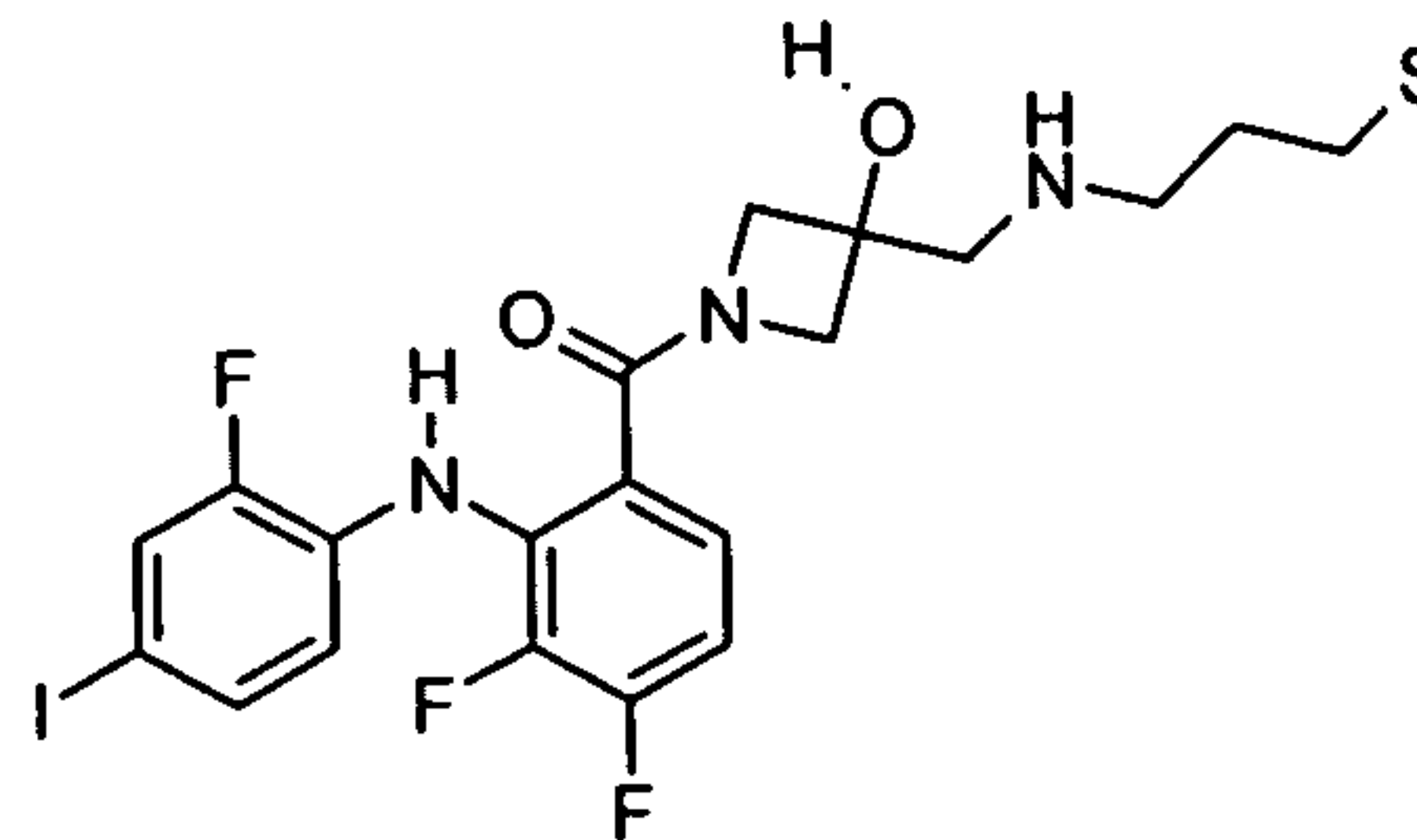
Cmpd No.	Structure	Name
141		3-[(cyclooctylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
142		3-[(1-cyclohexylethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
143		3-[(cycloheptylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
144		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-pyridin-3-ylethylamino)methyl]azetidin-3-ol
145		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(3-(methylthio)propylamino)methyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

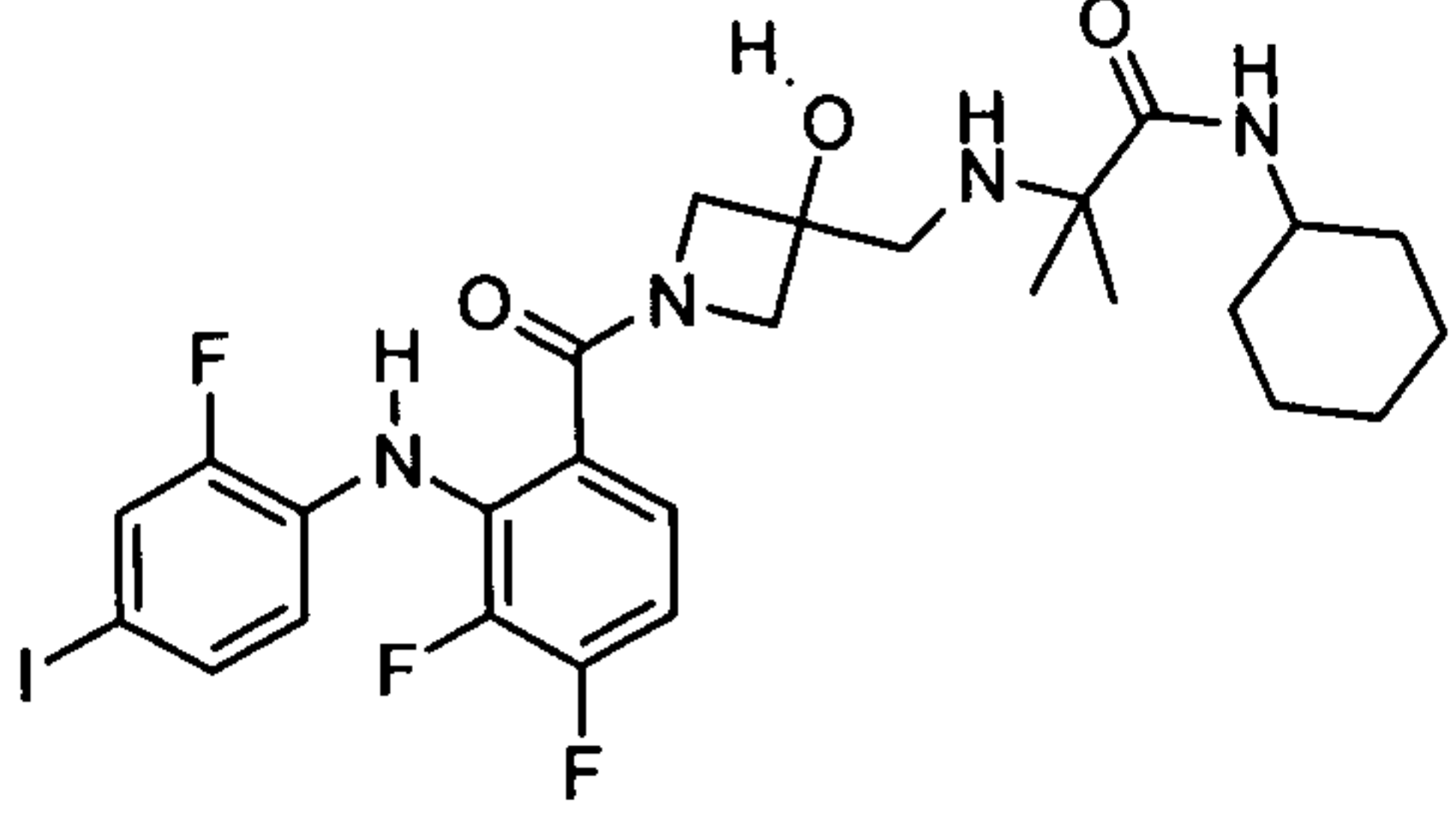
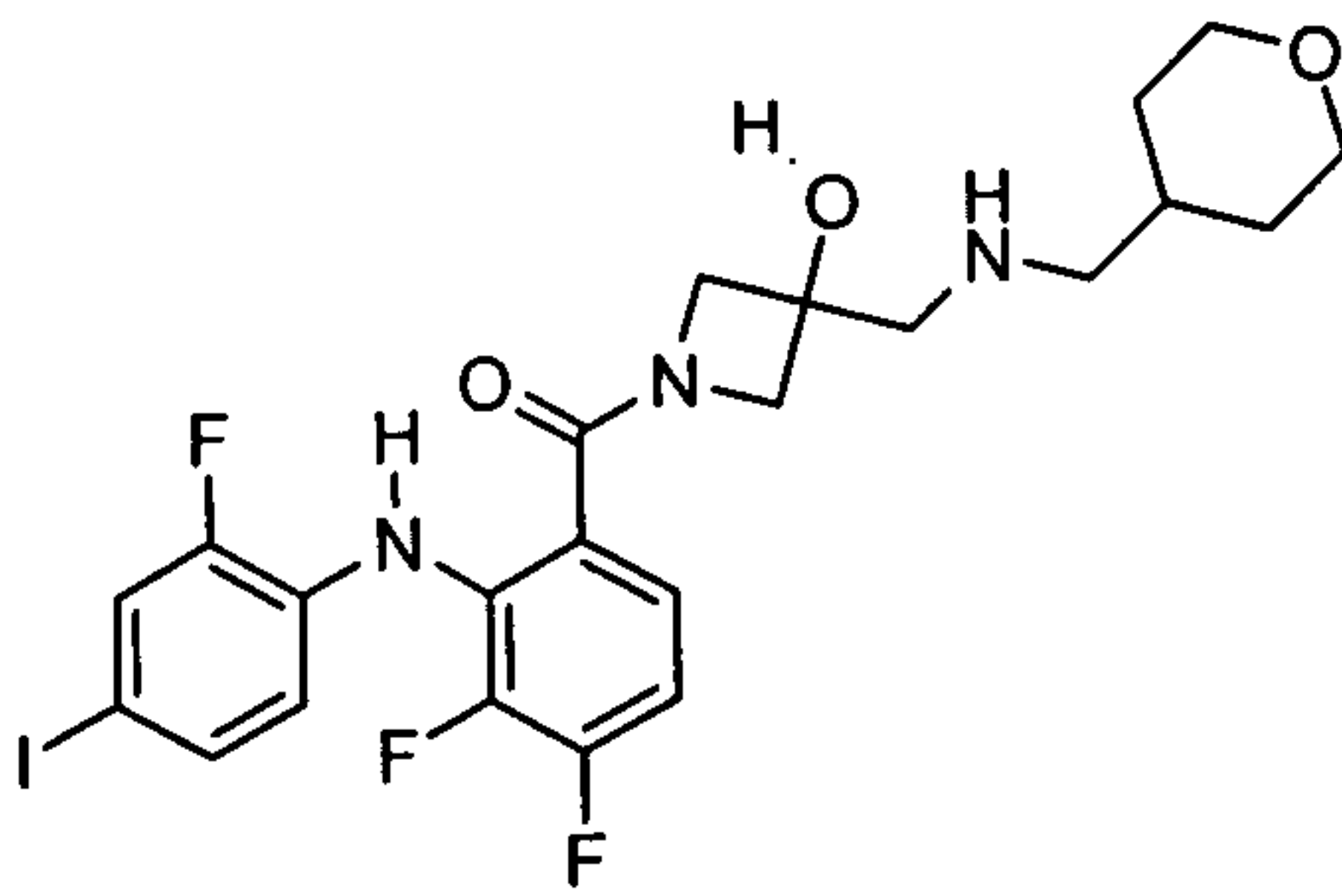
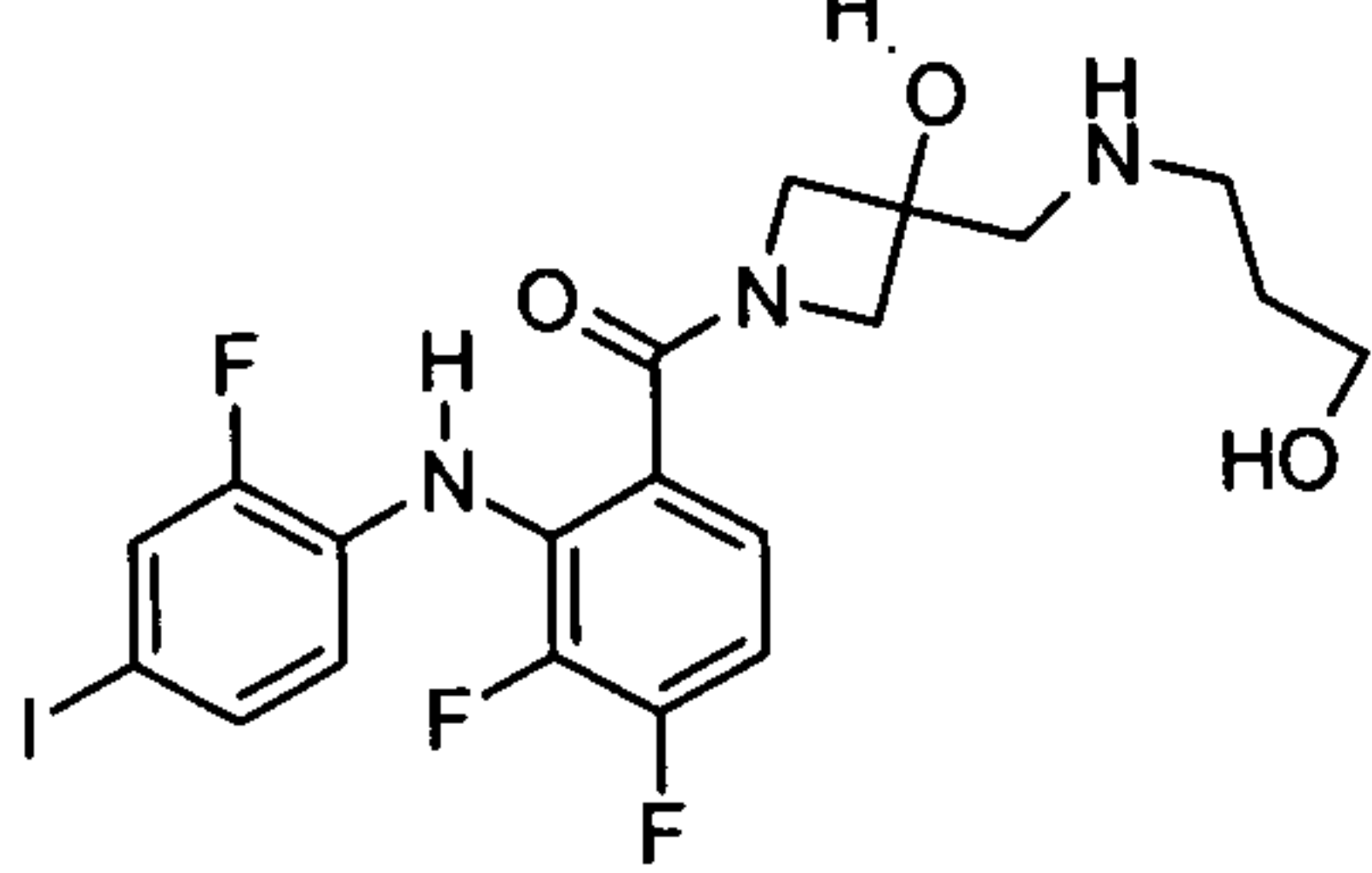
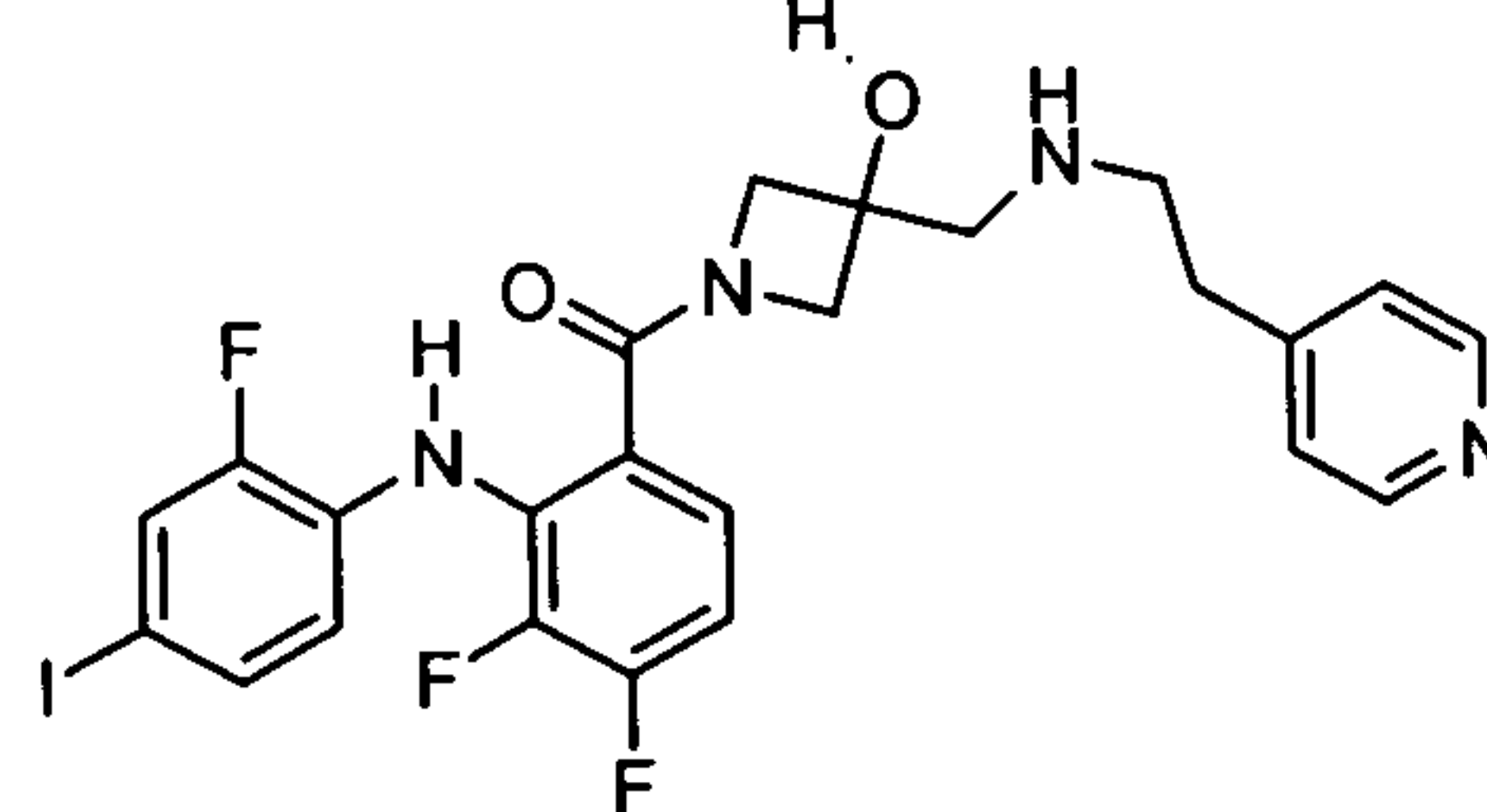
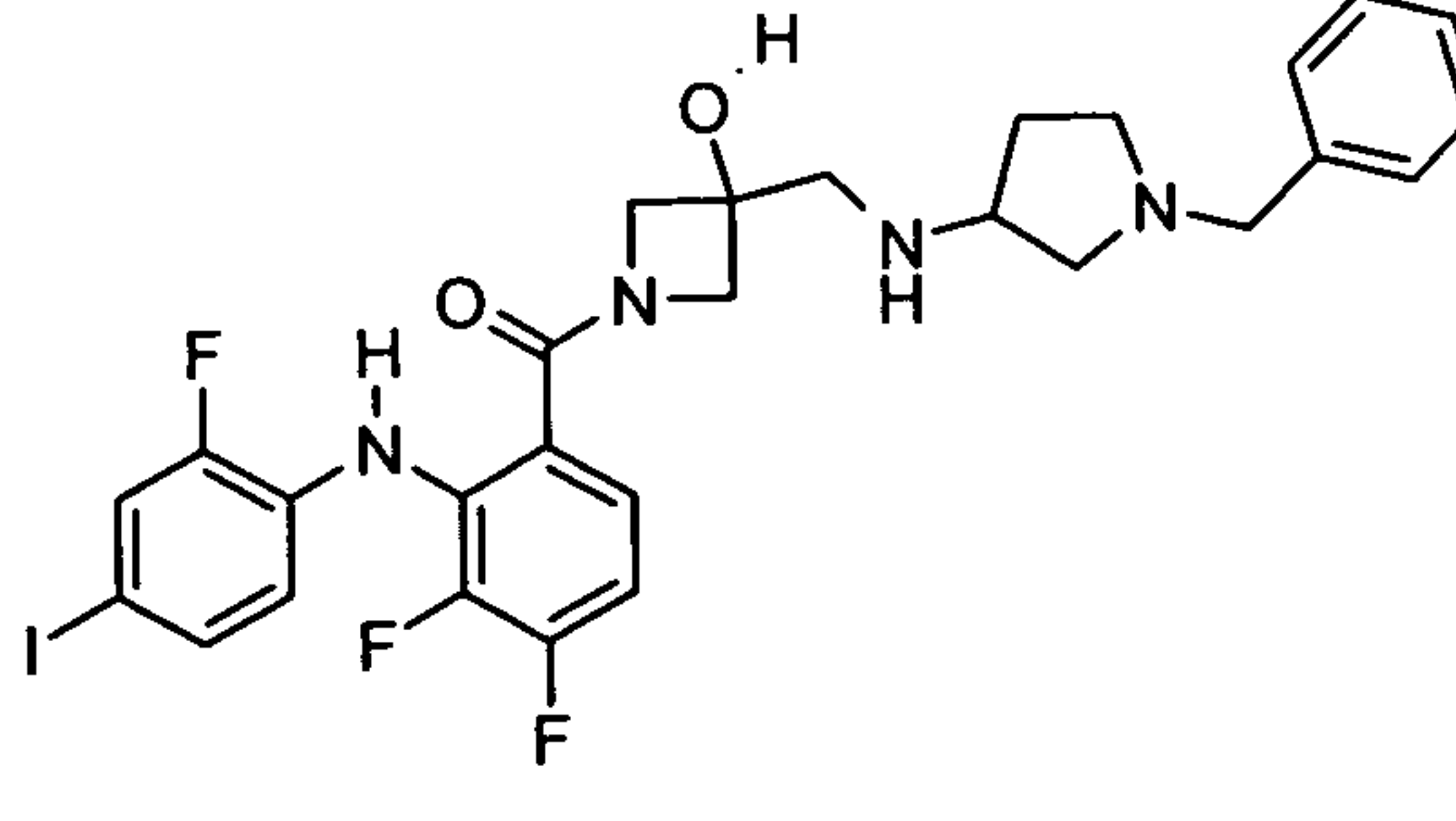
Cmpd No.	Structure	Name
146		N-cyclohexyl-N-2-[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl]-2-methylalaninamide
147		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[tetrahydro-2H-pyran-4-ylmethyl]amino]methylazetidin-3-ol
148		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[3-hydroxypropyl]amino]methylazetidin-3-ol
149		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[2-pyridin-4-ylethyl]amino]methylazetidin-3-ol
150		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[1-(phenylmethyl)pyrrolidin-3-yl]amino]methylazetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
151		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((2-(2-thienyl)ethyl)amino)methyl)azetidin-3-ol
152		3-(((2-bis(1-methylethyl)amino)ethyl)amino)methyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol
153		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((2-(phenyloxy)ethyl)amino)methyl)azetidin-3-ol
154		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((phenylamino)methyl)azetidin-3-ol
155		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((2-hydroxypropyl)amino)methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

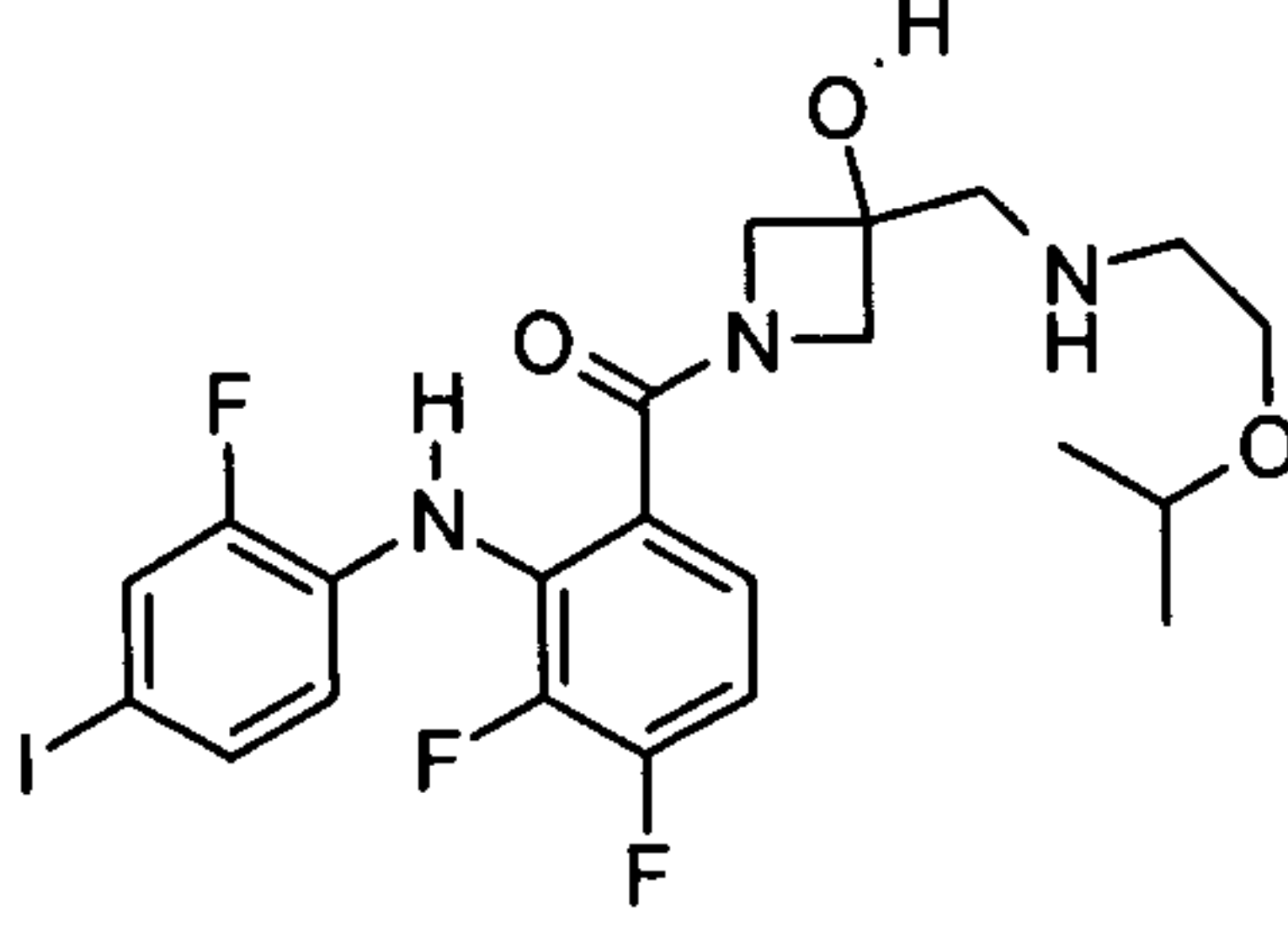
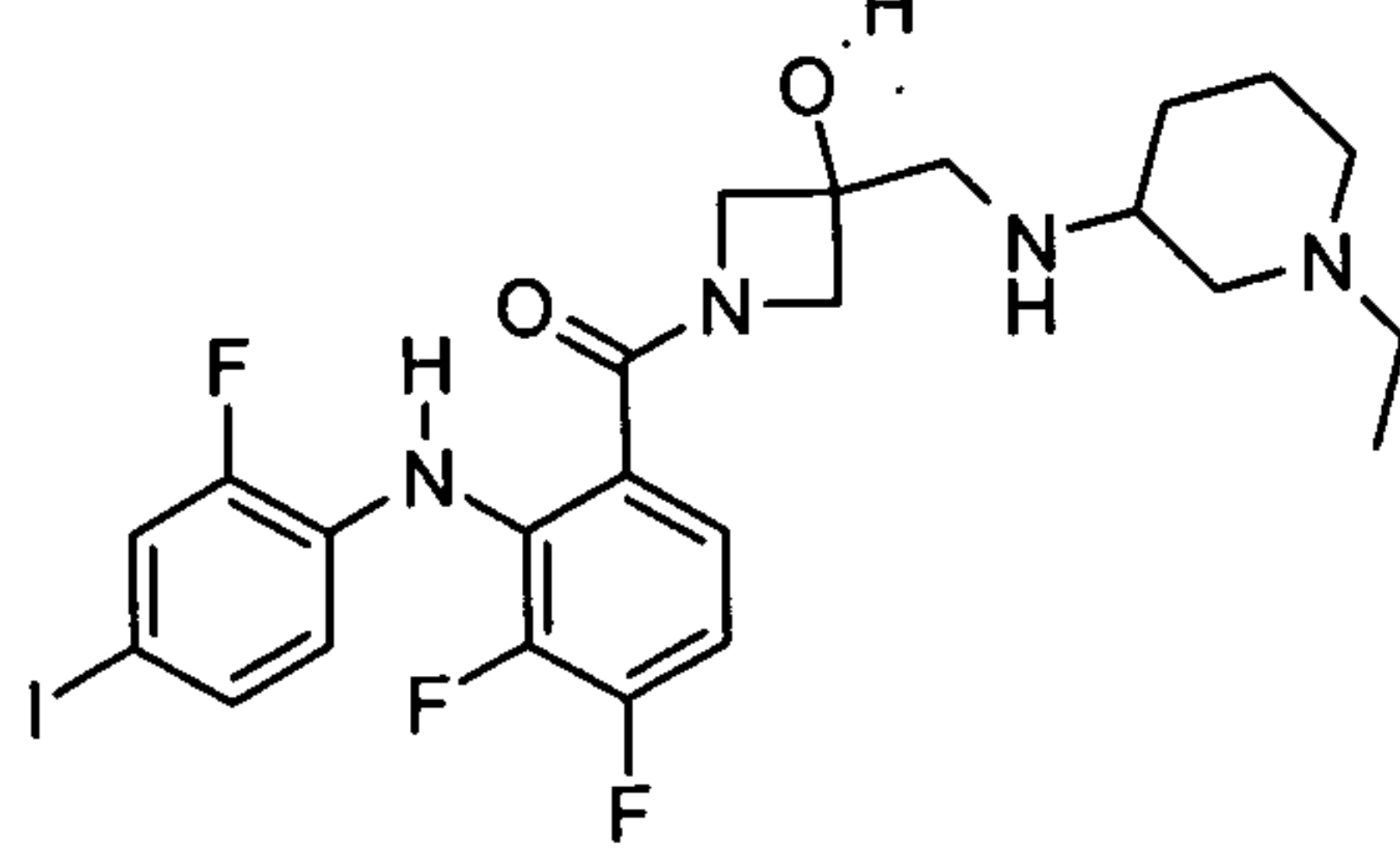
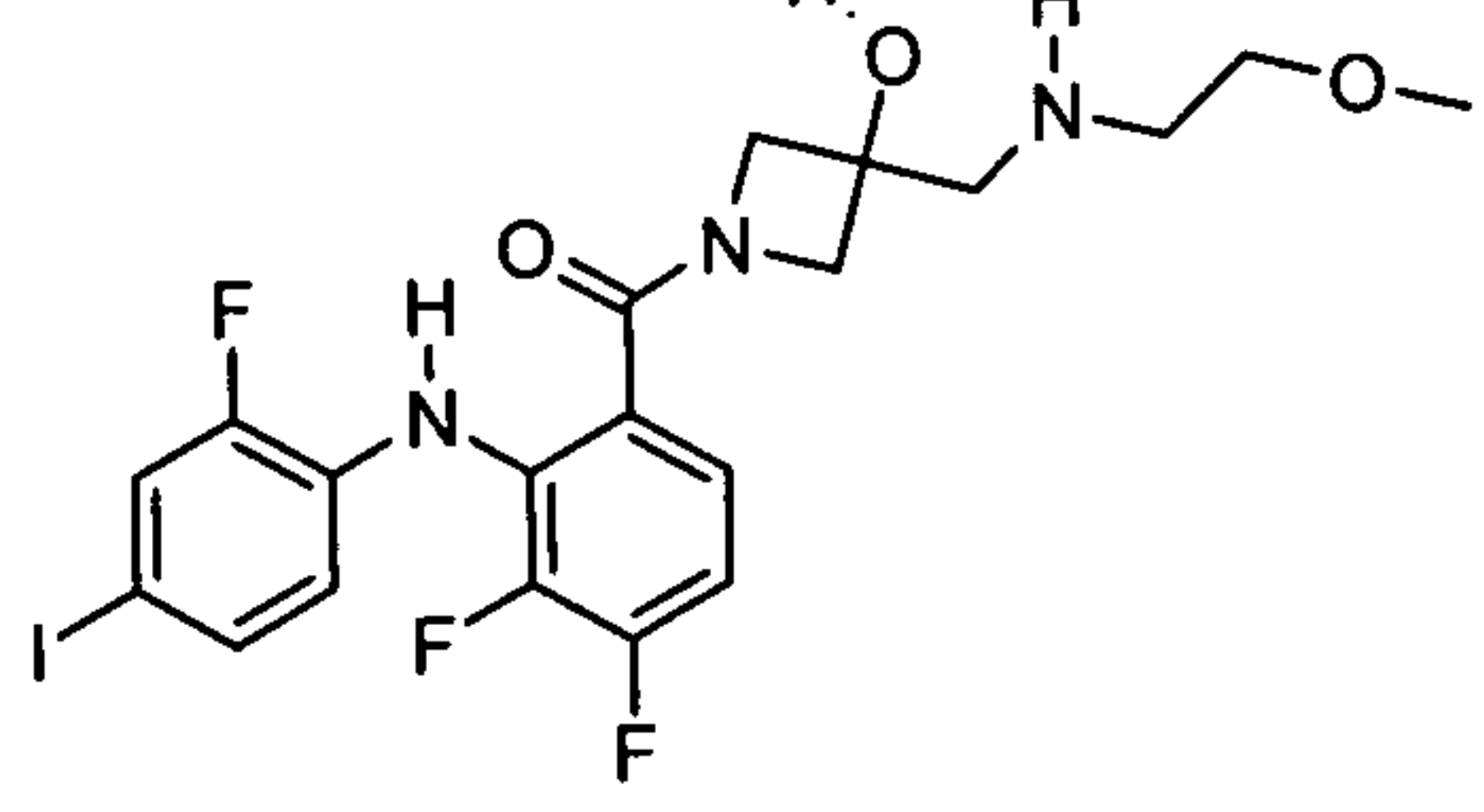
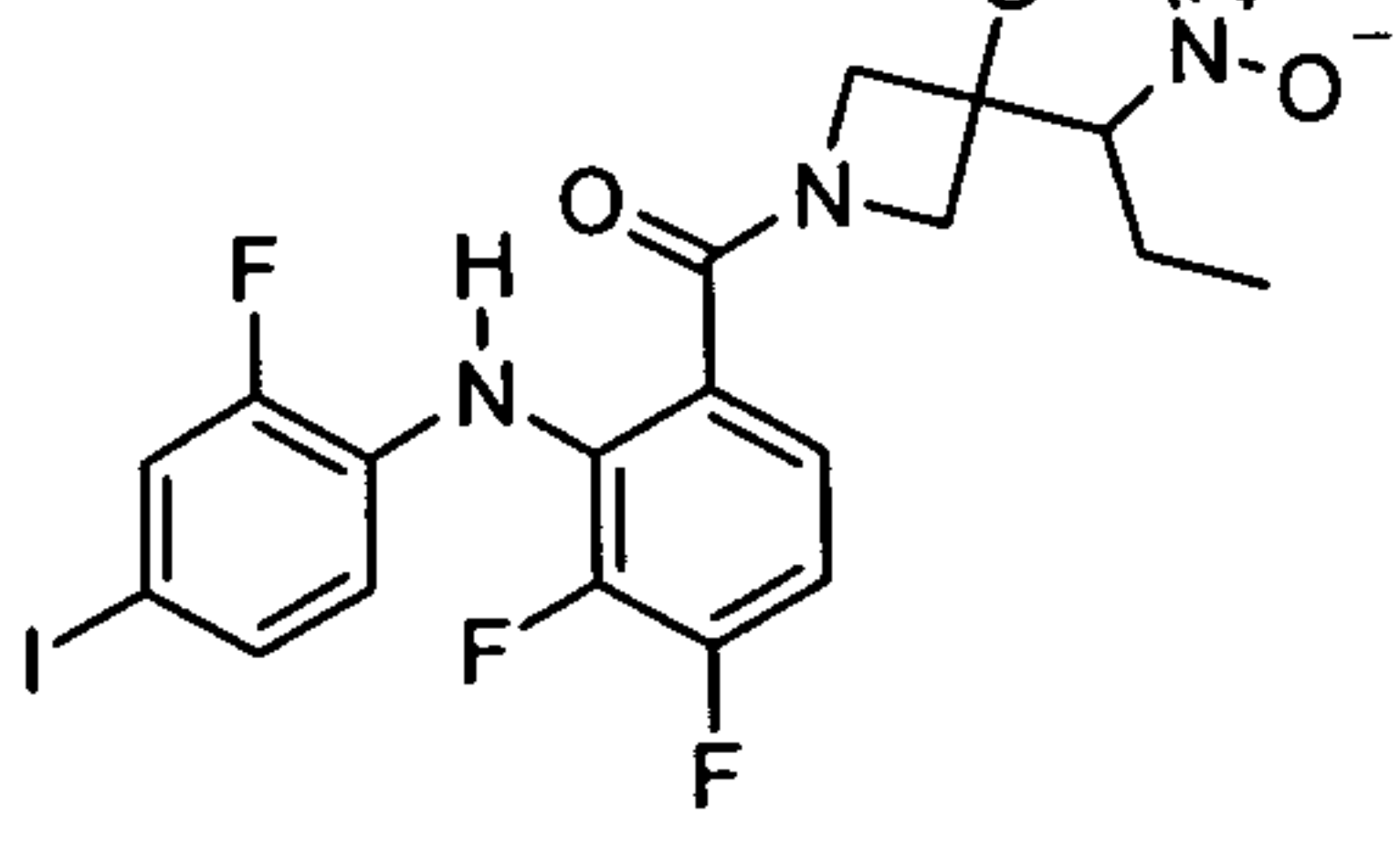
Cmpd No.	Structure	Name
156		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-[(1-methylethyl)oxy]ethyl)amino)methyl]azetidin-3-ol
157		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1-ethylpiperidin-3-yl)amino)methyl]azetidin-3-ol
158		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-(methyloxy)ethyl)amino)methyl]azetidin-3-ol
159		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitropropyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

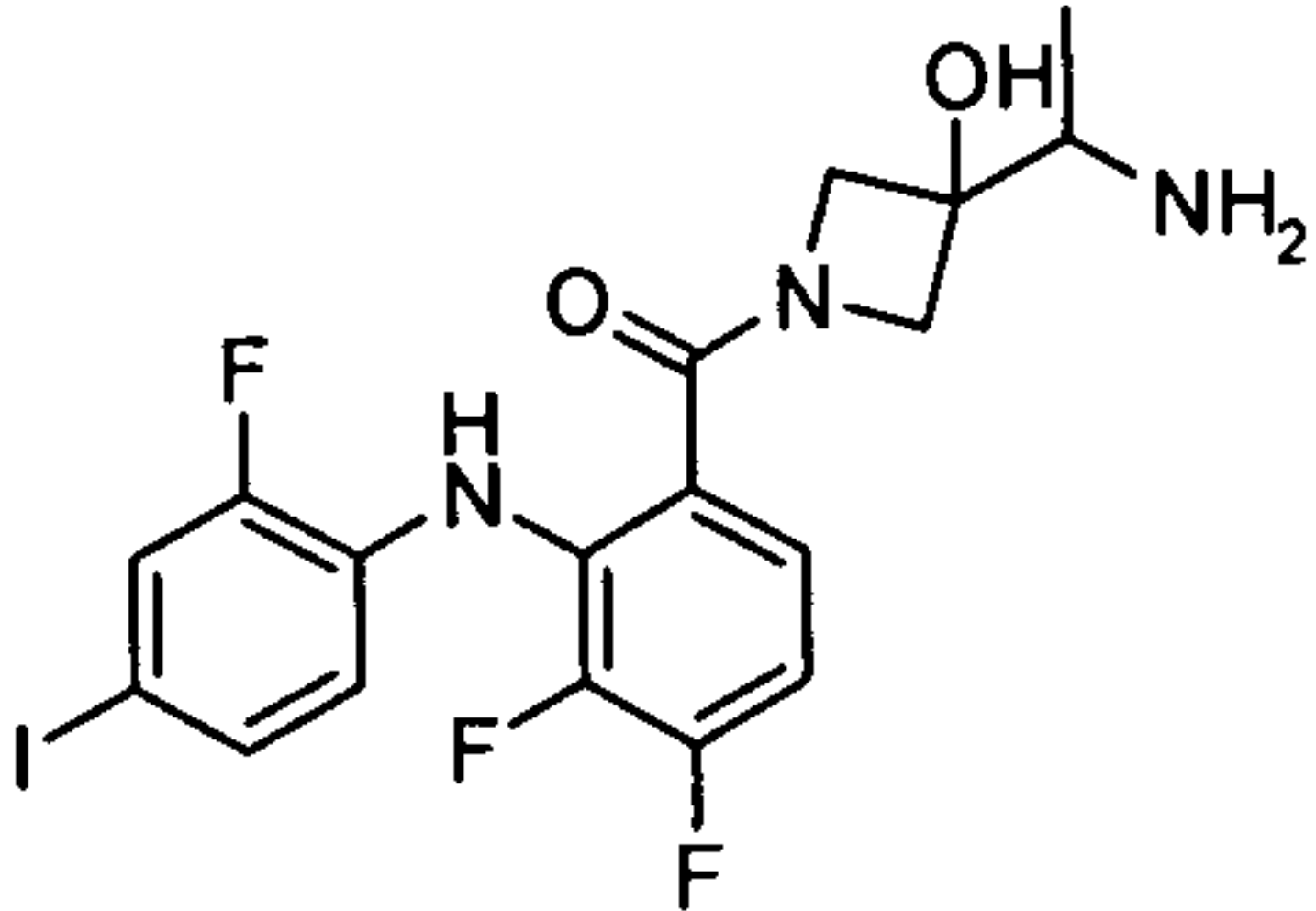
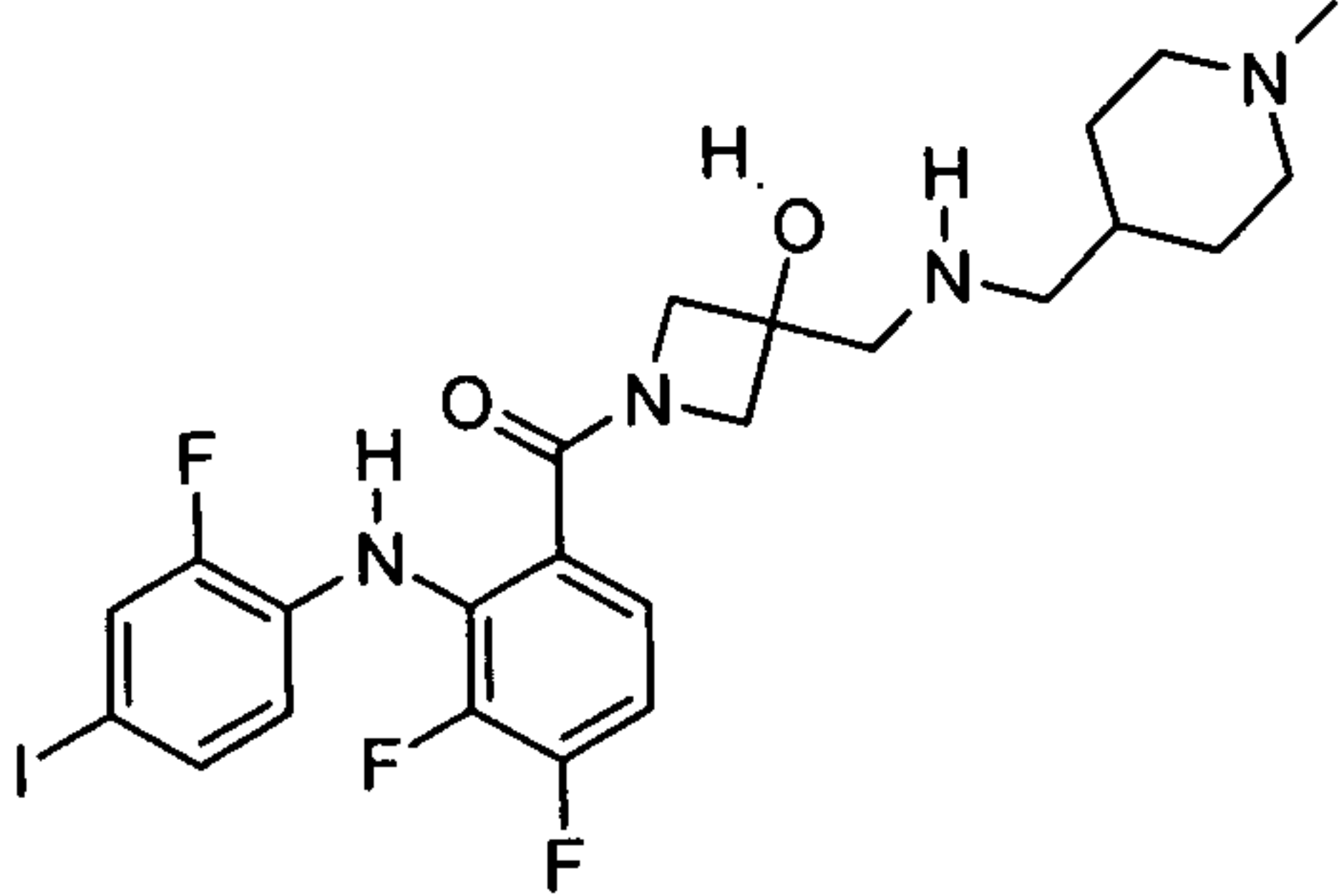
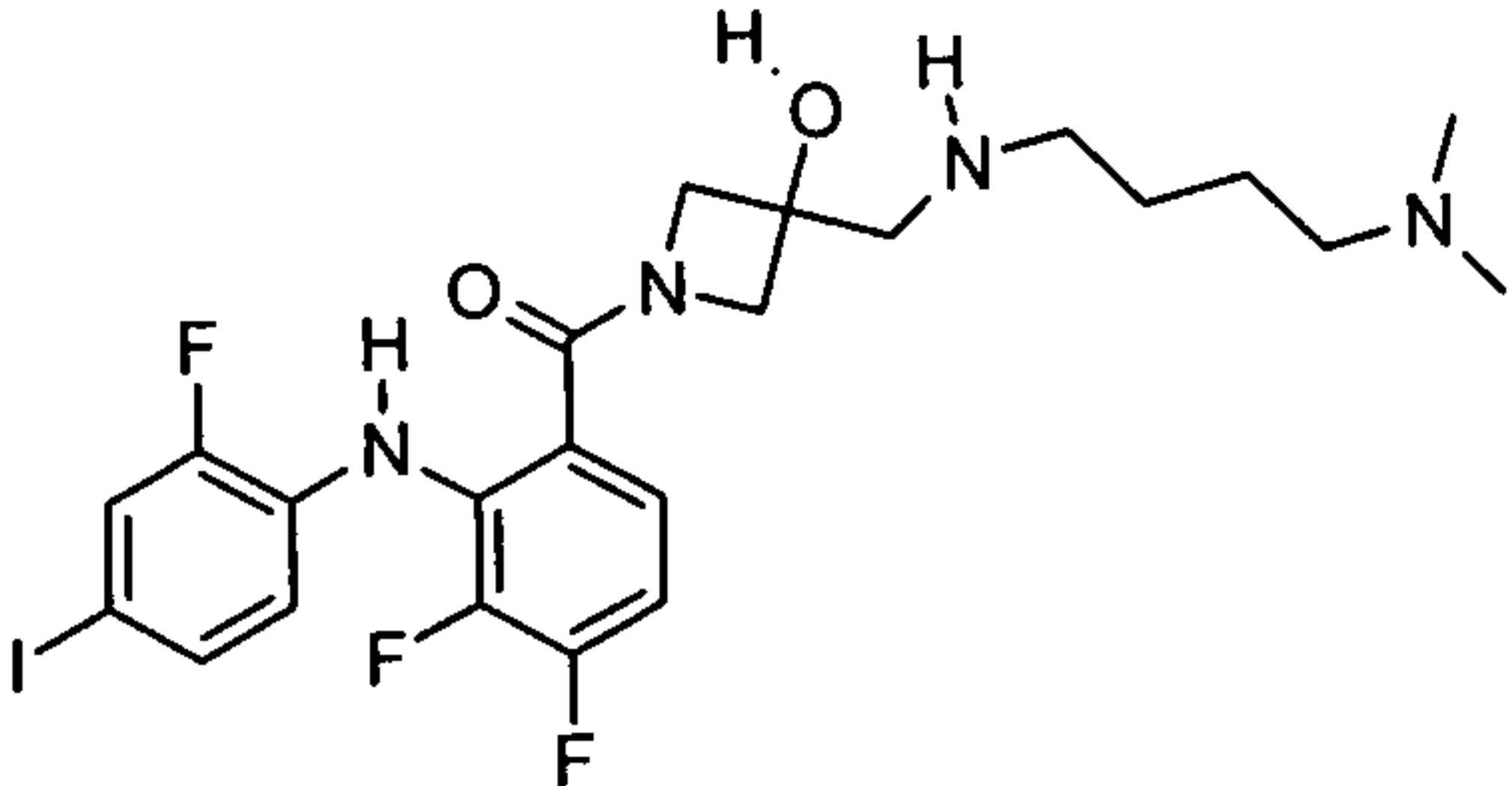
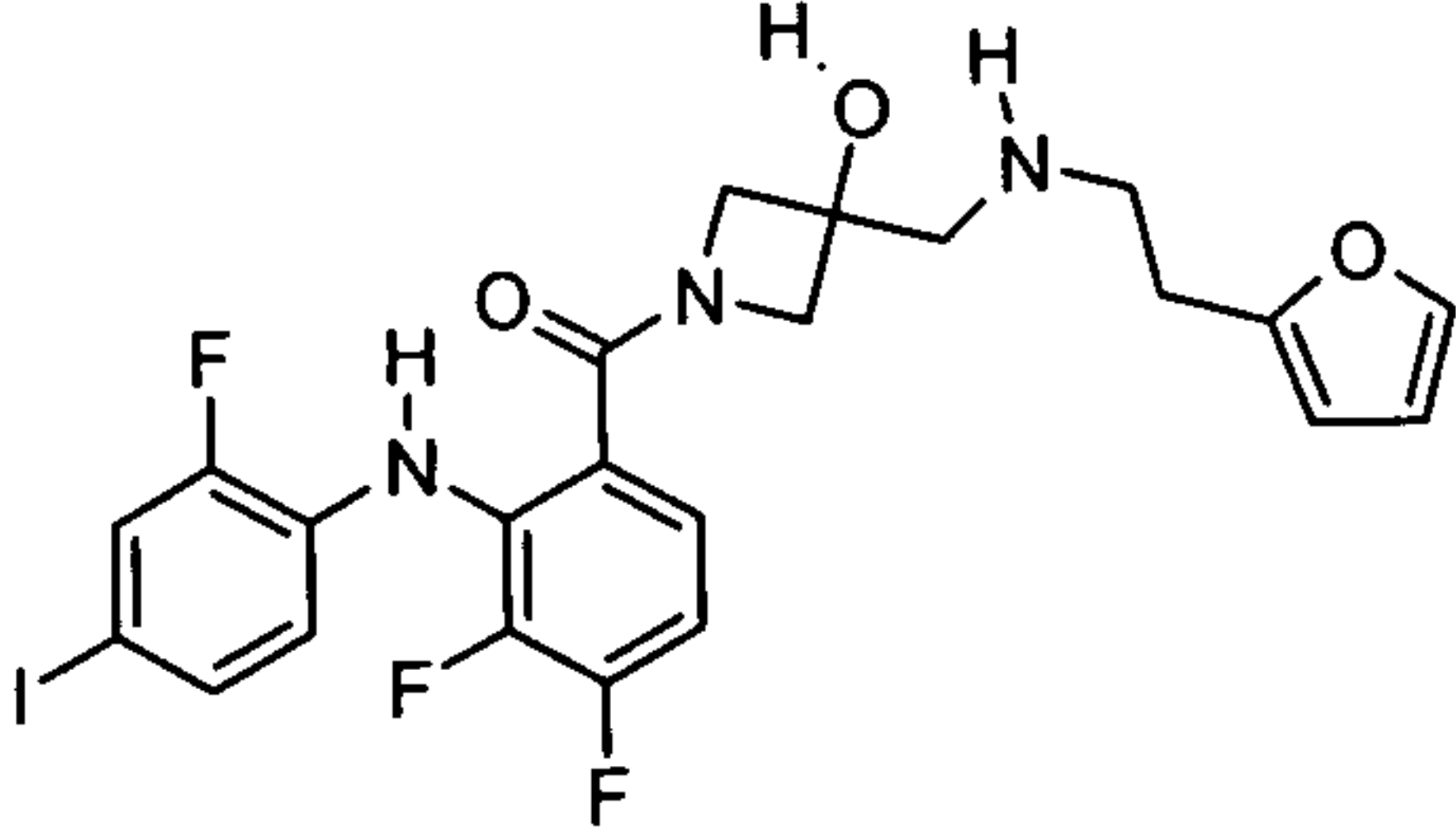
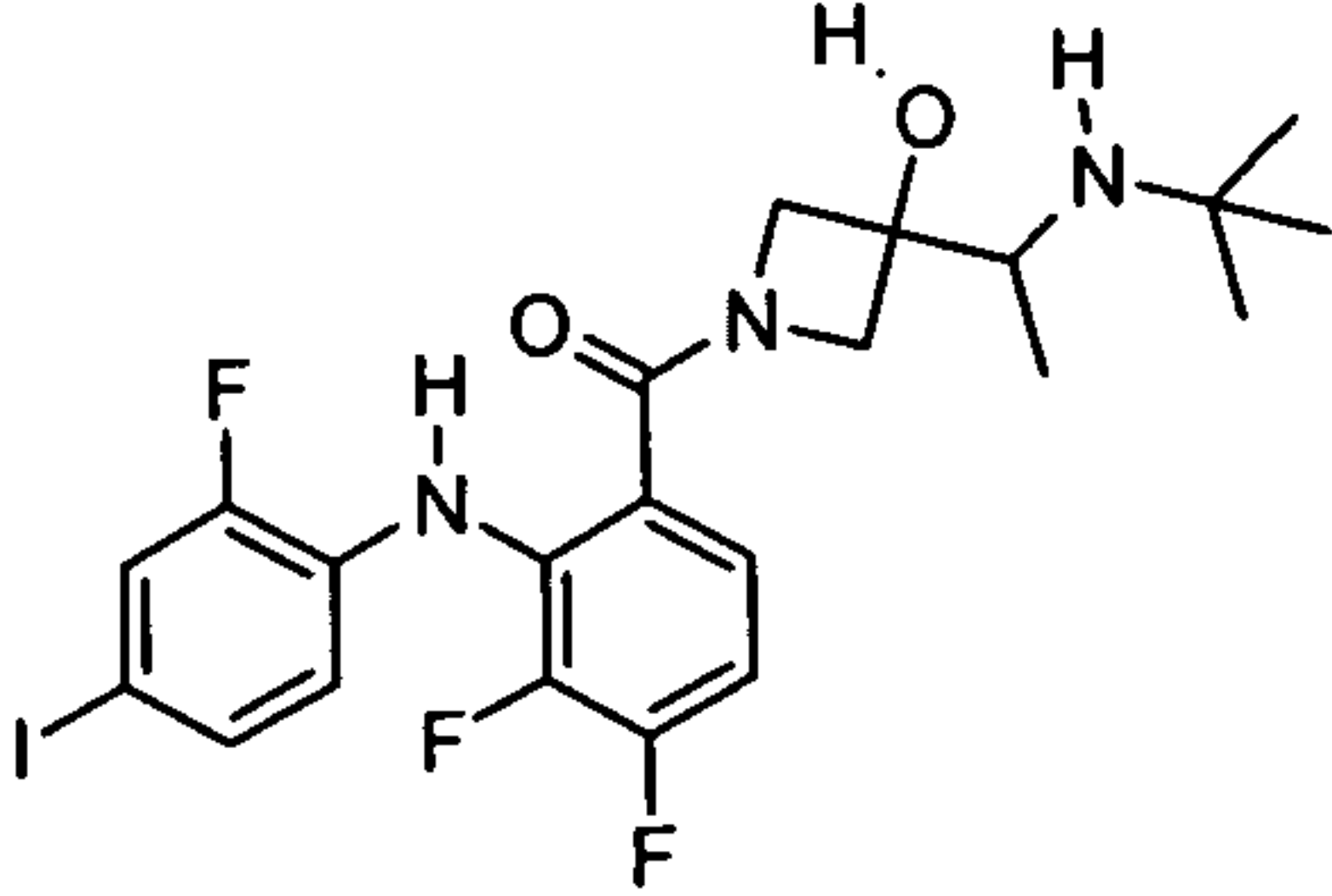
Cmpd No.	Structure	Name
160		3-(1-aminoethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
161		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(1-methylpiperidin-4-yl)methyl]amino}methyl)azetidin-3-ol
162		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[4-(dimethylamino)butyl]amino}methyl)azetidin-3-ol
163		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2-furan-2-ylethyl)amino]methyl}azetidin-3-ol
164		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(1,1-dimethylethyl)amino]ethyl}azetidin-3-ol

Table 1. Representative MEK Inhibitors

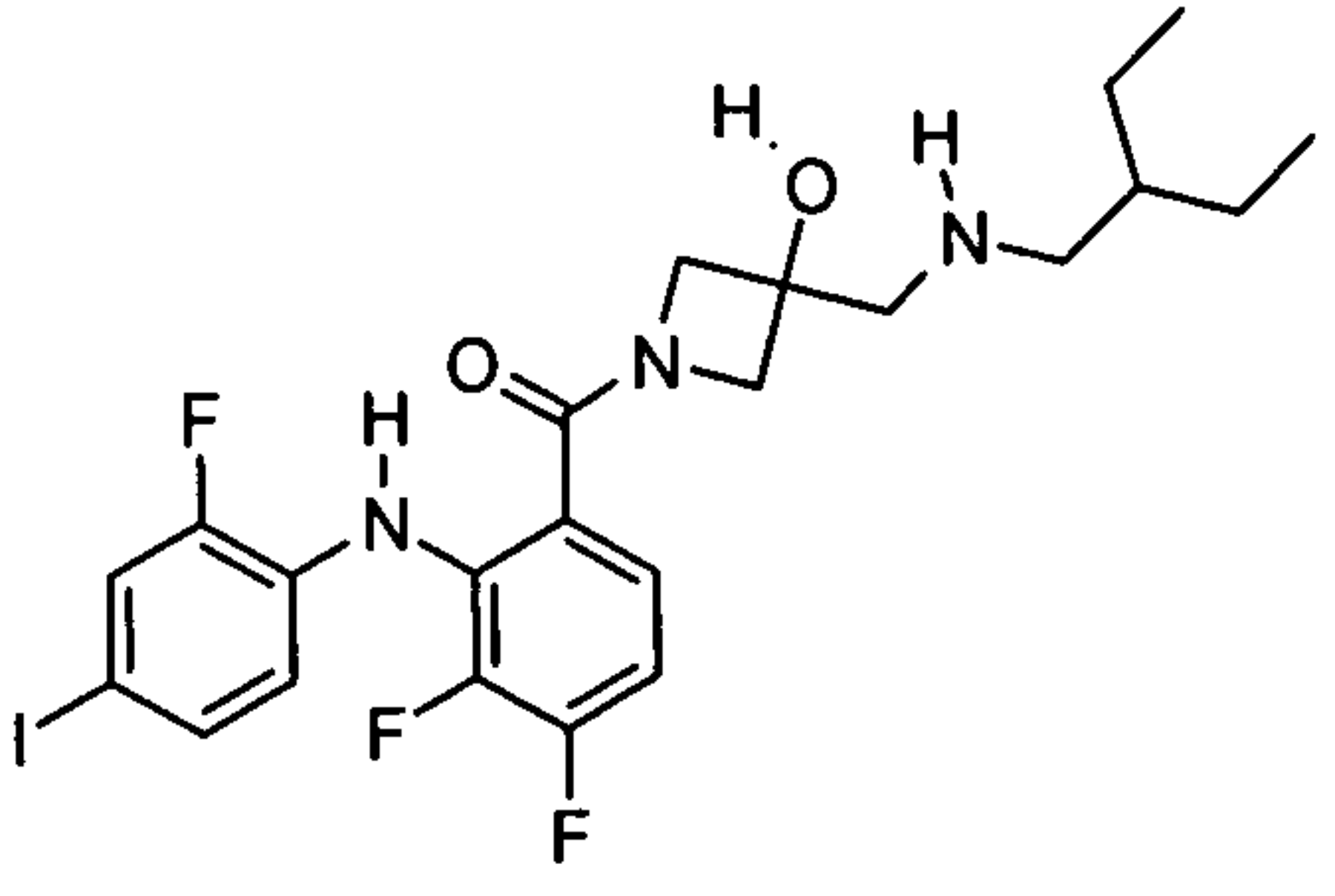
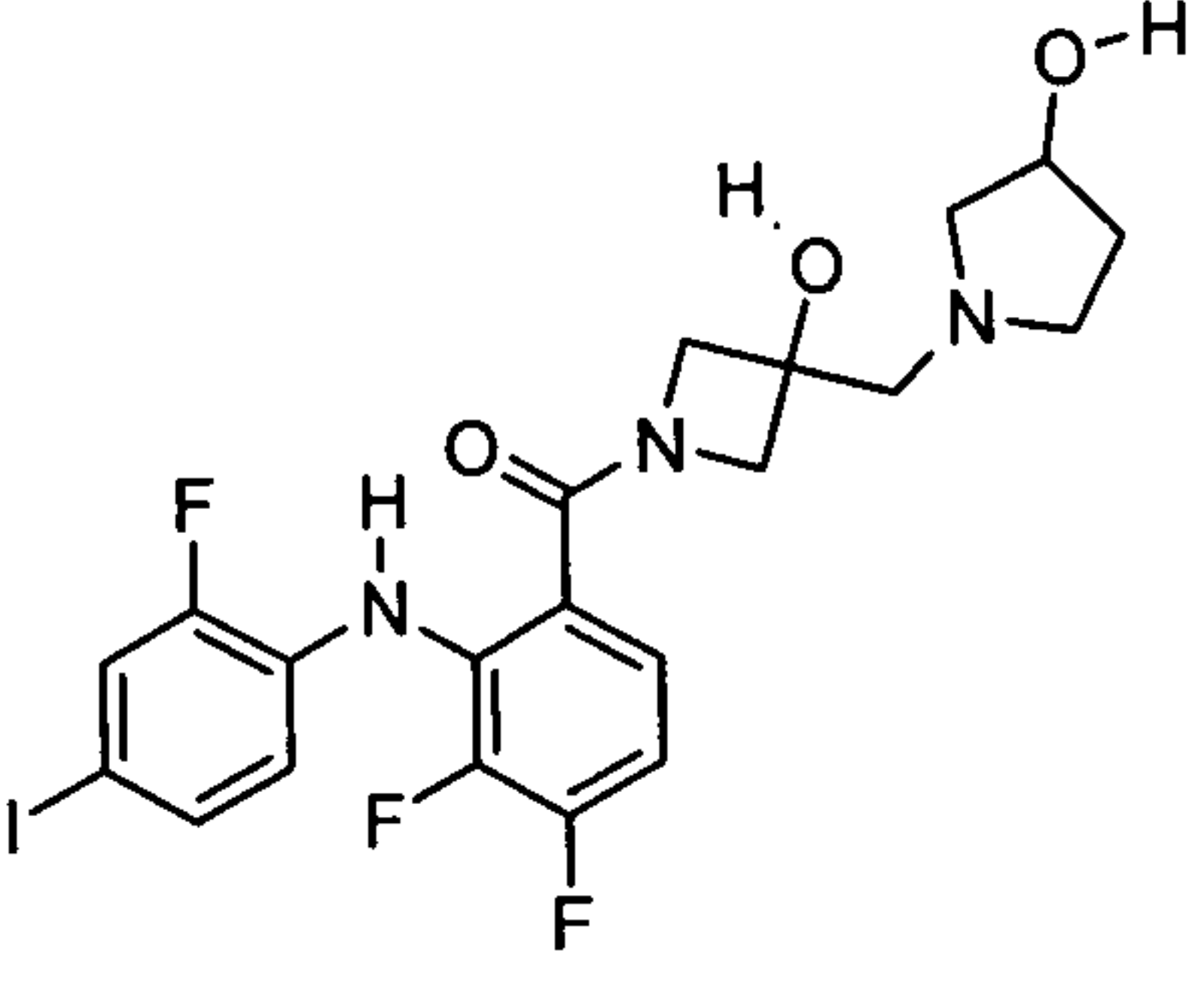
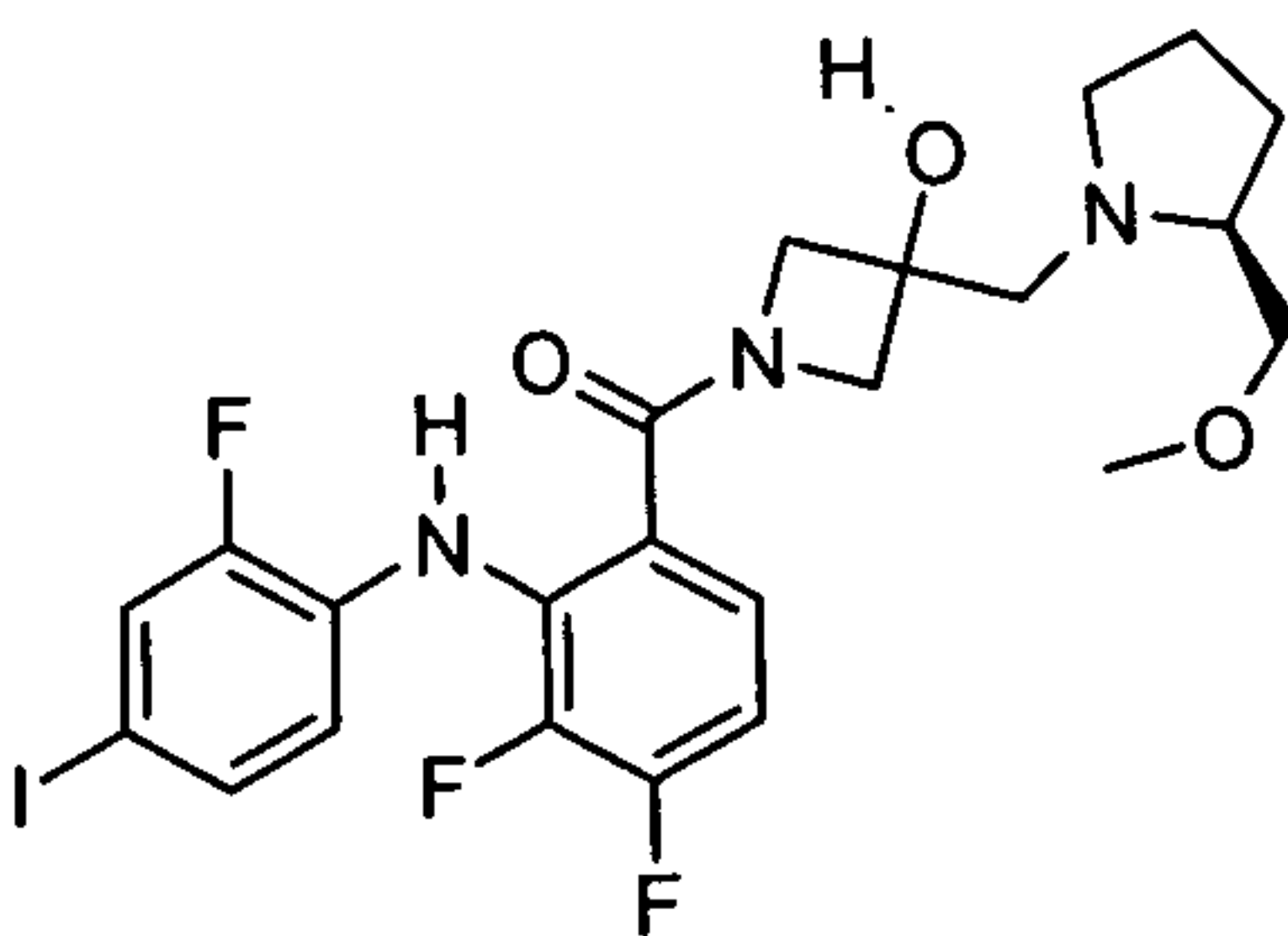
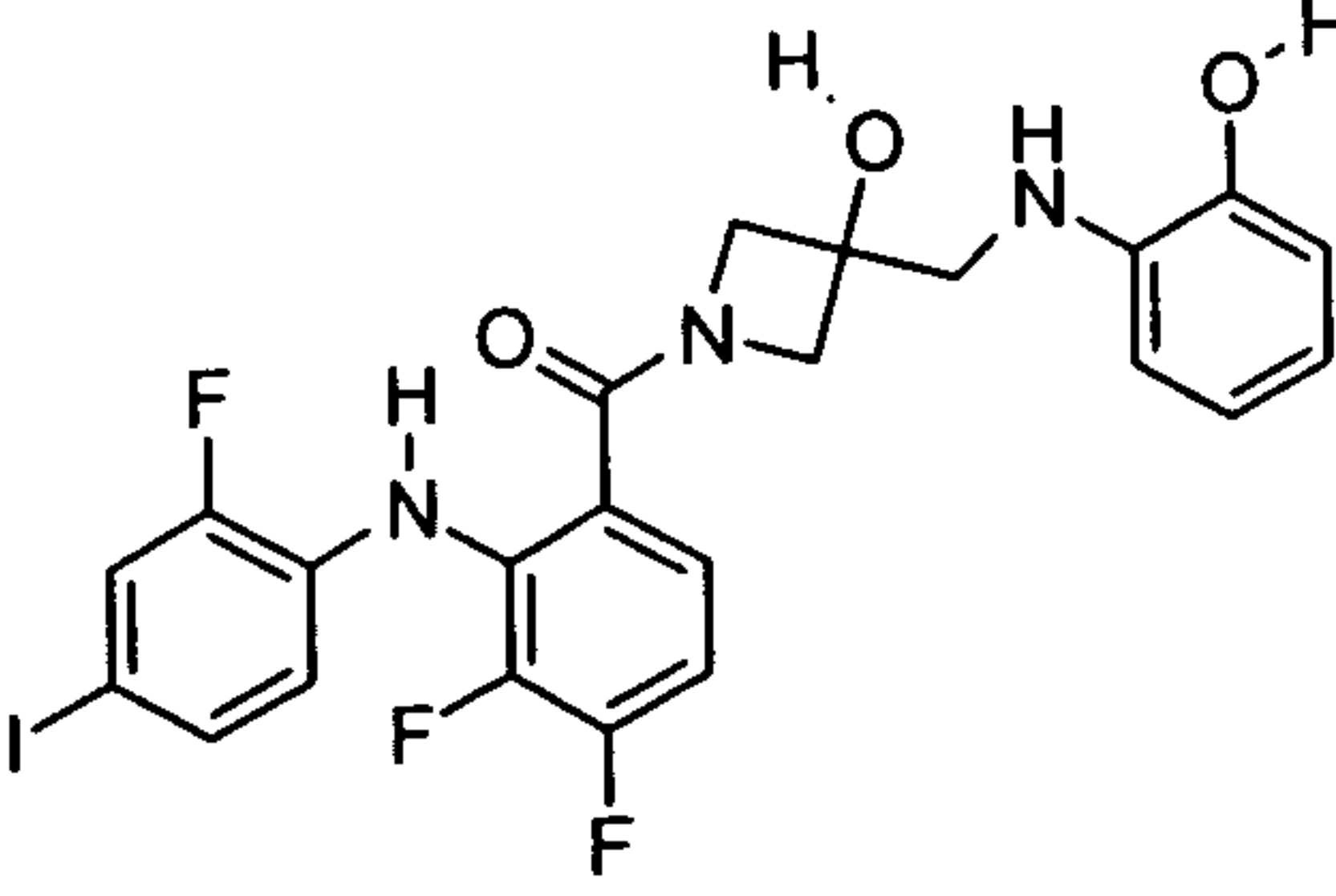
Cmpd No.	Structure	Name
165		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(2-ethylbutyl)amino}methyl}azetidin-3-ol
166		1-{{1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl}methyl}pyrrolidin-3-ol
167		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-((2 <i>S</i>)-2-[(methyloxy)methyl]pyrrolidin-1-yl)methyl}azetidin-3-ol
168		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(2-hydroxyphenyl)amino}methyl}azetidin-3-ol

Table 1. Representative MEK Inhibitors

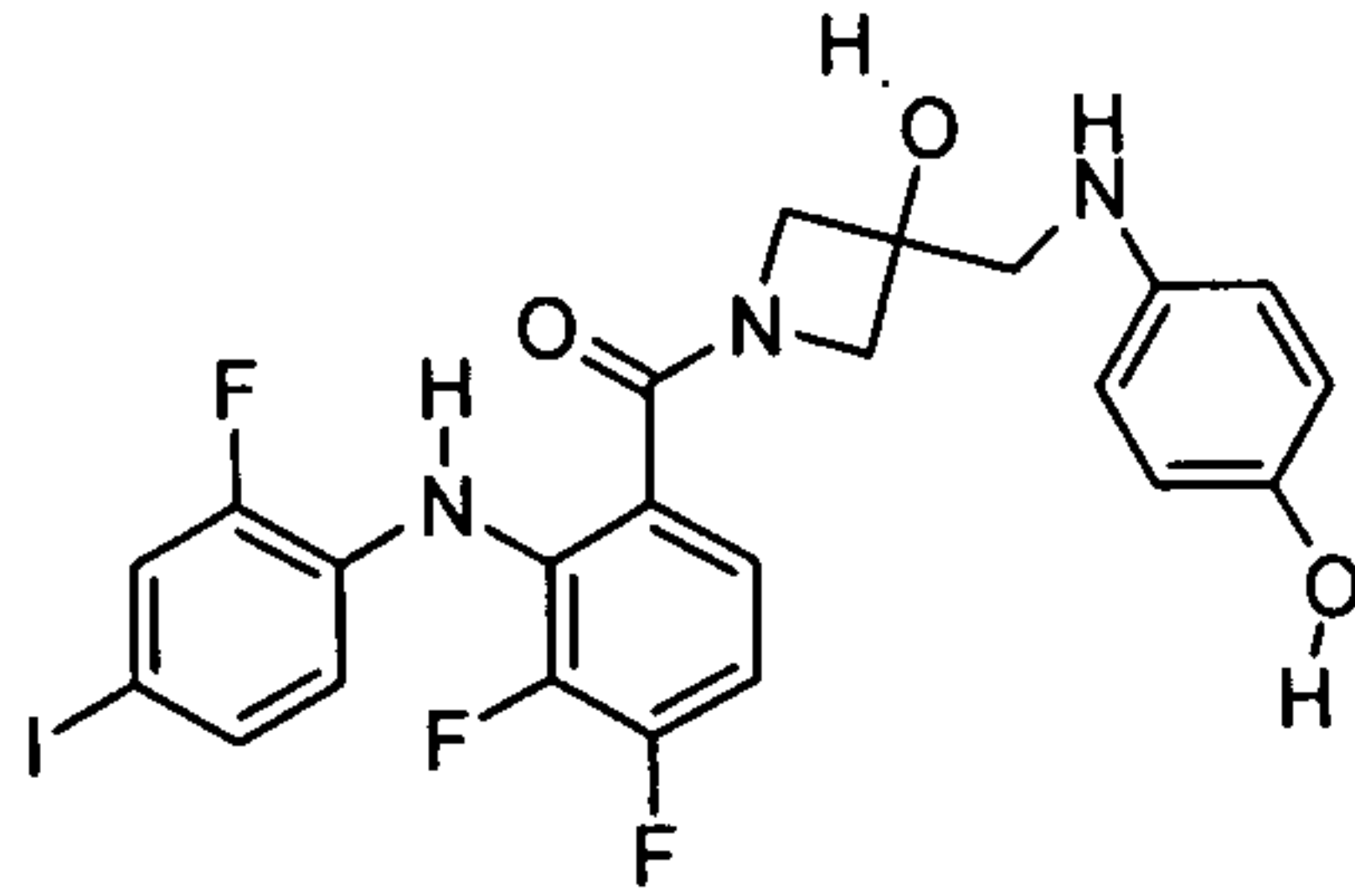
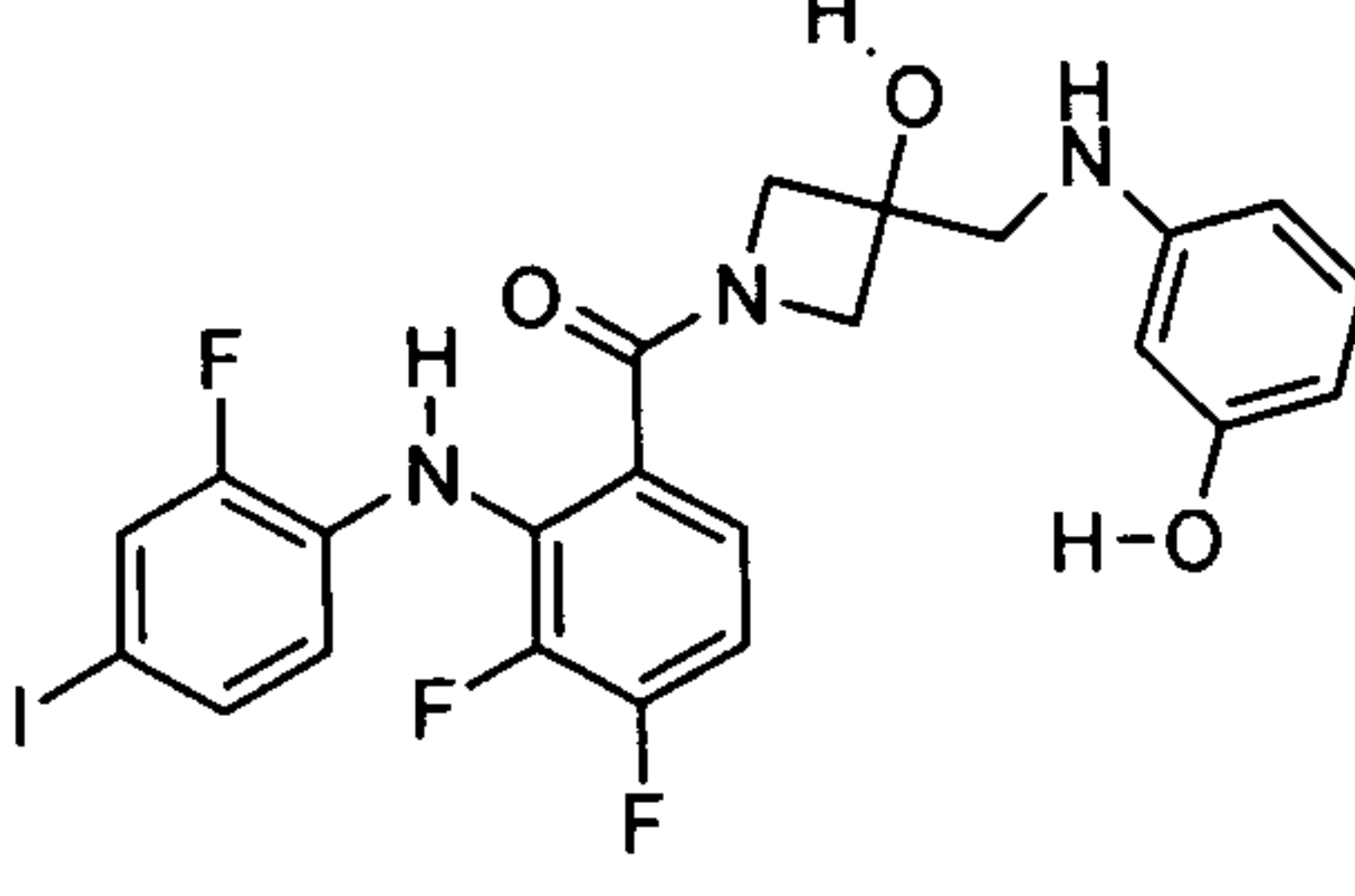
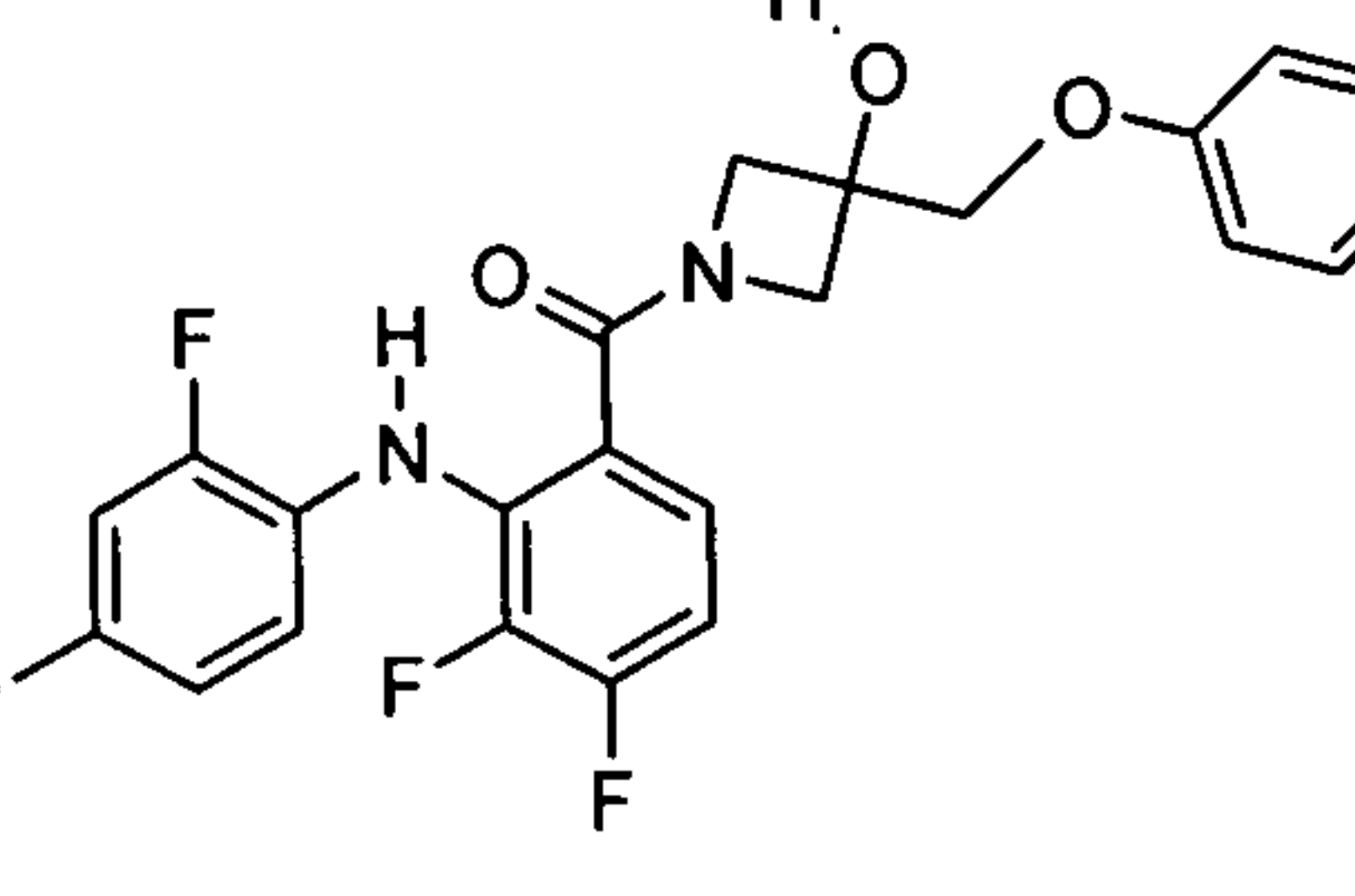
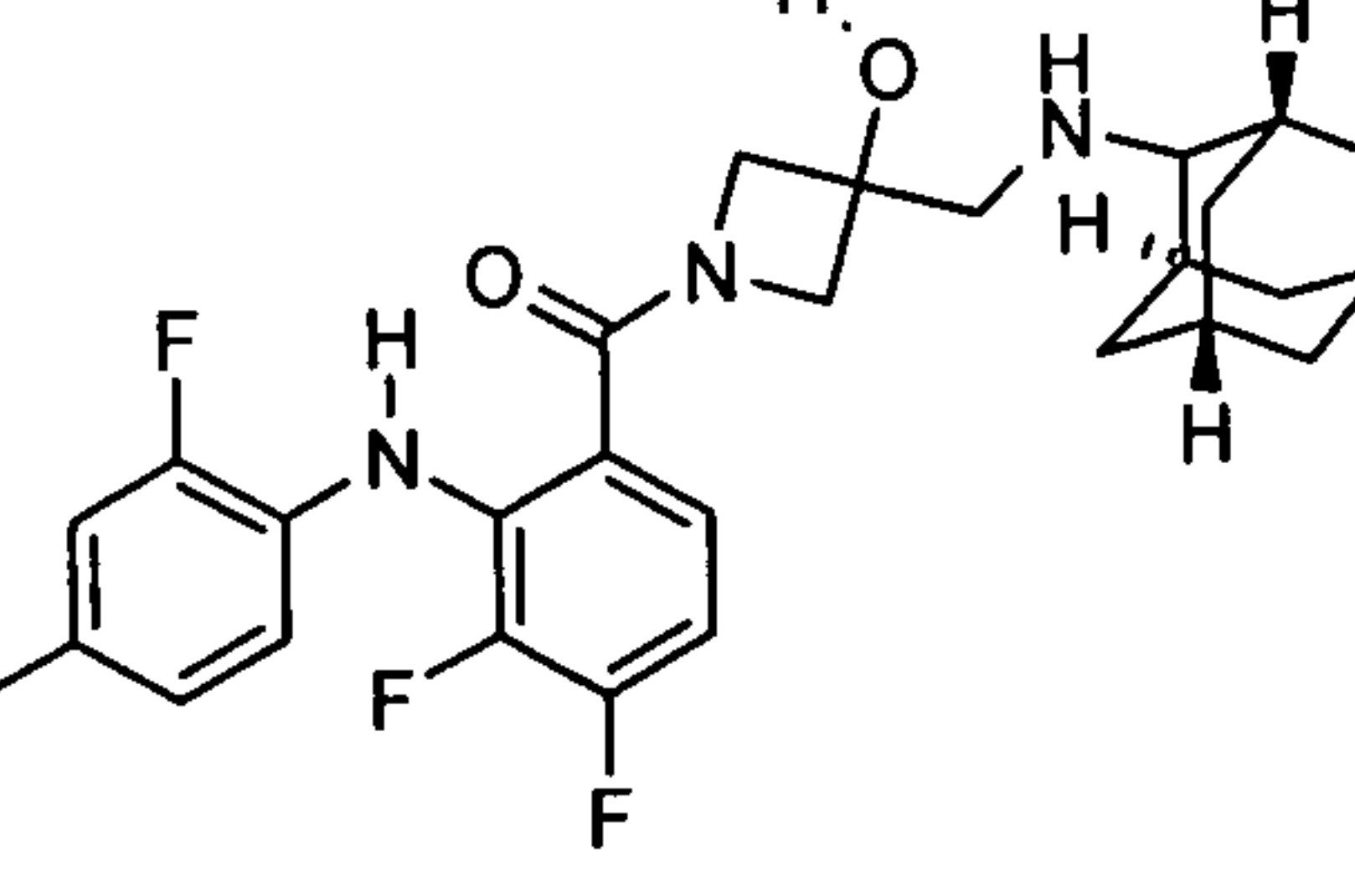
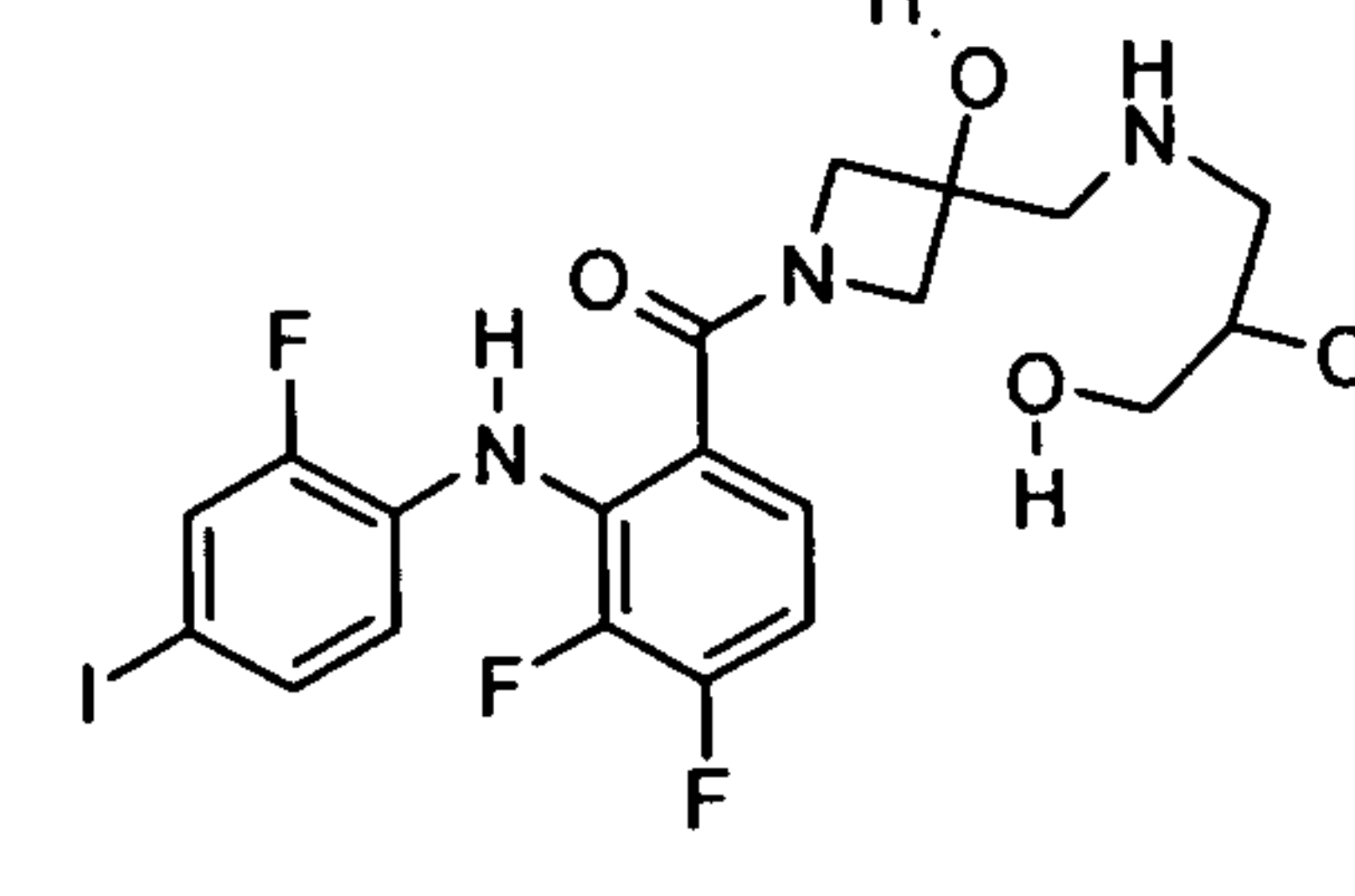
Cmpd No.	Structure	Name
169		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(4-hydroxyphenyl)amino}methyl}azetidin-3-ol
170		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(3-hydroxyphenyl)amino}methyl}azetidin-3-ol
171		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenyloxy)methyl]azetidin-3-ol
172		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[(1r,3r,5R,7R)-tricyclo[3.3.1.1 ^{3,7}]dec-2-ylamino}methyl}azetidin-3-ol
173		3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propane-1,2-diol

Table 1. Representative MEK Inhibitors

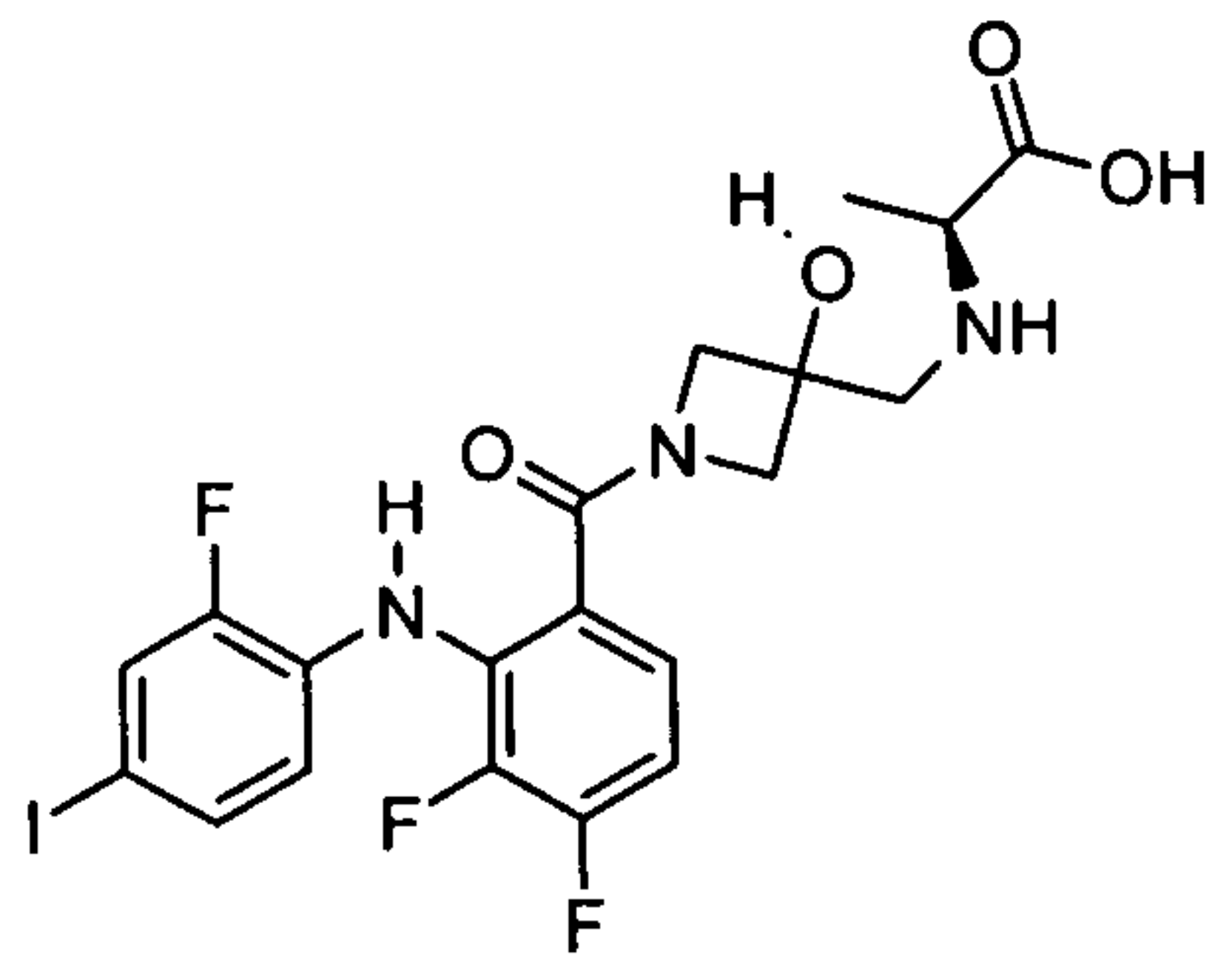
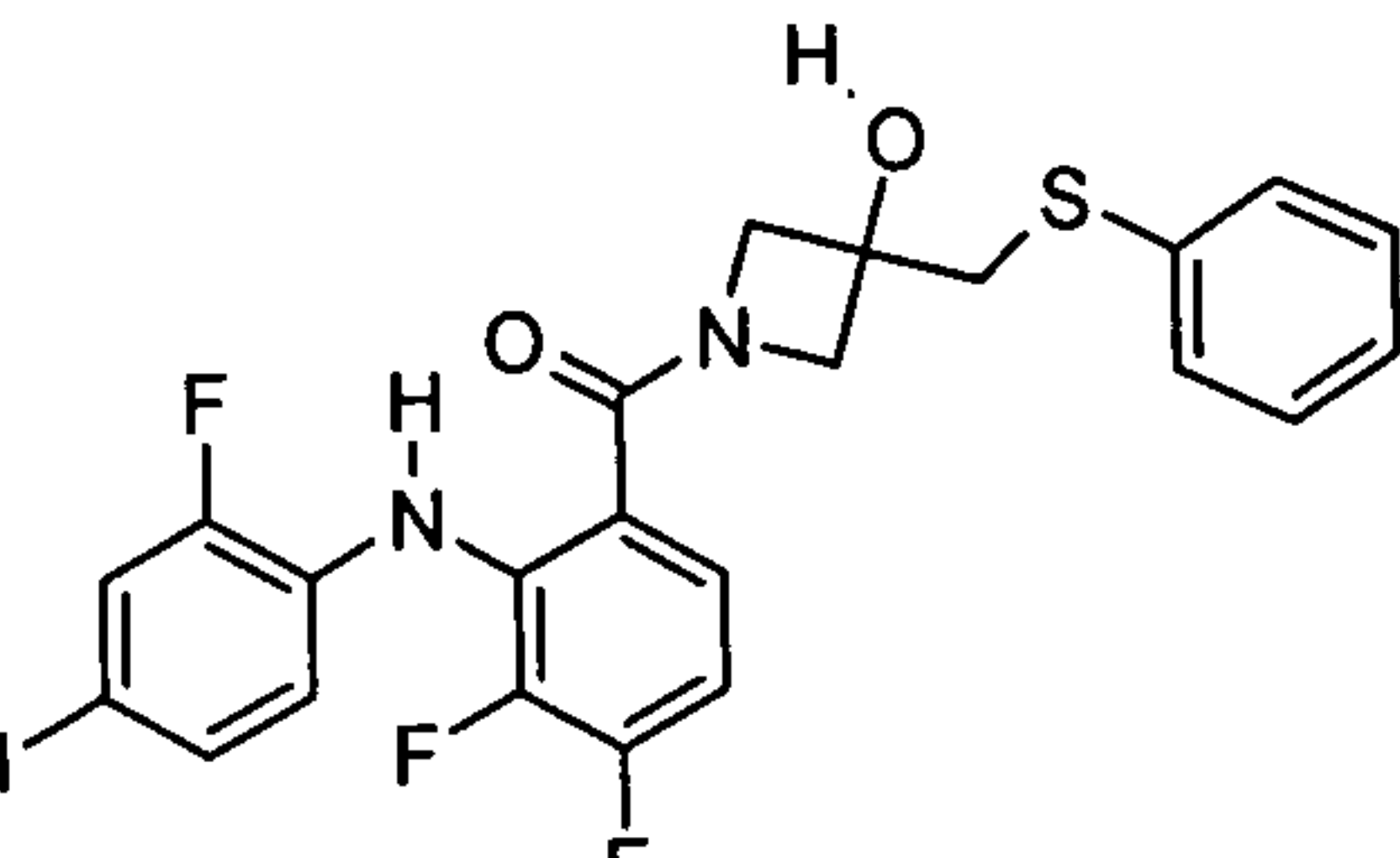
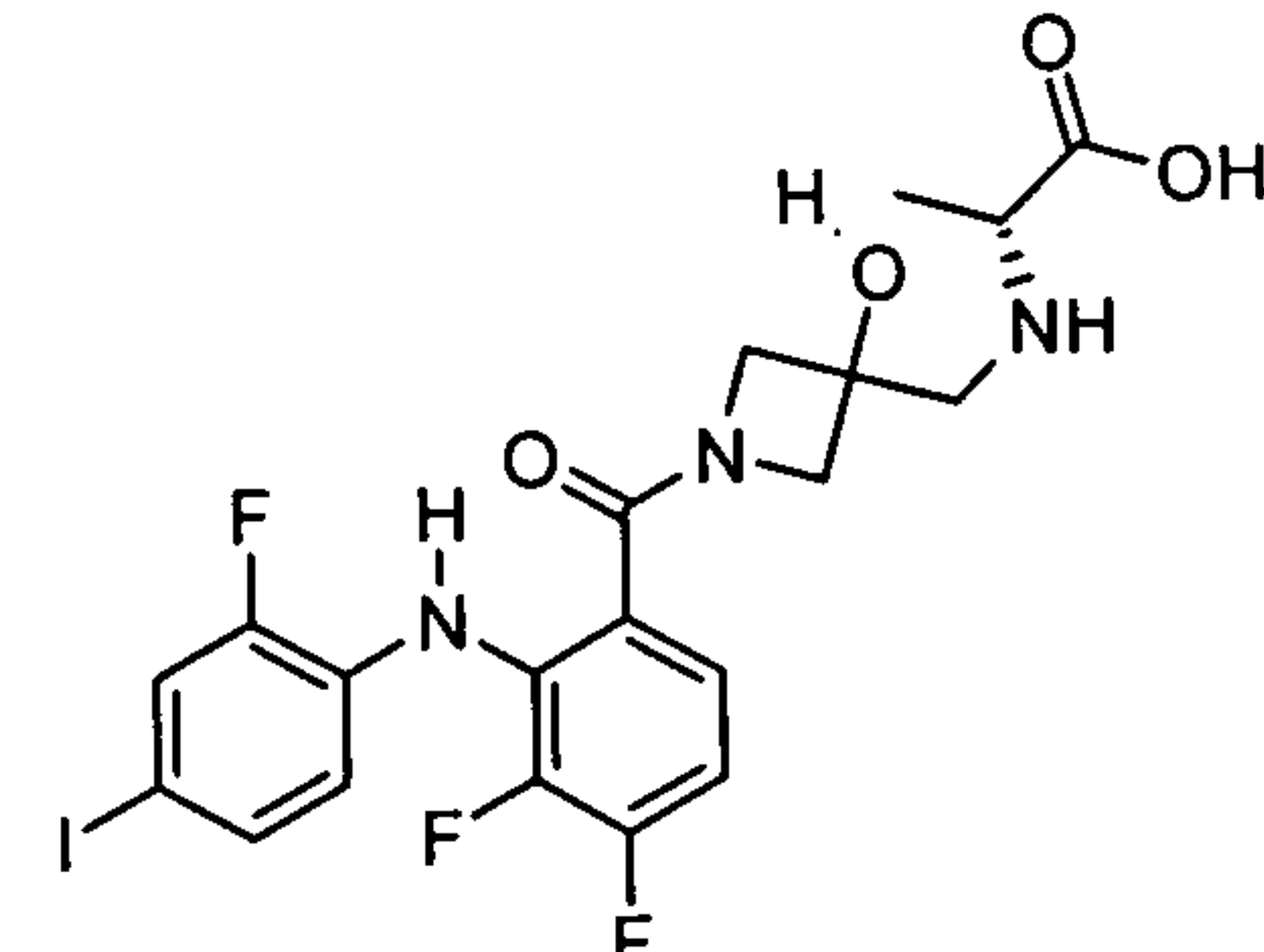
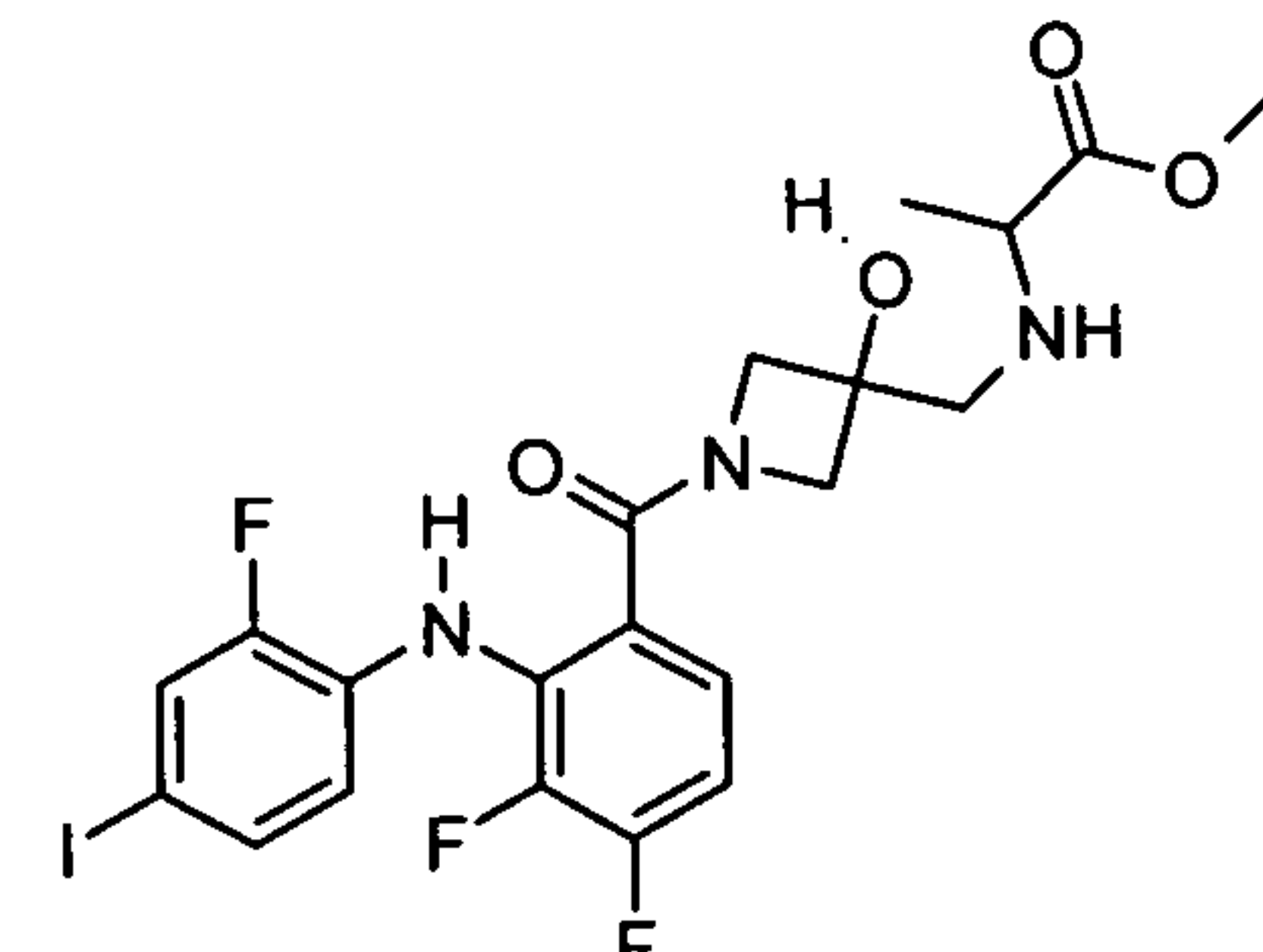
Cmpd No.	Structure	Name
174		<i>N</i> -[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl]-L-alanine
175		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(phenylthio)methyl]azetidin-3-ol
176		<i>N</i> -[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl]-D-alanine
177		methyl <i>N</i> -[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl]alaninate

Table 1. Representative MEK Inhibitors

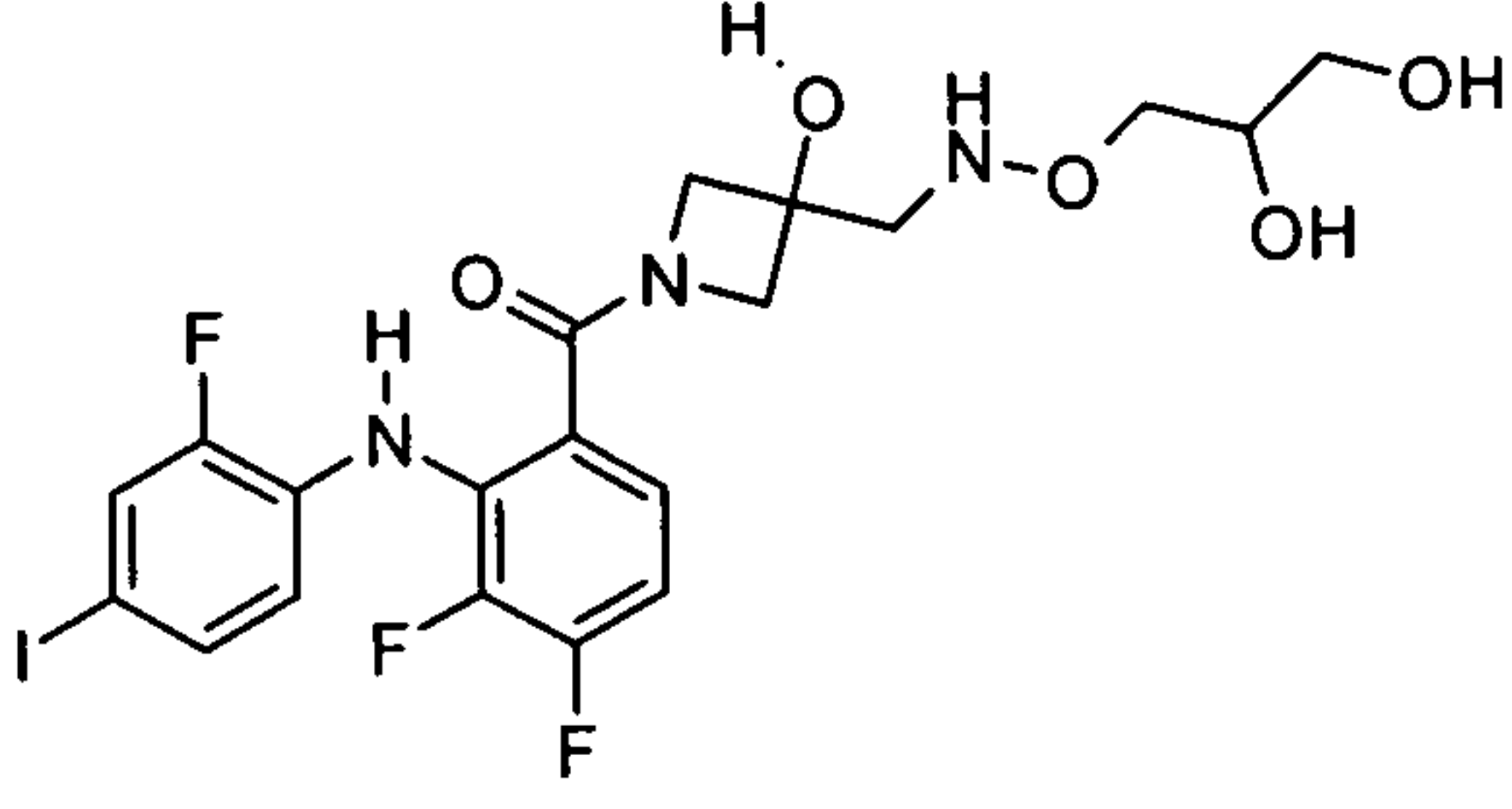
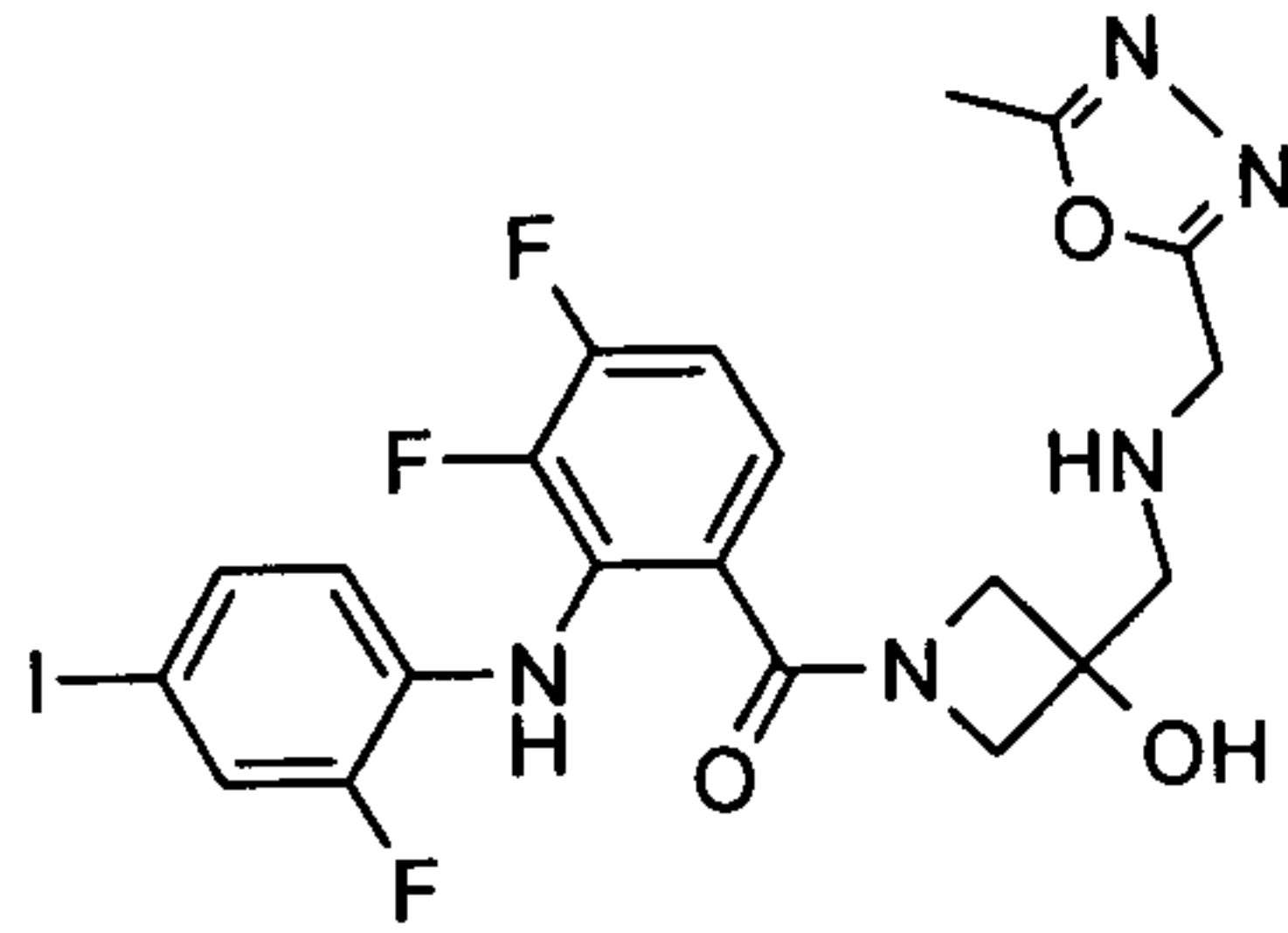
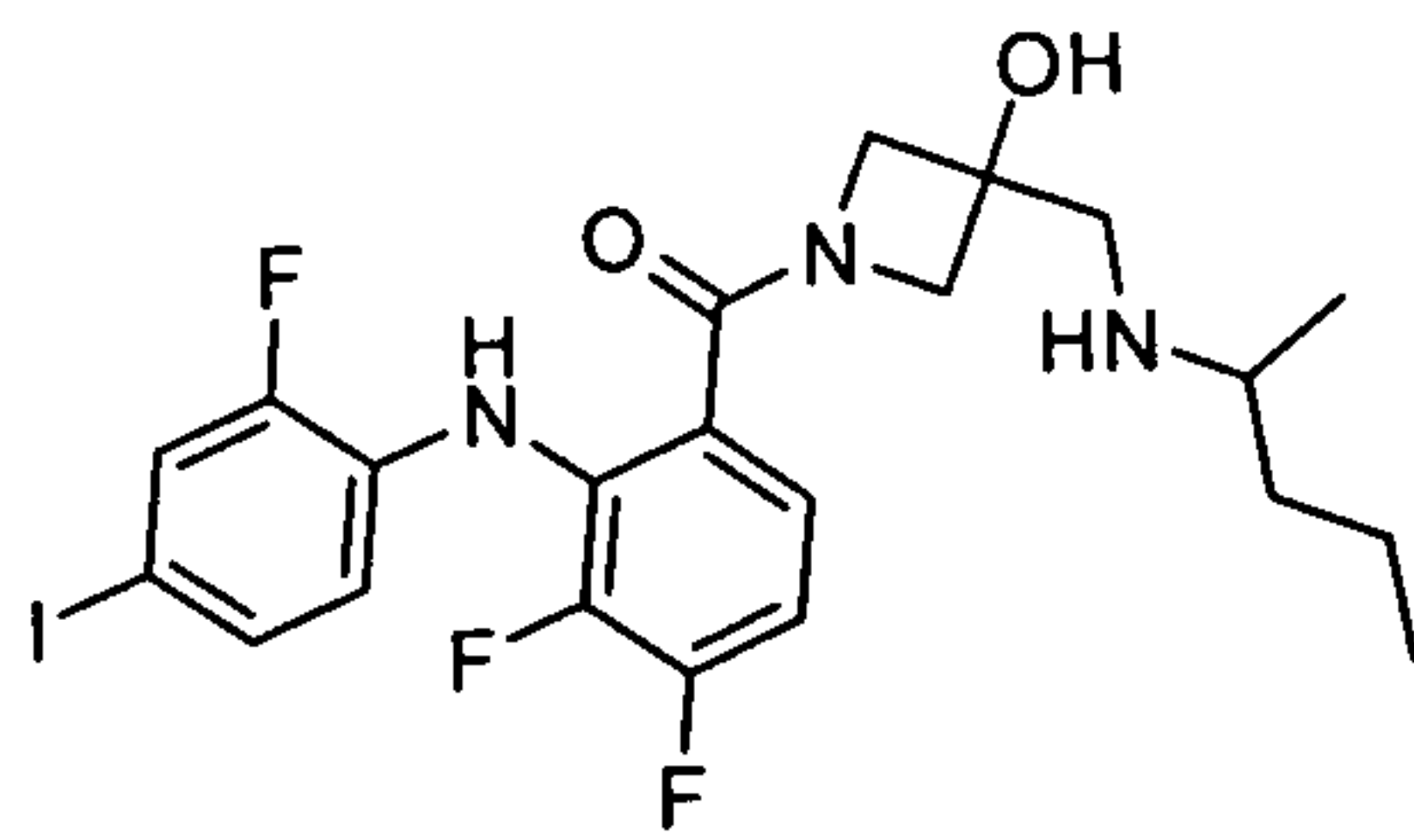
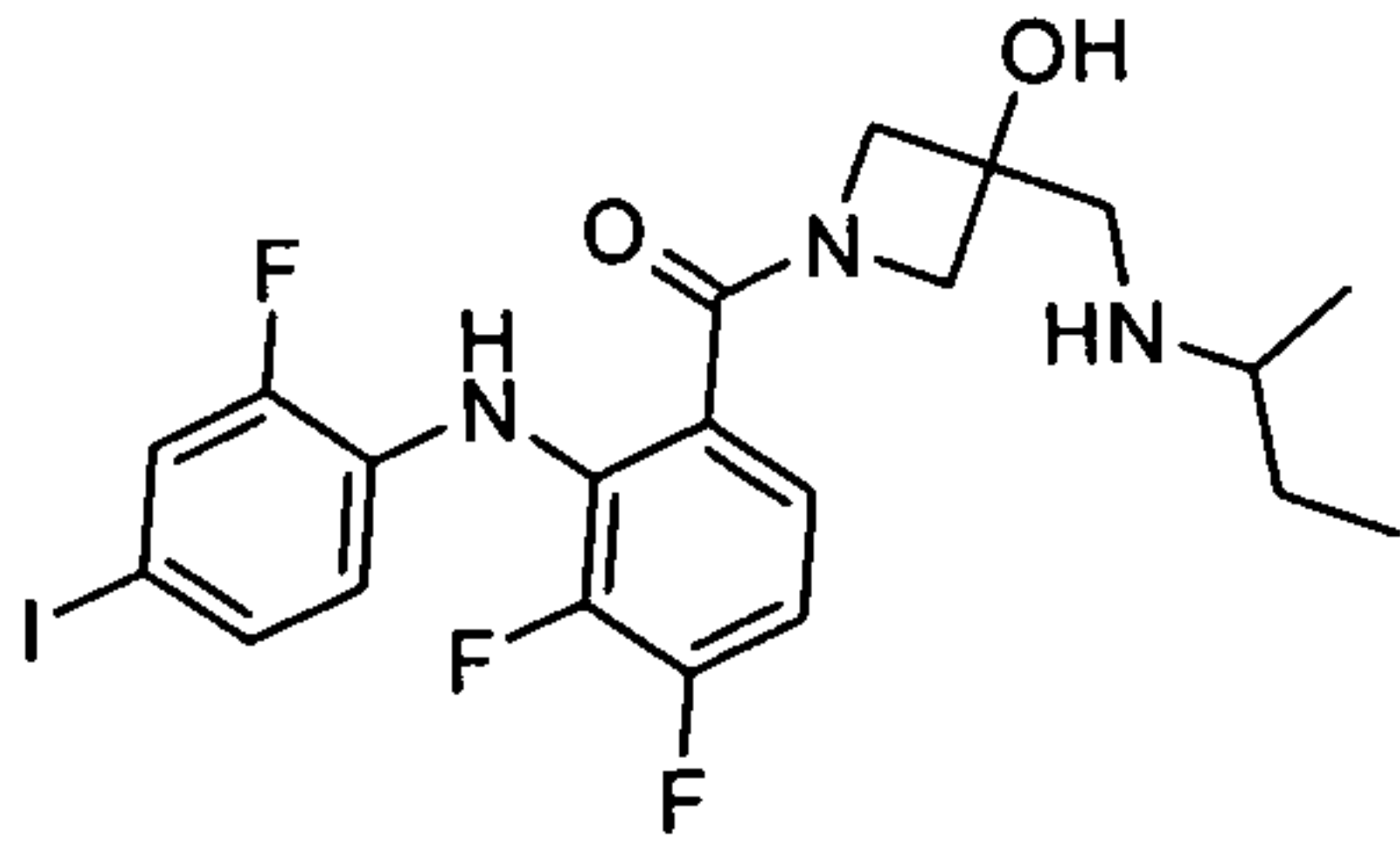
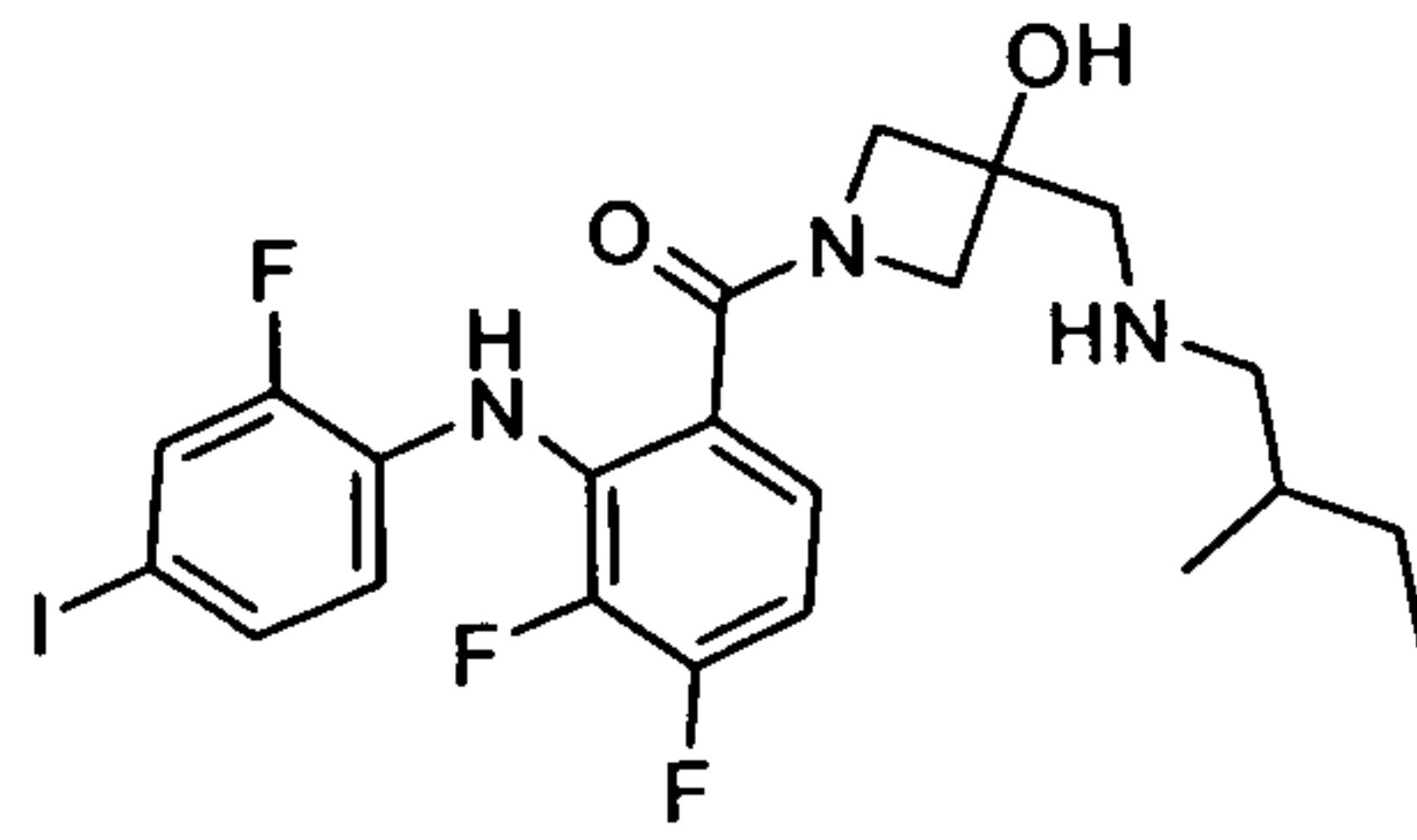
Cmpd No.	Structure	Name
178		3-(((1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-hydroxyazetidin-3-yl)methyl)amino)oxy]propane-1,2-diol
179		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((5-methyl-1,3,4-oxadiazol-2-yl)methyl)amino)methylazetidin-3-ol
180		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1-methylbutyl)amino)methyl)azetidin-3-ol
181		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1-methylpropyl)amino)methyl)azetidin-3-ol
182		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((2-methylbutyl)amino)methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

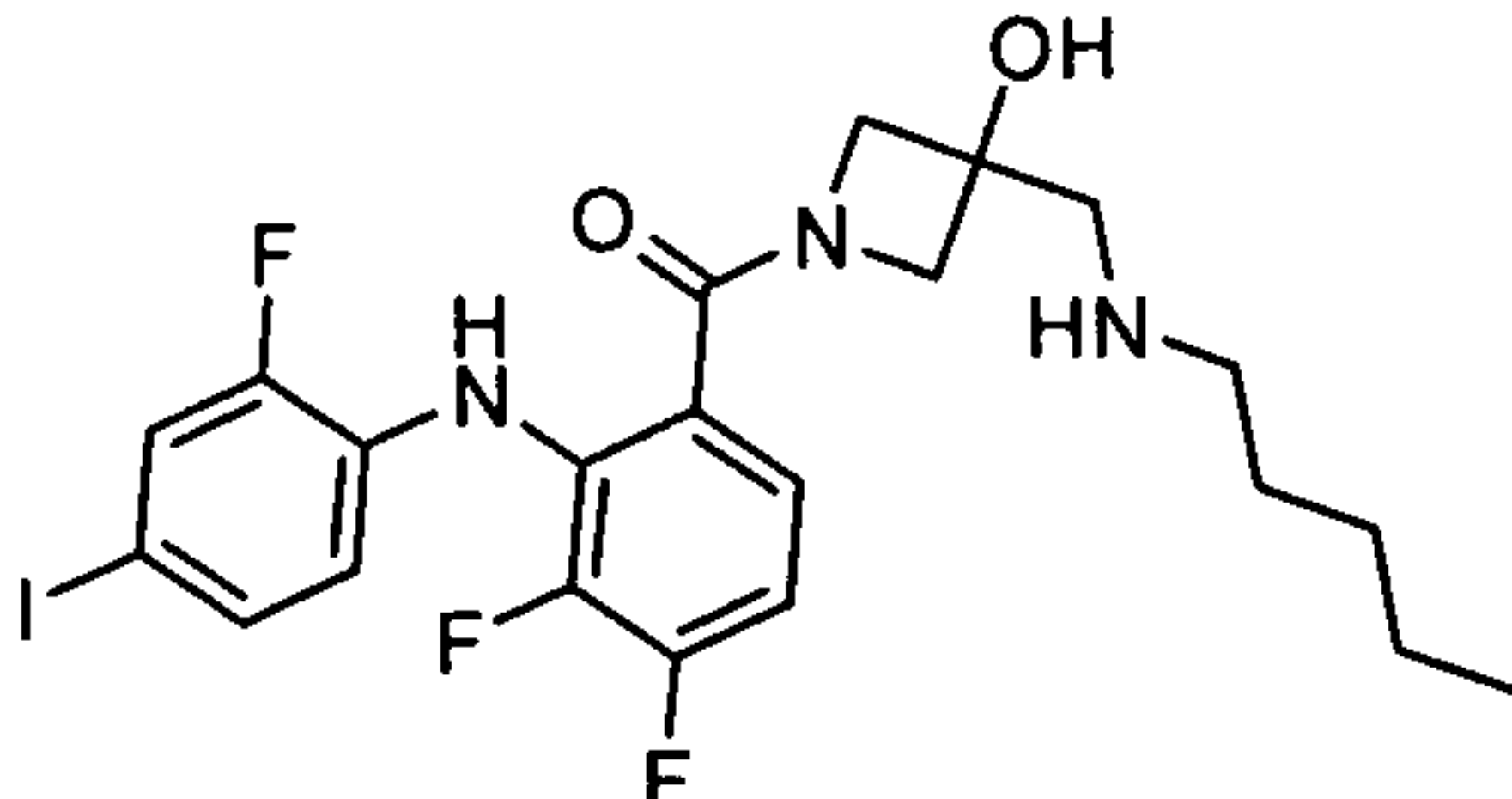
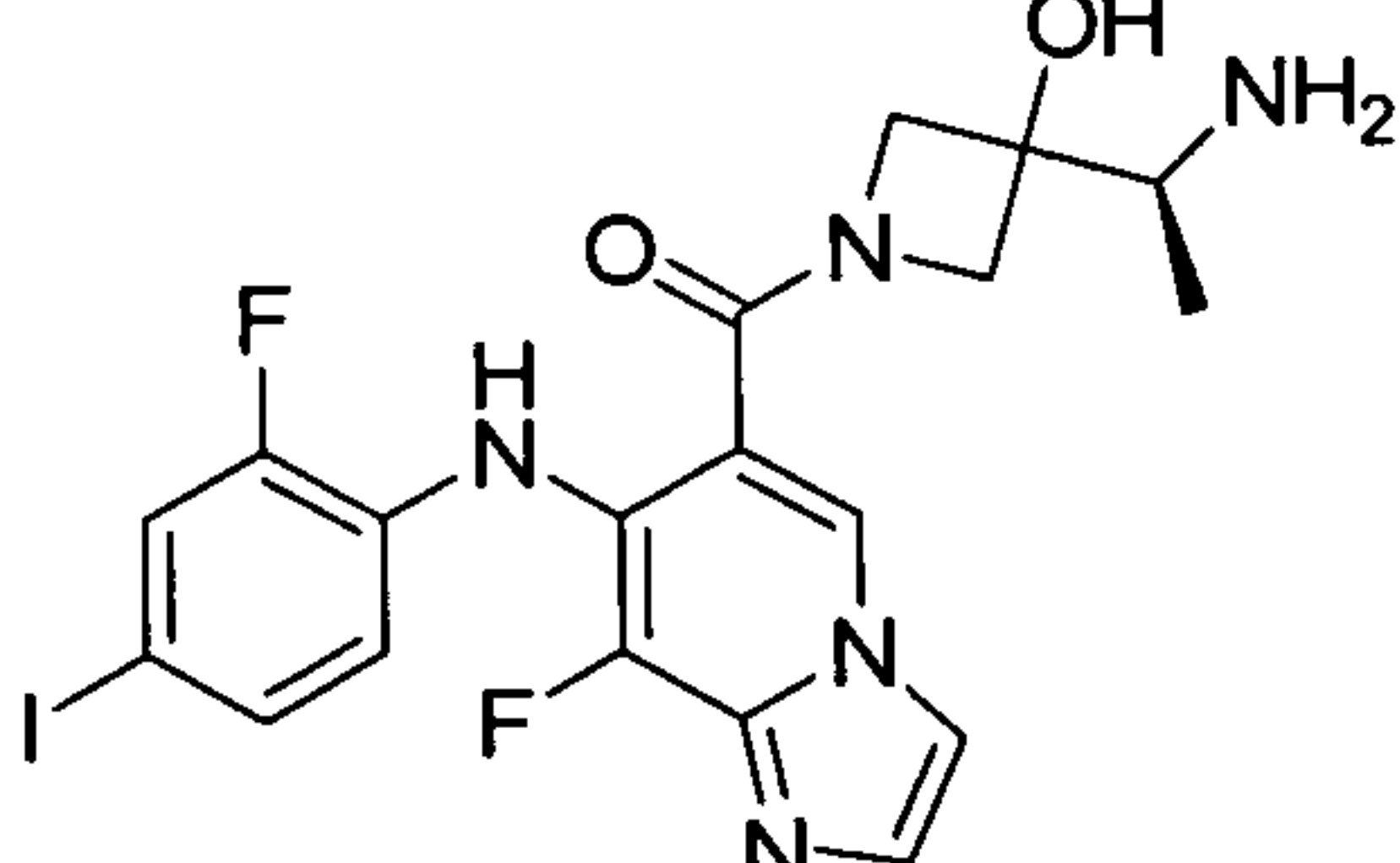
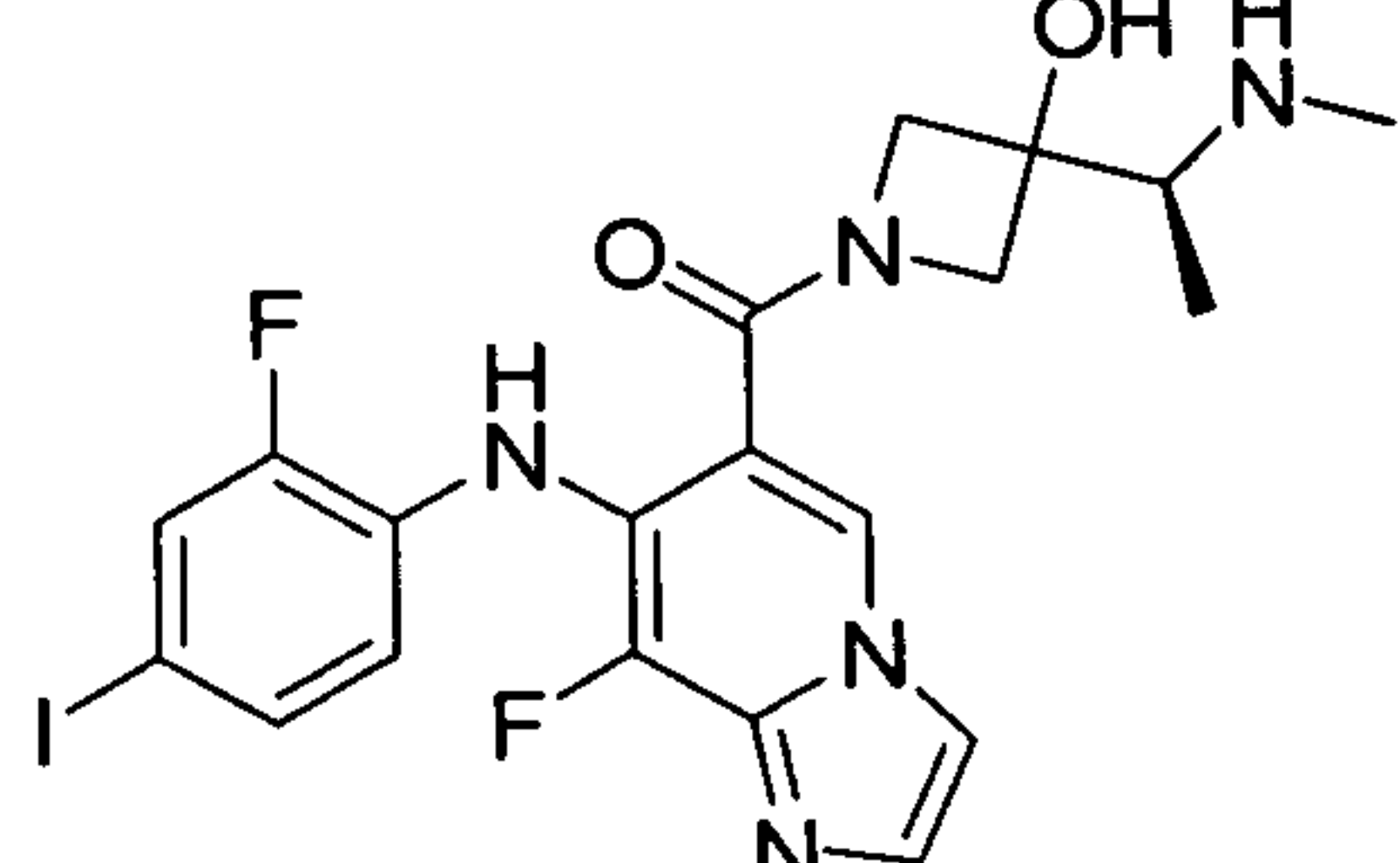
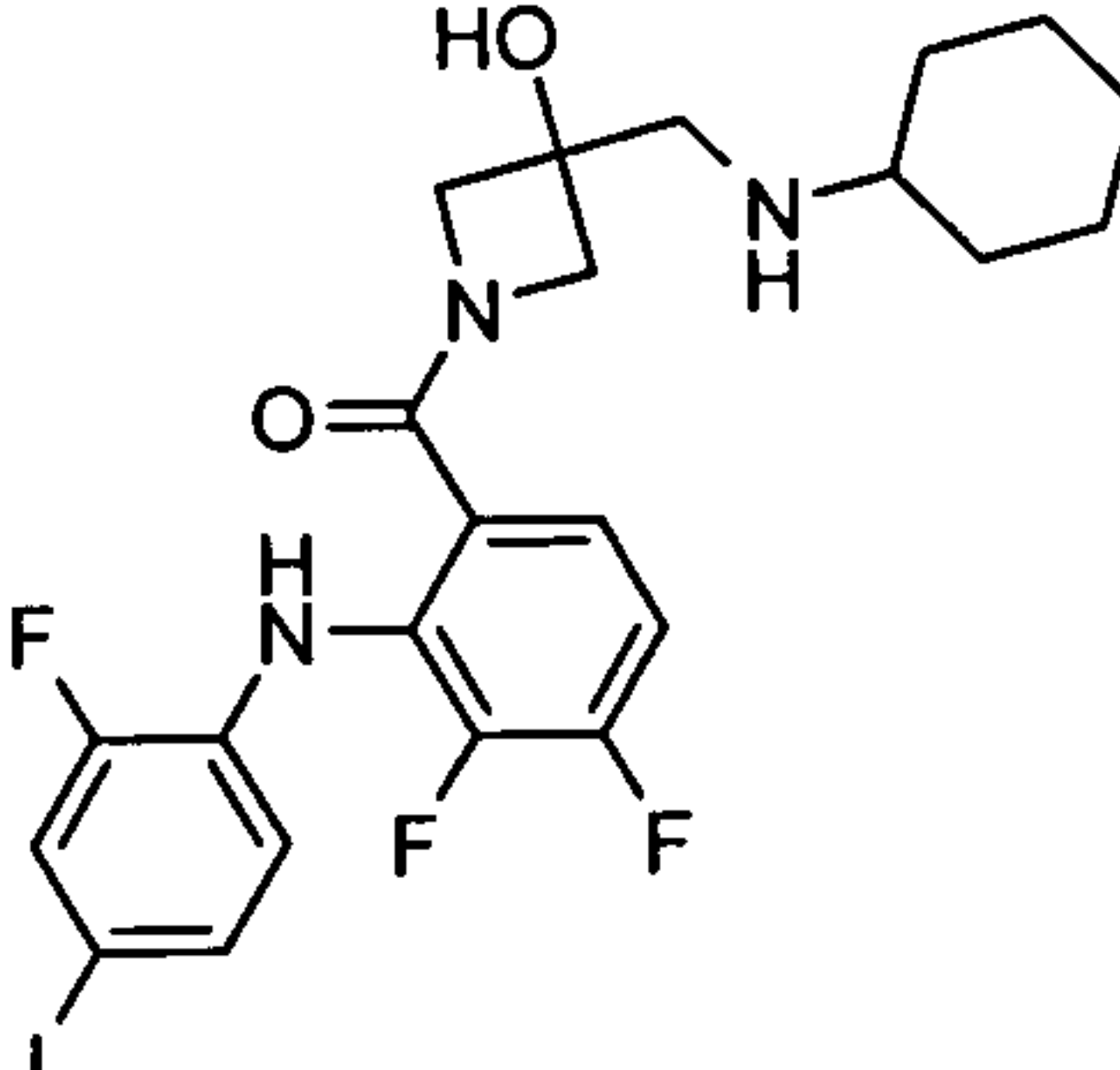
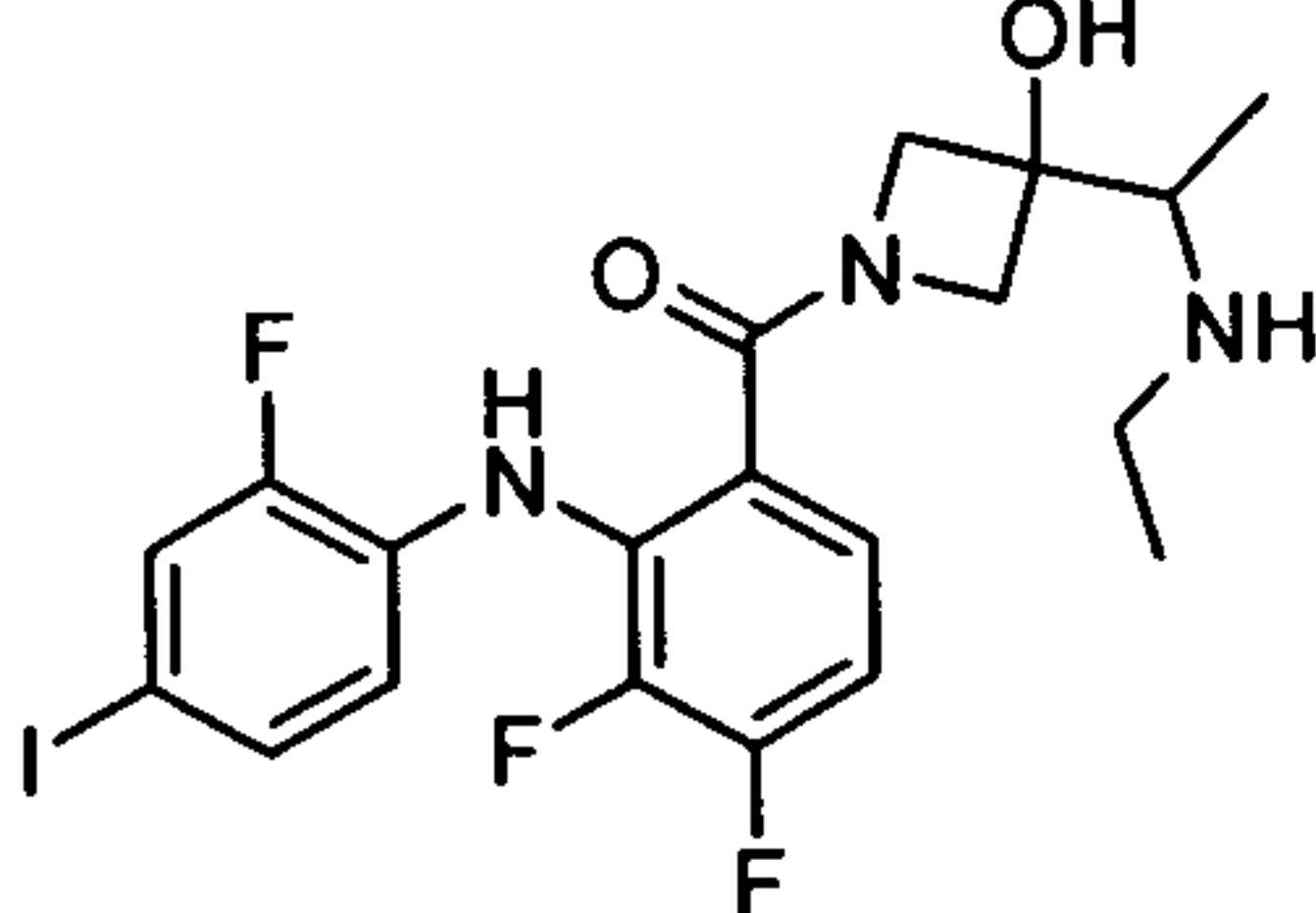
Cmpd No.	Structure	Name
183		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pentylamino)methyl]azetidin-3-ol
184		3-[(1 <i>S</i>)-1-aminoethyl]-1-({8-fluoro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2- <i>a</i>]pyridin-6-yl}carbonyl)azetidin-3-ol
185		1-({8-fluoro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2- <i>a</i>]pyridin-6-yl}carbonyl)-3-[(1 <i>S</i>)-1-(methylamino)ethyl]azetidin-3-ol
186		3-[(cyclohexylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
187		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)ethyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

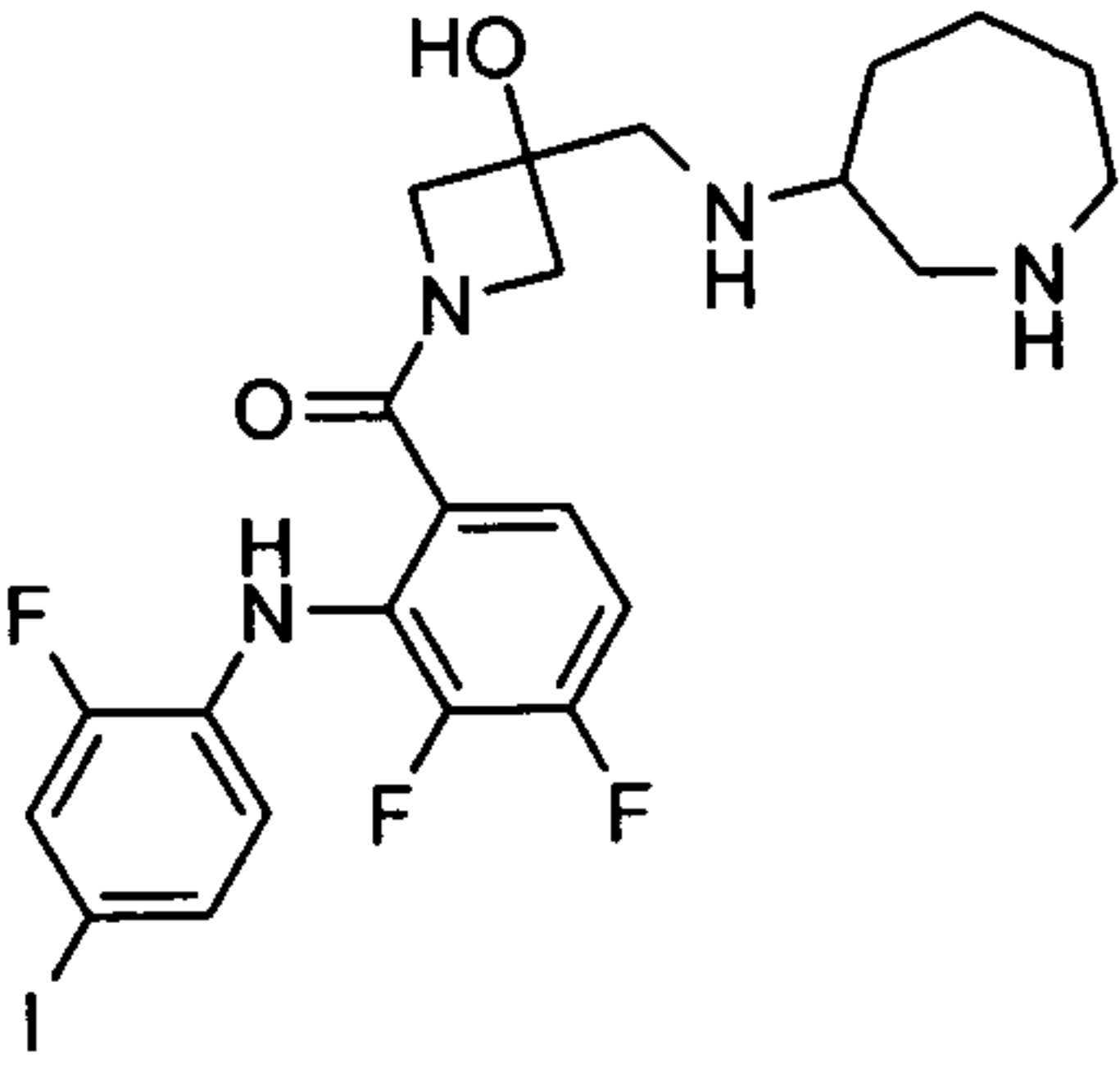
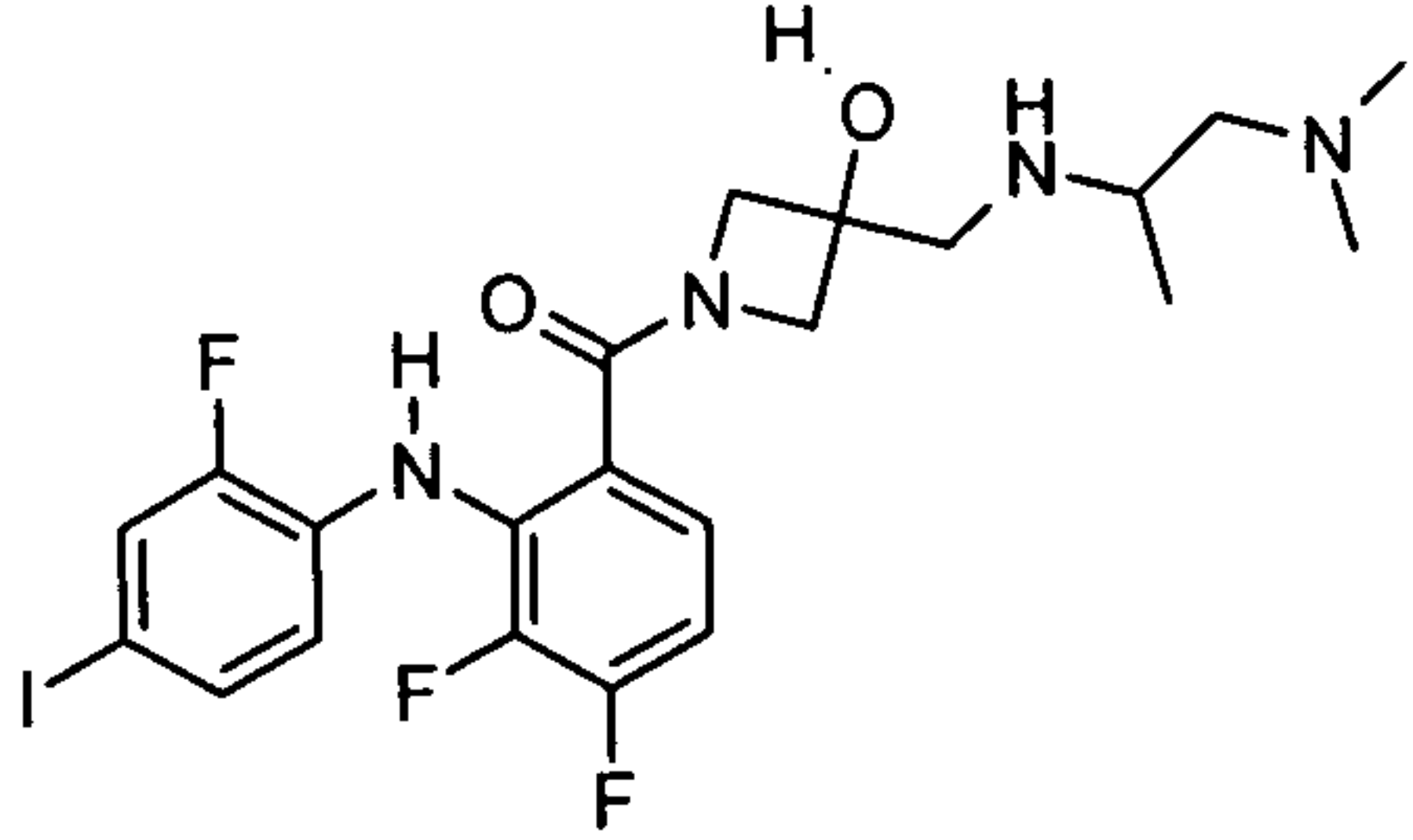
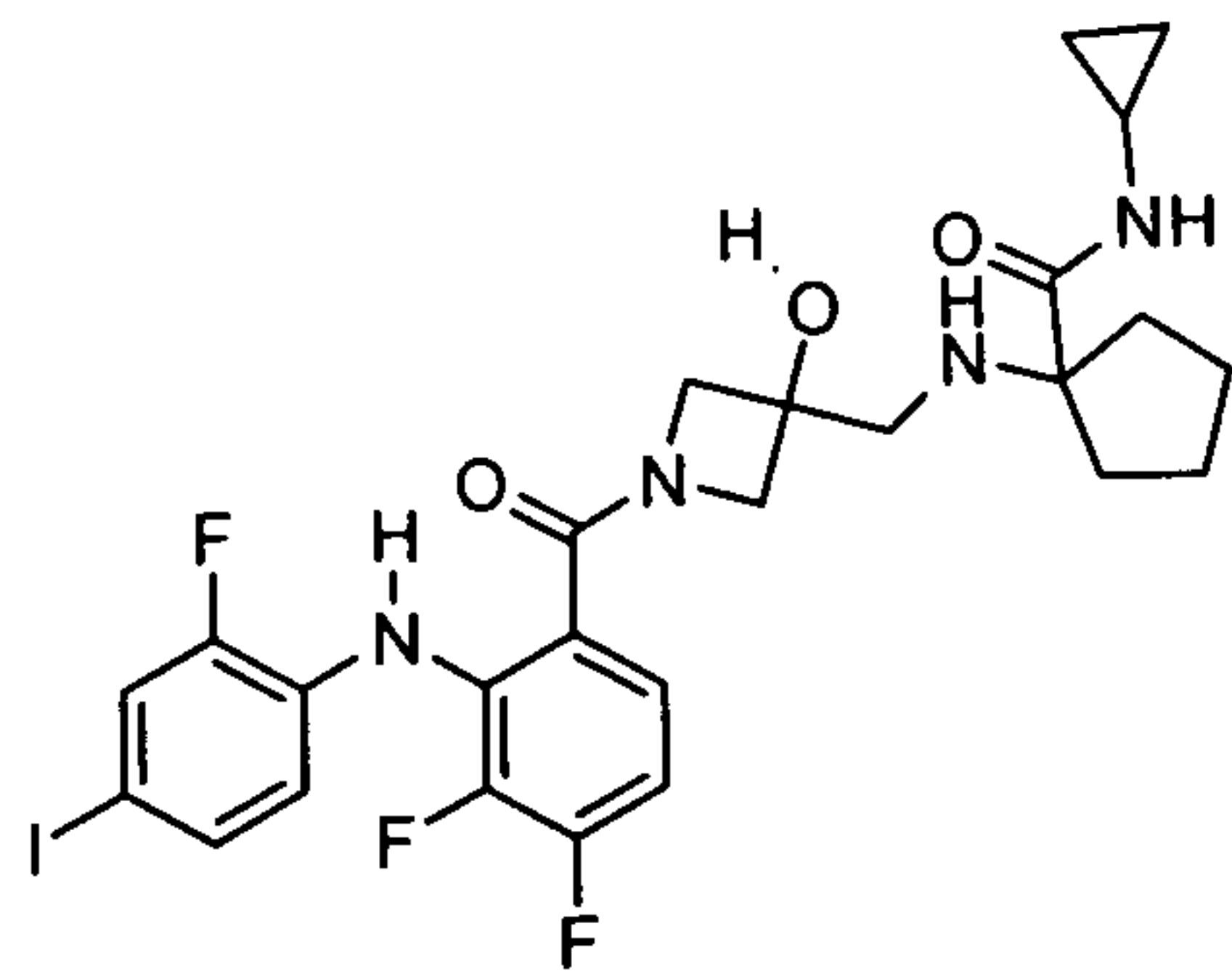
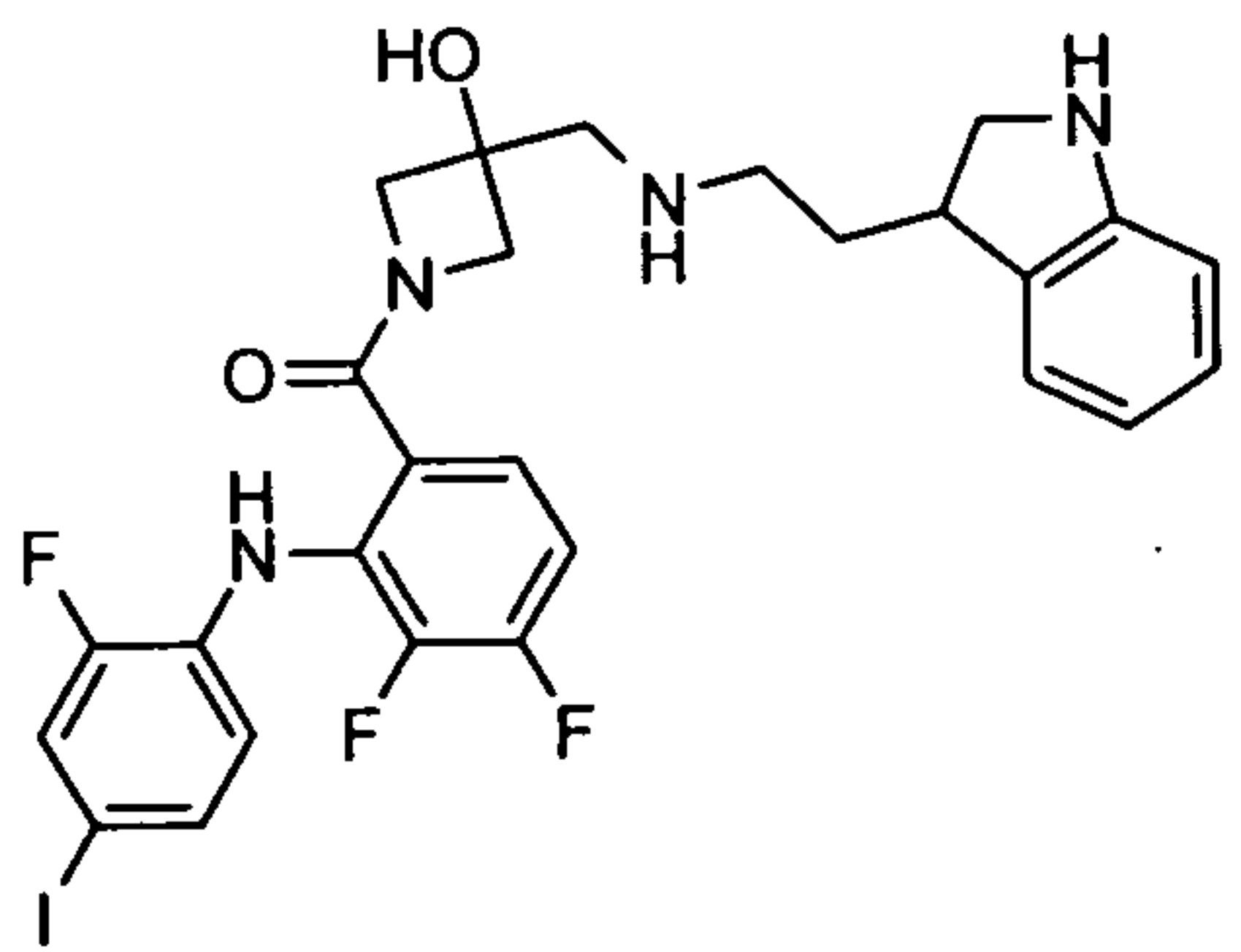
Cmpd No.	Structure	Name
188		3-[(azepan-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
189		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(dimethylamino)-1-methylethyl]amino}methyl)azetidin-3-ol
190		N-cyclopropyl-1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentanecarboxamide
191		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[2-(2,3-dihydro-1H-indol-3-yl)ethyl]amino}methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
192		<i>N</i> -2-([1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl)methyl]- <i>N</i> -ethyl-2-methylalaninamide
193		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2-methylhydrazino)methyl]azetidin-3-ol
194		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(hydroxyamino)methyl]azetidin-3-ol
195		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(methoxyamino)methyl]azetidin-3-ol
196		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(ethoxyamino)methyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

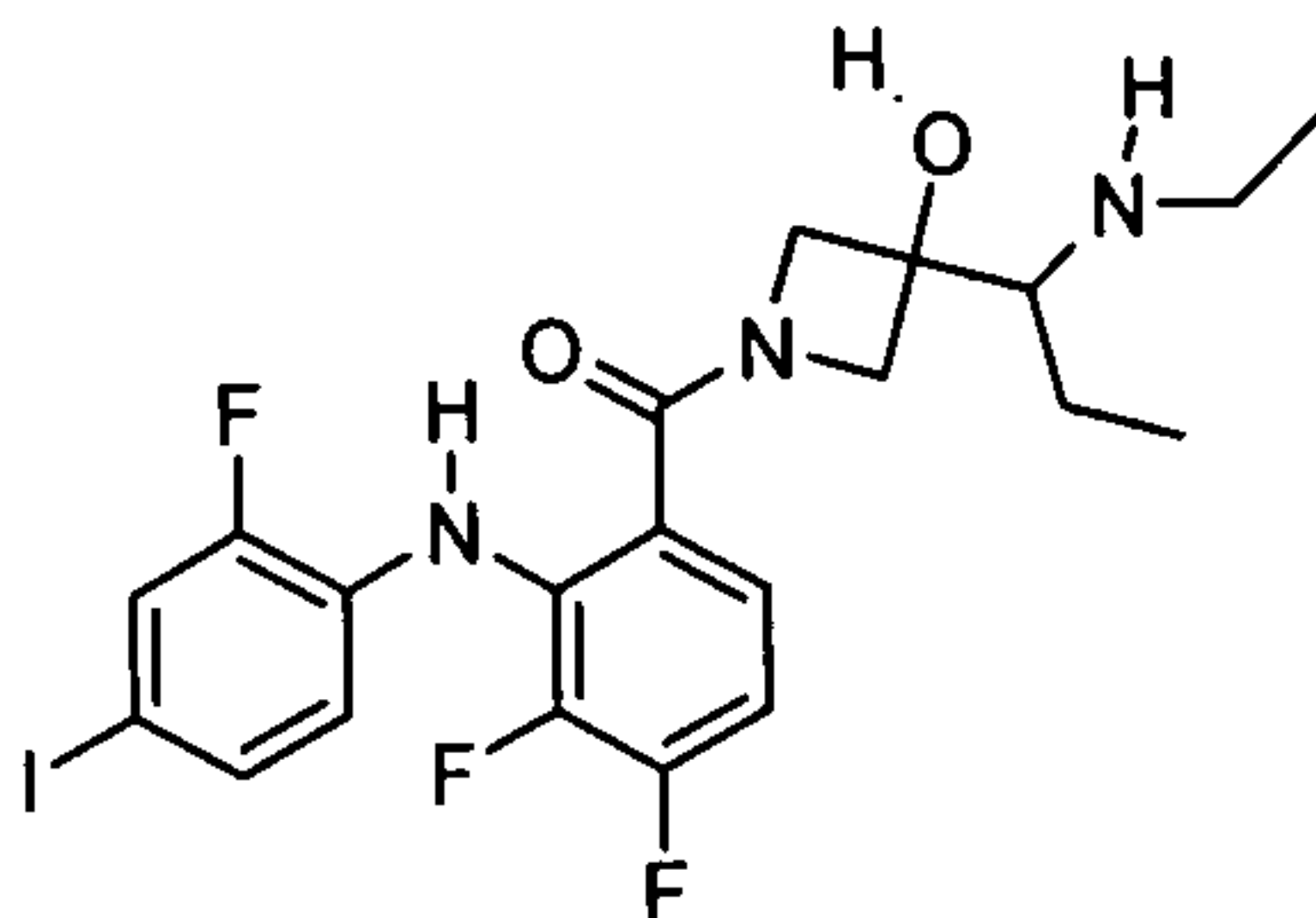
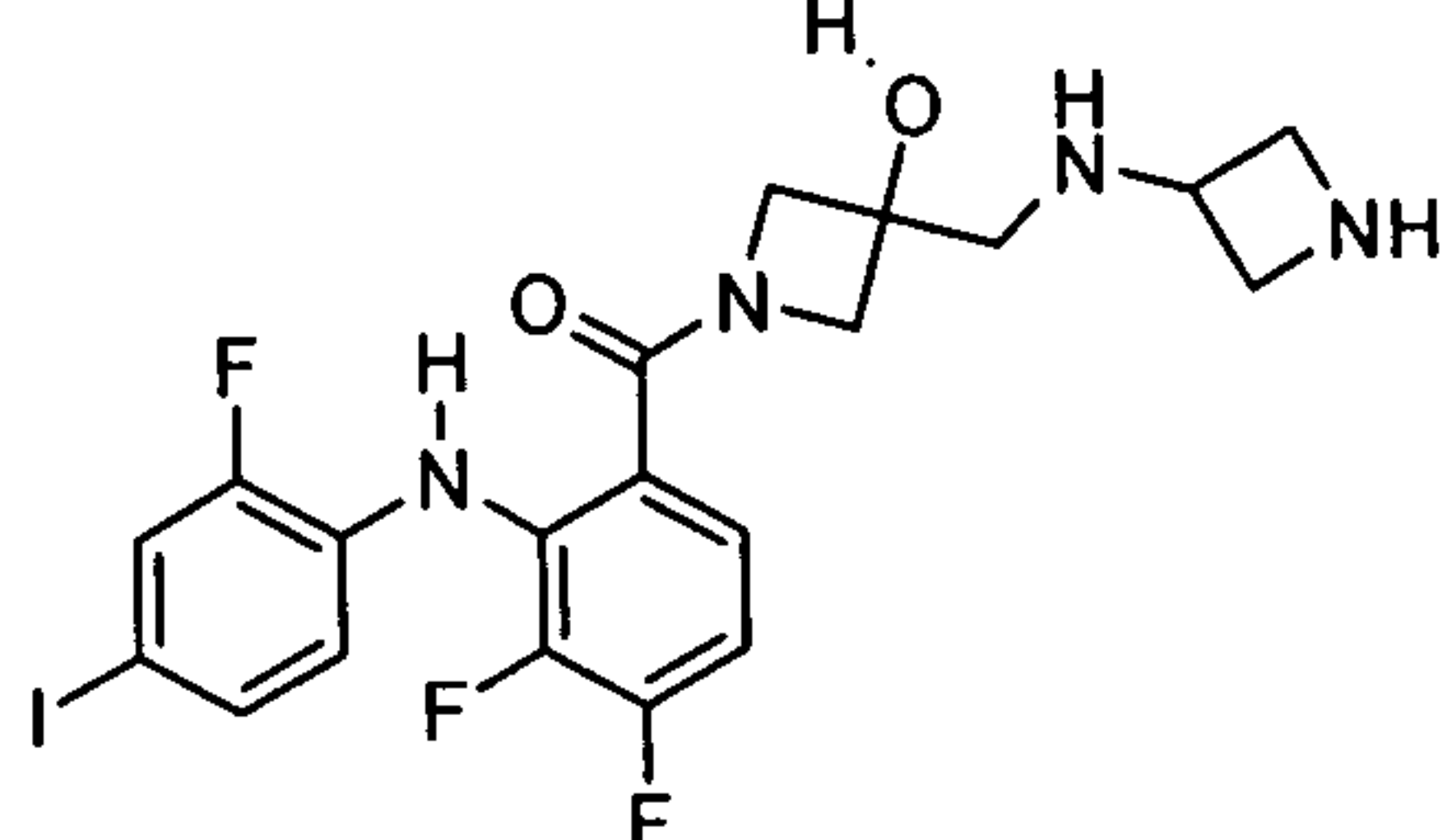
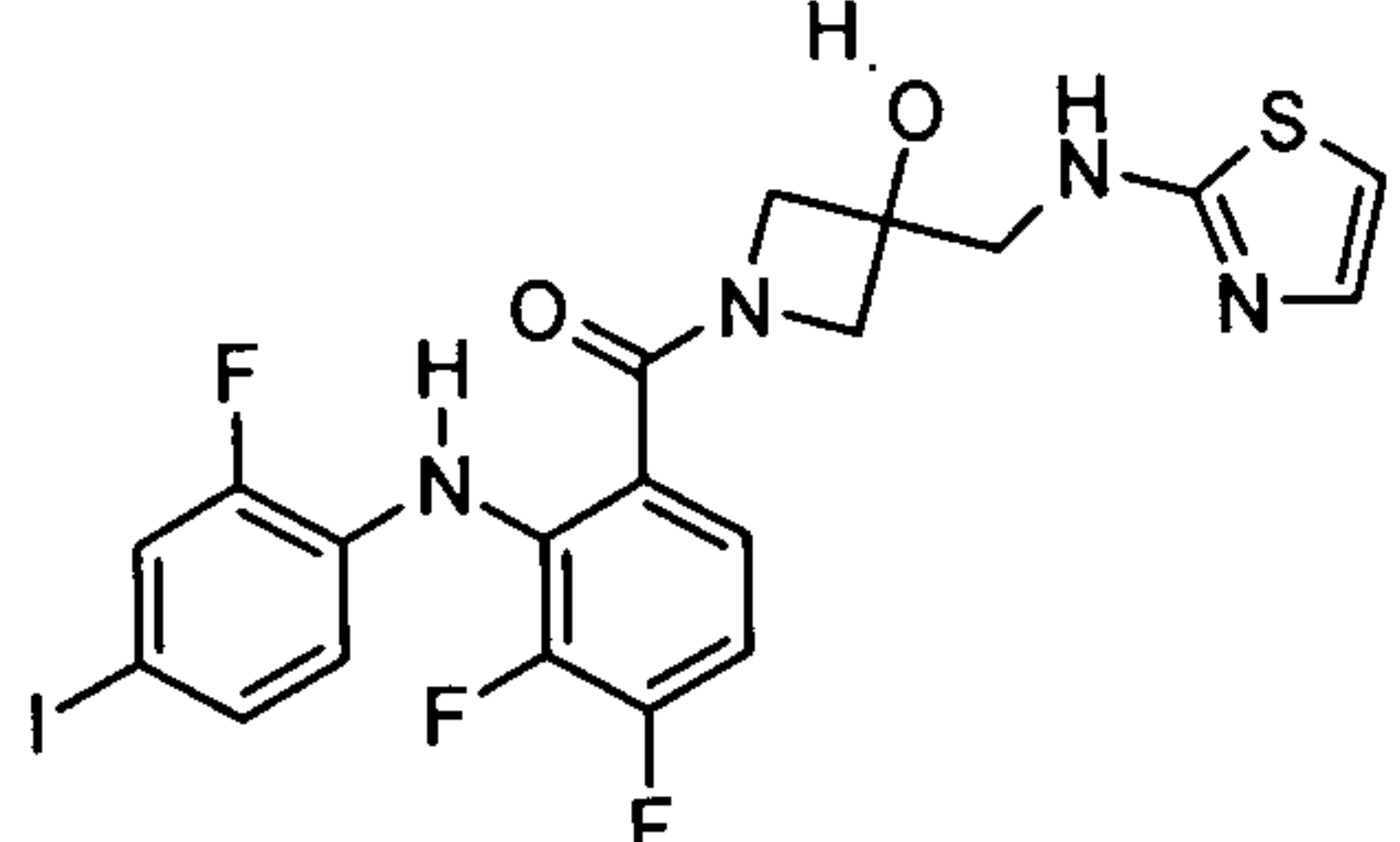
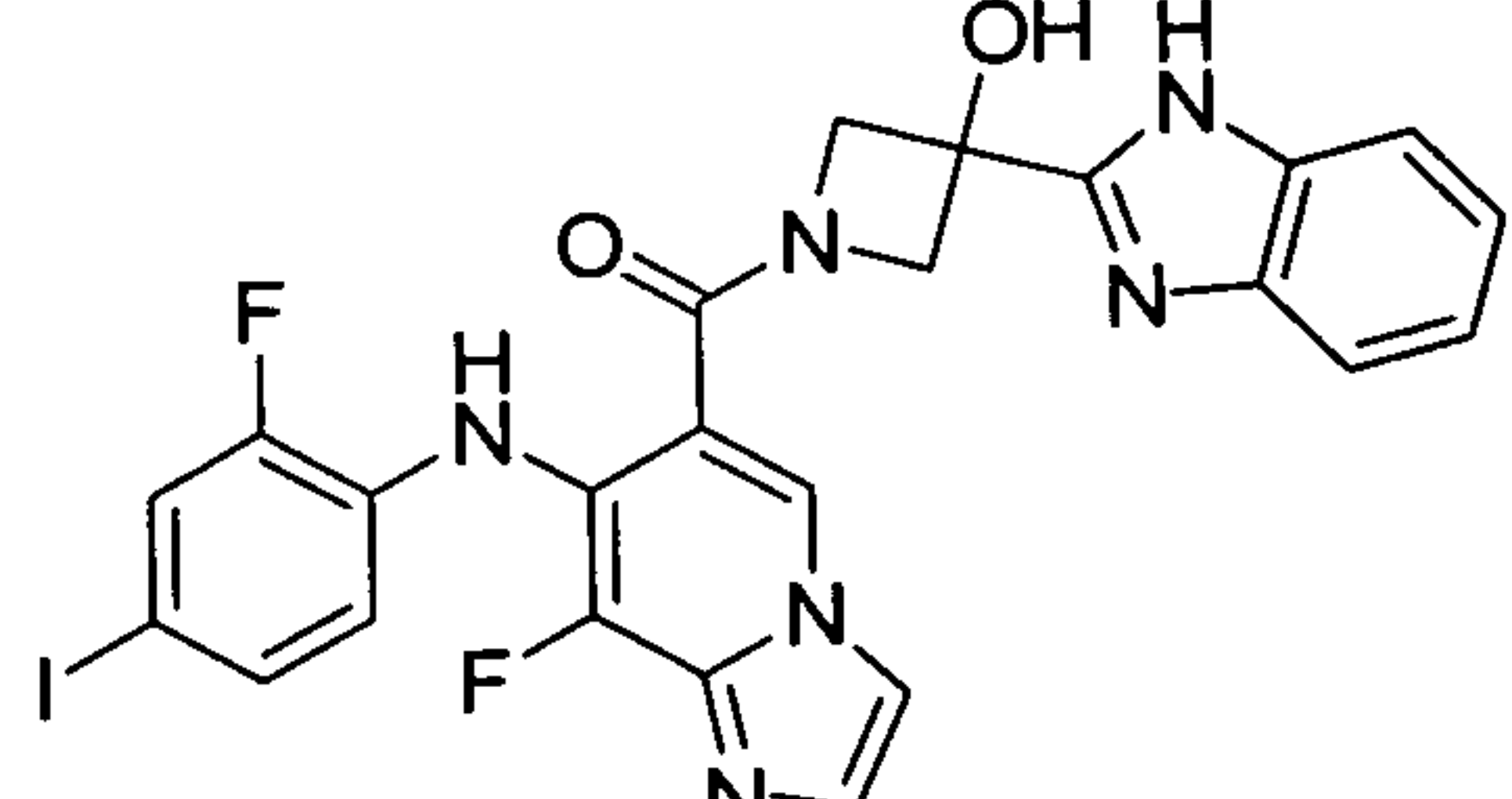
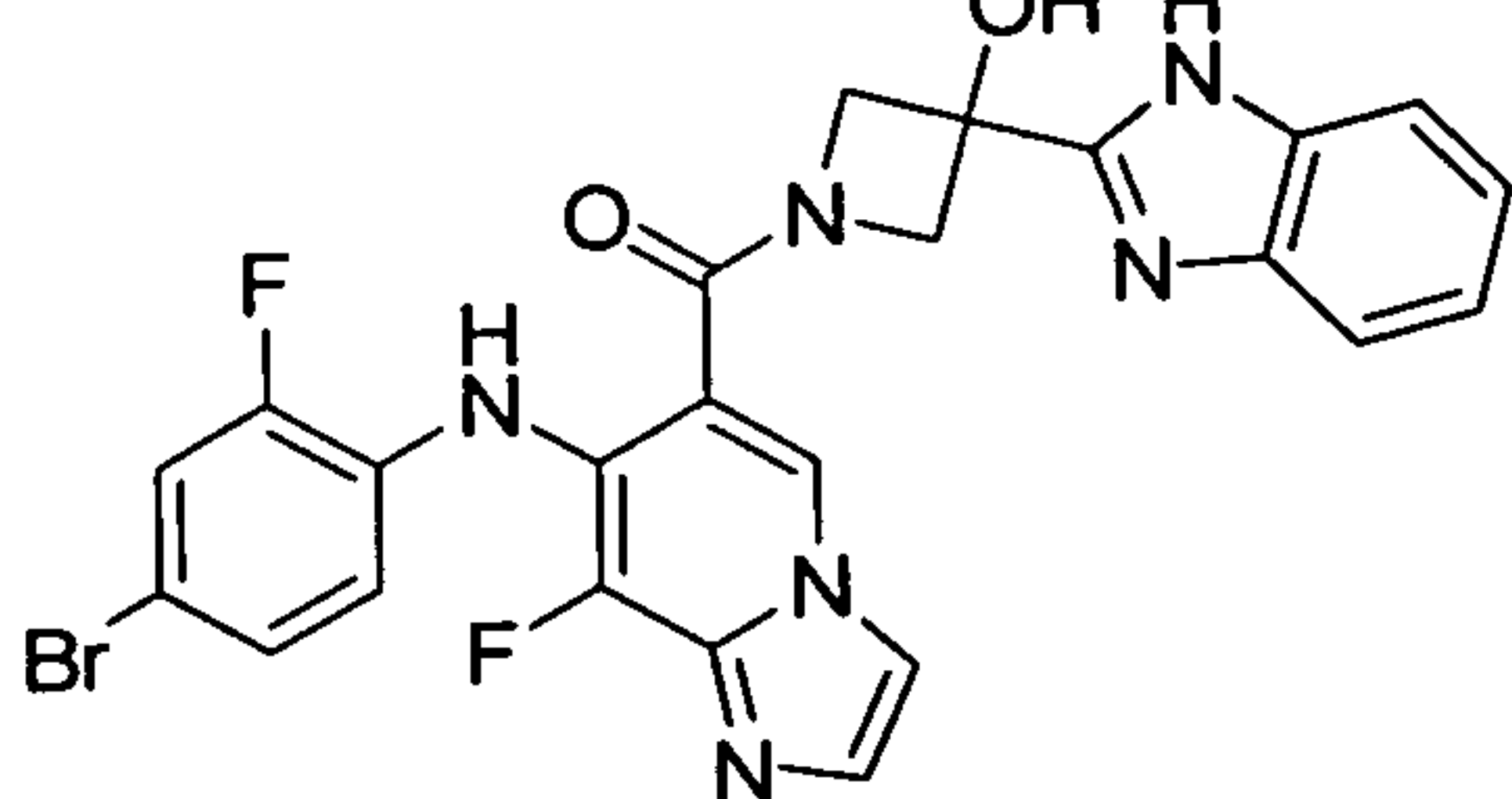
Cmpd No.	Structure	Name
197		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(ethylamino)propyl]azetidin-3-ol
198		3-[(azetidin-3-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
199		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3-thiazol-2-ylamino)methyl]azetidin-3-ol
200		3-(1 <i>H</i> -benzimidazol-2-yl)-1-({8-fluoro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2- <i>a</i>]pyridin-6-yl}carbonyl)azetidin-3-ol
201		3-(1 <i>H</i> -benzimidazol-2-yl)-1-({7-[(4-bromo-2-fluorophenyl)amino]-8-fluoroimidazo[1,2- <i>a</i>]pyridin-6-yl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

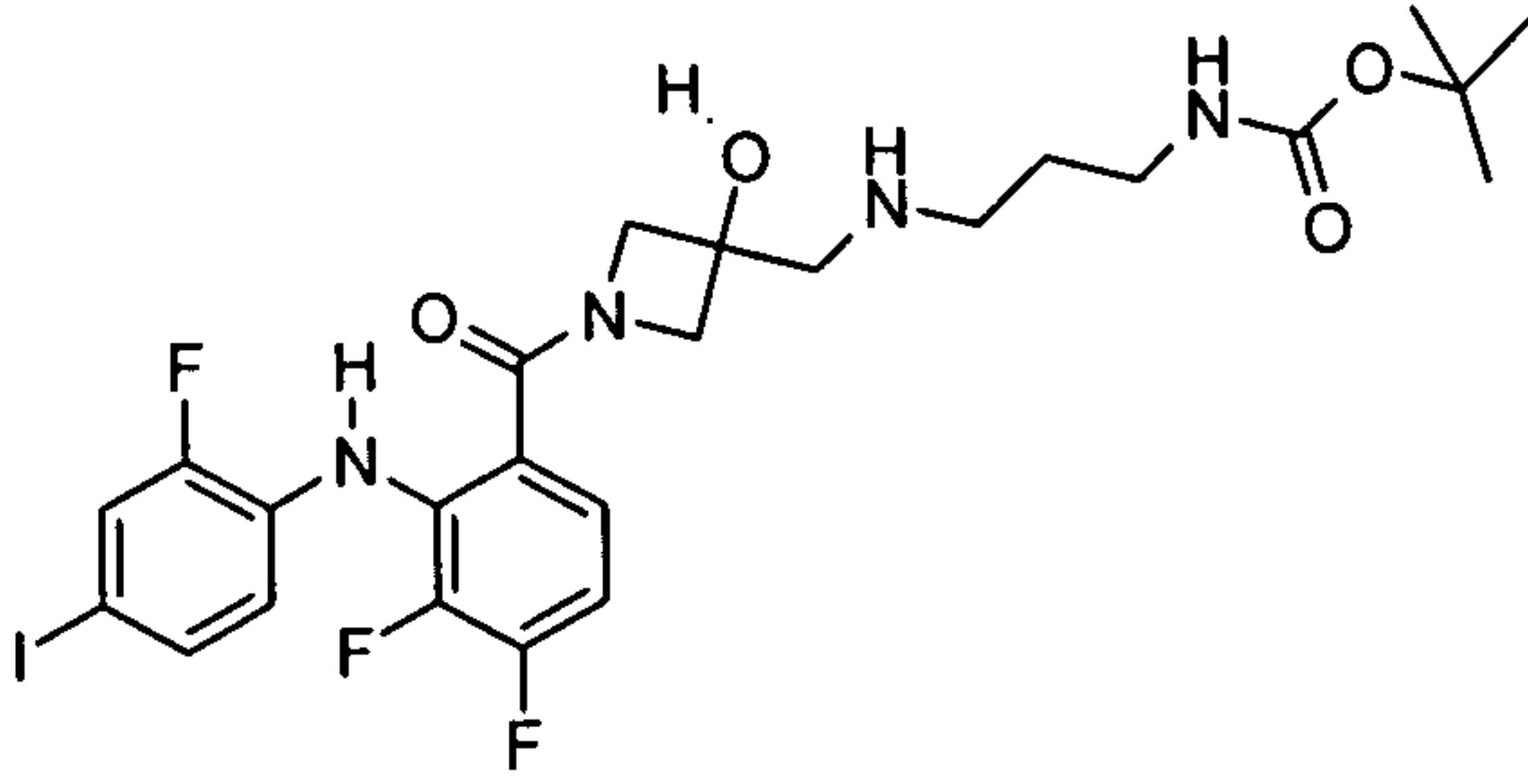
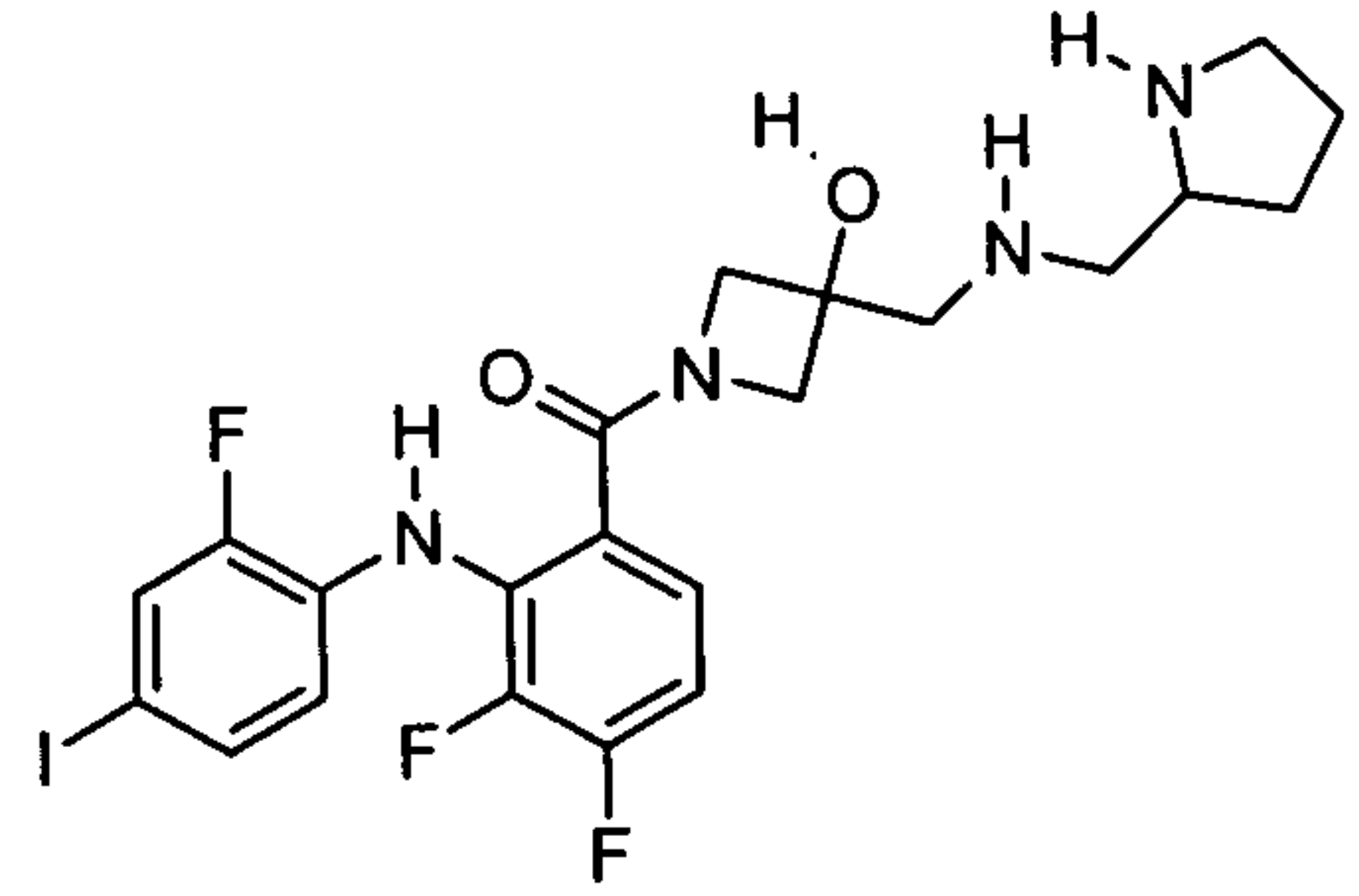
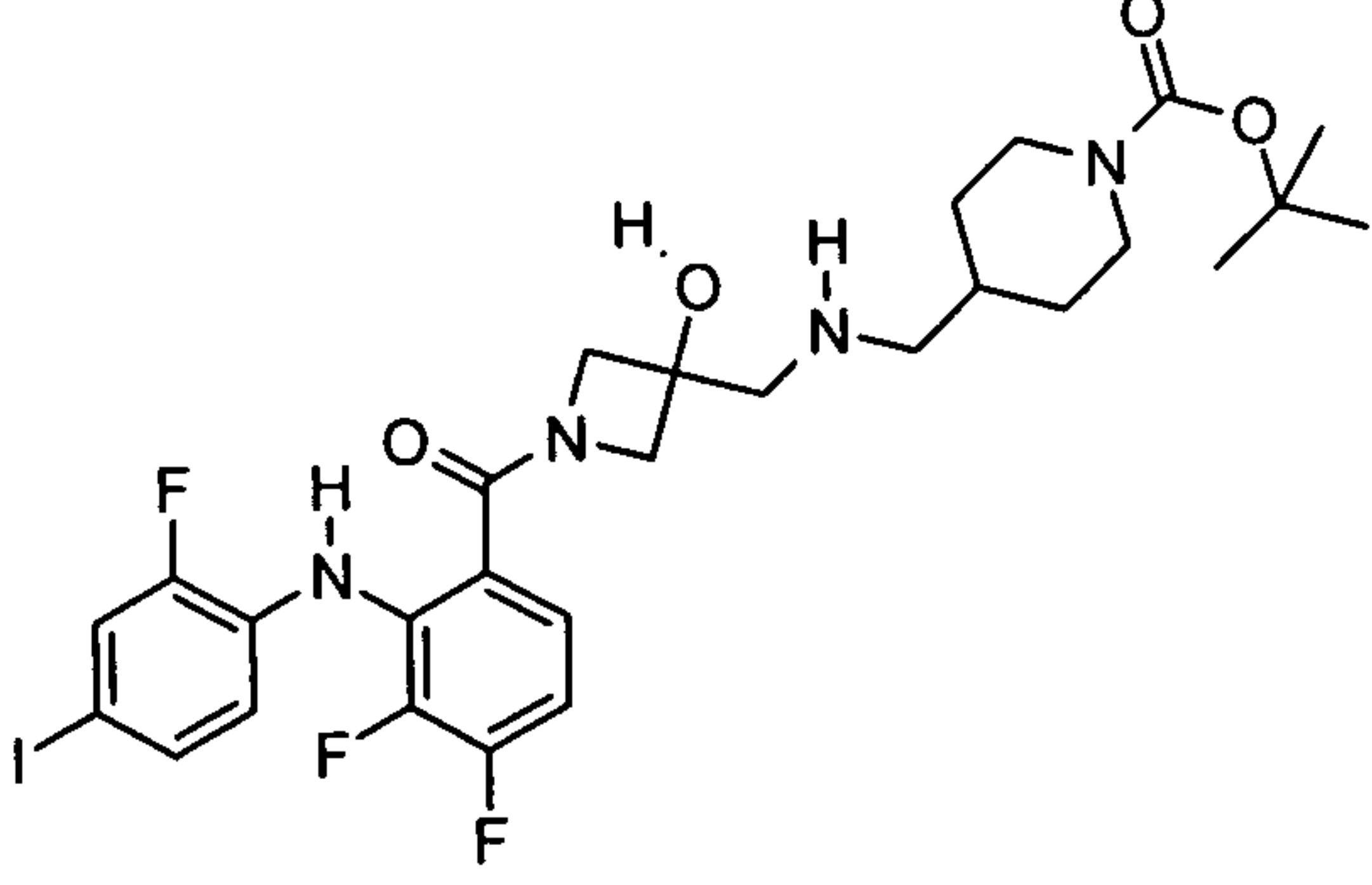
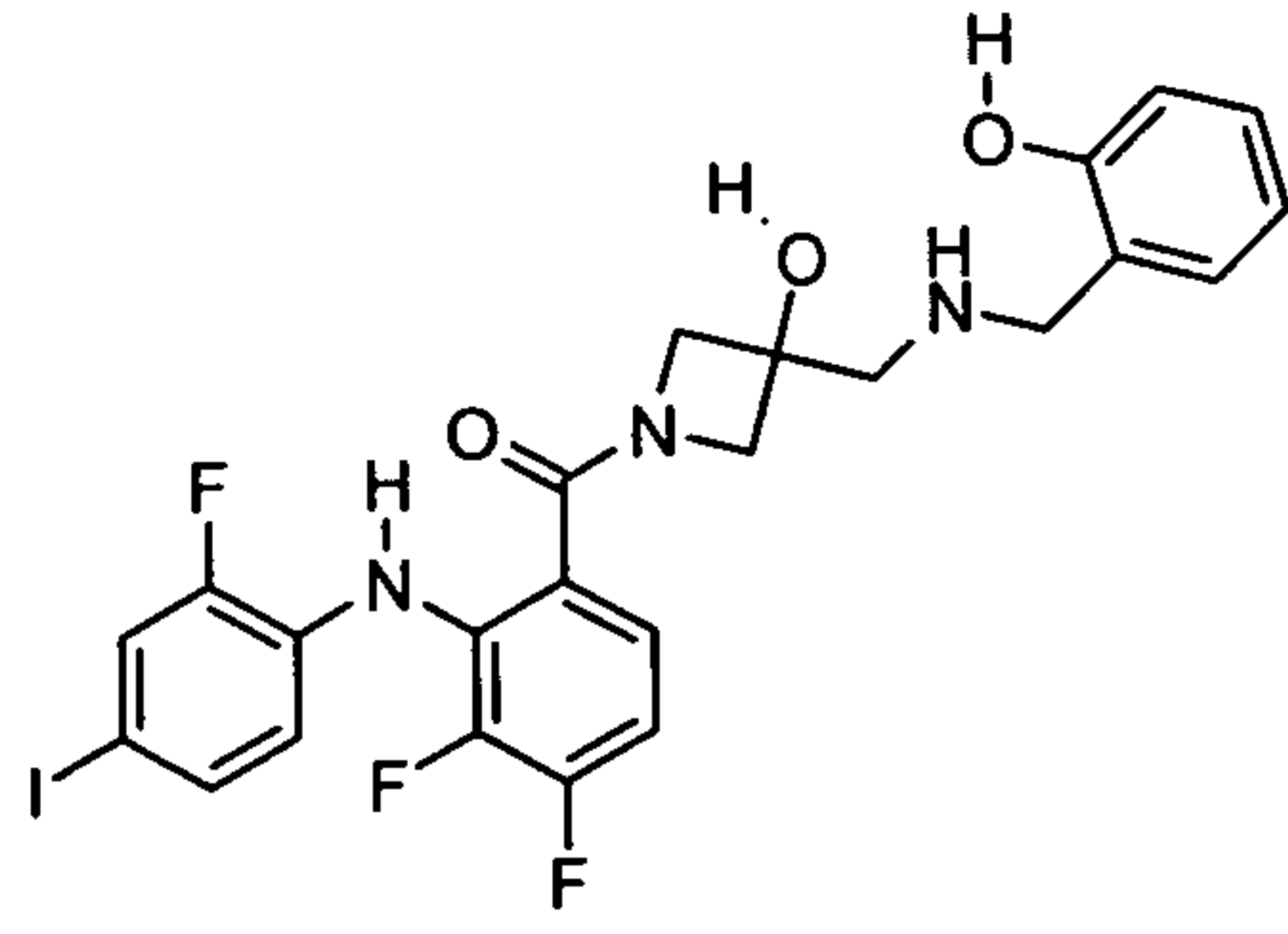
Cmpd No.	Structure	Name
202		1,1-dimethylethyl [3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)propyl]carbamate
203		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[(pyrrolidin-2-ylmethyl)amino]methyl}azetidin-3-ol
204		1,1-dimethylethyl 4-[[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)methyl]piperidine-1-carboxylate
205		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

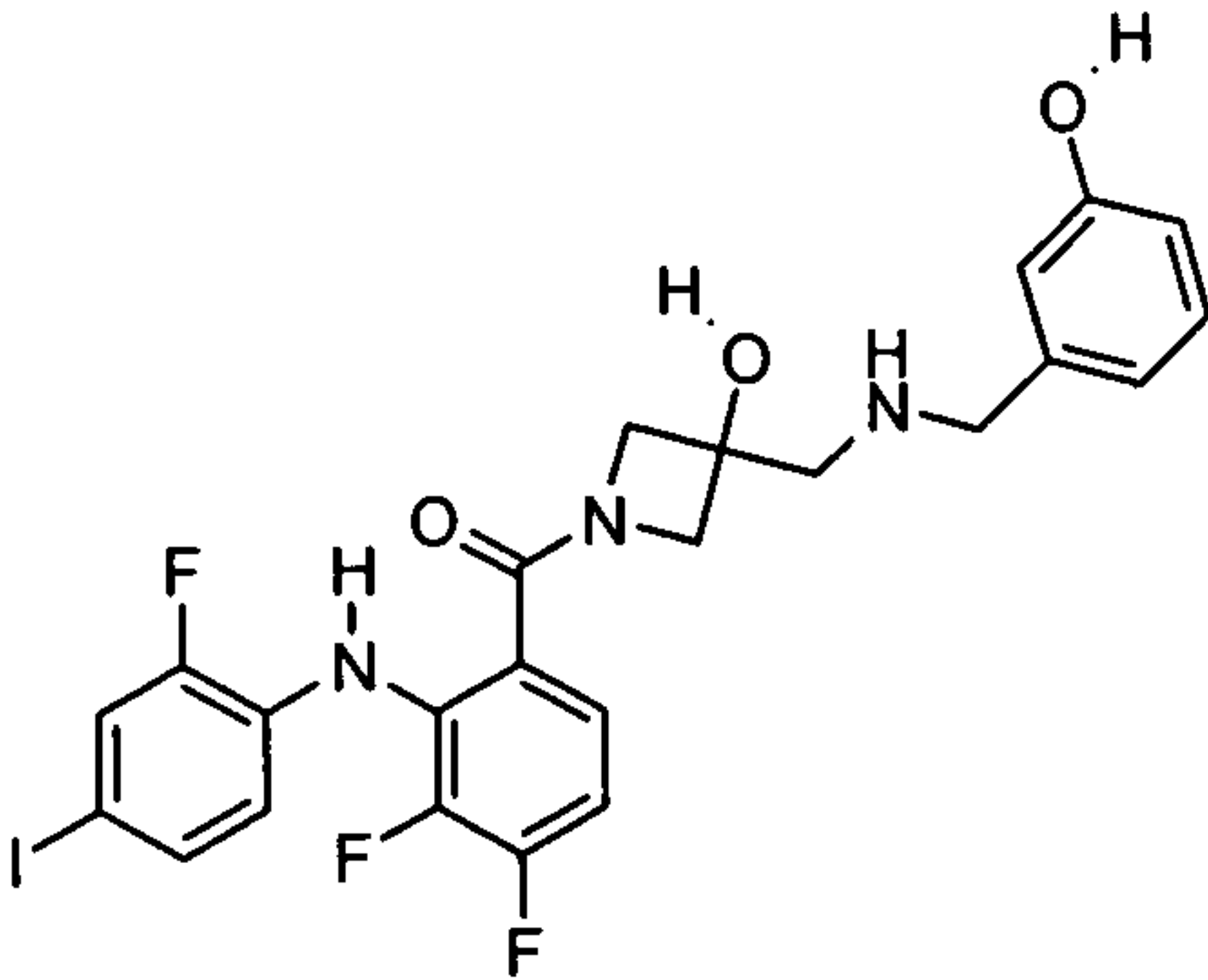
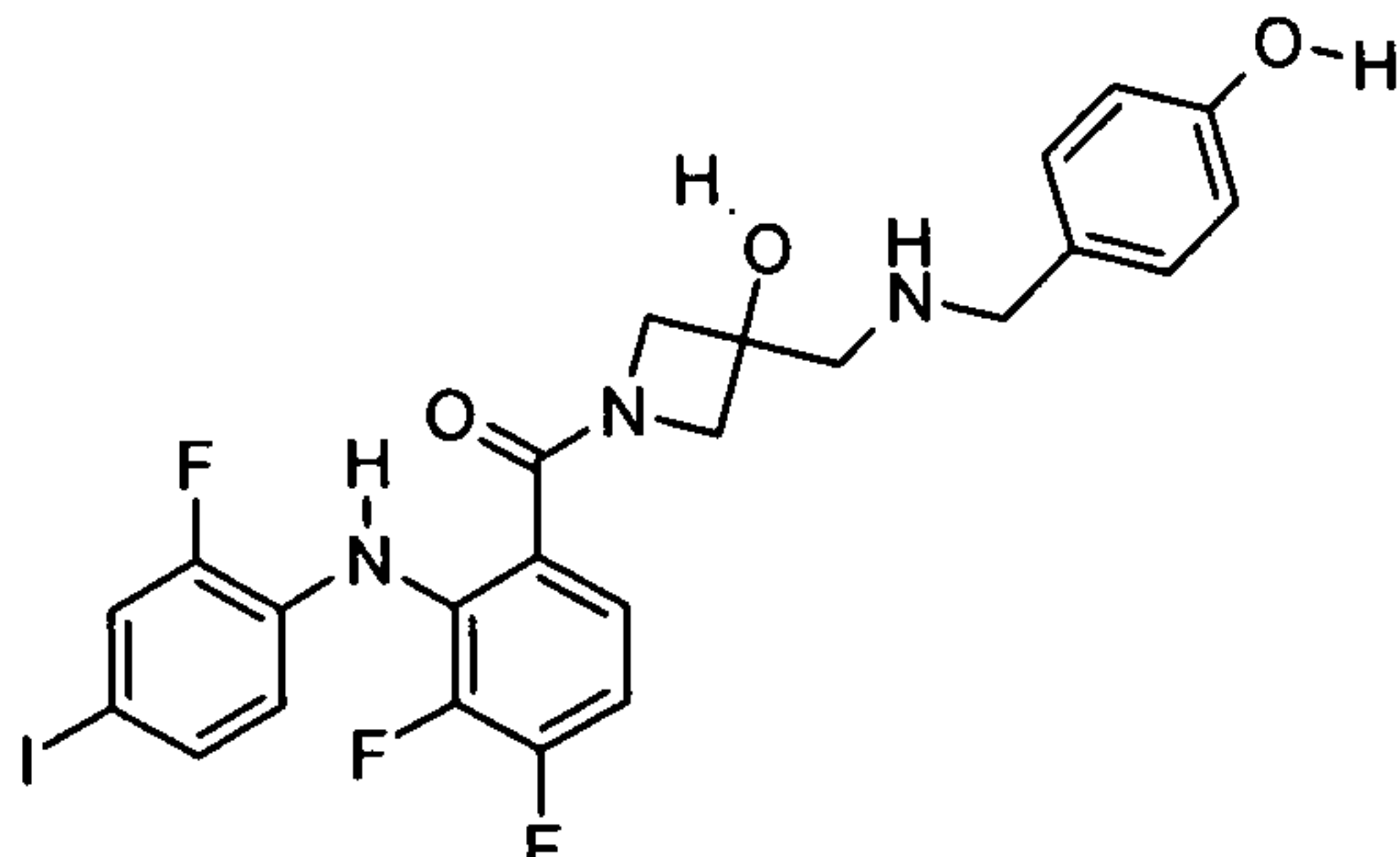
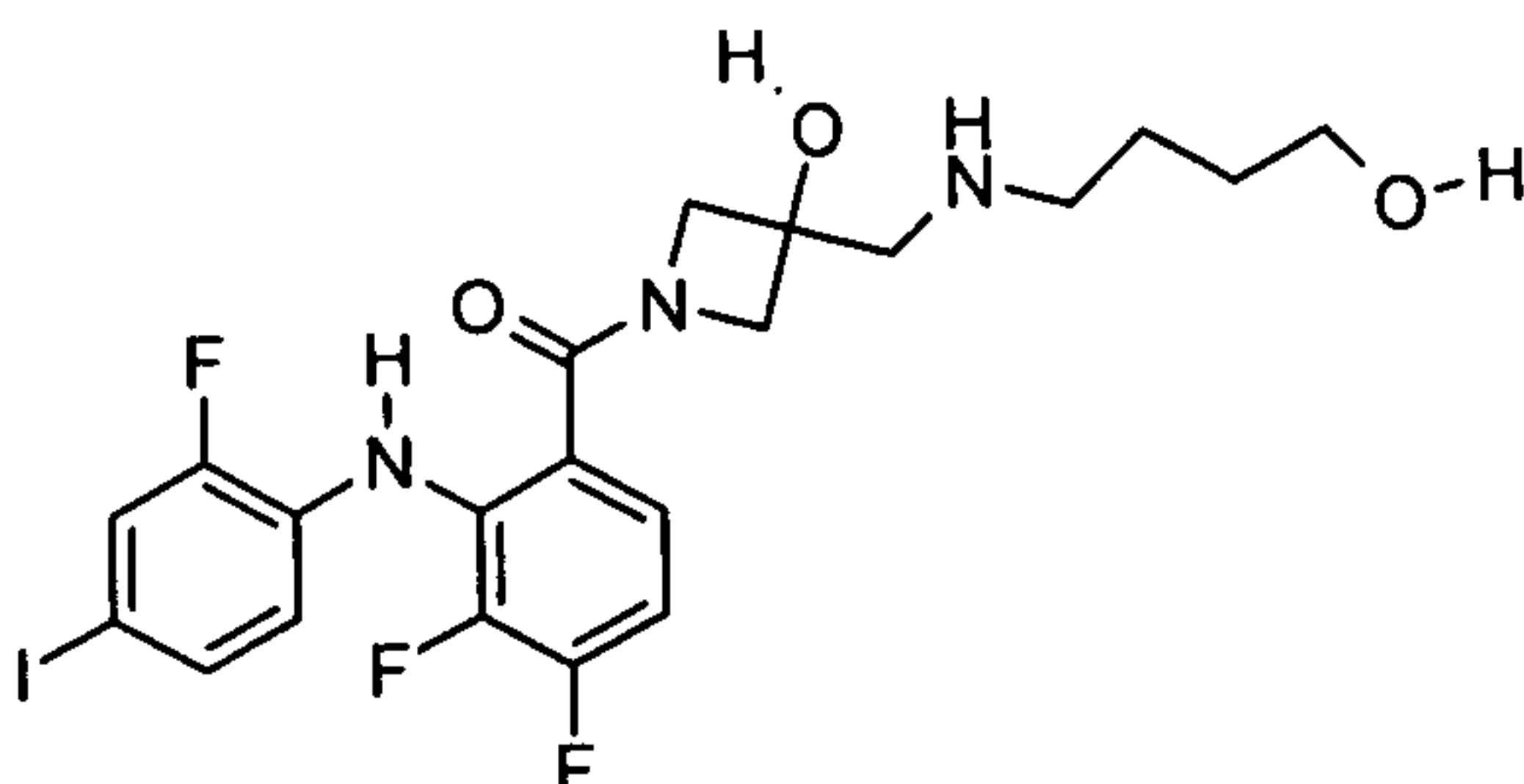
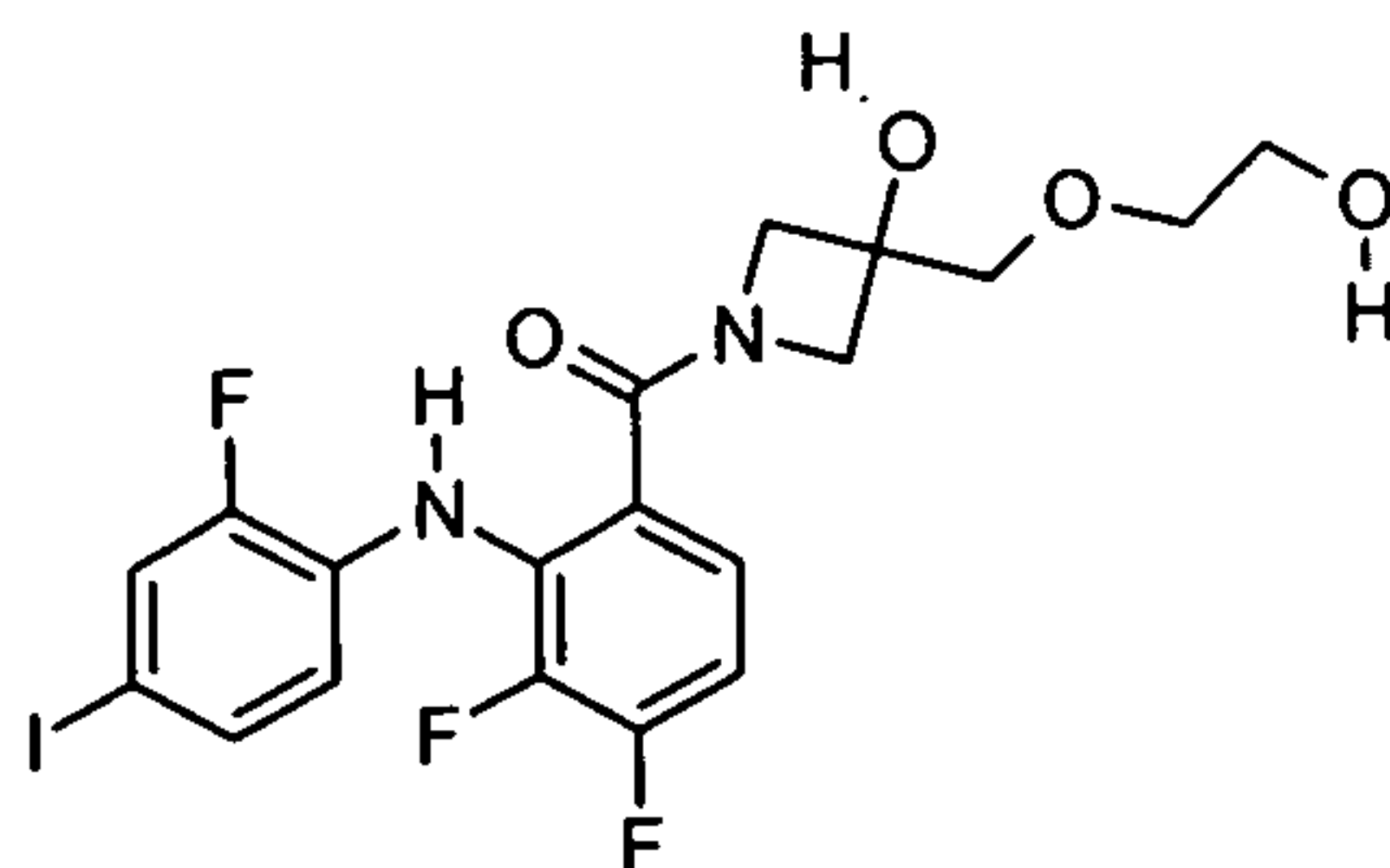
Cmpd No.	Structure	Name
206		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(3-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol
207		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(4-hydroxyphenyl)methyl]amino}methyl)azetidin-3-ol
208		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(4-hydroxybutyl)amino]methyl}azetidin-3-ol
209		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2-hydroxyethyl)oxy]methyl}azetidin-3-ol

Table 1. Representative MEK Inhibitors

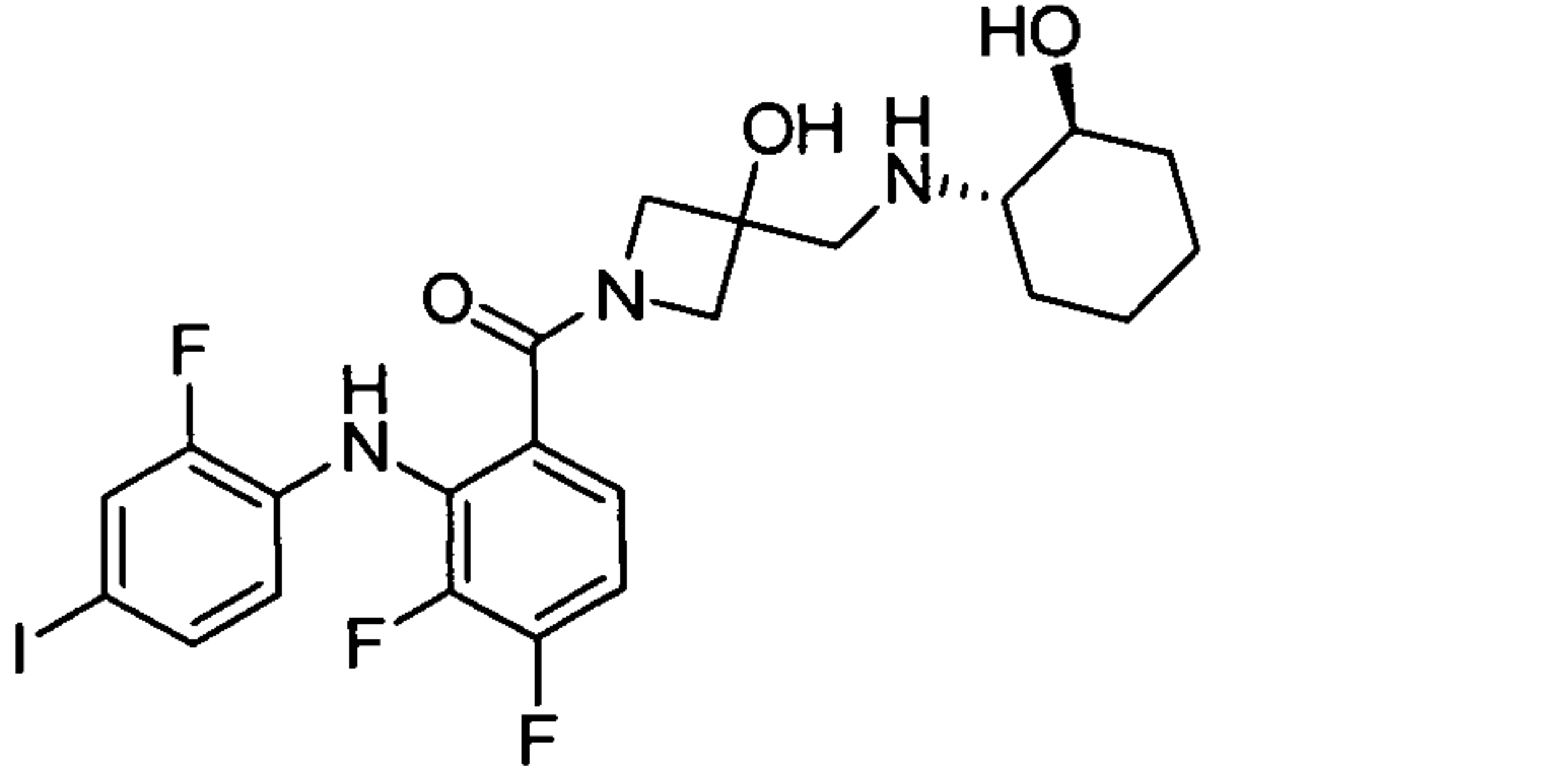
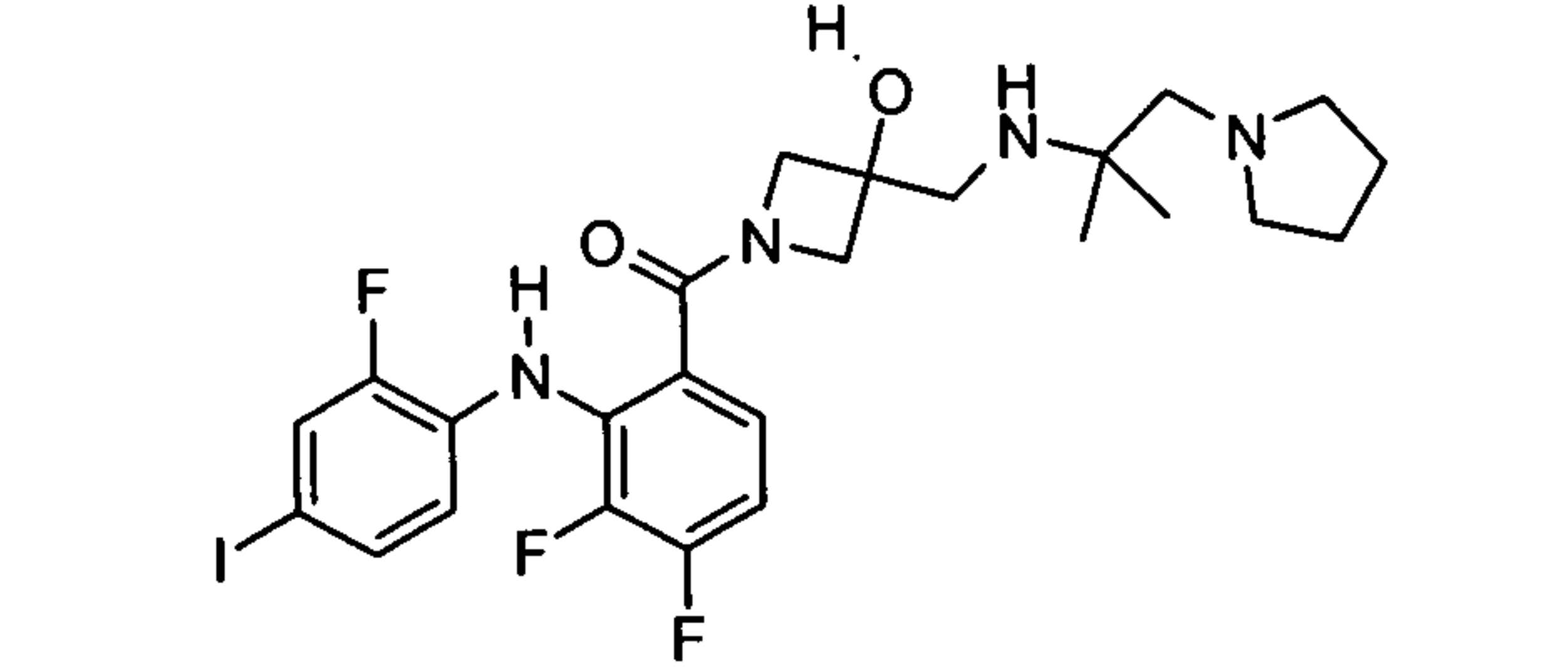
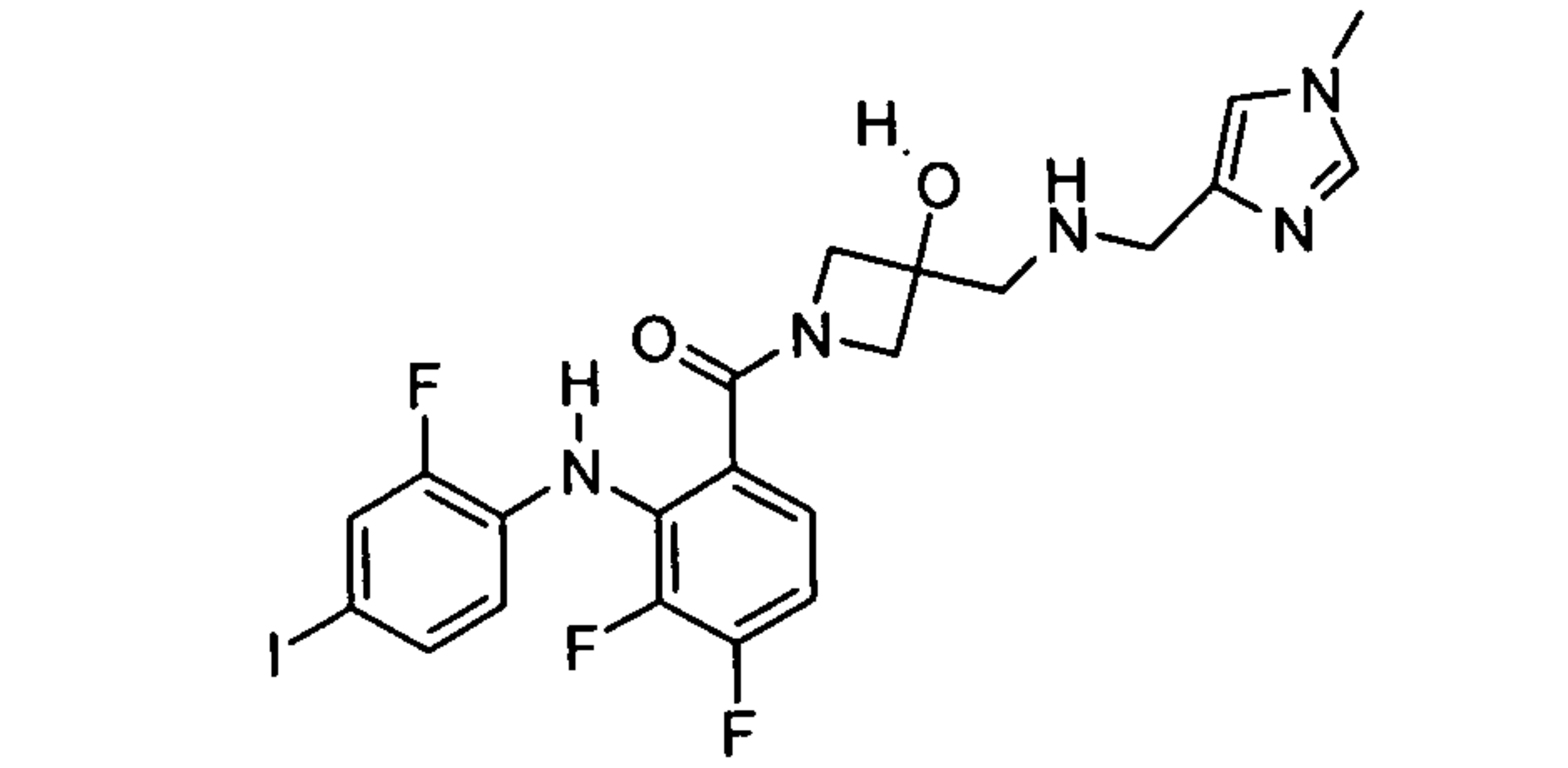
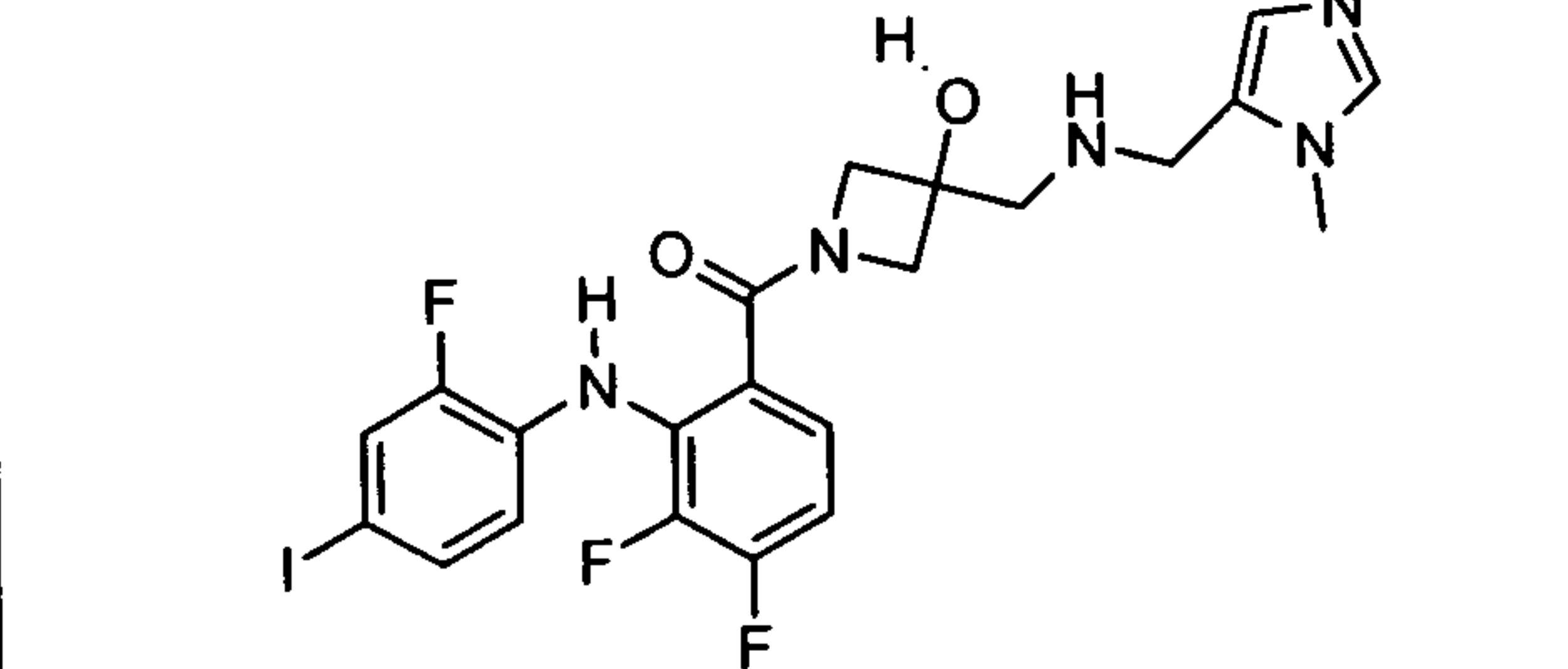
Cmpd No.	Structure	Name
210		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1S,2S)-2-hydroxycyclohexyl)amino)methyl)azetidin-3-ol
211		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1,1-dimethyl-2-pyrrolidin-1-ylethyl)amino)methyl)azetidin-3-ol
212		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1-methyl-1H-imidazol-4-yl)methyl)amino)methyl)azetidin-3-ol
213		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-(((1-methyl-1H-imidazol-5-yl)methyl)amino)methyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

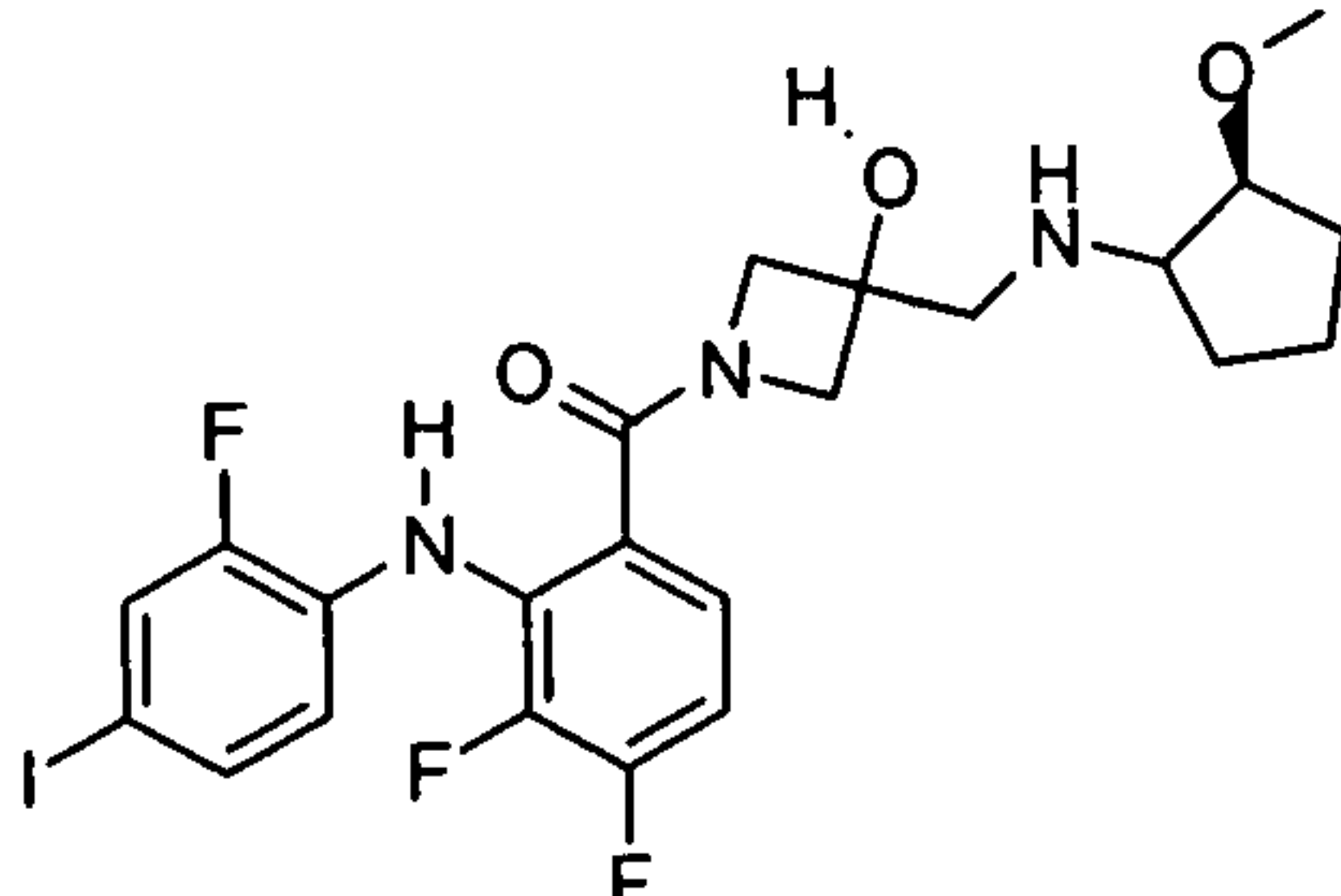
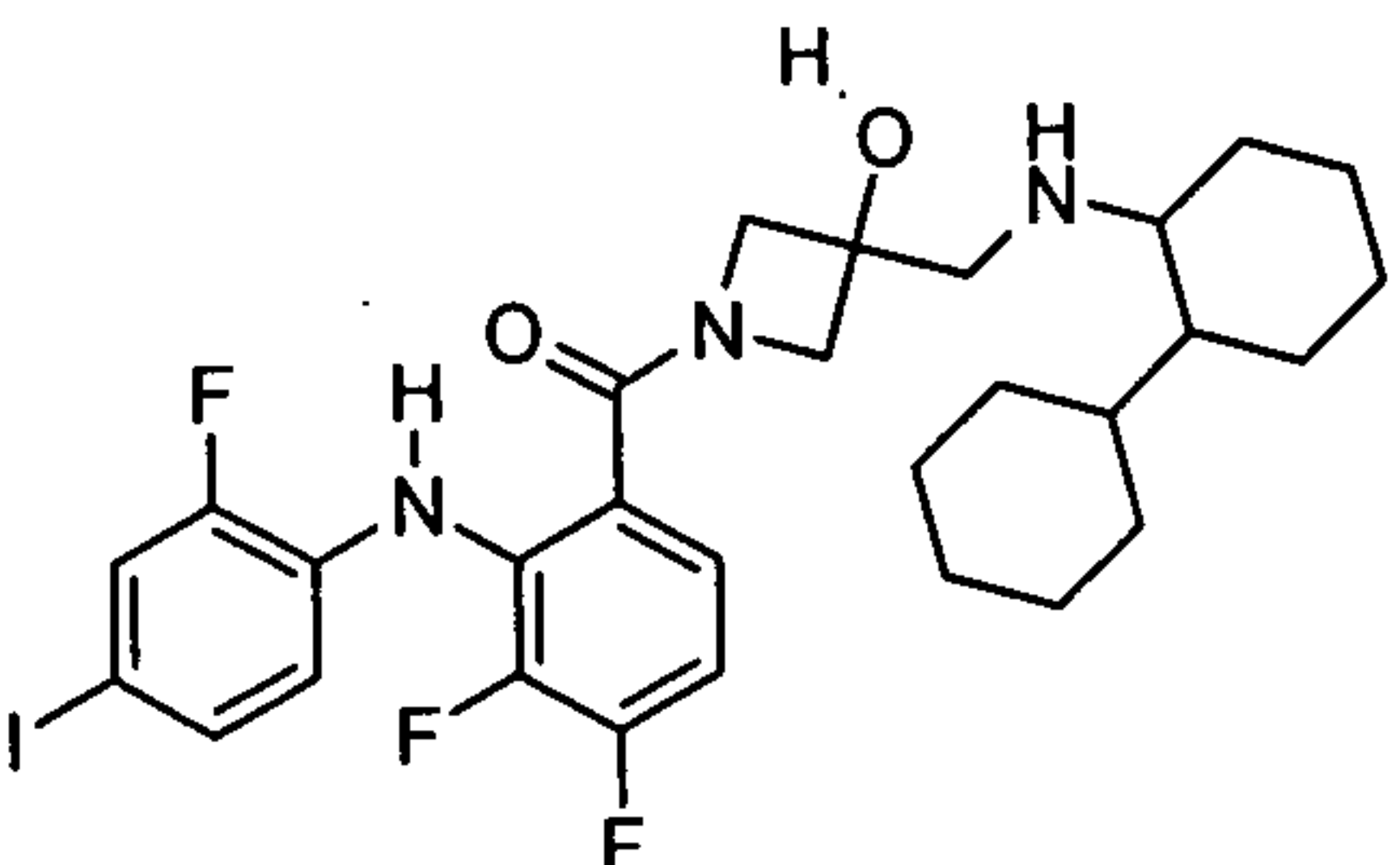
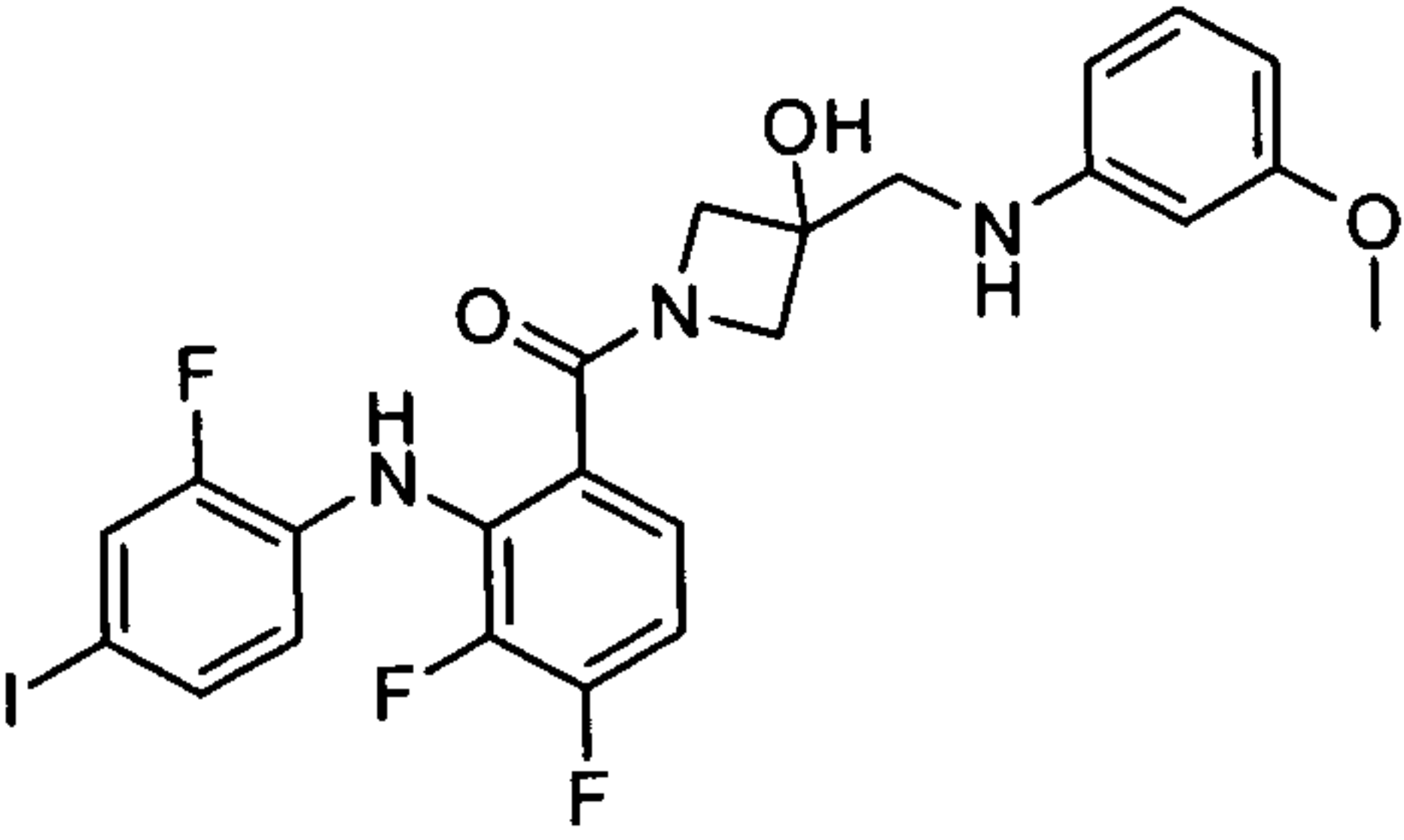
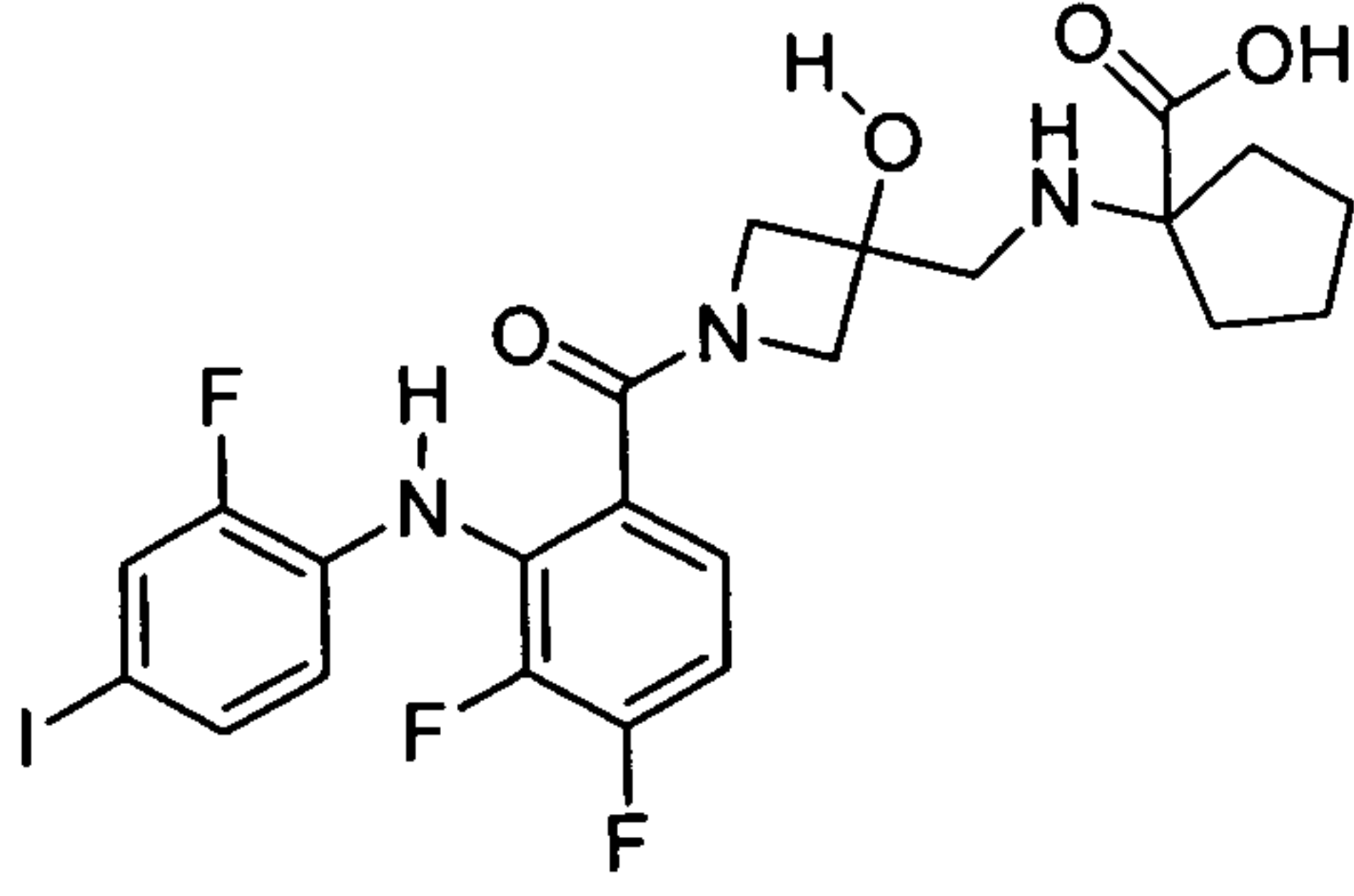
Cmpd No.	Structure	Name
214		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[(2S)-2-(methyloxy)cyclopentyl]amino}methyl)azetidin-3-ol
215		3-{{[1,1'-bi(cyclohexyl)-2-ylamino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
216		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[3-(methyloxy)phenyl]amino}methyl)azetidin-3-ol
217		1-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)cyclopentanecarboxylic acid

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
218		1-((3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[4-fluorophenyl]amino]methyl}azetidin-3-ol
219		1-((3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1,3,5-triazin-2-ylamino)methyl]azetidin-3-ol
220		1-((3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[<i>trans</i> -4-hydroxycyclohexyl]amino]methyl}azetidin-3-ol
221		3-[(cyclopent-3-en-1-ylamino)methyl]-1-((3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

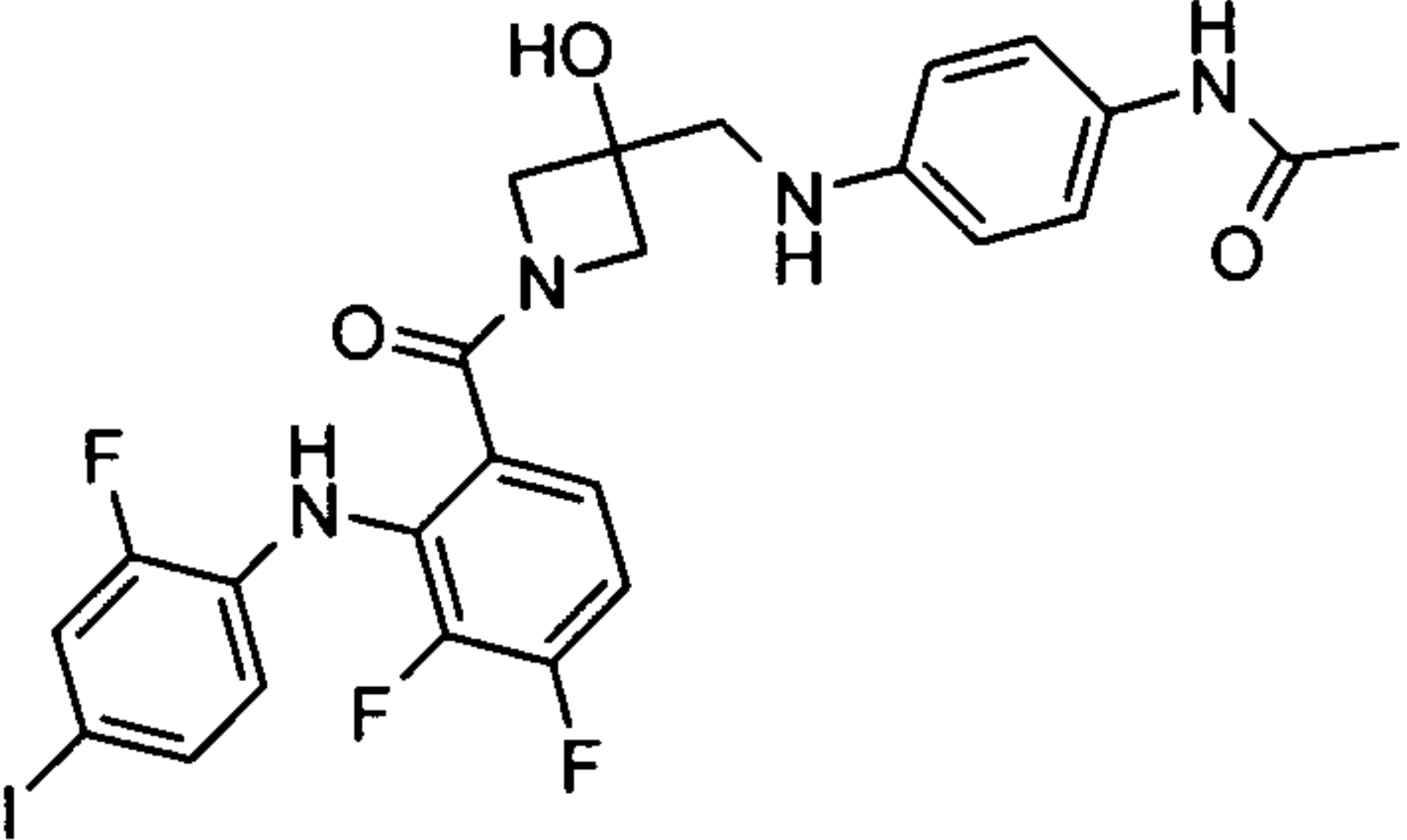
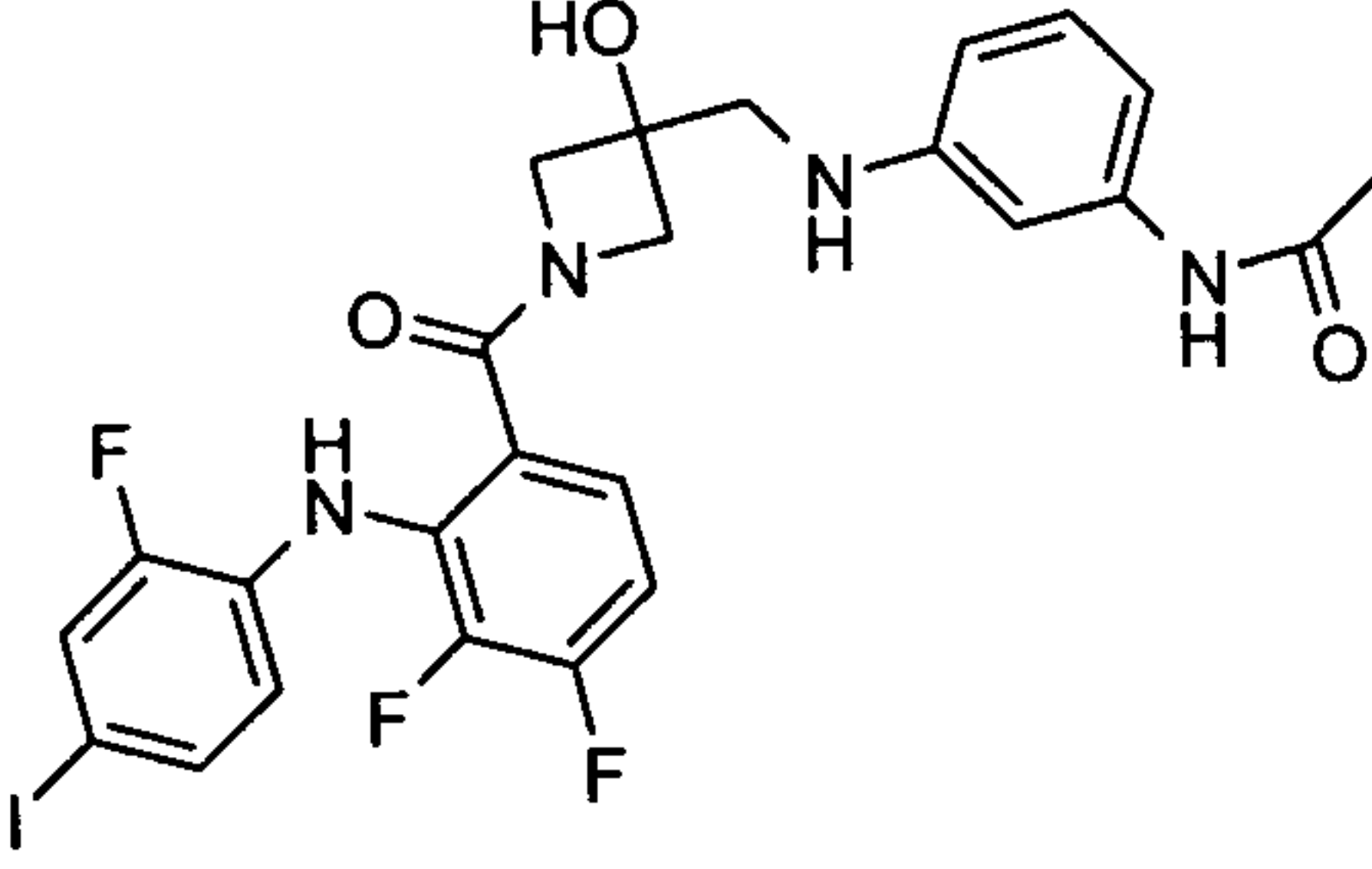
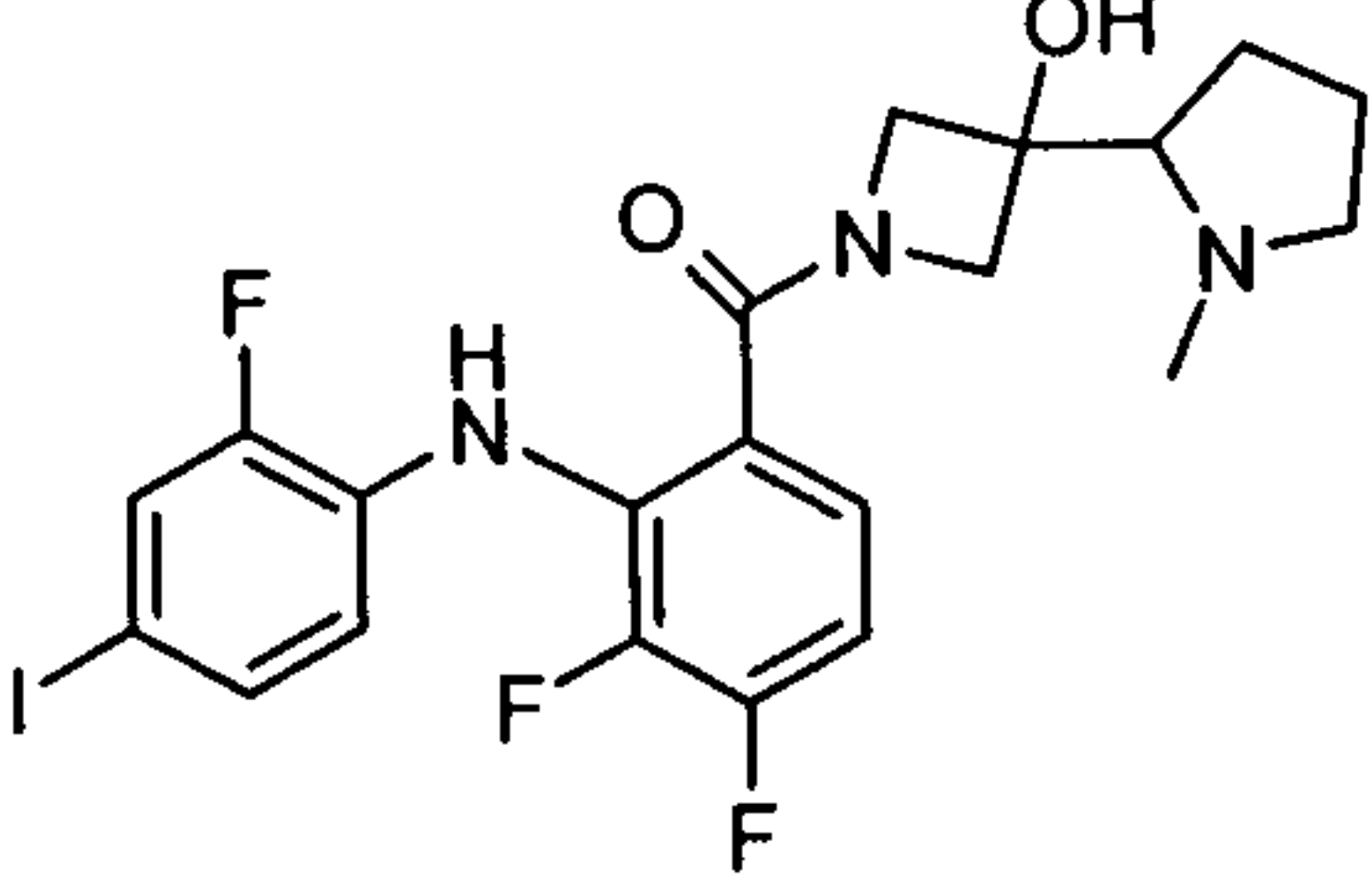
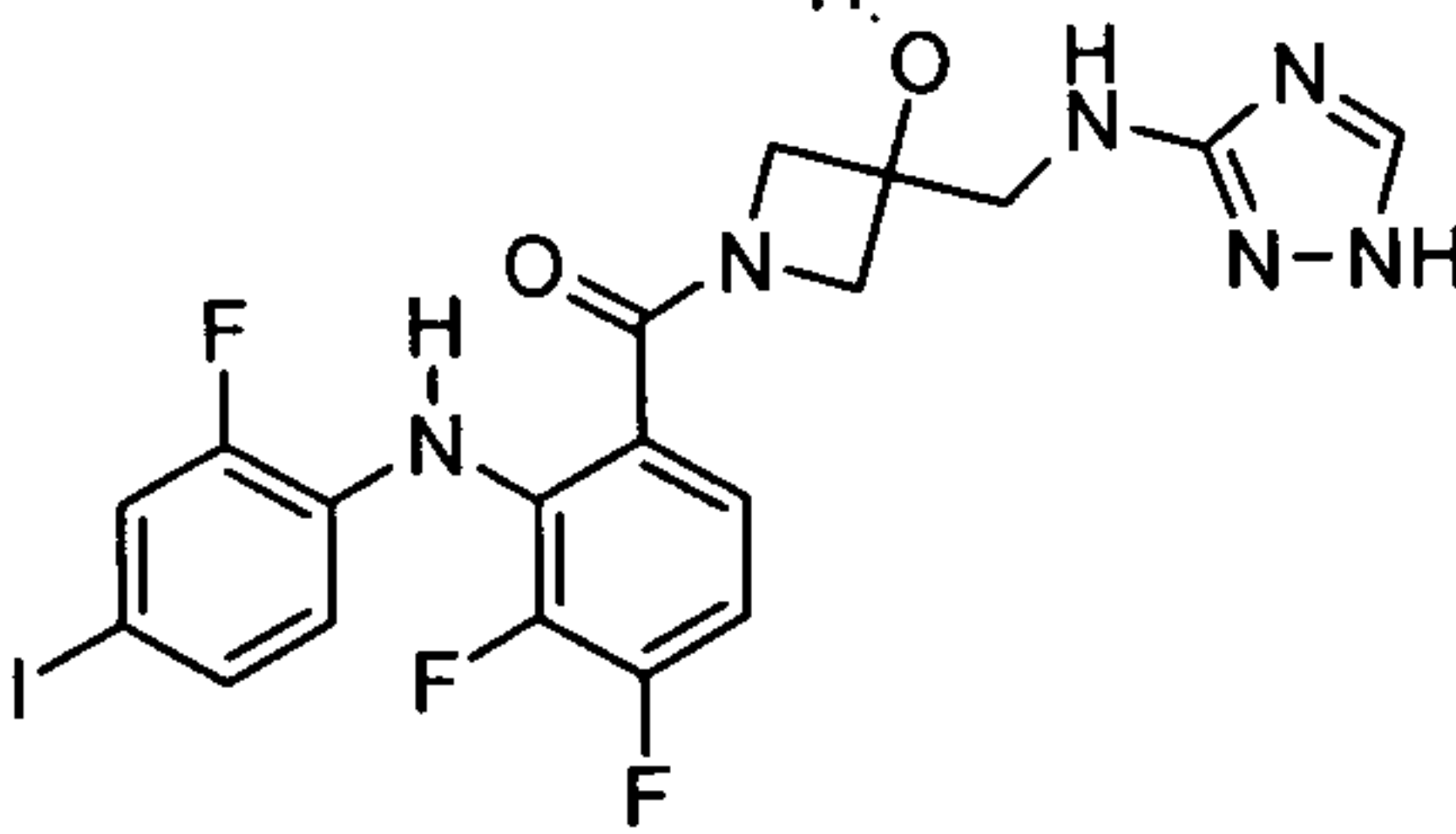
Cmpd No.	Structure	Name
222		N-[4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide
223		N-[3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)phenyl]acetamide
224		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methylpyrrolidin-2-yl)azetidin-3-ol
225		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1H-1,2,4-triazol-3-ylamino)methyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

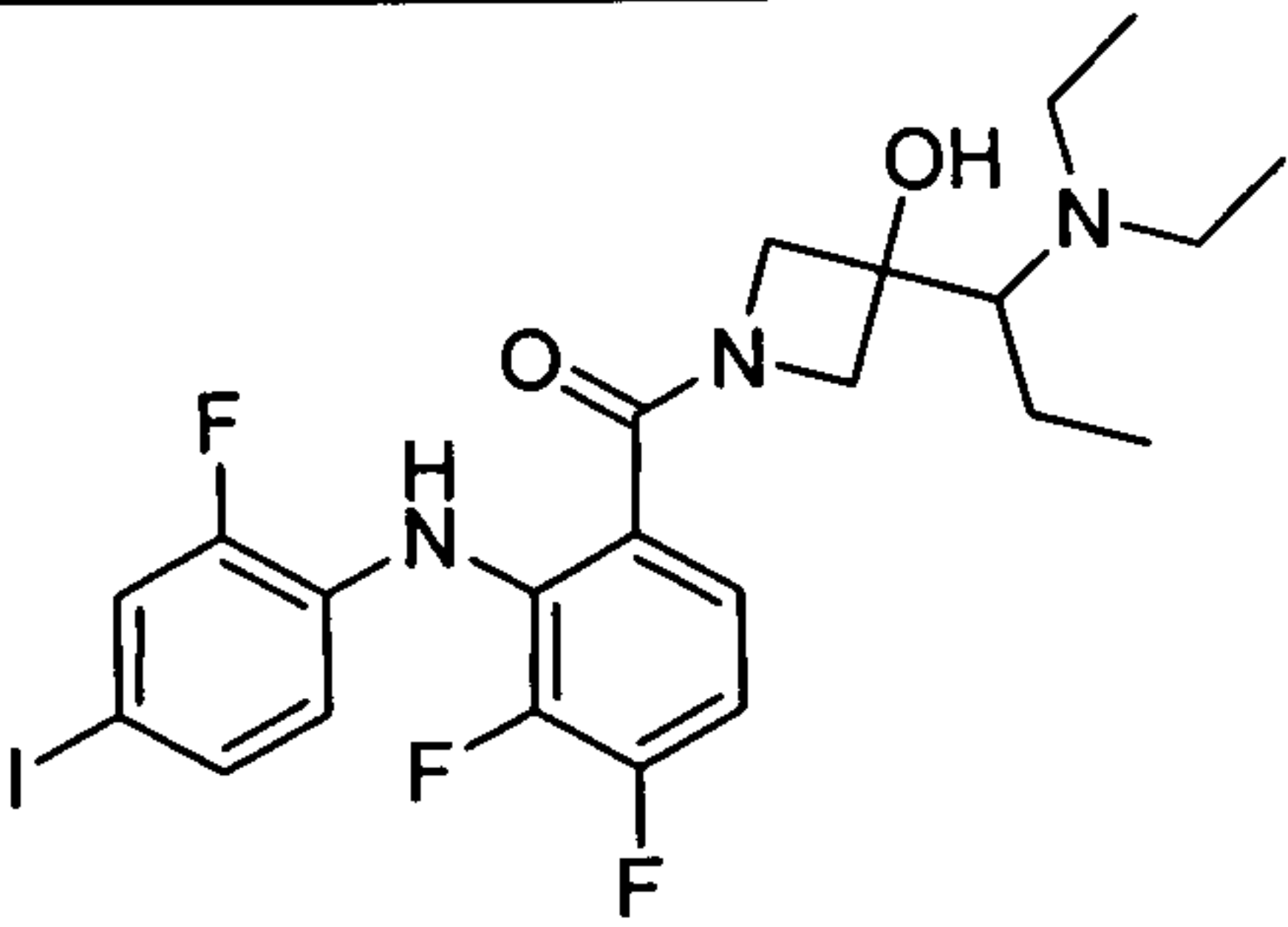
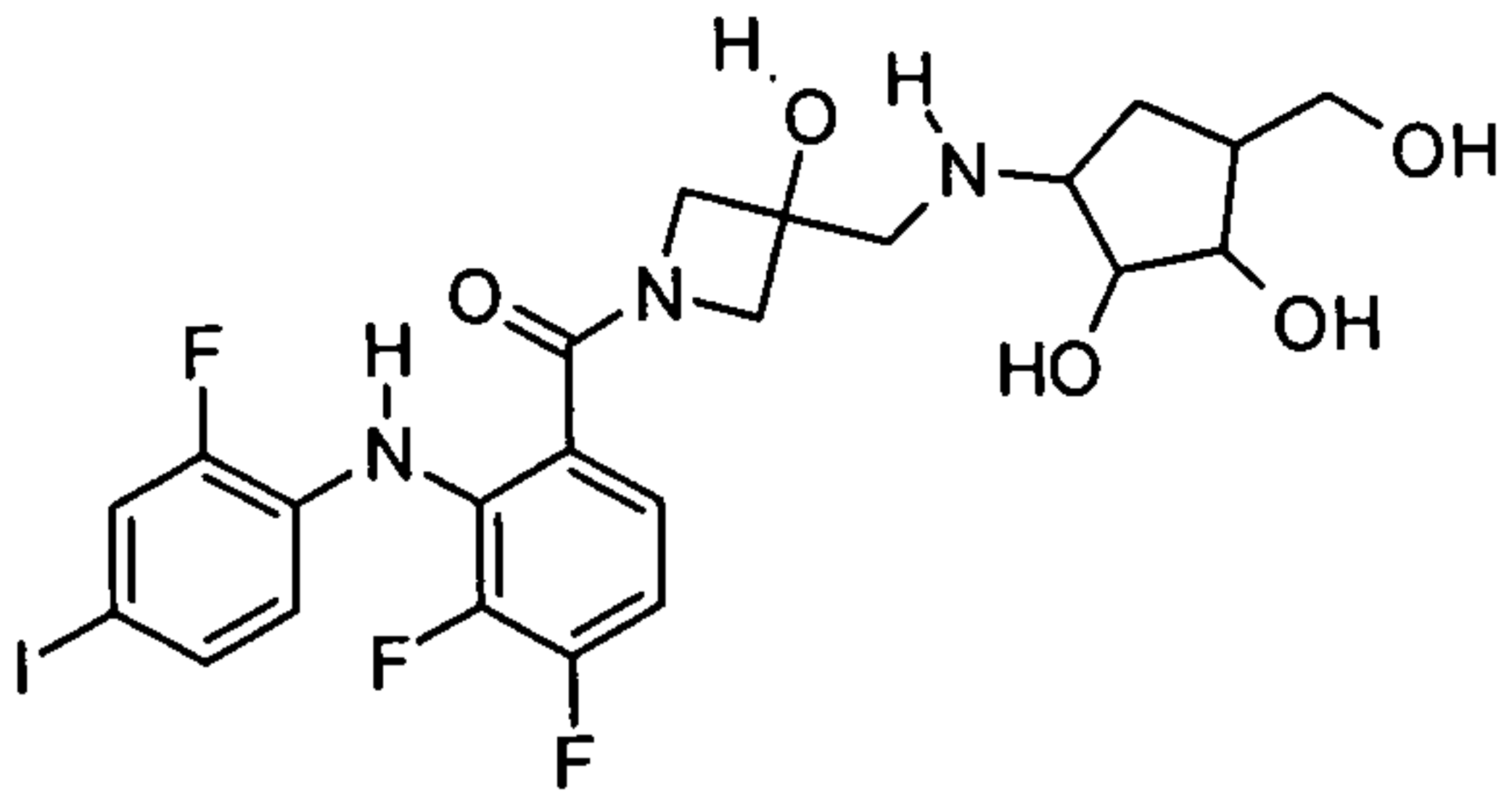
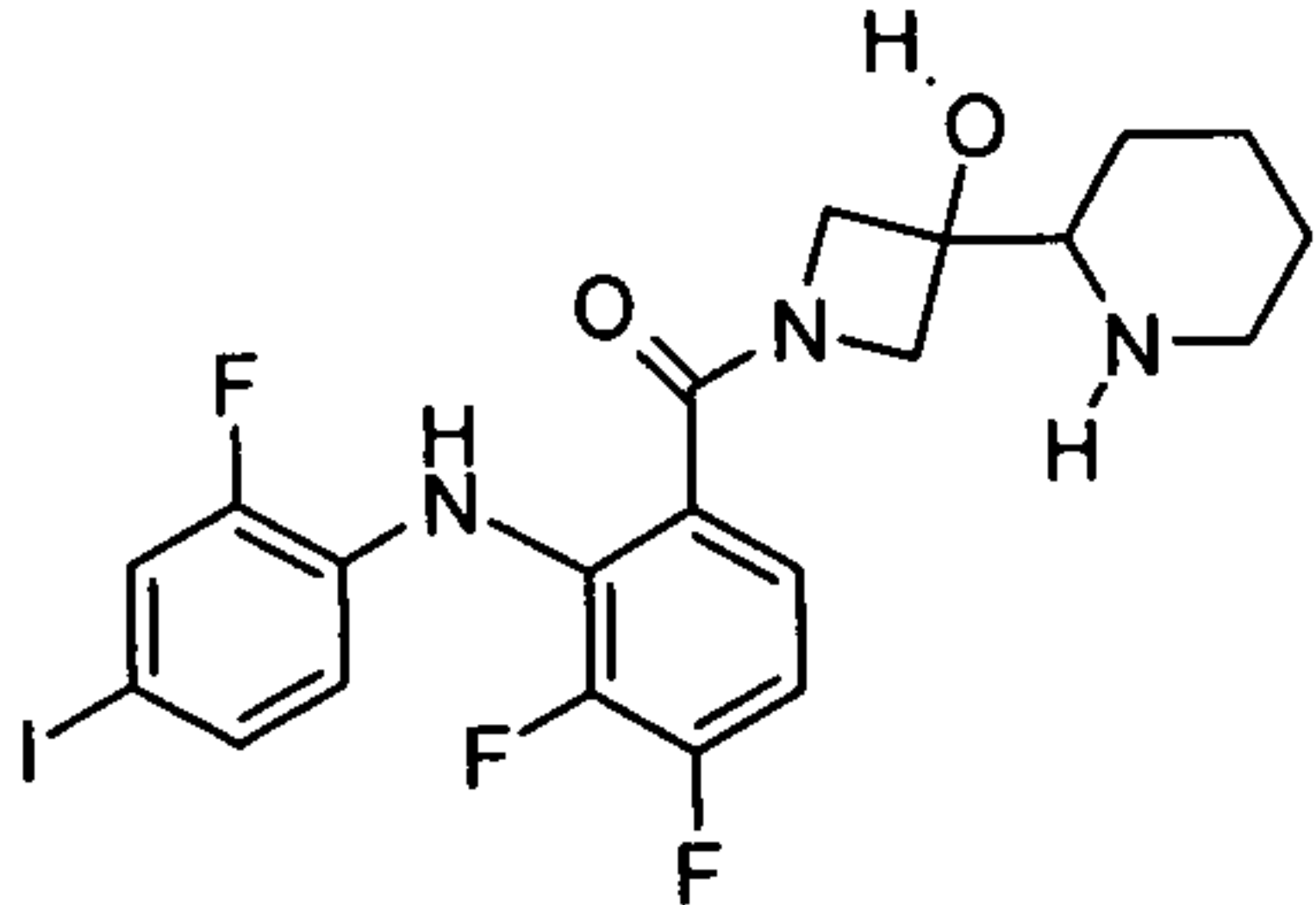
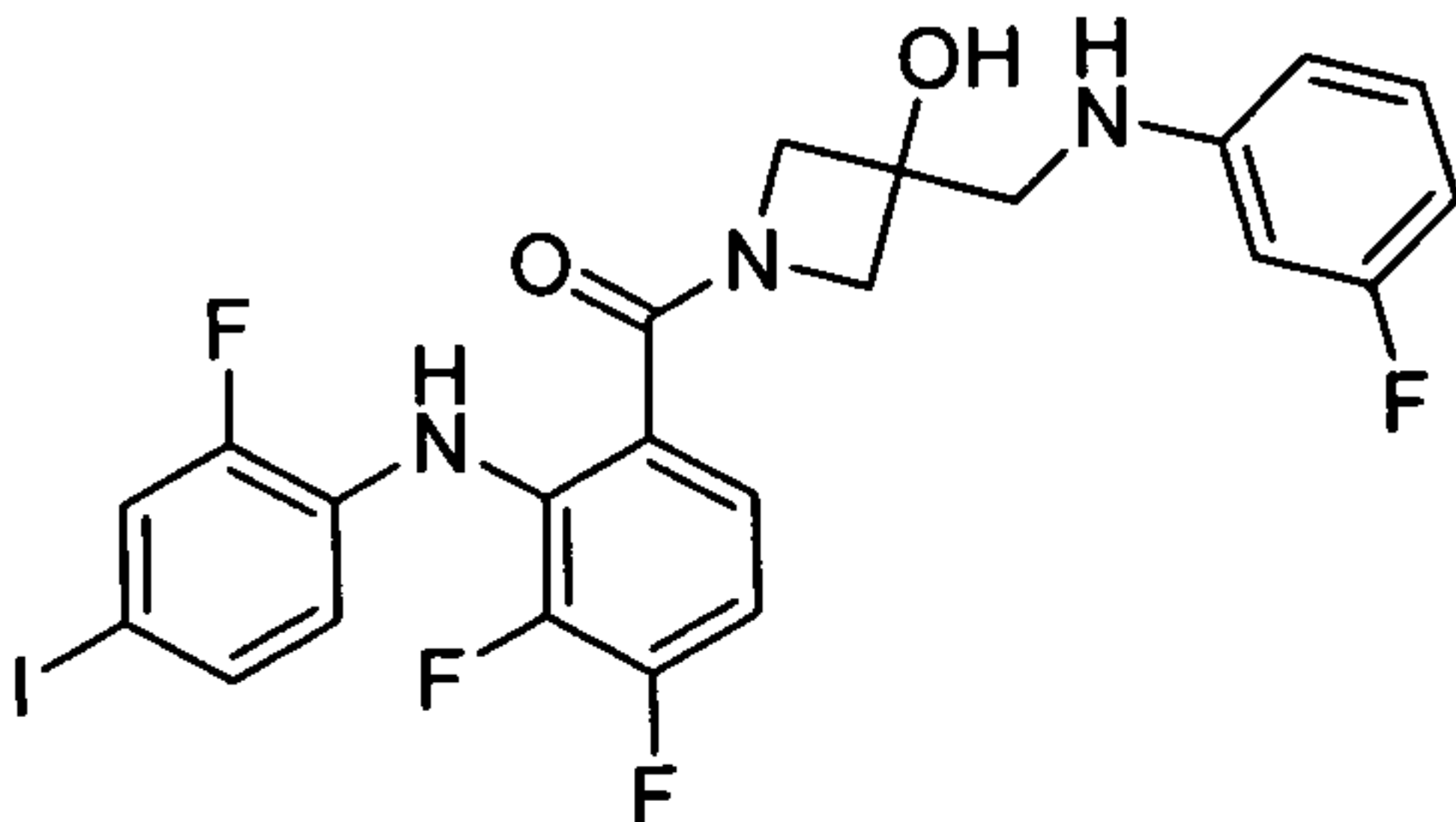
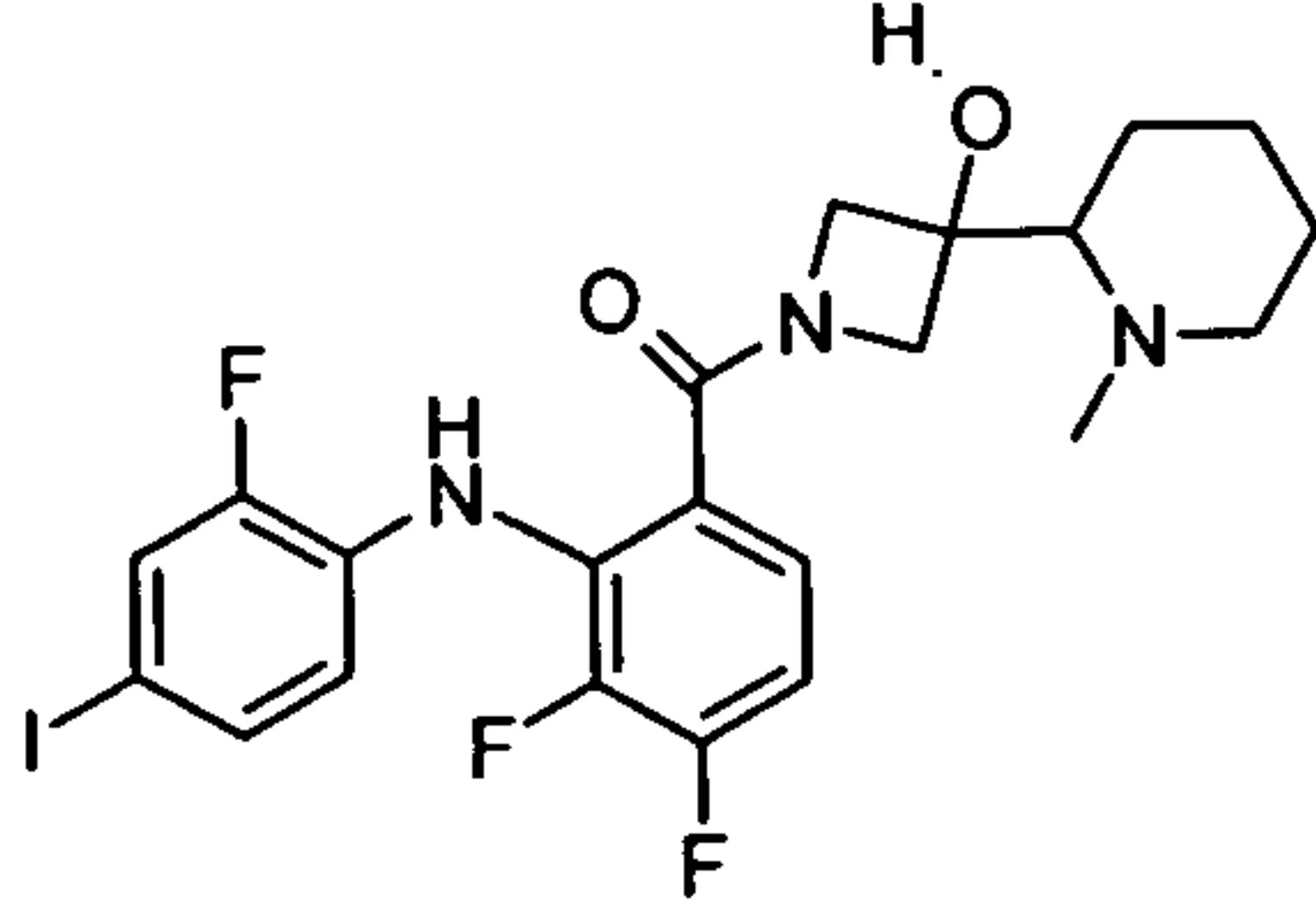
Cmpd No.	Structure	Name
226		3-[1-(diethylamino)propyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
227		3-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-5-(hydroxymethyl)cyclopentane-1,2-diol
228		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
229		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{[3-fluorophenyl]amino]methyl}azetidin-3-ol
230		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methylpiperidin-2-yl)azetidin-3-ol

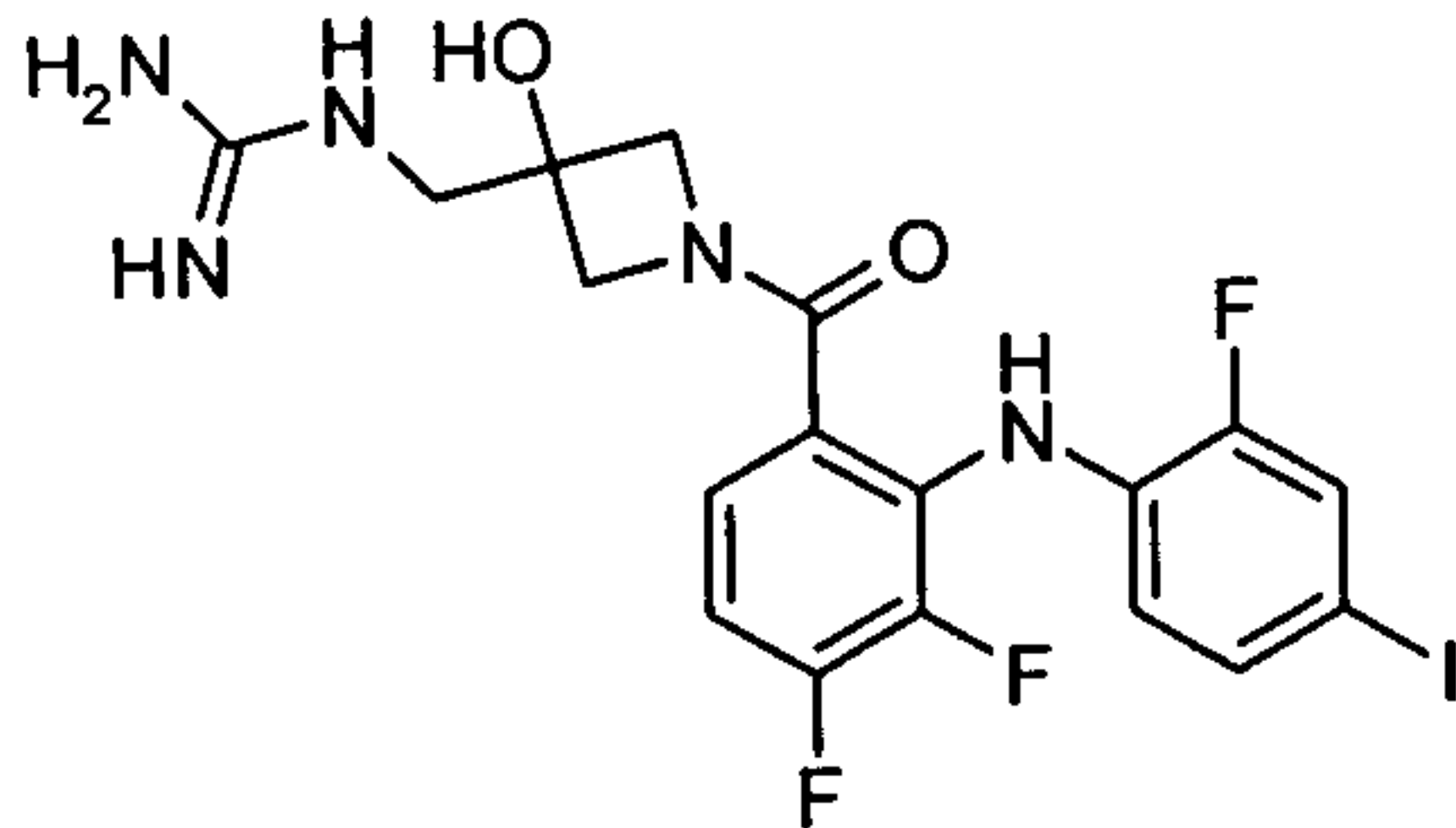
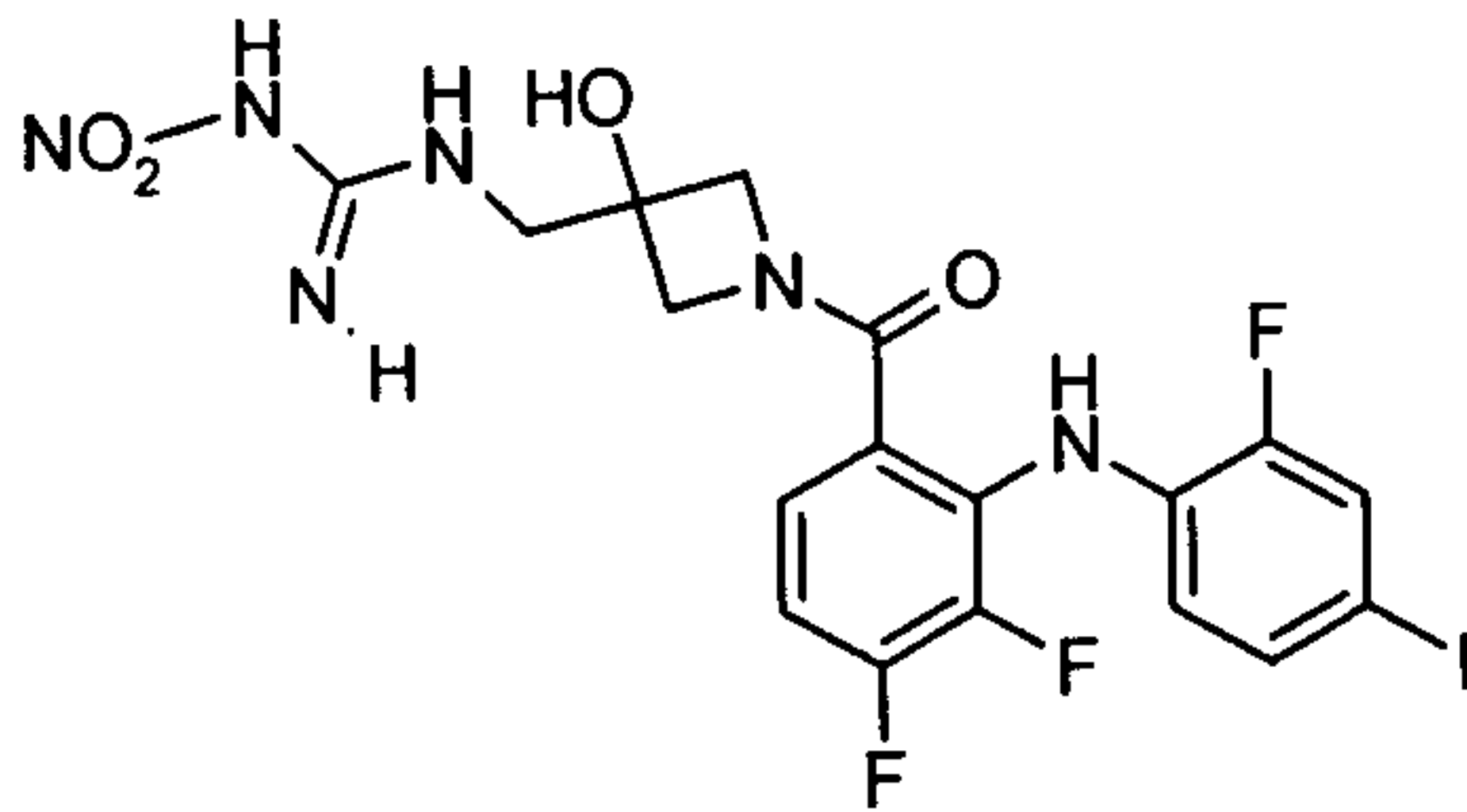
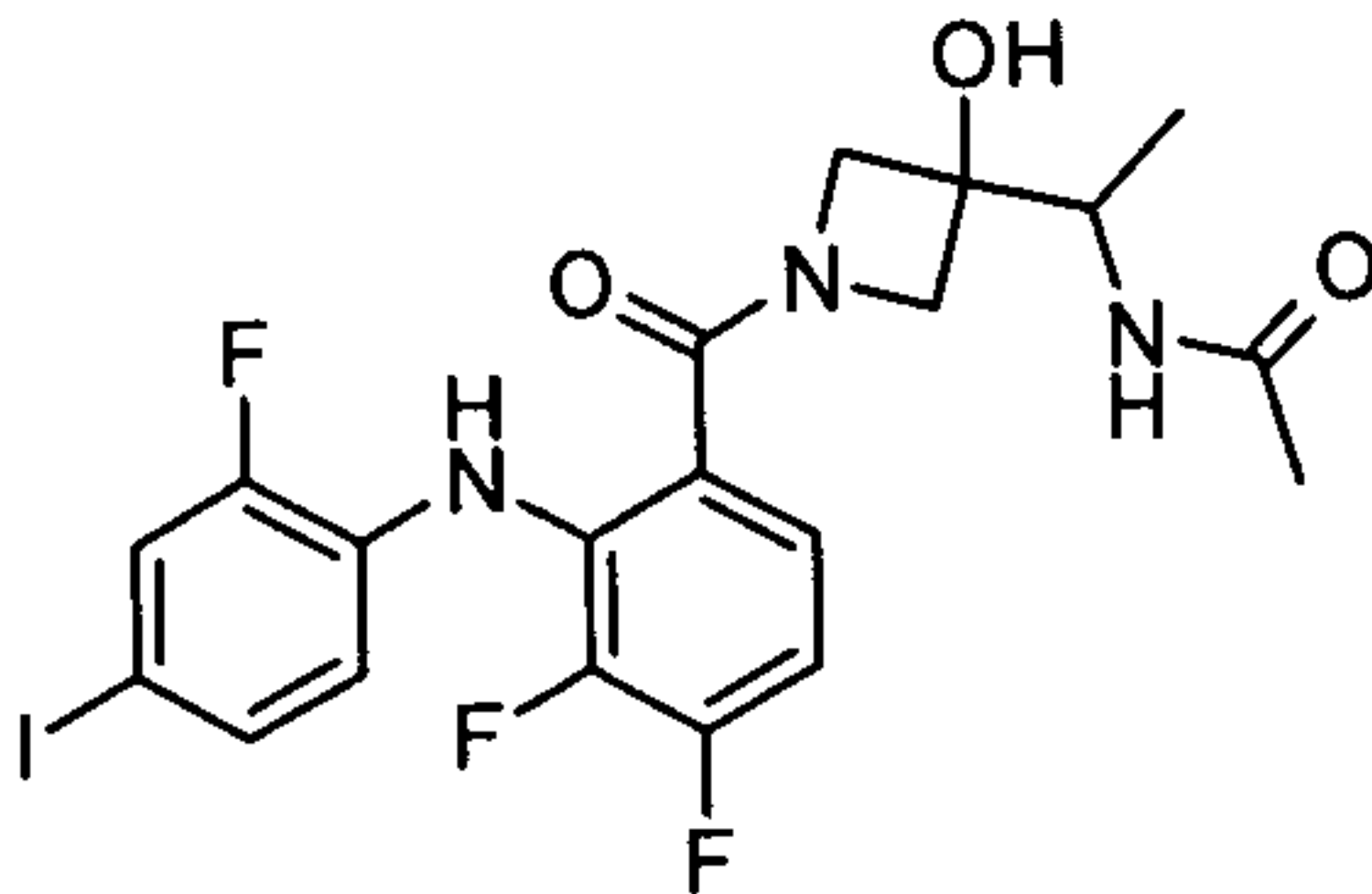
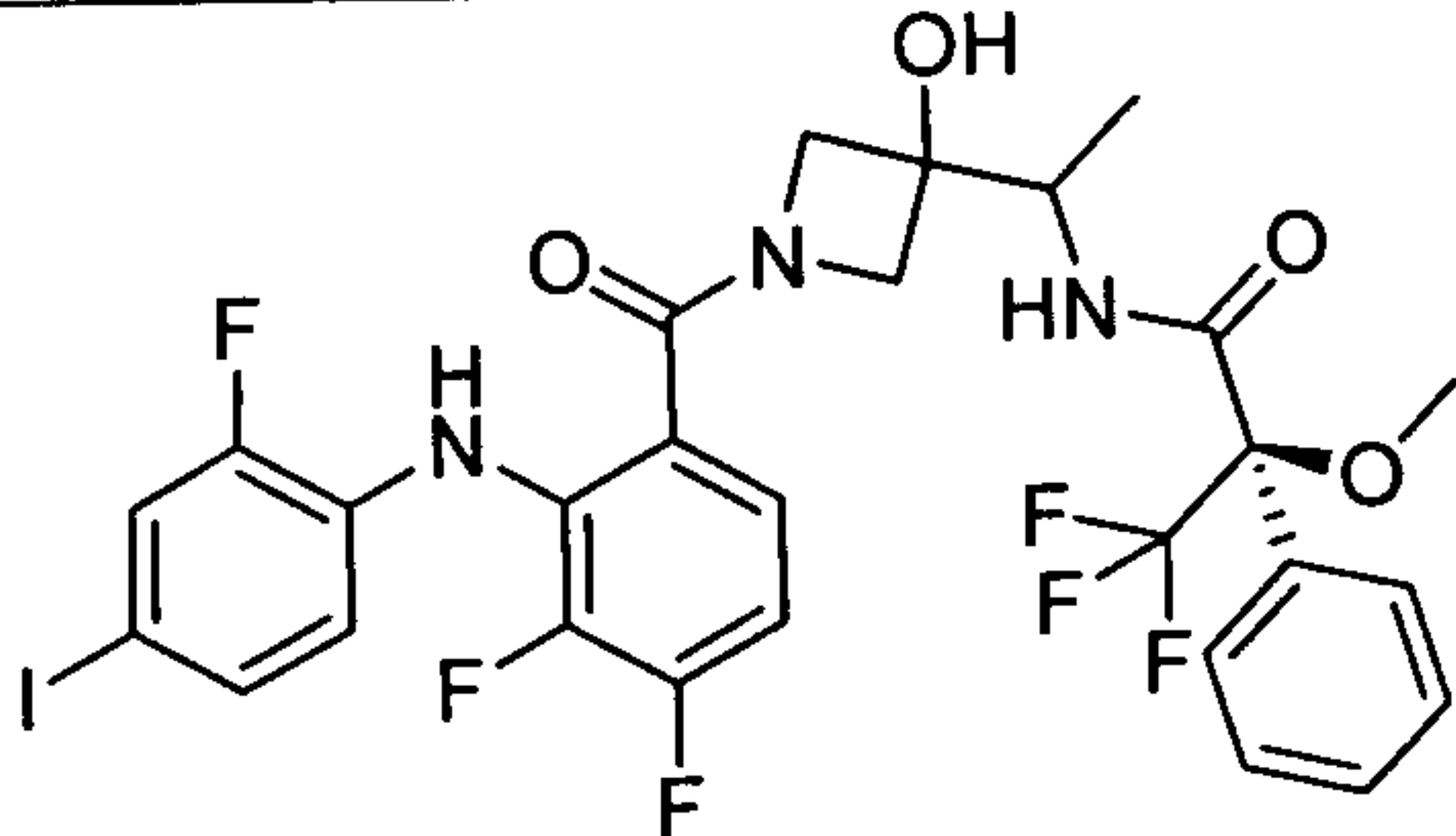
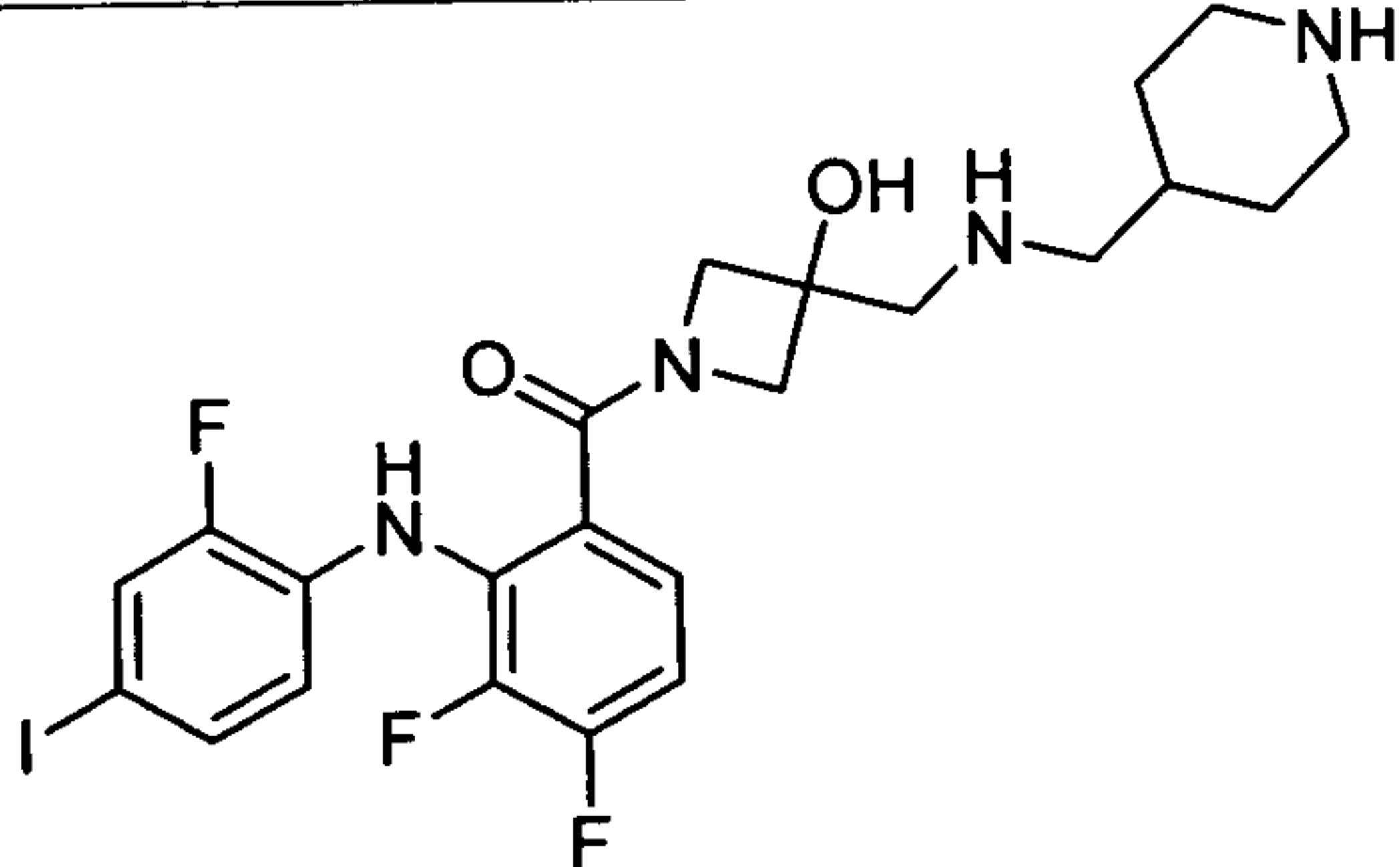
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
231		1-[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine
232		1-[[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}-3-nitroguanidine
233		<i>N</i> -{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}acetamide
234		(2 <i>R</i>)- <i>N</i> -{1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}-3,3,3-trifluoro-2-(methoxy)-2-phenylpropanamide
235		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[{(piperidin-4-ylmethyl)amino]methyl}azetidin-3-ol

Table 1. Representative MEK Inhibitors

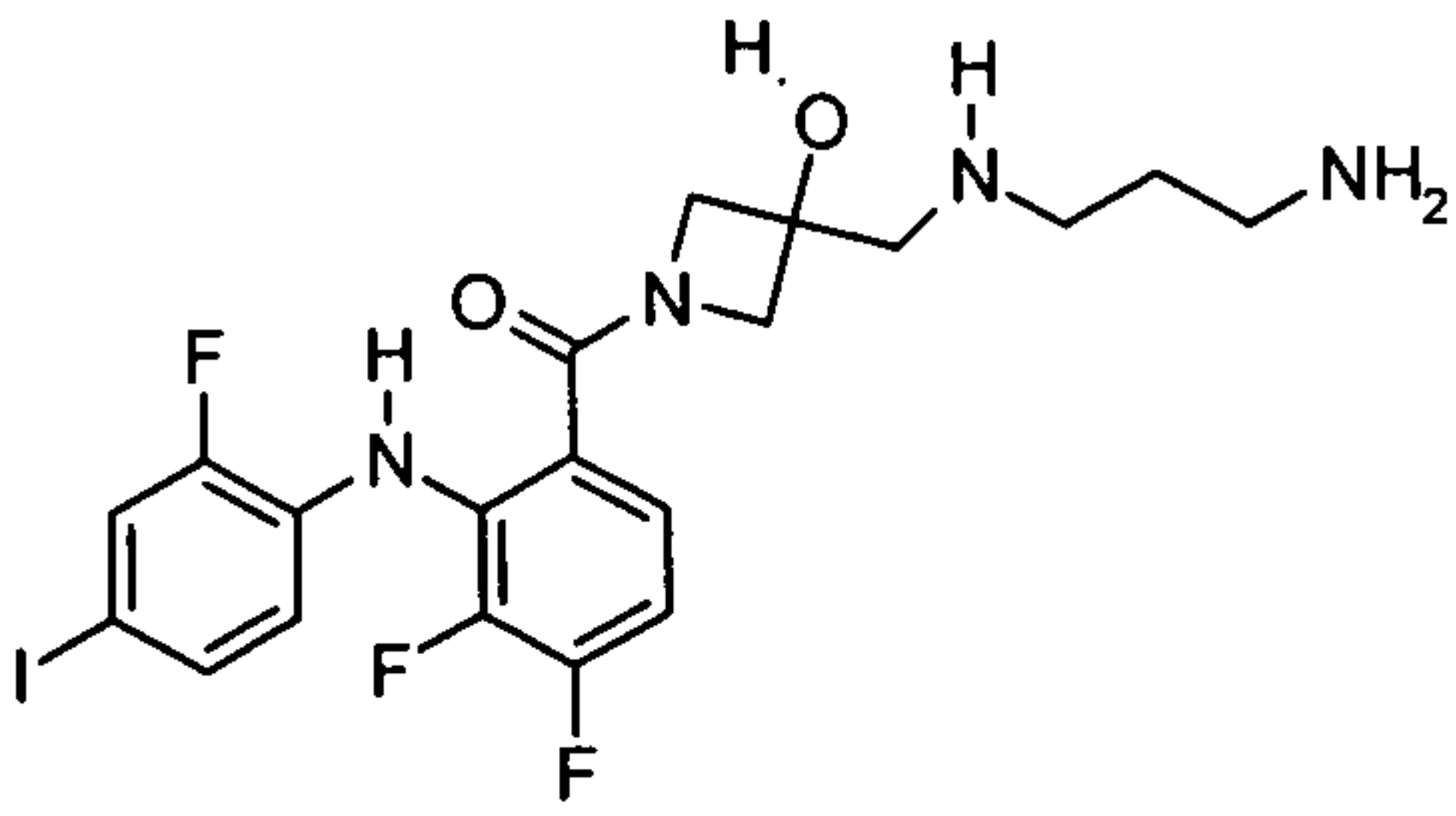
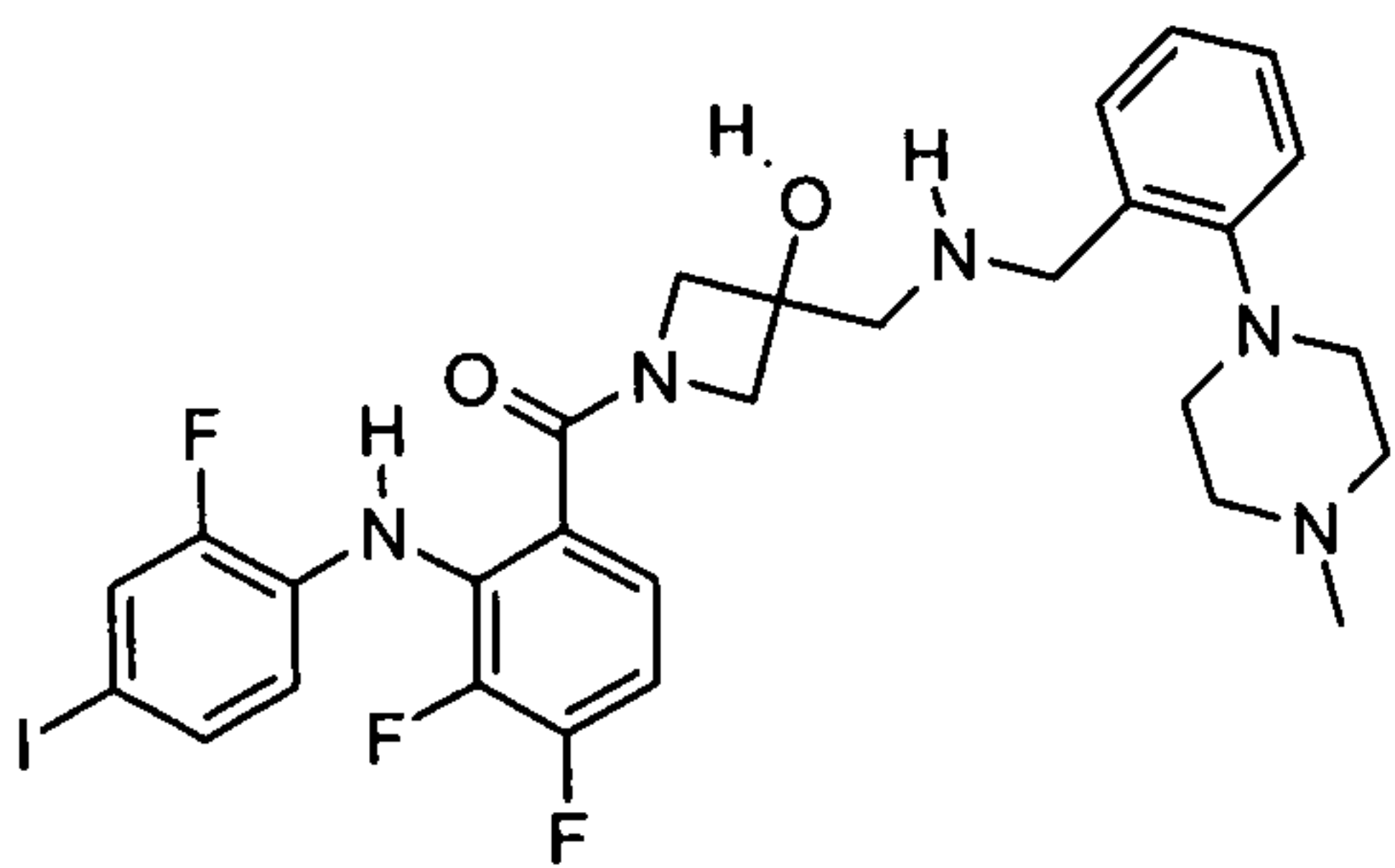
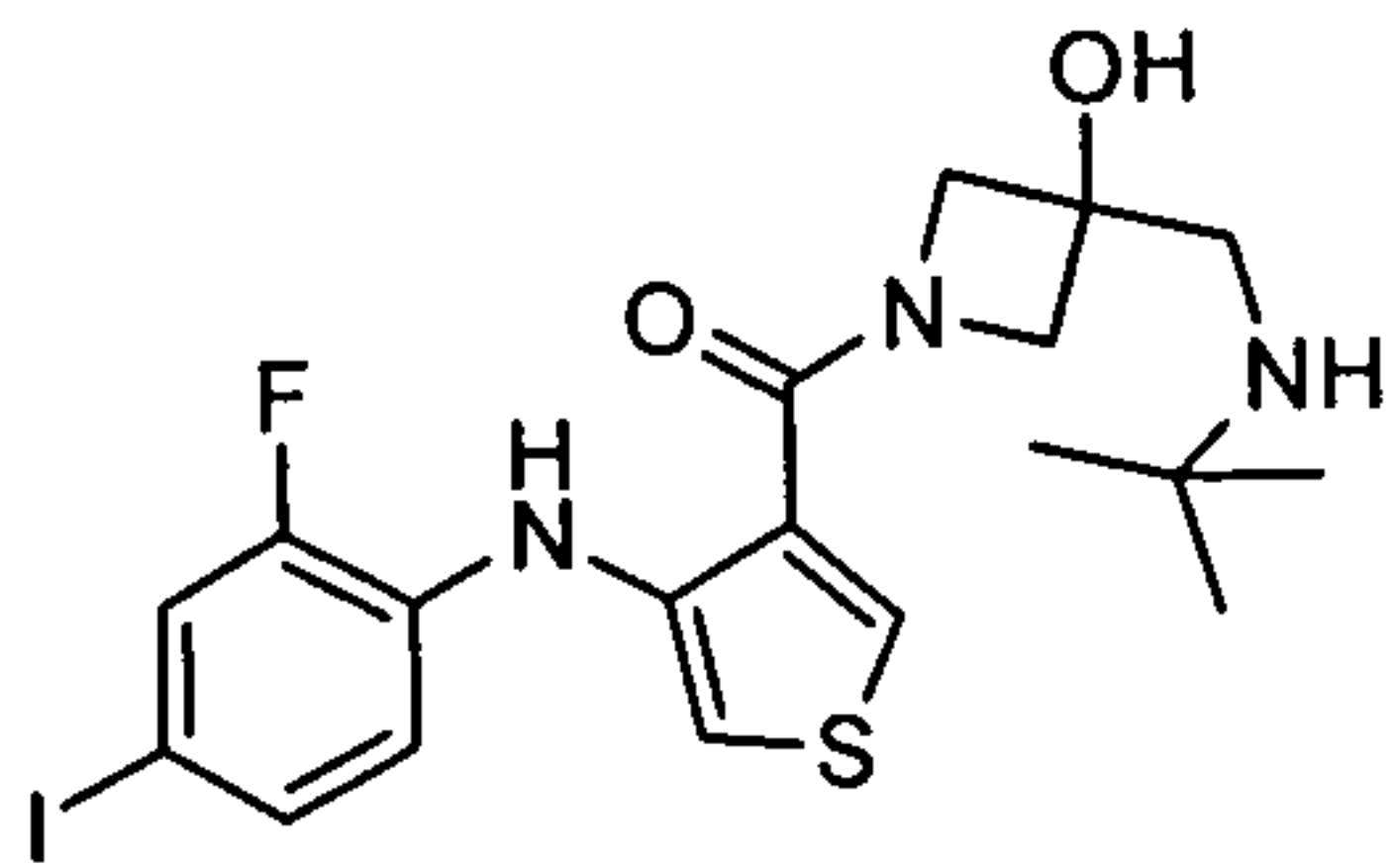
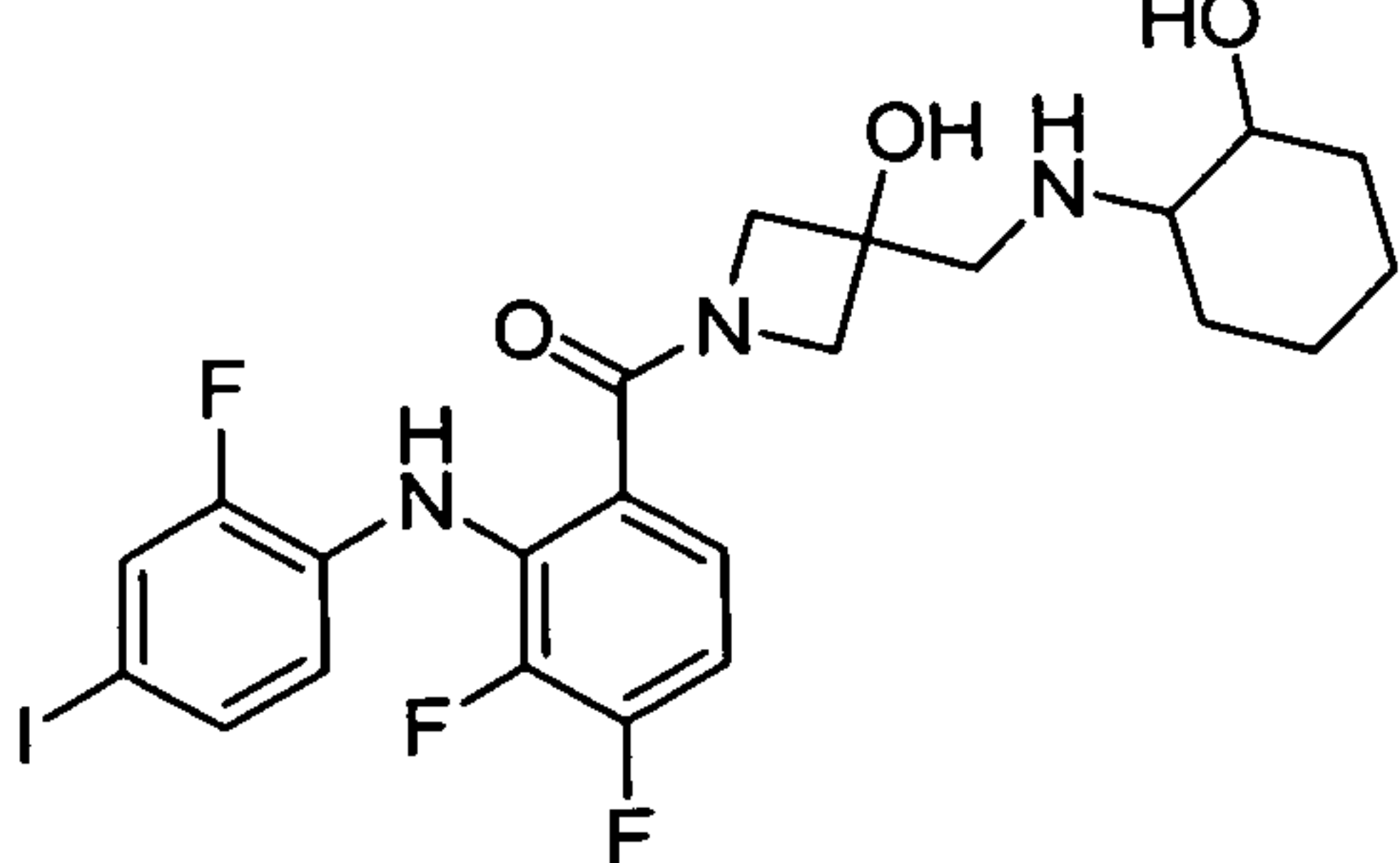
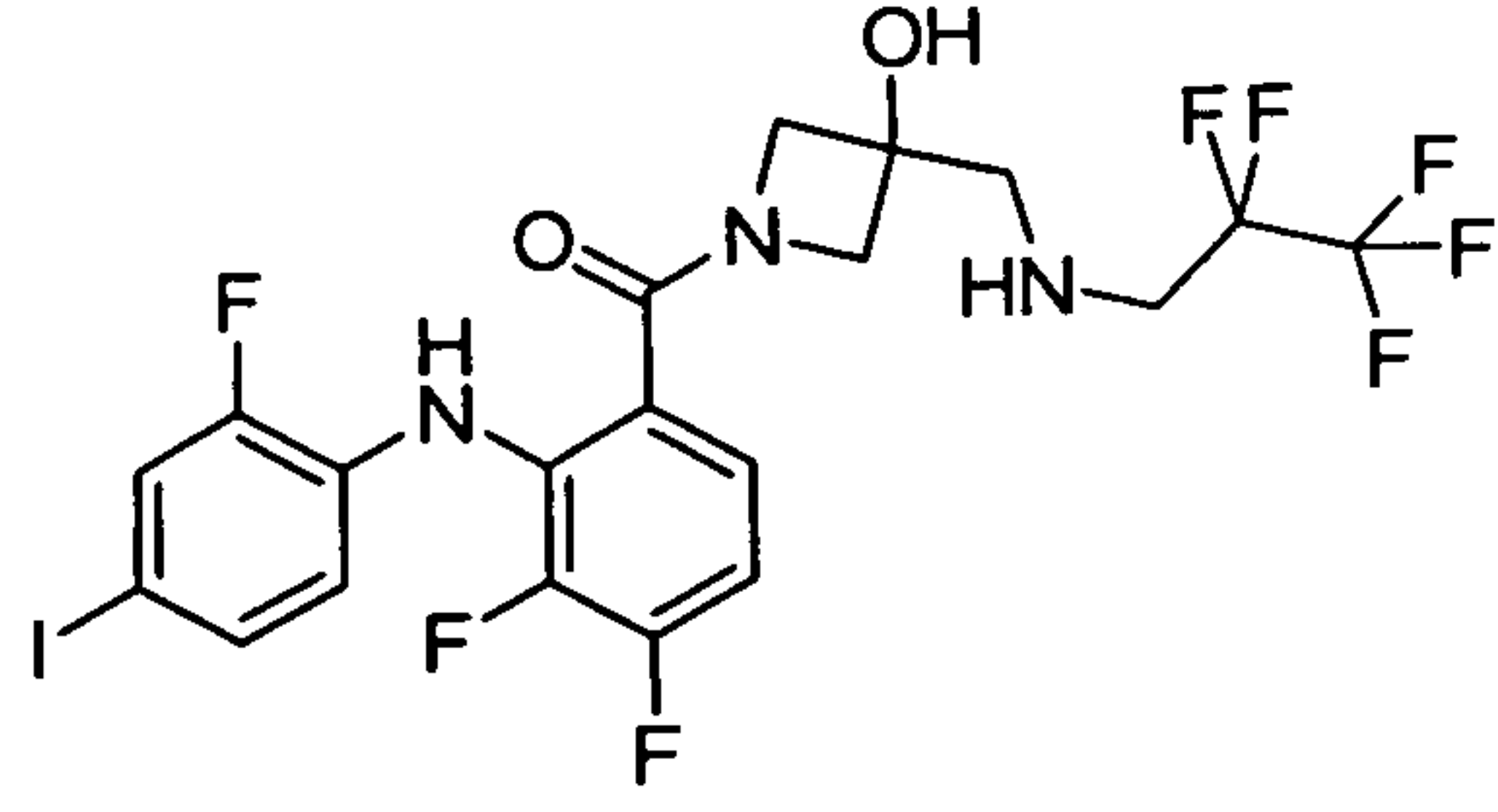
Cmpd No.	Structure	Name
236		3-[[[(3-aminopropyl)amino]methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
237		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[[2-(4-methylpiperazin-1-yl)phenyl]methyl]amino)methyl]azetidin-3-ol
238		3-[[[(1,1-dimethylethyl)amino]methyl]-1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol
239		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[[2-(hydroxycyclohexyl)amino]methyl]azetidin-3-ol
240		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[[2,2,3,3,3-pentafluoropropyl]amino]methyl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

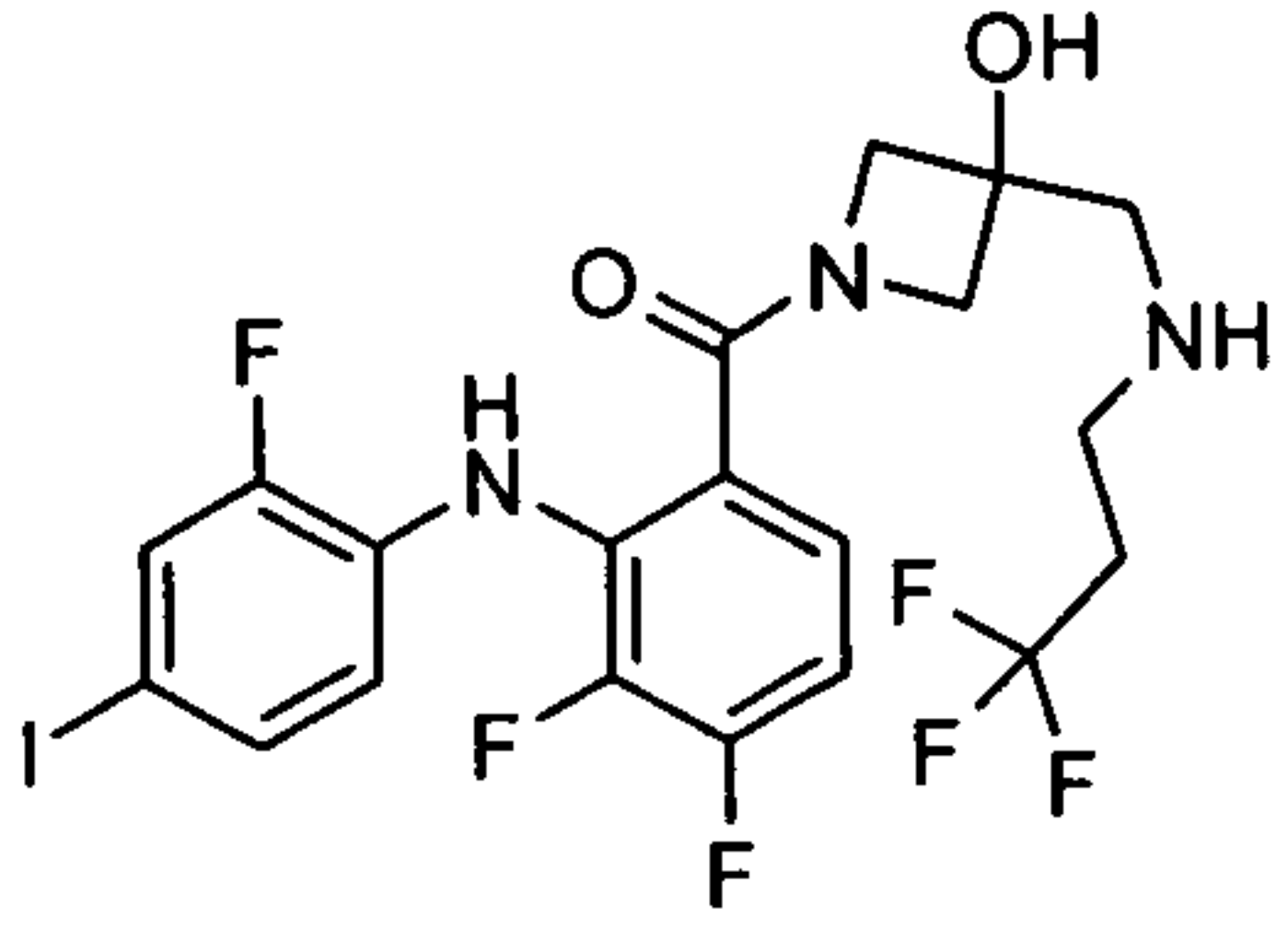
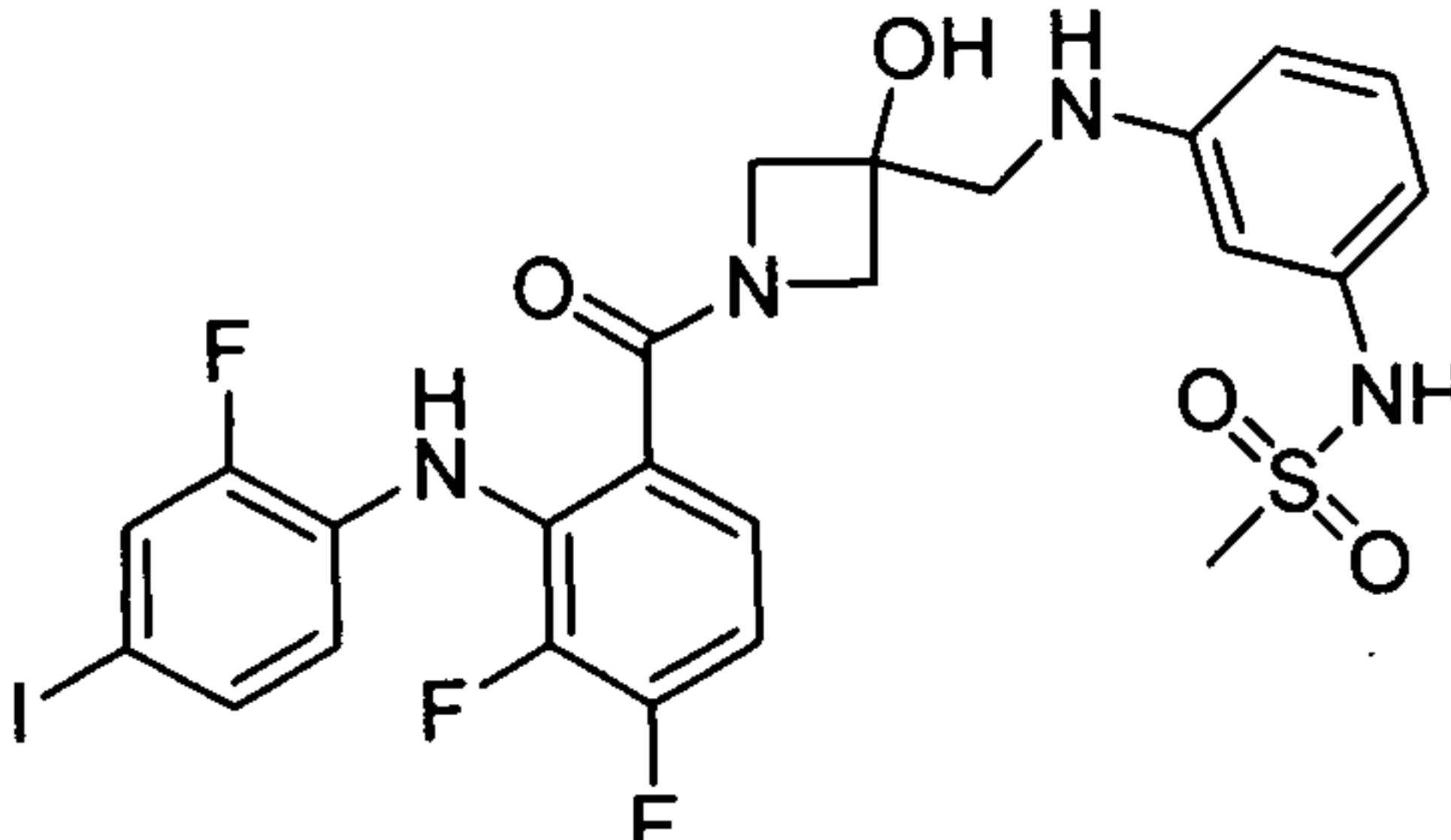
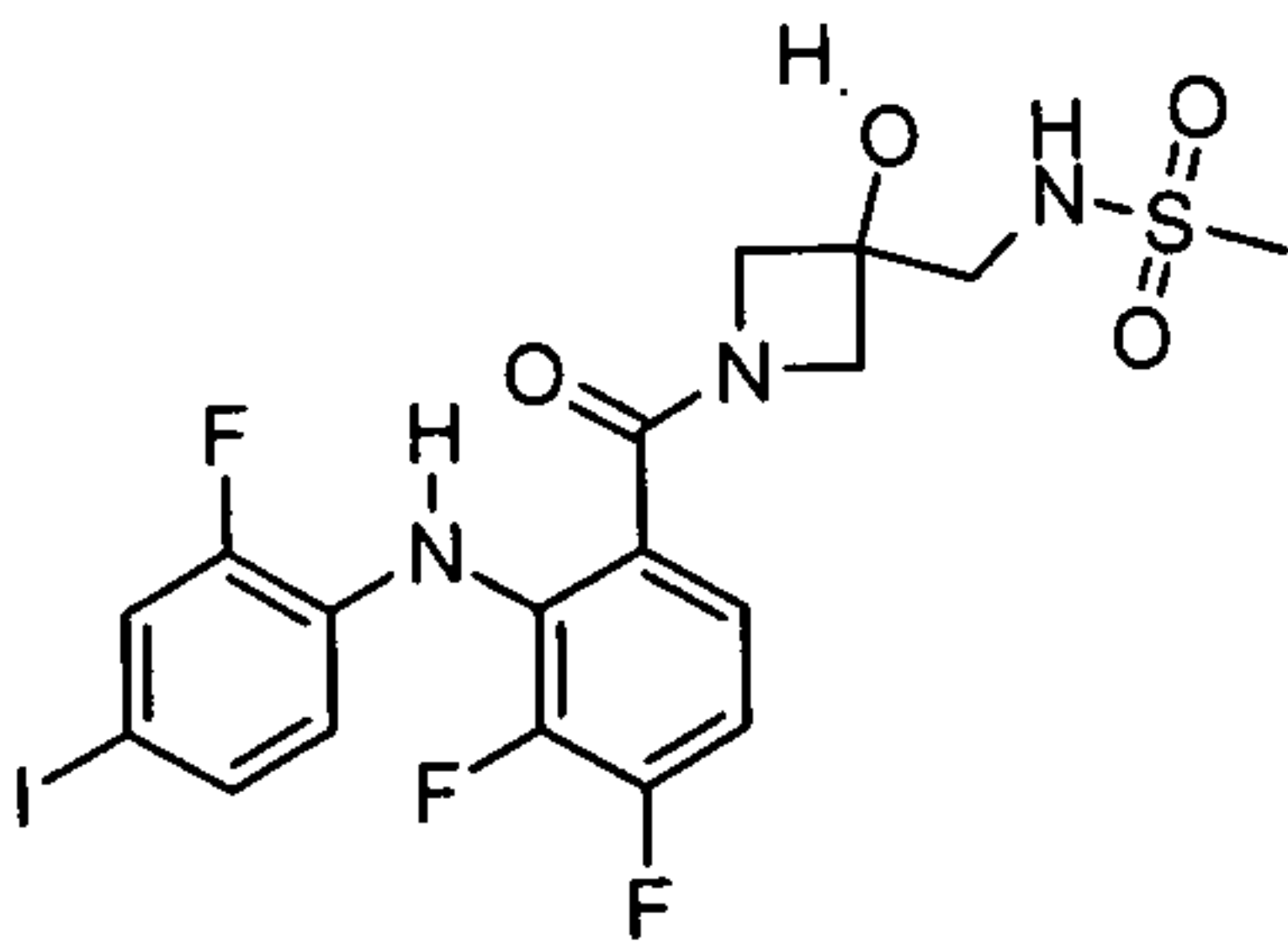
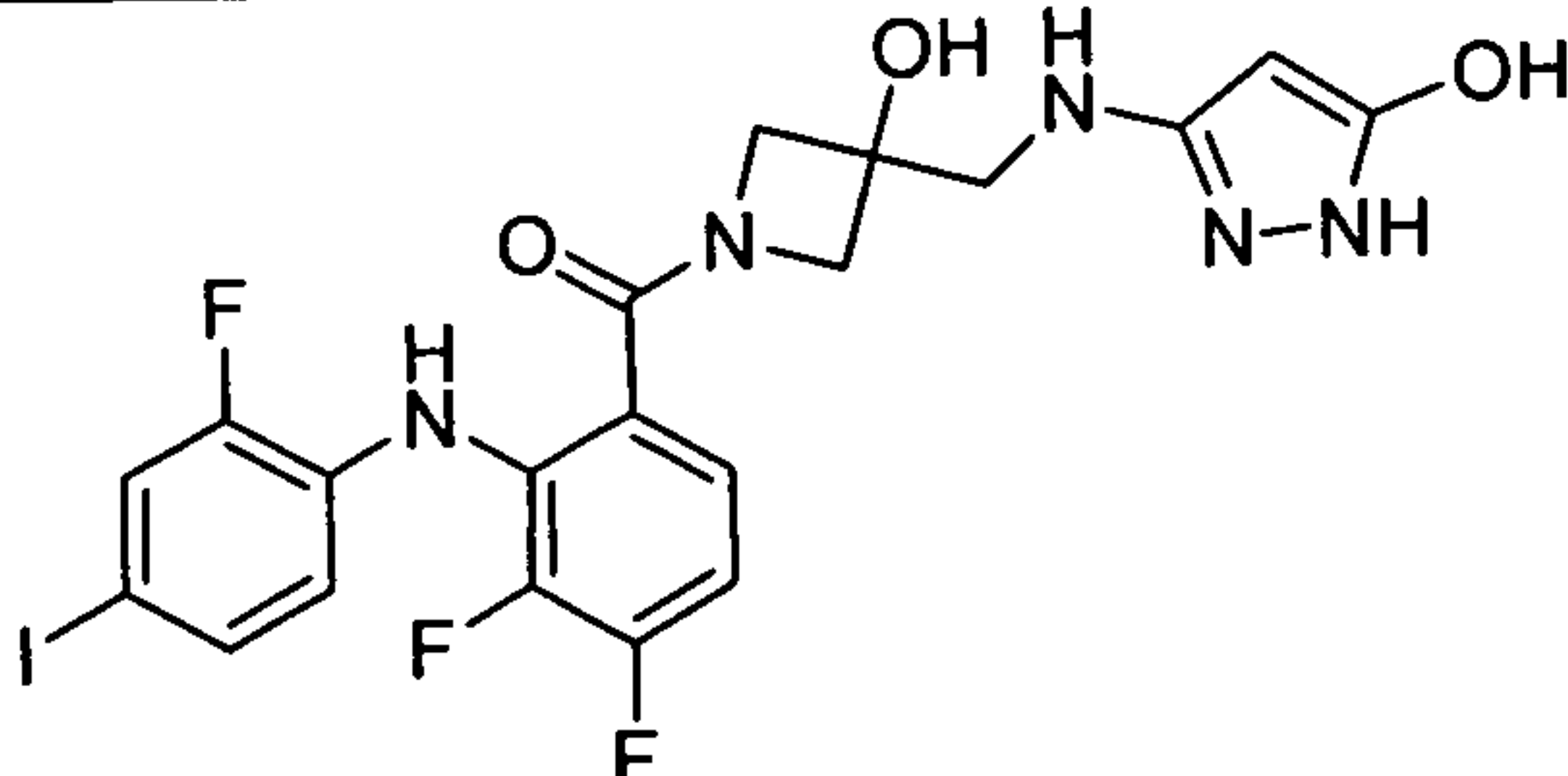
Cmpd No.	Structure	Name
241		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((3,3,3-trifluoropropyl)amino)methylazetidin-3-ol
242		<i>N</i> -[3-((1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-hydroxyazetidin-3-yl)methyl)amino)phenyl]methanesulfonamide
243		<i>N</i> -{[1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-hydroxyazetidin-3-yl]methyl}methanesulfonamide
244		3-((1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-hydroxyazetidin-3-yl)methyl)amino)-1 <i>H</i> -pyrazol-5-ol

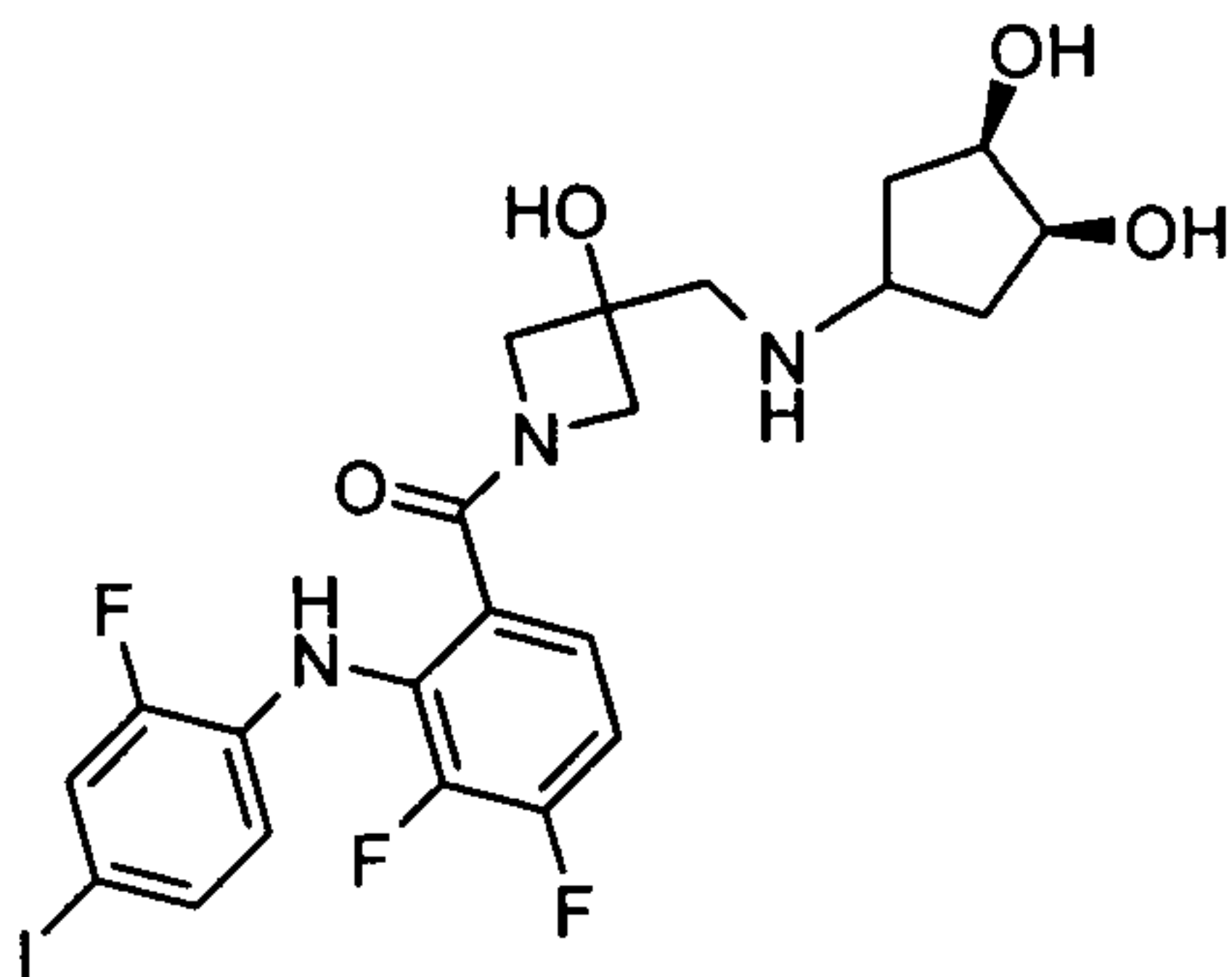
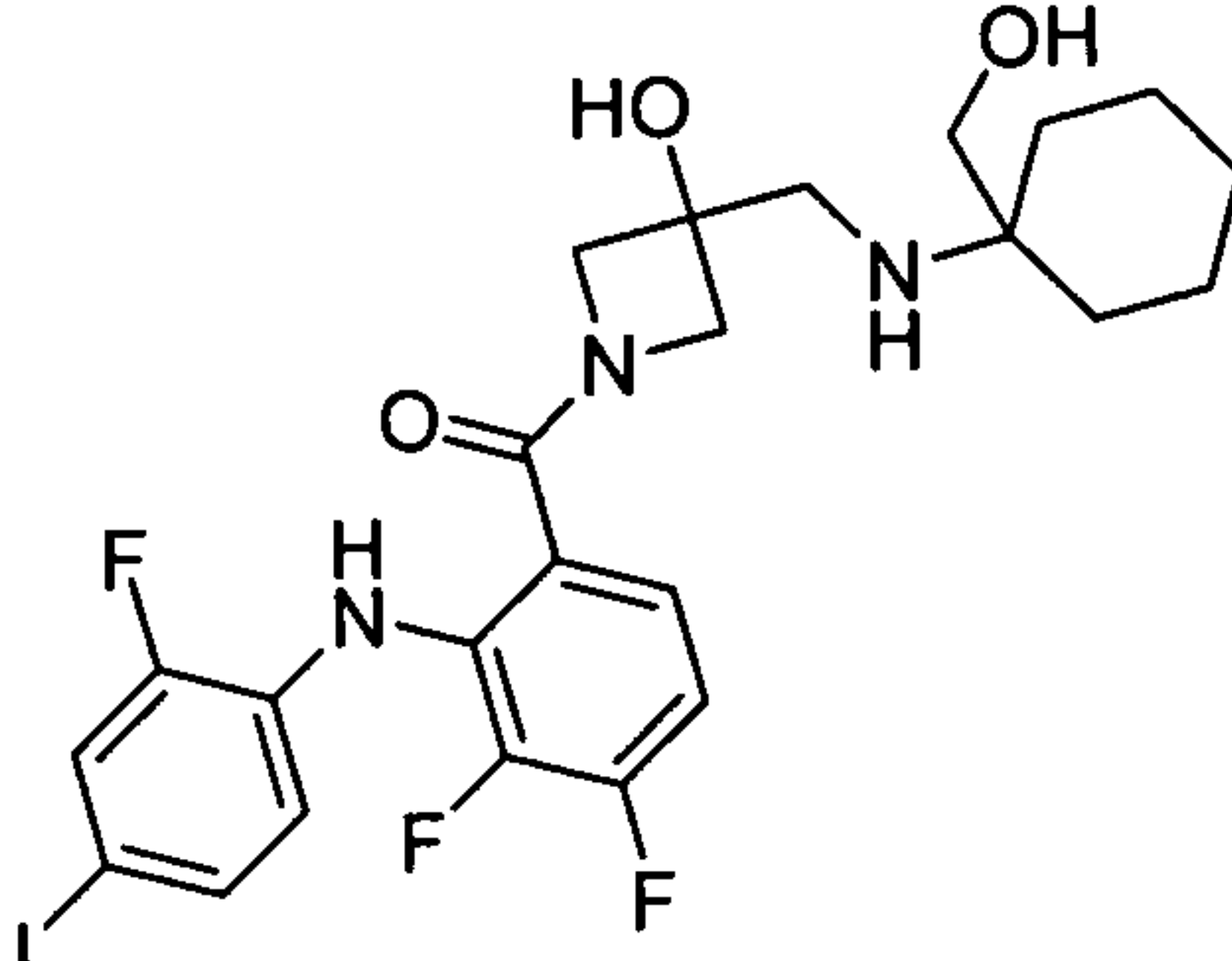
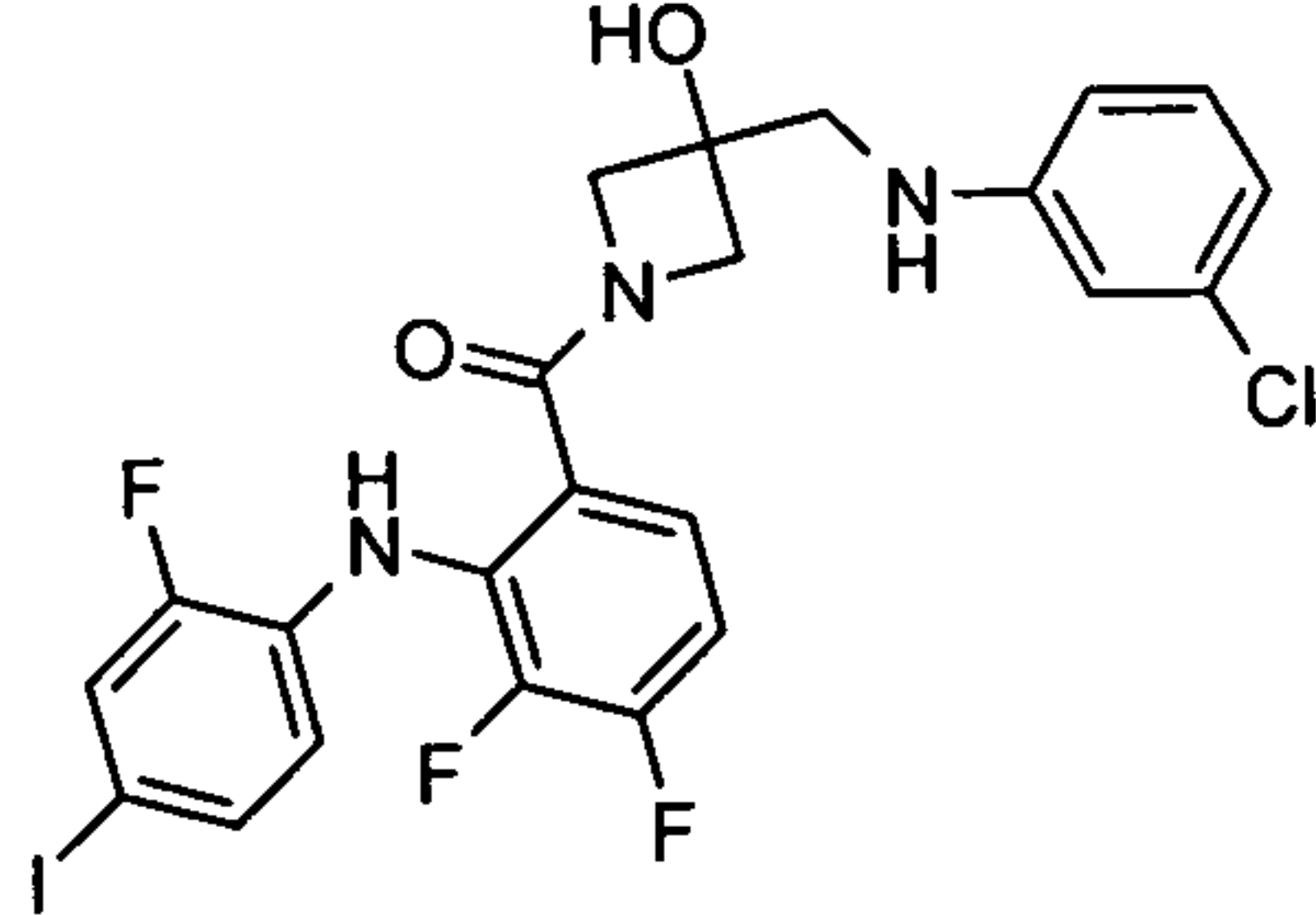
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
245		(1 <i>R</i> ,2 <i>S</i>)-4-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-hydroxyazetidin-3-yl]methyl} amino)cyclopentane-1,2-diol
246		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)-3-({[1-(hydroxymethyl)cyclohexyl]amino} methyl)azetidin-3-ol
247		3-{{[(3-chlorophenyl)amino]methyl}-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl} carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

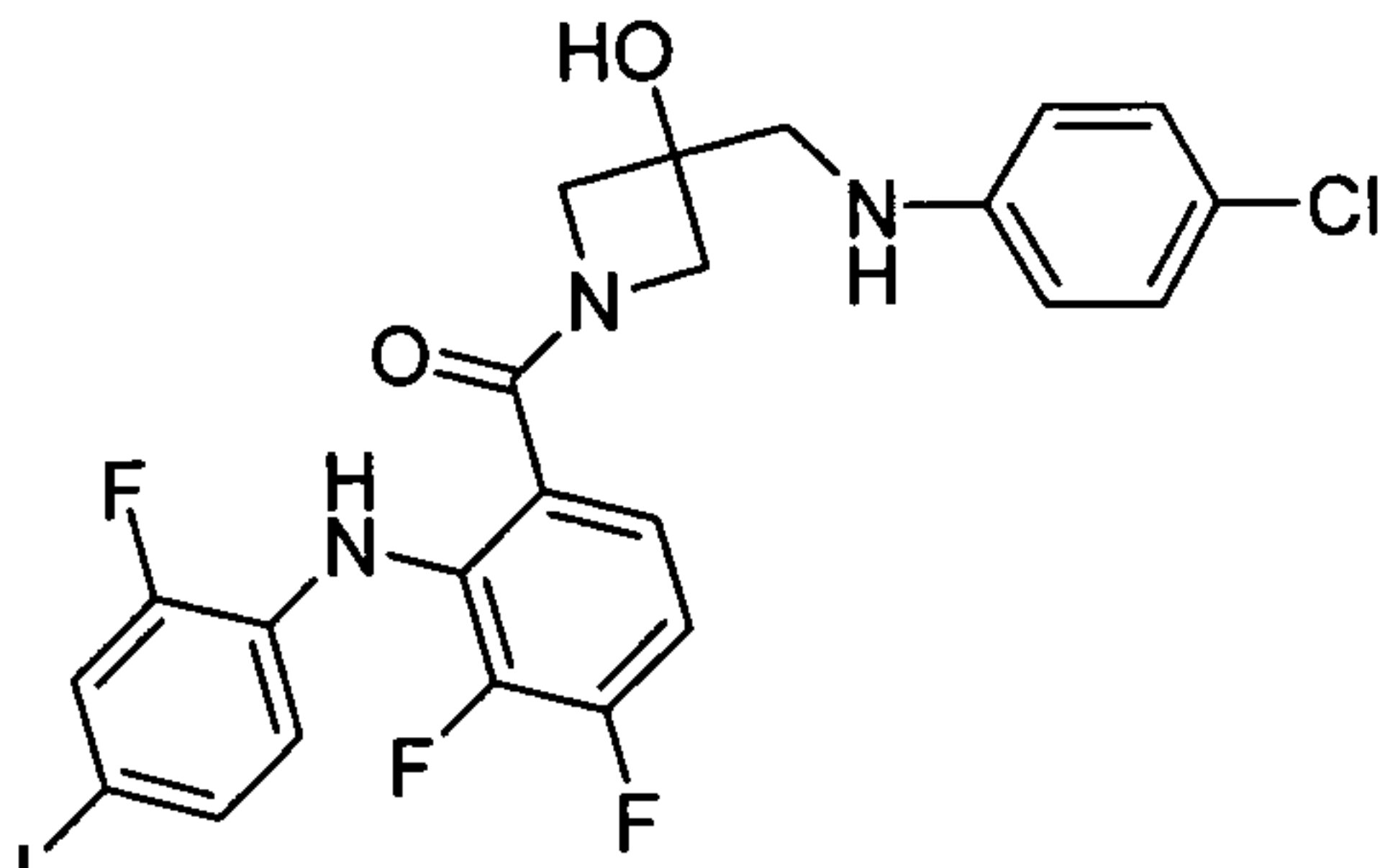
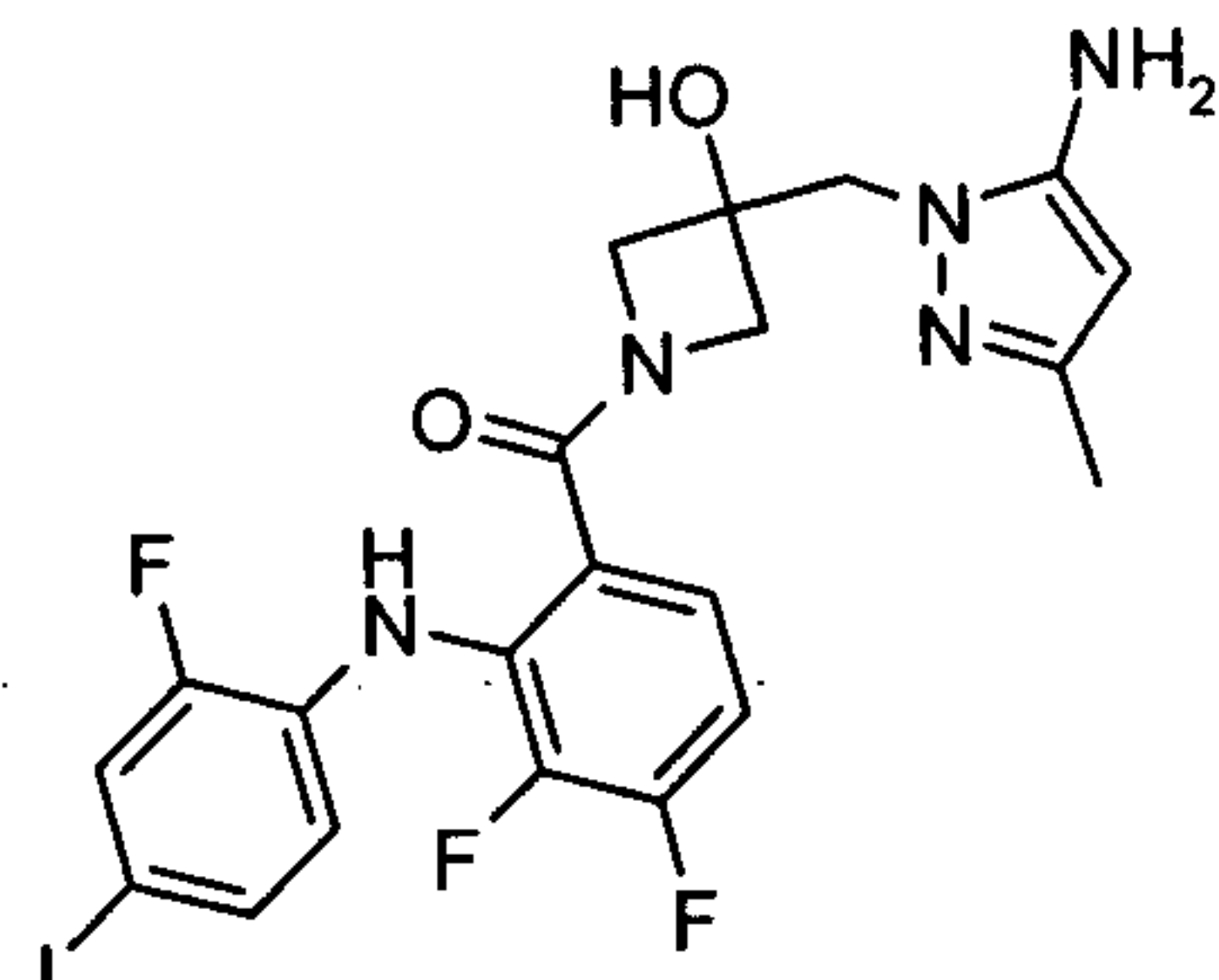
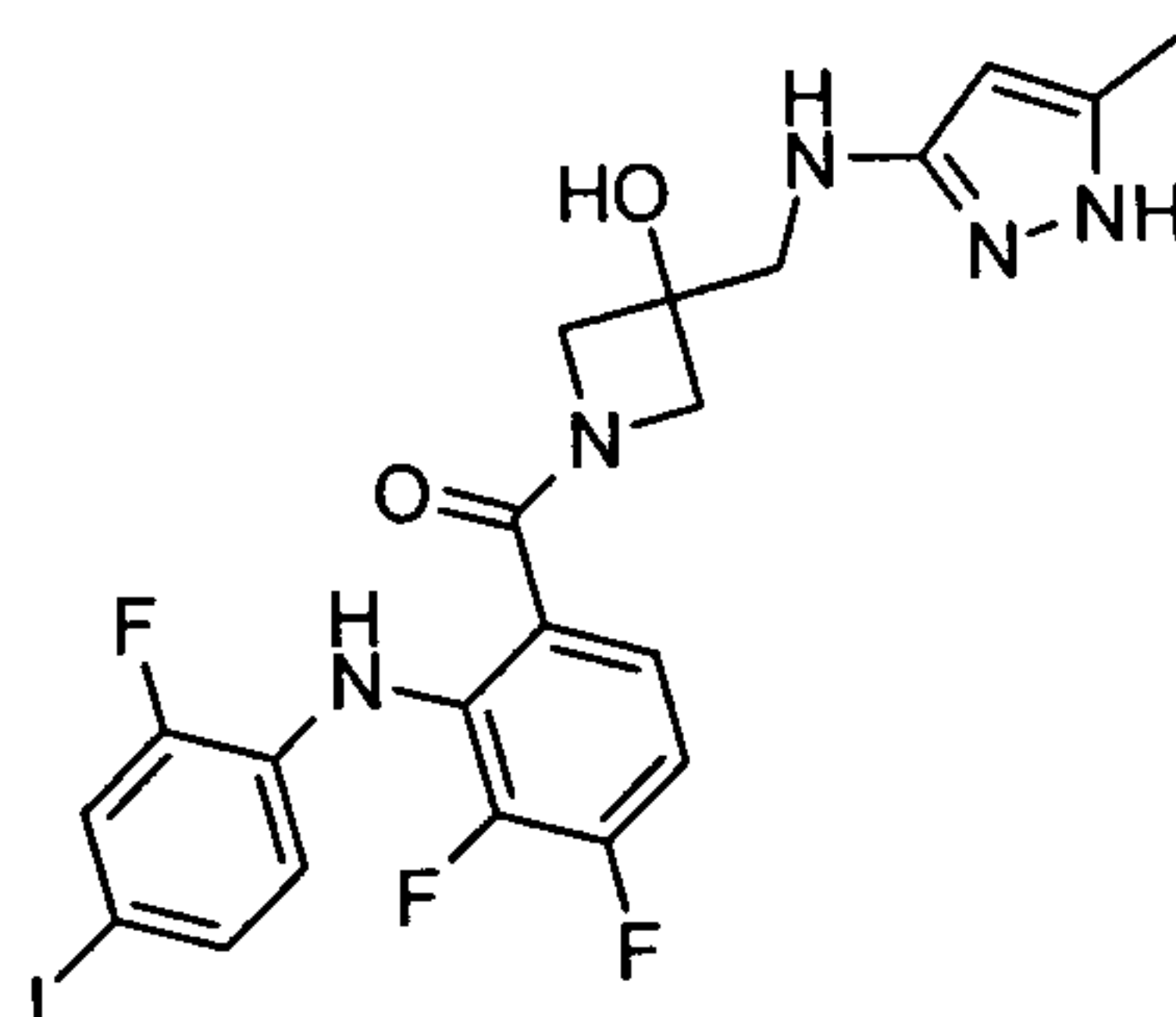
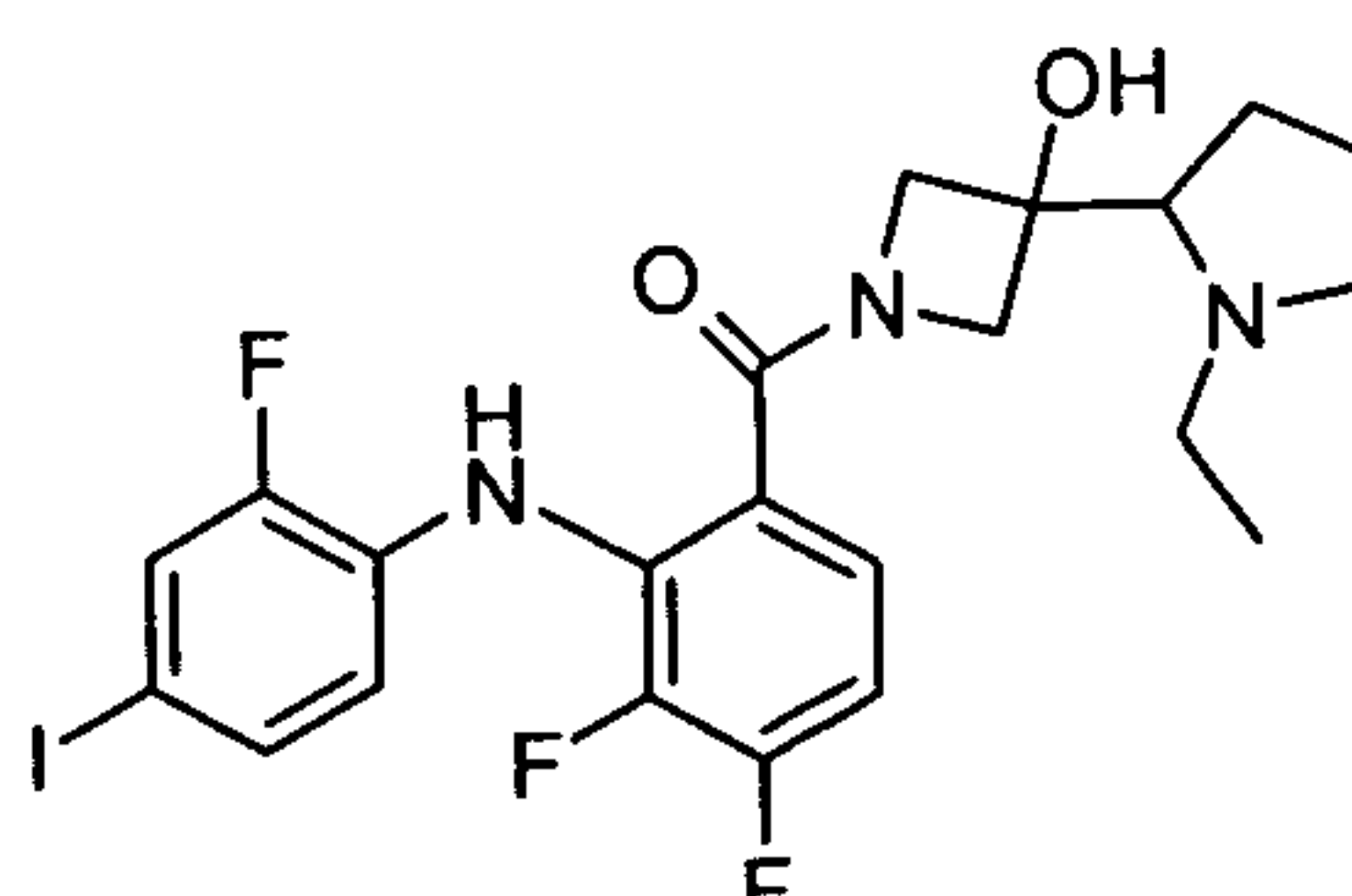
Cmpd No.	Structure	Name
248		3-[[[(4-chlorophenyl)amino]methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
249		3-[(5-amino-3-methyl-1 <i>H</i> -pyrazol-1-yl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
250		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[[[(5-methyl-1 <i>H</i> -pyrazol-3-yl)amino]methyl]azetidin-3-ol
251		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-ethylpyrrolidin-2-yl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

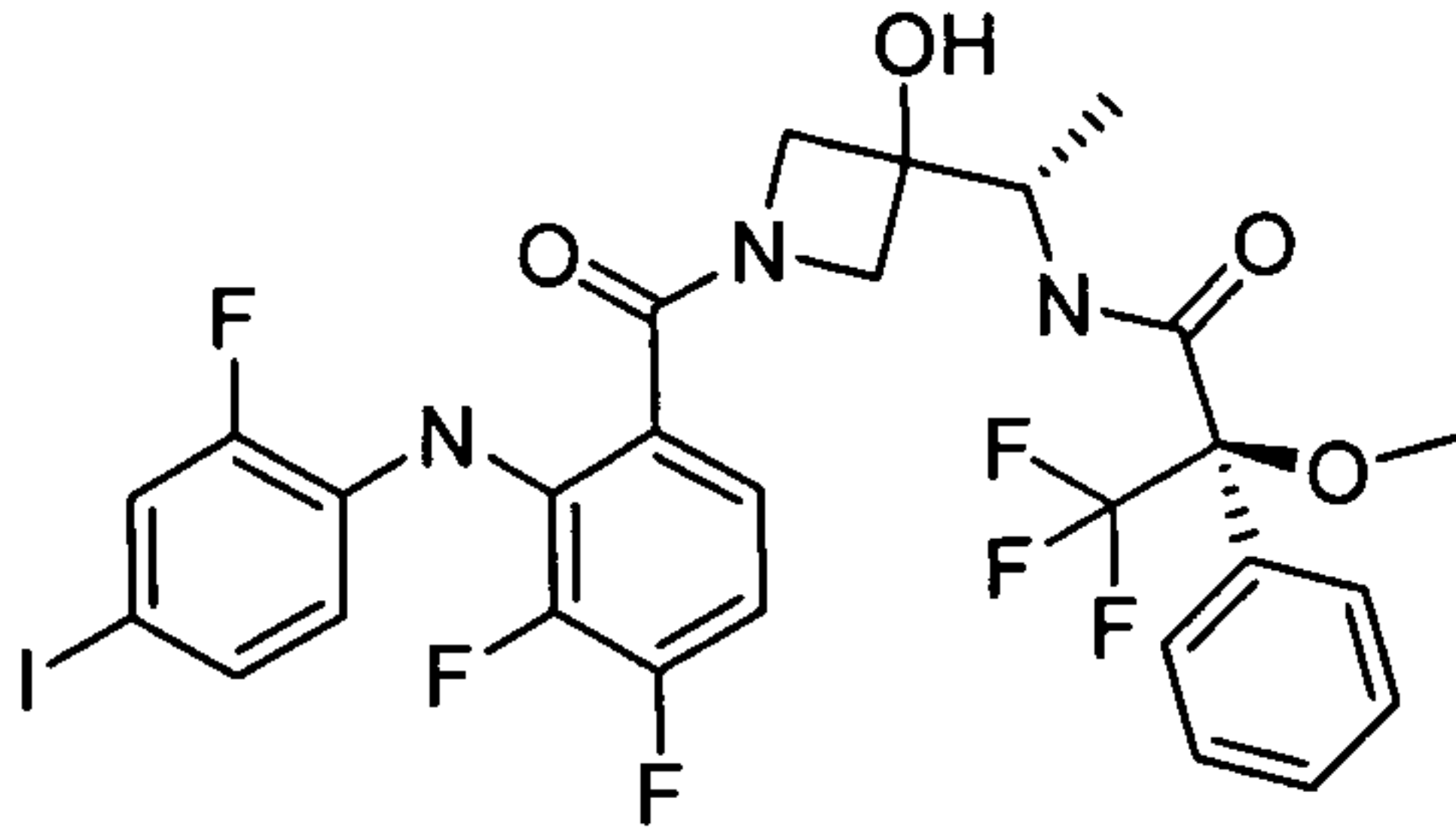
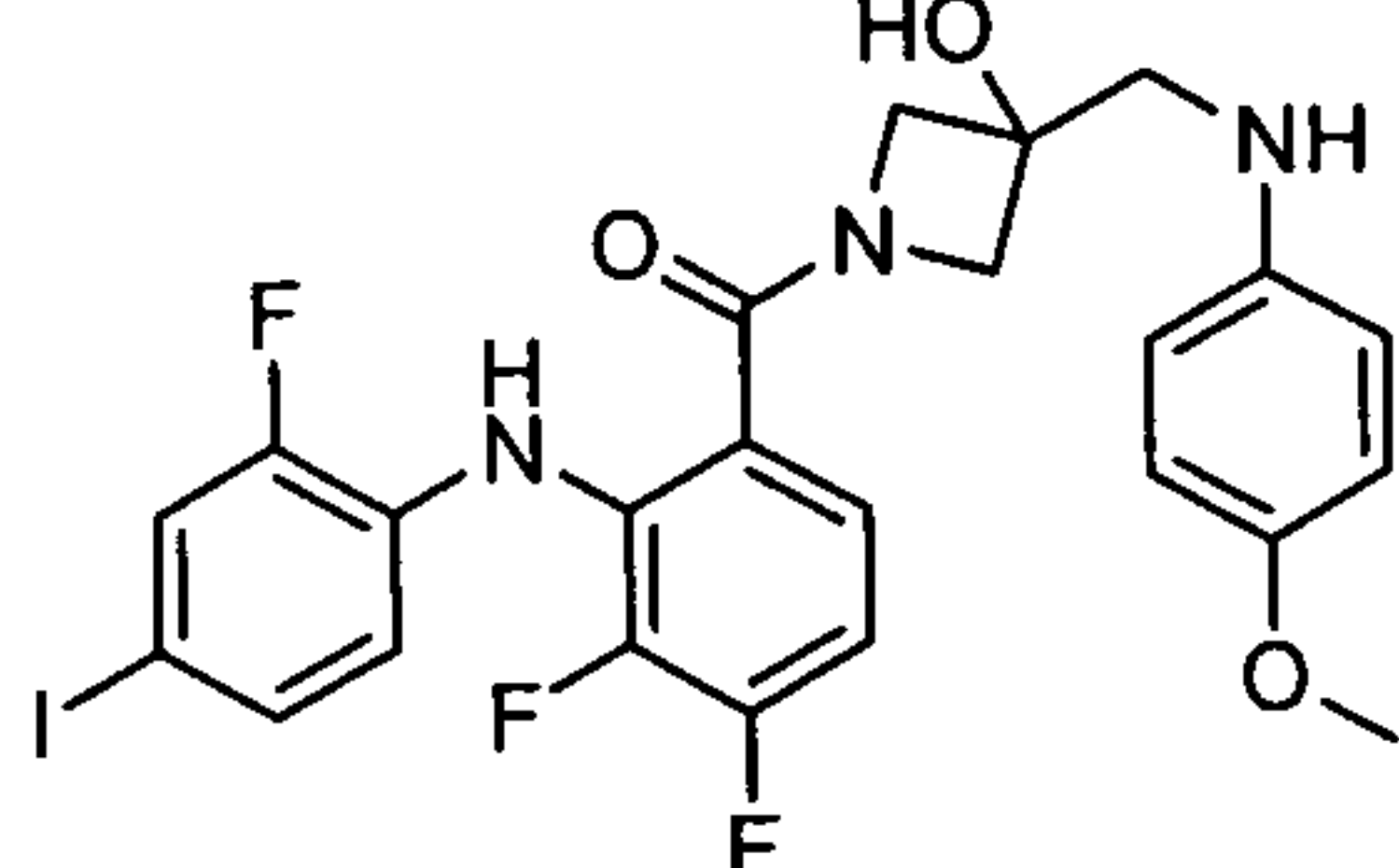
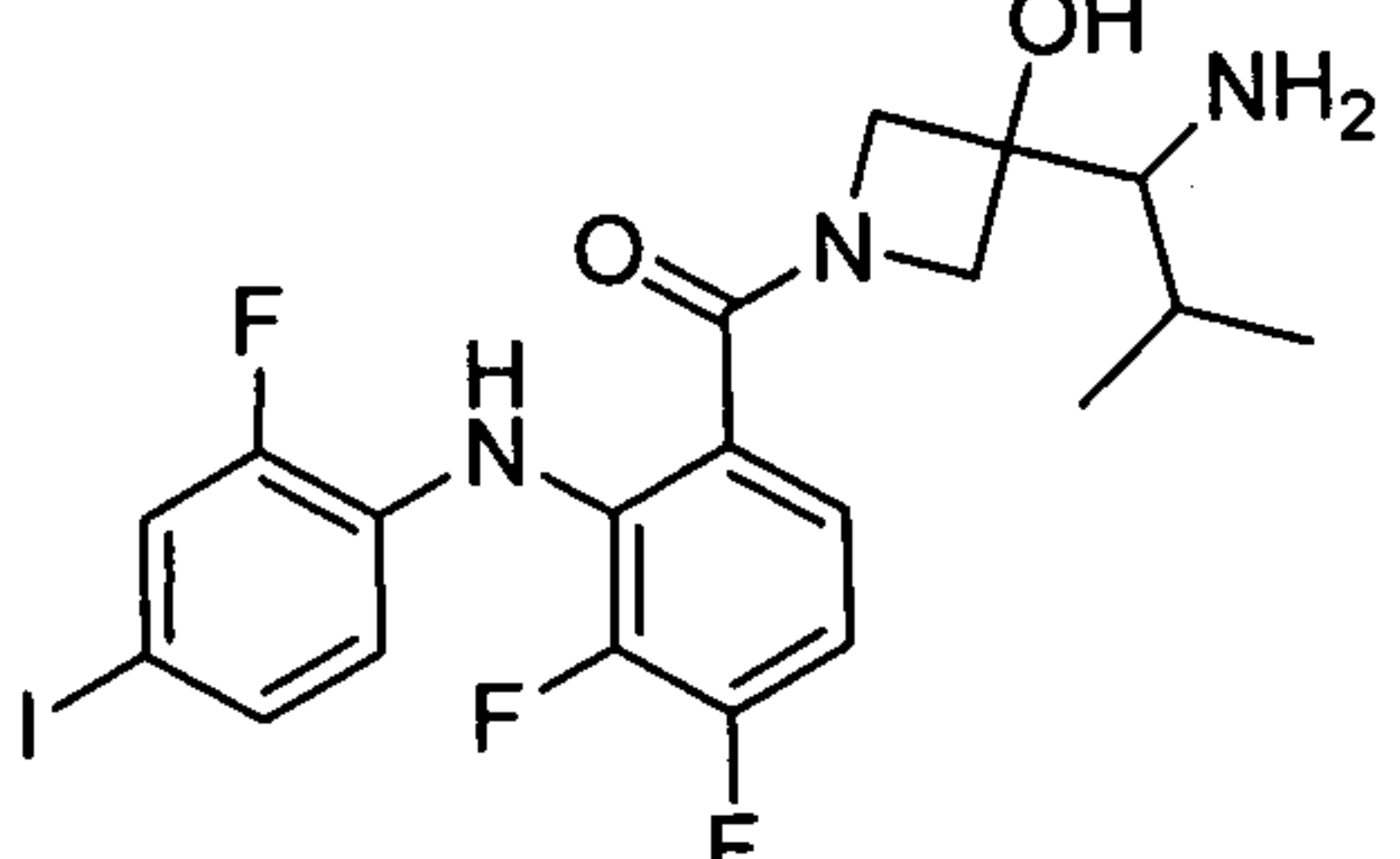
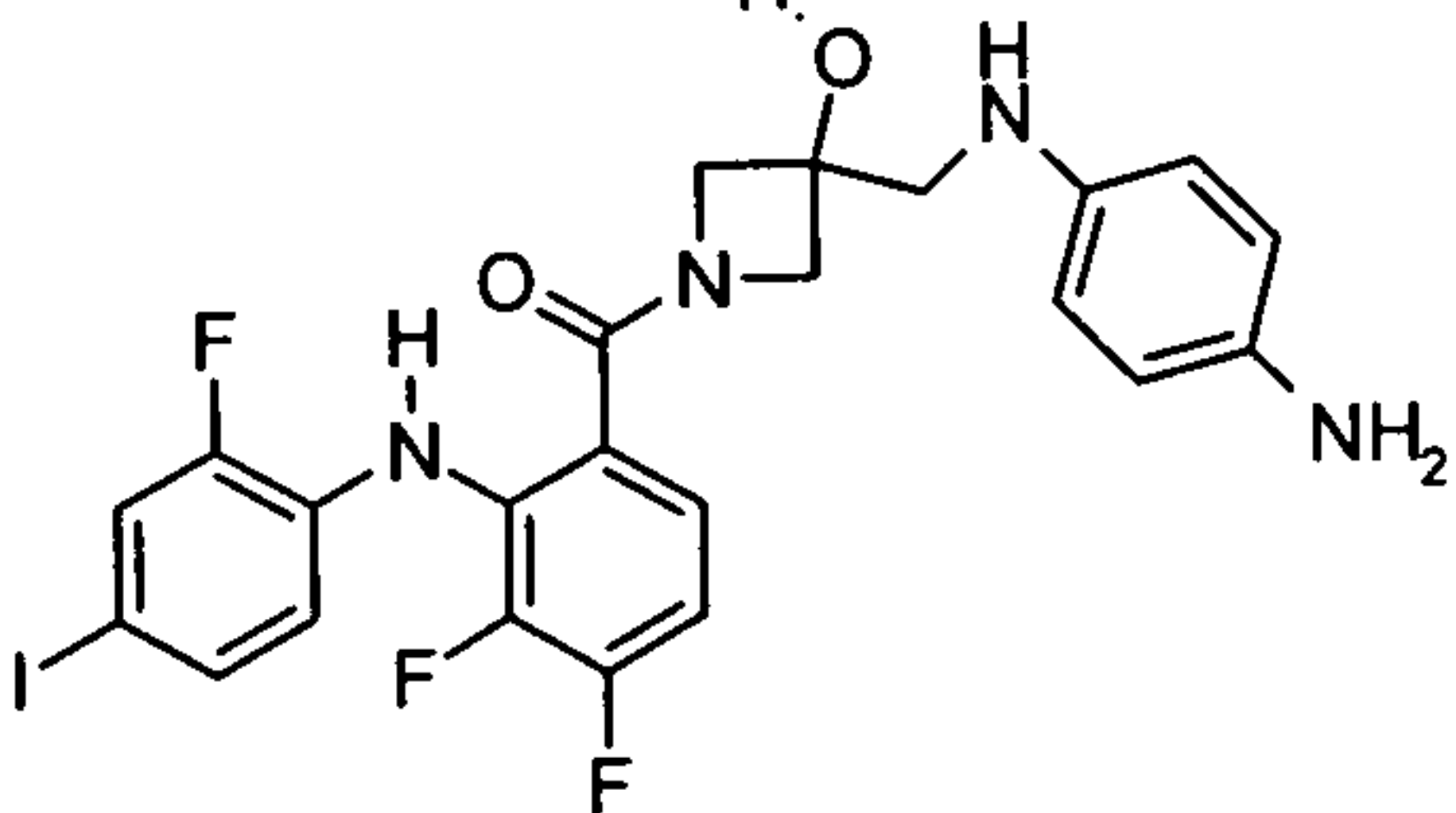
Cmpd No.	Structure	Name
252		(2 <i>R</i>)- <i>N</i> -{((1 <i>S</i>)-1-[1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-hydroxyazetidin-3-yl]ethyl)-3,3,3-trifluoro-2-(methoxy)-2-phenylpropanamide
253		1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)-3-((4-(methoxy)phenyl)amino)methylazetidin-3-ol
254		3-(1-amino-2-methylpropyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol
255		3-(((4-aminophenyl)amino)methyl)-1-((3,4-difluoro-2-((2-fluoro-4-iodophenyl)amino)phenyl)carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

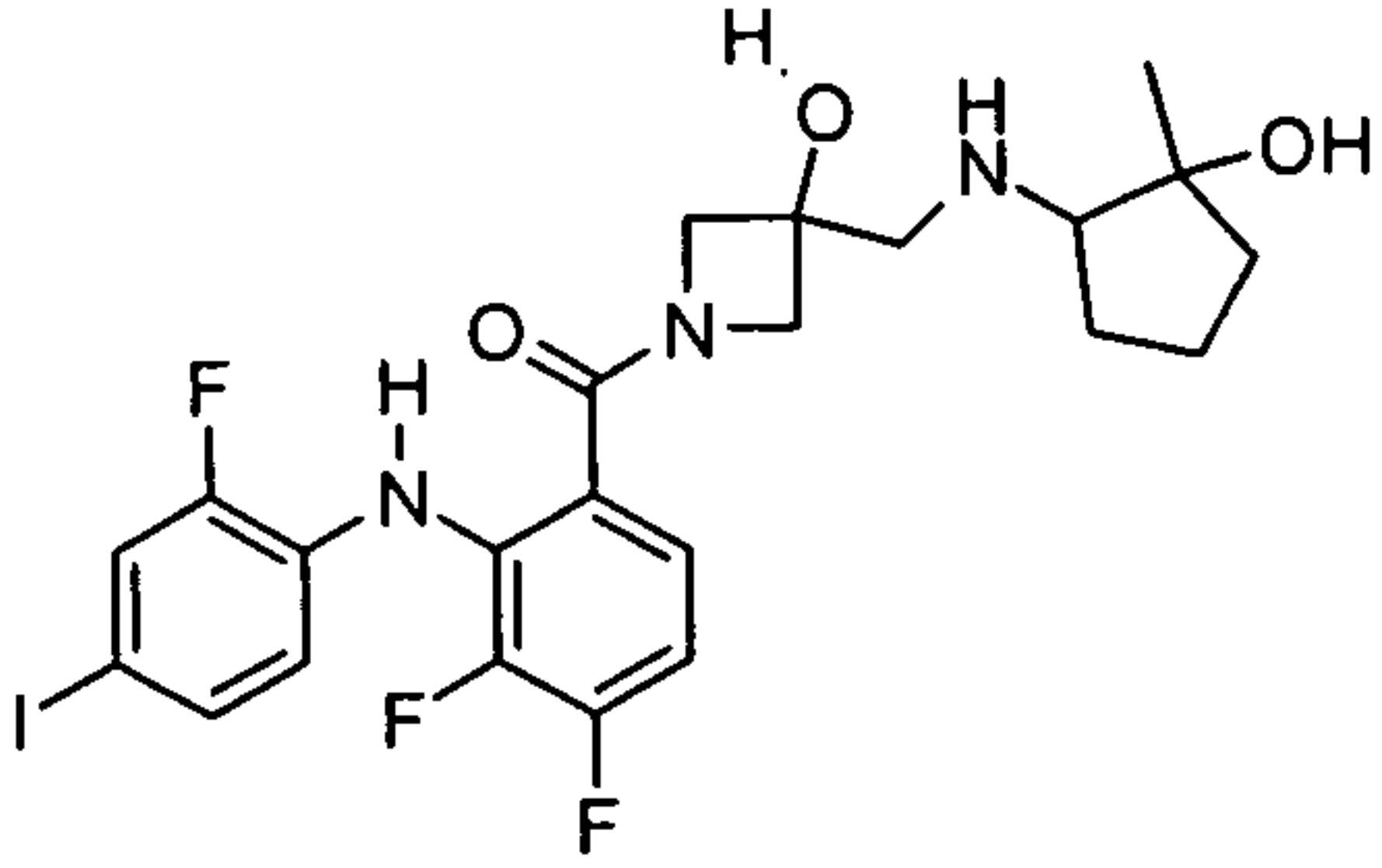
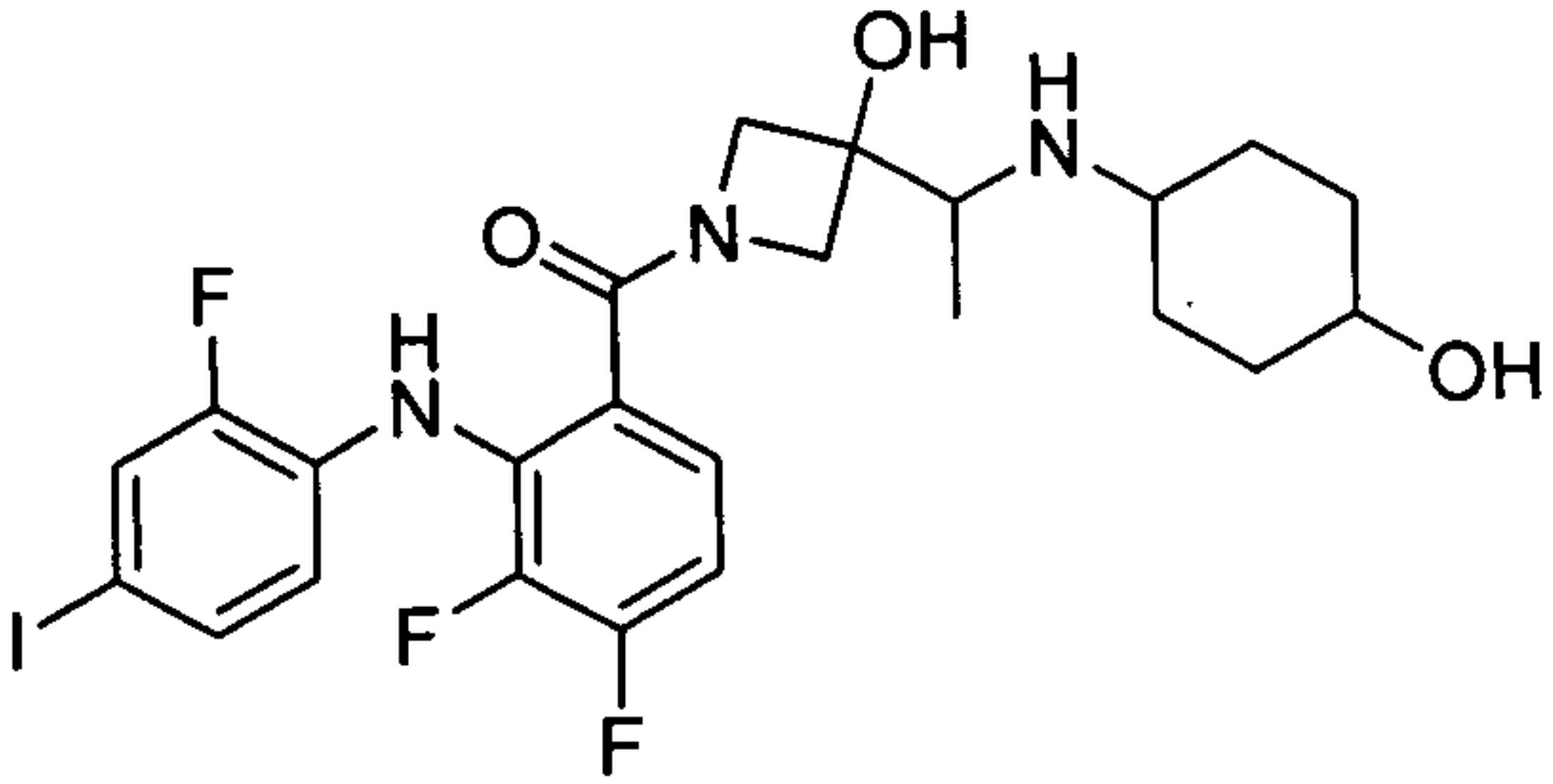
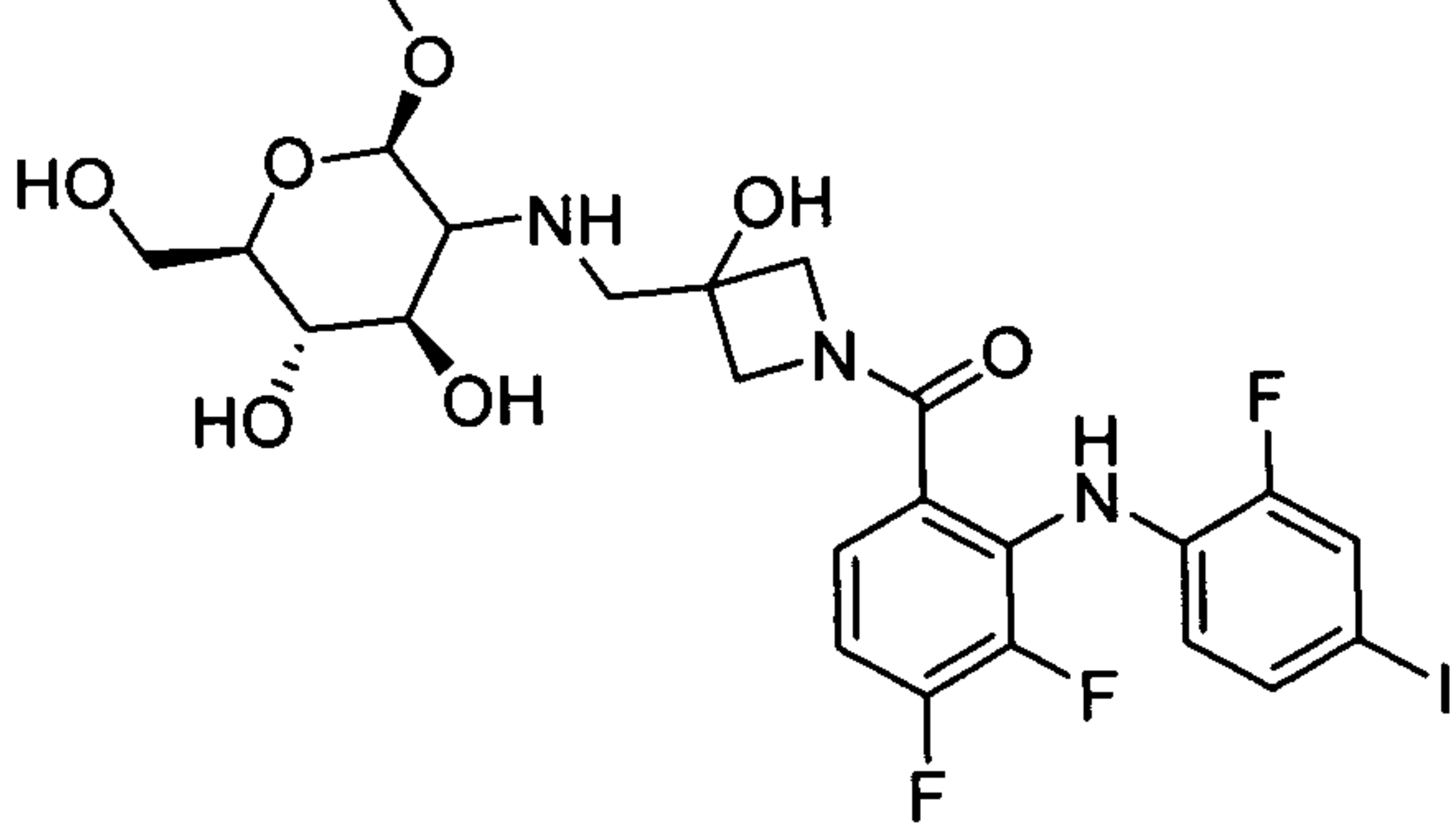
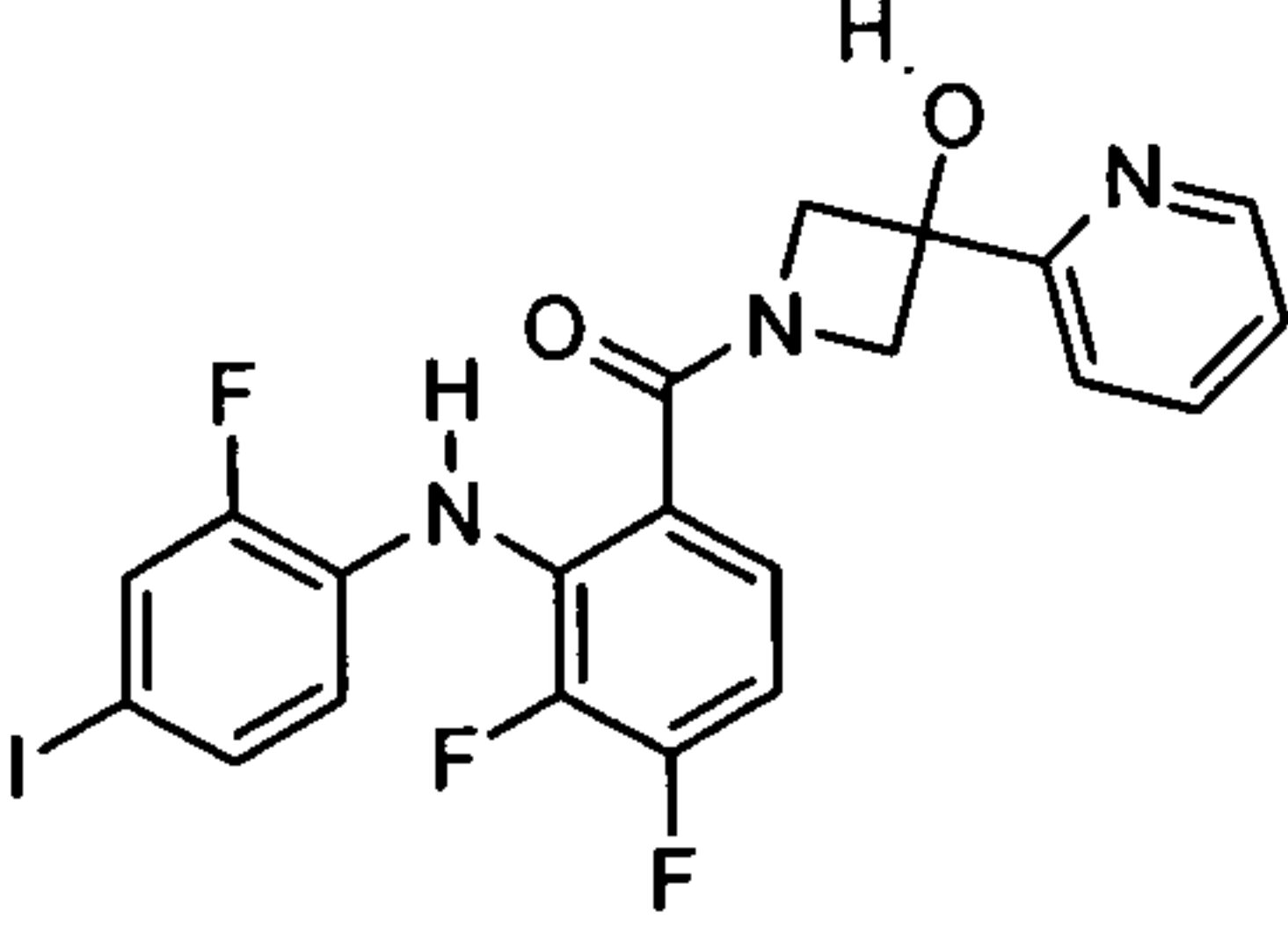
Cmpd No.	Structure	Name
256		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(2-hydroxy-2-methylcyclopentyl)amino}methyl}azetidin-3-ol
257		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{1-[(4-hydroxycyclohexyl)amino]ethyl}azetidin-3-ol
258		methyl (2xi)-2-deoxy-2-({[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}amino)-beta-D-arabino-hexopyranoside
259		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-pyridin-2-ylazetidin-3-ol

Table 1. Representative MEK Inhibitors

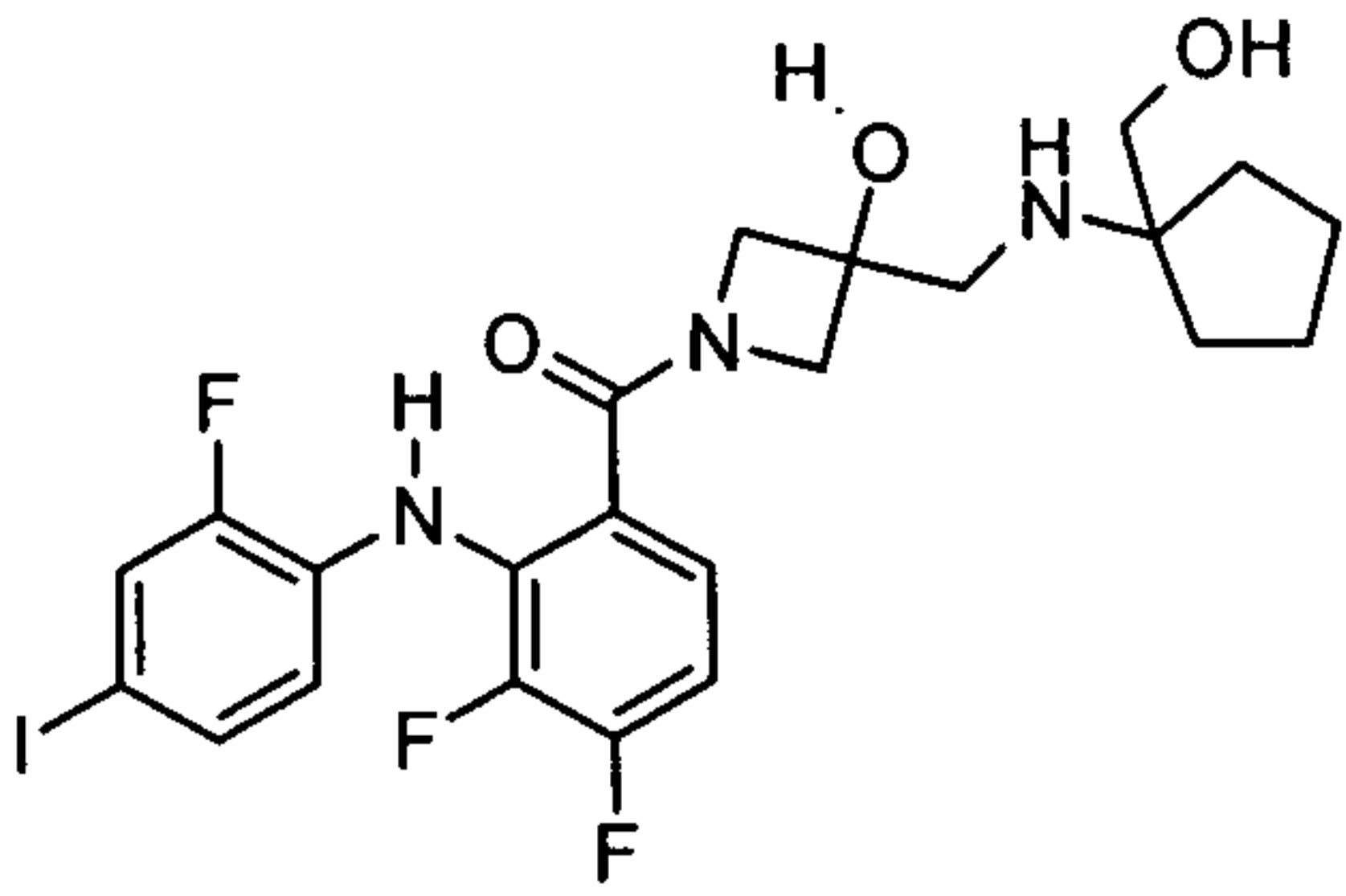
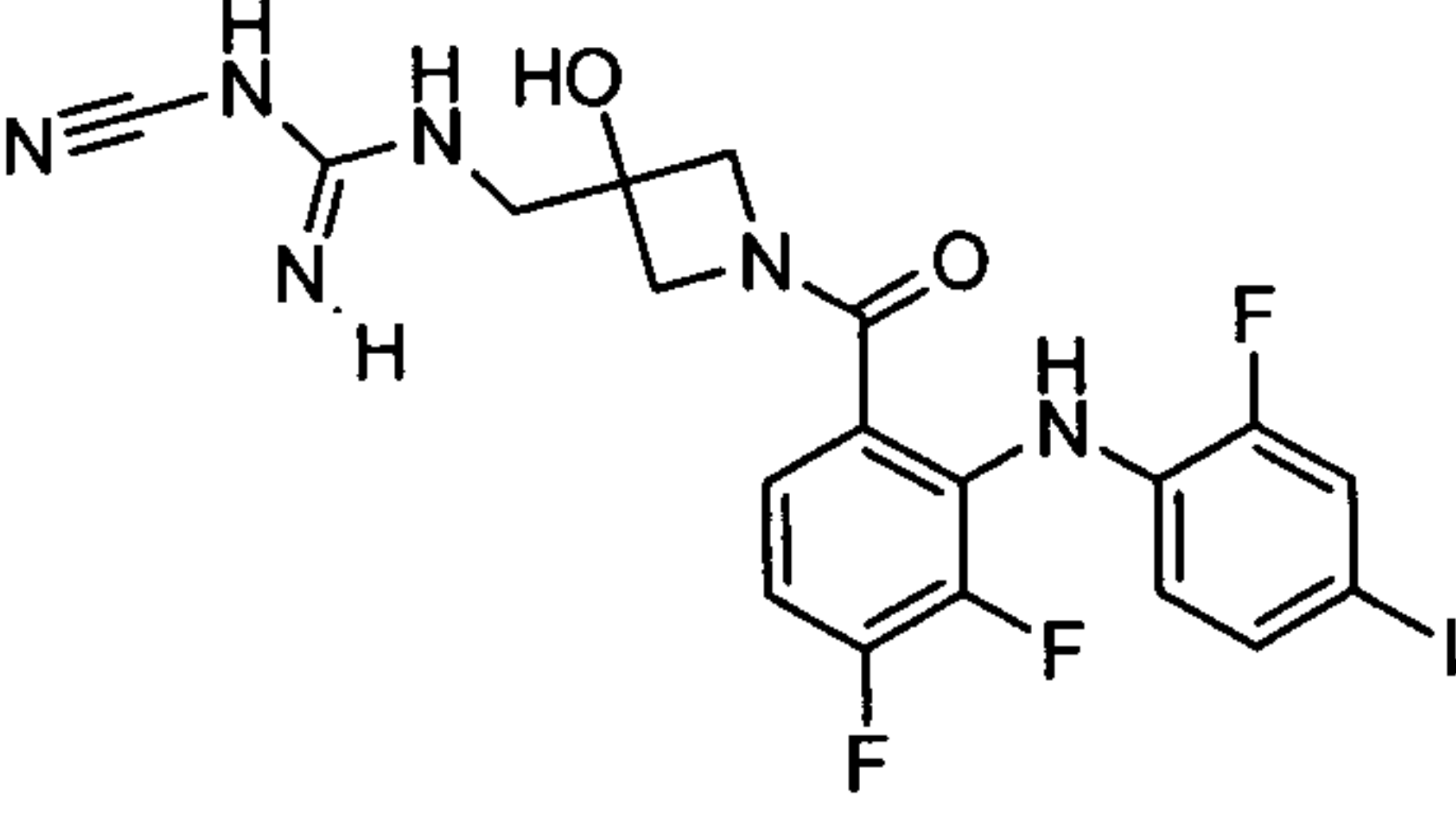
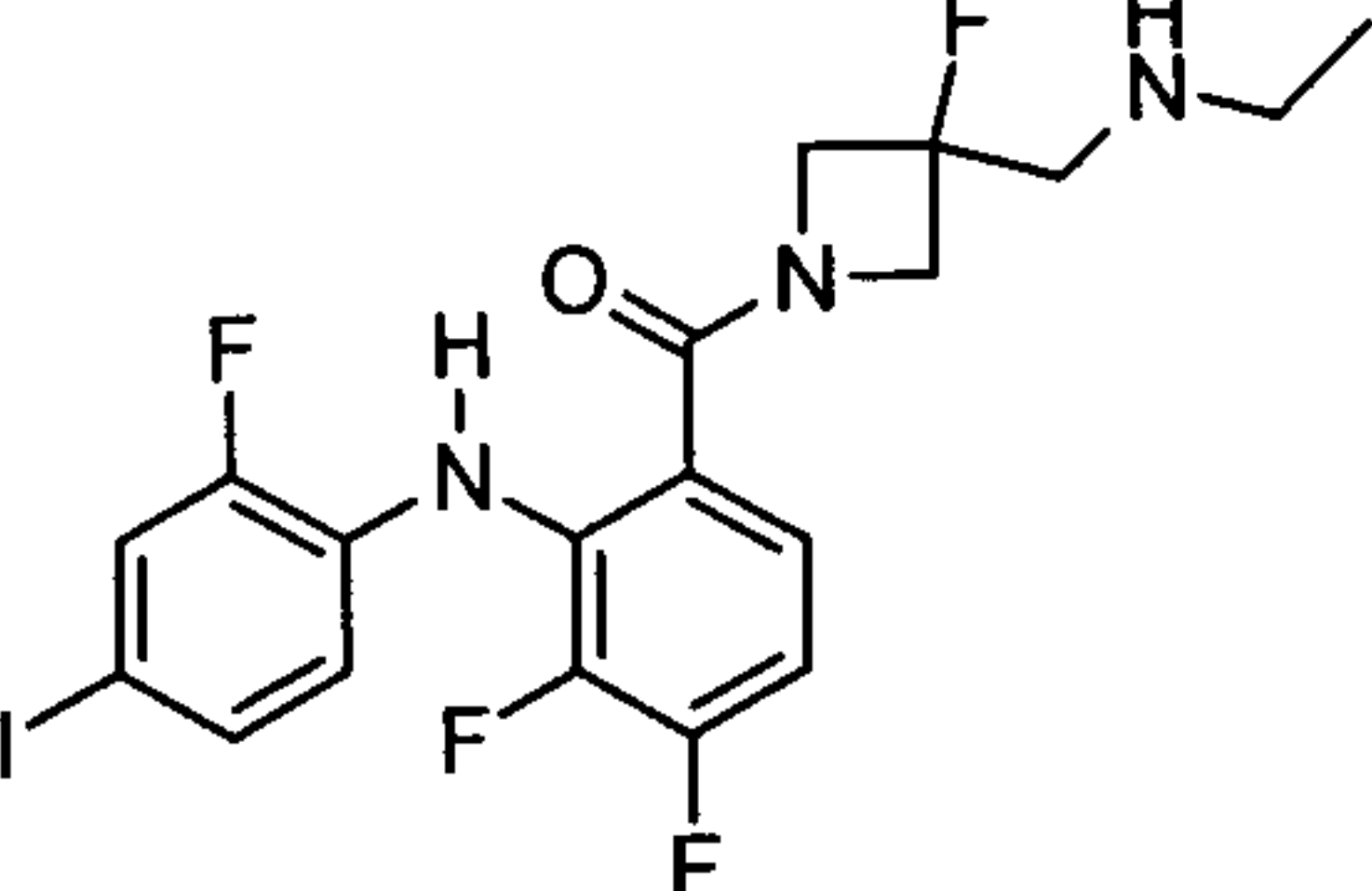
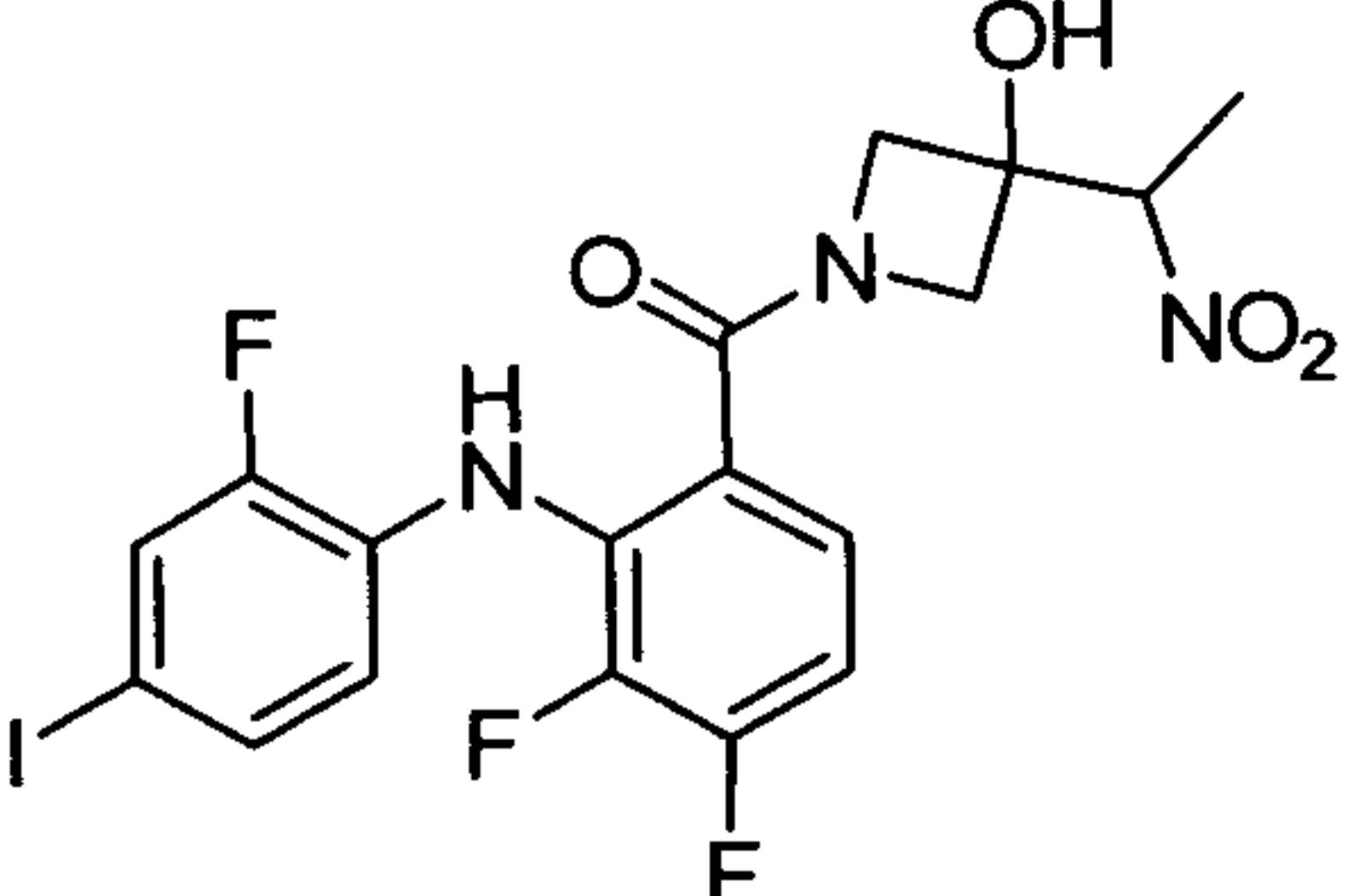
Cmpd No.	Structure	Name
260		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-({[1-(hydroxymethyl)cyclopentyl]amino}methyl)azetidin-3-ol
261		1-cyano-3-{{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}guanidine
262		6-({3-[(ethylamino)methyl]-3-fluoroazetidin-1-yl}carbonyl)-2,3-difluoro-N-(2-fluoro-4-iodophenyl)aniline
263		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-nitroethyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
264		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(3-fluoro-4-hydroxyphenyl)amino}methyl}azetidin-3-ol
265		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-{{(2-fluoro-4-hydroxyphenyl)amino}methyl}azetidin-3-ol
266		3-(1-aminoethyl)-1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)azetidin-3-ol
267		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(methylamino)ethyl]azetidin-3-ol
268		1-({8-fluoro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

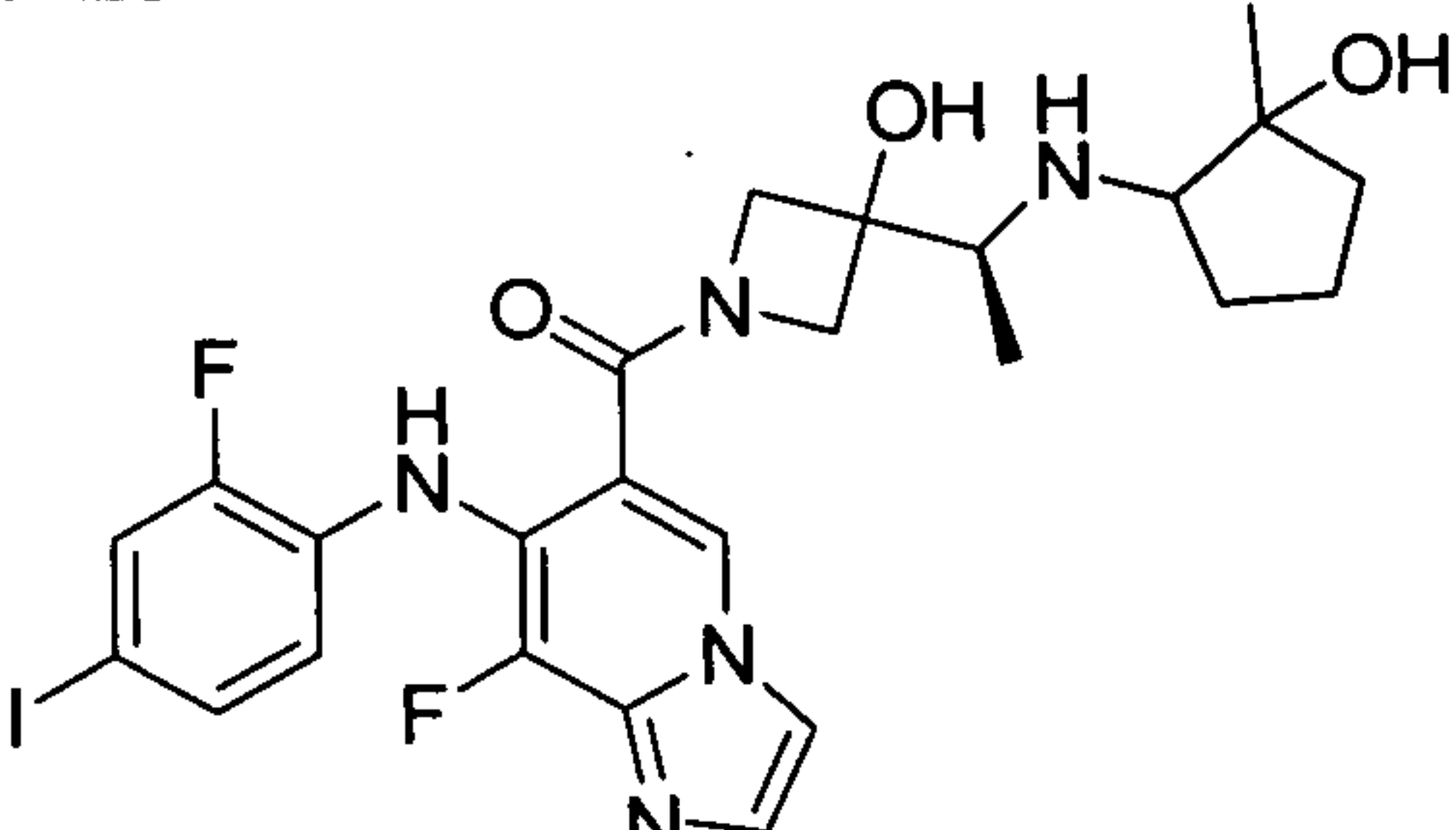
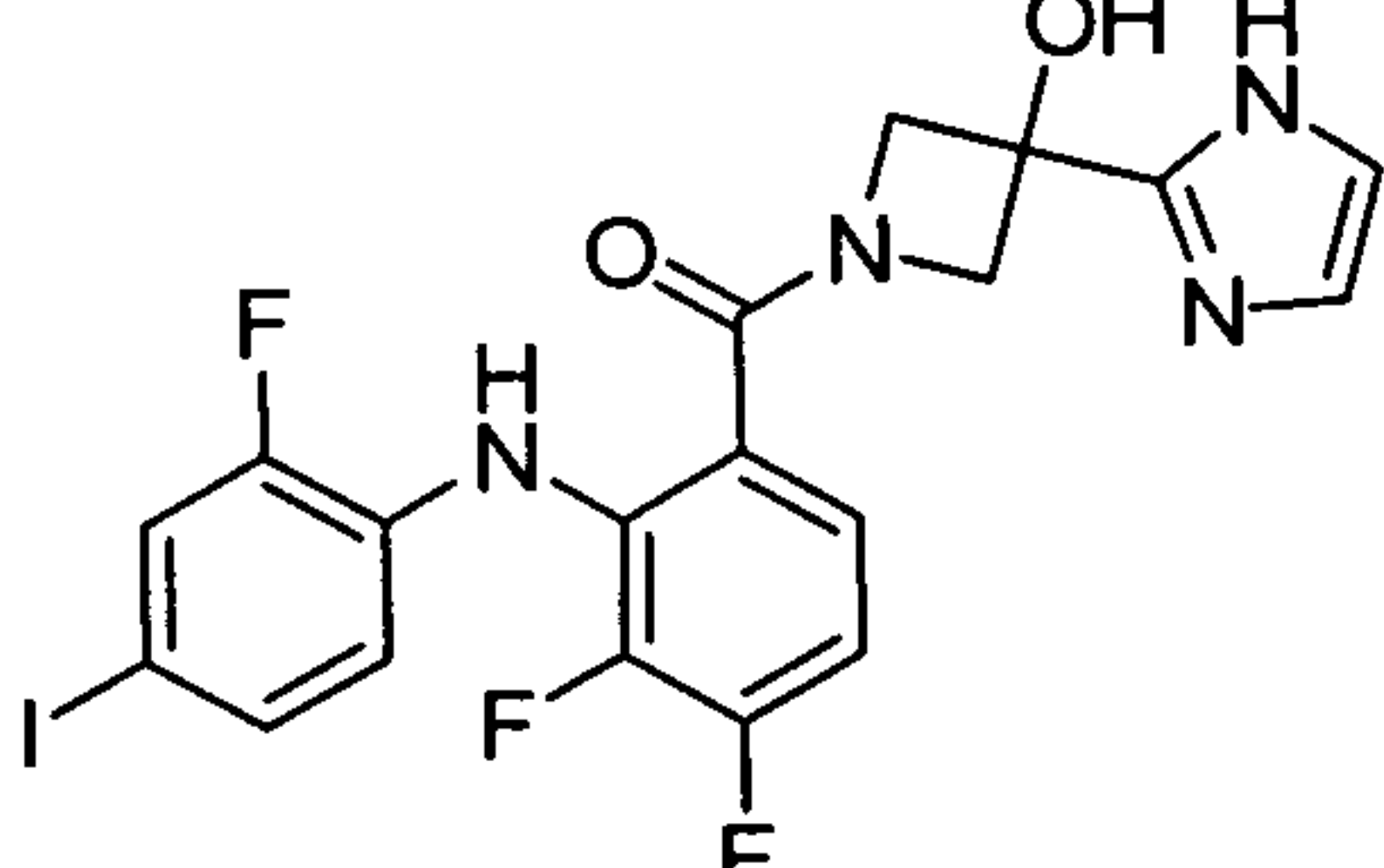
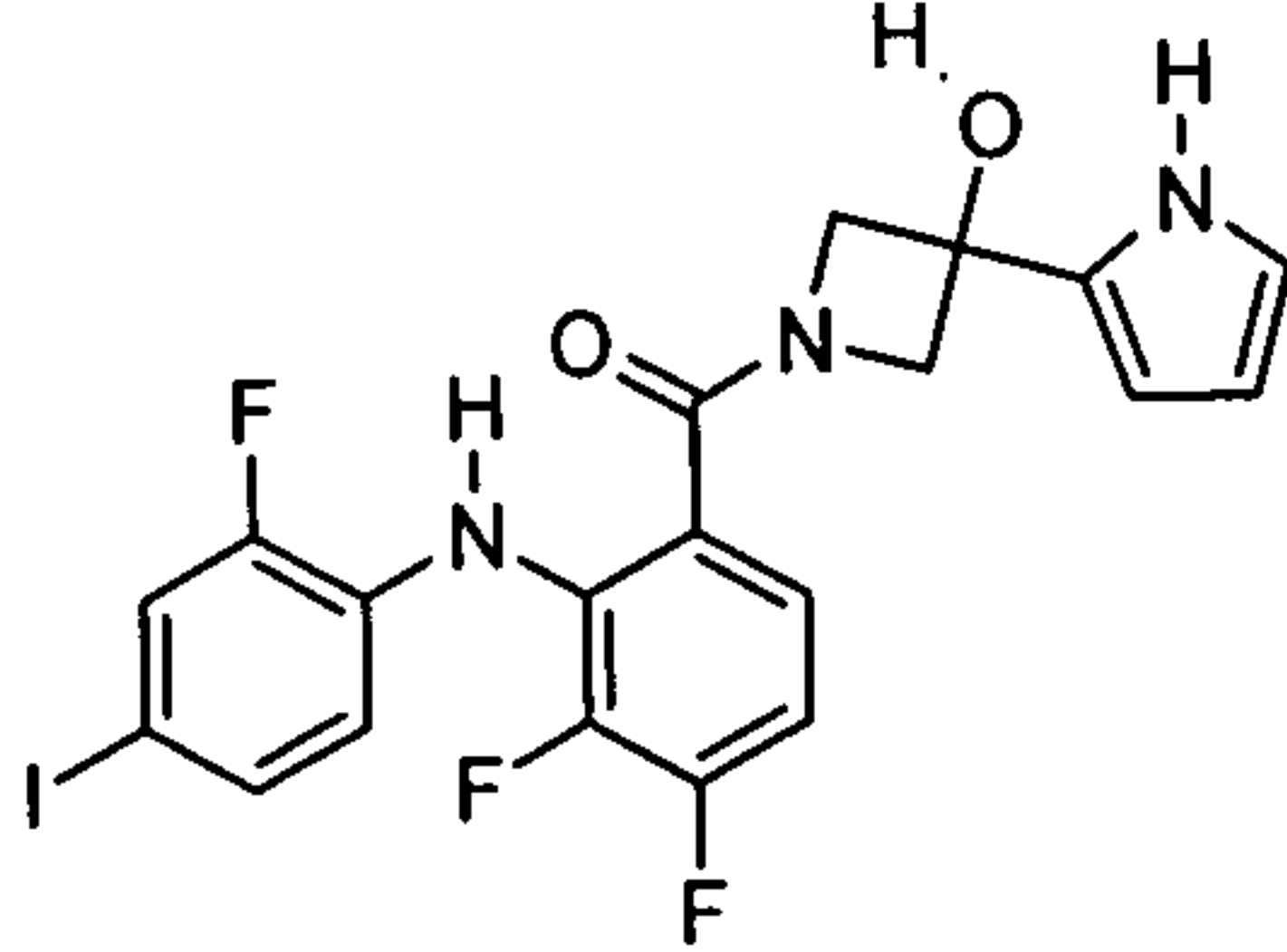
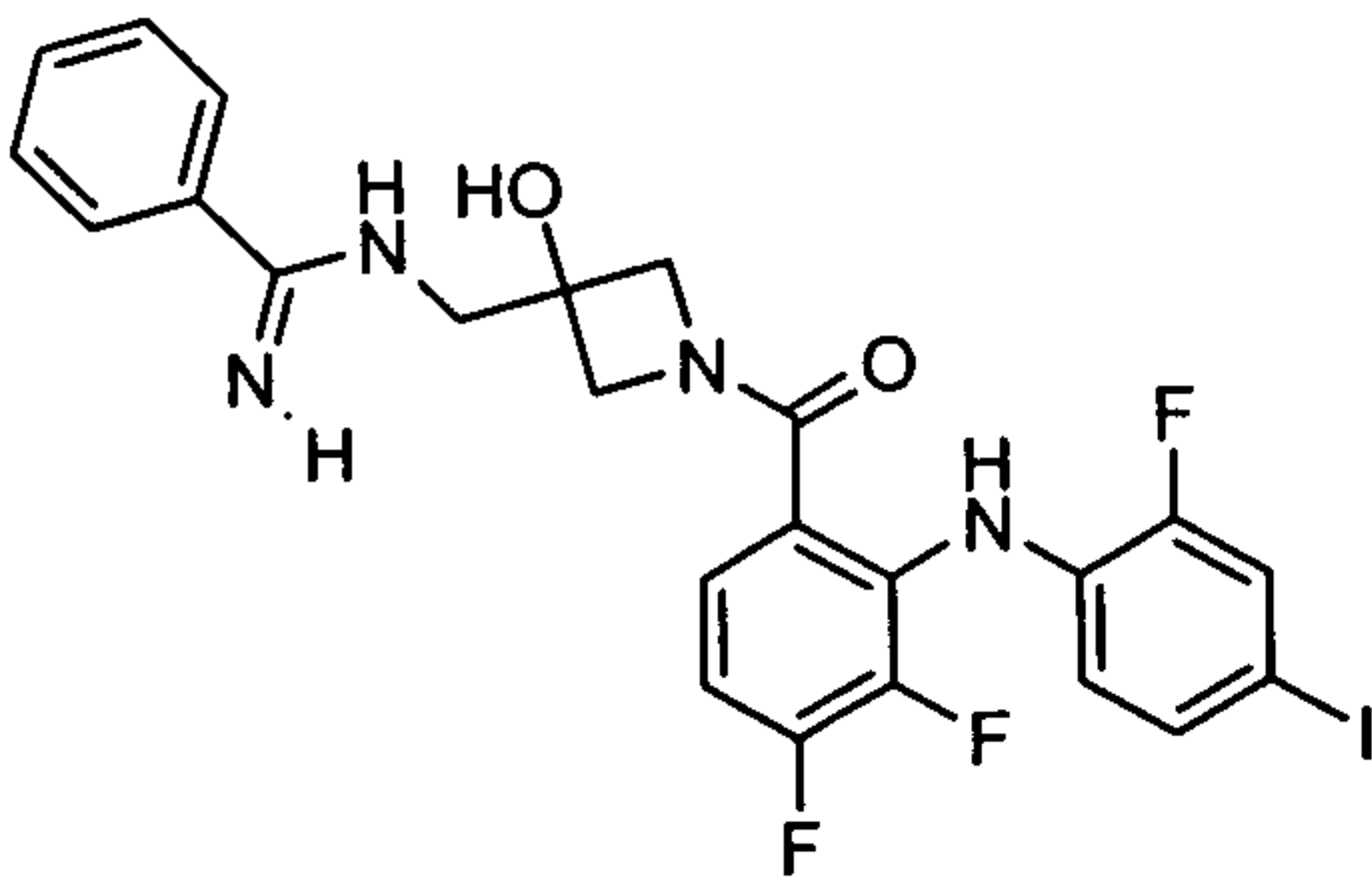
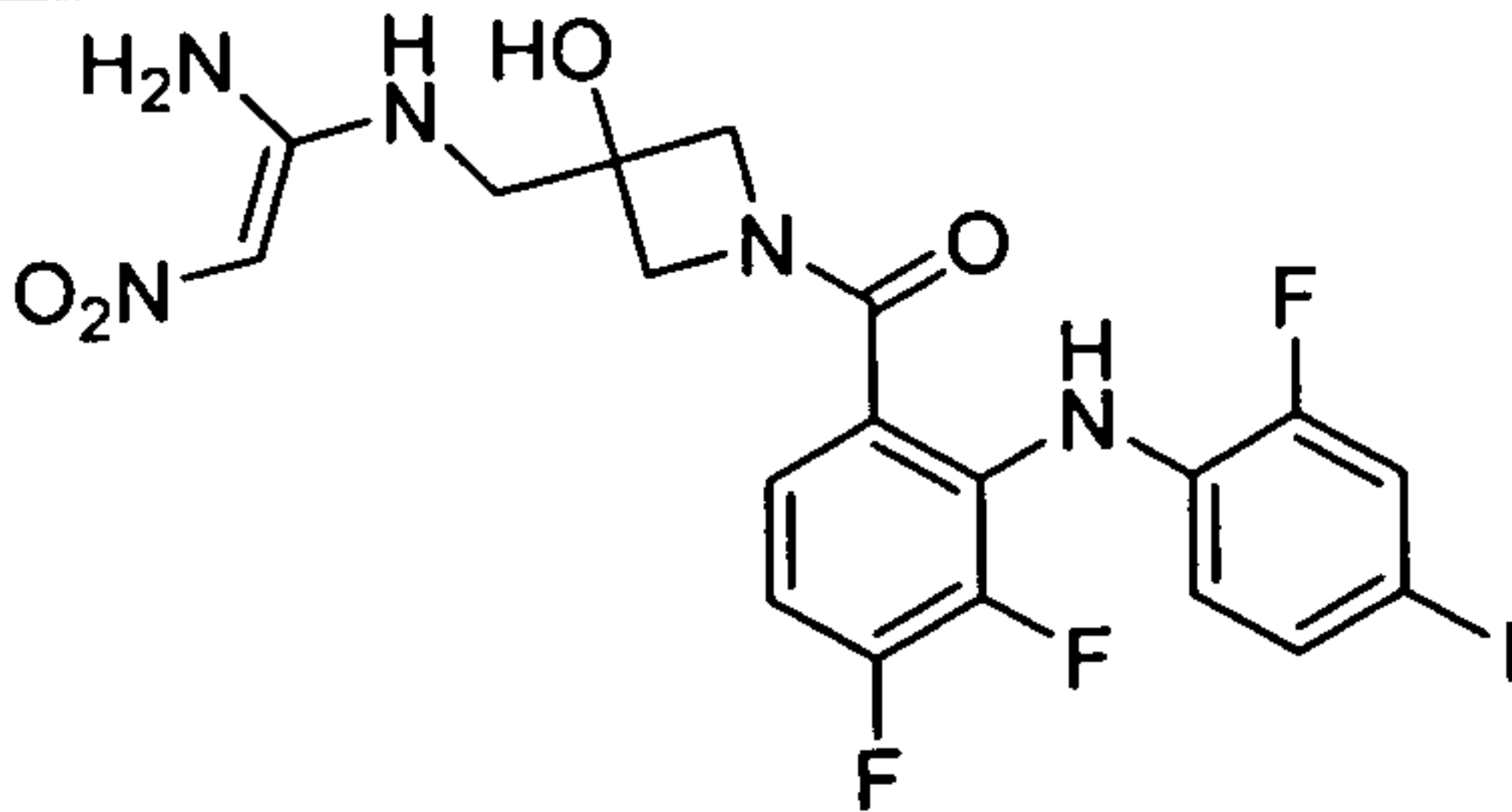
Cmpd No.	Structure	Name
269		1-({8-fluoro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2- <i>a</i>]pyridin-6-yl}carbonyl)-3-((1 <i>S</i>)-1-[(2-hydroxy-2-methylcyclopentyl)amino]ethyl)azetidin-3-ol
270		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1 <i>H</i> -imidazol-2-yl)azetidin-3-ol
271		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1 <i>H</i> -pyrrol-2-yl)azetidin-3-ol
272		<i>N</i> -{[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]methyl}benzenecarboximidamide
273		3-({[(<i>E</i>)-1-amino-2-nitroethenyl]amino}methyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
274		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1-nitroethyl)azetidin-3-ol
275		3-(1-amino-1-methylethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
276		3-[(1H-benzimidazol-2-ylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
277		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(1H-imidazol-2-ylamino)methyl]azetidin-3-ol
278		methyl {1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethyl}carbamate

Table 1. Representative MEK Inhibitors

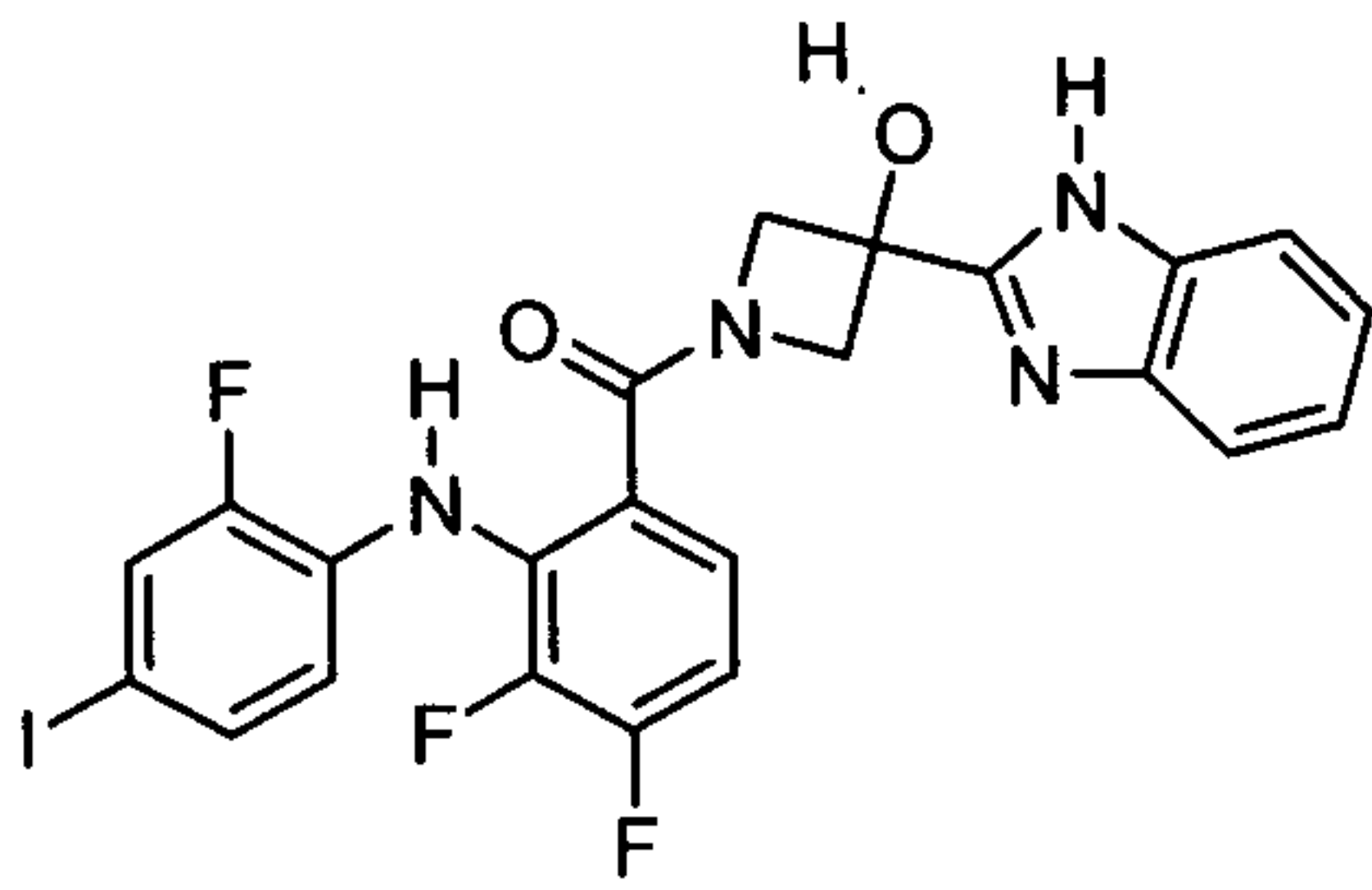
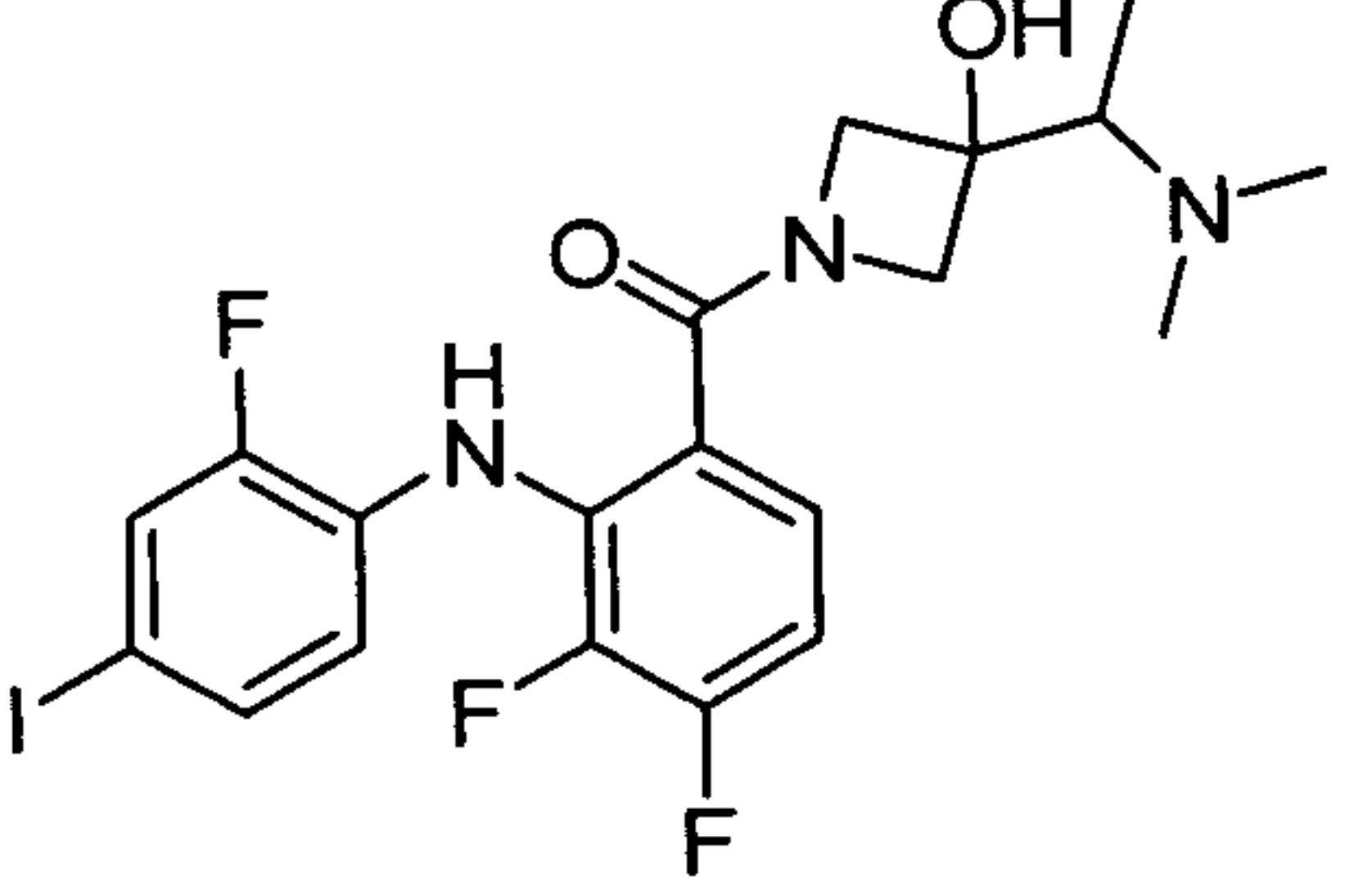
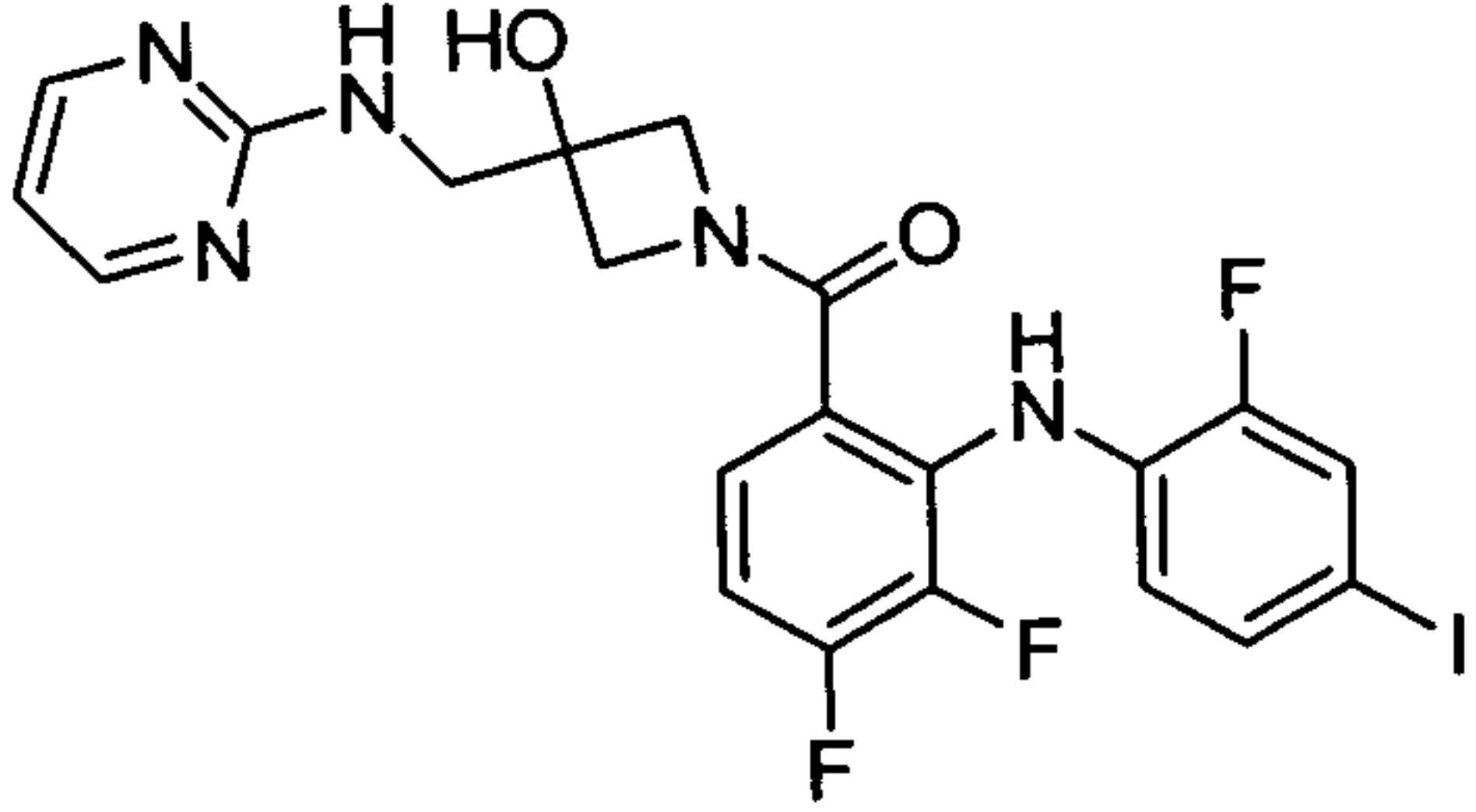
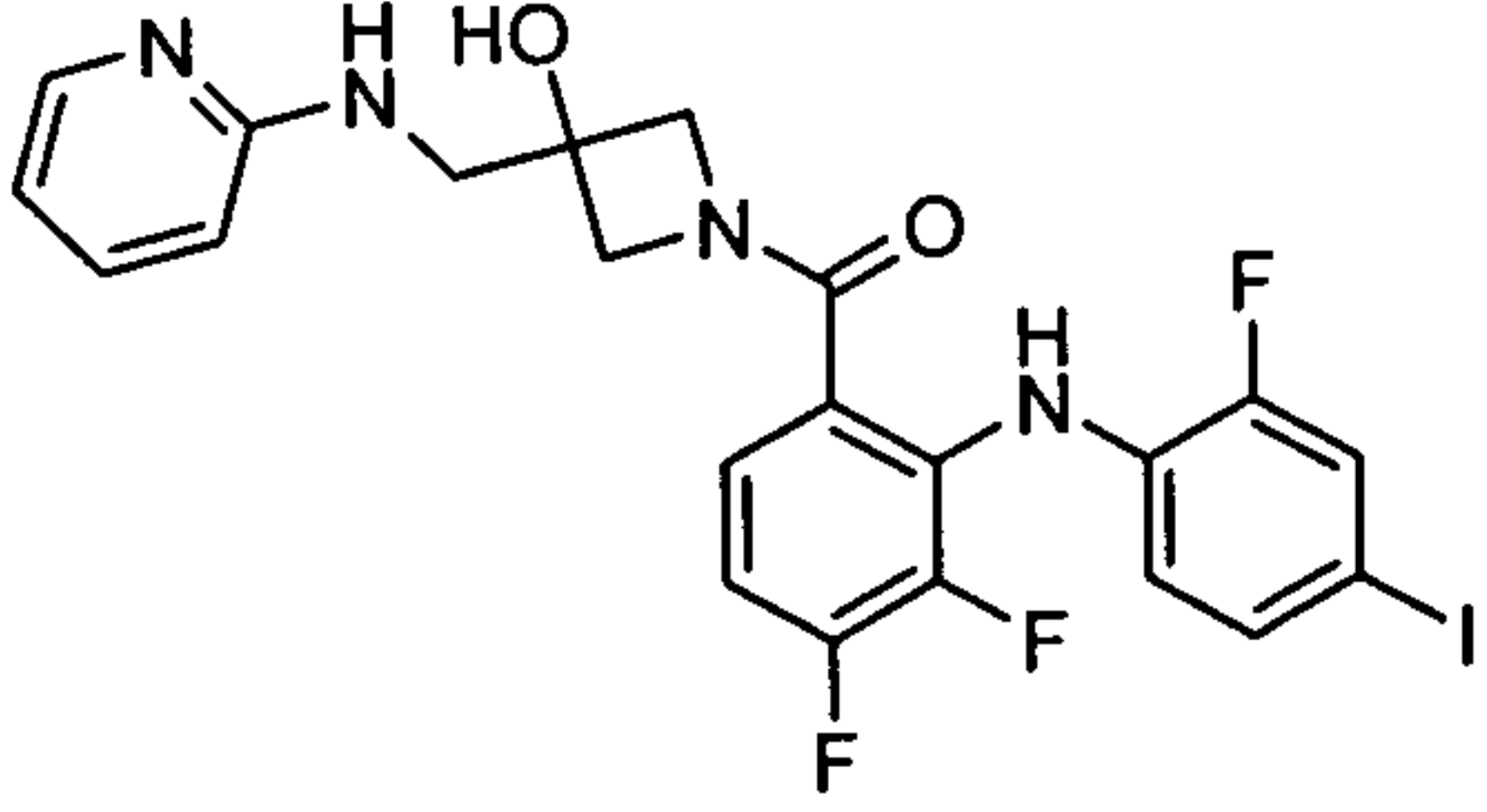
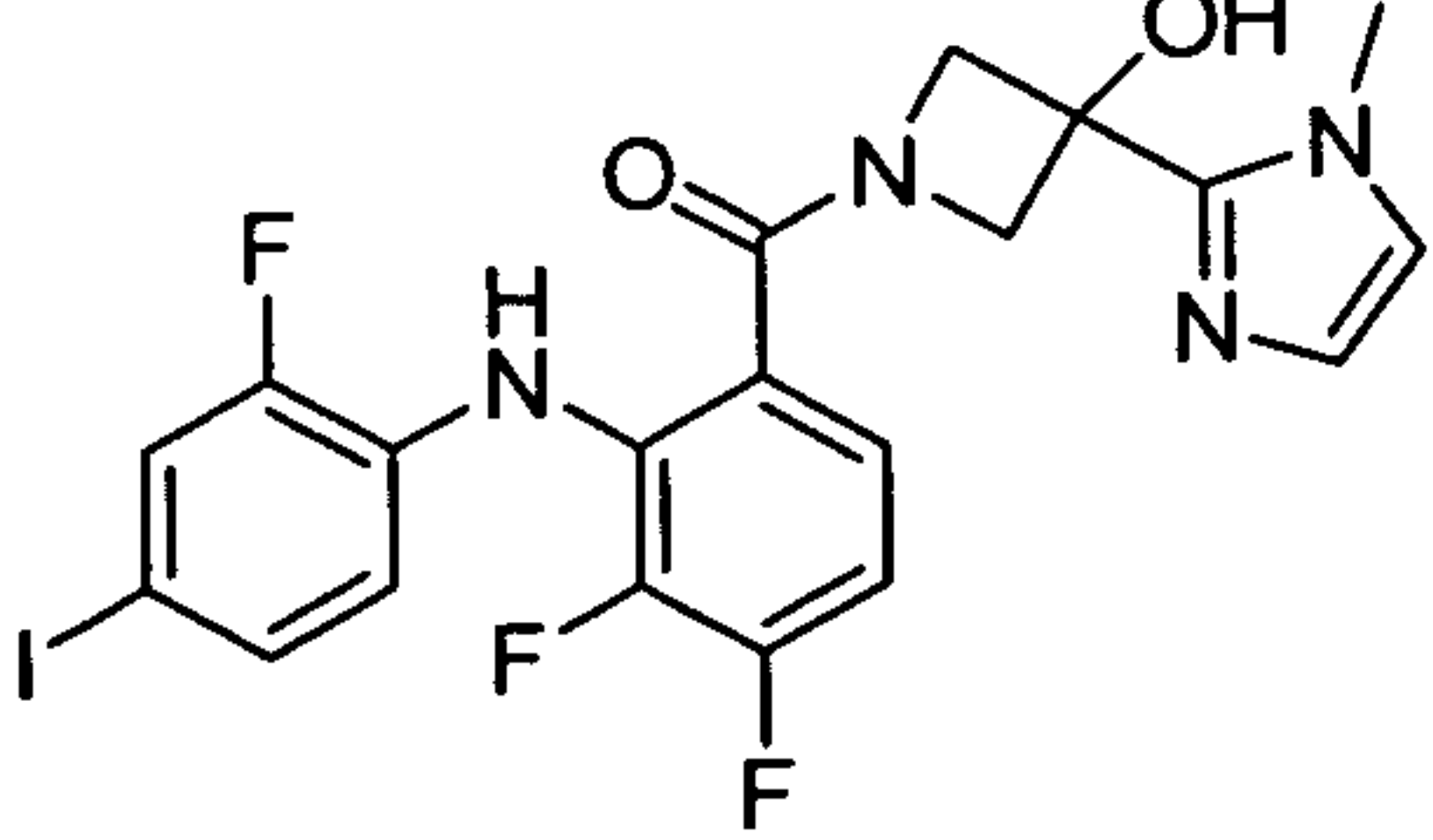
Cmpd No.	Structure	Name
279		3-(1 <i>H</i> -benzimidazol-2-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
280		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[1-(dimethylamino)ethyl]azetidin-3-ol
281		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyrimidin-2-ylamino)methyl]azetidin-3-ol
282		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(pyridin-2-ylamino)methyl]azetidin-3-ol
283		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1-methyl-1 <i>H</i> -imidazol-2-yl)azetidin-3-ol

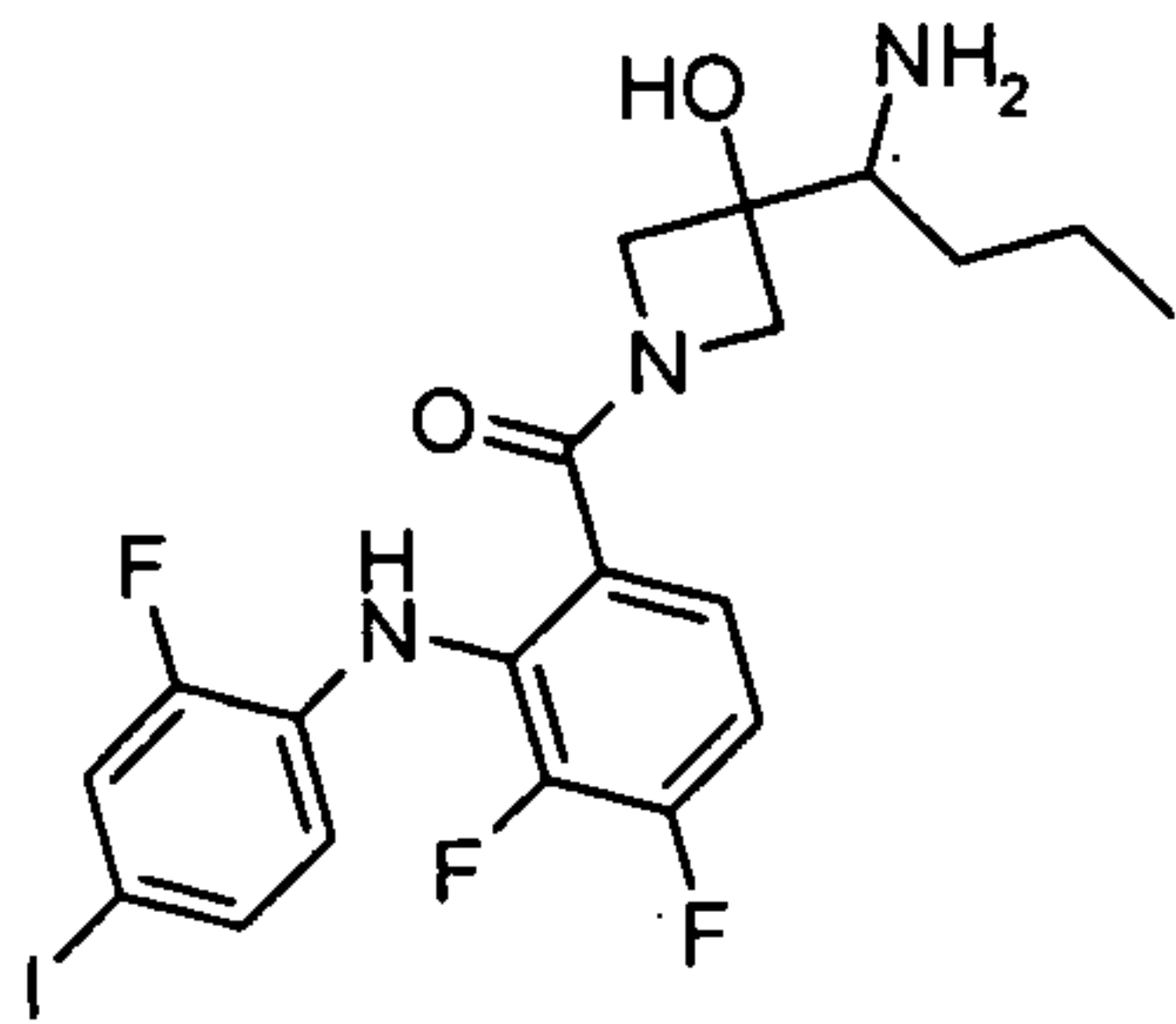
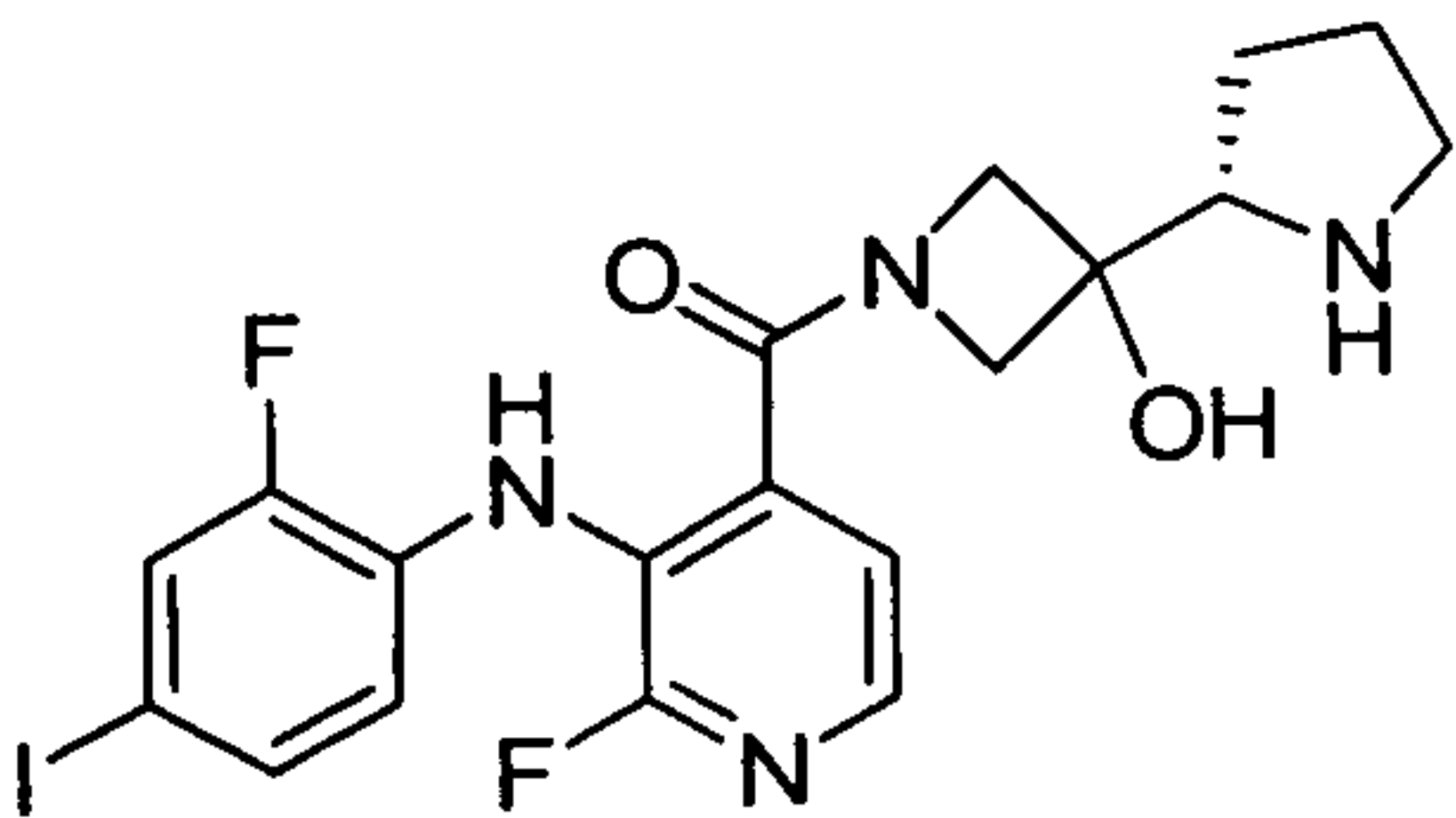
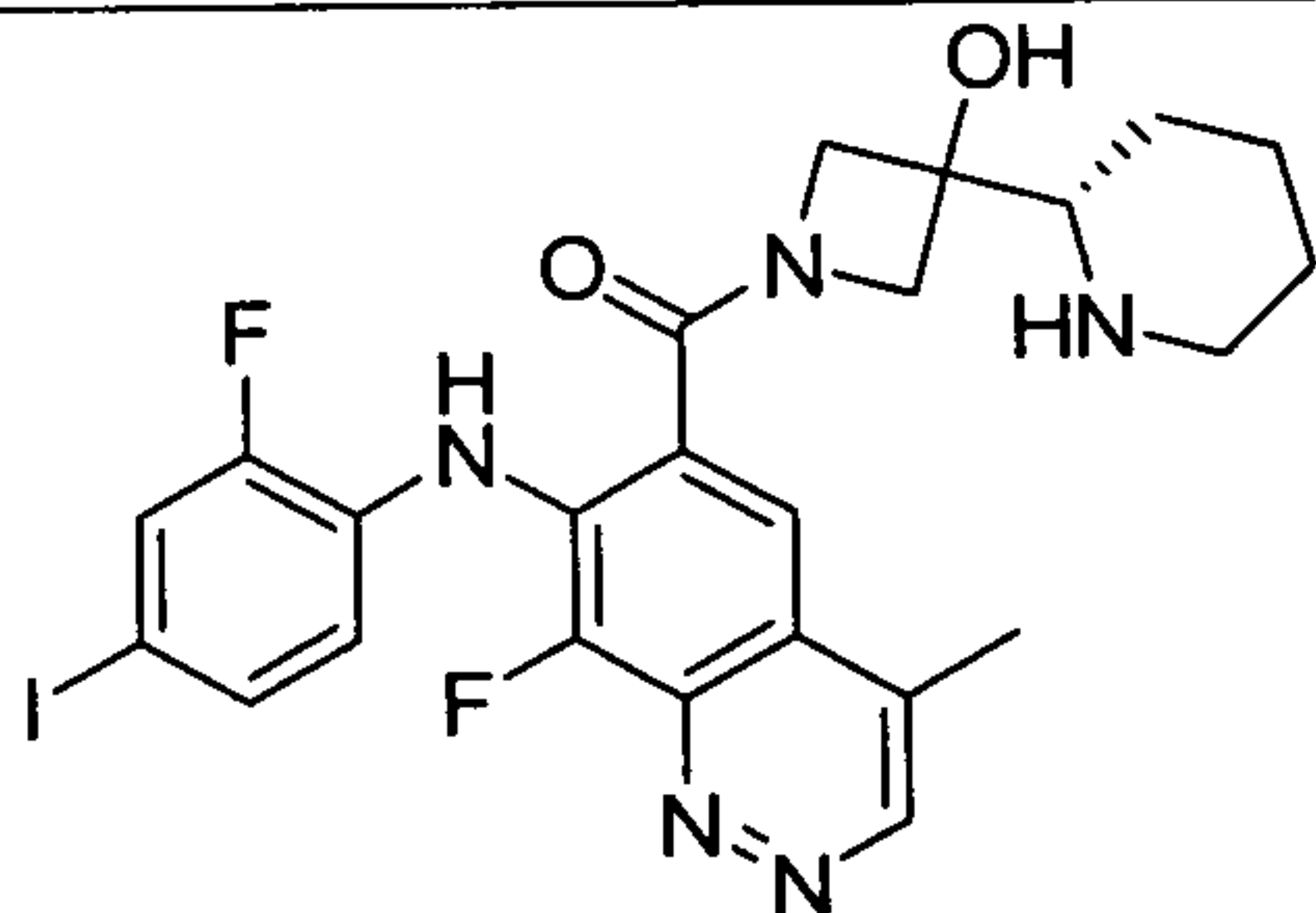
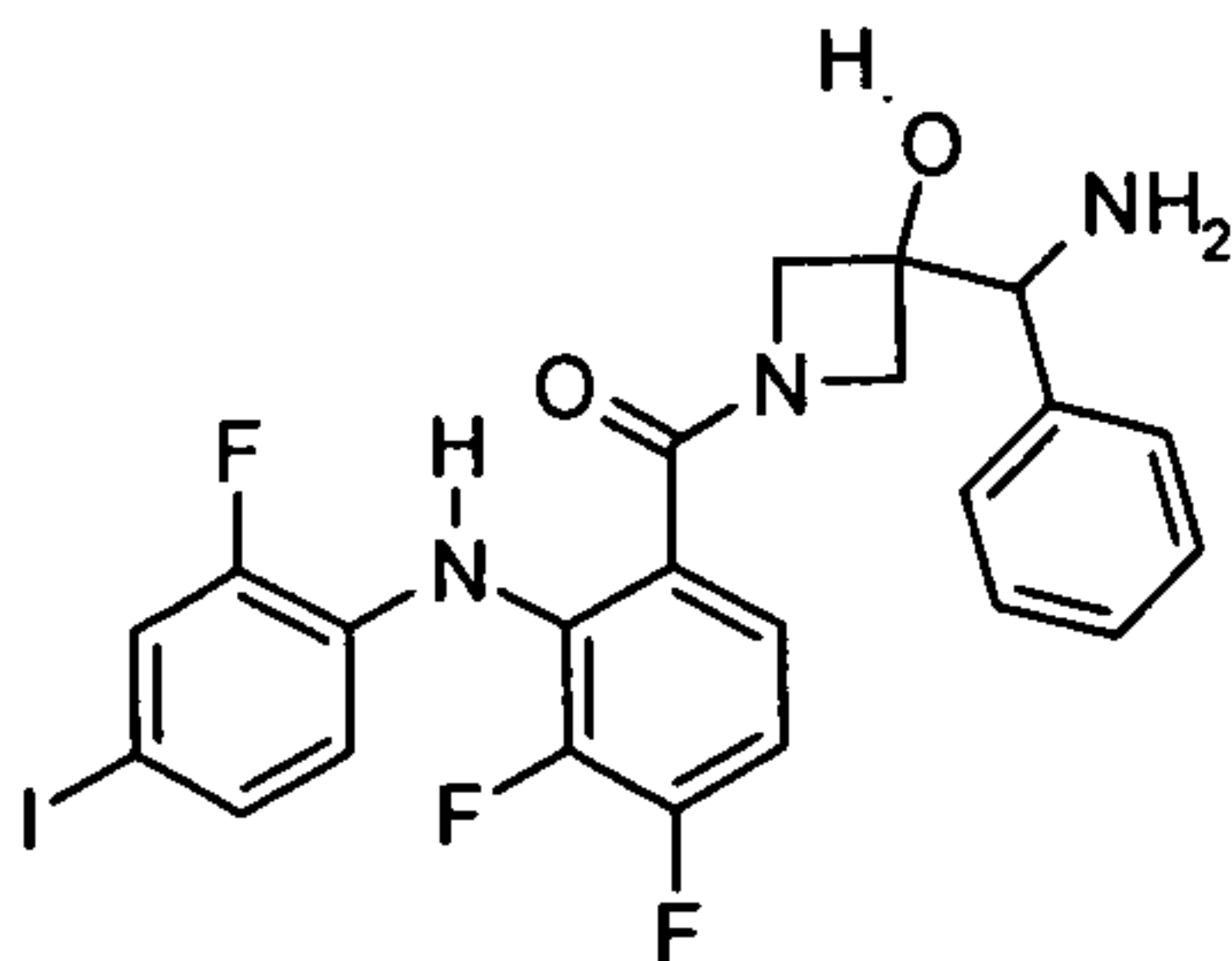
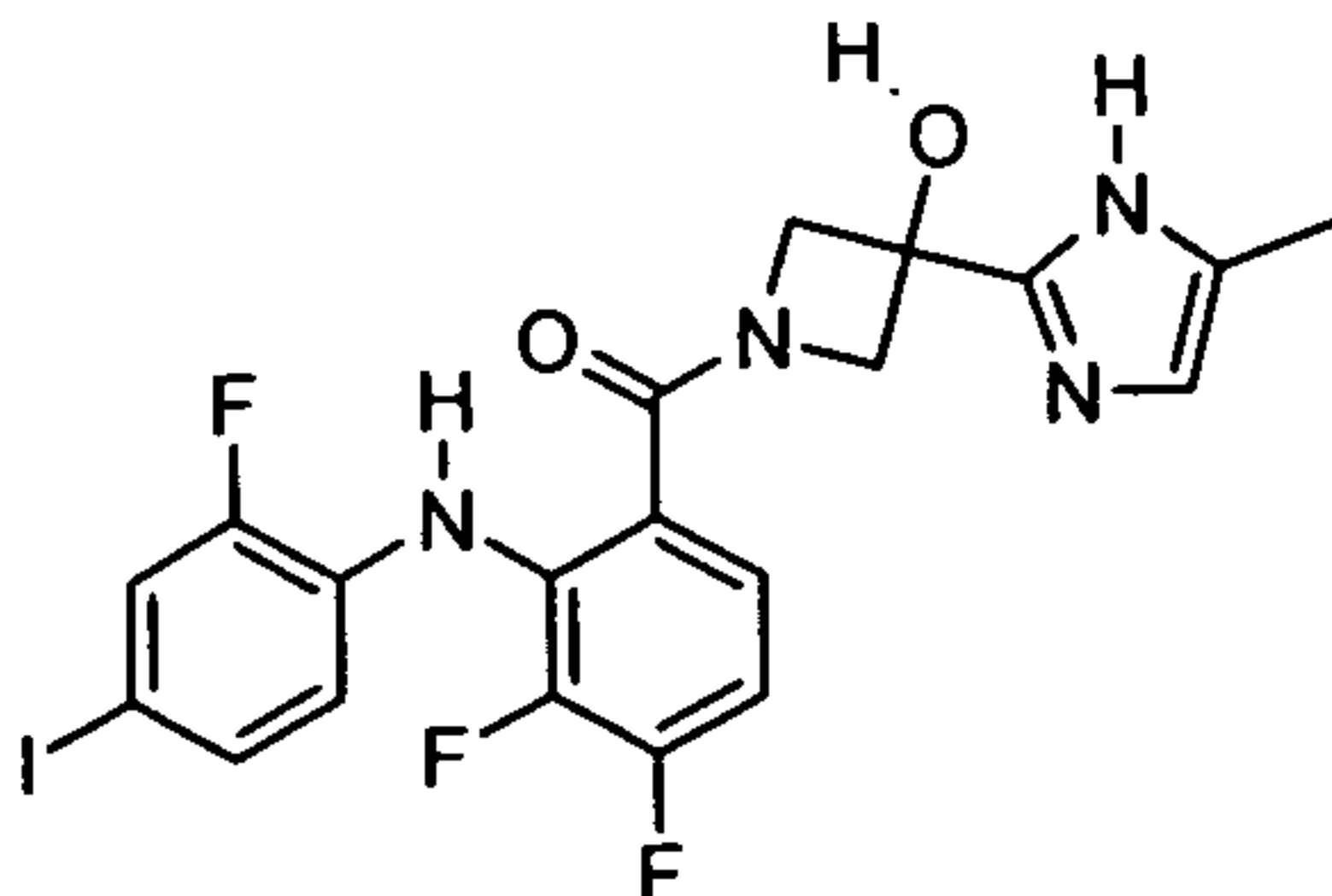
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
284		3-(1-aminobutyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
285		1-({2-fluoro-3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2S)-pyrrolidin-2-yl]azetidin-3-ol
286		1-({8-fluoro-7-[(2-fluoro-4-iodophenyl)amino]-4-methylcinnolin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
287		3-[amino(phenyl)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
288		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(5-methyl-1H-imidazol-2-yl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

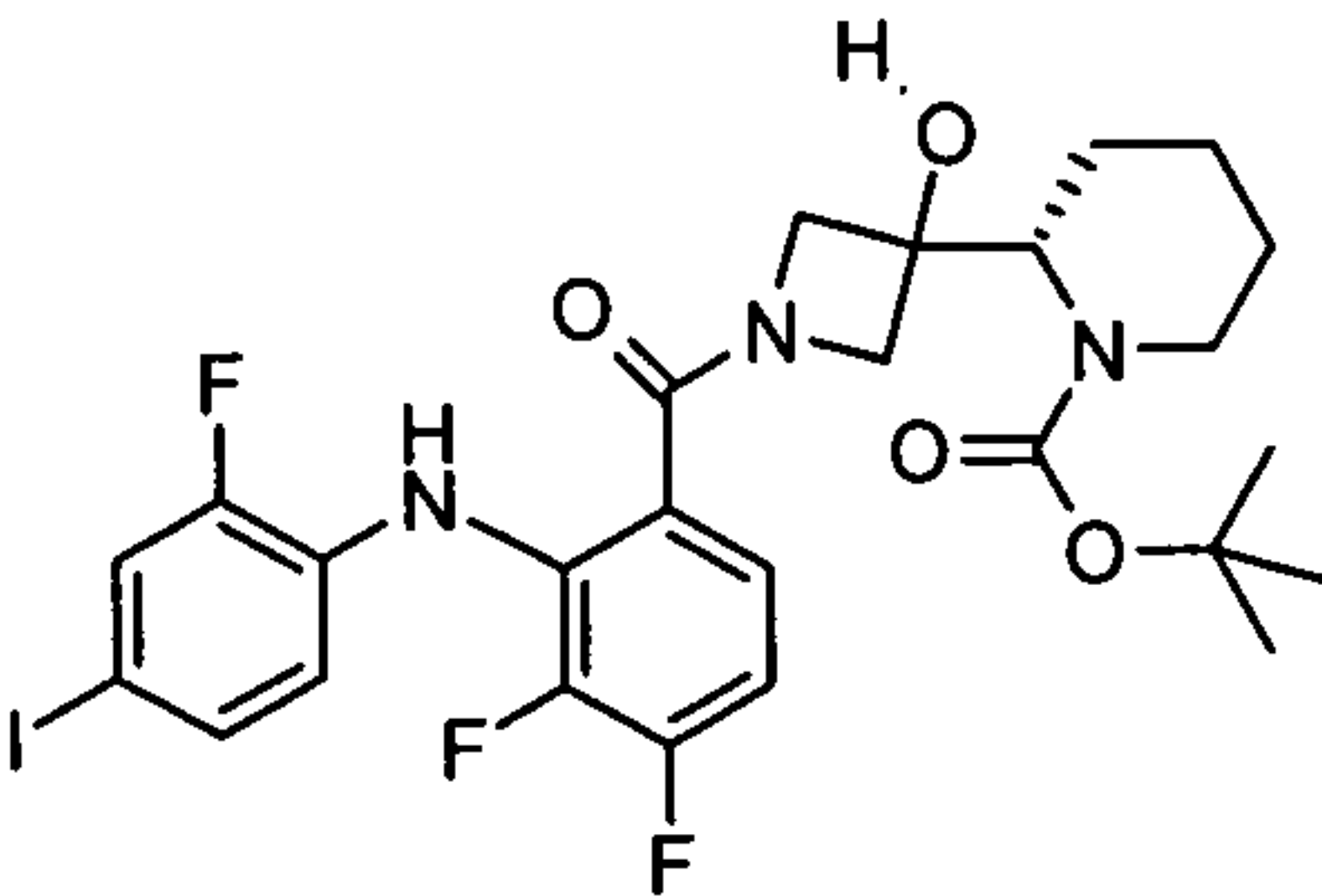
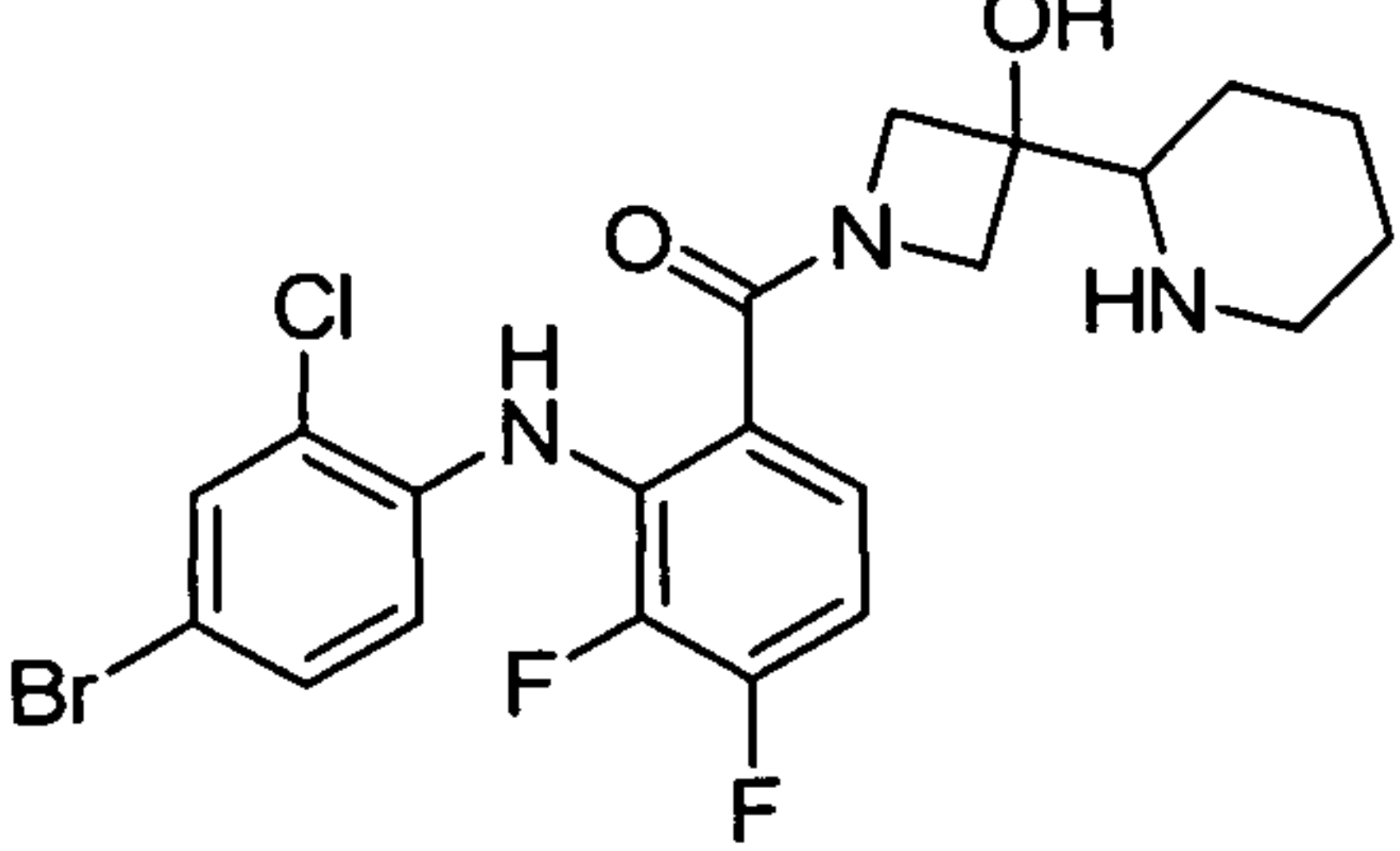
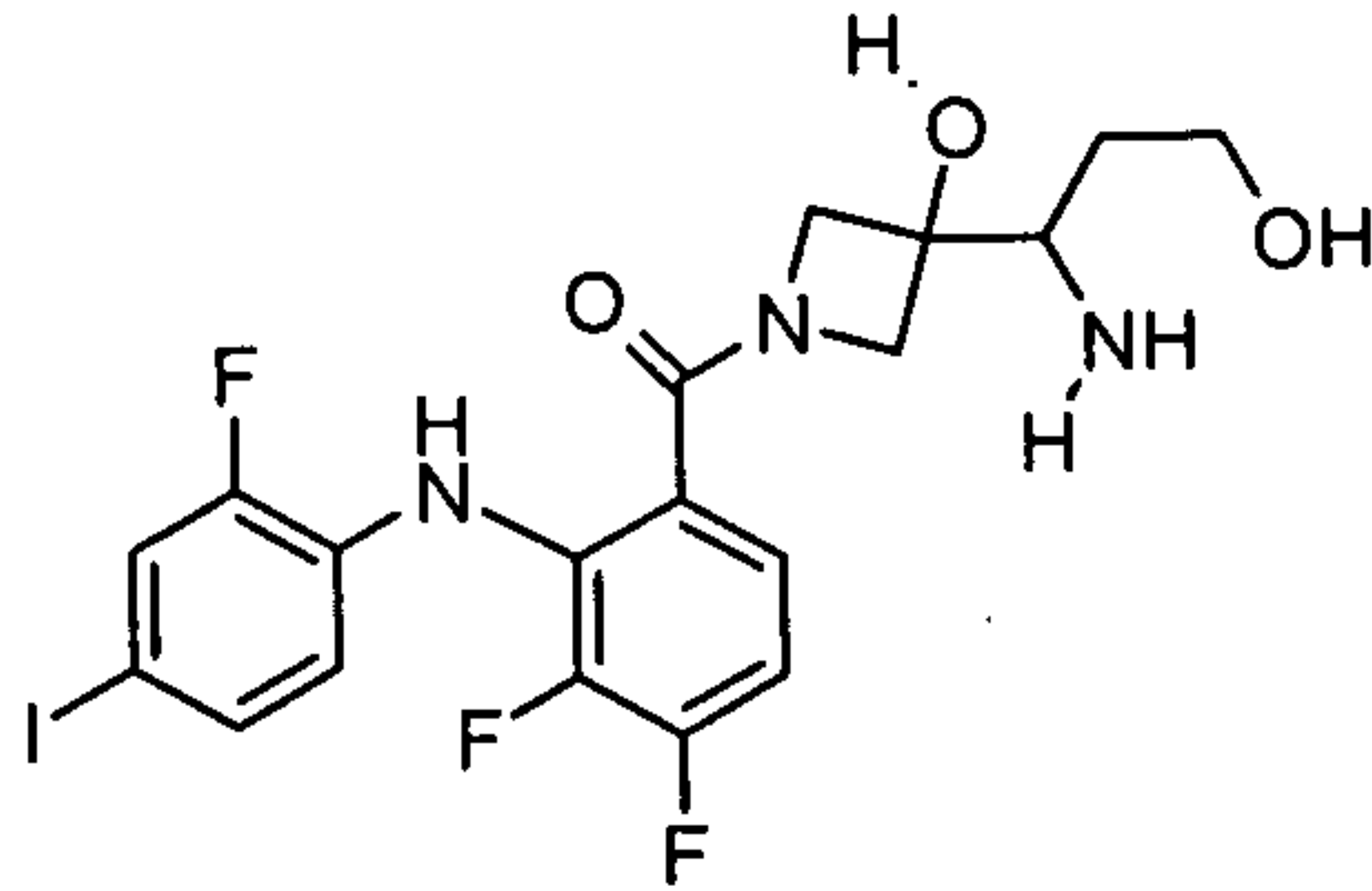
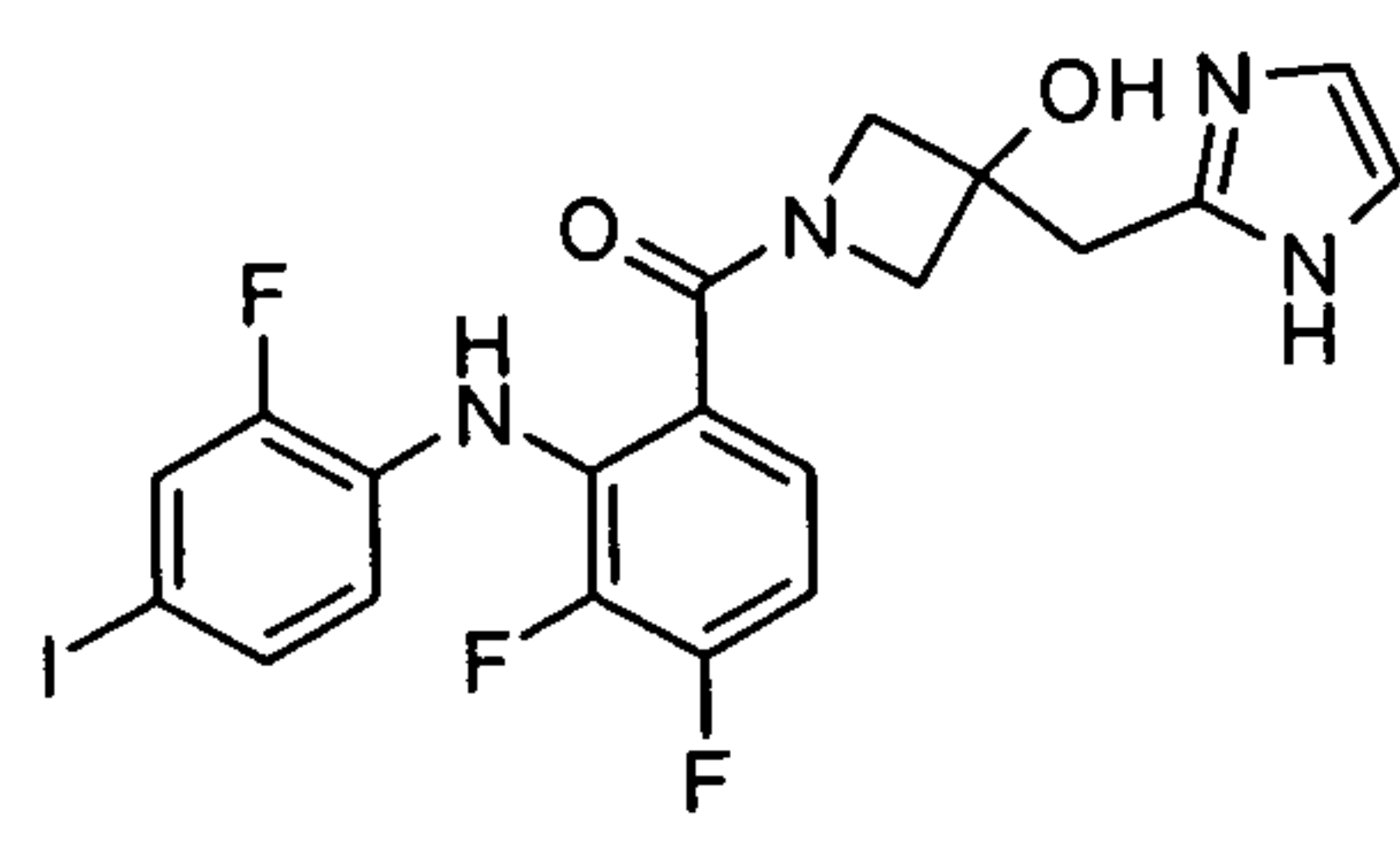
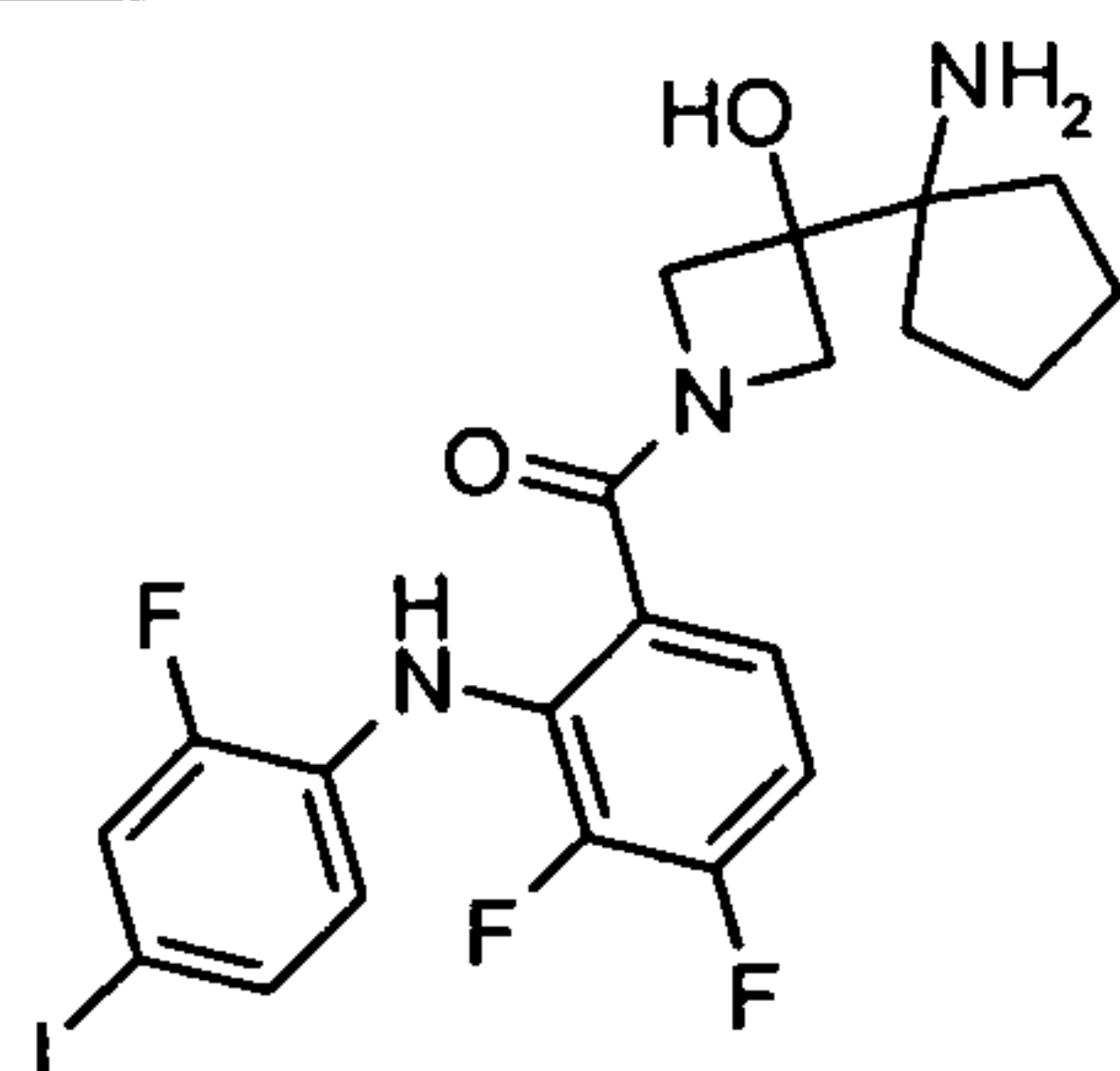
Cmpd No.	Structure	Name
289		1,1-dimethylethyl (2 <i>S</i>)-2-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]piperidine-1-carboxylate
290		1-({2-[(4-bromo-2-chlorophenyl)amino]-3,4-difluorophenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
291		3-(1-amino-3-hydroxypropyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
292		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(1 <i>H</i> -imidazol-2-ylmethyl)azetidin-3-ol
293		3-(1-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol

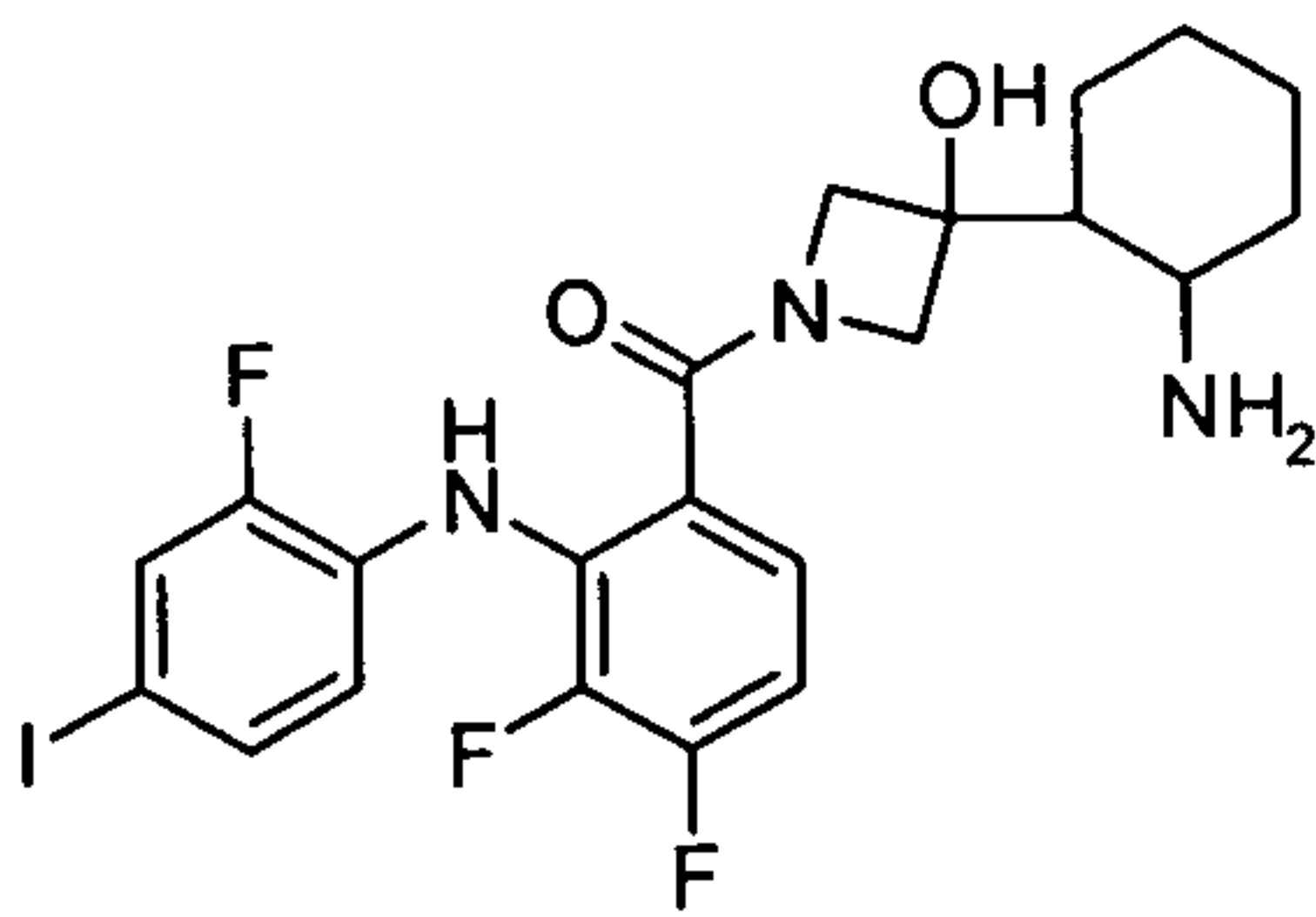
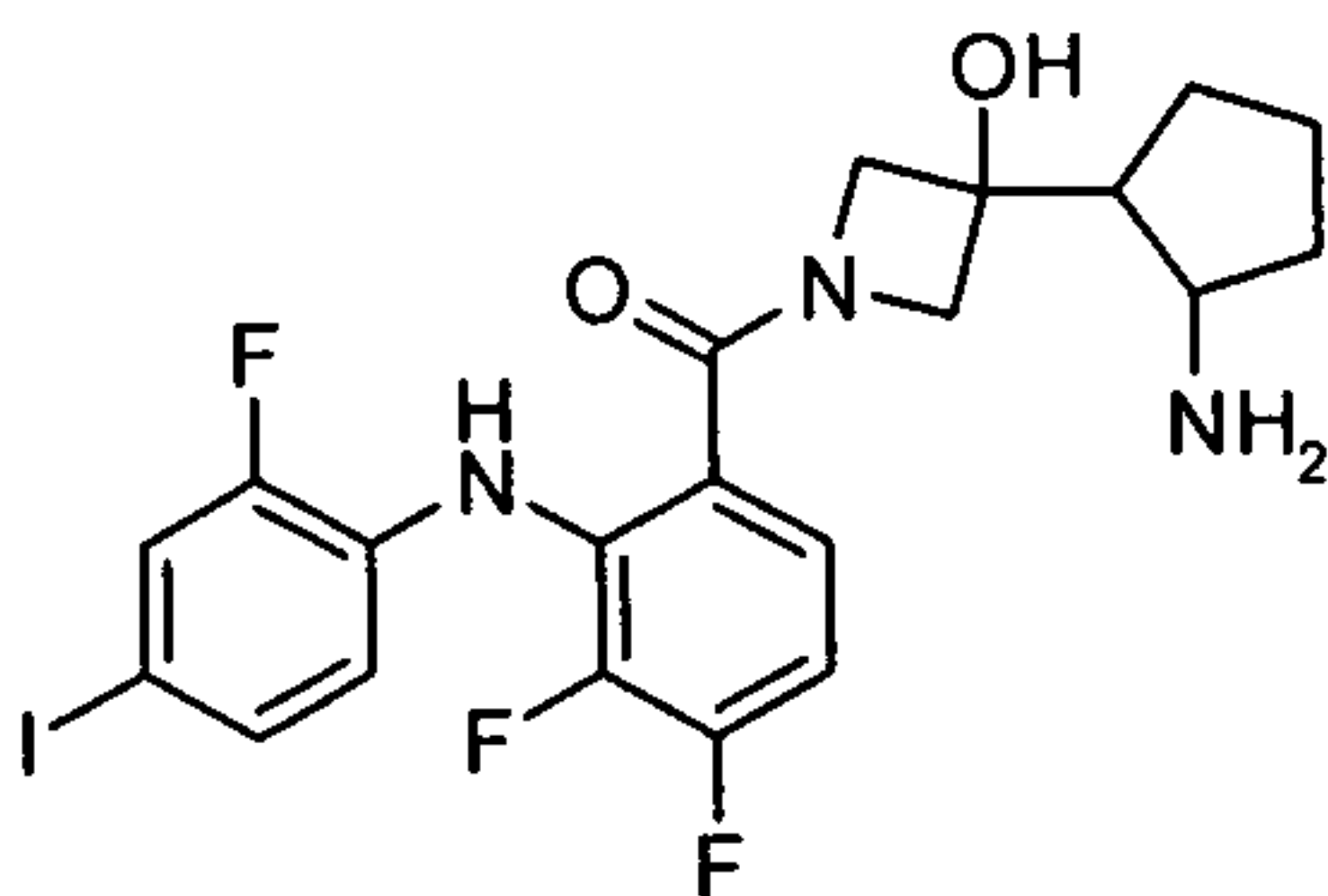
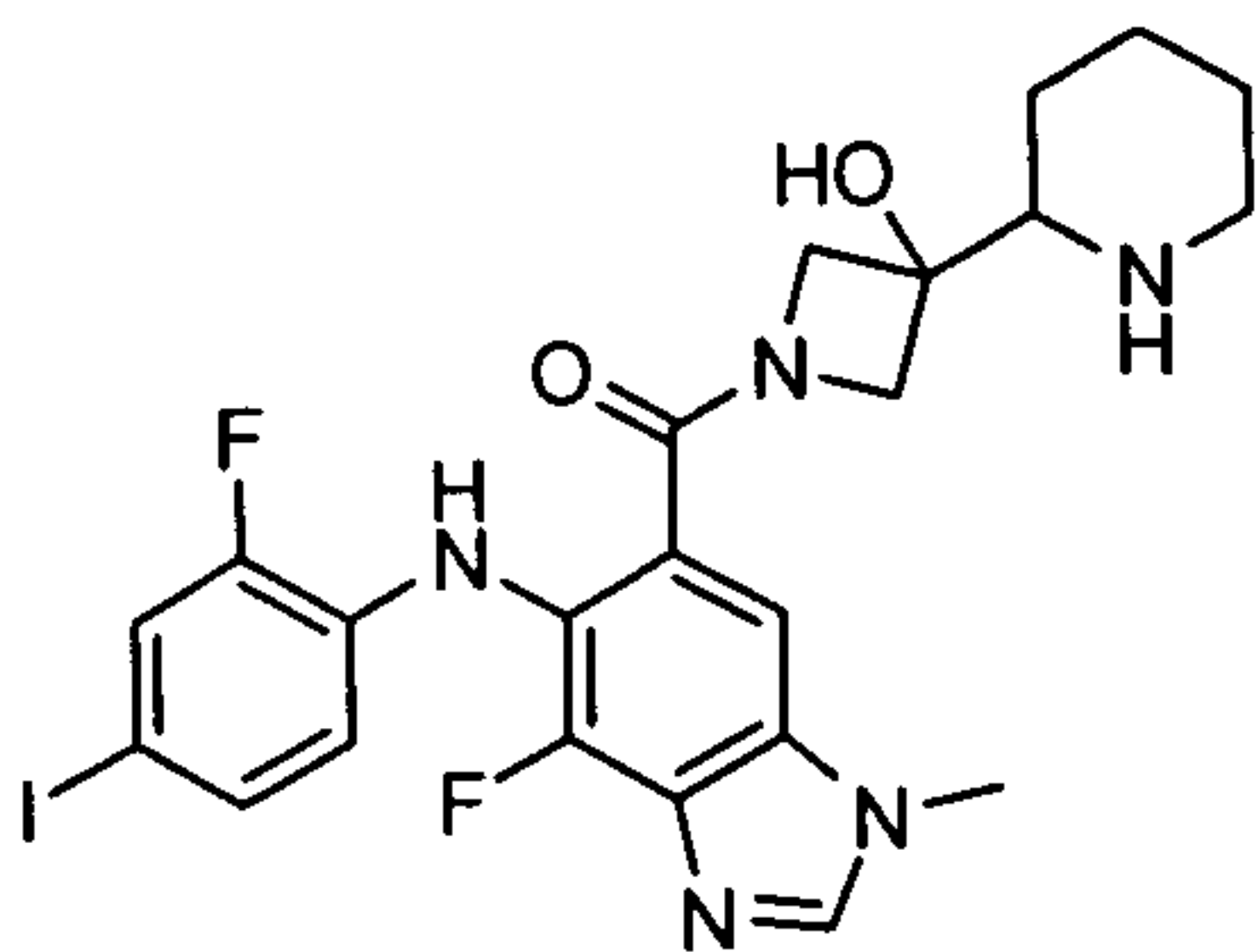
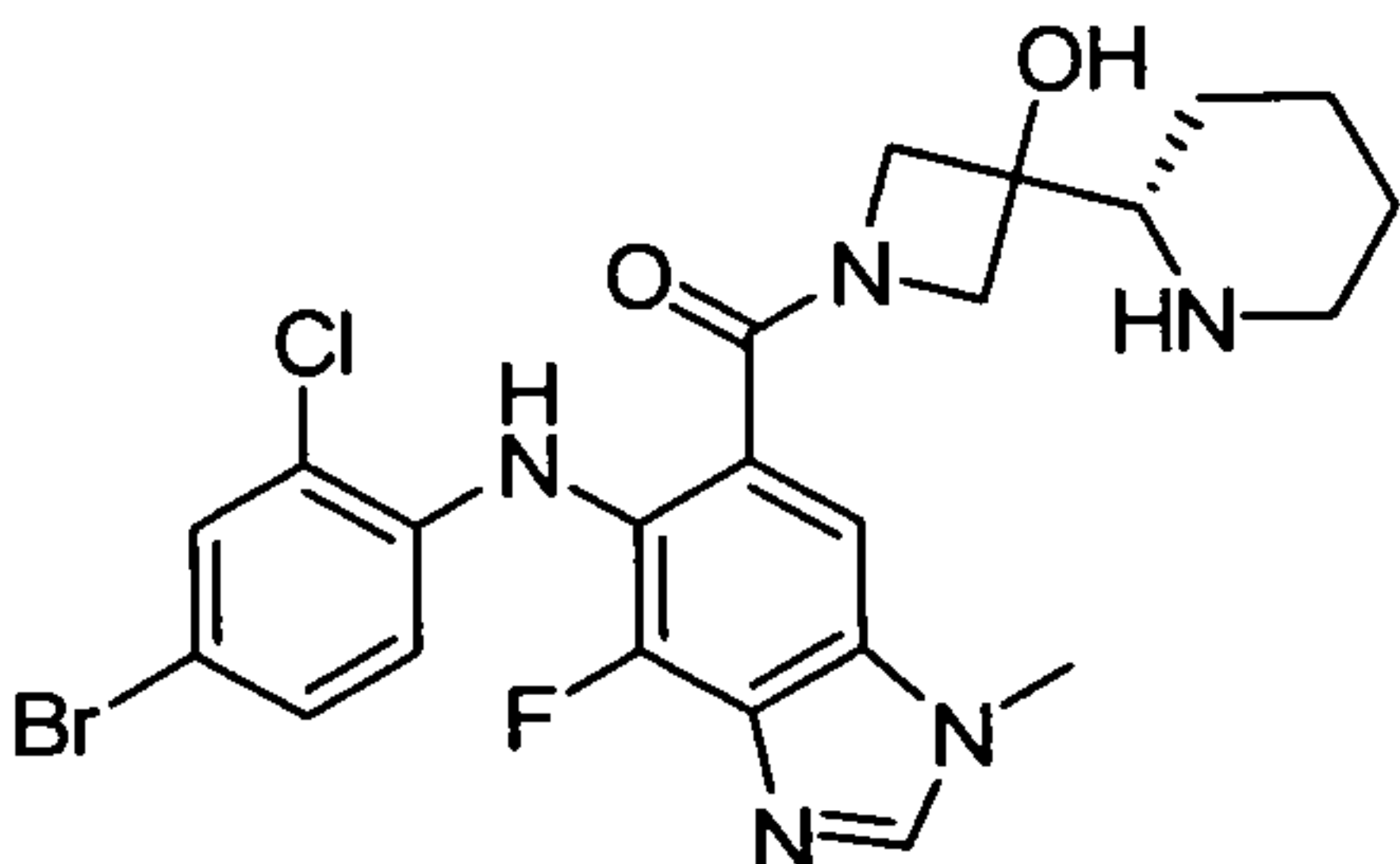
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
294		3-(2-aminocyclohexyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
295		3-(2-aminocyclopentyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-azetidin-3-ol
296		1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1H-benzimidazol-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
297		1-({5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-1-methyl-1H-benzimidazol-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol

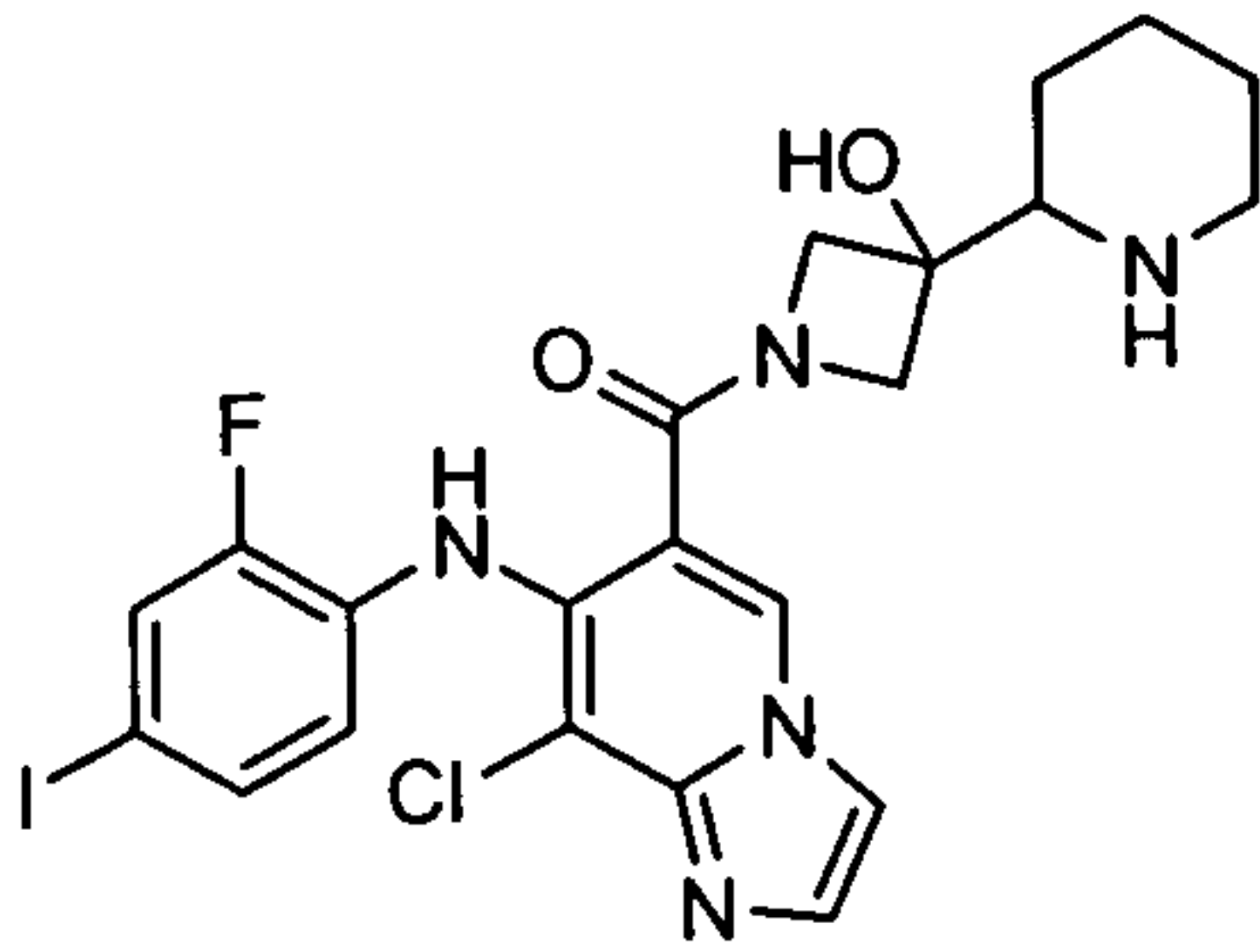
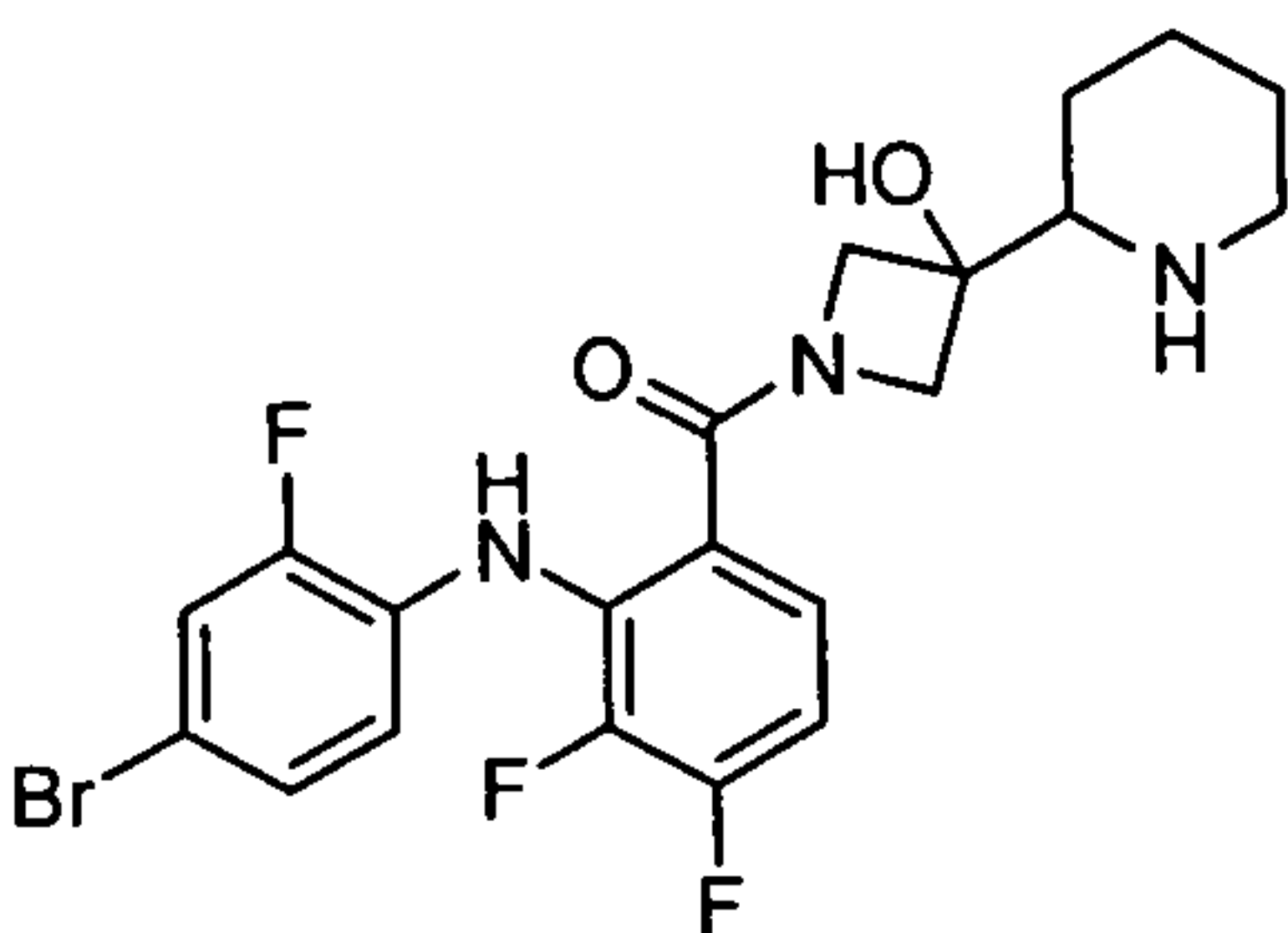
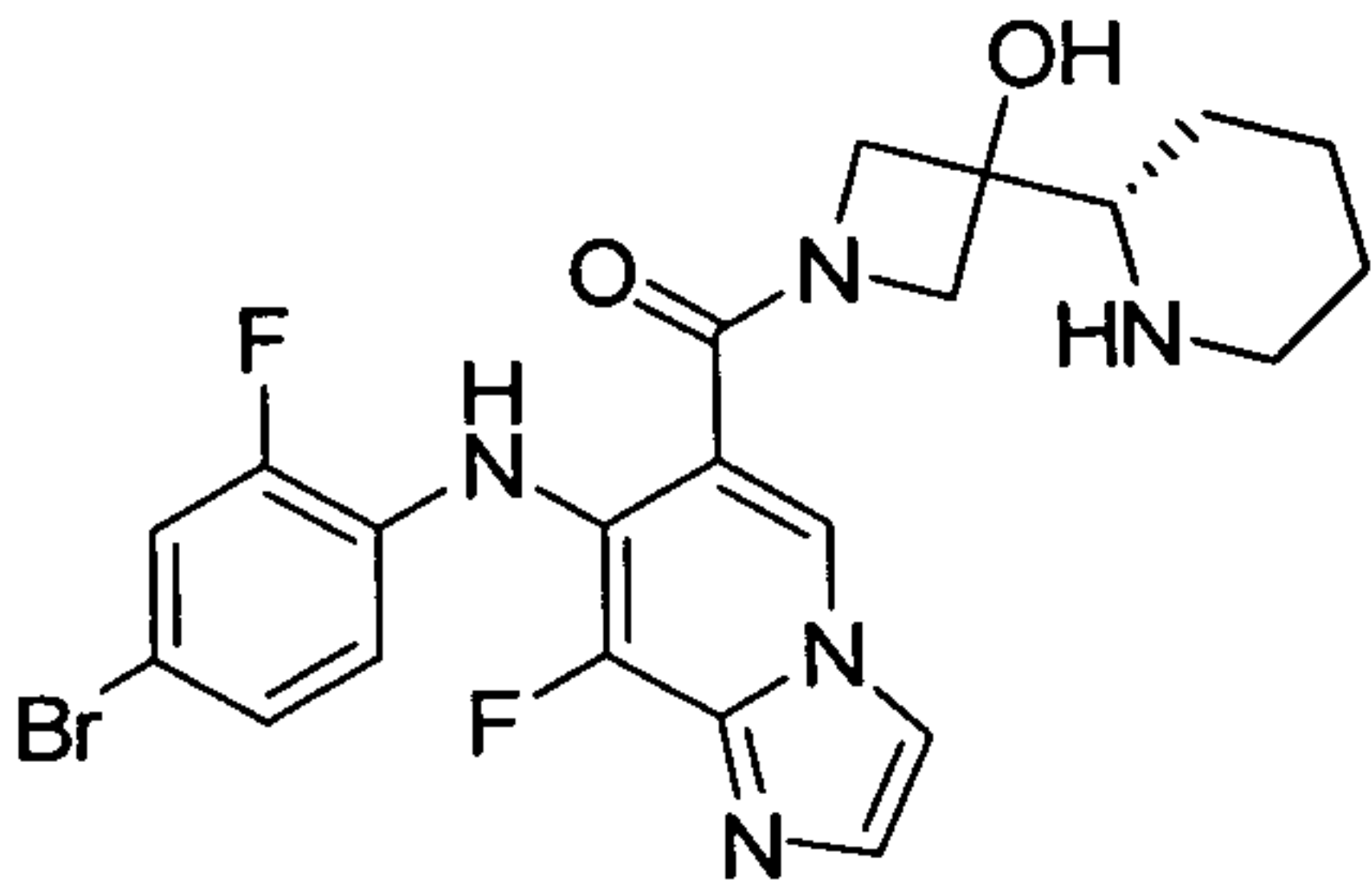
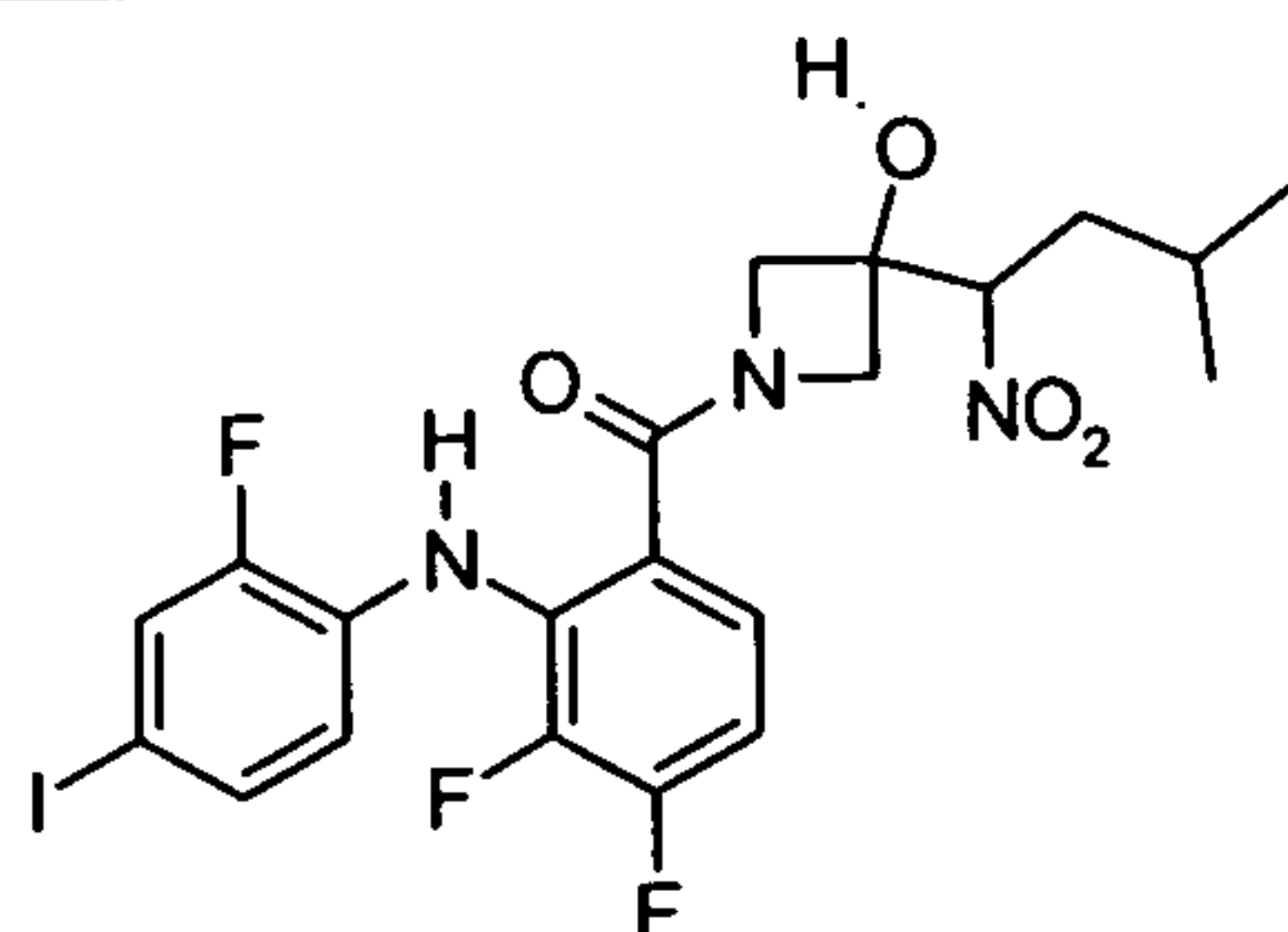
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
298		1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
299		1-({2-[(4-bromo-2-fluorophenyl)amino]-3,4-difluorophenyl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
300		1-({7-[(4-bromo-2-fluorophenyl)amino]-8-fluoroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
301		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(3-methyl-1-nitrobutyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors

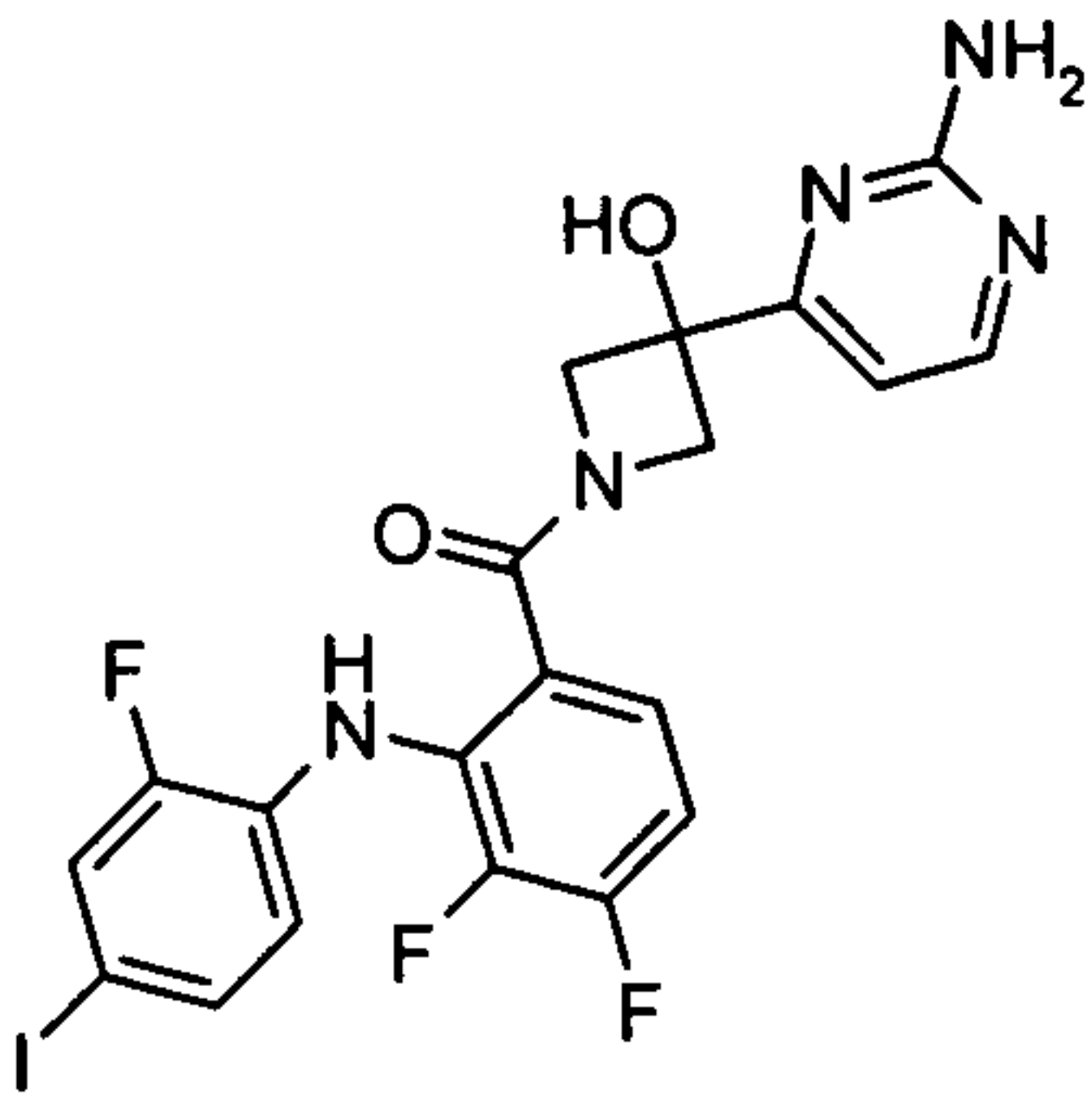
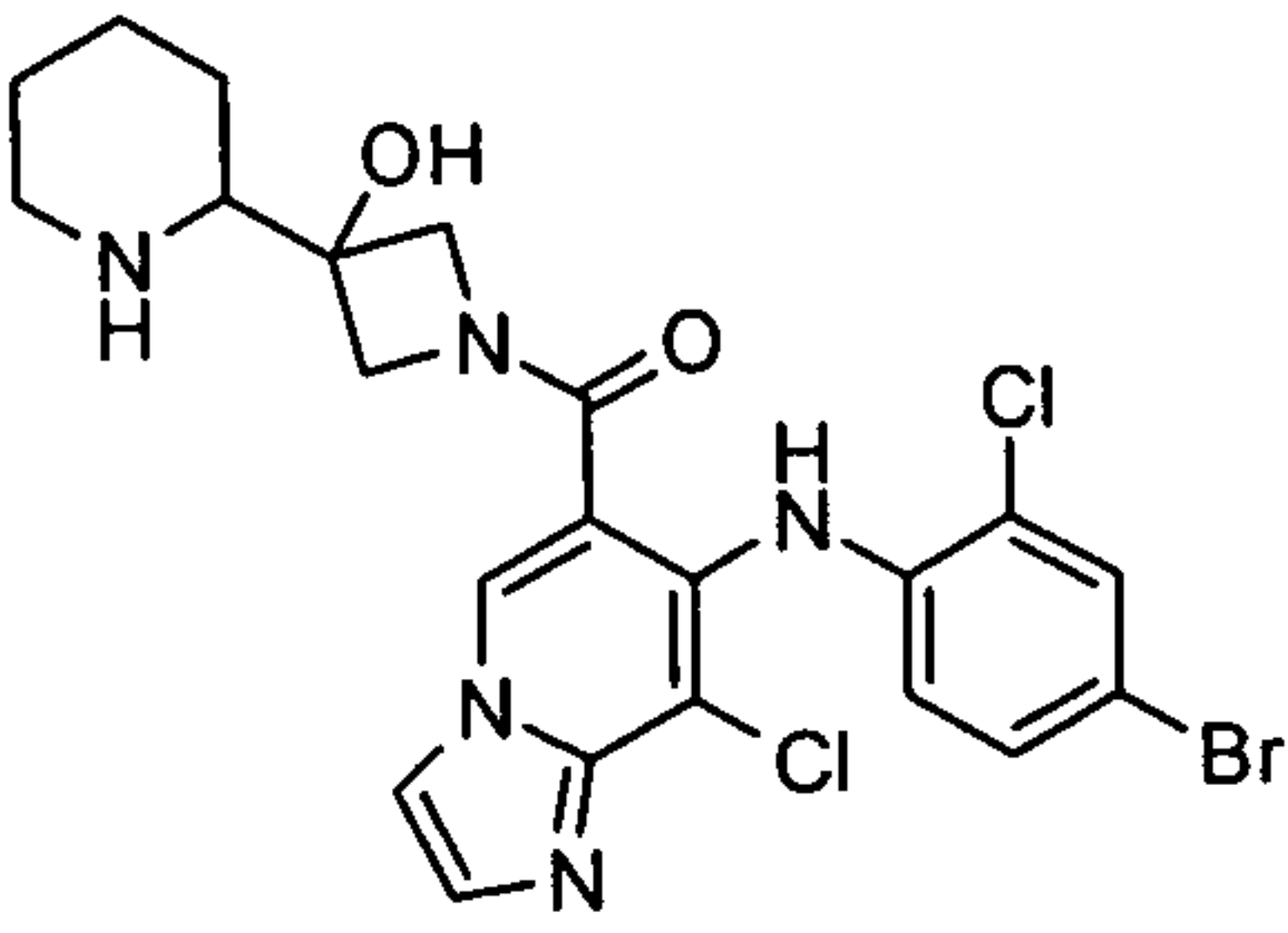
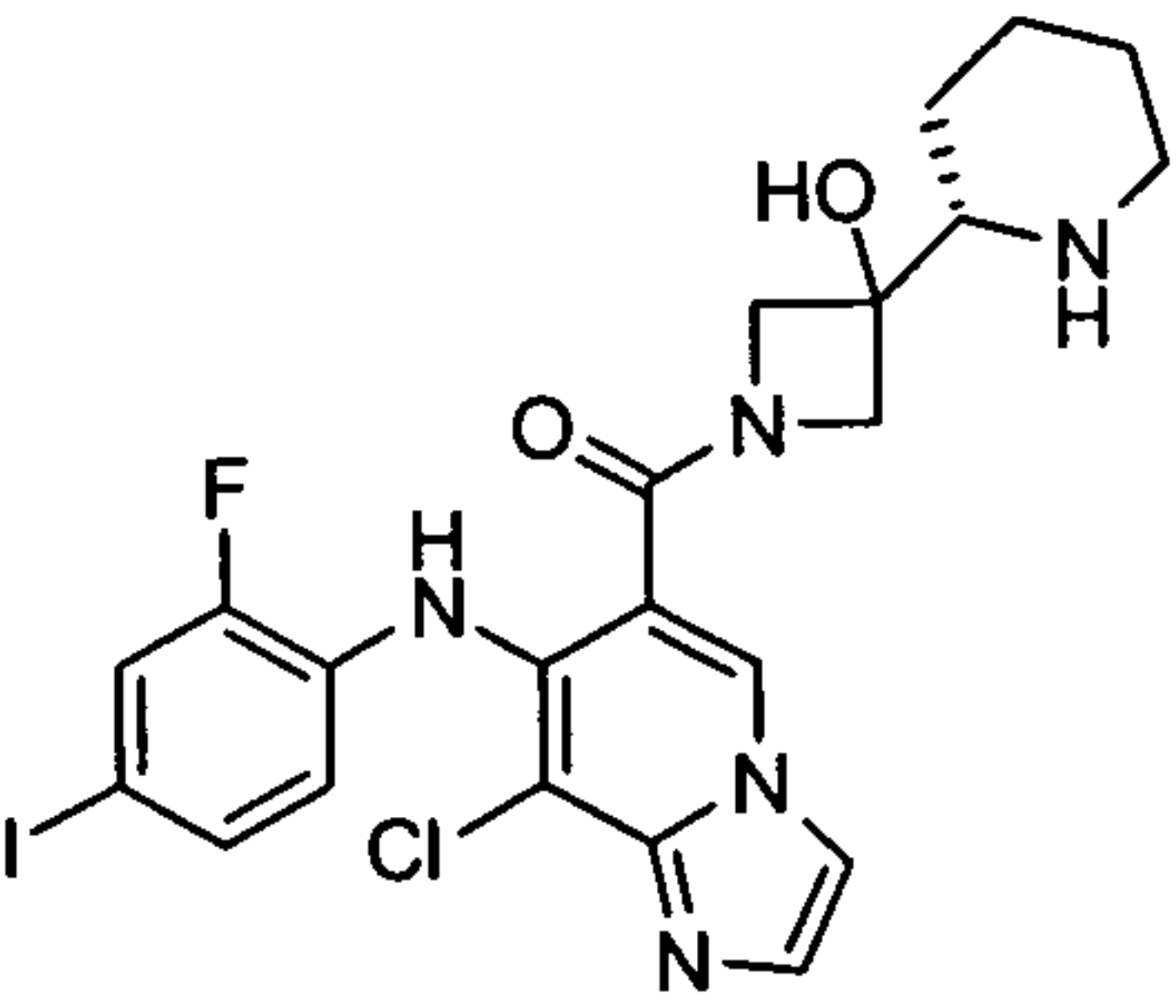
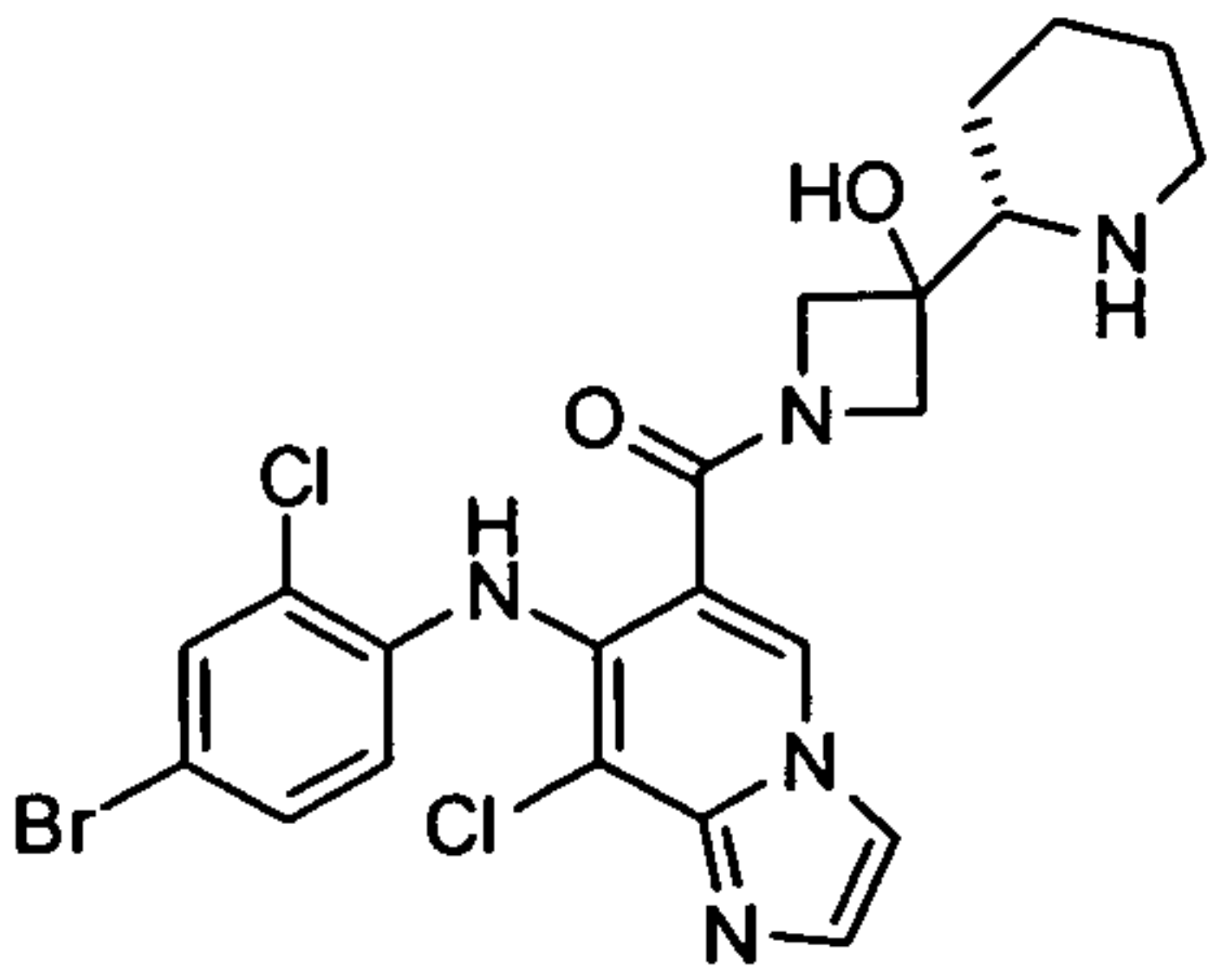
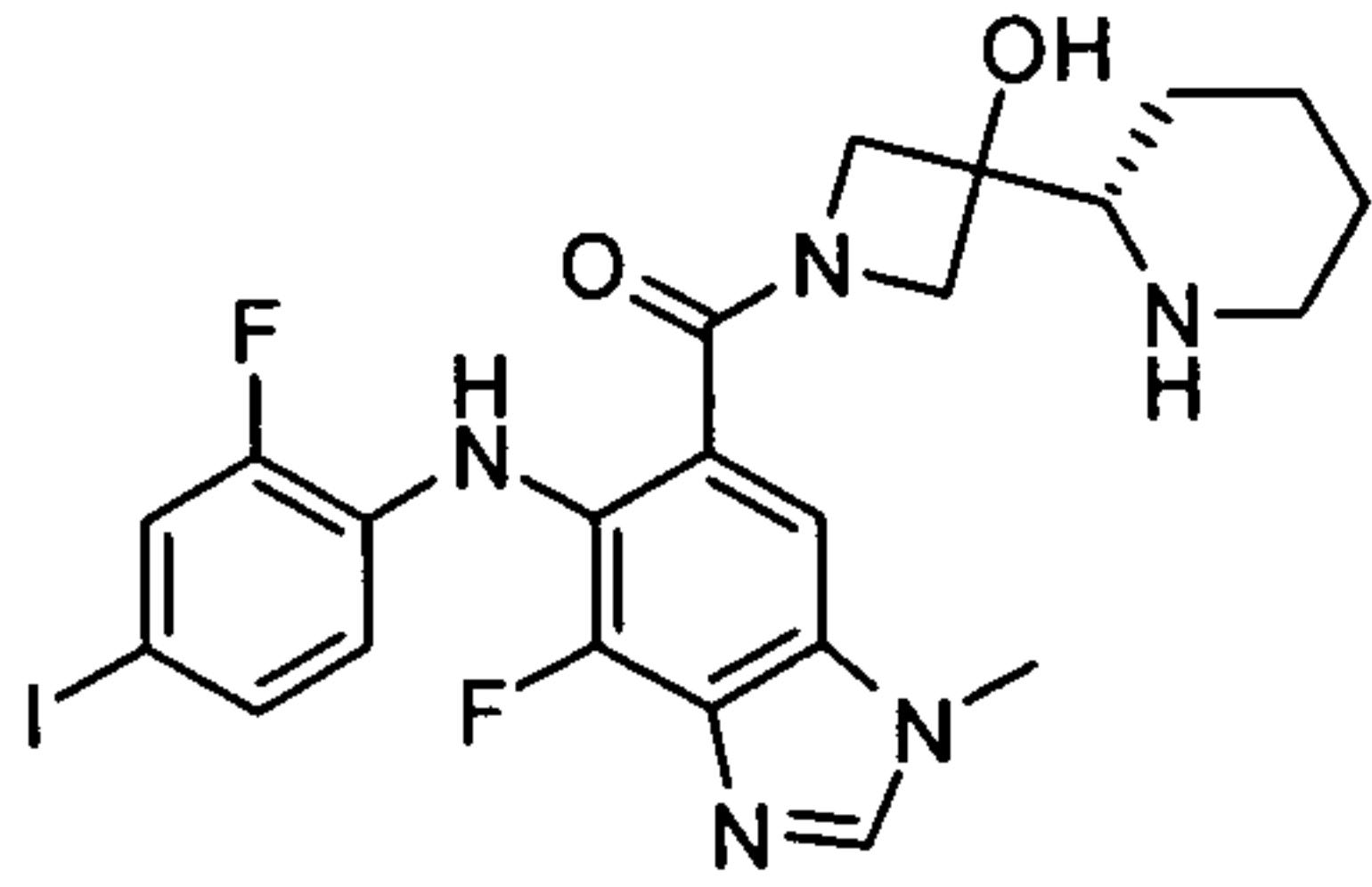
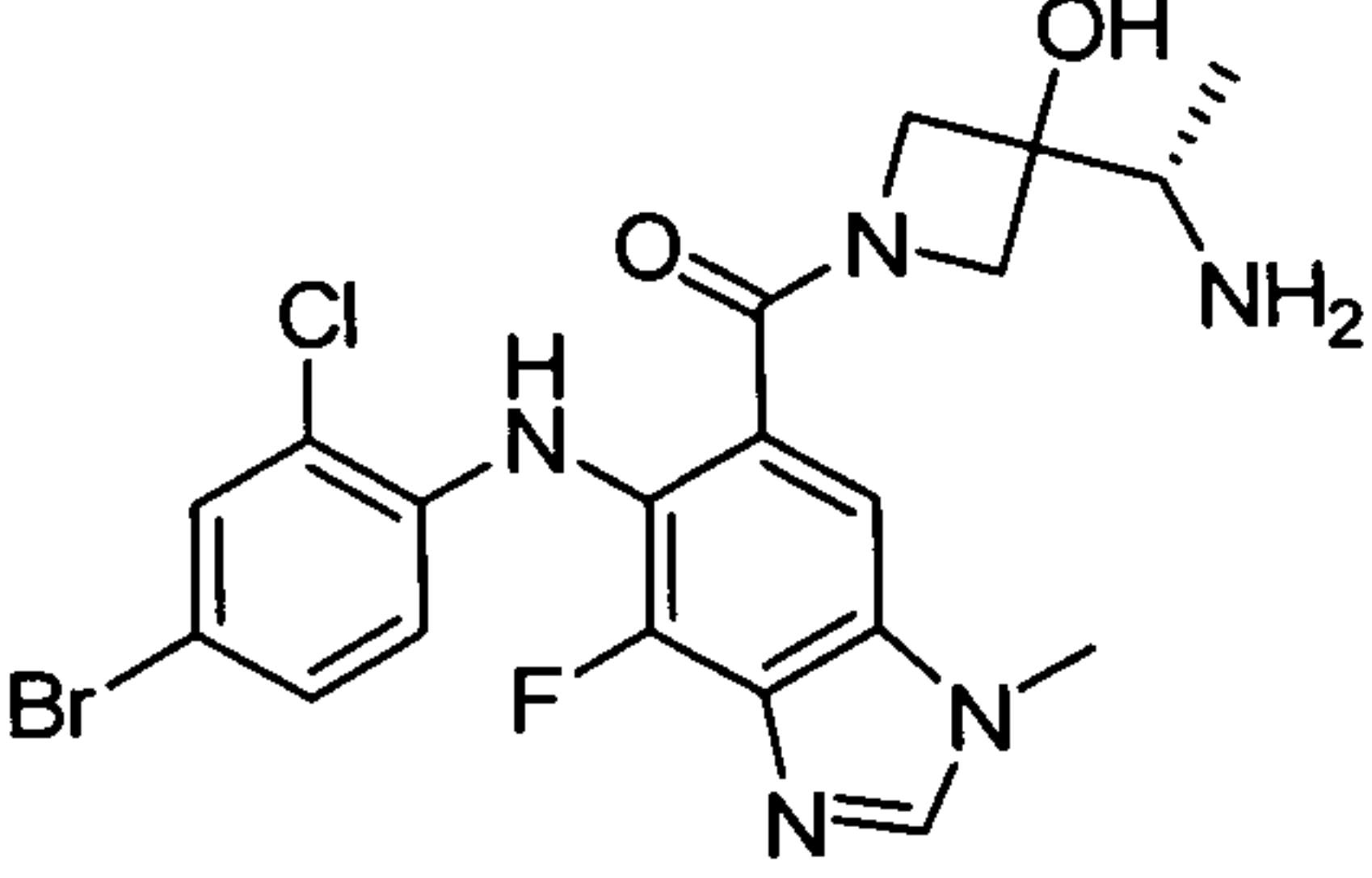
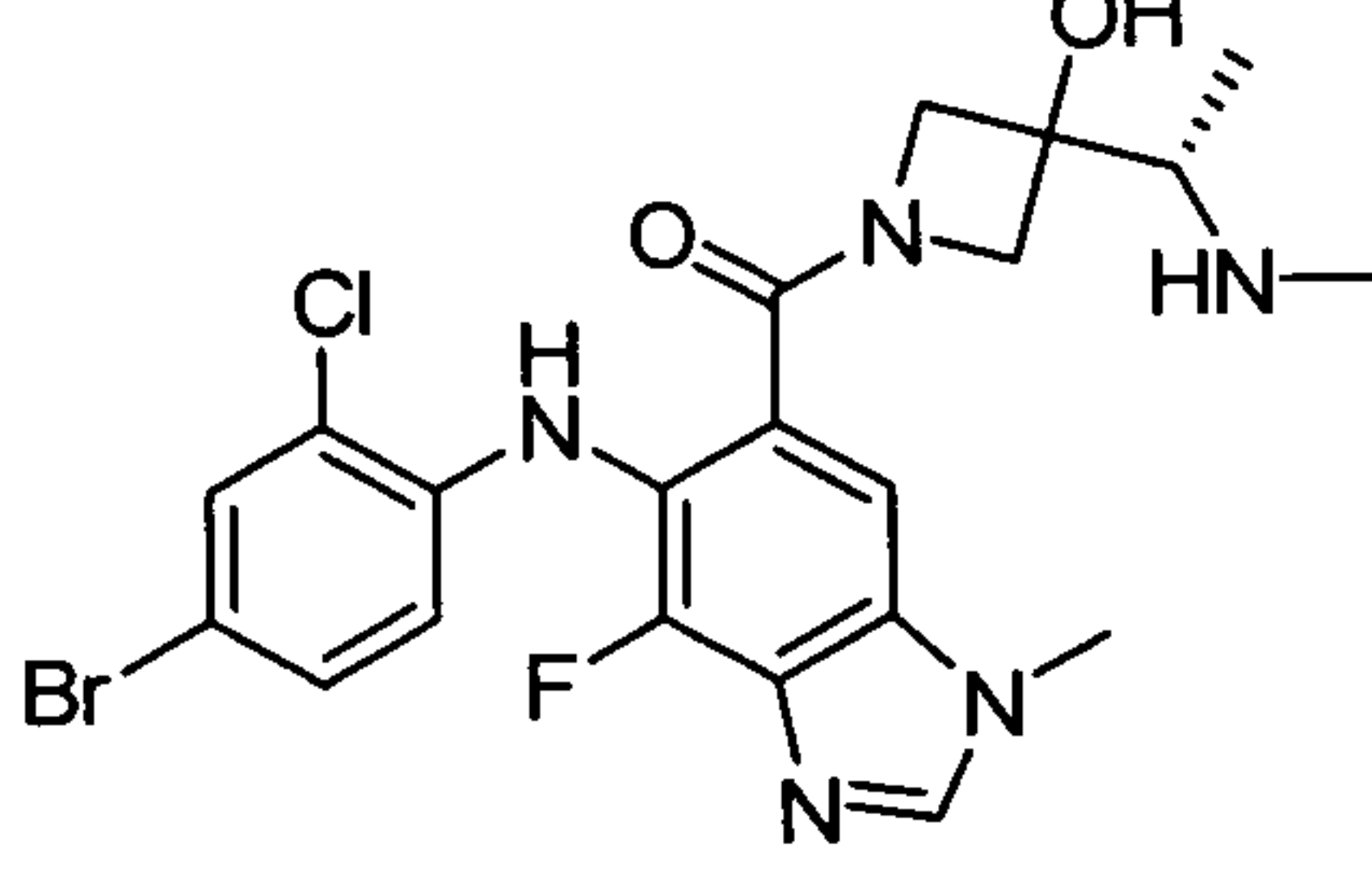
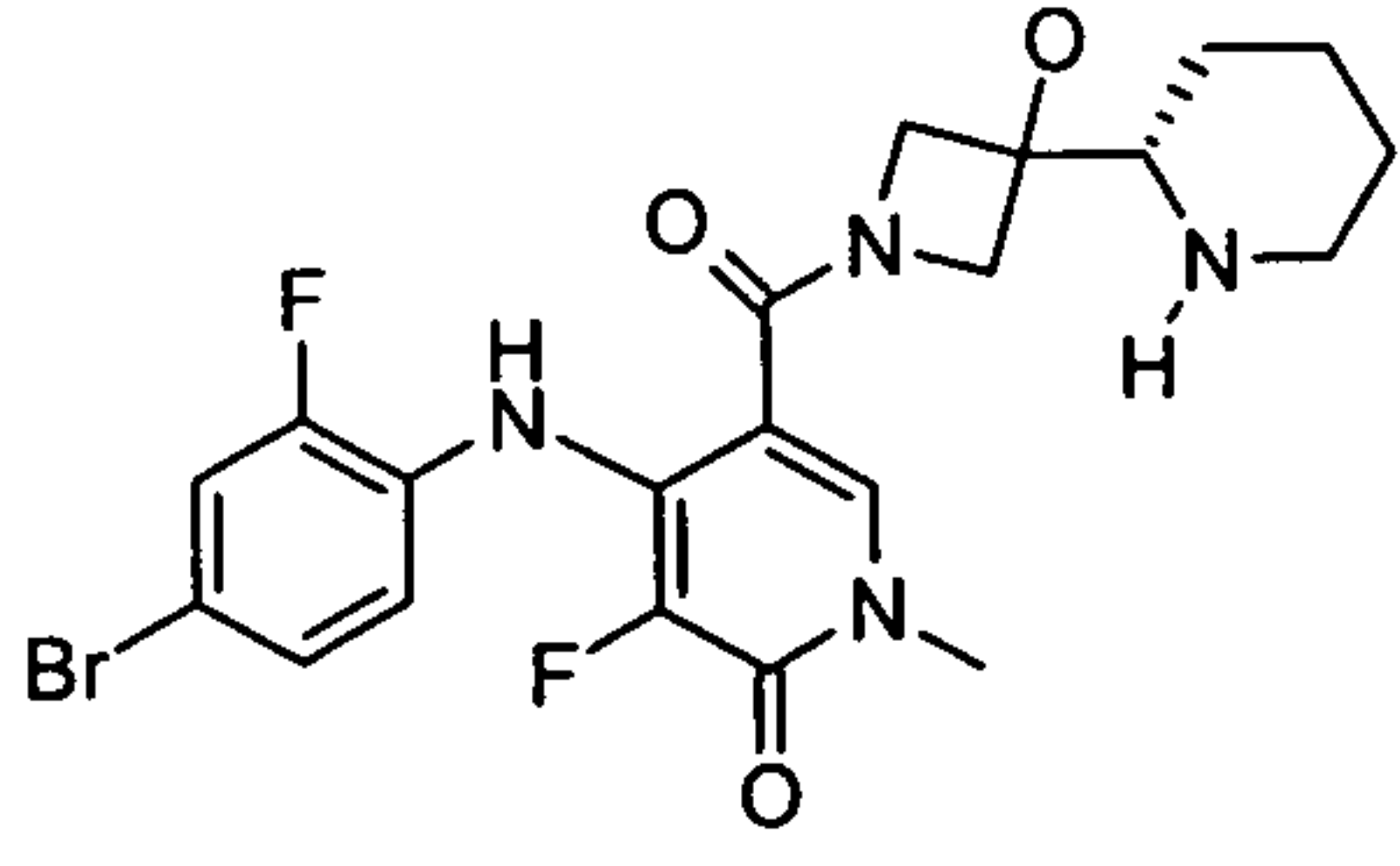
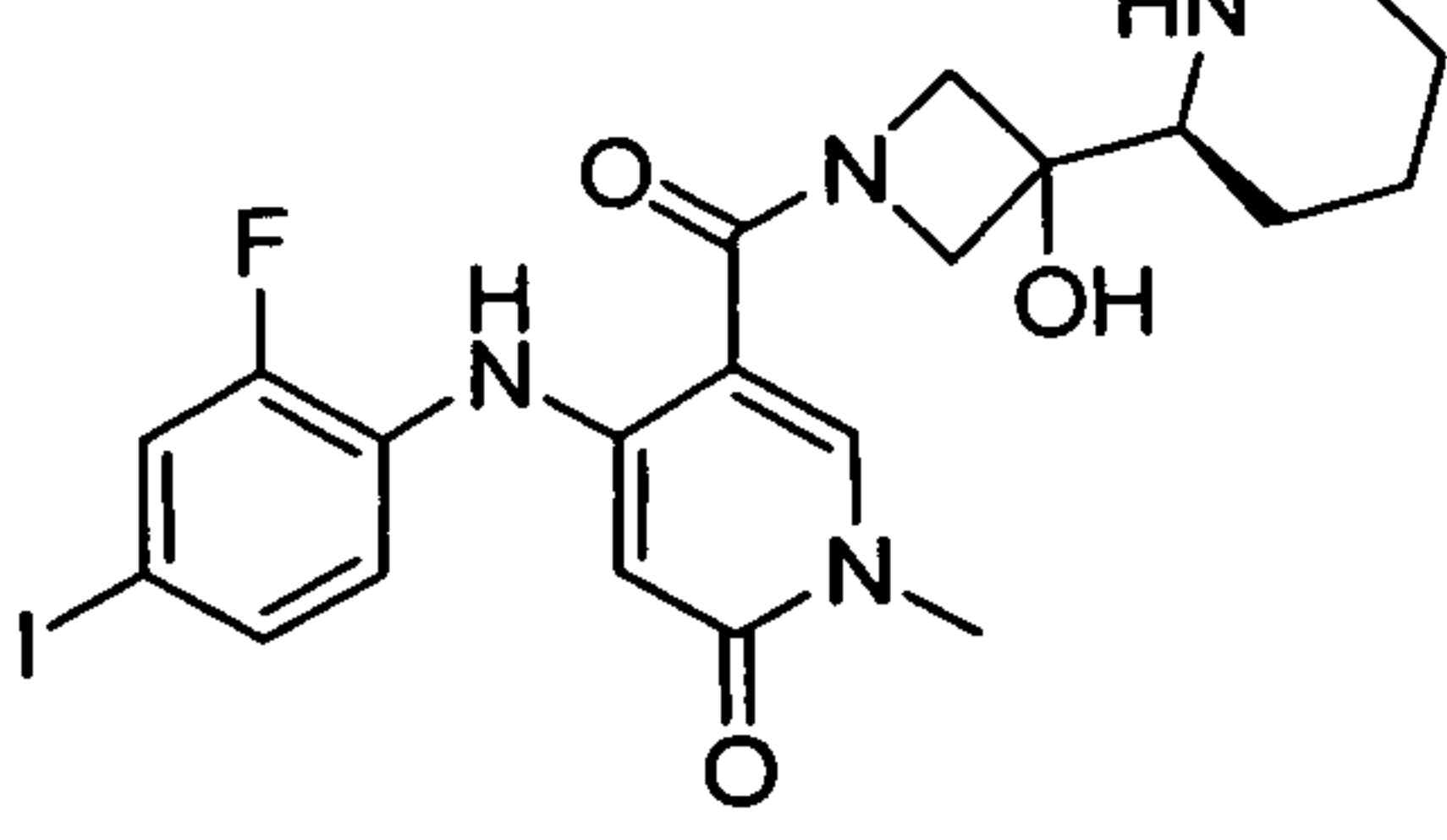
Cmpd No.	Structure	Name
302		3-(2-aminopyrimidin-4-yl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol
303		1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-piperidin-2-ylazetidin-3-ol
304		1-({8-chloro-7-[(2-fluoro-4-iodophenyl)amino]imidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
305		1-({7-[(4-bromo-2-chlorophenyl)amino]-8-chloroimidazo[1,2-a]pyridin-6-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
306		1-((4-fluoro-5-((2-fluoro-4-iodophenyl)amino)-1-methyl-1H-benzimidazol-6-yl)carbonyl)-3-((2S)-piperidin-2-yl)azetidin-3-ol
307		3-((1S)-1-aminoethyl)-1-((5-((4-bromo-2-chlorophenyl)amino)-4-fluoro-1-methyl-1H-benzimidazol-6-yl)carbonyl)azetidin-3-ol
308		1-((5-((4-bromo-2-chlorophenyl)amino)-4-fluoro-1-methyl-1H-benzimidazol-6-yl)carbonyl)-3-((1S)-1-(methylamino)ethyl)azetidin-3-ol
309		4-((4-bromo-2-fluorophenyl)amino)-3-fluoro-5-((3-hydroxy-3-((2S)-piperidin-2-yl)azetidin-1-yl)carbonyl)pyridin-2(1H)-one
310		4-((2-fluoro-4-iodophenyl)amino)-5-((3-hydroxy-3-((2S)-piperidin-2-yl)azetidin-1-yl)carbonyl)-1-methylpyridin-2(1H)-one

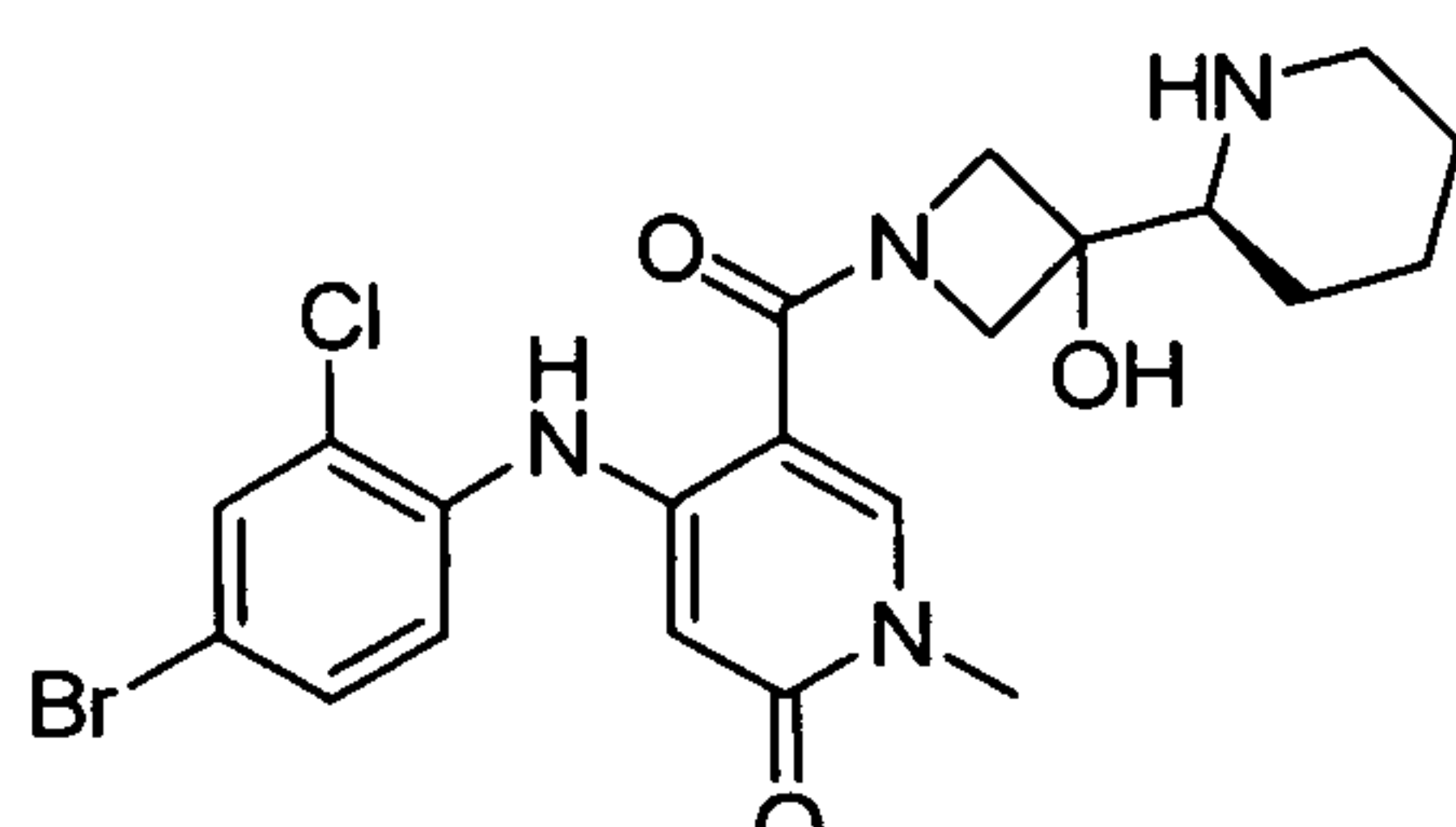
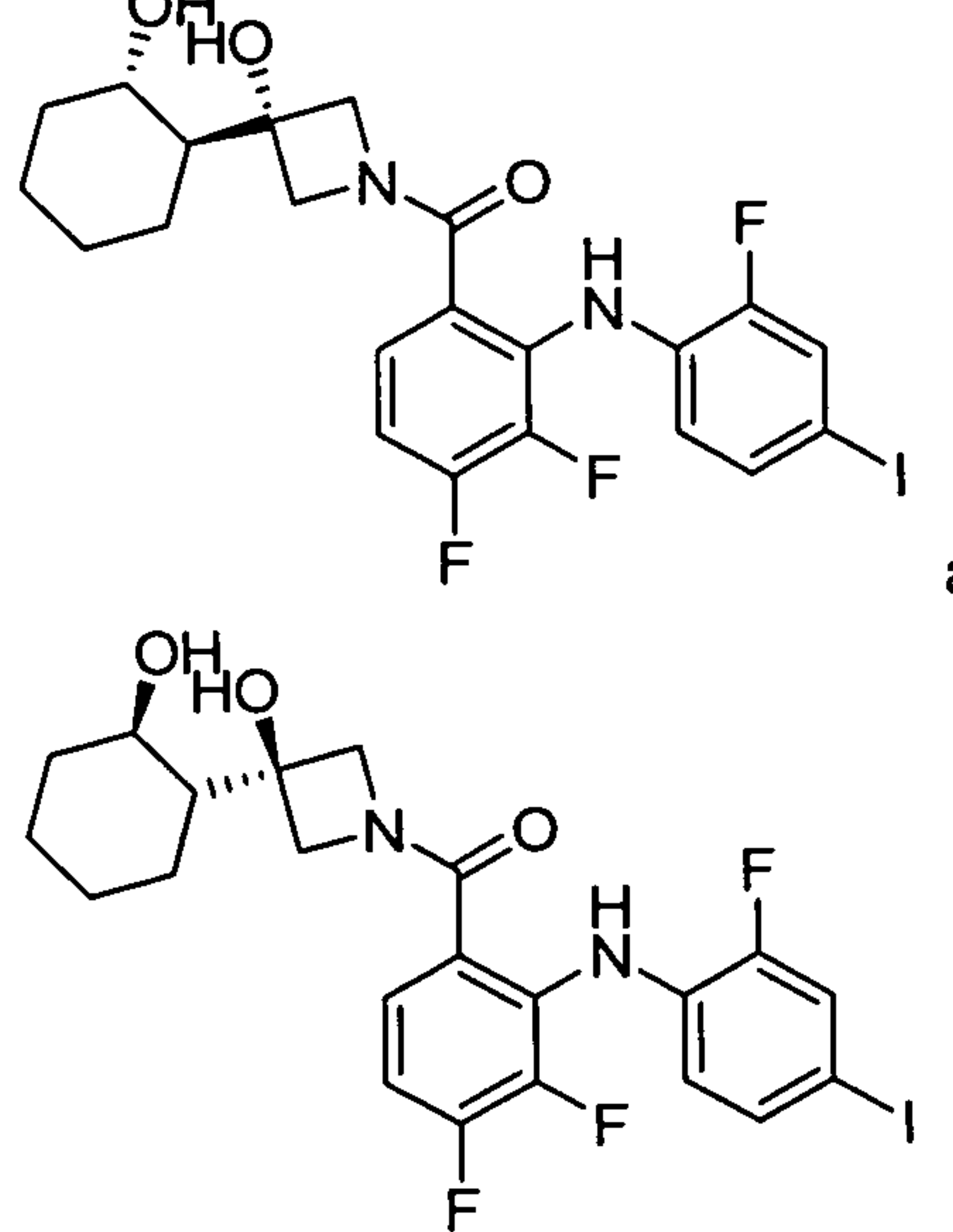
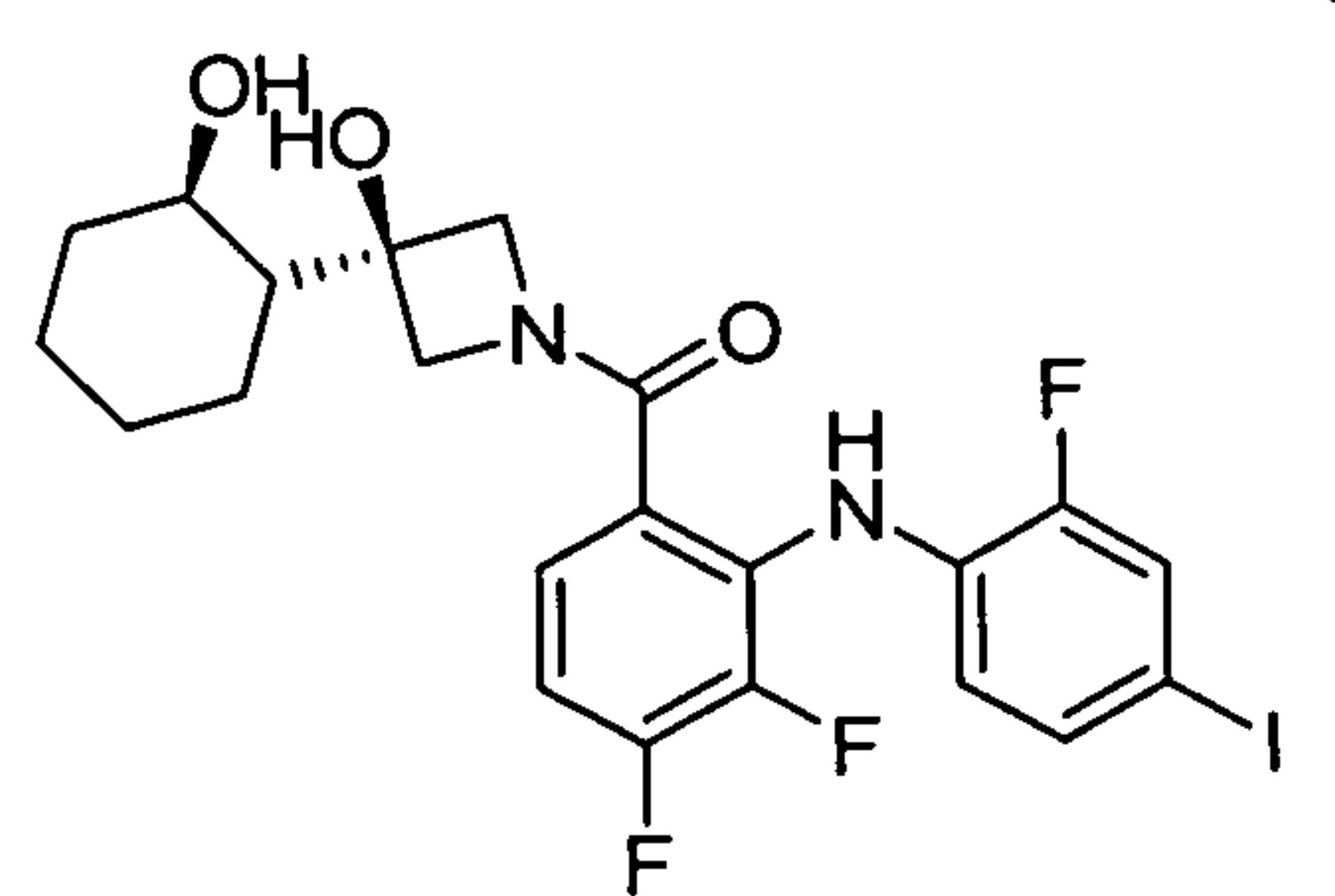
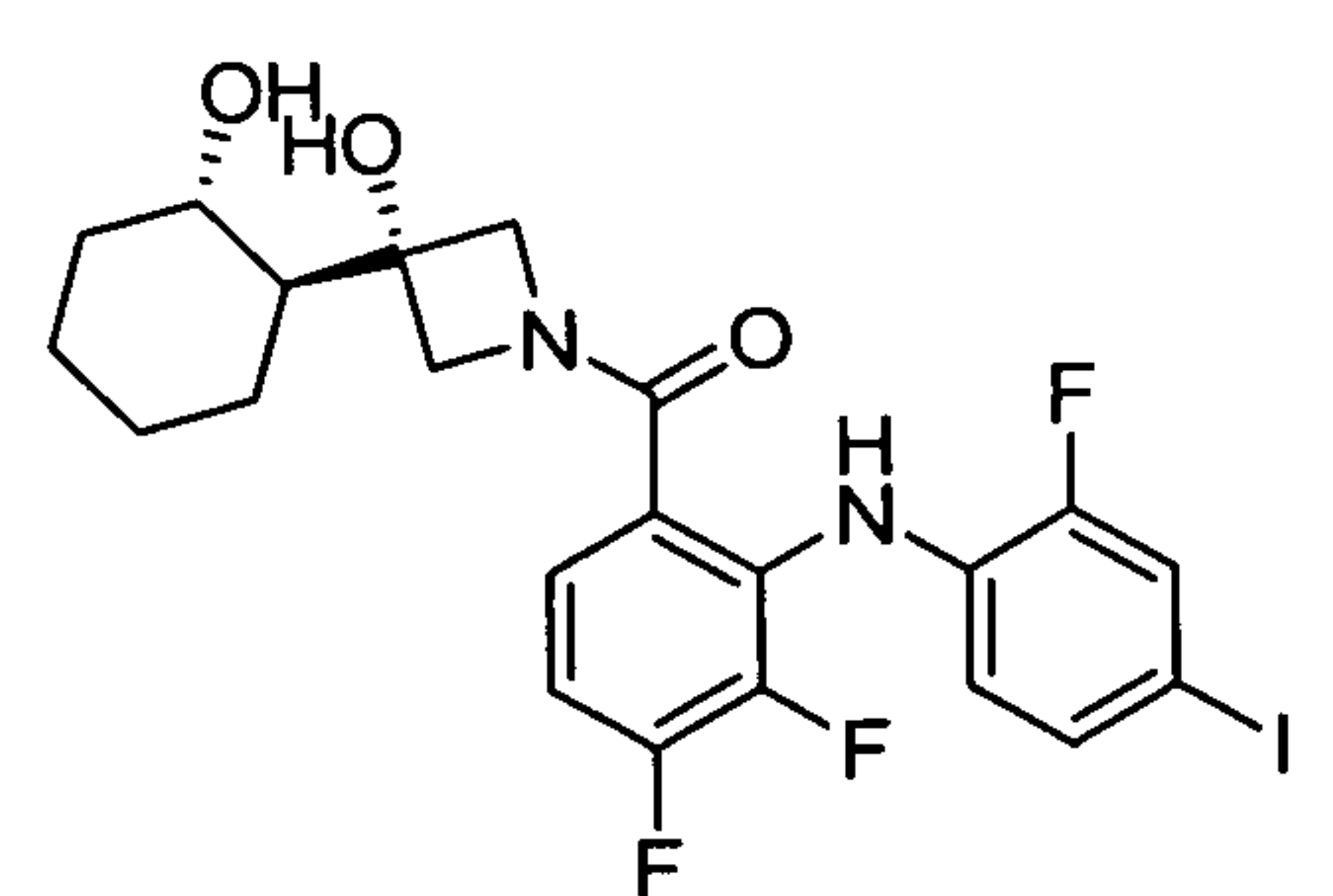
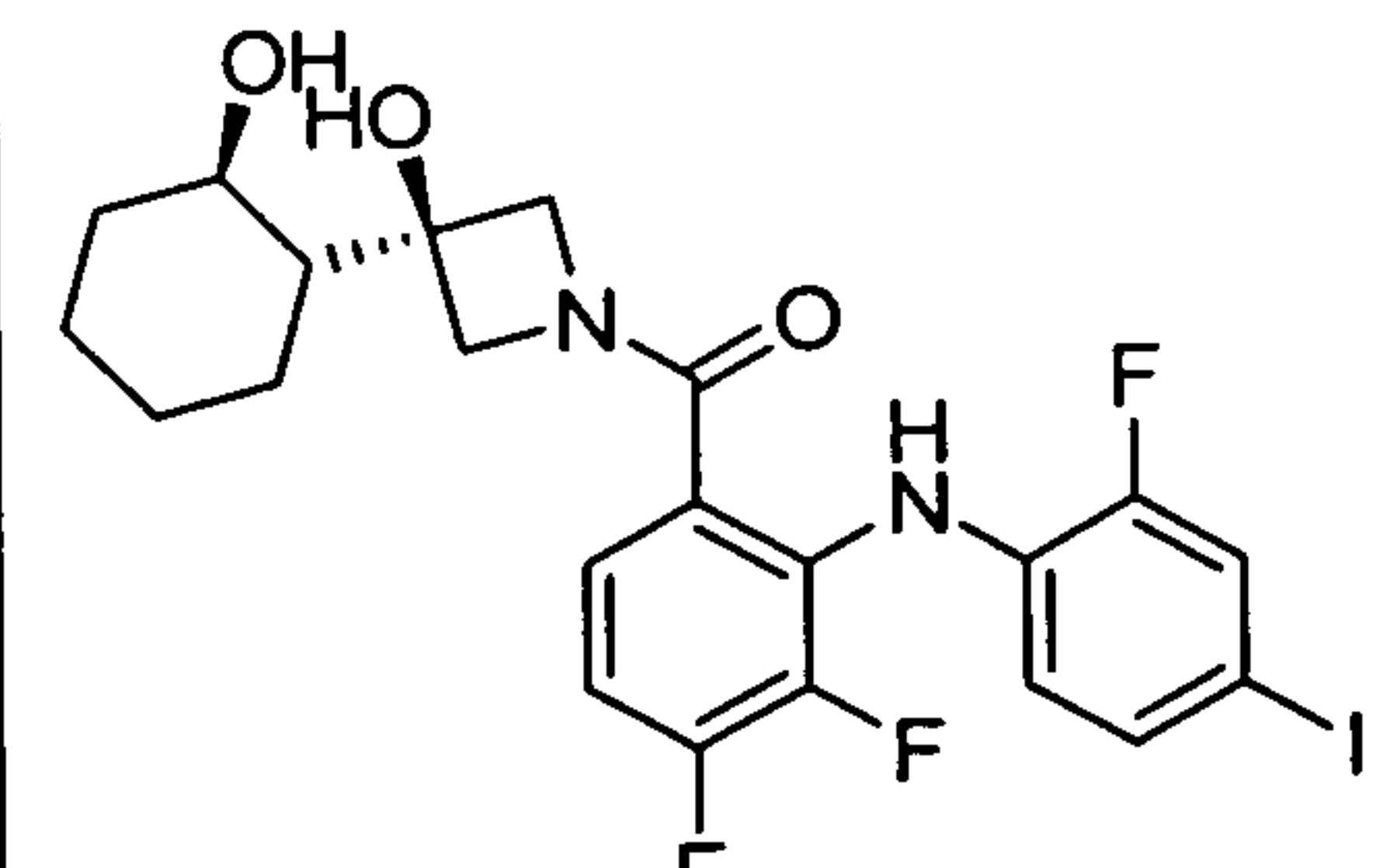
Cmpd No.	Structure	Name
311		4-[(2-fluoro-4-iodophenyl)amino]-5-({3-hydroxy-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-1-yl}carbonyl)-1-methylpyridin-2(1 <i>H</i>)-one
312	 and 	(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(<i>trans</i>)-2-hydroxycyclohexyl]azetidin-3-ol
313		(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)(3-hydroxy-3-((1 <i>S</i> ,2 <i>S</i>)-2-hydroxycyclohexyl)azetidin-1-yl)methanone
314		(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)(3-hydroxy-3-((1 <i>S</i> ,2 <i>R</i>)-2-hydroxycyclohexyl)azetidin-1-yl)methanone

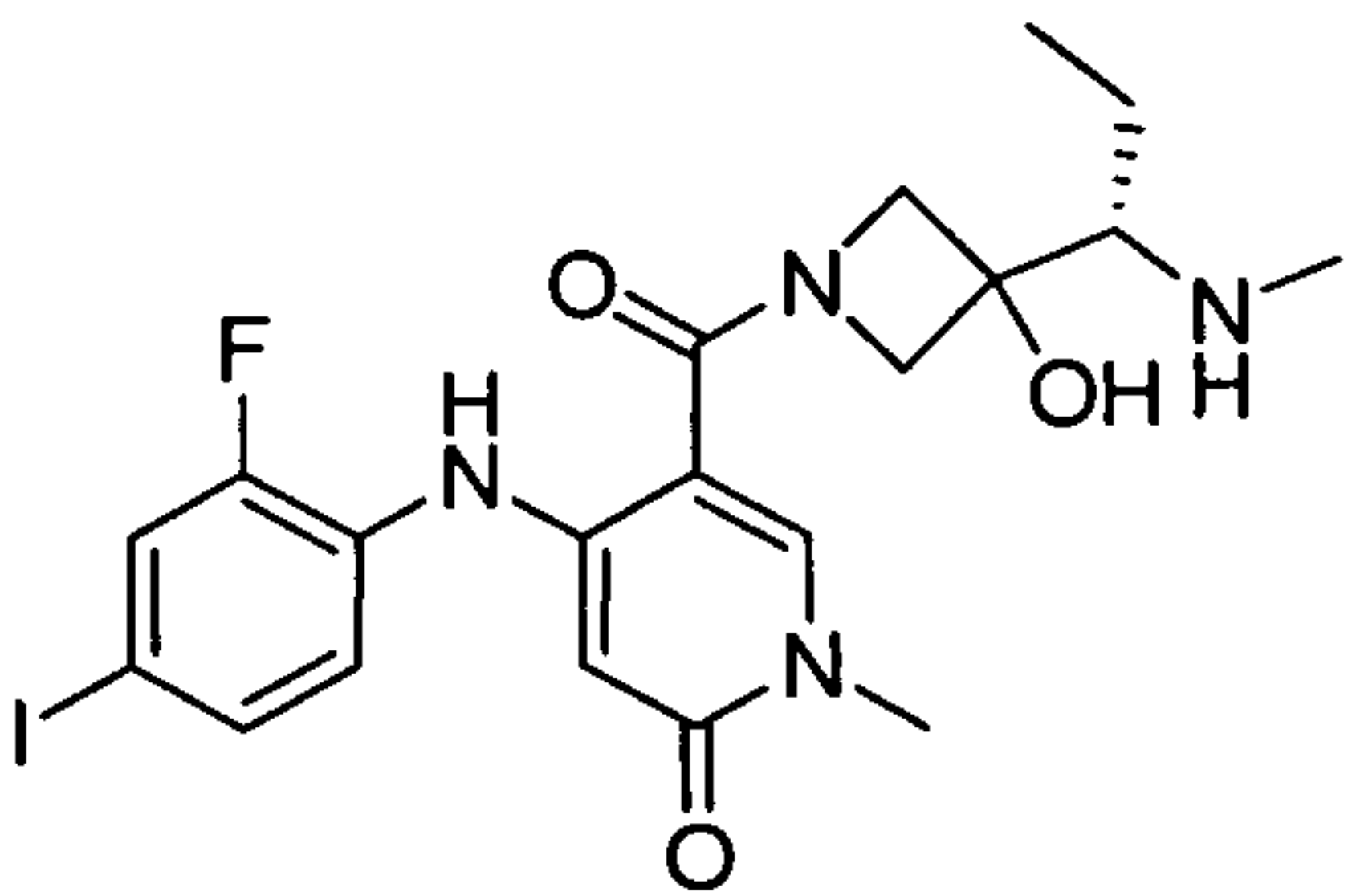
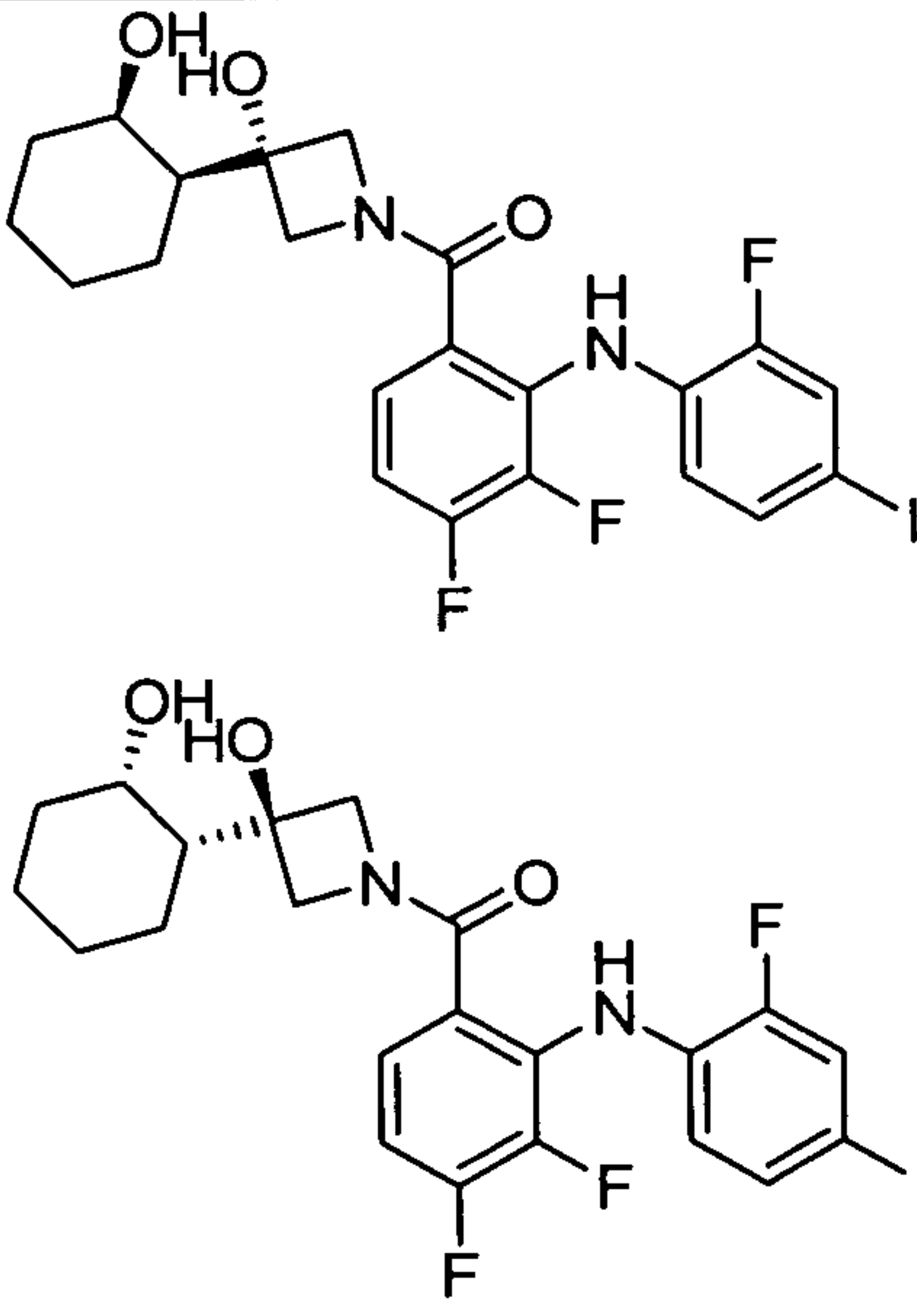
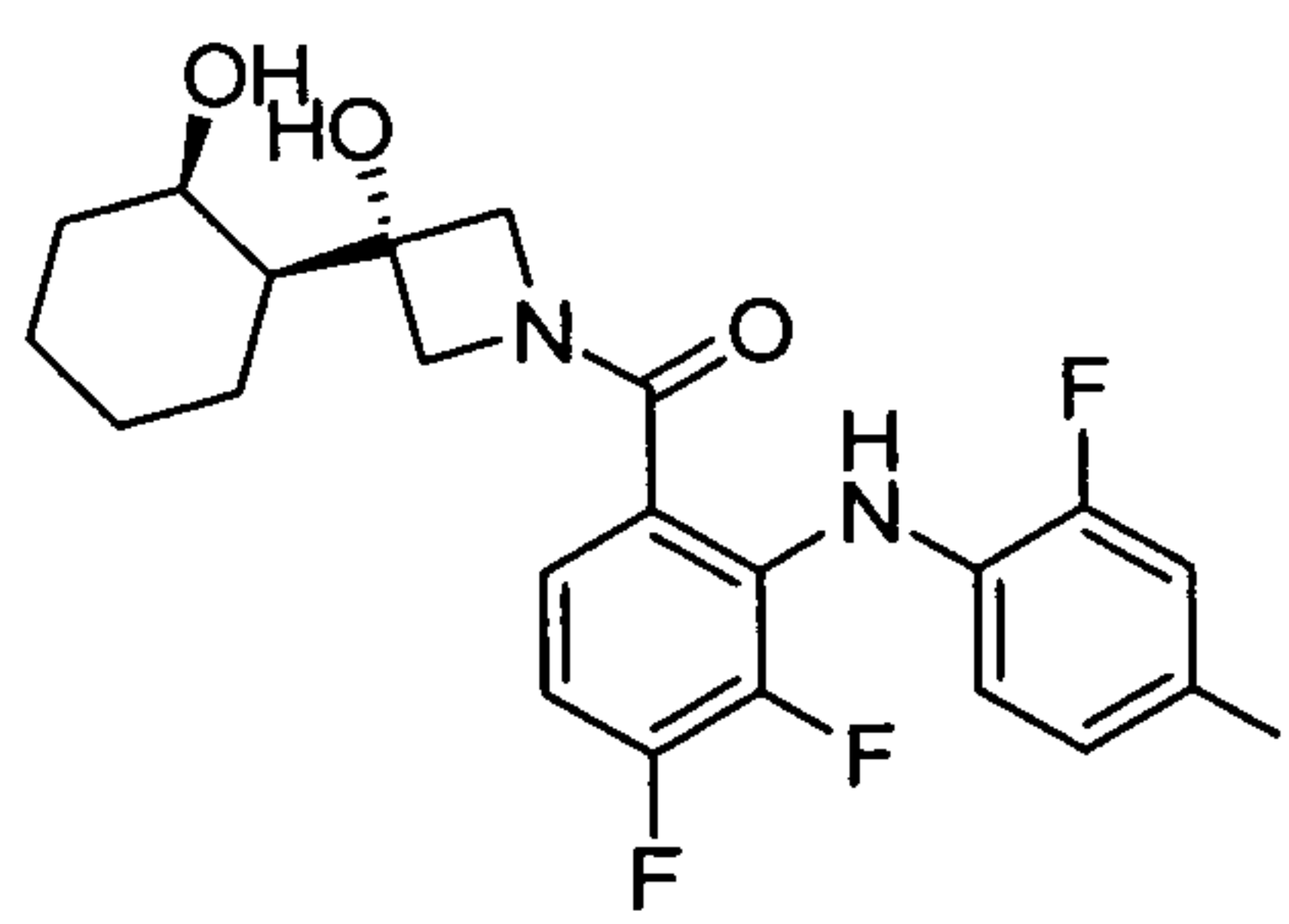
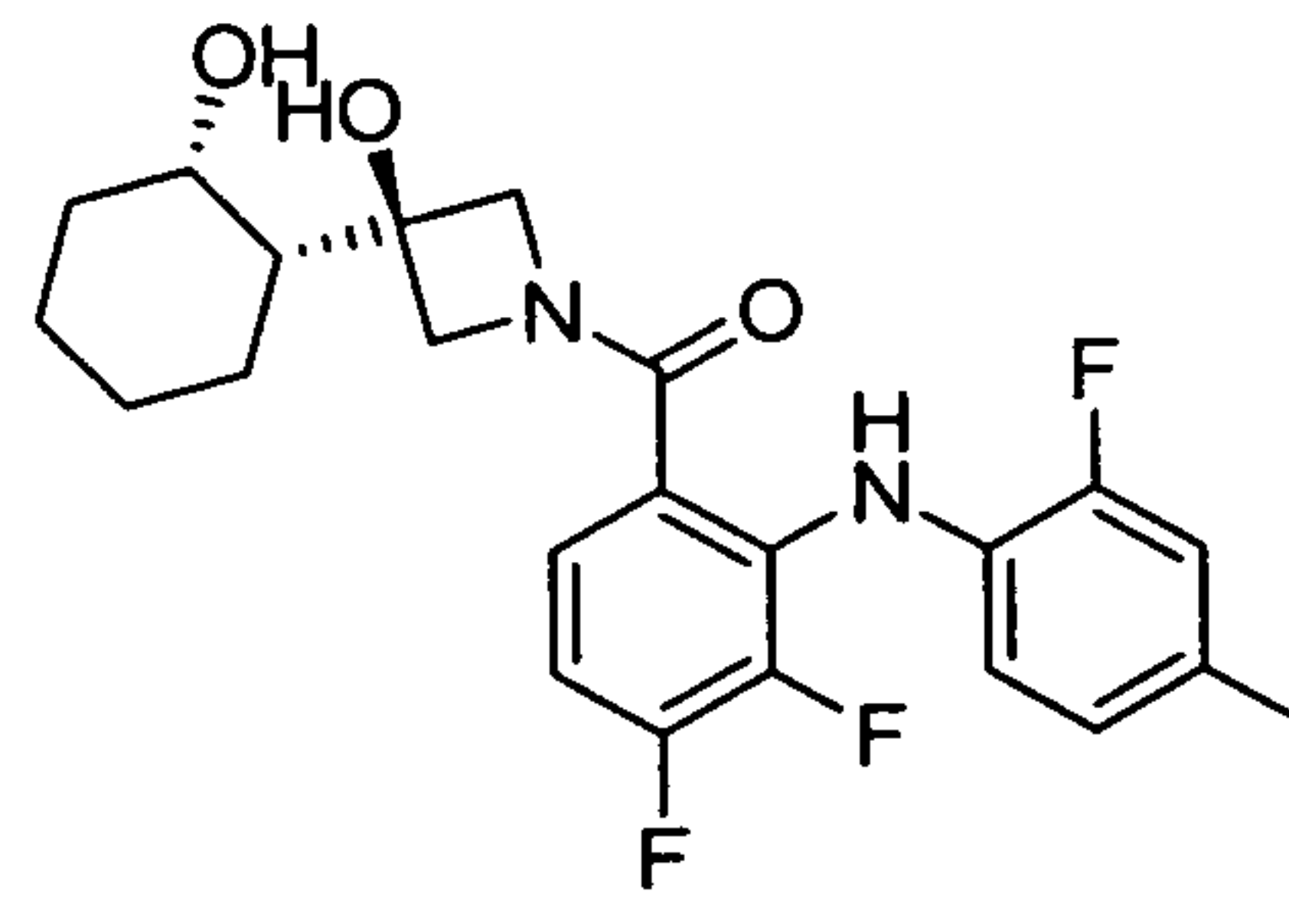
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
315		4-[(2-fluoro-4-iodophenyl)amino]-5-({3-hydroxy-3-[(1S)-1-(methylamino)propyl]azetidin-1-yl}carbonyl)-1-methylpyridin-2(1H)-one
316		(±)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(<i>cis</i>)-2-hydroxycyclohexyl]azetidin-3-ol
317		(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)(3-hydroxy-3-((1S,2R)-2-hydroxycyclohexyl)azetidin-1-yl)methanone
318		(3,4-difluoro-2-(2-fluoro-4-iodophenylamino)phenyl)(3-hydroxy-3-((1R,2S)-2-hydroxycyclohexyl)azetidin-1-yl)methanone

Table 1. Representative MEK Inhibitors

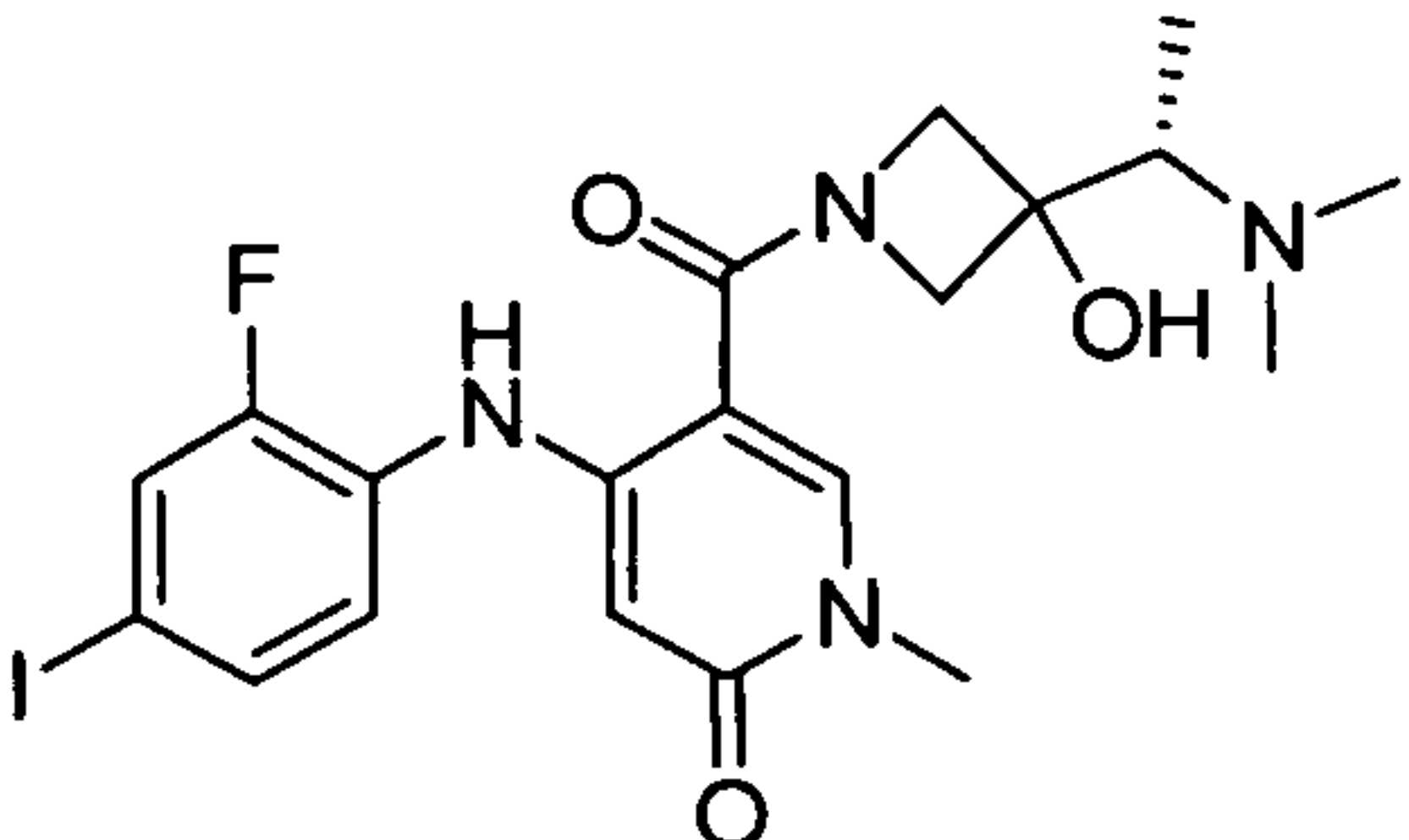
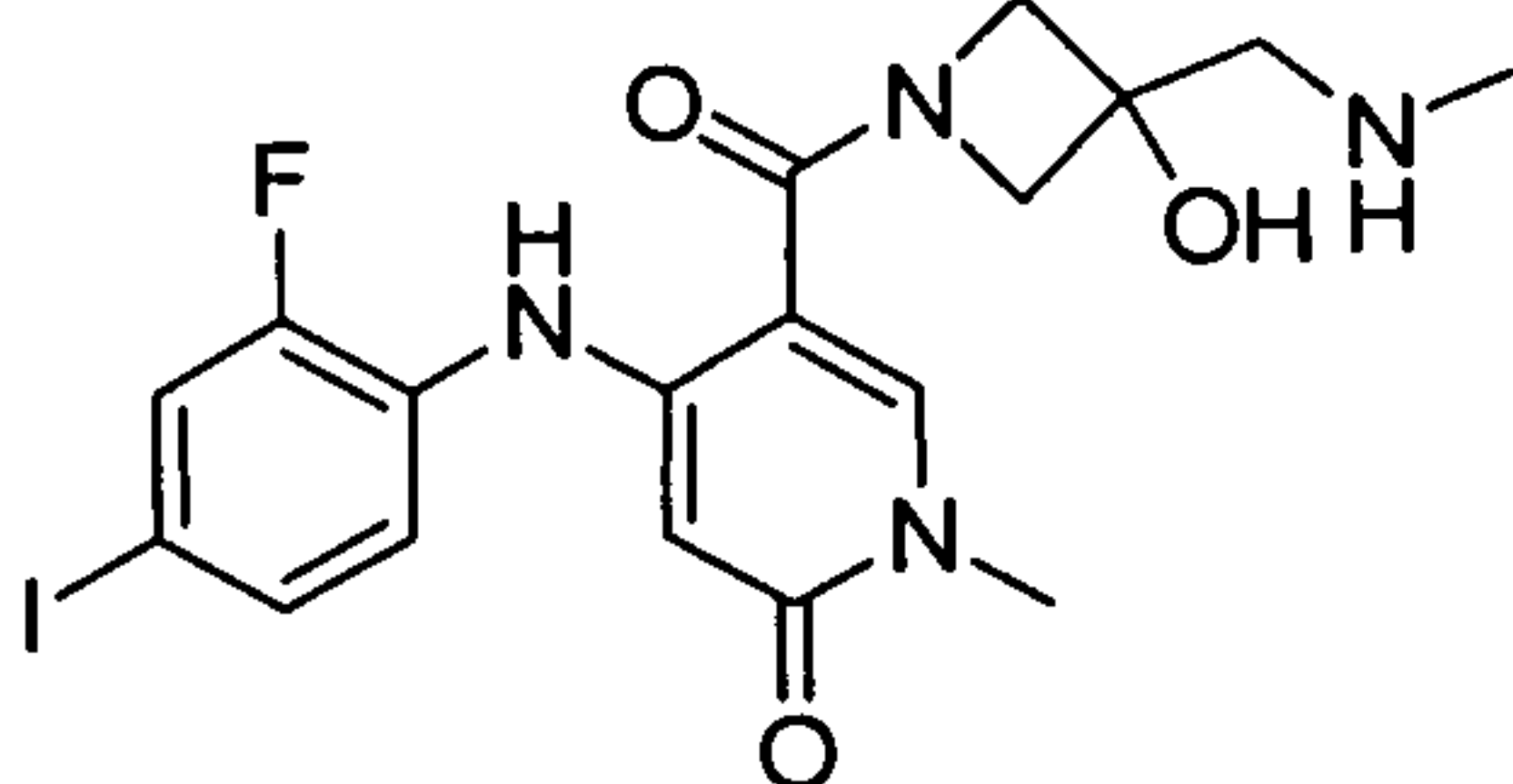
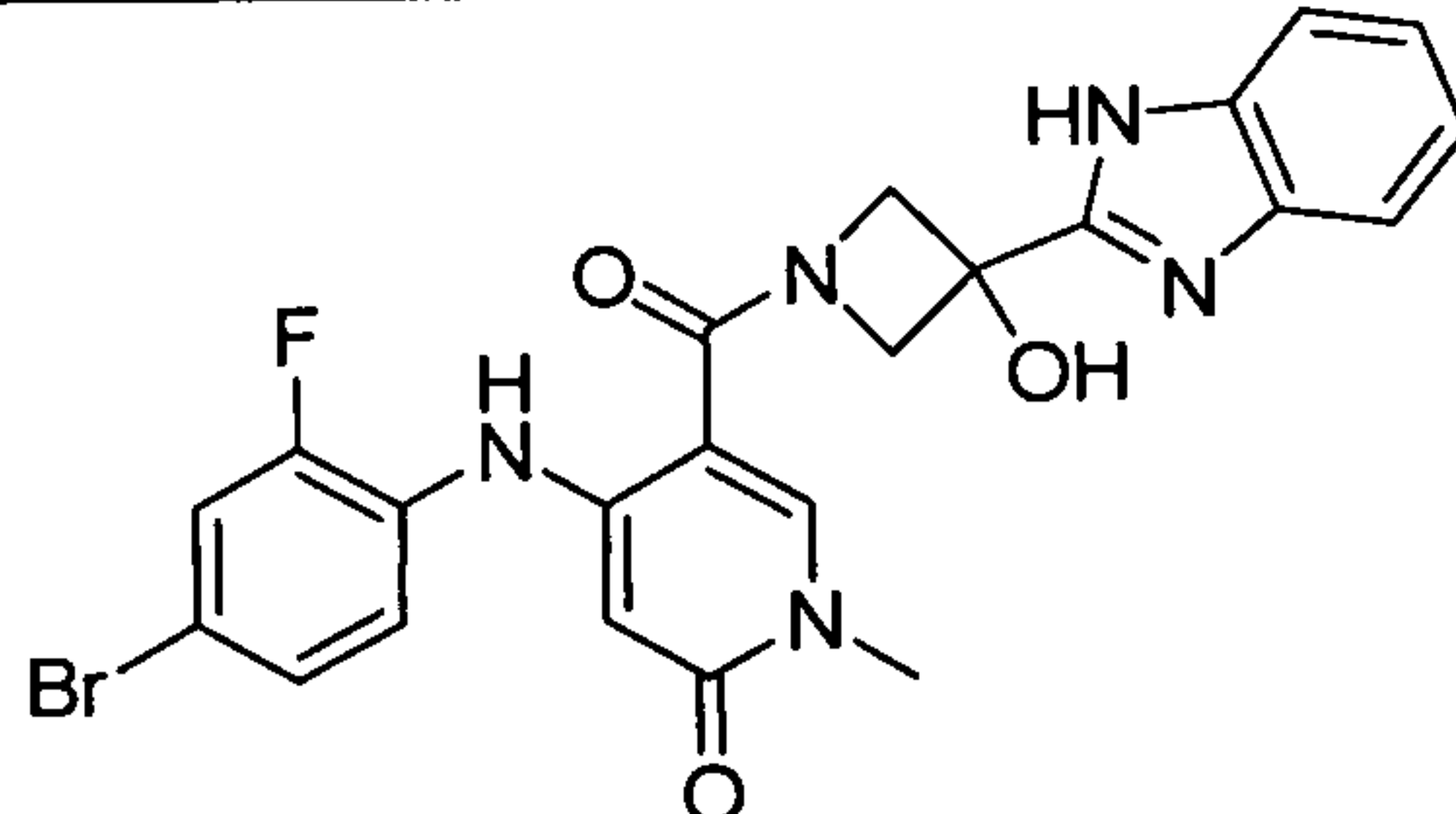
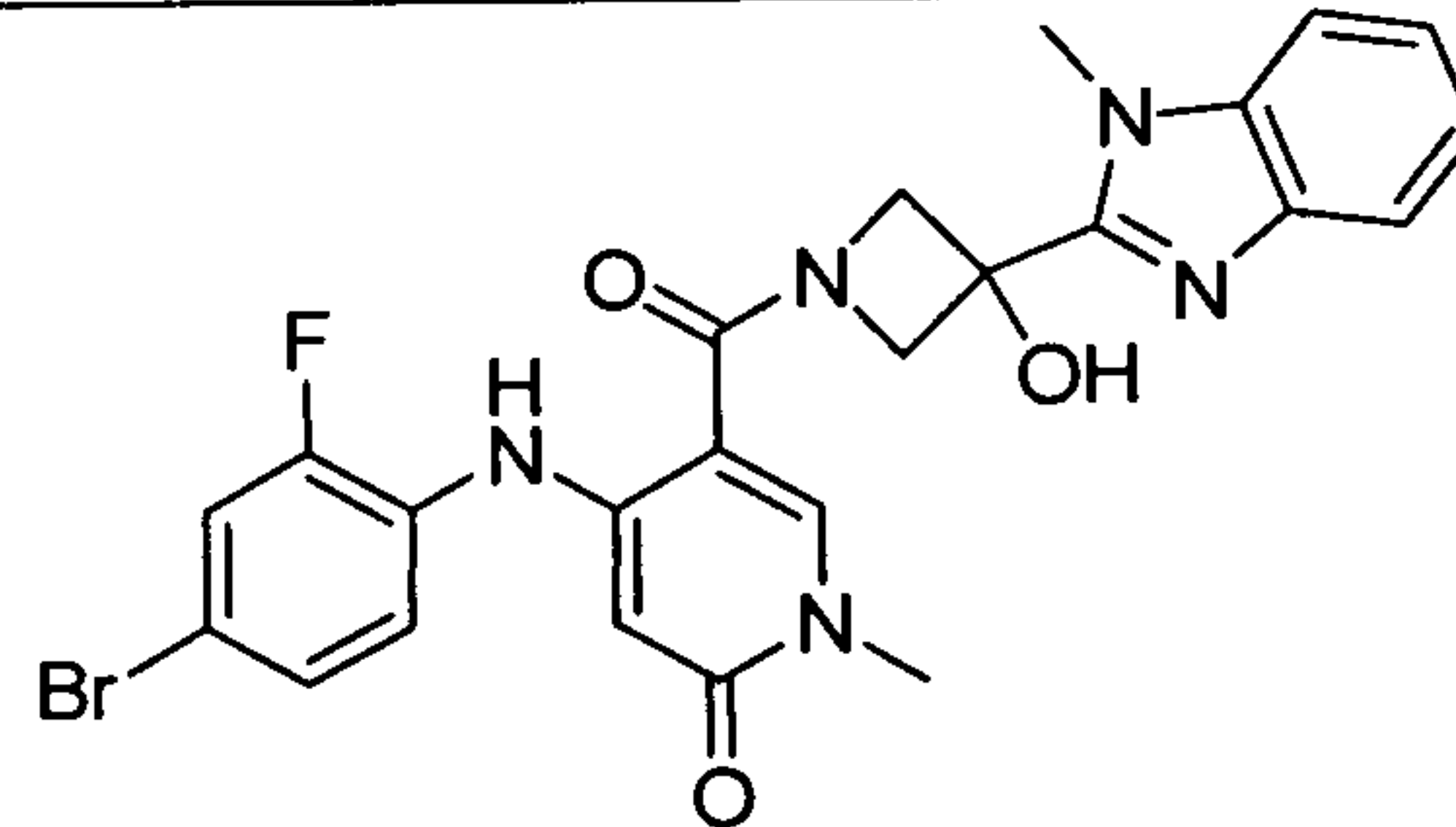
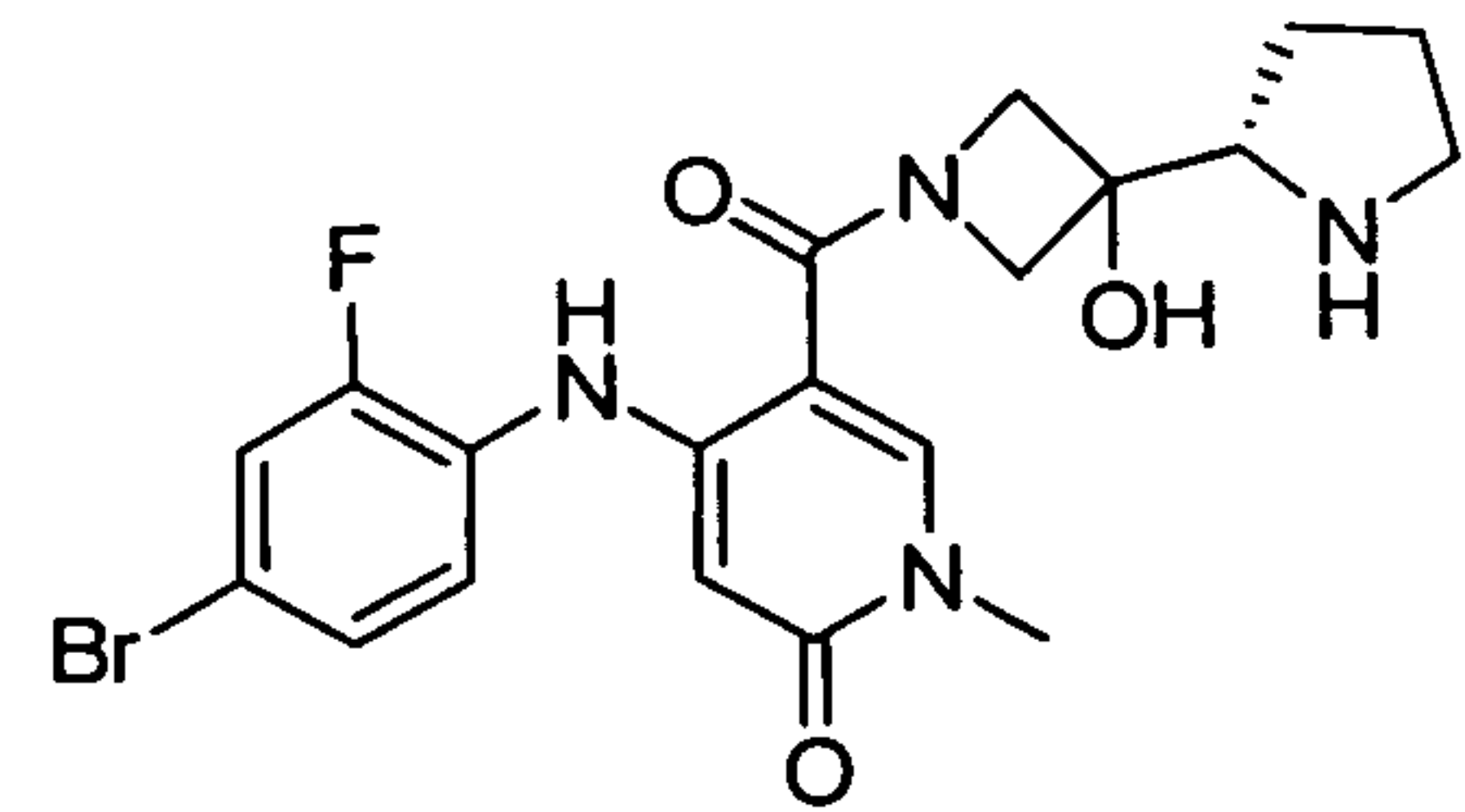
Cmpd No.	Structure	Name
319		5-({3-[(1S)-1-(dimethylamino)ethyl]-3-hydroxyazetidin-1-yl}carbonyl)-4-[(2-fluoro-4-iodophenyl)amino]-1-methylpyridin-2(1H)-one
320		4-[(2-fluoro-4-iodophenyl)amino]-5-({3-hydroxy-3-[(methylamino)methyl]azetidin-1-yl}carbonyl)-1-methylpyridin-2(1H)-one
321		5-{{3-[(1H-benzimidazol-2-yl)-3-hydroxyazetidin-1-yl]carbonyl}-4-[(4-bromo-2-fluorophenyl)amino]-1-methylpyridin-2(1H)-one
322		4-[(4-bromo-2-fluorophenyl)amino]-5-{{3-hydroxy-3-(1-methyl-1H-benzimidazol-2-yl)azetidin-1-yl}carbonyl}-1-methylpyridin-2(1H)-one
323		4-[(4-bromo-2-fluorophenyl)amino]-5-({3-hydroxy-3-[(2S)-pyrrolidin-2-yl]azetidin-1-yl}carbonyl)-1-methylpyridin-2(1H)-one

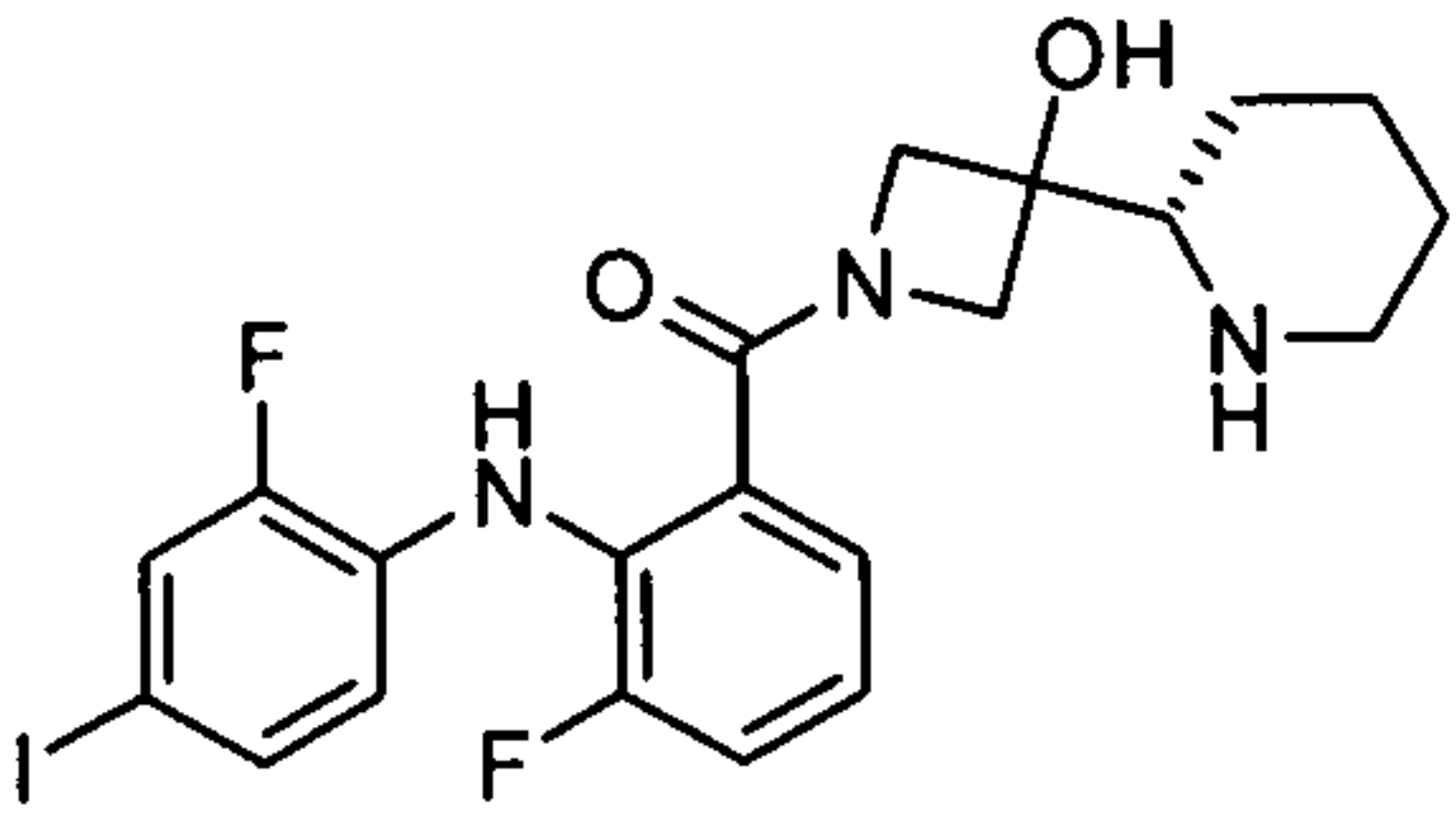
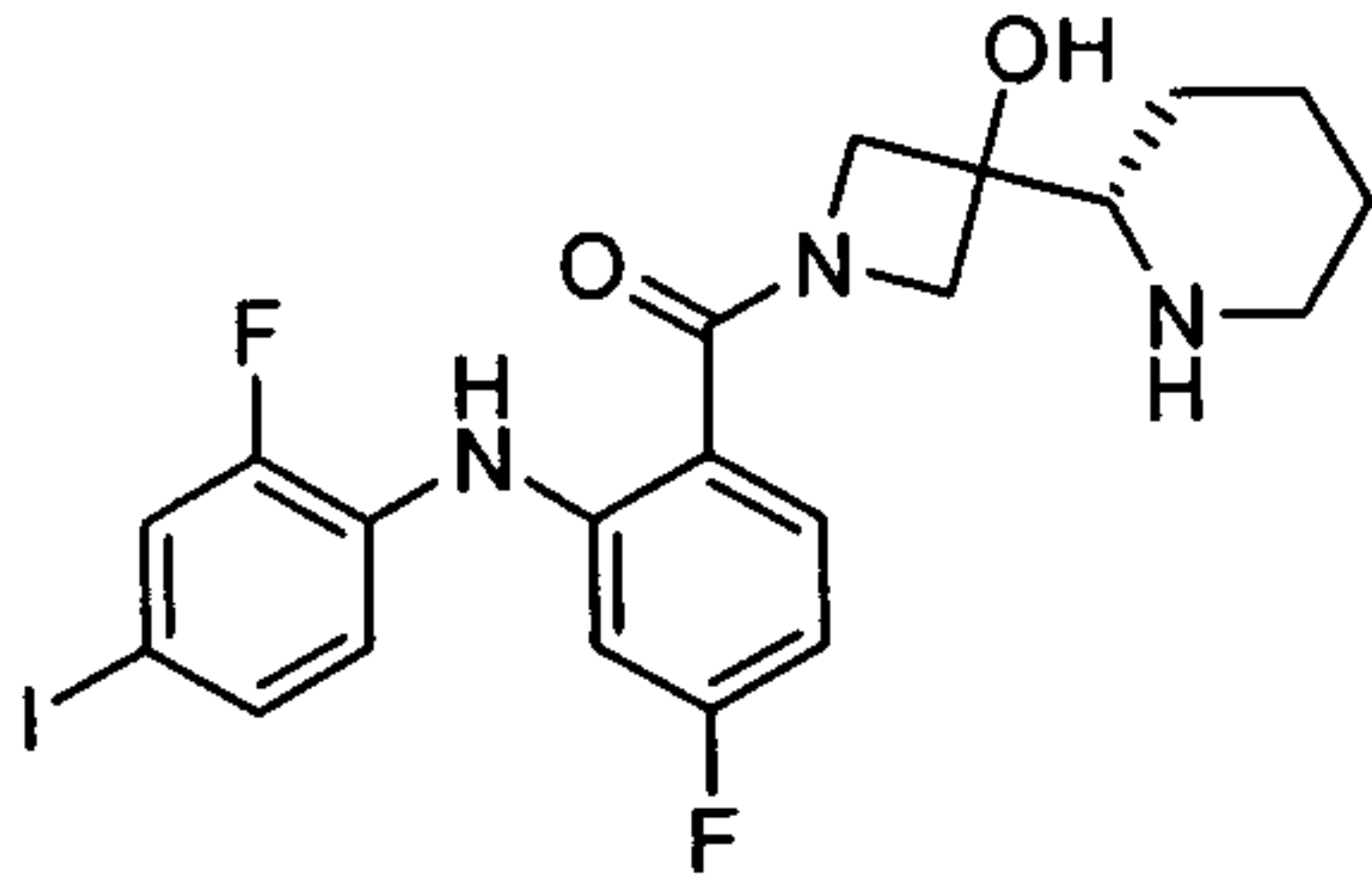
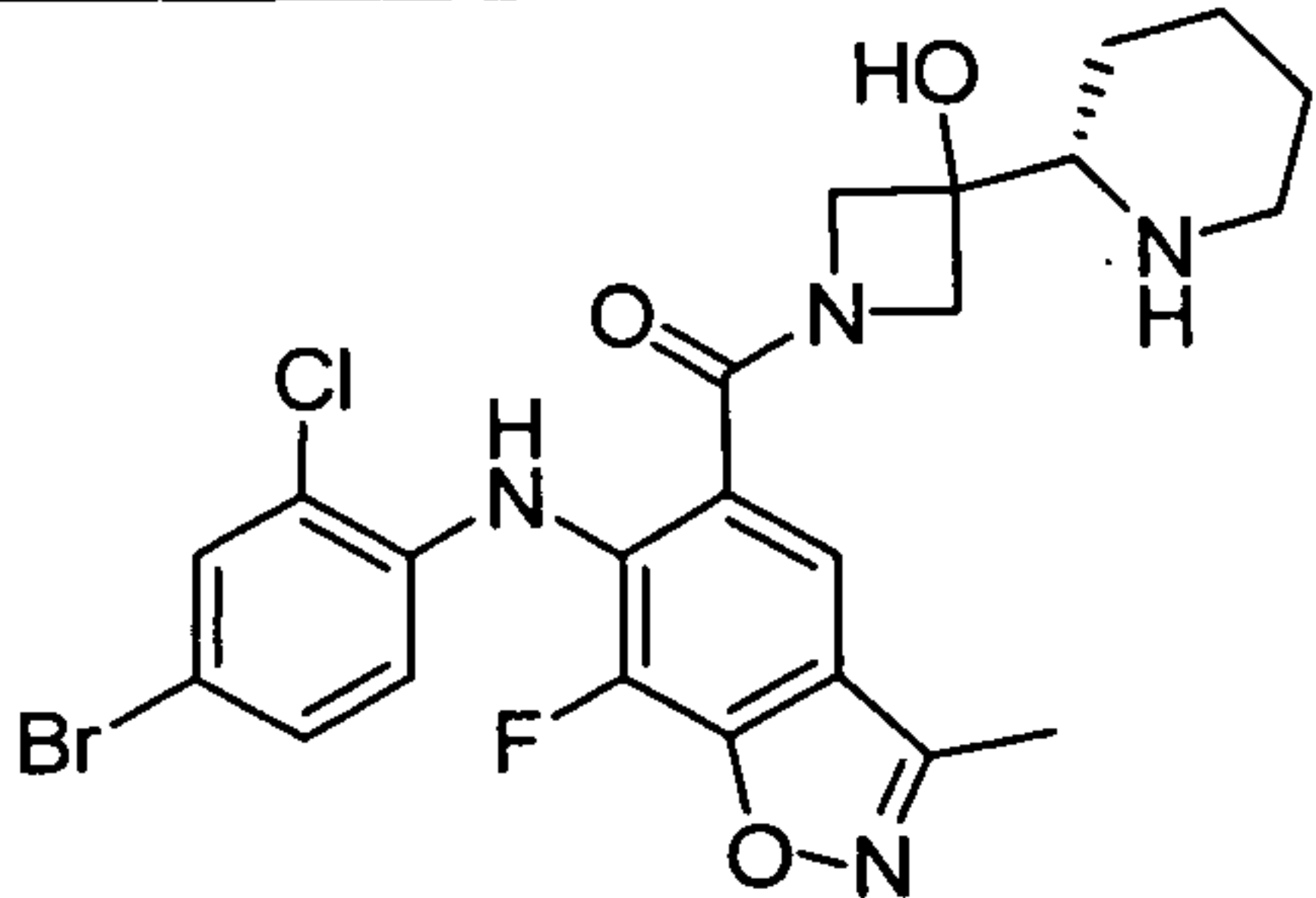
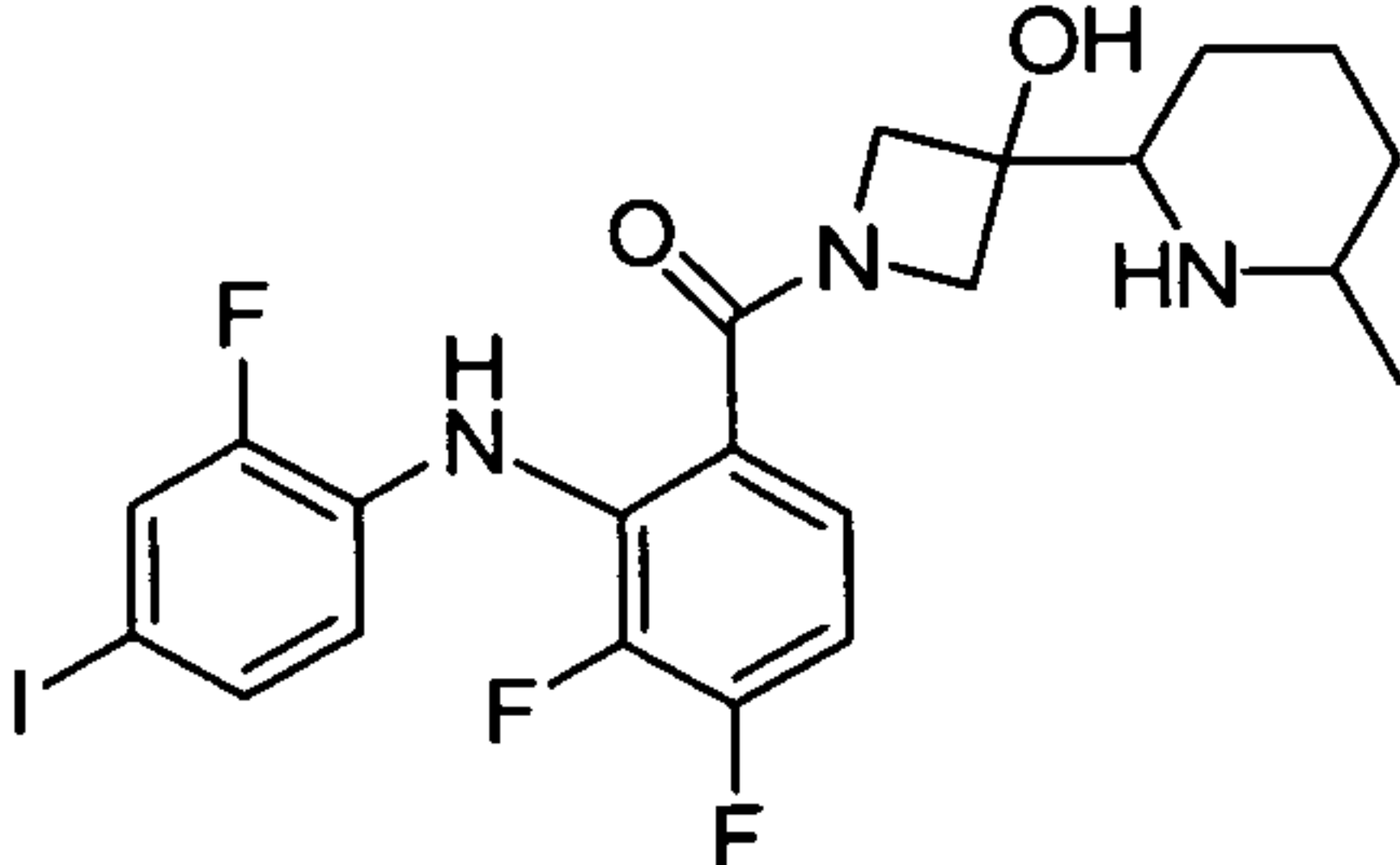
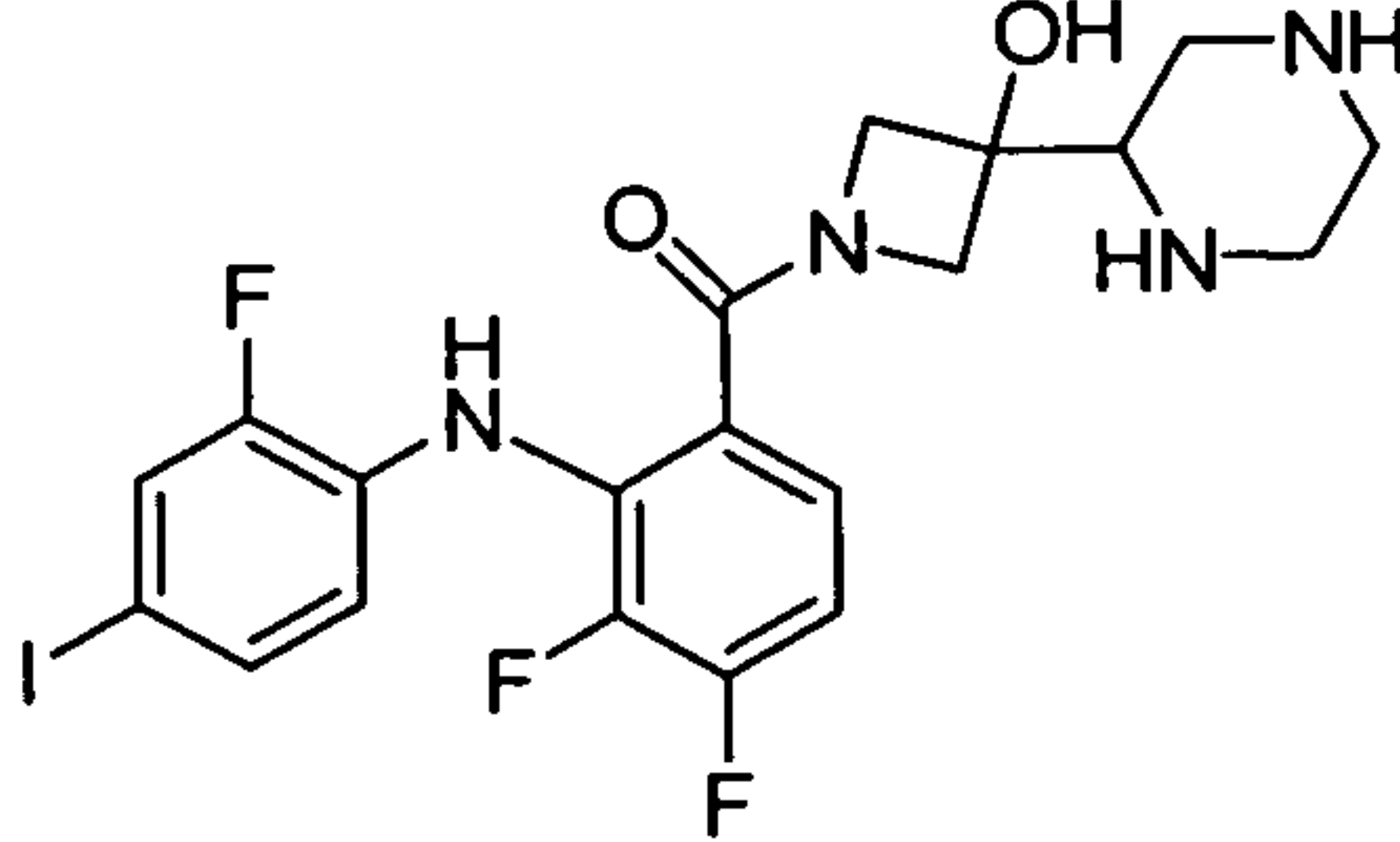
Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
324		1-({3-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
325		1-({4-fluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
326		1-({6-[(4-bromo-2-chlorophenyl)amino]-7-fluoro-3-methyl-1,2-benzisoxazol-5-yl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
327		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(6-methylpiperidin-2-yl)azetidin-3-ol
328		1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-piperazin-2-ylazetidin-3-ol

Table 1. Representative MEK Inhibitors

Cmpd No.	Structure	Name
329		5-[(2-fluoro-4-iodophenyl)amino]-6-({3-hydroxy-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2 <i>H</i>)-one
330		5-[(4-bromo-2-chlorophenyl)amino]-6-({3-hydroxy-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2 <i>H</i>)-one
331		5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-6-({3-hydroxy-3-[(2 <i>S</i>)-pyrrolidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2 <i>H</i>)-one
332		5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-6-({3-hydroxy-3-[(2 <i>R</i>)-pyrrolidin-2-yl]azetidin-1-yl}carbonyl)-2-methylpyridazin-3(2 <i>H</i>)-one
333		6-({3-[(1 <i>S</i>)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-5-[(2-fluoro-4-iodophenyl)amino]-2-methylpyridazin-3(2 <i>H</i>)-one

Table 1. Representative MEK Inhibitors

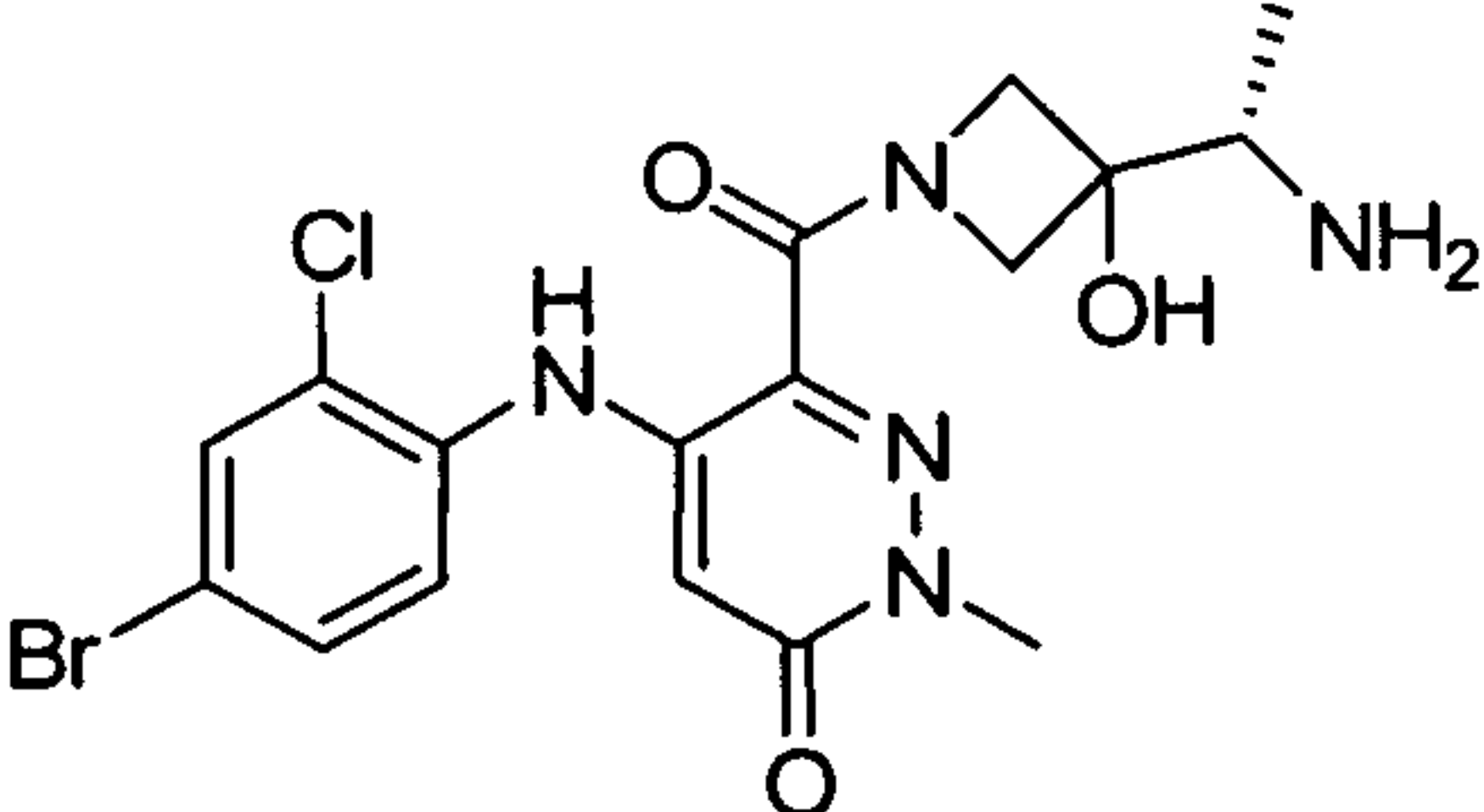
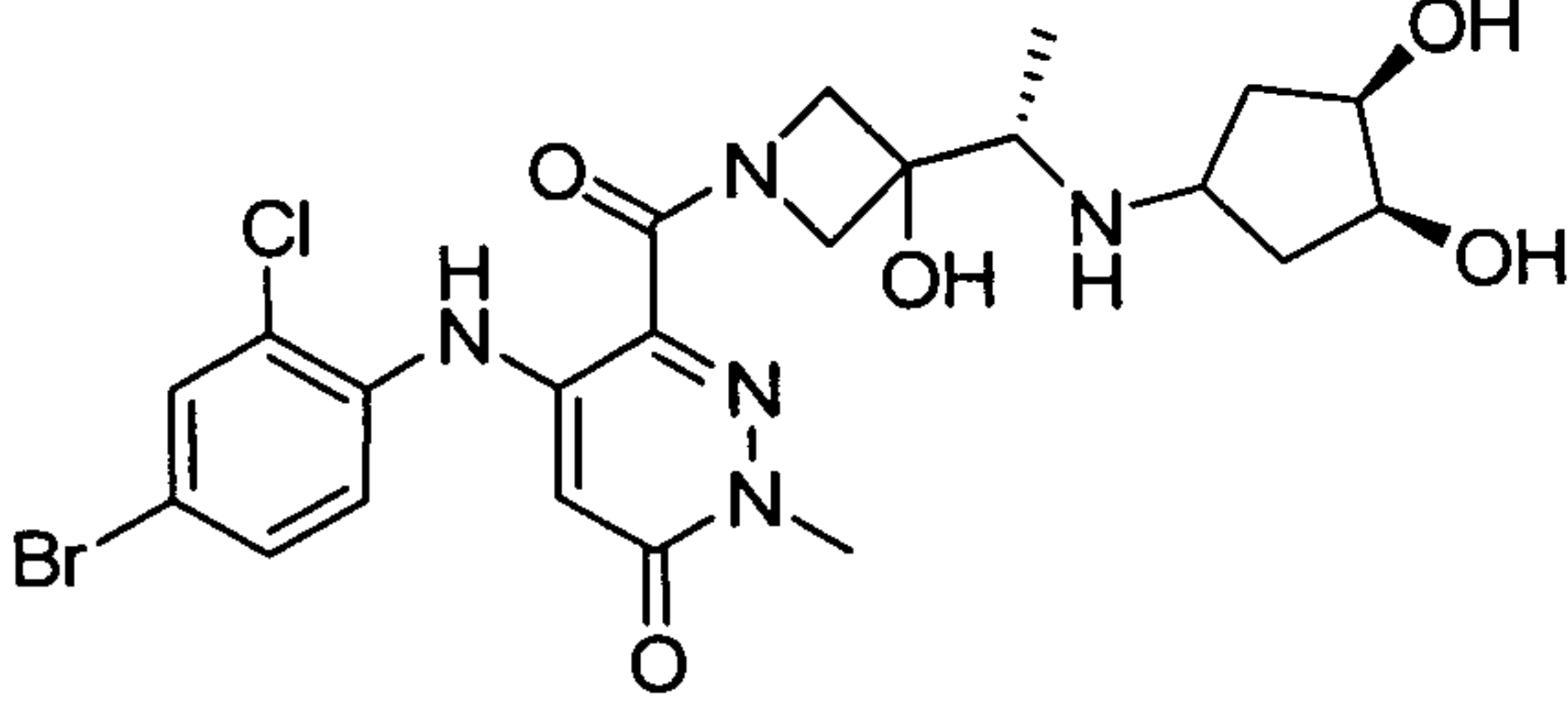
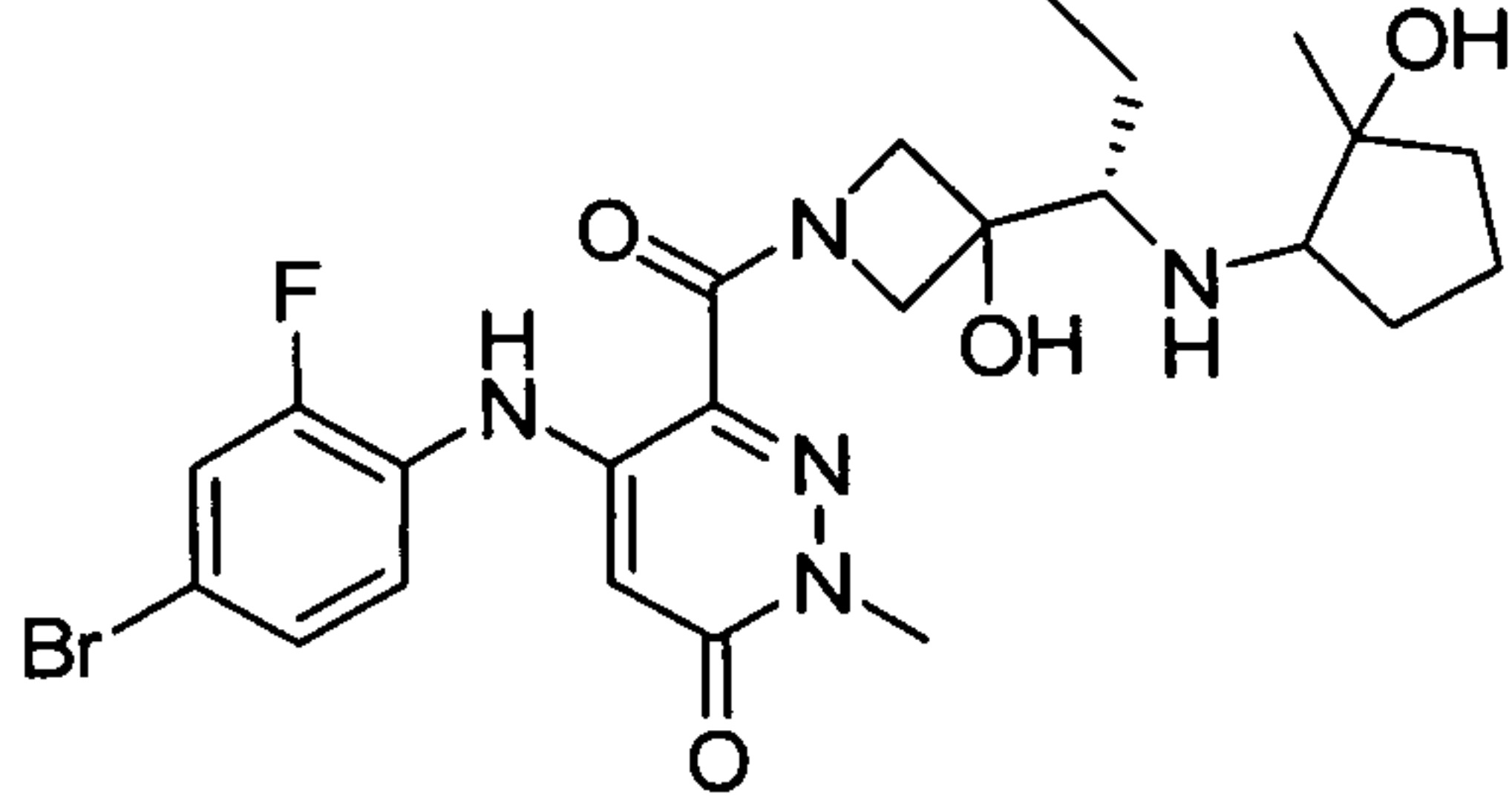
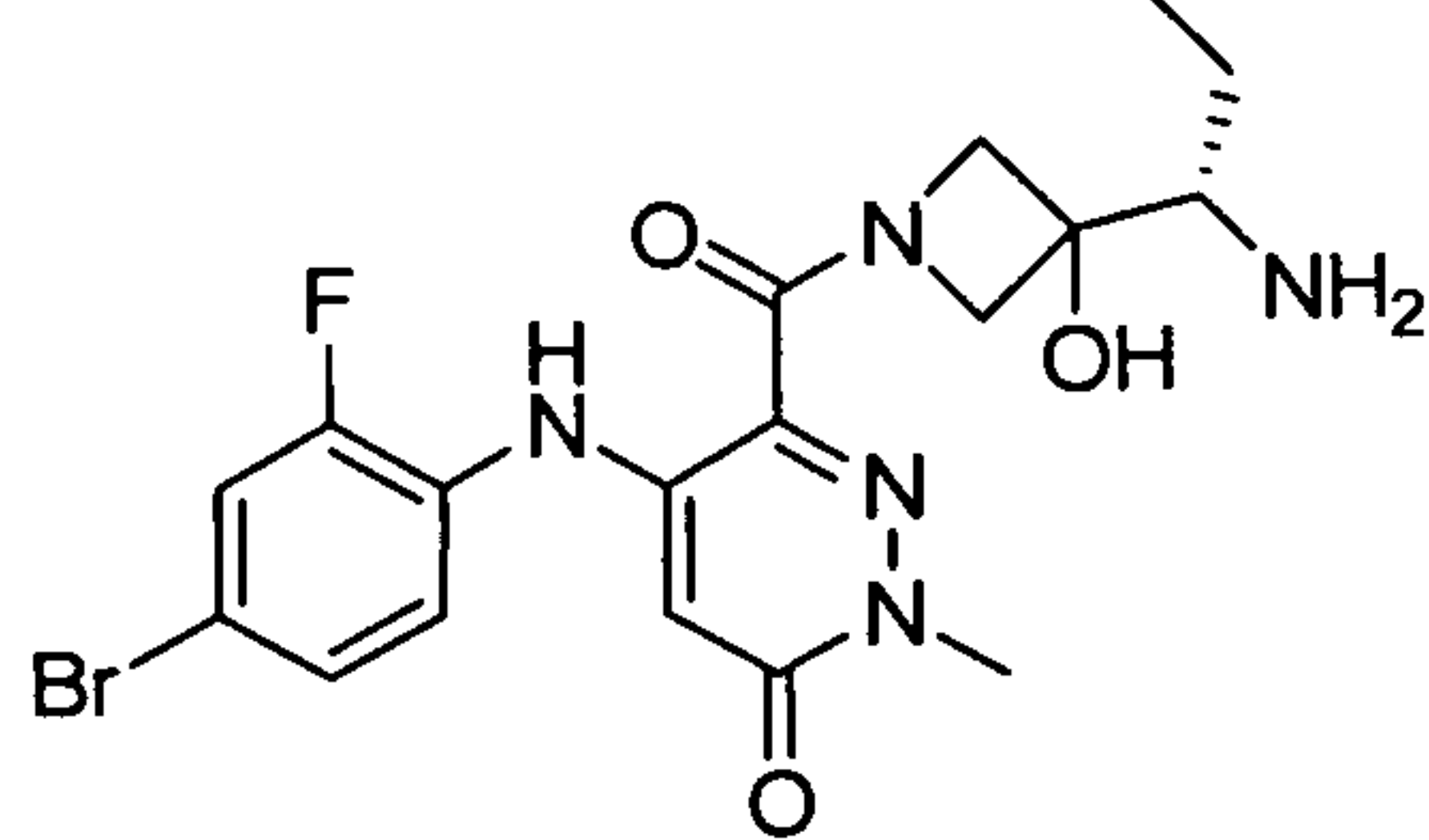
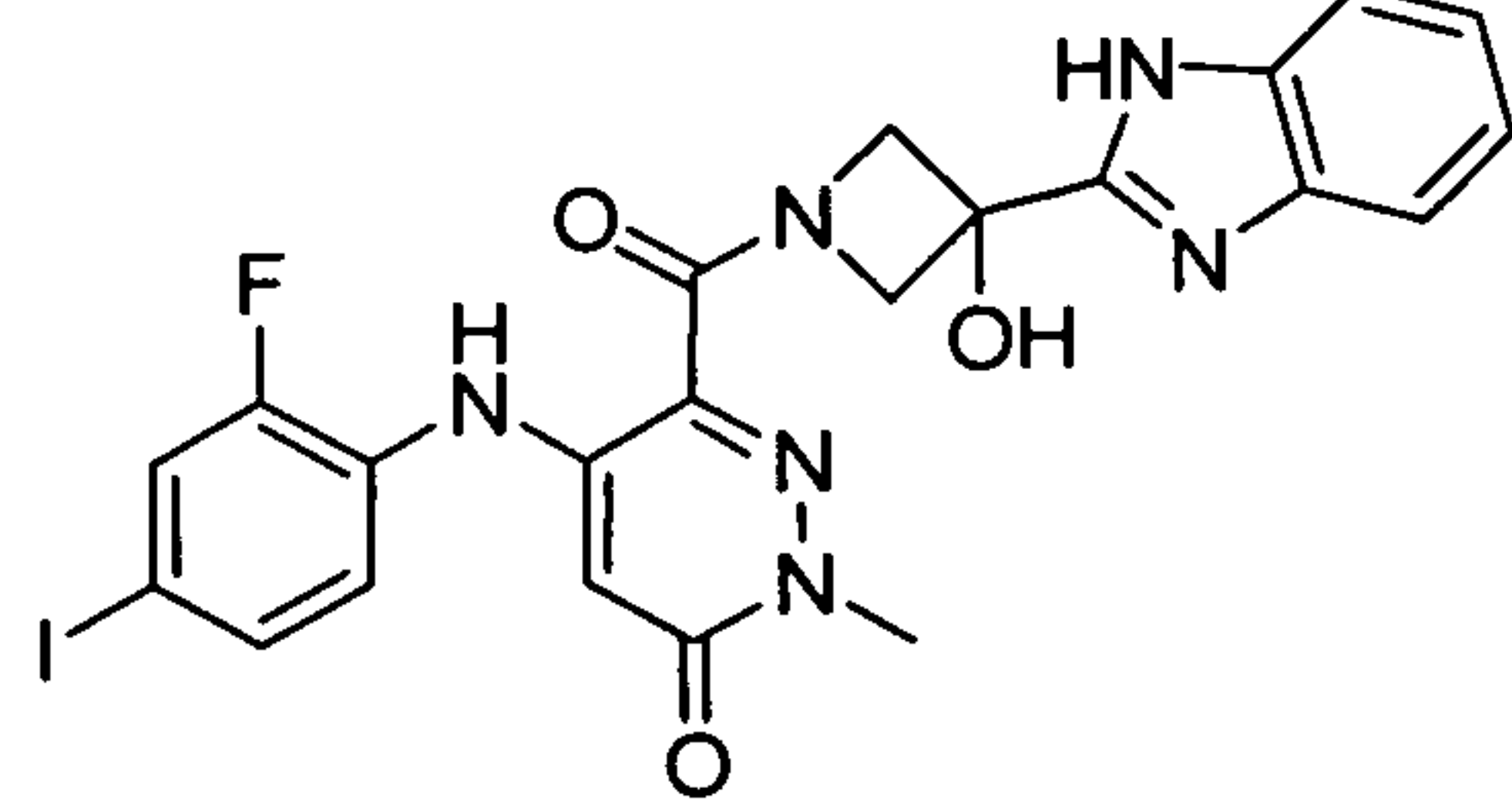
Cmpd No.	Structure	Name
334		6-((3-((1 <i>S</i>)-1-aminoethyl)-3-hydroxyazetidin-1-yl)carbonyl)-5-((4-bromo-2-chlorophenyl)amino)-2-methylpyridazin-3(2 <i>H</i>)-one
335		5-((4-bromo-2-chlorophenyl)amino)-6-((3-((1 <i>S</i>)-1-((3 <i>R</i> ,4 <i>S</i>)-3,4-dihydroxycyclopentyl)amino)ethyl)-3-hydroxyazetidin-1-yl)carbonyl)-2-methylpyridazin-3(2 <i>H</i>)-one
336		5-((4-bromo-2-fluorophenyl)amino)-6-((3-hydroxy-3-((1 <i>S</i>)-1-((2-hydroxy-2-methylcyclopentyl)amino)propyl)azetidin-1-yl)carbonyl)-2-methylpyridazin-3(2 <i>H</i>)-one
337		6-((3-((1 <i>S</i>)-1-aminopropyl)-3-hydroxyazetidin-1-yl)carbonyl)-5-((4-bromo-2-fluorophenyl)amino)-2-methylpyridazin-3(2 <i>H</i>)-one
338		6-((3-((1 <i>H</i>)-benzimidazol-2-yl)-3-hydroxyazetidin-1-yl)carbonyl)-5-((2-fluoro-4-iodophenyl)amino)-2-methylpyridazin-3(2 <i>H</i>)-one

Table 1. Representative MEK Inhibitors

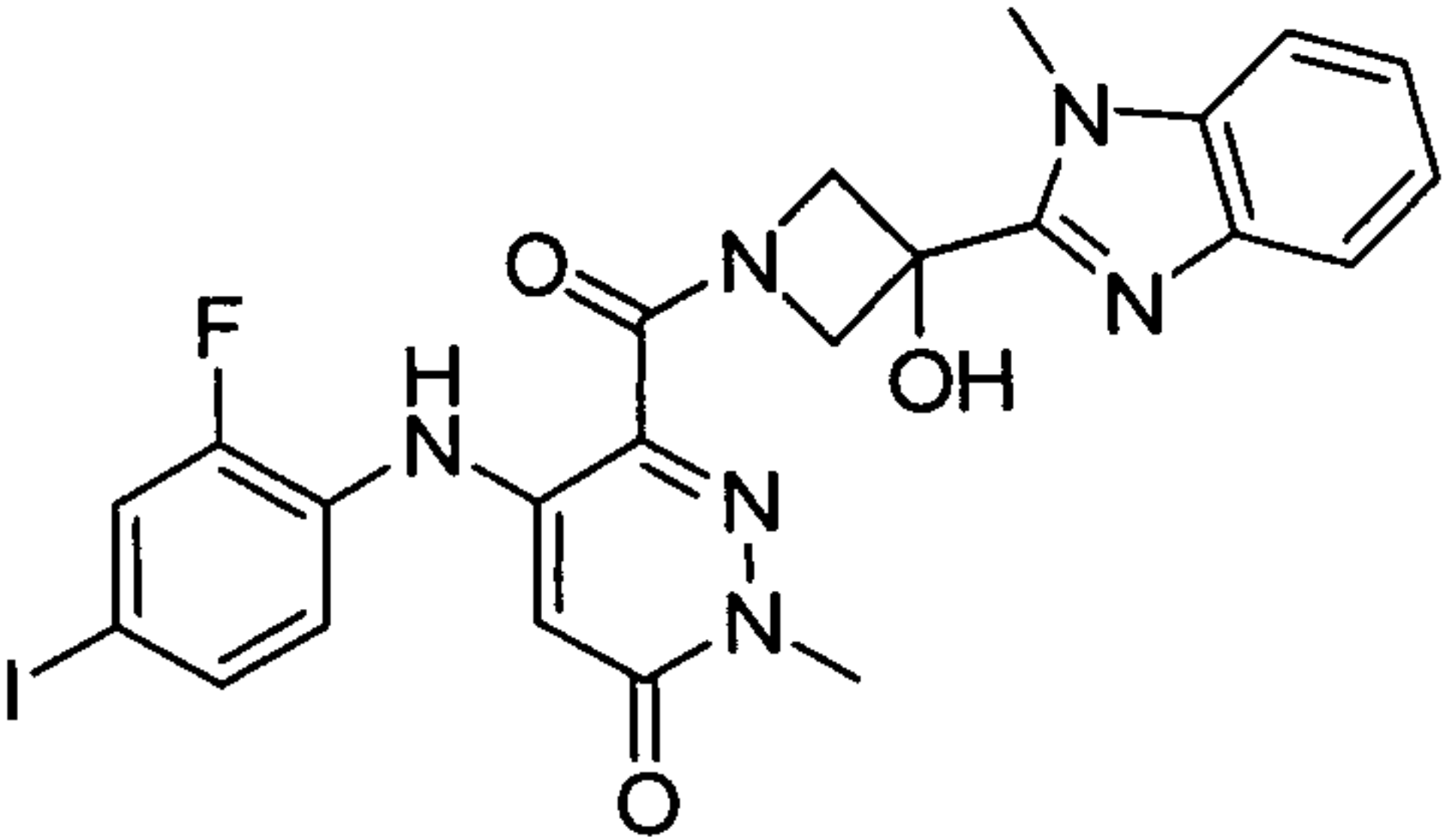
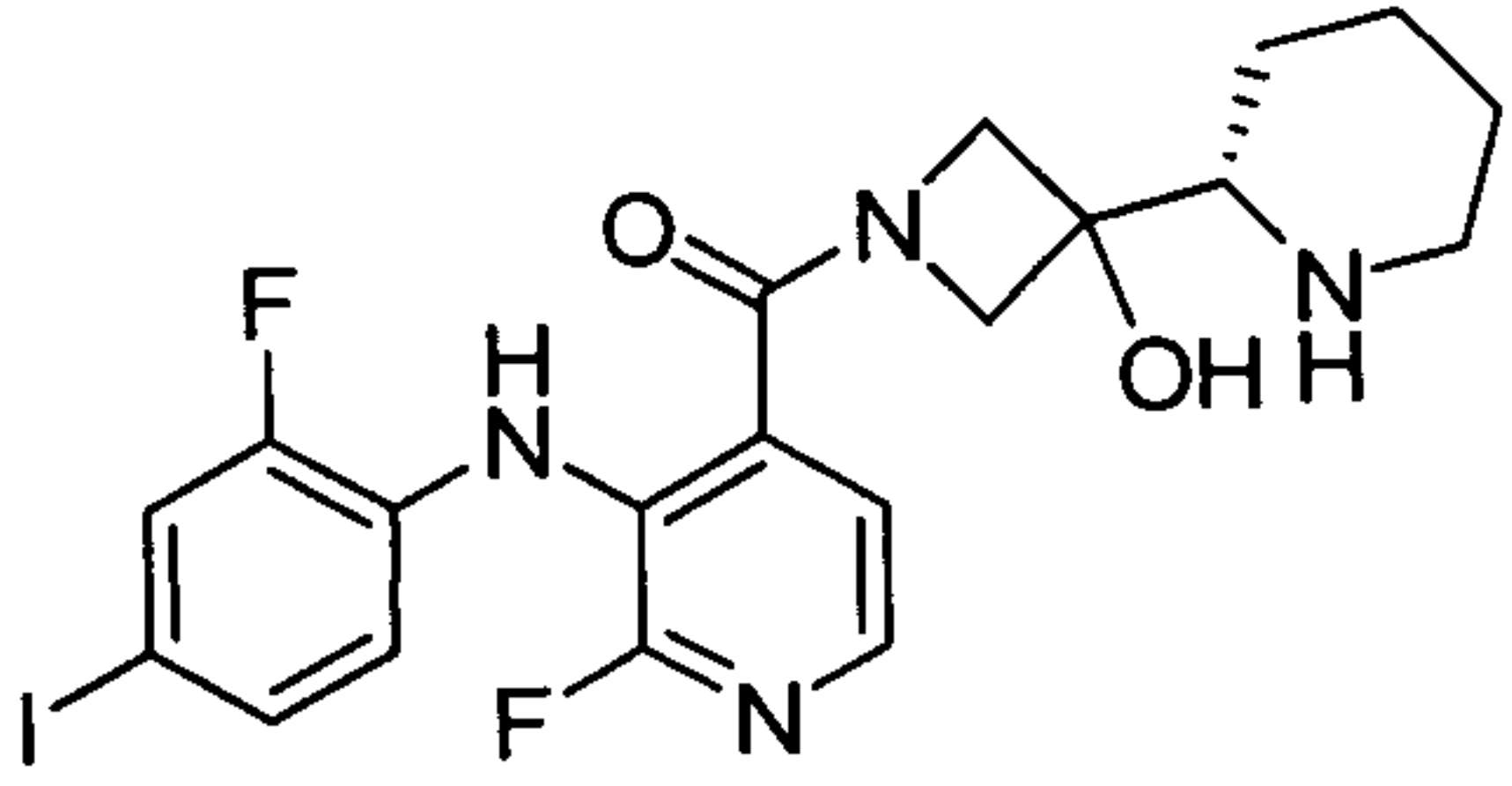
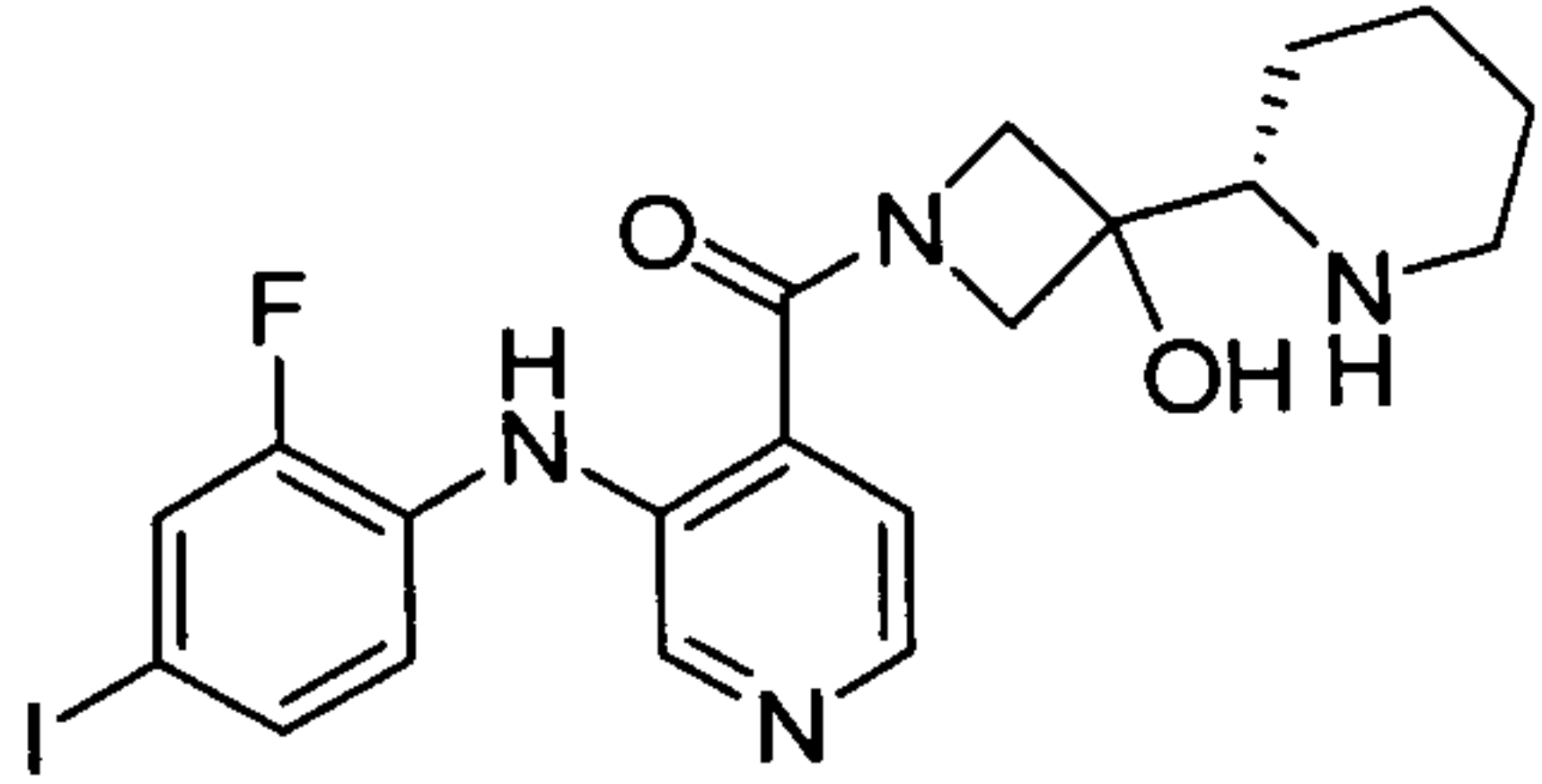
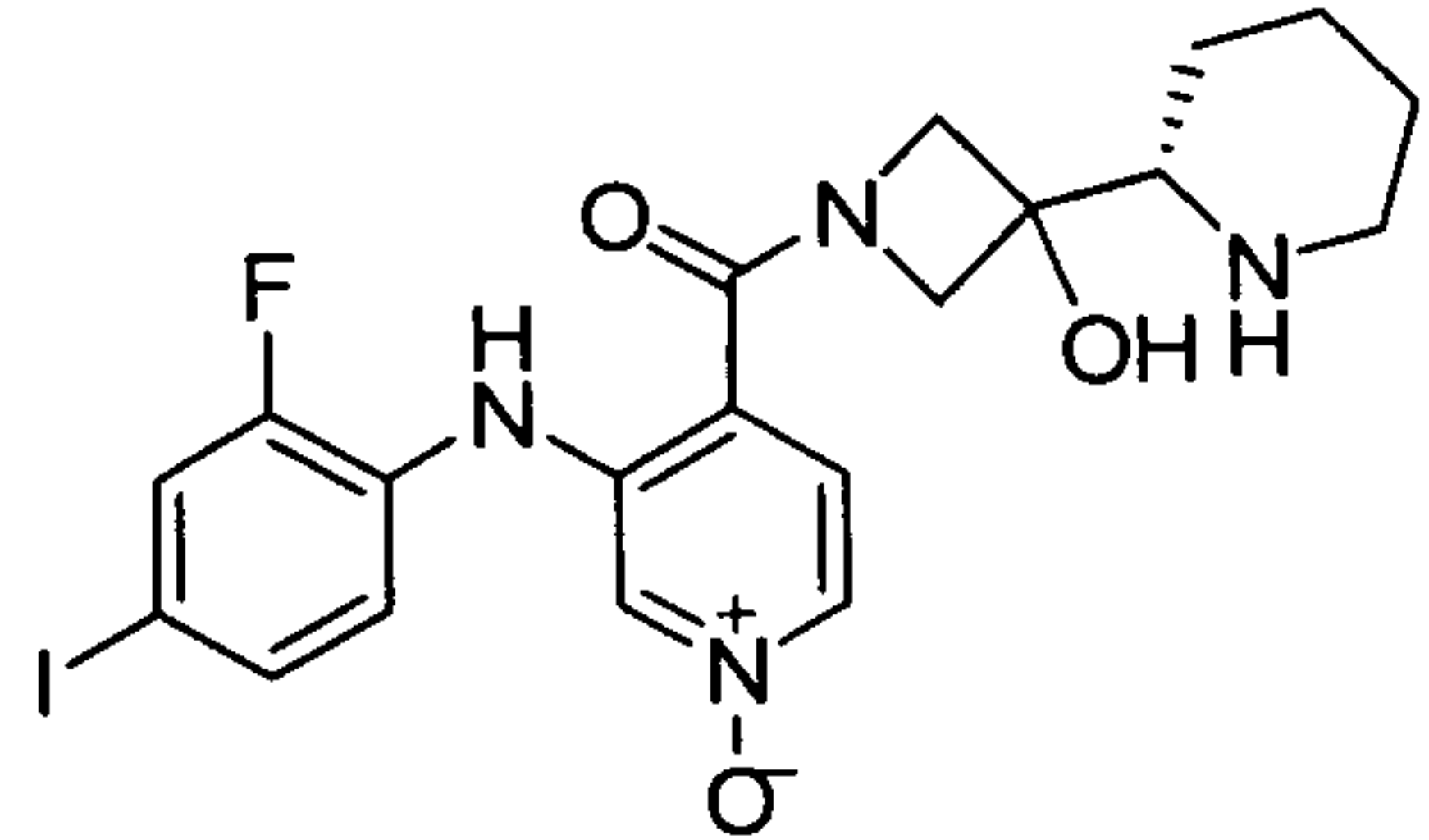
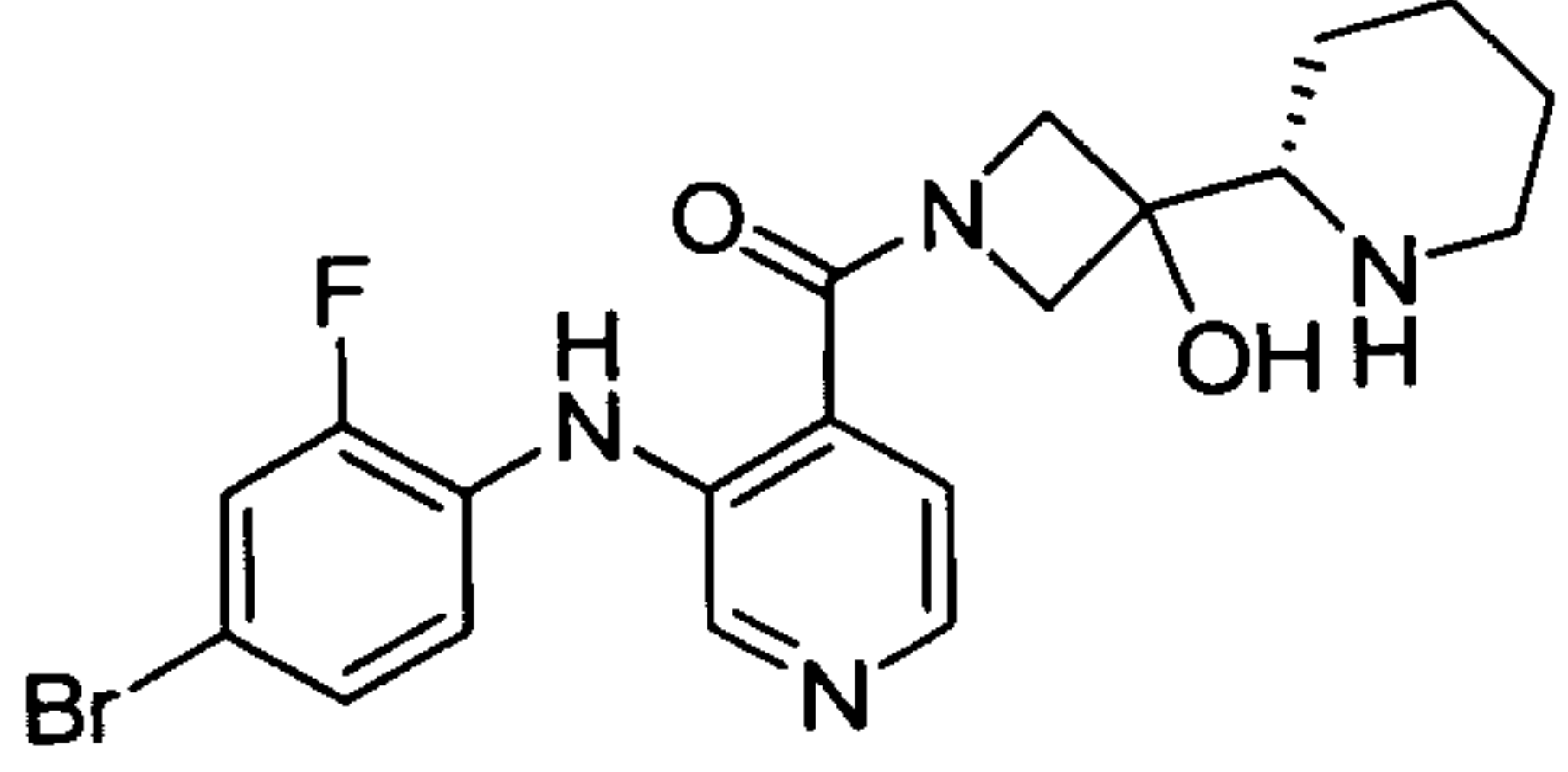
Cmpd No.	Structure	Name
339		5-[(2-fluoro-4-iodophenyl)amino]-6-[[3-hydroxy-3-(1-methyl-1H-benzimidazol-2-yl)azetidin-1-yl]carbonyl]-2-methylpyridazin-3(2H)-one
340		1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
341		1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
342		1-({3-[(2-fluoro-4-iodophenyl)amino]-1-oxidopyridin-4-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
343		1-({2-fluoro-3-[(2-fluoro-4-bromophenyl)amino]pyridin-4-yl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol

Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
344		3-[(1 <i>S</i>)-1-aminopropyl]-1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl} carbonyl)azetidin-3-ol
345		1-({3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl} carbonyl)-3-[(1 <i>S</i>)-1-(methylamino)propyl]azetidin-3-ol
346		(1 <i>R</i> ,2 <i>S</i>)-4-({(1 <i>S</i>)-1-[1-({2-fluoro-3-[(2-fluoro-4-iodophenyl)amino]pyridin-4-yl} carbonyl)-3-hydroxyazetidin-3-yl]propyl}amino)cyclopentane-1,2-diol
347		1-({7-[(4-bromo-2-chlorophenyl)amino]-8-fluoro-4-methylcinnolin-6-yl} carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
348		1-({7-[(4-bromo-2-fluorophenyl)amino]-8-fluoro-4-methylcinnolin-6-yl} carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol

Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
349		3-[(1 <i>S</i>)-1-aminoethyl]-1-({7-[(4-bromo-2-fluorophenyl)amino]cinnolin-6-yl}carbonyl)azetidin-3-ol
350		1-({7-[(4-bromo-2-fluorophenyl)amino]cinnolin-6-yl}carbonyl)-3-[(1 <i>S</i>)-1-[(2-hydroxy-2-methylcyclopentyl)amino]ethyl]azetidin-3-ol
351		1-({7-[(4-bromo-2-fluorophenyl)amino]cinnolin-6-yl}carbonyl)-3-[(1 <i>S</i>)-1-(dimethylamino)ethyl]azetidin-3-ol
352		3-[(1 <i>S</i>)-1-aminoethyl]-1-({5-[(2-fluoro-4-iodophenyl)amino]-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)azetidin-3-ol
353		3-[(1 <i>S</i>)-1-(dimethylamino)ethyl]-1-({5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)azetidin-3-ol

Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
354		1-({5-[(2-fluoro-4-iodophenyl)amino]-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
355		1-({5-[(2-fluoro-4-iodophenyl)amino]-1-methyl-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol
356		1-({5-[(2-fluoro-4-iodophenyl)amino]-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)-3-[(1 <i>S</i>)-1-[(2-hydroxy-2-methylcyclopentyl)amino]ethyl]azetidin-3-ol
357		3-[(1 <i>S</i>)-1-aminoethyl]-1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)azetidin-3-ol
358		1-({4-fluoro-5-[(2-fluoro-4-iodophenyl)amino]-1 <i>H</i> -1,2,3-benzotriazol-6-yl}carbonyl)-3-[(2 <i>S</i>)-piperidin-2-yl]azetidin-3-ol

Table 1. Representative MEK Inhibitors		
Cmpd No.	Structure	Name
359		5-({3-[(1S)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-6-[(2-fluoro-4-iodophenyl)amino]pyrimidin-2(1H)-one
360		6-[(2-fluoro-4-iodophenyl)amino]-5-({3-hydroxy-3-[(2S)-piperidin-2-yl]azetidin-1-yl}carbonyl)pyrimidin-2(1H)-one
361		4-[(2-fluoro-4-iodophenyl)amino]-5-({3-hydroxy-3-[(2S)-piperidin-2-yl]azetidin-1-yl}carbonyl)pyrimidin-2(1H)-one
362		5-({3-[(1S)-1-aminoethyl]-3-hydroxyazetidin-1-yl}carbonyl)-4-[(2-fluoro-4-iodophenyl)amino]pyrimidin-2(1H)-one

OTHER REPRESENTATIVE COMPOUNDS

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
1	3-(azetidin-3-ylidenemethyl)-4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
2	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(3-fluoropyridin-4-yl)-1H-pyrazolo[3,4-d]pyrimidine
3	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(3-chloropyridin-4-yl)-1H-pyrazolo[3,4-d]pyrimidine
4	2-({5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}oxy)-N,N-dimethylethanamine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
5	2-({5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}oxy)-N,N-diethylethanamine
6	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
7	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-piperazin-1-yl-1H-pyrazolo[3,4-d]pyrimidine
8	N-(3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}prop-2-yn-1-yl)acetamide
9	N,N-diethyl-2-({3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]phenyl}oxy)ethanamine
10	3-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methylphenyl}-N,N-diethylpropan-1-amine
11	3-bromo-4-{4-[5-chloro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
12	3-bromo-4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
13	2-({3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methylphenyl}oxy)-N,N-diethylethanamine
14	4-[4-(5-chloro-2-methyl-3-{[2-(1-methylpiperidin-4-yl)ethyl]oxy}phenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
15	5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
16	4-(4-{5-chloro-2-methyl-3-[(2-morpholin-4-ylethyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
17	4-(4-{5-chloro-2-methyl-3-[(2-piperidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
18	3-bromo-4-{4-[5-chloro-2-methyl-3-(3-morpholin-4-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
19	3-bromo-4-(4-{5-chloro-2-methyl-3-[3-(4-methylpiperazin-1-yl)propyl]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
20	3-bromo-4-(4-{5-chloro-2-methyl-3-[(2-piperidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
21	3-bromo-4-(4-{5-chloro-2-methyl-3-[(2-morpholin-4-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
22	4-{4-[5-chloro-2-methyl-3-(3-morpholin-4-ylpropyl)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
23	N'-(5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl)-N,N-diethylethane-1,2-diamine
24	4-{4-[5-chloro-2-methyl-3-(3-piperidin-1-ylpropyl)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
25	4-[4-(5-chloro-3-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-2-methylphenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
26	4-(4-{5-chloro-2-methyl-3-[(3-morpholin-4-ylpropyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
27	3-bromo-4-{4-[5-chloro-2-methyl-3-(3-piperidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
28	N'-(3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methylphenyl)-N,N-diethylethane-1,2-diamine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
29	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
30	4-[4-(5-chloro-2-methyl-3-{[2-(4-methylpiperazin-1-yl)ethyl]oxy}phenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
31	4-[4-(5-chloro-2-methyl-3-{[(1-methylpiperidin-4-yl)methyl]oxy}phenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
32	N,N-diethyl-2-({3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}oxy)ethanamine
33	2-[(5-chloro-3-{4-[1-(1,1-dimethylethyl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}-2-methylphenyl)oxy]-N,N-diethylethanamine
34	2-[(5-chloro-2-methyl-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}phenyl)oxy]-N,N-diethylethanamine
35	4-(4-{5-chloro-2-methyl-3-[(3-pyrrolidin-1-ylpropyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
36	4-[4-(5-chloro-2-methyl-3-{[3-(4-methylpiperazin-1-yl)propyl]oxy}phenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
37	3-bromo-4-(4-{5-chloro-2-methyl-3-[(3-piperidin-1-ylpropyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
38	3-bromo-4-(4-{5-chloro-2-methyl-3-[(3-morpholin-4-ylpropyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
39	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
40	4-(4-{5-chloro-2-methyl-3-[(3-morpholin-4-ylpropyl)oxy]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
41	4-(4-{5-chloro-2-methyl-3-[(2-morpholin-4-ylethyl)oxy]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
42	4-(4-{5-chloro-2-methyl-3-[(3-piperidin-1-ylpropyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
43	4-[4-(5-chloro-3-{[3-(4-ethylpiperazin-1-yl)propyl]oxy}-2-methylphenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
44	5-chloro-2-methyl-3-[4-(1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-(2-pyrrolidin-1-ylethyl)aniline
45	5-chloro-2-methyl-3-[4-(3-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-(2-pyrrolidin-1-ylethyl)aniline
46	N'-(5-chloro-2-methyl-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}phenyl)-N,N-dimethylethane-1,2-diamine
47	3-({5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}oxy)-N,N-diethylpropan-1-amine
48	N'-(5-chloro-2-methyl-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}phenyl)-N,N-diethylethane-1,2-diamine
49	5-chloro-2-methyl-N-(2-pyrrolidin-1-ylethyl)-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}aniline
50	3-bromo-4-(4-{4-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
51	4-(4-{4-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
52	3-methyl-4-(4-{4-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
53	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
54	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-methyl-1H-pyrazolo[3,4-d]pyrimidine
55	4-(4-{5-chloro-2-methyl-3-[(2-piperidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
56	3-[(5-chloro-2-methyl-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}phenyl)oxy]-N,N-diethylpropan-1-amine
57	5-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
58	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-fluoro-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
59	4-{4-[5-chloro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
60	3-bromo-4-{4-[5-fluoro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
61	4-{4-[5-chloro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
62	4-(4-{5-chloro-2-methyl-3-[3-(4-methylpiperazin-1-yl)propyl]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
63	3-bromo-4-(4-pyridin-2-ylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
64	3-bromo-4-[4-(2,4-dimethylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
65	3-bromo-4-{4-[3-(methyloxy)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
66	3-bromo-4-{4-[2-(methyloxy)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
67	3-bromo-4-{4-[4-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
68	4-(4-{5-chloro-2-methyl-3-[(3-pyrrolidin-1-ylpropyl)oxy]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
69	4-(4-{5-chloro-2-methyl-3-[(3-piperidin-1-ylpropyl)oxy]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
70	4-[4-(5-chloro-2-methyl-3-{[3-(4-methylpiperazin-1-yl)propyl]oxy}phenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
71	4-[4-(5-chloro-3-{[3-(4-ethylpiperazin-1-yl)propyl]oxy}-2-methylphenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
72	3-bromo-4-[4-(5-chloro-2-methyl-3-{[2-(4-methylpiperazin-1-yl)ethyl]oxy}phenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
73	4-[4-(5-chloro-2-methyl-3-{[2-(4-methylpiperazin-1-yl)ethyl]oxy}phenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
74	3-bromo-4-[4-(5-chloro-3-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
75	3-bromo-4-[4-(3,4-dichlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
76	3-bromo-4-[4-(3,4-difluorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
77	3-bromo-4-[4-(2,4-dichlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
78	3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-fluoro-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
79	5-fluoro-2-methyl-N-(2-pyrrolidin-1-ylethyl)-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}aniline
80	4-{4-[3,5-bis(methyloxy)phenyl]piperazin-1-yl}-3-bromo-1H-pyrazolo[3,4-d]pyrimidine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
81	4-[4-(5-chloro-3-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-2-methylphenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
82	N-{5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}-N,N',N'-trimethylethane-1,2-diamine
83	3-({3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methylphenyl}oxy)-N,N-diethylpropan-1-amine
84	3-bromo-4-(4-{5-chloro-2-methyl-3-[(3-pyrrolidin-1-ylpropyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
85	3-bromo-4-[4-(5-chloro-2-methyl-3-{[3-(4-methylpiperazin-1-yl)propyl]oxy}phenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
86	3-bromo-4-[4-(5-chloro-3-{[3-(4-ethylpiperazin-1-yl)propyl]oxy}-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
87	3-(5-chloro-2-methyl-3-{4-[3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}phenyl)-N,N-diethylpropan-1-amine
88	3-bromo-4-[4-(5-chloro-2-methyl-3-{[(1-methylpiperidin-4-yl)methyl]oxy}phenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
89	3-bromo-4-[4-(5-chloro-2-methyl-3-{[2-(1-methylpiperidin-4-yl)ethyl]oxy}phenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
90	4-[4-(5-chloro-2-methyl-3-{[(1-methylpiperidin-4-yl)methyl]oxy}phenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
91	4-[4-(5-chloro-2-methyl-3-{[2-(1-methylpiperidin-4-yl)ethyl]oxy}phenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
92	4-(4-{5-chloro-2-methyl-3-[3-(4-methylpiperazin-1-yl)propyl]phenyl}piperazin-1-yl)-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
93	3-bromo-4-[4-(3-chloro-4-fluorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
94	1-[4-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]phenyl]ethanone
95	3-bromo-4-[4-(2,5-dichlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
96	3-bromo-4-[4-(3,4-dimethylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
97	3-bromo-4-[4-(4-nitrophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
98	3-ethyl-4-(4-phenylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
99	3-ethyl-4-{4-[3-(methyloxy)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
100	4-{4-[5-chloro-2-methyl-3-(3-piperidin-1-ylpropyl)phenyl]piperazin-1-yl}-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
101	4-[4-(3,6-dimethylpyrazin-2-yl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
102	1-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]isoquinoline
103	3-bromo-4-[4-(2,6-dimethylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
104	3-bromo-4-{4-[4-(ethyloxy)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
105	3-bromo-4-[4-(2-ethylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
106	4-{4-[2,4-bis(methyloxy)phenyl]piperazin-1-yl}-3-bromo-1H-pyrazolo[3,4-d]pyrimidine
107	3-bromo-4-(4-pyrazin-2-ylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
108	3-bromo-4-(4-pyrimidin-2-ylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
109	4-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(trifluoromethyl)quinoline
110	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]pyrazine-2-carbonitrile
111	4-[4-(4,6-dimethylpyrimidin-2-yl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
112	ethyl 4-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(trifluoromethyl)pyrimidine-5-carboxylate

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
113	4-{4-[3-chloro-5-(methyloxy)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
114	4-[4-(3-bromo-2-chloro-5-fluorophenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
115	2-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]pyridine-3-carboxamide
116	3-ethyl-4-{4-[4-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
117	3-bromo-4-{4-[4-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
118	3-bromo-4-{4-[4-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
119	2-({3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]pyrazin-2-yl}oxy)-N,N-dimethylethanamine
120	4-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylquinoline
121	3-bromo-4-[4-(2-nitrophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
122	2-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]benzonitrile
123	4-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]benzonitrile
124	3-bromo-4-{4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
125	3-bromo-4-(4-{4-[(phenylmethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
126	4-{4-[5-chloro-2-methyl-3-(methyloxy)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
127	2-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]pyridine-3-carbonitrile
128	3-bromo-4-[4-(3,5-dichlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
129	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-chloro-5-fluoro-N-(2-pyrrolidin-1-ylethyl)aniline
130	2-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-fluoro-N-(2-pyrrolidin-1-ylethyl)aniline
131	3-bromo-4-[4-(2,5-difluorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
132	4-[4-(2,5-difluorophenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
133	3-bromo-4-{4-[3-(methyloxy)pyrazin-2-yl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
134	3-bromo-4-[4-(3-chlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
135	3-bromo-4-{4-[3-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
136	3-bromo-4-{4-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
137	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-(1-methylethyl)-1H-pyrazolo[3,4-d]pyrimidine
138	5-chloro-2-methyl-3-{4-[3-(1-methylethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}-N-(2-pyrrolidin-1-ylethyl)aniline
139	2-({3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]phenyl}oxy)-N-ethylacetamide
140	2-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,N-diethylpyrimidin-4-amine
141	3-bromo-4-[4-(3-{[(3-methylphenyl)methyl]oxy}phenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
142	3-bromo-4-(4-{3-[(2-piperidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
143	3-bromo-4-[4-(4-furan-2-ylpyrimidin-2-yl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
144	6-{2-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]pyrimidin-4-yl}-2H-1,4-benzoxazin-3(4H)-one
145	3-ethyl-4-{4-[2-methyl-3-(methyloxy)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
146	N'-{5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}-N-methyl-N-(1-methylethyl)ethane-1,2-diamine
147	N'-{5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}-N-ethyl-N-methylethane-1,2-diamine
148	N'-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methylphenyl}-N,N-dimethylethane-1,2-diamine
149	3-((6-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-chloro-5-methylpyrimidin-4-yl)oxy)-N,N-diethylpropan-1-amine
150	3-bromo-4-[4-(2,3-dichlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
151	3-bromo-4-{4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
152	3-bromo-4-(4-phenylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
153	3-bromo-4-[4-(4-fluorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
154	3-bromo-4-[4-(4-chlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
155	3-bromo-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
156	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-6-amine
157	3-bromo-4-[4-(4-bromophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
158	3-bromo-4-[3-methyl-4-(3-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
159	4-[4-(3-bromo-5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-6-amine
160	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-cyclopropyl-1H-pyrazolo[3,4-d]pyrimidine
161	5-chloro-3-[4-(3-cyclopropyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
162	5-chloro-2-methyl-3-{4-[3-(2-methylpropyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]piperazin-1-yl}-N-(2-pyrrolidin-1-ylethyl)aniline
163	4-(4-{5-chloro-2-methyl-3-[(2-pyrrolidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-(2-methylpropyl)-1H-pyrazolo[3,4-d]pyrimidine
164	3-bromo-4-[(3S)-4-(5-chloro-2-methylphenyl)-3-methylpiperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
165	5-bromo-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylaniline
166	2-((3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]phenyl)oxy)-N-cyclopropylacetamide
167	3-bromo-4-(4-{3-[(2-piperidin-1-ylethyl)oxy]pyrazin-2-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
168	4-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-6,7-bis(methyloxy)quinazoline
169	2-((3-chloro-5-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]phenyl)oxy)-N,N-diethylethanamine
170	4-{4-[2-chloro-5-(trifluoromethyl)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
171	3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(2-methylpropyl)oxy]-N-(2-pyrrolidin-1-ylethyl)aniline
172	3-((4-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-6-chloro-5-methylpyrimidin-2-yl)oxy)-N,N-diethylpropan-1-amine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
173	3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(phenylmethyl)oxy]-N-(2-pyrrolidin-1-ylethyl)aniline
174	3-bromo-4-[(3R)-4-(5-chloro-2-methylphenyl)-3-methylpiperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
175	3-[(2S)-4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-2-methylpiperazin-1-yl]-4-methyl-N-phenylbenzamide
176	3-[(2S)-4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-2-methylpiperazin-1-yl]-4-methyl-N-(phenylmethyl)benzamide
177	methyl 3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methylbenzoate
178	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methylbenzoic acid
179	(2E)-3-(4-{4-[5-chloro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)prop-2-enoic acid
180	3-(4-{4-[5-chloro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidin-3-yl)prop-2-yn-1-ol
181	4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-1-(5-chloro-2-methylphenyl)piperazin-2-one
182	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(2-methylpropyl)oxy]-N-(2-pyrrolidin-1-ylethyl)aniline
183	N'-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(2-methylpropyl)oxy]phenyl}-N,N-diethylethane-1,2-diamine
184	methyl 3-bromo-5-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methylbenzoate
185	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-phenylbenzamide
186	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,4-dimethylbenzamide
187	2-({3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]phenyl}oxy)-N,N-diethylethanamine
188	methyl 3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzoate
189	3-bromo-5-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-phenylbenzamide
190	3-bromo-5-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-phenylbenzamide
191	N'-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-2-methylphenyl}-N-methyl-N-(1-methylethyl)ethane-1,2-diamine
192	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-phenyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
193	N'-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(2-methylpropyl)oxy]phenyl}-N,N-dimethylethane-1,2-diamine
194	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,N,4-trimethylbenzamide
195	3-[4-(3-chloro-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-(2-methylpropyl)benzamide
196	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,N,4-trimethyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
197	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-2-oxopiperazin-1-yl]-4-methyl-N-phenylbenzamide
198	3-[(2R)-4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-2-(hydroxymethyl)piperazin-1-yl]-4-methyl-N-phenylbenzamide
199	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(pyrrolidin-1-ylcarbonyl)-N-(2-pyrrolidin-1-ylethyl)aniline

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
200	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,4-dimethyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
201	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-(4-chlorophenyl)-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
202	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-(2-chlorophenyl)-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
203	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(cyclopropylmethyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
204	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(3-methylbutyl)oxy]-N-(2-pyrrolidin-1-ylethyl)aniline
205	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(2-ethylbutyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
206	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-(butyloxy)-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
207	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-(1-methylethyl)-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
208	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,4-dimethyl-N-(1-methylethyl)-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
209	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(cyclobutylmethyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
210	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-(ethyloxy)-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
211	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-[2-(dimethylamino)ethyl]-4-methylbenzamide
212	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-(1,1-dimethylethyl)-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
213	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-pyridin-3-yl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
214	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(2-fluoro-2-methylpropyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
215	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(cyclohexylmethyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
216	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(cyclopentylmethyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
217	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-ethyl-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
218	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-[(1-methylethyl)oxy]-N-(2-pyrrolidin-1-ylethyl)aniline
219	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(2,2-dimethylpropyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
220	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-[(tetrahydrofuran-2-ylmethyl)oxy]aniline
221	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-{[2-(methyloxy)ethyl]oxy}-N-(2-pyrrolidin-1-ylethyl)aniline
222	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(propyloxy)-N-(2-pyrrolidin-1-ylethyl)aniline
223	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-{[2-(dimethylamino)ethyl]amino}-4-methyl-N-phenylbenzamide

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
224	N'-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(2-fluoro-2-methylpropyl)oxy]-2-methylphenyl}-N,N-dimethylethane-1,2-diamine
225	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-{[2-(dimethylamino)ethyl]amino}-4-methyl-N-(1-methylethyl)benzamide
226	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}pentan-1-one
227	N'-(3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-2-methylphenyl)-N,N-dimethylethane-1,2-diamine
228	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
229	5-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-N-(2-pyrrolidin-1-ylethyl)biphenyl-3-amine
230	1-(3-{5-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methylbiphenyl-3-yl}propyl)pyridinium
231	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-(1,3-thiazol-2-yl)aniline
232	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzoic acid
233	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(phenylethynyl)-N-(2-pyrrolidin-1-ylethyl)aniline
234	{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}(phenyl)methanone
235	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-ethynyl-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
236	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-(3,3-dimethylbut-1-yn-1-yl)-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
237	3-bromo-4-{4-[5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
238	3-bromo-4-{4-[2-methyl-5-[(2-methylpropyl)oxy]-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
239	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(3-phenyl-1,2,4-oxadiazol-5-yl)-N-(2-pyrrolidin-1-ylethyl)aniline
240	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(3-methyl-1,2,4-oxadiazol-5-yl)-N-(2-pyrrolidin-1-ylethyl)aniline
241	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}propan-1-one
242	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-(3,3-dimethylbutyl)-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
243	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-ethyl-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
244	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-[2-(trimethylsilyl)ethyl]aniline
245	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(2-phenylethyl)-N-(2-pyrrolidin-1-ylethyl)aniline
246	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}butan-1-one
247	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N,4-dimethyl-N-(methoxy)-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
248	3-bromo-4-[4-(3-bromo-5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
249	4-[4-(3-bromo-5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-2-methylphenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
250	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}ethanone
251	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(difluoromethyl)oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
252	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[[[(difluoromethyl)oxy]methyl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
253	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(methyloxy)-N-(2-pyrrolidin-1-ylethyl)aniline
254	5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
255	2-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-3,5,6-trifluoro-N-(3-methylbutyl)pyridin-4-amine
256	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-[(cyclopropylmethyl)oxy]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]benzamide
257	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(5-methyl-1,2,4-oxadiazol-3-yl)-N-(2-pyrrolidin-1-ylethyl)aniline
258	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-(ethylsulfonyl)-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
259	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-5-(methylsulfonyl)-N-(2-pyrrolidin-1-ylethyl)aniline
260	1-{3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}pentan-1-one
261	3-bromo-4-[4-(5-{[2,3-difluoro-2-(fluoromethyl)propyl]oxy}-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
262	6-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-3,5-difluoro-N~4~-(3-methylbutyl)-N~2~-(2-pyrrolidin-1-ylethyl)pyridine-2,4-diamine
263	3-bromo-5-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-N-(2-pyrrolidin-1-ylethyl)aniline
264	3-bromo-4-[4-(3',4',6-trifluoro-4-methylbiphenyl-3-yl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
265	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-chloro-N-(2-pyrrolidin-1-ylethyl)aniline
266	{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}methanol
267	3-bromo-4-(4-{4-methyl-2'-[(2-pyrrolidin-1-ylethyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
268	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[[[(2,2-difluorocyclopropyl)methyl]oxy]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
269	5-bromo-3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
270	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(ethyloxy)methyl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
271	3-[4-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-1-methyl-6-(trifluoromethyl)-1H-benzimidazol-2-yl]propan-1-ol

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
272	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}-4,4,4-trifluorobutan-1-one
273	{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}(cyclopropyl)methanone
274	3-({3'-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4'-methylbiphenyl-2-yl}oxy)-N,N-dimethylpropan-1-amine
275	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-(1,1-difluorobutyl)-2-methyl-N-(2-pyrrolidin-1-ylethyl)aniline
276	3-bromo-4-(4-{4-methyl-2'-[(3-morpholin-4-ylpropyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
277	3-bromo-4-(4-{4-methyl-2'-[(2-morpholin-4-ylethyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
278	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-[(2,2,2-trifluoroethyl)oxy]methyl}aniline
279	1-[2-({3'-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4'-methylbiphenyl-2-yl}oxy)ethyl]pyrrolidine-2,5-dione
280	3-bromo-4-(4-{3'-fluoro-4-methyl-2'-[(2-pyrrolidin-1-ylethyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
281	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}butan-1-one
282	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-[(3,3,3-trifluoropropyl)oxy]aniline
283	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-[(2,2,2-trifluoroethyl)oxy]aniline
284	1-{3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-4-methyl-5-[(2-pyrrolidin-1-ylethyl)amino]phenyl}butan-1-ol
285	3-bromo-4-(4-{4-chloro-2'-[(2-pyrrolidin-1-ylethyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
286	3-[4-(4-{5-[[2,3-difluoro-2-(fluoromethyl)propyl]oxy]-2-methyl-3-[(2-pyrrolidin-1-ylethyl)amino]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]prop-2-yn-1-ol
287	3-bromo-4-(4-{4-chloro-4'-fluoro-2'-[(2-pyrrolidin-1-ylethyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
288	3-bromo-4-(4-{4-methyl-3'-[(2-pyrrolidin-1-ylethyl)oxy]biphenyl-3-yl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
289	(2E)-3-[4-(4-{5-[[2,3-difluoro-2-(fluoromethyl)propyl]oxy]-2-methyl-3-[(2-pyrrolidin-1-ylethyl)amino]phenyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidin-3-yl]prop-2-enoic acid
290	3-[4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methyl-N-(2-pyrrolidin-1-ylethyl)-5-[4,4,4-trifluoro-1,1-bis(methyloxy)butyl]aniline
291	6-(4-phenylpiperazin-1-yl)-9H-purine
292	6-[4-(3-chlorophenyl)piperazin-1-yl]-9H-purine
293	4-(4-phenylpiperazin-1-yl)-7H-pyrrolo[2,3-d]pyrimidine
294	4-[4-(3-chlorophenyl)piperazin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine
295	4-(4-phenylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
296	4-[4-(3-chlorophenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
297	6-[4-(2-chlorophenyl)piperazin-1-yl]-9H-purine
298	6-[4-(2-fluorophenyl)piperazin-1-yl]-9H-purine
299	4-[4-(2-methylphenyl)piperazin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine
300	4-{4-[2-(methyloxy)phenyl]piperazin-1-yl}-7H-pyrrolo[2,3-d]pyrimidine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
301	4-{4-[3-(methyloxy)phenyl]piperazin-1-yl}-7H-pyrrolo[2,3-d]pyrimidine
302	4-{4-[4-(methyloxy)phenyl]piperazin-1-yl}-7H-pyrrolo[2,3-d]pyrimidine
303	4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}-7H-pyrrolo[2,3-d]pyrimidine
304	6-{4-[4-(methyloxy)phenyl]piperazin-1-yl}-9H-purine
305	6-{4-[2-(methyloxy)phenyl]piperazin-1-yl}-9H-purine
306	6-[4-(4-chlorophenyl)piperazin-1-yl]-9H-purine
307	6-[4-(4-fluorophenyl)piperazin-1-yl]-9H-purine
308	4-[4-(4-chlorophenyl)piperazin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine
309	4-[4-(2-chlorophenyl)piperazin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine
310	4-[4-(4-fluorophenyl)piperazin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine
311	4-[4-(2-fluorophenyl)piperazin-1-yl]-7H-pyrrolo[2,3-d]pyrimidine
312	6-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}-9H-purine
313	6-[4-(2-methylphenyl)piperazin-1-yl]-9H-purine
314	4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
315	4-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
316	4-[4-(3-chlorophenyl)piperazin-1-yl]-3-methyl-1H-pyrazolo[3,4-d]pyrimidine
317	3-methyl-4-[4-(2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
318	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
319	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-methyl-1H-pyrazolo[3,4-d]pyrimidine
320	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-methyl-6-phenyl-1H-pyrazolo[3,4-d]pyrimidine
321	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
322	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-6-methyl-1H-pyrazolo[3,4-d]pyrimidine
323	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-6-ethyl-1H-pyrazolo[3,4-d]pyrimidine
324	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-6-(1-methylethyl)-1H-pyrazolo[3,4-d]pyrimidine
325	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-phenyl-1H-pyrazolo[3,4-d]pyrimidine
326	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-({[2-(methyloxy)ethyl]oxy}methyl)-1H-pyrazolo[3,4-d]pyrimidine
327	3-bromo-4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
328	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-propyl-1H-pyrazolo[3,4-d]pyrimidine
329	4-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}phenol
330	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-N-phenyl-1H-pyrazolo[3,4-d]pyrimidin-3-amine
331	4-[4-(3-chlorophenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
332	4-{4-[5-chloro-2-(methyloxy)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
333	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}phenol
334	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-{3-[(phenylmethyl)oxy]phenyl}-1H-pyrazolo[3,4-d]pyrimidine
335	3-(1,3-benzodioxol-5-yl)-4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
336	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(2-thienyl)-1H-pyrazolo[3,4-d]pyrimidine
337	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}aniline
338	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}benzoic acid

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
339	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(4-methylphenyl)-1H-pyrazolo[3,4-d]pyrimidine
340	N-(4-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}phenyl)acetamide
341	4-[4-(3-chlorophenyl)-1,4-diazepan-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
342	4-[5-(3-chlorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
343	4-(4-{3-chloro-4-[(2-morpholin-4-ylethyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
344	methyl 1-(3-chlorophenyl)-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazine-2-carboxylate
345	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(3-methylbut-2-en-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
346	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidine
347	methyl 4-(3-chlorophenyl)-1-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazine-2-carboxylate
348	4-(4-{3-chloro-4-[(2-piperidin-1-ylethyl)oxy]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
349	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(1-methylethyl)-1H-pyrazolo[3,4-d]pyrimidine
350	1-(3-chlorophenyl)-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazine-2-carboxylic acid
351	1-(3-chlorophenyl)-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-N-methylpiperazine-2-carboxamide
352	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(phenylmethyl)-1H-pyrazolo[3,4-d]pyrimidine
353	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(2-methylpropyl)-1H-pyrazolo[3,4-d]pyrimidine
354	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-[4-(methyloxy)phenyl]-1H-pyrazolo[3,4-d]pyrimidine
355	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(4-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidine
356	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-[4-(phenyloxy)phenyl]-1H-pyrazolo[3,4-d]pyrimidine
357	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-{4-[(piperidin-4-ylmethyl)oxy]phenyl}-1H-pyrazolo[3,4-d]pyrimidine
358	1-(3-chlorophenyl)-N-[2-(dimethylamino)ethyl]-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazine-2-carboxamide
359	4-[4-(5-chloro-2-methyl-3-morpholin-4-ylphenyl)piperazin-1-yl]-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
360	4-(3-chlorophenyl)-1-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-N-methylpiperazine-2-carboxamide
361	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-[2-(methyloxy)phenyl]-1H-pyrazolo[3,4-d]pyrimidine
362	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-pyridin-4-yl-1H-pyrazolo[3,4-d]pyrimidine
363	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-[3-(methyloxy)phenyl]-1H-pyrazolo[3,4-d]pyrimidine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
364	4-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}benzonitrile
365	[5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)phenyl]methanol
366	methyl 5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)benzoate
367	(2E)-3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}prop-2-enoic acid
368	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}propanoic acid
369	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}propan-1-ol
370	methyl (2E)-3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}prop-2-enoate
371	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-{4-[(2-morpholin-4-ylethyl)oxy]phenyl}-1H-pyrazolo[3,4-d]pyrimidine
372	5-chloro-N-[2-(dimethylamino)ethyl]-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)benzamide
373	4-(4-{5-chloro-2-(methyloxy)-3-[(4-methylpiperazin-1-yl)carbonyl]phenyl}piperazin-1-yl)-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine
374	2-(dimethylamino)ethyl 5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)benzoate
375	1-[5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)phenyl]-N,N-dimethylmethanamine
376	N'-{[5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)phenyl]methyl}-N,N-dimethylethane-1,2-diamine
377	[1-(3-chlorophenyl)-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-2-yl]methanol
378	3-[(4-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}phenyl)oxy]-N,N-dimethylpropan-1-amine
379	2-chloro-4-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-methylphenol
380	1-(3-chlorophenyl)-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-N-(1-methylpiperidin-4-yl)piperazine-2-carboxamide
381	1-(3-chlorophenyl)-4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-N-(2-morpholin-4-ylethyl)piperazine-2-carboxamide
382	2-{[5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-(methyloxy)phenyl]oxy}-N,N-dimethylethanamine
383	3-{5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}-N,N-dimethylprop-2-yn-1-amine
384	N'-{5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}-N,N-dimethylethane-1,2-diamine
385	1,1-dimethylethyl (2E)-3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}prop-2-enoate
386	3-({2-chloro-4-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-methylphenyl}oxy)-N,N-dimethylpropan-1-amine
387	2-({2-chloro-4-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-5-methylphenyl}oxy)-N,N-dimethylethanamine
388	4-{4-[5-chloro-2-methyl-4-(methyloxy)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine

Table 2a. Representative AKT Inhibitors	
Cmpd No.	Name
389	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(4-methylpiperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
390	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-N,N-diethylprop-2-yn-1-amine
391	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}prop-2-yn-1-ol
392	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(piperidin-4-ylmethyl)-1H-pyrazolo[3,4-d]pyrimidine
393	phenylmethyl (3aR,6aS)-5-({4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}methylidene)hexahydrocyclopenta[c]pyrrole-2(1H)-carboxylate
394	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-[(E)-(3aR,6aS)-hexahydrocyclopenta[c]pyrrol-5(1H)-ylidenemethyl]-1H-pyrazolo[3,4-d]pyrimidine
395	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(3-pyrrolidin-1-ylprop-1-yn-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
396	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-[3-(4-methylpiperazin-1-yl)prop-1-yn-1-yl]-1H-pyrazolo[3,4-d]pyrimidine
397	3-{4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidin-3-yl}-N,N-diethylpropan-1-amine
398	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(3-pyrrolidin-1-ylpropyl)-1H-pyrazolo[3,4-d]pyrimidine
399	4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-3-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-d]pyrimidine
400	3-{5-chloro-3-[4-(3-ethyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]-2-methylphenyl}-N,N-diethylpropan-1-amine
401	4-{4-[5-chloro-2-methyl-3-(3-pyrrolidin-1-ylpropyl)phenyl]piperazin-1-yl}-3-ethyl-1H-pyrazolo[3,4-d]pyrimidine and
	a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt, solvate, or hydrate thereof.

Table 2b. Additional Representative AKT Inhibitors	
Entry	Name
1	[1-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methanol
2	2-{[[1-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]oxy}-N,N-dimethylethanamine
3	3-{[[1-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]oxy}-N,N-dimethylpropan-1-amine
4	3-bromo-4-{4-[(4-bromophenyl)methyl]piperazin-1-yl}-1H-pyrazolo[3,4-d]pyrimidine
5	{4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-1-[(4-chlorophenyl)methyl]piperazin-2-yl}methanol
6	N'-[[1-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]-N,N-diethylethane-1,2-diamine
7	3-bromo-4-(4-{[4-(1,1-dimethylethyl)phenyl]methyl}piperazin-1-yl)-1H-pyrazolo[3,4-d]pyrimidine
8	4-(3-bromo-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-1-[(4-chlorophenyl)methyl]piperazin-2-one

Table 2b. Additional Representative AKT Inhibitors	
Entry	Name
9	2-[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperazin-1-yl]-2-(4-chlorophenyl)- <i>N</i> -[2-(dimethylamino)ethyl]acetamide
10	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)- <i>N</i> ', <i>N</i> '-diethylpropane-1,3-diamine
11	3-bromo-4-(4-{[4-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
12	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)- <i>N</i> '-[2-(dimethylamino)ethyl]urea
13	<i>N</i> -[[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]- <i>N</i> '-[2-(dimethylamino)ethyl]urea
14	2-[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)-2-oxopiperazin-1-yl]-2-(4-chlorophenyl)- <i>N</i> -[2-(dimethylamino)ethyl]acetamide
15	2-(dimethylamino)ethyl [1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)carbamate
16	3-bromo-4-{4-[(4-chloro-3-fluorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
17	3-bromo-4-{4-[(4-chloro-2-fluorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
18	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)- <i>N</i> ', <i>N</i> '-diethylethane-1,2-diamine
19	3-bromo-4-{4-[(4-chlorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
20	[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-fluorophenyl)methanone
21	<i>N</i> -[[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]- <i>N</i> ', <i>N</i> '-diethyl- <i>N</i> -methylethane-1,2-diamine
22	[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-fluorophenyl)methanol
23	3-bromo-4-(4-{[2-fluoro-4-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
24	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)- <i>N</i> ~3~, <i>N</i> ~3~-diethyl-beta-alaninamide
25	2-{[[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-fluorophenyl)methyl]oxy}- <i>N</i> , <i>N</i> -dimethylethanamine
26	<i>N</i> -[[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]- <i>N</i> ~3~, <i>N</i> ~3~-diethyl-beta-alaninamide
27	3-bromo-4-{4-[(3,4-dichlorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
28	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)- <i>N</i> '-[2-(dimethylamino)ethyl]ethanediamide
29	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)-2-(diethylamino)ethanesulfonamide
30	4-[4-(biphenyl-4-ylmethyl)piperazin-1-yl]-3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
31	3-bromo-4-{(3 <i>S</i>)-4-[(4-chlorophenyl)methyl]-3-methylpiperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
32	3-bromo-4-(4-{[4-(methyloxy)phenyl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
33	4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)- <i>N</i> -[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide
34	3-bromo-4-{4-[(4-fluorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
35	<i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N</i> -(4-chlorophenyl)pent-4-enamide
36	3-bromo-4-[4-(2,3-dihydro-1,4-benzodioxin-6-ylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine

Table 2b. Additional Representative AKT Inhibitors	
Entry	Name
37	4-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
38	[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methanone
39	3-bromo-4-(4-{[4-(phenyloxy)phenyl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
40	3-bromo-4-{4-[(3,4-dichlorophenyl)methyl]piperidin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
41	4-{[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]methyl}- <i>N,N</i> -dimethylaniline
42	methyl 4-{[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]methyl}benzoate
43	3-bromo-4-{4-[(2 <i>E</i>)-3-phenylprop-2-enoyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
44	1-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)-4-[(4-chlorophenyl)methyl]- <i>N</i> -[3-(diethylamino)propyl]piperidine-4-carboxamide
45	3-bromo-4-{4-[(2-bromophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
46	3-bromo-4-{4-[(2-chlorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
47	3-bromo-4-{4-[(2,4-dichlorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
48	3-bromo-4-{4-[(2-chloro-4-fluorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
49	1-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)-4-(4-chlorophenyl)- <i>N</i> -[3-(diethylamino)propyl]piperidine-4-carboxamide
50	3-bromo-4-[4-(phenylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
51	2-[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]- <i>N</i> -pyridin-2-ylacetamide
52	3-bromo-4-[4-(1 <i>H</i> -imidazol-2-ylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
53	3-bromo-4-(4-{[3-(phenyloxy)phenyl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
54	3-bromo-4-{4-[(3-methylphenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
55	3-{[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)piperazin-1-yl]methyl}benzonitrile
56	3-bromo-4-{4-[(2-chloro-6-fluorophenyl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
57	3-bromo-4-[4-(1-phenylethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
58	3-bromo-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
59	1-(3-bromo-1 <i>H</i> -pyrazolo[3,4-d]pyrimidin-4-yl)- <i>N</i> -(4-chlorophenyl)piperidin-4-amine
60	3-bromo-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
61	3-bromo-4-(4-{[2,3,4-tris(methyloxy)phenyl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
62	3-bromo-4-[4-({3-[(phenylmethyl)oxy]phenyl}methyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
63	3-bromo-4-[4-(naphthalen-1-ylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine
64	3-bromo-4-(4-{[5-(4-chlorophenyl)furan-2-yl]methyl}piperazin-1-yl)-1 <i>H</i> -pyrazolo[3,4-d]pyrimidine

Table 2b. Additional Representative AKT Inhibitors	
Entry	Name
65	3-bromo-4-[4-({4-[(4-fluorophenyl)oxy]-3-nitrophenyl}methyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
66	3-bromo-4-[4-(furan-2-ylcarbonyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
67	3-bromo-4-[4-(1 <i>H</i> -indol-6-ylcarbonyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
68	3-bromo-4-{4-[2-(2-thienyl)ethyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
69	3-bromo-4-[4-(3-pyrrolidin-1-ylpropyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
70	3-bromo-4-[4-(cyclohexylmethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
71	3-bromo-4-{4-[(10-chloroanthracen-9-yl)methyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
72	3-bromo-4-[4-(1-methylpropyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
73	4-(4-{[4,6-bis(methyloxy)pyrimidin-2-yl]methyl}piperazin-1-yl)-3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
74	3-bromo-4-{4-[2-(methyloxy)ethyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
75	3-bromo-4-[4-(2-morpholin-4-yl-2-oxoethyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
76	3-bromo-4-{4-[3-(methyloxy)propyl]piperazin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
77	4-{4-[[4,6-bis(methyloxy)pyrimidin-2-yl](phenyl)methyl]piperazin-1-yl}-3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
78	3-bromo-4-[4-(6,7,8,9-tetrahydro-5 <i>H</i> -benzocyclohepten-5-yl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
79	3-bromo-4-[4-({4-[(phenylmethyl)oxy]phenyl}methyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
80	3-bromo-4-[4-({3-chloro-4-[(phenylmethyl)oxy]phenyl}methyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
81	4-{[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperazin-1-yl]methyl}- <i>N</i> -(3-morpholin-4-ylpropyl)benzamide
82	4-{[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperazin-1-yl]methyl}- <i>N</i> -[3-(methyloxy)propyl]benzamide
83	2-[(4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)-1-[(4-chlorophenyl)methyl]piperazin-2-yl)methyl]oxy)- <i>N,N</i> -dimethylethanamine
84	3-bromo-4-[4-({4-[(4-chlorophenyl)oxy]-3-nitrophenyl}methyl)piperazin-1-yl]-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
85	2-[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperazin-1-yl]- <i>N,N</i> -dimethylacetamide
86	2-{[(<i>R</i>)-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]oxy}- <i>N,N</i> -dimethylethanamine
87	<i>N</i> -(4-bromo-3-fluorophenyl)- <i>N</i> -[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]- <i>N'</i> -[2-(dimethylamino)ethyl]urea
88	2-[(<i>R</i>)-(4-chlorophenyl)[1-(3-ethyl-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]methyl]oxy)- <i>N,N</i> -dimethylethanamine
89	2-{[(<i>S</i>)-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]oxy}- <i>N,N</i> -dimethylethanamine
90	3-bromo-4-(4-{(<i>R</i>)-(4-chlorophenyl)[(2-pyrrolidin-1-ylethyl)oxy]methyl}piperidin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
91	1-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]-1-(4-chlorophenyl)-4-(dimethylamino)butan-1-ol
92	2-{[(<i>R</i>)-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chloro-3-fluorophenyl)methyl]oxy}- <i>N,N</i> -dimethylethanamine

Table 2b. Additional Representative AKT Inhibitors	
Entry	Name
93	3-bromo-4-(4-((R)-(4-chlorophenyl)[(2-piperidin-1-ylethyl)oxy]methyl)piperidin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
94	4-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]-4-(4-chlorophenyl)- <i>N,N</i> -dimethylbutan-1-amine
95	3-bromo-4-(4-((R)-(4-chlorophenyl)[(2-morpholin-4-ylethyl)oxy]methyl)piperidin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
96	1-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]-1-(4-fluorophenyl)- <i>N</i> -(furan-2-ylmethyl)- <i>N</i> -methylmethanamine
97	1-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]-1-(4-fluorophenyl)- <i>N</i> -methyl- <i>N</i> -(pyridin-2-ylmethyl)methanamine
98	4-{{[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-fluorophenyl)methyl}(methyl)amino)methyl}- <i>N,N</i> -dimethylaniline
99	[4-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperazin-1-yl](1 <i>H</i> -indol-6-yl)methanol
100	3-bromo-4-(4-((R)-(4-chloro-3-fluorophenyl)[(2-pyrrolidin-1-ylethyl)oxy]methyl)piperidin-1-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
101	3-bromo-4-{4-[(4-chlorophenyl)oxy]piperidin-1-yl}-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidine
102	2-{{[(R)-[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl](4-chlorophenyl)methyl]oxy}- <i>N,N</i> -diethylethanamine
103	2-{{[1-(3-bromo-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl)piperidin-4-yl]oxy}-5-chloro- <i>N</i> -(2-pyrrolidin-1-ylethyl)aniline and
	a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt, solvate, or hydrate thereof.

Table 3a. Representative c-MET Inhibitors	
Cmpd No.	Name
1	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[3-fluoro-4-(7 <i>H</i> -pyrrolo[2,3- <i>d</i>]pyrimidin-4-yloxy)phenyl]propanediamide
2	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[3-fluoro-4-(7 <i>H</i> -pyrrolo[2,3- <i>d</i>]pyrimidin-4-yloxy)phenyl]cyclopropane-1,1-dicarboxamide
3	<i>N</i> -({[3-fluoro-4-(7 <i>H</i> -pyrrolo[2,3- <i>d</i>]pyrimidin-4-yloxy)phenyl]amino}carbonothioyl)-2-phenylacetamide
4	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -(4-{{[1-(tetrahydro-2 <i>H</i> -pyran-2-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl]oxy}phenyl}cyclopropane-1,1-dicarboxamide
5	2-phenyl- <i>N</i> -{{(4-{{[1-(tetrahydro-2 <i>H</i> -pyran-2-yl)-1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yl]oxy}phenyl]amino}carbonothioyl}acetamide
6	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[4-(1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yloxy)phenyl]cyclopropane-1,1-dicarboxamide
7	2-phenyl- <i>N</i> -({[4-(1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-yloxy)phenyl]amino}carbonothioyl)acetamide
8	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -(4-{{[9-(tetrahydro-2 <i>H</i> -pyran-2-yl)-9 <i>H</i> -purin-6-yl]oxy}phenyl}cyclopropane-1,1-dicarboxamide
9	2-phenyl- <i>N</i> -{{(4-{{[9-(tetrahydro-2 <i>H</i> -pyran-2-yl)-9 <i>H</i> -purin-6-yl]oxy}phenyl]amino}carbonothioyl}acetamide
10	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[4-(9 <i>H</i> -purin-6-yloxy)phenyl]cyclopropane-1,1-dicarboxamide
11	2-phenyl- <i>N</i> -({[4-(9 <i>H</i> -purin-6-yloxy)phenyl]amino}carbonothioyl)acetamide
12	<i>N</i> -{3-fluoro-4-[(6-{{[(2-morpholin-4-ylethyl)amino]carbonyl}-7 <i>H</i> -pyrrolo[2,3- <i>d</i>]pyrimidin-4-yl]oxy}phenyl]}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide and

Table 3a. Representative c-MET Inhibitors	
Cmpd No.	Name
	a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt, solvate, or hydrate thereof.

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
1	<i>N</i> -[({3-fluoro-4-[(6-(methyloxy)-7-{{(3aR,6aS)-octahydrocyclopenta[c]pyrrol-5-ylmethyl}oxy}quinazolin-4-yl)oxy]phenyl}amino)carbonothioyl]-2-phenylacetamide
2	<i>N</i> -{[(3-fluoro-4-{[7-{{(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-yl]oxy}phenyl]amino}carbonothioyl]-2-phenylacetamide
3	<i>N</i> -{[(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)(methyl)amino]carbonothioyl}-2-phenylacetamide
4	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)imidazolidin-2-one
5	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-(phenylmethyl)imidazolidin-2-one
6	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-(phenylacetyl)imidazolidin-2-one
7	ethyl [(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)amino](oxo)acetate
8	<i>N</i> -{[(4-{[6,7-bis(methyloxy)quinazolin-4-yl]amino}-3-fluorophenyl)amino]carbonothioyl}-2-phenylacetamide
9	<i>N'</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> -methyl- <i>N</i> -(2-phenylethyl)sulfamide
10	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-(phenylmethyl)-1,2,4-oxadiazol-5-amine
11	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)piperidin-2-one
12	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(phenylmethyl)ethanediamide
13	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-4-phenyl-1,3-thiazol-2-amine
14	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(2-phenylethyl)ethanediamide
15	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-1-phenylmethanesulfonamide
16	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-2-phenylethanesulfonamide
17	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -(phenylmethyl)benzenesulfonamide
18	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -methyl- <i>N</i> -(phenylmethyl)benzenesulfonamide
19	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -(2-phenylethyl)benzenesulfonamide
20	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -methyl- <i>N</i> -(2-phenylethyl)benzenesulfonamide
21	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -(3-phenylpropyl)benzenesulfonamide
22	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)pyrrolidin-2-one
23	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl (phenylmethyl)carbamate
24	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl (2-phenylethyl)carbamate
25	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -methyl- <i>N</i> -(3-phenylpropyl)benzenesulfonamide
26	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -phenylethanediamide
27	<i>N</i> -{[(3-fluoro-4-{[7-{{(2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy}-6-(methyloxy)quinolin-4-yl]oxy}phenyl]amino}carbonothioyl]-2-phenylacetamide
28	<i>N</i> -[(<i>Z</i>)-[(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)amino](imino)methyl]-2-phenylacetamide
29	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro- <i>N</i> -[2-(phenyloxy)ethyl]benzenesulfonamide

Table 3b. Additional Representative c-MET Inhibitors

Entry	Name
30	<i>N,N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-bis-(3-phenylpropane-1-sulfonamide)
31	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-phenylpropane-1-sulfonamide
32	<i>N</i> 2-[(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)sulfonyl]- <i>N</i> 1-phenylglycinamide
33	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-2-phenylacetamide
34	<i>N</i> -{[(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)amino]carbonothioyl}-2-phenylacetamide
35	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-1,3-benzothiazol-2-amine
36	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-amine
37	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-phenylacetamide
38	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(2-morpholin-4-ylethyl)ethanediamide
39	benzyl-{[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenylcarbamoyl]-methyl}-carbamic acid tert-butyl ester
40	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-(phenylmethyl)glycinamide
41	<i>N</i> 2-acetyl- <i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-(phenylmethyl)glycinamide
42	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-1,3-benzothiazol-2-yl)-2-phenylacetamide
43	benzyl-{[6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-ylcarbamoyl]-methyl}-carbamic acid tert-butyl ester
44	<i>N</i> 1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)- <i>N</i> 2-(phenylmethyl)glycinamide
45	<i>N</i> 2-acetyl- <i>N</i> 1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)- <i>N</i> 2-(phenylmethyl)glycinamide
46	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-3-phenylpropanamide
47	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-4-phenylbutanamide
48	<i>N</i> 1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)- <i>N</i> 2-methyl- <i>N</i> 2-(phenylmethyl)glycinamide
49	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -{2-[4-(methyloxy)phenyl]ethyl}ethanediamide
50	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-methyl- <i>N</i> 2-(phenylmethyl)glycinamide
51	4-[(2-amino-1,3-benzothiazol-6-yl)oxy]-6,7-bis(methyloxy)-1-(2-oxo-2-phenylethyl)quinolinium
52	<i>N</i> -{[(4-{[6,7-bis(methyloxy)quinolin-4-yl]amino}phenyl)amino]carbonothioyl}-2-phenylacetamide
53	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-3-phenylpropanamide
54	<i>N</i> -{[(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)amino]carbonothioyl}-2-phenylacetamide
55	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(2,3-dihydro-1 <i>H</i> -inden-1-yl)ethanediamide
56	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(2,3-dihydro-1 <i>H</i> -inden-2-yl)ethanediamide
57	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(1,2,3,4-tetrahydronaphthalen-1-yl)ethanediamide
58	<i>N'</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> -(2-phenylethyl)- <i>N</i> -(phenylmethyl)sulfamide
59	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
	(trifluoroacetyl)glycinamide
60	<i>N</i> -{[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenylcarbamoyl]-methyl}-benzamide
61	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)- <i>N'</i> -(4-fluorophenyl)propanediamide
62	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[(2 <i>S</i>)-1,2,3,4-tetrahydronaphthalen-2-yl]ethanediamide
63	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[2-(4-methylphenyl)ethyl]ethanediamide
64	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(2-phenylpropyl)ethanediamide
65	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[2-(4-chlorophenyl)ethyl]ethanediamide
66	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N,N'</i> -bis(phenylmethyl)sulfamide
67	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N,N'</i> -bis(2-phenylethyl)sulfamide
68	ethyl [(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)amino](oxo)acetate
69	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(2-phenylethyl)ethanediamide
70	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(4-fluorophenyl)propanediamide
71	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(1,2,3,4-tetrahydronaphthalen-2-yl)ethanediamide
72	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[2-(1-methylpyrrolidin-2-yl)ethyl]ethanediamide
73	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[2-(phenyloxy)ethyl]ethanediamide
74	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[2-hydroxy-1-(phenylmethyl)ethyl]urea
75	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)imidazolidin-2-one
76	<i>N'</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> -methyl- <i>N</i> -(2-phenylethyl)ethanediamide
77	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -{[3-(trifluoromethyl)phenyl]methyl}ethanediamide
78	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -{2-[3-(trifluoromethyl)phenyl]ethyl}ethanediamide
79	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-3-oxo-4-phenylbutanamide
80	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-2-[3-(trifluoromethyl)phenyl]acetamide
81	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro- <i>N</i> -[2-(phenyloxy)ethyl]-1,3-benzothiazol-2-amine
82	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro- <i>N</i> -(2-piperidin-1-ylethyl)-1,3-benzothiazol-2-amine
83	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro- <i>N</i> -methyl- <i>N</i> -(2-phenylethyl)-1,3-benzothiazol-2-amine
84	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro- <i>N</i> -(2-pyrrolidin-1-ylethyl)-1,3-benzothiazol-2-amine
85	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro- <i>N</i> -{[3-(trifluoromethyl)phenyl]methyl}-1,3-benzothiazol-2-amine
86	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro- <i>N</i> -{2-[3-(trifluoromethyl)phenyl]ethyl}-1,3-benzothiazol-2-amine
87	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -[3-

Table 3b. Additional Representative c-MET Inhibitors

Entry	Name
	(trifluoromethyl)phenyl]propanediamide
88	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-[3-(trifluoromethyl)phenyl]acetamide
89	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-{[3-(trifluoromethyl)phenyl]methyl}glycinamide
90	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-(2-phenylethyl)glycinamide
91	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-{2-[3-(trifluoromethyl)phenyl]ethyl}glycinamide
92	benzyl-{[5-chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-ylcarbamoyl]-methyl}-carbamic acid tert-butyl ester
93	<i>N</i> 1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N</i> 2-(phenylmethyl)glycinamide
94	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-[3,5-bis(trifluoromethyl)phenyl]acetamide
95	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-[2-chloro-5-(trifluoromethyl)phenyl]acetamide
96	<i>N</i> -(3-fluoro-4-[(6-(methyloxy)-7-{[(1-methylpiperidin-4-yl)methyl]oxy}quinolin-4-yl)oxy]phenyl)- <i>N'</i> -(2-phenylethyl)ethanediamide
97	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(1,2,3,4-tetrahydroisoquinolin-1-ylmethyl)ethanediamide
98	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -[(2-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl]ethanediamide
99	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-methyl- <i>N</i> 2-{[3-(trifluoromethyl)phenyl]methyl}glycinamide
100	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-methyl- <i>N</i> 2-{2-[3-(trifluoromethyl)phenyl]ethyl}glycinamide
101	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N</i> 2-methyl- <i>N</i> 2-(2-phenylethyl)glycinamide
102	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-4-(phenylmethyl)imidazolidin-2-one
103	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridazin-3-yl)- <i>N'</i> -(4-fluorophenyl)propanediamide
104	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(2-chlorophenyl)propanediamide
105	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(3-chlorophenyl)propanediamide
106	<i>N</i> 1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N</i> 2-methyl- <i>N</i> 2-(phenylmethyl)glycinamide
107	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(4-chlorophenyl)propanediamide
108	(2 <i>E</i>)- <i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-2-[(methyloxy)imino]propanamide
109	(2 <i>E</i>)- <i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-2-[(ethyloxy)imino]propanamide
110	(2 <i>E</i>)- <i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-2-[[phenylmethyl]oxy]imino]propanamide
111	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-1-(phenylmethyl)prolinamide
112	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)imidazolidin-2-one
113	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-4-(phenylmethyl)imidazolidin-2-one
114	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-4-(phenylmethyl)-4,5-dihydro-1,3-oxazol-2-amine
115	6,7-bis(methyloxy)-4-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}oxy)quinoline
116	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-4-(phenylmethyl)piperazin-2-one

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
117	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N</i> 2-(phenylmethyl)alaninamide
118	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N</i> 2-methyl- <i>N</i> 2-(phenylmethyl)alaninamide
119	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N</i> 2-(phenylmethyl)leucinamide
120	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N</i> 2-methyl- <i>N</i> 2-(phenylmethyl)leucinamide
121	<i>N</i> 1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N</i> 2-(phenylmethyl)valinamide
122	4-(6,7-dimethoxy-quinolin-4-ylamino)- <i>N</i> -(3-phenyl-propyl)-benzamide
123	4-benzyl-1-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-tetrahydro-pyrimidin-2-one
124	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
125	2-(Benzyl-methyl-amino)- <i>N</i> -[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-3-methyl-butylamide (note: Alphabetic order of prefixes ignored while selecting parent chain)
126	<i>N</i> -[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-phenoxyimino-propionamide
127	2-Benzoyloxyimino- <i>N</i> -[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-phenyl-acetamide
128	4-[4-(4-Benzyl-piperidin-1-yl)-phenoxy]-6,7-dimethoxy-quinoline
129	<i>N</i> -[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]- <i>N'</i> -(2-isopropyl-1,2,3,4-tetrahydro-isoquinolin-1-ylmethyl)-oxalamide
130	<i>N</i> -[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]- <i>N'</i> -(2-ethyl-1,2,3,4-tetrahydro-isoquinolin-1-ylmethyl)-oxalamide
131	4-(4-{3-Chloro-5-[2-(4-fluoro-phenylcarbamoyl)-acetylamino]-pyridin-2-yloxy}-6-methoxy-quinolin-7-yloxymethyl)-piperidine-1-carboxylic acid tert-butyl ester
132	<i>N</i> -{5-Chloro-6-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-pyridin-3-yl}- <i>N'</i> -(4-fluoro-phenyl)-malonamide
133	<i>N</i> -{5-Chloro-6-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-pyridin-3-yl}- <i>N'</i> -(4-fluoro-phenyl)-malonamide
134	<i>N</i> -{4-[7-(3-Diethylamino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}- <i>N'</i> -phenethyl-oxalamide
135	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
136	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(3-piperidin-1-yl-propoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
137	<i>N</i> -{4-[7-(2-Diethylamino-ethoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}- <i>N'</i> -phenethyl-oxalamide
138	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -methyl- <i>N'</i> -phenethyl-oxalamide
139	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(2-methyl-octahydro-cyclopenta[c]pyrrol-5-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
140	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(2-methyl-octahydro-cyclopenta[c]pyrrol-5-ylmethoxy)-quinazolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
141	2-(3,4-Dihydro-1 <i>H</i> -isoquinolin-2-yl)- <i>N</i> -{3-fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-2-oxo-acetamide
142	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-2-oxo-2-(3-phenyl-pyrrolidin-1-yl)-acetamide
143	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-2-oxo-2-(2-phenyl-morpholin-4-yl)-acetamide
144	<i>N</i> -(2-Dimethylamino-2-phenyl-ethyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
145	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-oxo-2-phenyl-ethyl)-oxalamide

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
146	<i>N</i> -[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]-2,2-difluoro- <i>N'</i> -(4-fluoro-phenyl)-malonamide
147	<i>N</i> -Benzyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
148	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(2-fluoro-phenyl)-ethyl]-oxalamide
149	<i>N</i> -[2-(3-Chloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
150	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(2-methoxy-phenyl)-ethyl]-oxalamide
151	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-pyridin-3-yl-ethyl)-oxalamide
152	<i>N</i> -Benzyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
153	<i>N</i> -[2-(2,5-Dimethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
154	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(2-trifluoromethyl-phenyl)-ethyl]-oxalamide
155	<i>N</i> -[2-(2-Ethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
156	<i>N</i> -[2-(2,4-Dimethyl-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
157	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>S</i> -phenyl-2- <i>p</i> -tolyl-ethyl)-oxalamide
158	<i>N</i> -[2-(4-Chloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
159	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamic acid
160	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(3-fluoro-phenyl)-ethyl]-oxalamide
161	<i>N</i> -[2-(2-Chloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
162	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(3-methoxy-phenyl)-ethyl]-oxalamide
163	<i>N</i> -(1,2-Diphenyl-ethyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
164	<i>N</i> -[2-(2,4-Dichloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
165	<i>N</i> -[2-(3,4-Dimethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
166	<i>N</i> -[2-(4-Ethyl-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
167	<i>N</i> -[2-(4-Ethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
168	<i>N</i> -[2-(4-Ethoxy-3-methoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
169	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(4-phenoxy-phenyl)-ethyl]-oxalamide
170	<i>N</i> -[2-(3-Ethoxy-4-methoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
171	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-pyridin-2-yl-ethyl)-oxalamide
172	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-

Table 3b. Additional Representative c-MET Inhibitors

Entry	Name
	pyridin-4-yl-ethyl)-oxalamide
173	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(4-fluoro-phenyl)-ethyl]-oxalamide
174	<i>N</i> -[2-(2-Bromo-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
175	<i>N</i> -[2-(2-Chloro-6-fluoro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
176	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2 <i>R</i> -phenyl-propyl)-oxalamide
177	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -indan-1-yl-oxalamide
178	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -isobutyl-oxalamide
179	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-methyl-butyl)-oxalamide
180	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2 <i>R</i> -phenyl-propyl)-oxalamide
181	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-phenyl-propyl)-oxalamide
182	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -indan-2-yl-oxalamide
183	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>R</i> -phenyl-ethyl)-oxalamide
184	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>S</i> -phenyl-ethyl)-oxalamide
185	<i>N</i> -[2-(3-Bromo-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
186	<i>N</i> -[2-(2,6-Dichloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
187	<i>N</i> -[2-(2,4-Dichloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
188	<i>N</i> -(2-Benzo[1,3]dioxol-5-yl-ethyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
189	<i>N</i> -[2-(3-Bromo-4-methoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
190	<i>N</i> -[2-(3,5-Dimethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
191	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2- <i>o</i> -tolyl-ethyl)-oxalamide
192	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2- <i>m</i> -tolyl-ethyl)-oxalamide
193	<i>N</i> -[2-(3-Ethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
194	<i>N</i> -[2-(3,4-Dimethyl-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
195	<i>N</i> -[2-(2,5-Dimethyl-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
196	<i>N</i> -[2-(3-Chloro-4-propoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
197	<i>N</i> -[2-(4-Butoxy-3-chloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
198	<i>N</i> -[2-(4- <i>tert</i> -Butyl-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
199	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(4-sulfamoyl-phenyl)-ethyl]-oxalamide
200	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(4-hydroxy-3-methoxy-phenyl)-ethyl]-oxalamide
201	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(3-hydroxy-4-methoxy-phenyl)-ethyl]-oxalamide
202	<i>N</i> -(2,4-Dichloro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
203	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-fluoro-2-trifluoromethyl-benzyl)-oxalamide
204	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1-p-tolyl-ethyl)-oxalamide
205	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-fluoro-4-trifluoromethyl-benzyl)-oxalamide
206	<i>N</i> -(3-Chloro-4-fluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
207	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[1-(3-methoxy-phenyl)-ethyl]-oxalamide
208	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1-naphthalen-2-yl-ethyl)-oxalamide
209	<i>N</i> -(4-Chloro-3-trifluoromethyl-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
210	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1-p-tolyl-ethyl)-oxalamide
211	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(6-trifluoromethyl-pyridin-3-ylmethyl)-oxalamide
212	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-methyl-benzyl)-oxalamide
213	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-methyl-benzyl)-oxalamide
214	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-fluoro-3-trifluoromethyl-benzyl)-oxalamide
215	<i>N</i> -(3,5-Dichloro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
216	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>R</i> ,2,3,4-tetrahydro-naphthalen-1-yl)-oxalamide
217	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>S</i> ,2,3,4-tetrahydro-naphthalen-1-yl)-oxalamide
218	<i>N</i> -Cyclopentyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
219	<i>N</i> -[1-(4-Bromo-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
220	<i>N</i> -(2-Fluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
221	<i>N</i> -[2-(3,4-Dichloro-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
222	<i>N</i> -(4-Fluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
223	<i>N</i> -(2,3-Difluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
224	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-phenoxy-ethyl)-oxalamide
225	<i>N</i> -(2,2-Diphenyl-ethyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
	yloxy]-phenyl}-oxalamide
226	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(4-methoxy-phenyl)-ethyl]-oxalamide
227	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-phenyl-propyl)-oxalamide
228	<i>N</i> -[2-(4-Bromo-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
229	<i>N</i> -{4-[7-(1-Ethyl-piperidin-4-ylmethoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-oxo-2-(2-phenyl-morpholin-4-yl)-acetamide
230	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-fluoro-5-trifluoromethyl-benzyl)-oxalamide
231	<i>N</i> -(3,5-Difluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
232	<i>N</i> -(2-Chloro-5-trifluoromethyl-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
233	<i>N</i> -[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]- <i>N'</i> -(2-dimethylamino-2-phenyl-ethyl)-oxalamide
234	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-methoxy-benzyl)-oxalamide
235	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-trifluoromethyl-benzyl)-oxalamide
236	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-methoxy-benzyl)-oxalamide
237	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-trifluoromethyl-benzyl)-oxalamide
238	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-trifluoromethoxy-benzyl)-oxalamide
239	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-methoxy-benzyl)-oxalamide
240	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-trifluoromethyl-benzyl)-oxalamide
241	<i>N</i> -(3-Chloro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
242	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-trifluoromethoxy-benzyl)-oxalamide
243	<i>N</i> -(2-Chloro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
244	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-trifluoromethoxy-benzyl)-oxalamide
245	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-methoxy-benzyl)-oxalamide
246	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(4-trifluoromethyl-benzyl)-oxalamide
247	<i>N</i> -{4-[7-(Azetidin-3-ylmethoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}- <i>N'</i> -phenethyl-oxalamide
248	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-azetidin-3-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
249	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-hydroxy-2-phenyl-ethyl)-oxalamide
250	<i>N</i> -[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]- <i>N'</i> -(2,4-difluoro-phenyl)-malonamide
251	<i>N</i> -[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]- <i>N'</i> -(4-fluoro-phenyl)- <i>N'</i> -methyl-malonamide

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
252	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>R</i> -phenyl-propyl)-oxalamide
253	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(1 <i>R</i> -phenyl-propyl)-oxalamide
254	<i>N</i> -(3,4-Difluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
255	<i>N</i> -(2,6-Difluoro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
256	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[2-(4-fluoro-phenyl)-ethyl]-oxalamide
257	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -phenyl-oxalamide
258	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-fluoro-phenyl)-oxalamide
259	<i>N</i> -(4-Chloro-3-fluoro-phenyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
260	<i>N</i> -(3,4-Dimethoxy-phenyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
261	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(3-methyl-butyl)-oxalamide
262	<i>N</i> -(3,3-Dimethyl-butyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
263	<i>N</i> -{5-Chloro-6-[6-methoxy-7-(3-piperidin-1-yl-propoxy)-quinolin-4-yloxy]-pyridin-3-yl}- <i>N'</i> -(4-fluoro-phenyl)-malonamide
264	<i>N</i> -{5-Chloro-6-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-pyridin-3-yl}- <i>N'</i> -(4-fluoro-phenyl)-malonamide
265	<i>N</i> -{5-Chloro-6-[7-(3-diethylamino-propoxy)-6-methoxy-quinolin-4-yloxy]-pyridin-3-yl}- <i>N'</i> -(4-fluoro-phenyl)-malonamide
266	<i>N</i> -(4-Chloro-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
267	<i>N</i> -(3,5-Dimethoxy-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
268	<i>N</i> -(4-Butyl-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
269	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2- <i>p</i> -tolyl-ethyl)-oxalamide
270	<i>N</i> -(3,5-Bis-trifluoromethyl-benzyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
271	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -pyrazin-2-ylmethyl-oxalamide
272	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -pyridin-2-ylmethyl-oxalamide
273	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinazolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
274	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(1-methyl-piperidin-4-ylmethoxy)-quinazolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
275	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-fluoro-3-trifluoromethyl-benzyl)-oxalamide
276	<i>N</i> -[2-(2-Bromo-6-methoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
277	<i>N</i> -[2-(3,4-Dimethoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N</i> -methyl-oxalamide
278	<i>N</i> -[2-(5-Bromo-2-methoxy-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-

Table 3b. Additional Representative c-MET Inhibitors	
Entry	Name
	ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
279	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-fluoro-5-trifluoromethyl-benzyl)-oxalamide
280	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -[1-(4-fluoro-phenyl)-ethyl]-oxalamide
281	<i>N</i> -(1 <i>S</i> -Benzyl-2-oxo-2-pyrrolidin-1-yl-ethyl)- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
282	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(octahydro-cyclopenta[<i>c</i>]pyrrol-5-ylmethoxy)-quinazolin-4-yloxy]-phenyl}- <i>N'</i> -phenethyl-oxalamide
283	<i>N</i> -[2-(4-Amino-phenyl)-ethyl]- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
284	2-(4-Benzyl-piperidin-1-yl)- <i>N</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-2-oxo-acetamide
285	<i>N</i> -[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]- <i>N'</i> -(4-fluoro-phenyl)-malonamide
286	<i>N</i> -[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]- <i>N'</i> -(3-fluoro-phenyl)-malonamide
287	<i>N</i> -[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]- <i>N'</i> -phenyl-malonamide
288	<i>N</i> -[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]- <i>N'</i> -(4-fluoro-phenyl)-2,2-dimethyl-malonamide
289	<i>N</i> -Ethyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
290	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -isopropyl-oxalamide
291	<i>N</i> -Butyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
292	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-methoxy-ethyl)-oxalamide
293	<i>N</i> -Cyclopropylmethyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide
294	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -(2-morpholin-4-yl-ethyl)-oxalamide
295	<i>N</i> -{3-Fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-2-oxo-2-pyrrolidin-1-yl-acetamide
296	<i>N</i> -Ethyl- <i>N'</i> -{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}- <i>N'</i> -methyl-oxalamide and
	a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt, solvate, or hydrate thereof.

Table 3c. Additional Representative c-MET Inhibitors	
Entry	Name
1	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
2	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
3	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(phenylmethyl)cyclopropane-1,1-dicarboxamide
4	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -phenylcyclopropane-1,1-dicarboxamide
5	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide

Table 3c. Additional Representative c-MET Inhibitors	
Entry	Name
6	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperidin-1-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
7	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperidin-1-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
8	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)- <i>N'</i> -(2-phenylethyl)cyclopropane-1,1-dicarboxamide
9	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-methylpyridin-3-yl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
10	<i>N</i> -{4-[(7-chloroquinolin-4-yl)oxy]-3-fluorophenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
11	<i>N</i> -{4-[(7-chloroquinolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
12	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
13	<i>N</i> -(4-{[6,7-bis(methyloxy)quinazolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
14	<i>N</i> -(4-{[6,7-bis(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
15	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
16	<i>N</i> -{5-chloro-6-[(6-(methyloxy)-7-[(1-methylpiperidin-4-yl)methyl]oxy}quinolin-4-yl)oxy]pyridin-3-yl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
17	<i>N</i> -[5-chloro-6-({6-(methyloxy)-7-[(piperidin-4-ylmethyl)oxy]quinolin-4-yl}oxy)pyridin-3-yl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
18	<i>N</i> -[5-chloro-6-({6-(methyloxy)-7-[(phenylmethyl)oxy]quinolin-4-yl}oxy)pyridin-3-yl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
19	<i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
20	<i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
21	<i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-[(1-methylpiperidin-4-yl)methyl]oxy}quinazolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
22	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-methylphenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
23	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[2-methyl-6-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)pyridin-3-yl]cyclopropane-1,1-dicarboxamide
24	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
25	<i>N</i> -(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloro-2-methylpyridin-3-yl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
26	<i>N</i> -[3-fluoro-4-({7-(methyloxy)-6-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
27	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3,5-difluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
28	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2,5-difluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
29	<i>N</i> -[3-fluoro-4-({7-(methyloxy)-6-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
30	<i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-(2-methyl octahydrocyclopenta[c]pyrrol-5-ylmethoxy)quinazolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
31	<i>N</i> -{3-fluoro-4-[(7-(methyloxy)-6-[(1-methylpiperidin-4-yl)methyl]oxy}quinazolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
32	<i>N</i> -[5-fluoro-2-methyl-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
33	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2,3,5-trifluorophenyl)- <i>N'</i> -(4-

Table 3c. Additional Representative c-MET Inhibitors	
Entry	Name
	fluorophenyl)cyclopropane-1,1-dicarboxamide
34	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-2-methylphenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
35	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-chloro-5-methylphenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
36	<i>N</i> -(3-fluoro-4-{[6-hydroxy-7-(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
37	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[2-methyl-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]cyclopropane-1,1-dicarboxamide
38	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperazin-1-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
39	<i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
40	<i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[(1-methylpiperidin-4-yl)methyl]oxy}quinolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
41	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -[4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]cyclopropane-1,1-dicarboxamide
42	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
43	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-chloro-5-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
44	<i>N</i> -(4-{[6,7-bis(methyloxy)-2-(methylthio)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
45	<i>N</i> -(4-fluorophenyl)- <i>N'</i> -(4-{[2-methyl-6,7-bis(methyloxy)quinazolin-4-yl]oxy}phenyl)cyclopropane-1,1-dicarboxamide
46	<i>N</i> -(4-{[2-amino-6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
47	<i>N</i> -(3-fluoro-4-{[2-(methylamino)-6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
48	(1 <i>S</i> ,2 <i>R</i>)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
49	(1 <i>R</i> ,2 <i>R</i>)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
50	<i>N</i> -(4-{[6-{[3-(diethylamino)propyl]oxy}-7-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
51	<i>N</i> -(4-{[6-{[2-(diethylamino)ethyl]oxy}-7-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
52	1,1-dimethylethyl 4-(3-{[4-[(2-fluoro-4-{[(1-{[(4-fluorophenyl)amino]carbonyl}cyclopropyl)carbonyl]amino}phenyl)oxy]-6-(methyloxy)quinolin-7-yl]oxy}propyl)piperazine-1-carboxylate
53	(1 <i>R</i> ,2 <i>R</i>)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
54	(1 <i>R</i> ,2 <i>R</i>)- <i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
55	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
56	<i>N</i> -(4-{[7-{[3-(4-acetylpiperazin-1-yl)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
57	1,1-dimethylethyl 4-(3-{[4-[(2-fluoro-4-{[(1 <i>R</i> ,2 <i>R</i>)-1-{[(4-fluorophenyl)amino]carbonyl}-2-methylcyclopropyl)carbonyl]amino}phenyl)oxy]-6-(methyloxy)quinolin-7-yl]oxy}propyl)piperazine-1-carboxylate
58	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)-1-(phenylmethyl)azetidine-3,3-dicarboxamide
59	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)azetidine-3,3-

Table 3c. Additional Representative c-MET Inhibitors	
Entry	Name
	dicarboxamide
60	(1R,2S)- <i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
61	(1R,2R)- <i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
62	(1R,2R)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperazin-1-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
63	<i>N</i> -(3-fluoro-4-{[7-({3-[4-(1-methylethyl)piperazin-1-yl]propyl}oxy)-6-(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
64	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclopropane-1,1-dicarboxamide
65	(1R,2R)- <i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
66	(1R,2R)- <i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
67	(1R,2S)- <i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
68	(1R,2S)- <i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
69	<i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
70	(1R,2S)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperazin-1-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
71	(1R,2R,3S)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
72	(1R,2R,3S)- <i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
73	(1R,2R,3S)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
74	(1R,2R,3S)- <i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinazolin-4-yl)oxy]phenyl}- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
75	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
76	(2R,3R)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
77	(2R,3R)- <i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
78	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide
79	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide
80	(1R,2R,3S)- <i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
81	<i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide
82	(1R,2R,3S)- <i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
83	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide
84	<i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide
85	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)-

Table 3c. Additional Representative c-MET Inhibitors	
Entry	Name
	<i>N'</i> -(4-fluorophenyl)-2,2-dimethylcyclopropane-1,1-dicarboxamide
86	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
87	<i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinazolin-4-yl]oxy}phenyl}- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
88	<i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperazin-1-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
89	(2R,3R)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
90	<i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
91	<i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinolin-4-yl]oxy}phenyl}- <i>N'</i> -(4-fluorophenyl)cyclobutane-1,1-dicarboxamide
92	(1R,2R)- <i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
93	(1R,2R)- <i>N</i> -{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinazolin-4-yl]oxy}phenyl}- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
94	(2R,3R)- <i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
95	(2R,3R)- <i>N</i> -(4-{[7-{[3-(diethylamino)propyl]oxy}-6-(methyloxy)quinazolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
96	(1R,2R)- <i>N</i> -[3-fluoro-4-({6-(methyloxy)-7-[(3-piperazin-1-ylpropyl)oxy]quinazolin-4-yl}oxy)phenyl]- <i>N'</i> -(4-fluorophenyl)-2-methylcyclopropane-1,1-dicarboxamide
97	(2R,3R)- <i>N</i> -(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)- <i>N'</i> -(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide
98	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[(4-fluorophenyl)methyl]cyclopropane-1,1-dicarboxamide
99	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -(2-morpholin-4-ylethyl)cyclopropane-1,1-dicarboxamide
100	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[2-(piperidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide
101	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[2-(pyrrolidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide
102	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[3-(morpholin-4-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide
103	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[2-(morpholin-4-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide
104	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -phenylcyclopropane-1,1-dicarboxamide
105	<i>N</i> -[3-(aminomethyl)phenyl]- <i>N'</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)cyclopropane-1,1-dicarboxamide
106	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[3-(piperidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide
107	<i>N</i> -(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)- <i>N'</i> -[3-(pyrrolidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide
	a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt, solvate, or hydrate thereof.

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
1	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-(1-

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
	methylethyl)octahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
2	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
3	7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-acetyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)- <i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine
4	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-octahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy}quinazolin-4-amine
5	ethyl (3 <i>aR</i> ,6 <i>aS</i>)-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[c]pyrrole-2(1 <i>H</i>)-carboxylate
6	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-(methysulfonyl)octahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)quinazolin-4-amine
7	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
8	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)quinazolin-4-amine
9	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
10	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
11	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
12	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
13	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
14	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
15	<i>N</i> -(3,4-dichlorophenyl)-7-({[(3 <i>aR</i> ,5 <i>s</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
16	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)-6-(methyloxy)quinazolin-4-amine
17	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl)methyl}oxy)quinazolin-4-amine
18	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-({[(3 <i>R</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
19	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-({[(3 <i>R</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
20	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3 <i>R</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
21	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-({[(3 <i>R</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
22	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3 <i>S</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
23	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3 <i>S</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
24	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-({[(3 <i>S</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl}oxy}-6-(methyloxy)quinazolin-4-amine
25	<i>N</i> -(3,4-dichlorophenyl)-7-[(hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
26	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-{[(3 <i>S</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
27	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-{[(3 <i>S</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
28	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-{[(3 <i>S</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
29	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-{[(3 <i>R</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
30	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-{[(3 <i>R</i> ,9 <i>aS</i>)-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
31	<i>N</i> -(3,4-dichlorophenyl)-7-{[(3 <i>R</i> ,8 <i>aR</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
32	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
33	<i>N</i> -(3,4-dichlorophenyl)-7-{[(3 <i>S</i> ,8 <i>aR</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
34	<i>N</i> -(3,4-dichlorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
35	<i>N</i> -(3,4-dichlorophenyl)-7-{[(3 <i>R</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
36	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
37	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
38	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
39	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
40	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-{[(3 <i>S</i> ,8 <i>aS</i>)-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i>][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine
41	1,4:3,6-dianhydro-5-({[4-[(4-bromo-5-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2- <i>O</i> -methyl- <i>D</i> -xylo-hexitol
42	1,4:3,6-dianhydro-5-deoxy-5-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2- <i>O</i> -methyl- <i>D</i> -glucitol
43	1,4:3,6-dianhydro-5-deoxy-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2- <i>O</i> -methyl- <i>D</i> -xylo-hexitol
44	1,4:3,6-dianhydro-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2- <i>O</i> -methyl- <i>D</i> -xylo-hexitol
45	1,4:3,6-dianhydro-5-({[4-[(3-chloro-2,4-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2- <i>O</i> -methyl- <i>D</i> -xylo-hexitol
46	1,4:3,6-dianhydro-5-({[4-[(4-bromo-2,3-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2- <i>O</i> -methyl- <i>D</i> -glucitol
47	1,4:3,6-dianhydro-2-deoxy-2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5- <i>O</i> -methyl- <i>D</i> -threo-hexitol
48	1,4:3,6-dianhydro-5-deoxy-5-({[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2- <i>O</i> -methyl- <i>D</i> -glucitol
49	(3 <i>S</i> ,9 <i>aS</i>)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydro-2 <i>H</i> -pyrido[1,2- <i>a</i>]pyrazin-1(6 <i>H</i>)-one
50	(3 <i>S</i> ,9 <i>aR</i>)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydro-2 <i>H</i> -pyrido[1,2- <i>a</i>]pyrazin-1(6 <i>H</i>)-one
51	(3 <i>S</i> ,8 <i>aS</i>)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydropyrrolo[1,2- <i>a</i>]pyrazin-1(2 <i>H</i>)-one

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
52	(3S,8aR)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy} methyl)hexahydropyrrolo[1,2-a]pyrazin-1(2H)-one
53	(3S,8aS)-3-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy} methyl)hexahydropyrrolo[1,2-a]pyrazin-1(2H)-one
54	(3S,8aS)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy} methyl)-2-methylhexahydropyrrolo[1,2-a]pyrazin-1(2H)-one
55	<i>N</i> -(3,4-dichlorophenyl)-7-({2-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)amino]ethyl}oxy)-6-(methyloxy)quinazolin-4-amine
56	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{(8aR)-tetrahydro-1H-[1,3]thiazolo[4,3-c][1,4]oxazin-6-ylmethyl}oxy} quinazolin-4-amine
57	<i>N</i> -(3,4-dichlorophenyl)-7-{{2-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)ethyl]oxy}-6-(methyloxy)quinazolin-4-amine
58	<i>N</i> -(3,4-dichlorophenyl)-7-{{[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
59	<i>N</i> -(3,4-dichlorophenyl)-7-{{[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]oxy}-6-(methyloxy)quinazolin-4-amine
60	<i>N</i> -(3,4-dichlorophenyl)-7-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]-6-(methyloxy)quinazolin-4-amine
61	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-5-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
62	1,4:3,6-dianhydro-2-O-[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
63	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
64	1,4:3,6-dianhydro-2-O-methyl-5-O-{6-(methyloxy)-4-[(2,3,4-trichlorophenyl)amino]quinazolin-7-yl}-L-iditol
65	1,4:3,6-dianhydro-5-O-[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-O-methyl-D-xylo-hexitol
66	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-2,3-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
67	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-L-sorbose ethylene glycol acetal
68	1,4:3,6-dianhydro-2-O-[4-[(3-chloro-2,4-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
69	1,4:3,6-dianhydro-2-O-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
70	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-(difluoromethyl)-L-iditol
71	1,4:3,6-dianhydro-2-O-[4-[(3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
72	1,4:3,6-dianhydro-2-O-[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
73	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
74	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-ethyl-L-iditol
75	1,4:3,6-dianhydro-2-O-[4-[(3-bromo-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
76	1,4:3,6-dianhydro-2-O-[4-[(3-chloro-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-L-iditol
77	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-deoxy-D-xylo-hexitol

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
78	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-D-glucitol
79	methyl 3,6-anhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-O-methyl- α -L-idofuranoside
80	3,6-anhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-1,2-O-(1-methylethylidene)- β -L-xylo-hexofuranose
81	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-deoxy-5-methylidene-D-xylo-hexitol
82	methyl 3,6-anhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-O-methyl- β -L-idofuranoside
83	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-[(octahydro-2H-quinolizin-3-ylmethyl)oxy]quinazolin-4-amine
84	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-{6-(methyloxy)-4-[(2,3,4-trifluorophenyl)amino]quinazolin-7-yl}-D-iditol
85	1,4:3,6-dianhydro-5-O-[4-[(2-chloro-4-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
86	1,4:3,6-dianhydro-5-O-[4-[(2-bromo-4-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
87	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(2,6-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
88	1,4:3,6-dianhydro-5-O-[4-[(3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
89	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-[4-{[4-fluoro-3-(trifluoromethyl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-D-iditol
90	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(2,4-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
91	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(2,5-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
92	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(2,3-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
93	1,4:3,6-dianhydro-5-O-[4-[(5-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
94	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(3,5-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
95	1,4:3,6-dianhydro-5-O-[4-[(3-chloro-4-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
96	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-2-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
97	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
98	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-5-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
99	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-{6-(methyloxy)-4-[(2,4,5-trifluorophenyl)amino]quinazolin-7-yl}-D-iditol
100	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-{6-(methyloxy)-4-[(2,4,6-trifluorophenyl)amino]quinazolin-7-yl}-D-iditol
101	1,4:3,6-dianhydro-5-O-[4-({4-[(4-chlorophenyl)oxy]-3,5-difluorophenyl}amino)-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
102	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
103	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-2,3-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
104	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chloro-5-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
105	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
106	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-{6-(methyloxy)-4-[(2,3,4-trichlorophenyl)amino]quinazolin-7-yl}-D-iditol
107	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-{6-(methyloxy)-4-[(3,4,5-trichlorophenyl)amino]quinazolin-7-yl}-D-iditol
108	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
109	1,4:3,6-dianhydro-5-O-[4-[(4-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
110	1,4:3,6-dianhydro-5-O-[4-[(3-chloro-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
111	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(3,4-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
112	1,4:3,6-dianhydro-5-O-[4-[(2-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
113	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-[4-[(2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-D-iditol
114	1,4:3,6-dianhydro-5-O-[4-[(3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
115	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-[4-[(4-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-D-iditol
116	1,4:3,6-dianhydro-5-O-[4-[(4-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
117	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(2,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
118	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(2,5-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
119	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
120	1,4:3,6-dianhydro-5-O-[4-[(2-bromo-4,6-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
121	1,4:3,6-dianhydro-5-O-[4-[[4-chloro-3-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
122	1,4:3,6-dianhydro-5-O-[4-[[2-chloro-5-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
123	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-[4-[[2-fluoro-3-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-D-iditol
124	1,4:3,6-dianhydro-5-O-[4-[[2-bromo-5-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
125	1,4:3,6-dianhydro-5-O-[4-[[2-bromo-4-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
126	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-[4-[[4-fluoro-2-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-D-iditol
127	1,4:3,6-dianhydro-5-O-[4-[[3-bromo-5-(trifluoromethyl)phenyl]amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
128	1,4:3,6-dianhydro-5-O-[4-[(2-bromophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
129	1,4:3,6-dianhydro-5-O-[4-[(3-bromophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
130	1,4:3,6-dianhydro-5-O-[4-[(4-bromophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
131	1,4:3,6-dianhydro-5-O-[4-[(3-bromo-4-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
132	1,4:3,6-dianhydro-5-O-[4-[(5-chloro-2-methylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
133	1,4:3,6-dianhydro-2-deoxy-5-O-[4-[(3,5-dimethylphenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
134	1,4:3,6-dianhydro-5-O-[4-{[2,5-bis(methyloxy)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
135	1,4:3,6-dianhydro-5-O-[4-{[5-chloro-2,4-bis(methyloxy)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
136	1,4:3,6-dianhydro-5-O-[4-{[4-chloro-2,5-bis(methyloxy)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
137	1,4:3,6-dianhydro-5-O-[4-[(3-chloro-2,4-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-fluoro-D-iditol
138	<i>N</i> -(3,4-dichlorophenyl)-7-[(5-{[(dimethylamino)methyl]-1,2,4-oxadiazol-3-yl}methyl)oxy]-6-(methyloxy)quinazolin-4-amine
139	<i>N</i> -(3,4-dichlorophenyl)-7-[(3-{[(dimethylamino)methyl]-1,2,4-oxadiazol-5-yl}methyl)oxy]-6-(methyloxy)quinazolin-4-amine
140	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-{[(4-methylpiperazin-1-yl)methyl]-1,2,4-oxadiazol-5-yl}methyl)oxy]quinazolin-4-amine
141	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-piperidin-4-yl-1,2,4-oxadiazol-3-yl)methyl]oxy]quinazolin-4-amine
142	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-(1-methylpiperidin-4-yl)-1,2,4-oxadiazol-3-yl)methyl]oxy]quinazolin-4-amine
143	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-(morpholin-4-ylmethyl)-1,2,4-oxadiazol-5-yl)methyl]oxy]quinazolin-4-amine
144	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(morpholin-2-ylmethyl)oxy]quinazolin-4-amine
145	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-piperidin-2-yl-1,2,4-oxadiazol-3-yl)methyl]oxy]quinazolin-4-amine
146	<i>N</i> -(3,4-dichlorophenyl)-7-[(2-{[(dimethylamino)methyl]-1,3-thiazol-4-yl}methyl)oxy]-6-(methyloxy)quinazolin-4-amine
147	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-(phenylmethyl)morpholin-2-yl)methyl]oxy]quinazolin-4-amine
148	1,1-dimethylethyl 2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholine-4-carboxylate
149	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl)methyl]oxy]quinazolin-4-amine
150	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-{[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}methyl)oxy]quinazolin-4-amine
151	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-methylmorpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
152	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(1,4-oxazepan-2-ylmethyl)oxy]quinazolin-4-amine
153	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-piperidin-3-yl-1,2,4-oxadiazol-3-yl)methyl]oxy]quinazolin-4-amine
154	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-(1-methylpiperidin-2-yl)-1,2,4-oxadiazol-3-yl)methyl]oxy]quinazolin-4-amine
155	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-methyl-1,4-oxazepan-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
156	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([5-(1-methylpiperidin-3-yl)-1,2,4-oxadiazol-3-yl]methyl)oxy]quinazolin-4-amine
157	<i>N</i> -(3,4-dichlorophenyl)-7-([5-(1,1-dimethylethyl)-1,2,4-oxadiazol-3-yl]methyl)oxy)-6-(methyloxy)quinazolin-4-amine
158	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-phenyl-1,3-thiazol-4-yl)methyl]oxy} quinazolin-4-amine
159	7-[(2,1,3-benzothiadiazol-4-ylmethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
160	<i>N</i> -(3,4-dichlorophenyl)-7-[(5-methylisoxazol-3-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
161	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-methyl-4-phenylisoxazol-3-yl)methyl]oxy} quinazolin-4-amine
162	7-[(1,3-benzothiazol-2-ylmethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
163	7-[(2,1,3-benzoxadiazol-5-ylmethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
164	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([2-(2-thienyl)-1,3-thiazol-4-yl]methyl)oxy]quinazolin-4-amine
165	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(1-phenyl-1H-pyrazol-4-yl)methyl]oxy} quinazolin-4-amine
166	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-[3-(trifluoromethyl)phenyl]-1,2,4-oxadiazol-3-yl]methyl)oxy]quinazolin-4-amine
167	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-[4-(trifluoromethyl)phenyl]-1,2,4-oxadiazol-3-yl]methyl)oxy]quinazolin-4-amine
168	7-([3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]methyl)oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
169	7-([6-bromo-2-(methyloxy)naphthalen-1-yl]methyl)oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
170	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(1,3-thiazol-4-ylmethyl)oxy]quinazolin-4-amine
171	7-[(6-chloropyridin-3-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
172	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(pyridin-4-ylmethyl)oxy]quinazolin-4-amine
173	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-methyl-1,3-thiazol-4-yl)methyl]oxy} quinazolin-4-amine
174	7-[(6-chloro-4H-1,3-benzodioxin-8-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
175	7-[(5-chloro-1-methyl-3-phenyl-1H-pyrazol-4-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
176	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([1-methyl-3-(trifluoromethyl)-1H-thieno[2,3-c]pyrazol-5-yl]methyl)oxy]quinazolin-4-amine
177	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-phenylisoxazol-5-yl)methyl]oxy} quinazolin-4-amine
178	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2,4,6-trimethylphenyl)methyl]oxy} quinazolin-4-amine
179	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(pyridin-3-ylmethyl)oxy]quinazolin-4-amine
180	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-[4-(methyloxy)phenyl]isoxazol-5-yl]methyl)oxy]quinazolin-4-amine
181	<i>N</i> -(3,4-dichlorophenyl)-7-([5-[(2,4-dichlorophenyl)oxy]-1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl]methyl)oxy)-6-(methyloxy)quinazolin-4-amine
182	7-[(cyclopropylmethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
183	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(tetrahydrofuran-2-ylmethyl)oxy]quinazolin-4-amine
184	7-(cyclopentyloxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
185	7-[(2-cyclohexylethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
186	7-[(cyclohexylmethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
187	7-[(cyclobutylmethyl)oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
188	<i>N</i> -(3,4-dichlorophenyl)-7-{[2-(1,3-dioxolan-2-yl)ethyl]oxy}-6-(methyloxy)quinazolin-4-amine
189	<i>N</i> -(3,4-dichlorophenyl)-7-{[2-(1,3-dioxan-2-yl)ethyl]oxy}-6-(methyloxy)quinazolin-4-amine
190	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-morpholin-4-ylethyl)oxy]quinazolin-4-amine
191	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-pyrrolidin-1-ylethyl)oxy]quinazolin-4-amine
192	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-piperidin-1-ylethyl)oxy]quinazolin-4-amine
193	2-(2-{[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}ethyl)-1 <i>H</i> -isoindole-1,3(2 <i>H</i>)-dione
194	methyl 6-O-[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-alpha-D-glucopyranoside
195	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-morpholin-4-yl-2-oxoethyl)oxy]quinazolin-4-amine
196	1,1-dimethylethyl 2-[3-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,2,4-oxadiazol-5-yl]piperidine-1-carboxylate
197	1,1-dimethylethyl 4-[3-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,2,4-oxadiazol-5-yl]piperidine-1-carboxylate
198	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(4-pyrrolidin-1-ylphenyl)-1,3-thiazol-2-yl]methyl}oxy)quinazolin-4-amine
199	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-[(4-diethylamino)phenyl]-1,3-thiazol-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
200	5-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,3-thiazol-4-yl]-2-hydroxybenzamide
201	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(4-pyridin-3-yl-1,3-thiazol-2-yl)methyl]oxy}quinazolin-4-amine
202	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(4-pyridin-2-yl-1,3-thiazol-2-yl)methyl]oxy}quinazolin-4-amine
203	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(4-pyridin-4-yl-1,3-thiazol-2-yl)methyl]oxy}quinazolin-4-amine
204	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[2-morpholin-4-yl-1,3-thiazol-4-yl)methyl]oxy}quinazolin-4-amine
205	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[3-morpholin-4-yl-1,2,4-oxadiazol-5-yl)methyl]oxy}quinazolin-4-amine
206	<i>N</i> -(3,4-dichlorophenyl)-7-({[3-(dimethylamino)-1,2,4-oxadiazol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
207	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-2-yl]methyl}oxy)quinazolin-4-amine
208	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4,5,6,7-tetrahydro[1,3]thiazolo[5,4- <i>c</i>]pyridin-2-ylmethyl)oxy]quinazolin-4-amine
209	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(morpholin-4-ylmethyl)-1,3-thiazol-2-yl]methyl}oxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
210	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-[(4-methyl-1,4-diazepan-1-yl)methyl]-1,3-thiazol-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
211	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-[(phenylmethyl)oxy]methyl)-1,2,4-oxadiazol-3-yl)methyl]oxy}quinazolin-4-amine
212	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-ethylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
213	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-piperidin-4-yl-1,3-thiazol-4-yl)methyl]oxy}quinazolin-4-amine
214	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([2-(1-methylpiperidin-4-yl)-1,3-thiazol-4-yl)methyl]oxy}quinazolin-4-amine
215	1,1-dimethylethyl 4-[5-([4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,2,4-oxadiazol-3-yl]piperazine-1-carboxylate
216	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-piperazin-1-yl-1,2,4-oxadiazol-5-yl)methyl]oxy}quinazolin-4-amine
217	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([3-(4-methylpiperazin-1-yl)-1,2,4-oxadiazol-5-yl)methyl]oxy}quinazolin-4-amine
218	<i>N</i> -(3,4-dichlorophenyl)-7-([5-(1-ethylpiperidin-2-yl)-1,2,4-oxadiazol-3-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
219	<i>N</i> -(3,4-dichlorophenyl)-7-([3-(4-ethylpiperazin-1-yl)-1,2,4-oxadiazol-5-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
220	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-[4-(methyloxy)phenyl]-1,2,4-oxadiazol-3-yl)methyl]oxy}quinazolin-4-amine
221	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([2-[4-(trifluoromethyl)phenyl]-1,3-thiazol-4-yl)methyl]oxy}quinazolin-4-amine
222	7-([2-(4-chlorophenyl)-1,3-thiazol-4-yl)methyl]oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
223	<i>N</i> -(3,4-dichlorophenyl)-7-([5-(3,5-dimethylisoxazol-4-yl)-1,2,4-oxadiazol-3-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
224	7-[(5-chloro-1-benzothien-3-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
225	<i>N</i> -(3,4-dichlorophenyl)-7-([3-[4-(1,1-dimethylethyl)phenyl]-1,2,4-oxadiazol-5-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
226	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-[2-(methyloxy)phenyl]-1,2,4-oxadiazol-3-yl)methyl]oxy}quinazolin-4-amine
227	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl)methyl]oxy}quinazolin-4-amine
228	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([1-(phenylmethyl)-1H-imidazol-2-yl)methyl]oxy}quinazolin-4-amine
229	<i>N</i> -(3,4-dichlorophenyl)-7-([3-(2,6-dichlorophenyl)-5-methylisoxazol-4-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
230	<i>N</i> -(3,4-dichlorophenyl)-7-[(6-fluoro-4H-1,3-benzodioxin-8-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
231	7-[(3,5-dibromophenyl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
232	<i>N</i> -(3,4-dichlorophenyl)-7-[(2,6-difluorophenyl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
233	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-([3-[(pyridin-2-ylsulfonyl)methyl]-1,2,4-oxadiazol-5-yl)methyl]oxy}quinazolin-4-amine
234	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]oxy}quinazolin-4-amine
235	7-([4-chloro-2-(trifluoromethyl)quinolin-6-yl)methyl]oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
236	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{[2-(1-methylpyrrolidin-2-yl)ethyl]oxy}quinazolin-4-amine
237	<i>N</i> -(3,4-dichlorophenyl)-7-({[5-(1-ethylpiperidin-4-yl)-1,2,4-oxadiazol-3-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
238	<i>N</i> -(3,4-dichlorophenyl)-7-({[5-(1-ethylpiperidin-3-yl)-1,2,4-oxadiazol-3-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
239	<i>N</i> -(3,4-dichlorophenyl)-7-({[2-(dimethylamino)-1,3-thiazol-4-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
240	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-ethyl-1,4-oxazepan-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
241	<i>N</i> -(3,4-dichlorophenyl)-7-({[2-(1-ethylpiperidin-4-yl)-1,3-thiazol-4-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
242	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-[(2 <i>S</i>)-pyrrolidin-2-yl]-1,2,4-oxadiazol-5-yl)methyl]oxy]quinazolin-4-amine
243	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-[(2 <i>S</i>)-pyrrolidin-2-yl]-1,3-thiazol-4-yl)methyl]oxy]quinazolin-4-amine
244	[4-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,3-thiazol-2-yl]methyl benzoate
245	[4-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,3-thiazol-2-yl]methanol
246	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(5-methyl-4,5,6,7-tetrahydro[1,3]thiazolo[5,4- <i>c</i>]pyridin-2-yl)methyl]oxy}quinazolin-4-amine
247	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-[(4 <i>S</i>)-1,3-thiazolidin-4-yl]-1,3-thiazol-4-yl)methyl]oxy]quinazolin-4-amine
248	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(2-piperidin-2-yl)-1,3-thiazol-4-yl]methyl}oxy}quinazolin-4-amine
249	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[2-(1-methylpiperidin-2-yl)-1,3-thiazol-4-yl]methyl}oxy)quinazolin-4-amine
250	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(2-piperidin-3-yl)-1,3-thiazol-4-yl]methyl}oxy}quinazolin-4-amine
251	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[2-(1-methylpiperidin-3-yl)-1,3-thiazol-4-yl]methyl}oxy)quinazolin-4-amine
252	<i>N</i> -(3,4-dichlorophenyl)-7-({[2-(1-ethylpiperidin-2-yl)-1,3-thiazol-4-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
253	<i>N</i> -(3,4-dichlorophenyl)-7-({[2-(1-ethylpiperidin-3-yl)-1,3-thiazol-4-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
254	<i>N</i> -(3,4-dichlorophenyl)-7-[(3-[(2 <i>S</i>)-1-ethylpyrrolidin-2-yl]-1,2,4-oxadiazol-5-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
255	<i>N</i> -(3,4-dichlorophenyl)-7-[(2-[(2 <i>S</i>)-1-ethylpyrrolidin-2-yl]-1,3-thiazol-4-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
256	<i>N</i> -(3,4-dichlorophenyl)-7-({[(5-ethyl-4,5,6,7-tetrahydro[1,3]thiazolo[5,4- <i>c</i>]pyridin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
257	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(4-propyl-1,4-oxazepan-2-yl)methyl]oxy}quinazolin-4-amine
258	7-({[4-(cyclopropylmethyl)-1,4-oxazepan-2-yl]methyl}oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
259	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-[2-(methyloxy)ethyl]-1,4-oxazepan-2-yl)methyl]oxy]quinazolin-4-amine
260	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(1-methylethyl)-1,4-oxazepan-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
261	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(2-piperazin-1-yl)-1,3-thiazol-4-yl]methyl]oxy}quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
262	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{[(5-pyrrolidin-2-yl-1,2,4-oxadiazol-3-yl)methyl]oxy}quinazolin-4-amine
263	<i>N</i> -(3,4-dichlorophenyl)-7-({[5-(1-ethylpyrrolidin-2-yl)-1,2,4-oxadiazol-3-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
264	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(3-[(2 <i>S</i>)-1-methylpyrrolidin-2-yl]-1,2,4-oxadiazol-5-yl)methyl]oxy]quinazolin-4-amine
265	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(2-[(2 <i>S</i>)-1-methylpyrrolidin-2-yl]-1,3-thiazol-4-yl)methyl]oxy]quinazolin-4-amine
266	<i>N</i> -(3,4-dichlorophenyl)-7-({[2-(4-ethylpiperazin-1-yl)-1,3-thiazol-4-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
267	<i>N</i> -(3,4-dichlorophenyl)-7-[(1,4-dimethylpiperazin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
268	7-{[(4-cyclopentylmorpholin-2-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
269	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(1-methylethyl)morpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
270	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(3-phenylpropyl)morpholin-2-yl)methyl]oxy}quinazolin-4-amine
271	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-[2-(methyloxy)ethyl]morpholin-2-yl)methyl]oxy]quinazolin-4-amine
272	ethyl 2-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]propanoate
273	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-hex-5-en-1-ylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
274	2-({2-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]ethyl}oxy)ethanol
275	methyl 3-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]propanoate
276	6-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]hexanenitrile
277	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(tetrahydro-2 <i>H</i> -pyran-2-yl)methyl]morpholin-2-yl)methyl}oxy]quinazolin-4-amine
278	4-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]butanenitrile
279	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-[(4-fluorophenyl)methyl]morpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
280	methyl 5-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]pentanoate
281	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-oct-7-en-1-ylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
282	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-propylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
283	6-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]hexan-1-ol
284	7-[(4-acetylmorpholin-2-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
285	7-({[4-(cyclopropylmethyl)morpholin-2-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
286	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-prop-2-yn-1-ylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
287	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-pyridin-4-ylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
288	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(pyridin-2-ylmethyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
289	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(pent-2-yn-1-ylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
290	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[2-(4-methylpiperazin-1-yl)-1,3-thiazol-4-yl]methyl}oxy)quinazolin-4-amine
291	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[5-(1-methylpyrrolidin-2-yl)-1,2,4-oxadiazol-3-yl]methyl}oxy)quinazolin-4-amine
292	<i>N</i> -(3-chloro-4-fluorophenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
293	7-{{[4-butyl-1,4-oxazepan-2-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
294	(3,4-dichlorophenyl)[7-(methyloxy)-6-({[4-(2-methylpropyl)-1,4-oxazepan-2-yl]methyl}oxy)quinazolin-4-amine
295	7-{{[4-acetyl-1-ethylpiperazin-2-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
296	(3,4-dichlorophenyl)(6-(methyloxy)-7-{{[4-pentyl-1,4-oxazepan-2-yl)methyl]oxy}quinazolin-4-amine
297	(3,4-dichlorophenyl)[6-(methyloxy)-7-({[4-(tetrahydro-2H-pyran-2-ylmethyl)-1,4-oxazepan-2-yl]methyl}oxy)quinazolin-4-amine
298	(3,4-dichlorophenyl)[6-(methyloxy)-7-({[4-(3-thienylmethyl)-1,4-oxazepan-2-yl]methyl}oxy)quinazolin-4-amine
299	<i>N</i> -[4-chloro-2,5-bis(methyloxy)phenyl]-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
300	<i>N</i> -(3-bromo-2-methylphenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
301	7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)- <i>N</i> -(3,4,5-trichlorophenyl)quinazolin-4-amine
302	<i>N</i> -(3-chloro-2-methylphenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
303	<i>N</i> -(3,4-dichlorophenyl)-7-{{[4-ethanimidoyl-1,4-oxazepan-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
304	<i>N</i> -(4-bromo-2-fluorophenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
305	<i>N</i> -(5-chloro-2-fluorophenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
306	<i>N</i> -(4-chloro-2-fluorophenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
307	<i>N</i> -(2,4-dichlorophenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
308	<i>N</i> -(2,4-dibromophenyl)-7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
309	7-{{[4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)- <i>N</i> -(2,3,4-trichlorophenyl)quinazolin-4-amine
310	<i>N</i> -(3,4-dichlorophenyl)-7-{{[1-ethyl-4-methylpiperazin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
311	<i>N'</i> -cyano-2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholine-4-carboximidamide
312	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[2-(pyrrolidin-1-ylmethyl)-1,3-thiazol-4-yl]methyl}oxy)quinazolin-4-amine
313	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(tetrahydro-2H-pyran-4-yl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
314	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(2-ethylbutyl)morpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
315	7-({[4-(cyclohexylmethyl)morpholin-2-yl]methyl}oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
316	2-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]ethanol
317	7-{{[4-but-2-yn-1-ylmorpholin-2-yl]methyl}oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
318	7-{{[4-cyclobutylmorpholin-2-yl]methyl}oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
319	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-[2-(1,3-dioxolan-2-yl)ethyl]morpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
320	7-({[4-(2-cyclohexylethyl)morpholin-2-yl]methyl}oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
321	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-[2-(1,3-dioxan-2-yl)ethyl]morpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
322	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-(pent-4-en-1-ylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
323	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-[(2 <i>R</i>)-2-methylbutyl]morpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
324	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(4-fluorobutyl)morpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
325	3-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]butan-2-one
326	1-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]butan-2-one
327	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-pentylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
328	<i>N</i> -(3,4-dichlorophenyl)-7-{{[4-hexylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
329	<i>N</i> -(3,4-dichlorophenyl)-7-{{[4-heptylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
330	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-octylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
331	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(2-phenylethyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
332	7-{{[4-butylmorpholin-2-yl)methyl]oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
333	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-prop-2-en-1-ylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
334	2-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]-1-phenylethanone
335	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(2-fluoroethyl)morpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
336	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(3-methylbut-2-en-1-yl)morpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
337	7-[(4-[(2 <i>E</i>)-3-bromoprop-2-en-1-yl]morpholin-2-yl)methyl]oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
338	2-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]acetamide
339	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-[3-(tetrahydro-2 <i>H</i> -pyran-2-yloxy)propyl]-1,4-oxazepan-2-yl)methyl]oxy]quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
340	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(3-methylbutyl)-1,4-oxazepan-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
341	7-({[4-(cyclohexylmethyl)-1,4-oxazepan-2-yl]methyl}oxy)-4-[(3,4-dichlorophenyl)methyl]-6-(methyloxy)quinazoline
342	7-({[4-(2-cyclohexylethyl)-1,4-oxazepan-2-yl]methyl}oxy)-4-[(3,4-dichlorophenyl)methyl]-6-(methyloxy)quinazoline
343	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(2-ethylbutyl)-1,4-oxazepan-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
344	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(methylsulfonyl)-1,4-oxazepan-2-yl]methyl}oxy)quinazolin-4-amine
345	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(1-methylpiperidin-4-yl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
346	<i>N</i> -(3-chloro-2-fluorophenyl)-7-{{[4-(methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
347	<i>N</i> -cyano-2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,4-oxazepan-4-carboximidamide
348	<i>N</i> -(3-bromo-4-methylphenyl)-7-{{[4-(methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
349	<i>N</i> -(3,4-dichlorophenyl)-7-{{[1,4-diethylpiperazin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
350	4-({[4-[(4-bromo-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)- <i>N</i> -cyanopiperidine-1-carboximidamide
351	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(methylsulfonyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
352	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-[(phenylmethyl)sulfonyl]morpholin-2-yl]methyl}oxy}quinazolin-4-amine
353	<i>N</i> -(3,4-dichlorophenyl)-7-{{[4-[(4-fluorophenyl)sulfonyl]morpholin-2-yl]methyl}oxy}-6-(methyloxy)quinazolin-4-amine
354	<i>N</i> -(3,4-dichlorophenyl)-7-({[4-(ethylsulfonyl)morpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
355	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(phenylsulfonyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
356	7-{{[4-[(3-chloropropyl)sulfonyl]morpholin-2-yl]methyl}oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
357	7-({[4-(butylsulfonyl)morpholin-2-yl]methyl}oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
358	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-[(4-methylphenyl)sulfonyl]morpholin-2-yl]methyl}oxy}quinazolin-4-amine
359	<i>N</i> -(3,4-dichlorophenyl)-7-{{[4-[(3,5-dimethylisoxazol-4-yl)carbonyl]morpholin-2-yl]methyl}oxy}-6-(methyloxy)quinazolin-4-amine
360	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[4-{{[3-(methyloxy)phenyl]acetyl}morpholin-2-yl]methyl}oxy}quinazolin-4-amine
361	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(2-methylpentanoyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
362	7-{{[4-[(4-butylphenyl)carbonyl]morpholin-2-yl]methyl}oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
363	7-{{[4-[(4-chlorophenyl)acetyl]morpholin-2-yl]methyl}oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
364	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(2-propylpentanoyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine
365	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[4-(4-methylpentanoyl)morpholin-2-yl]methyl}oxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
366	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-[(2,5-difluorophenyl)carbonyl]morpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
367	7-[(4-(cyclopentylcarbonyl)morpholin-2-yl)methyl]oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
368	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-(2-phenylbutanoyl)morpholin-2-yl)methyl]oxy]quinazolin-4-amine
369	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-[(2,3,6-trifluorophenyl)carbonyl]morpholin-2-yl)methyl]oxy]quinazolin-4-amine
370	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-(furan-3-ylcarbonyl)morpholin-2-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
371	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-propanoylmorpholin-2-yl)methyl]oxy]quinazolin-4-amine
372	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-hexanoylmorpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
373	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-(2-ethylhexanoyl)morpholin-2-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
374	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-(3-phenylpropanoyl)morpholin-2-yl)methyl]oxy]quinazolin-4-amine
375	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-(2,2-dimethylpropanoyl)morpholin-2-yl)methyl]oxy)-6-(methyloxy)quinazolin-4-amine
376	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[(4-(naphthalen-1-ylcarbonyl)morpholin-2-yl)methyl]oxy]quinazolin-4-amine
377	7-[(4-[(2-chloropyridin-3-yl)carbonyl]morpholin-2-yl)methyl]oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
378	7-[(4-[(6-chloropyridin-3-yl)carbonyl]morpholin-2-yl)methyl]oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
379	7-[(4-(1,3-benzodioxol-5-ylcarbonyl)morpholin-2-yl)methyl]oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
380	<i>N</i> -(3,4-dichlorophenyl)-6-[(1-methylethyl)oxy]-7-[(morpholin-2-yl)methyl]oxy]quinazolin-4-amine
381	<i>N</i> -(3,4-dichlorophenyl)-6-[[2-(methyloxy)ethyl]oxy]-7-[(morpholin-2-yl)methyl]oxy]quinazolin-4-amine
382	<i>N</i> -(3,4-dichlorophenyl)-6-(ethyloxy)-7-[(morpholin-2-yl)methyl]oxy]quinazolin-4-amine
383	<i>N</i> -(3,4-dichlorophenyl)-6-(ethyloxy)-7-[(4-methylmorpholin-2-yl)methyl]oxy]quinazolin-4-amine
384	<i>N</i> -(4-bromo-2-methylphenyl)-7-[(4-methylmorpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
385	<i>N</i> -(4-chloro-3-methylphenyl)-7-[(4-methylmorpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
386	<i>N</i> -cyano-2-[(4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy)methyl]- <i>N</i> -methylmorpholine-4-carboximidamide
387	<i>N</i> -(4-bromo-3-chlorophenyl)-7-[(4-methylmorpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
388	<i>N</i> -(3,4-dichlorophenyl)-6-[(1-methylethyl)oxy]-7-[(4-methylmorpholin-2-yl)methyl]oxy]quinazolin-4-amine
389	<i>N</i> -(3,4-dichlorophenyl)-7-[(4-methylmorpholin-2-yl)methyl]oxy]-6-[[2-(methyloxy)ethyl]oxy]quinazolin-4-amine
390	<i>N</i> -(4-bromo-2-chlorophenyl)-7-[(4-methylmorpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine
391	7-[(4-(4-acetyl-1,4-oxazepan-2-yl)methyl]oxy]- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
392	4-[(3,4-dichlorophenyl)amino]-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}quinazolin-6-ol
393	<i>N</i> -(3-bromo-4-chlorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
394	3-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]-3-oxopropanoic acid
395	methyl 4-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl]-4-oxobutanoate
396	<i>N</i> -(3,4-dichlorophenyl)-7-[[[(4-methylmorpholin-3-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
397	<i>N</i> -(3-bromo-2-chlorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
398	<i>N'</i> -cyano-2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)- <i>N</i> -[2-(methyloxy)ethyl]morpholine-4-carboximidamide
399	<i>N'</i> -cyano-2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)- <i>N</i> -ethylmorpholine-4-carboximidamide
400	[(1E)-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl](piperidin-1-yl)methylidene]cyanamide
401	[(1E)-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl](pyrrolidin-1-yl)methylidene]cyanamide
402	[(1E)-[2-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)morpholin-4-yl](4-methylpiperazin-1-yl)methylidene]cyanamide
403	<i>N</i> -(3,4-dichlorophenyl)-7-[[[(6-ethyl-4,6-dimethylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
404	<i>N</i> -(4-bromo-3-methylphenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
405	<i>N</i> -(3,4-dichlorophenyl)-7-[[[(6,6-dimethylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
406	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[[[(4,6,6-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
407	<i>N</i> -(3,4-dichlorophenyl)-7-[[2-(5,5-dimethylmorpholin-2-yl)ethyl]oxy}-6-(methyloxy)quinazolin-4-amine
408	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[[2-(4,5,5-trimethylmorpholin-2-yl)ethyl]oxy}quinazolin-4-amine
409	1,1-dimethylethyl 2-(2-{{[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}ethyl}-5,5-dimethylmorpholine-4-carboxylate
410	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[[[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
411	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
412	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
413	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-[[2-(4,6,6-trimethylmorpholin-2-yl)ethyl]oxy}quinazolin-4-amine
414	<i>N</i> -(4-bromo-2,3-difluorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
415	<i>N</i> -(4-bromo-2,5-difluorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
416	<i>N</i> -(4-bromo-3,5-difluorophenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
417	<i>N</i> -(3,4-dichloro-2-methylphenyl)-7-[[[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
418	<i>N</i> -(3,4-dichlorophenyl)-7-({[(2R,5S,6S)-5,6-dimethylmorpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
419	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(2R,5S,6S)-4,5,6-trimethylmorpholin-2-yl]methyl}oxy)quinazolin-4-amine
420	<i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)-7-({[(2S,5S,6S)-4,5,6-trimethylmorpholin-2-yl]methyl}oxy)quinazolin-4-amine
421	<i>N</i> -(4-bromo-3-chloro-2-methylphenyl)-7-{{[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
422	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-{{[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
423	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-{{[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
424	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-{{[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
425	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-{{[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
426	<i>N</i> -(2,3-dichloro-4-methylphenyl)-7-{{[(4-methylmorpholin-2-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine
427	6-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-3,3,4-trimethylmorpholin-2-one
428	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-6-(methyloxy)-7-{{[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
429	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
430	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
431	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
432	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
433	<i>N</i> -(3-chloro-2,4-difluorophenyl)-6-(methyloxy)-7-{{[(4,5,5-trimethylmorpholin-2-yl)methyl]oxy}quinazolin-4-amine
434	(6S)-6-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-4-methylpiperazin-2-one
435	(6S)-6-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-4-methylpiperazin-2-one
436	(6S)-6-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,4-dimethylpiperazin-2-one
437	(6S)-6-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-1,4-dimethylpiperazin-2-one
438	<i>N</i> -(4-bromo-3-chlorophenyl)-7-{{[(3a'S,4R,6'S,6a'R)-2,2-dimethyltetrahydrospiro[1,3-dioxolane-4,3'-furo[3,2-b]furan]-6'-yl]oxy}-6-(methyloxy)quinazolin-4-amine
439	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-5-C-[(methyloxy)methyl]-L-glucitol
440	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-(methylsulfonyl)-L-glucitol
441	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-L-glucitol
442	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-S-methyl-5-thio-D-iditol
443	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-morpholin-4-yl-D-iditol

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
444	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(4-methylpiperazin-1-yl)-D-iditol
445	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-pyrrolidin-1-yl-D-iditol
446	2-O-acetyl-1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-D-iditol
447	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-D-iditol
448	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(methylsulfonyl)-D-iditol
449	2-amino-1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-D-iditol
450	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(dimethylamino)-D-iditol
451	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(diethylamino)-D-iditol
452	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-piperidin-1-yl-D-iditol
453	2-(acetylamino)-1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-D-iditol
454	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-O-methyl-5-C-(trifluoromethyl)-L-glucitol
455	1,4:3,6-dianhydro-5-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-[(methylsulfonyl)amino]-D-iditol
456	<i>N</i> -(4-bromo-3-chlorophenyl)-6-(methyloxy)-7-[(1-methylpyrrolidin-3-yl)oxy]quinazolin-4-amine
457	<i>N</i> -(4-bromo-3-chlorophenyl)-6-(methyloxy)-7-[(3 <i>R</i>)-tetrahydrofuran-3-yloxy]quinazolin-4-amine
458	<i>N</i> -(4-bromo-3-chlorophenyl)-6-(methyloxy)-7-{[(3 <i>S</i> ,4 <i>R</i>)-4-(methyloxy)tetrahydrofuran-3-yl]oxy} quinazolin-4-amine
459	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-(6-(methyloxy)-4-{[4-(4-methylpiperazin-1-yl)phenyl]amino} quinazolin-7-yl)-D-iditol
460	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5-O-[4-{[3-fluoro-4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-D-iditol
461	1,4:3,6-dianhydro-2-deoxy-5-O-[4-{[2,3-dichloro-4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
462	1,4:3,6-dianhydro-2-deoxy-5-O-[4-{[3,4-dichloro-2-(4-methylpiperazin-1-yl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-fluoro-D-iditol
463	1,4:3,6-dianhydro-2-O-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-C-(trifluoromethyl)-D-glucitol
464	(3,4-dichlorophenyl)[6-(methyloxy)-7-({[4-(tetrahydrofuran-2-ylmethyl)-1,4-oxazepan-2-yl]methyl}oxy)quinazolin-4-amine
465	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,6 <i>aS</i>)-2-(1-methylethyl)octahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
466	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3 <i>aR</i> ,6 <i>aS</i>)-2-(1-methylethyl)octahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
467	7-({[(3 <i>aR</i> ,6 <i>aS</i>)-2-acetyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)- <i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine
468	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3 <i>aR</i> ,6 <i>aS</i>)-octahydrocyclopenta[<i>c</i>]pyrrol-5-ylmethyl]oxy} quinazolin-4-amine

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
469	ethyl (3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-5-[(4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy)methyl]hexahydrocyclopenta[<i>c</i>]pyrrole-2(1 <i>H</i>)-carboxylate
470	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-(methylsulfonyl)octahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine
471	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-ethyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
472	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-(2-methylpropyl)octahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine
473	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
474	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
475	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
476	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
477	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
478	<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
479	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
480	<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
481	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
482	<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
483	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
484	<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
485	<i>N</i> -(3,4-dichlorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
486	<i>N</i> -(3,4-dichlorophenyl)-7-([(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-2-methyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
487	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-ethyloctahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
488	<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-([(3 <i>aR</i> ,6 <i>aS</i>)-2-(2-methylpropyl)octahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine
489	<i>N</i> -(3,4-dichlorophenyl)-7-[(2-[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino}ethyl)oxy]-6-(methyloxy)quinazolin-4-amine
490	<i>N</i> -(3,4-dichlorophenyl)-7-[(2-[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]ethyl)oxy]-6-(methyloxy)quinazolin-4-amine
491	<i>N</i> -(3,4-dichlorophenyl)-7-[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine
492	<i>N</i> -(3,4-dichlorophenyl)-7-[(3-exo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]oxy}-6-(methyloxy)quinazolin-4-amine
493	1,1-dimethylethyl (3 <i>aR</i> ,6 <i>aS</i>)-5-[(4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyl-oxy)quinazolin-7-yl]oxy)methyl]hexahydrocyclopenta[<i>c</i>]pyrrole-2(1 <i>H</i>)-carboxylate

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
494	1,1-dimethylethyl (3 <i>aR</i> ,6 <i>aS</i>)-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl) hexahydrocyclopenta-[<i>c</i>]pyrrole-2(1 <i>H</i>)-carboxylate
495	<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{{{(3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i>)-octahydrocyclopenta[<i>c</i>]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine
496	7-{{{(3- <i>endo</i>)-8-azabicyclo[3.2.1]oct-3-ylmethyl}oxy}- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine
497	1,1-dimethylethyl (3- <i>endo</i>)-3-(2-{{[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}ethyl)-8-azabicyclo[3.2.1]octane-8-carboxylate and
498	7-({2-[(3- <i>endo</i>)-8-azabicyclo[3.2.1]oct-3-yl]ethyl}oxy)- <i>N</i> -(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine and
499	1,4:3,6-Dianhydro-5- <i>O</i> -[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2- <i>O</i> -methyl-D-glucitol
500	3,6-Anhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-1,2- <i>O</i> -(1-methylethylidene)- β -D-idofuranose
501	1,4:3,6-dianhydro-5- <i>O</i> -{4-[(3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl}-2-deoxy-2-fluoro-L- <i>iditol</i>
502	1,4:3,6-dianhydro-2- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5- <i>O</i> -(methylsulfonyl)-D-glucitol
503	1,4:3,6-dianhydro-2- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-D-glucitol
504	1,4:3,6-dianhydro-2- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5- <i>S</i> -methyl-5-thio-L- <i>iditol</i>
505	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-morpholin-4-yl-L- <i>iditol</i>
506	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(4-methylpiperazin-1-yl)-L- <i>iditol</i>
507	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-pyrrolidin-1-yl-L- <i>iditol</i>
508	2- <i>O</i> -acetyl-1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-L- <i>iditol</i>
509	1,4:3,6-dianhydro-2- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-L- <i>iditol</i>
510	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(methylsulfonyl)-L- <i>iditol</i>
511	2-amino-1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-L- <i>iditol</i>
512	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(dimethylamino)-L- <i>iditol</i>
513	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-(diethylamino)-L- <i>iditol</i>
514	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-piperidin-1-yl-L- <i>iditol</i>
515	2-(acetylamino)-1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-L- <i>iditol</i>
516	1,4:3,6-dianhydro-2- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5- <i>O</i> -methyl-5- <i>C</i> -(trifluoromethyl)-D-glucitol
517	1,4:3,6-dianhydro-5- <i>O</i> -[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-deoxy-2-[(methylsulfonyl)amino]-L- <i>iditol</i>
518	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5- <i>O</i> -(6-(methyloxy)-4-{{[4-(4-methylpiperazin-1-yl)phenyl]amino}quinazolin-7-yl})-L- <i>iditol</i>
519	1,4:3,6-dianhydro-2-deoxy-2-fluoro-5- <i>O</i> -[4-{{[3-fluoro-4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl}]L- <i>iditol</i>

Table 4. Representative EGFR and/or VEGFR Inhibitors	
Entry	Name
520	1,4:3,6-dianhydro-2-deoxy-5-O-[4-{[2,3-dichloro-4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-fluoro-L-iditol and
521	1,4:3,6-dianhydro-2-deoxy-5-O-[4-{[3,4-dichloro-2-(4-methylpiperazin-1-yl)phenyl]amino}-6-(methyloxy)quinazolin-7-yl]-2-fluoro-L-iditol and
	a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt, solvate, or hydrate thereof.

Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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Table 5a. Representative IGF-1R Inhibitors	
Entry	Structure
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DEMANDES OU BREVETS VOLUMINEUX

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

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

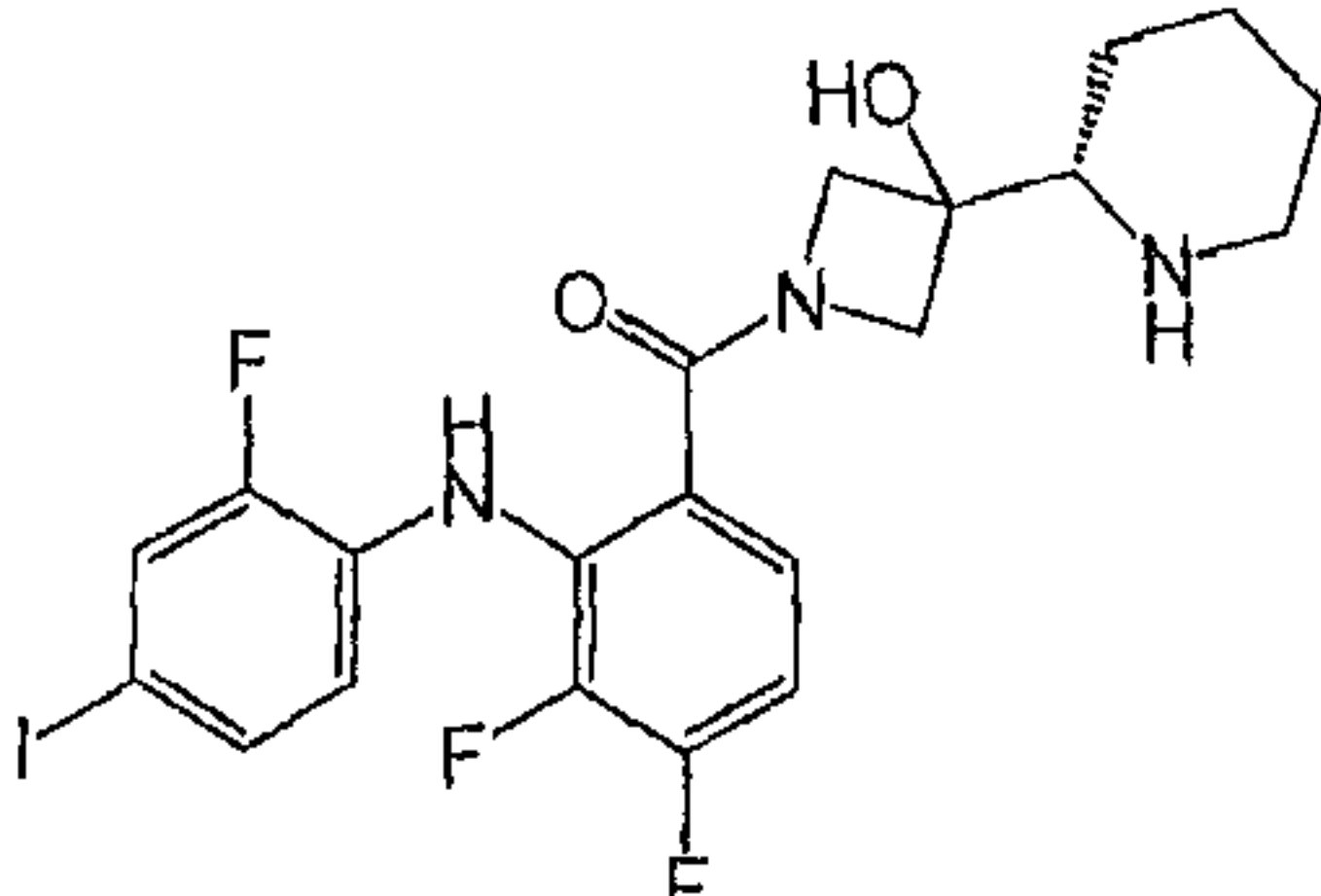
**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

THIS IS VOLUME __1__ OF __2__

NOTE: For additional volumes please contact the Canadian Patent Office.

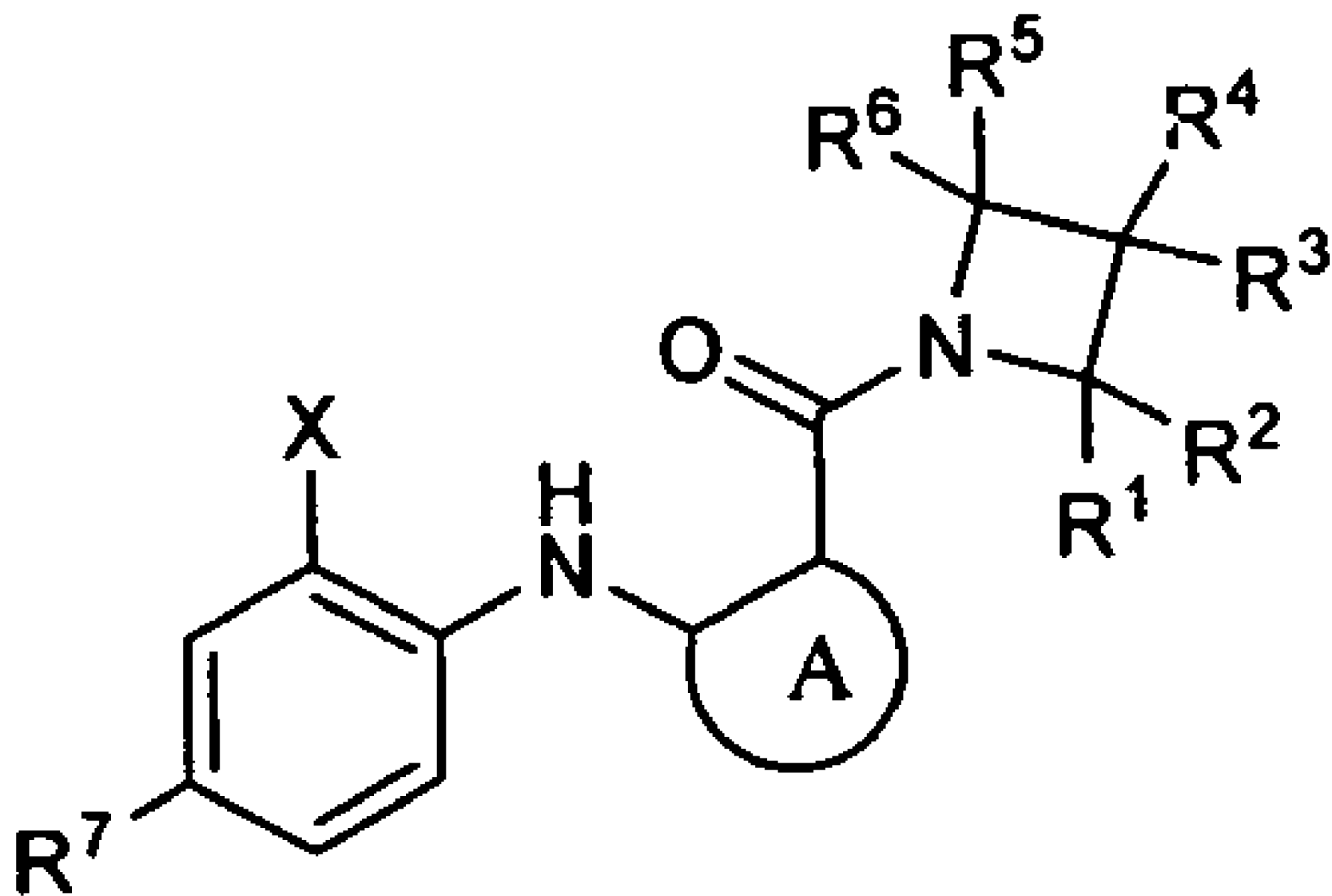
THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. Use of a compound which is:

	1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2S)-piperidin-2-yl]azetidin-3-ol
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or a pharmaceutically acceptable salt thereof; or a pharmaceutical composition comprising a therapeutically effective amount of said compound and a pharmaceutically acceptable carrier, excipient, or diluent; in combination with rapamycin for treatment of melanoma.



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