(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 February 2015 (05.02.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/014993 A2

(51) International Patent Classification:
*C07D 471/04* (2006.01)

(21) International Application Number:
PCT/EP2014/066614

(22) International Filing Date:
1 August 2014 (01.08.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/861,750 2 August 2013 (02.08.2013) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM,

*[Continued on next page]*

(54) Title: ANTI-INFECTIVE COMPOUNDS

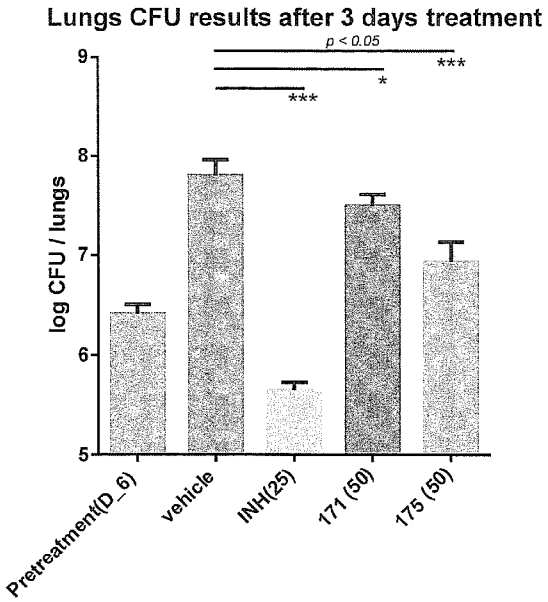


Figure 1

(57) Abstract: The present invention relates to small molecule compounds and their use in the treatment of bacterial infections, in particular Tuberculosis.

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AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

**(84) Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published**:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

## Anti-infective compounds

The present invention relates to small molecule compounds and their use in the treatment of bacterial infections, in particular Tuberculosis.

### Background of the Invention

Tuberculosis (TB) still claims the life of more than 1.8 million people each year. Inadequate use of chemotherapy has led to an increasing number in multi-drug resistant (MDR) TB, and the situation is likely to worsen with the emergence and spread of exensively drug resistant form of the disease (Chaisson R.E.&Nuermberger E.L., N Engl J Med 2012; Zhao Y. et al., N Engl J Med 2012). The most urgent clinical need is to discover potent agents capable of reducing the time of M-XDR tuberculosis therapy with a success rate comparable to susceptible tuberculosis. The last decade has seen the discovery of promising new agent classes for the management of tuberculosis (Stover C.K. *et al.* Nature 2000 ; Andreis K. *et al.* Science 2005; Makarov V. *et al.* Science 2009), several of which are currently under clinical development (Diacon A.H. *et al.* Antimicrob Agents Chemother 2010; Diacon A.H. *et al.* Antimicrob Agents Chemother 2012 ; Gler M.T. *et al.* N Engl J Med 2012). However, given the high attrition rate during clinical development and emergence of resistance, the discovery of additional clinical candidates is clearly needed.

Current chemotherapy consists of compounds that directly target *Mycobacterium tuberculosis* bacillus, by targeting either the synthesis of macromolecules such as DNA, RNA or protein synthesis, or key components of the cell-wall. The most widely used dedicated anti-tubercular drugs isoniazid, ethionamide and pyrazinamide are pro-drugs that first require activation. As active forms, they demonstrate inhibitory activity on primarily cell-wall synthesis and/or on a wide range of mycobacterial targets, which have not yet been fully characterized.

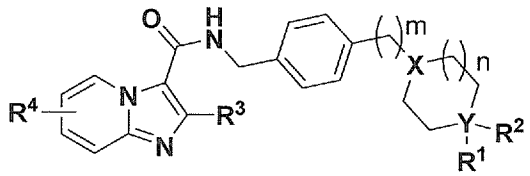
One of the most challenging obstacle in the discovery of new anti-TB drugs is the lack of predictive *in vitro* screening methods that reproduce critical features found *in vivo*. Although there is still a lack of understanding of the biological mechanisms behind tubercle bacillus persistence, i.e. the location and state of latent bacteria in humans, *M. tuberculosis* is thought to persists in primary granulomas (Lenaerts *et al.*, 2007) and within various cell types (Houben *et al.*, 2006; Neyrolles *et al.*, 2006). The bacillus mainly localizes inside phagocytic

cells, such as macrophages and dendritic cells, where it adapts drastically its metabolism to survive the harsh environment found in professional phagocytic cells (Rohde *et al.*, 2007; Schnappinger *et al.*, 2003). Therefore, we developed and used a phenotypic high-content screening technology in infected macrophages to identify novel antitubercular compounds (WO2010003533A2), overcoming many of the numerous and burdensome steps involved with other methodologies (Arain *et al.*, 1996). The technology has several advantages compared to traditional phenotypic screening approaches since it allows i) screening under physiologically relevant conditions, which is notoriously challenging in the field (Pethe K. *et al.* Nat Commun 2010; Stanley S.A. *et al.*, ACS Chem Biol 2012), ii) selection of non-cytotoxic compounds that penetrate effectively inside macrophages, and iii) selection of compounds that are poor substrates for macrophage-induced efflux mechanisms (Adams K.N. *et al.* Cell 2011), thereby compressing the discovery and optimization time of new lead molecules.

It was an object of the present invention to identify compounds effective against bacterial infections, in particular compounds that would prevent *M. tuberculosis* multiplication inside the host macrophage.

**Description of the Invention**

In one aspect, the present invention relates to compounds having the general formula I:



I

wherein

X is CH or N;

Y is CH, O or N;

m is 0 or 1;

n is 0 or 1;

$R^1$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, t-butyl, phenyl, $-NC(O)R^5$, $-OR^5$, $-C(O)R^5$, $-C(O)OR^5$, any of which is optionally substituted;

$R^2$ is, at each occurrence, independently selected from the group consisting of hydrogen and hydroxyl;

$R^3$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^4$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^5$ is, at each occurrence, independently selected from the group consisting of $C_1$-$C_3$ alkylhetorocycle, phenyl and benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof;

wherein, if m is 0, n is 1, X is N, Y is O and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro, 6-methyl, 6-methoxy, 6-bromo, 6-trifluoromethyl, 6-fluoro, 7-chloro, 7-methyl, 7-methoxy, 7-trifluoromethyl, 7-bromo, 8-fluoro, 8-trifluoromethyl, 8-methoxy, or 8-bromo;

wherein, if m is 0, n is 1, X is N and Y is C, $R^1$ is H, $R^2$ is H, $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

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wherein, if m is 0, n is 1, X is N and Y is N, $R^1$ is methyl, $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^2$ is hydroxyl, $R^3$ is ethyl and $R^4$ is 7-chloro, then $R^1$ is not hydrogen;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-fluorobenzyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-chlorophenyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-fluorophenyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-(trifluoromethyl)phenyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-(trifluoromethoxy)phenyl, then $R^4$ is not 6-chloro, 6-trifluoromethyl or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is methyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not 6- chloro or 7-chloro;

wherein, if m is 0, n is 0, X is N, Y is C, $R^1$ is methyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not 6- chloro or 7-chloro;

wherein, if m is 1, n is 1, X is N, Y is N, $R^1$ is 4-(butyramidomethyl)phenyl and $R^3$ is ethyl, then $R^4$ is not 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is N, $R^1$ is 4-fluorophenyl and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-fluoro, 6-chloro, 6-methyl, 6-methoxy, 6-bromo, 7-bromo, 7-chloro, 7-methyl, 7-methoxy , 8-methoxy, 8-bromo or 8-fluoro;

wherein, if m is 0, n is 1, X is N, Y is N, $R^1$ is 4-(trifluoromethoxy)phenyl and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-fluorophenyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-(trifluoromethoxy)phenyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-chlorophenyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

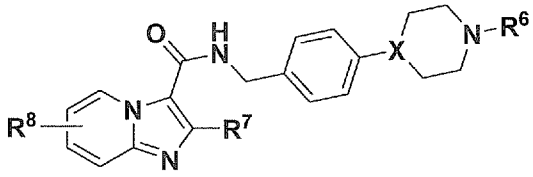
wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-fluorophenyl, $R^2$ is hydroxy and $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is phenyl, $R^2$ is hydroxy and $R^3$ is ethyl, then $R^4$ is not 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is N, $R^1$ is phenyl and $R^3$ is ethyl, then $R^4$ is not 7-chloro.

In one embodiment, m is 0. In one embodiment, m is 0, and $R^1$ is at each occurrence, independently, selected from the group consisting of halogen, methyl, ethyl, t-butyl, phenyl, -$NC(O)R^5$, -$OR^5$, -$C(O)R^5$, -$C(O)OR^5$, any of which is optionally substituted, $R^5$ being as defined further above.

In one aspect, the invention relates to a compound which has the general formula II:



II

wherein
X is CH or N

$R^6$ is, at each occurrence, independently selected from the group consisting of phenyl and $C(O)R^9$ , any of which is optionally substituted;

$R^7$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^8$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^9$ is, at each occurrence, independently selected from the group consisting of phenyl, benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof;

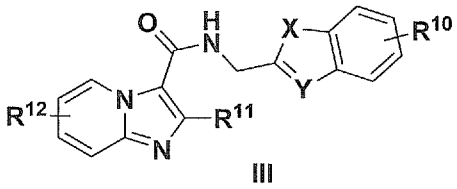
wherein, if X is N, $R^6$ is phenyl and $R^7$ is ethyl, then $R^8$ is not 7-chloro;

wherein, if X is N, $R^6$ is 4-fluorophenyl and $R^7$ is ethyl, then $R^8$ is not hydrogen, 6-fluoro, 6-chloro, 6-methyl, 6-methoxy, 6-bromo, 7-bromo, 7-chloro, 7-methyl, 7-methoxy , 8-methoxy, 8-bromo or 8-fluoro;

wherein, if X is N, $R^6$ is 4-(butyramidomethyl)phenyl and $R^7$ is ethyl, then $R^8$ is not 7-chloro;

wherein, if X is N, $R^6$ is 4-(trifluoromethoxy)phenyl and $R^7$ is ethyl, then $R^8$ is not hydrogen, 6-chloro or 7-chloro.

In one aspect, the invention relates to a compound which has the general formula III:



III

wherein
X is S, O or $NR^{13}$
Y is CH or N

$R^{10}$ is, at each occurrence, independently selected from the group consisting of halogen and phenyl, any of which is optionally substituted;

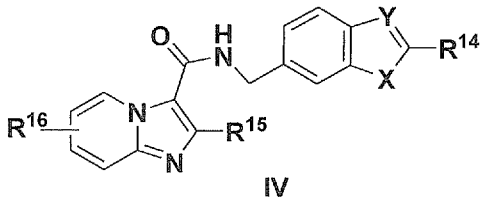
$R^{11}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{12}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^{13}$ is, at each occurrence, independently selected from the group consisting of hydrogen, methyl and benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof.

In one aspect, the invention relates to a compound which has the general formula IV:



IV

wherein

X is S, O or $NR^{17}$

Y is CH or N

$R^{14}$ is, at each occurrence, independently selected from the group consisting of hydrogen, $C_1$-$C_3$ alkyl, $C_1$-$C_3$ alkylheterocycle, phenyl, any of which is optionally substituted;

$R^{15}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{16}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^{17}$ is, at each occurrence, independently selected from the group consisting of hydrogen, methyl and benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof;

wherein, if X is $NR^{17}$, Y is N, $R^{14}$ is 4-(trifluoromethoxy)phenyl, $R^{15}$ is ethyl and $R^{17}$ is hydrogen, then $R^{16}$ is not 6-chloro or 7-chloro;

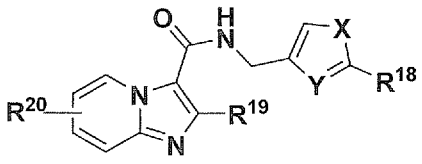
wherein, if X is $NR^{17}$, Y is N, $R^{14}$ is morpholinomethyl, $R^{15}$ is ethyl and $R^{17}$ is hydrogen, then $R^{16}$ is not 7-chloro;

wherein, if X is O, Y is N, $R^{14}$ is 4-(trifluoromethoxy)phenyl, and $R^{15}$ is ethyl, then $R^{16}$ is not 6-chloro or 7-chloro;

wherein, if X is O, Y is N, $R^{14}$ is 4-fluorophenyl, and $R^{15}$ is ethyl, then $R^{16}$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if X is O, Y is N, $R^{14}$ is cyclohexyl, and $R^{15}$ is ethyl, then $R^{16}$ is not 6-chloro or 7-chloro.

In one aspect, the present invention relates to a compound which has the general formula V:



V

wherein

X is S, O or NH

Y is CH or N

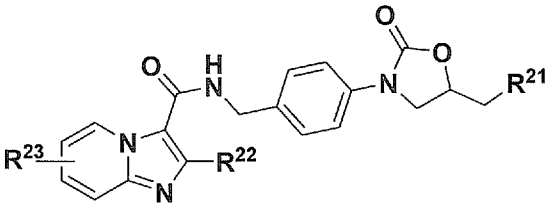
$R^{18}$ is, at each occurrence, independently selected from the group consisting of $C_1$-$C_3$ alkylheterocycle, phenyl and benzyl, any of which is optionally substituted;

$R^{19}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{20}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

In one aspect, the invention relates to a compound which has the general formula VI:



VI

wherein

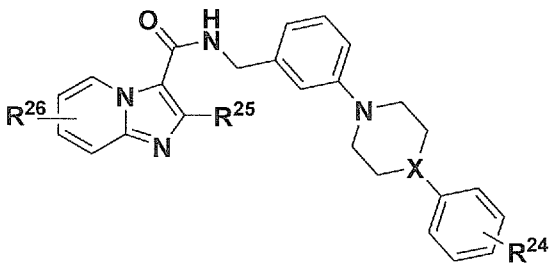
$R^{21}$ is, at each occurrence, independently selected from the group consisting of phenyl and O-phenyl, any of which is optionally substituted;

$R^{22}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{23}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

In one aspect, the invention relates to a compound which has the general formula VII:



VII

wherein
X is CH or N

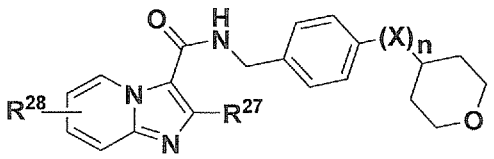
$R^{24}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogens, $C_1$-$C_2$ alkyl, -methoxy, $-CF_3$ and $-OCF_3$;

$R^{25}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{26}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, –methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

In one aspect, the invention relates to a compound which has the general formula VIII:



VIII

wherein

X is $CH_2$ or NH

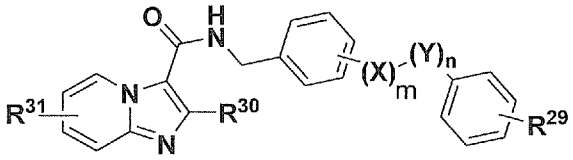
n is 0 or 1

$R^{27}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{28}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

In one aspect, the invention relates to a compound which has the general formula IX:



IX

wherein

X is $CH_2$, $NR^{32}$, O, C(O)NH or –HC=CH-

Y is $CH_2$, or C(O)NH,

m is 0 or 1

n is 0 or 1

$R^{29}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogens, $C_1$-$C_2$ alkyl, -methoxy, COOH, $-CF_3$ and $-OCF_3$;

$R^{30}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{31}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^{32}$ is, at each occurrence, independently selected from the group consisting of hydrogen and methyl;

and pharmaceutically acceptable salts thereof;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is methyl, then $R^{31}$ is not hydrogen;

wherein, if X is *para*-C, m is 0, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is methyl, then $R^{31}$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if X is *para*-C, m is 0, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-chloro or 6-methyl;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-methyl or 6-chloro;

wherein, if X is *para*-C, m is 0, n is 0, $R^{30}$ is ethyl and $R^{31}$ is 6-chloro, then $R^{29}$ is not 2-chloro, 4-chloro, 2-methyl, 3-methyl, 2-trifluoromethyl or 4-methyl;

wherein, if X is *para*-C, m is 0, n is 0, $R^{30}$ is ethyl, $R^{31}$ is 7-chloro, then $R^{29}$ is not hydrogen, 2-chloro, 4-chloro, 2-methyl, 3-methyl, 4-methyl, 4-fluoro, 4-methoxy, 4-trifluoromethoxy, 4-trifluoromethyl or 2-trifluoromethyl;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is 4-trifluoromethoxy and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-chloro or 7-chloro, 6-fluoro, 6-bromo, 6-methyl, 7-methyl or 8-fluoro;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is 4-fluoro and $R^{30}$ is ethyl, then $R^{31}$ is not 6-chloro, 6-bromo or 7-chloro;

Wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is 4-chloro and $R^{30}$ is ethyl, then $R^{31}$ is not 6-chloro or 7-chloro.

wherein, if X is *para*-N, Y is C, m is 1, $R^{29}$ is 4-trifluoromethoxy, $R^{30}$ is ethyl, $R^{31}$ is 7-chloro and $R^{32}$ is hydrogen, then n is not 0 or 1;

wherein, if X is *para*-O, Y is C, m is 1, n is 1, $R^{29}$ is 4-trifluoromethoxy and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-chloro, 6-fluoro, 6-bormo or 7-chloro;

wherein, if X is *para*-O, Y is C, m is 1, n is 1, $R^{29}$ is 4-fluoro and $R^{30}$ is ethyl, then $R^{31}$ is not 6-chloro or 7-chloro;

wherein, if X is *meta*-C, m is 0, n is 0, $R^{30}$ is ethyl and $R^{31}$ is 7-chloro, then $R^{29}$ is not 4-trifluoromethoxy;

wherein, if X is *para*-N, Y is C, m is 1, n is 1, $R^{29}$ is 4-trifluoromethoxy, $R^{30}$ is ethyl and $R^{31}$ is hydrogen, then $R^{32}$ is not methyl.

The term "optionally substituted" as used herein is meant to indicate that a hydrogen atom attached to a member atom within a group, or several such hydrogen atoms, is replaced by a group, such as halogen including fluorine, $C_1$-$C_3$ alkyl, $C_1$-$C_3$ haloalkyl, methylhydroxyl, COOMe, C(O)H, COOH, OMe, or $OCF_3$;

In one embodiment, the present invention also relates to pharmeceutically acceptable salts of the compounds according to the present invention.

The term "alkyl" refers to a monovalent straight or branched chain, saturated aliphatic hydrocarbon radical having a number of carbon atoms in the specified range. Thus, for example, "$C_1$-$C_6$ alkyl" refers to any of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec-, and t-butyl, n- and isopropyl, ethyl and methyl.

The term "alkenyl" refers to a monovalent straight or branched chain aliphatic hydrocarbon radical containing one carbon-carbon double bond and having a number of carbon atoms in the specified range. Thus, for example, "$C_2$-$C_6$ alkenyl" refers to all of the hexenyl and

pentenyl isomers as well as 1-butenyl, 2-butenyl, 3-butenyl, isobutenyl, 1-propenyl, 2-propenyl, and ethenyl (or vinyl).

The term "cycloalkyl", alone or in combination with any other term, refers to a group, such as optionally substituted or non-substituted cyclic hydrocarbon, having from three to eight carbon atoms, unless otherwise defined. Thus, for example, "$C_3$-$C_8$ cycloalkyl" refers to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl.

The term "haloalkyl" refers to an alkyl group, as defined herein that is substituted with at least one halogen. Examples of straight or branched chained "haloalkyl" groups useful in the present invention include, but are not limited to, methyl, ethyl, propyl, isopropyl, *n*-butyl, and *t*-butyl substituted independently with one or more halogens. The term "haloalkyl" should be interpreted to include such substituents such as -$CHF_2$, –$CF_3$, -$CH_2$-$CH_2$-F, -$CH_2$-$CF_3$, and the like.

The term "heteroalkyl" refers to an alkyl group where one or more carbon atoms have been replaced with a heteroatom, such as, O, N, or S. For example, if the carbon atom of alkyl group which is attached to the parent molecule is replaced with a heteroatom (*e.g.*, O, N, or S) the resulting heteroalkyl groups are, respectively, an alkoxy group (*e.g.*, -$OCH_3$, etc.), an amine (*e.g.*, -$NHCH_3$, -$N(CH_3)_2$, etc.), or thioalkyl group (*e.g.*, -$SCH_3$, etc.). If a non-terminal carbon atom of the alkyl group which is not attached to the parent molecule is replaced with a heteroatom (*e.g.*, O, N, or S) and the resulting heteroalkyl groups are, respectively, an alkyl ether (*e.g.*, -$CH_2CH_2$-O-$CH_3$, etc.), alkyl amine (*e.g.*, -$CH_2NHCH_3$, -$CH_2N(CH_3)_2$, etc.), or thioalkyl ether (e.g., -$CH_2$-S-$CH_3$).

The term "halogen" refers to fluorine, chlorine, bromine, or iodine.

The term "phenyl" as used herein is meant to indicate that optionally substituted or non-substituted phenyl group.

The term "benzyl" as used herein is meant to indicate that optionally substituted or non-substituted benzyl group.

The term "heteroaryl" refers to (i) optionally substituted 5- and 6-membered heteroaromatic rings and (ii) optionally substituted 9- and 10-membered bicyclic, fused ring systems in which at least one ring is aromatic, wherein the heteroaromatic ring or the bicyclic, fused ring system contains from 1 to 4 heteroatoms independently selected from N, O, and S, where each N is optionally in the form of an oxide and each S in a ring which is not aromatic is optionally S(O) or $S(O)_2$. Suitable 5- and 6-membered heteroaromatic rings include, for example, pyridyl, pyrrolyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, thienyl, furanyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, and thiadiazolyl. Suitable 9-and 10-membered heterobicyclic, fused ring systems include, for example, benzofuranyl, indolyl, indazolyl, naphthyridinyl, isobenzofuranyl, benzopiperidinyl, benzisoxazolyl, benzoxazolyl, chromenyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, isoindolyl, benzodioxolyl, benzofuranyl, imidazo[1,2-a]pyridinyl, benzotriazolyl, dihydroindolyl, dihydroisoindolyl, indazolyl, indolinyl, isoindolinyl, quinoxalinyl, quinazolinyl, 2,3-dihydrobenzofuranyl, and 2,3-dihydrobenzo-1,4-dioxinyl.

The term "heterocyclyl" refers to (i) optionally substituted 4- to 8-membered, saturated and unsaturated but non-aromatic monocyclic rings containing at least one carbon atom and from 1 to 4 heteroatoms, (ii) optionally substituted bicyclic ring systems containing from 1 to 6 heteroatoms, and (iii) optionally substituted tricyclic ring systems, wherein each ring in (ii) or (iii) is independent of fused to, or bridged with the other ring or rings and each ring is saturated or unsaturated but nonaromatic, and wherein each heteroatom in (i), (ii), and (iii) is independently selected from N, O, and S, wherein each N is optionally in the form of an oxide and each S is optionally oxidized to S(O) or $S(O)_2$. Suitable 4- to 8-membered saturated heterocyclyls include, for example, azetidinyl, piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, azepanyl, diazepanyl, tetrahydropyranyl, tetrahydrothiopyranyl, dioxanyl, and azacyclooctyl. Suitable unsaturated heterocyclic rings include those corresponding to the saturated heterocyclic rings listed in the above sentence in which a single bond is replaced with a double bond. It is understood that the specific rings and ring systems suitable for use in the present invention are not limited to those listed in this and the preceding paragraphs. These rings and ring systems are merely representative.

The term "$MIC_{80}$" refers to the concentration of compound which inhibits bacterial growth, preferably growth of M. tuberculosis, in comparison to a control without any drug after five days by 80%.

In another aspect, the present invention relates to compounds having one of the formulae 1-350 as shown in Tables 1 and 2, preferably one of the formulae 1-21, 23-24, 26, 28-33, 35-57, 59-77, 79-83, 85-87, 90-98, 100-102, 106-111, 113-116 118-124, 126-128, 130-142, 144-150, 153, 155-167, 169-184, 186-188, 190-197, 199, 201, 203-208, 210-211, 213-214, 216, 218-231, 233, 235-246, 252-254, 256-259, 261, 267-270, 273, 279-280, 284-303, 307-316, 319-328, 333-338, 340-350 as shown in Tables 1 and 2, and pharmaceutically acceptable salts thereof. Particularly preferred compounds are compounds having one of the formulae 55, 171, 175 and 325 as shown in Tables 1 and 2. Their pharmaceutical acitivity is also shown in Figure 1.

Preferably, the compounds as defined above have an inhibitory activity on bacterial growth, preferably on the growth of *M. tuberculosis*, inside a host cell, preferably a macrophage, at a concentration between 1-20 μM, preferably less than 1 μM. Preferably, the compounds as defined above have a $MIC_{80}$ of less than 1 μM.

In one aspect, the present invention relates to compounds as defined above for use in the treatment of a bacterial infection, e.g. tuberculosis.

In one aspect, the present invention relates to compounds as defined above for use in the treatment of Tuberculosis.

In one aspect, the present invention relates to a pharmaceutical composition comprising a compound as defined above, and a pharmaceutically acceptable carrier.

In one aspect, the present invention relates to a method of treatment of a bacterial infection, in particular Tuberculosis, comprising the application of a suitable amount of a compound as defined above or of a pharmaceutical composition as defined above to a person in need thereof.

In one embodiment, a "suitable amount", as used herein, is meant to refer to an amount in the range of from 0.01 mg/kg body weight to 1 g/kg body weight.

The objects of the present invention are also solved by a compound that competitively inhibits the specific binding of a compound according to the present invention. Preferably, such specific binding is with respect to a target protein of said compound according to the present invention.

The objects of the present invention are also solved by a method of treatment of a bacterial infection, in particular tuberculosis comprising the application of a suitable amount of a compound which compound is characterized by an ability to competitively inhibit the specific binding of a compound according to the present invention or a pharmaceutical composition according to the present invention, to a target protein, to a person in need thereof.

Pharmaceutical compositions

Pharmaceutically acceptable salts

Examples of pharmaceutically acceptable addition salts include, without limitation, the non-toxic inorganic and organic acid addition salts such as the acetate derived from acetic acid, the aconate derived from aconitic acid, the ascorbate derived from ascorbic acid, the benzenesulfonate derived from benzensulfonic acid, the benzoate derived from benzoic acid, the cinnamate derived from cinnamic acid, the citrate derived from citric acid, the embonate derived from embonic acid, the enantate derived from enanthic acid, the formate derived from formic acid, the fumarate derived from fumaric acid, the glutamate derived from glutamic acid, the glycolate derived from glycolic acid, the hydrochloride derived from hydrochloric acid, the hydrobromide derived from hydrobromic acid, the lactate derived from lactic acid, the maleate derived from maleic acid, the malonate derived from malonic acid, the mandelate derived from mandelic acid, the methanesulfonate derived from methane sulphonic acid, the naphthalene-2-sulphonate derived from naphtalene-2-sulphonic acid, the nitrate derived from nitric acid, the perchlorate derived from perchloric acid, the phosphate derived from phosphoric acid, the phthalate derived from phthalic acid, the salicylate derived from salicylic acid, the sorbate derived from sorbic acid, the stearate derived from stearic acid, the succinate derived from succinic acid, the sulphate derived from sulphuric acid, the tartrate derived from tartaric acid, the toluene-p-sulphonate derived from p-toluene sulphonic acid, and the like. Such salts may be formed by procedures well known and described in the art.

Other acids such as oxalic acid, which may not be considered pharmaceutically acceptable, may be useful in the preparation of salts useful as intermediates in obtaining a chemical compound of the invention and its pharmaceutically acceptable acid addition salt.

In another embodiment, the compounds of the invention are used in their respective free base form according to the present invention.

Metal salts of a chemical compound of the invention include alkali metal salts, such as the sodium salt of a chemical compound of the invention containing a carboxy group.

The chemical compounds of the invention may be provided in unsolvated or solvated forms together with a pharmaceutically acceptable solvent(s) such as water, ethanol, and the like. Solvated forms may also include hydrated forms such as the monohydrate, the dihydrate, the hemihydrate, the trihydrate, the tetrahydrate, and the like. In general, solvated forms are considered equivalent to unsolvated forms for the purposes of this invention.

Administration and Formulation

The production of medicaments containing the compounds of the invention, its active metabolites or isomers and salts according to the invention and their application can be performed according to well-known pharmaceutical methods.

While the compounds of the invention, useable according to the invention for use in therapy, may be administered in the form of the raw chemical compound, it is preferred to introduce the active ingredient, optionally in the form of a physiologically acceptable salt in a pharmaceutical composition together with one or more adjuvants, excipients, carriers, buffers, diluents, and/or other customary pharmaceutical auxiliaries. Such salts of the compounds of the invention may be anhydrous or solvated.

In a preferred embodiment, the invention provides medicaments comprising a compound useable according to the invention, or a pharmaceutically acceptable salt or derivative thereof, together with one or more pharmaceutically acceptable carriers therefor, and, optionally, other therapeutic and/or prophylactic ingredients. The carrier(s) must be "acceptable" in the sense

of being compatible with the other ingredients of the formulation and not harmful to the recipient thereof.

A medicament of the invention may be those suitable for oral, rectal, bronchial, nasal, topical, buccal, sub-lingual, transdermal, vaginal or parenteral (including cutaneous, subcutaneous, intramuscular, intraperitoneal, intravenous, intraarterial, intracerebral, intraocular injection or infusion) administration, or those in a form suitable for administration by inhalation or insufflation, including powders and liquid aerosol administration, or by sustained release systems. Suitable examples of sustained release systems include semipermeable matrices of solid hydrophobic polymers containing the compound of the invention, which matrices may be in form of shaped articles, e.g. films or microcapsules.

The compounds useable according to the invention, together with a conventional adjuvant, carrier, or diluent, may thus be placed into the form of medicament and unit dosages thereof. Such forms include solids, and in particular tablets, filled capsules, powder and pellet forms, and liquids, in particular aqueous or non-aqueous solutions, suspensions, emulsions, elixirs, and capsules filled with the same, all for oral use, suppositories for rectal administration, and sterile injectable solutions for parenteral use. Such medicament and unit dosage forms thereof may comprise conventional ingredients in conventional proportions, with or without additional active compounds or principles, and such unit dosage forms may contain any suitable effective amount of the active ingredient commensurate with the intended daily dosage range to be employed.

The compounds useable according to the invention can be administered in a wide variety of oral and parenteral dosage forms. It will be obvious to those skilled in the art that the following dosage forms may comprise, as the active component, either a compound(s) useable according to the invention or a pharmaceutically acceptable salt of a compound(s) useable according to the invention.

For preparing a medicament from a compound useable according to the invention, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances which may also act as diluents, flavouring agents,

solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

In powders, the carrier is a finely divided solid which is in a mixture with the finely divided active component. In tablets, the active component is mixed with the carrier having the necessary binding capacity in suitable proportions and compacted in the shape and size desired. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as carrier providing a capsule in which the active component, with or without carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid forms suitable for oral administration.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glyceride or cocoa butter, is first melted and the active component is dispersed homogeneously therein, as by stirring. The molten homogenous mixture is then poured into convenient sized moulds, allowed to cool, and thereby to solidify. Compositions suitable for vaginal administration may be presented as pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate. Liquid preparations include solutions, suspensions, and emulsions, for example, water or water-propylene glycol solutions. For example, parenteral injection liquid preparations can be formulated as solutions in aqueous polyethylene glycol solution.

The chemical compounds according to the present invention may thus be formulated for parenteral administration (e.g. by injection, for example bolus injection or continuous infusion) and may be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers with an added preservative. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulation agents such as suspending, stabilising and/or dispersing agents. Alternatively, the active ingredient may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilization from solution, for constitution with a suitable vehicle, e.g. sterile, pyrogen-free water, before use.

Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavours, stabilising and thickening agents, as desired. Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, or other well known suspending agents.

Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for oral administration. Such liquid forms include solutions, suspensions, and emulsions. These preparations may contain, in addition to the active component, colorants, flavours, stabilisers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

In one embodiment of the present invention, the medicament is applied topically or systemically or via a combination of the two routes.

For administration, the compounds of the present invention may, in one embodiment, be administered in a formulation containing 0,001% to 70% per weight of the compound, preferably between 0,01% to 70% per weight of the compound, even more preferred between 0,1% and 70% per weight of the compound. In one embodiment, a suitable amount of compound administered is in the range of from 0.01 mg/kg body weight to 1 g/kg body weight.

Compositions suitable for administration also include lozenges comprising the active agent in a flavoured base, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert base such as gelatin and glycerol or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

Solutions or suspensions are applied directly to the nasal cavity by conventional means, for example with a dropper, pipette or spray. The compositions may be provided in single or multi-dose form. In the latter case of a dropper or pipette, this may be achieved by the patient administering an appropriate, predetermined volume of the solution or suspension. In the case of a spray, this may be achieved for example by means of a metering atomising spray pump.

Administration to the respiratory tract may also be achieved by means of an aerosol formulation in which the active ingredient is provided in a pressurised pack with a suitable propellant such as a chlorofluorocarbon (CFC) for example dichlorodifluoromethane, trichlorofluoromethane, or dichlorotetrafluoroethane, carbon dioxide, or other suitable gas. The aerosol may conveniently also contain a surfactant such as lecithin. The dose of drug may be controlled by provision of a metered valve.

Alternatively the active ingredients may be provided in the form of a dry powder, for example a powder mix of the compound in a suitable powder base such as lactose, starch, starch derivatives such as hydroxypropylmethyl cellulose and polyvinylpyrrolidone (PVP). Conveniently the powder carrier will form a gel in the nasal cavity. The powder composition may be presented in unit dose form for example in capsules or cartridges of, e.g., gelatin, or blister packs from which the powder may be administered by means of an inhaler.

In compositions intended for administration to the respiratory tract, including intranasal compositions, the compound will generally have a small particle size for example of the order of 5 microns or less. Such a particle size may be obtained by means known in the art, for example by micronization.

When desired, compositions adapted to give sustained release of the active ingredient may be employed.

The pharmaceutical preparations are preferably in unit dosage forms. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packaged tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form. Tablets or capsules for oral administration and liquids for intravenous administration and continuous infusion are preferred compositions.

Further details on techniques for formulation and administration may be found in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing Co. Easton, Pa.).

**Figures and Tables**

Reference is now made to the figures and tables, wherein

**Figure 1** shows the in vivo efficacy of compounds 171 and 175 in a murine model of acute tuberculosis infection.

**Table 1** summarizes imidazopyridine derivatives (general scaffolds I-VId) with their respective inhibitory activities.

**Table 2** summarizes compounds 1-350 in terms of their structures and corresponding characteristics.

**Examples**

The invention is now further described by reference to the following examples which are intended to illustrate, not to limit the scope of the invention.

Example 1: Determination the Minimum Inhibitory Concentration 80% ($MIC_{80}$) of new chemical entities against *M. tuberculosis*

Cell-based assays are key tools in lead finding and optimization of new chemical entities for *Mycobacterium tuberculosis*. The availability of a robust *in vitro* assay for testing the Minimum inhibitory concentration (MIC) of a new chemical entity is an absolute requirement for the success of a program. The microplate broth dilution assay using a *M. tuberculosis* strain expressing the green-fluorescent protein (GFP) was selected as this method i) delivers highly reproducible results, ii) allows screening of large number of compounds, and iii) can be partially automated if required.

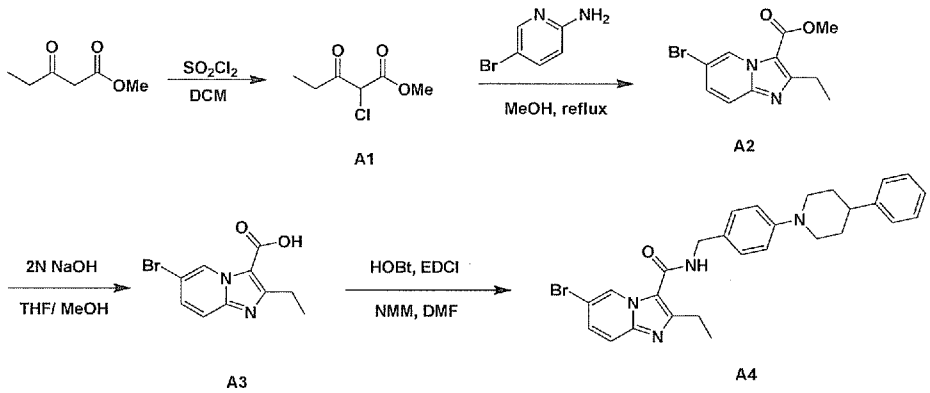
Breiefly, a starting culture of *M. tuberculosis* was prepared by diluting a frozen aliquot in 50mL of 7H9 medium supplemented with glycerol, to an optical density at 600nM ($OD_{600}$) of 0.02. The culture was incubated for 3 days at 37°C to an $OD_{600}$ of 0.2-0.3. The bacteria were the harvested by centrifugation at 3000 rpm, washed once and resuspended to an $OD_{600}$ of 0.1 in 7H9 medium without glycerol. The $OD_{600}$ was finally adjusted to 0.02 and the culture was kept at room temperature before dispensing to the assay plate.

The assay was carried out in 384-well flat bottom microplates in a final volume of 50µl. 25µl of the prepared bacterial working culture was added to the compound test plate containing 0.5µl of serial diluted test compounds.

The plates were incubated at 37°C for 5 days. Bacterial growth was determined after 5 days of incubation by measuring fluorescence intensity at 488nm after 5 days of incubation using the plate reader SPECTRA MAX plus (Molecular Devices®). $MIC_{80}$, the concentration of the compound that inhibits growth compared to the drug free control after 5 days by 80%, were determined using Graph Pad PRISM® software.

Example 2: Derivatization of the imidazopyridine general scaffold

The imidazopyridine compounds (scaffolds I - IX; see **Table 1**) underwent derivatization according to the methods outlined below (**Schemes 1-22**). Resulting derivatives were examined for inhibitory activity (MIC) using the assays described above (Example 1) and the results are summarized in **Table 1**. The synthesized compounds 1-350 are shown in **Table 2**.




**Scheme 1**

**General procedure for the synthesis of A1**

To a solution of methyl 3-oxopentanoate (200 g, 1.55 mol) in anhydrous DCM (500 mL) was added $SO_2Cl_2$ (220 g, 1.63 mol) dropwise at 0 °C, then the mixture was stirred at 25 °C for 16 hours. The reaction mixture was poured into water (500 mL). The organic layer was separated and washed with water (500 mL×3), brine (500 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to afford compound **A1** (245 g, yield: 96%) as a colorless oil which was used for next step without further purification.

**General procedure for the synthesis of A2**

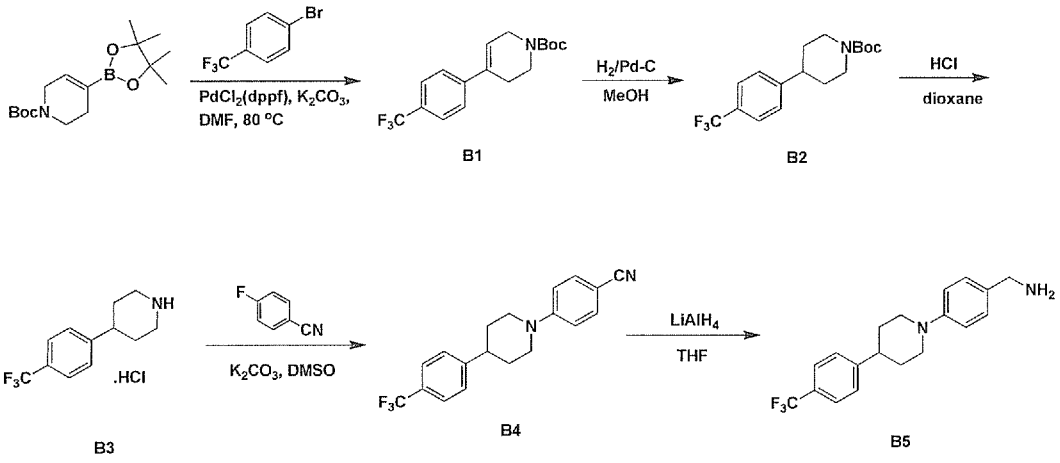
To a solution of 5-bromopyridin-2-amine (10.0 g, 57.8 mmol) in MeOH (10 mL) was added compound **A1** (10.5 g, 63.6 mmol) dropwise at 25 °C, then the mixture was stirred at reflux for 16 hours. The reaction mixture was concentrated. The residue was partitioned between EtOAc (100 mL) and water (100 mL). The organic layer was separated and washed with water (100 mL x 3), brine (100 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by combi flash (PE: EtOAc = 4: 1) to afford compound **A2** (4.00 g, yield: 25%) as a yellow powder.

**General procedure for the synthesis of A3**

To a solution of compound **A2** (3.00 g, 10.6 mmol) in THF (40 mL) and MeOH (20 mL) was added 2N NaOH (40 mL) at 25 °C, then the mixture was stirred at 25 °C for 16 hours. Most of the MeOH and THF were evaporated under reduced pressure. The mixture was then washed with DCM (40 mL x 2). The aqueous layer was then acidified with HCl to pH = 6, No solid was precipitated. The aqueous phase was concentrated under reduced pressure and suspended in DCM/ MeOH= 5: 1 (40 mL) under stirring. The mixture was filtered and the filtrate was concentrated under reduced pressure to afford compound **A3** (2.60 g, yield: 91%) as a white powder.

**General procedure for the synthesis of A4**

To a solution of compound **A3** (60 mg, 0.224 mmol), HOBt (45 mg, 0.336 mmol), EDCI (86 mg, 0.448 mmol) in 1.5 mL DMF was added NMM (136 mg, 1.34mmol). The mixture was stirred at 20°C for 10 minutes. Then (4-(4-phenylpiperidin-1-yl)phenyl)methanamine (40 mg, 0.212 mmol) was added to the mixture and stirred at 30°C for 18 hours. 15 mL of water was added into the mixture and the solid was formed. The mixture was filtered and the filter cake was dissolved in 20 mL DCM and concentrated under reduced pressure to give the crude product **A4**, which was triturated with 3 mL x 2 of $CH_3OH$ twice and 3 mL of $CH_3CN$ in sequence and then filtered and the filter cake was dried to give the pure product **A4** (12 mg, 12%) as a white solid.




**Scheme 2**

**General procedure for the synthesis of B1**

To a suspension of compound 1-bromo-4-(trifluoromethyl)benzene (20.0 g, 89.3 mmol), compound tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (33.1 g, 107 mmol) in DMF (200 mL) was added $K_2CO_3$ (30.3 g, 223 mmol) and $PdCl_2(dppf)$ (1.33 g, 1.79 mmol) under nitrogen. The reaction mixture was stirred at 80 °C under nitrogen for 16 hours. TLC and LCMS showed the reaction was finished. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was partitioned between water (200 mL) and EtOAc (400 mL). The layers were separated and the aqueous layer was extracted with EtOAc (400 mL×2). The combined extracts were washed with water (100 mL×2), dried over anhydrous Na2SO4 and concentrated under reduced pressure. The residue pressure was purified by combi flash (Eluents: PE : THF = 19 : 1) to afford compound Y05_1A (16.0 g, 54.6%yield) as a yellow oil.

**General procedure for the synthesis of B2**

To a solution of **B1** (16.0 g, 48.8 mmol) in MeOH (250 mL) was added Pd/C (10%, 2.50 g) under Ar atmosphere. The suspension was degassed under vacuum and purged with $H_2$ for 3 times. The reaction mixture was stirred at 20℃ under $H_2$ atmosphere (40 psi) for 24 hours. LCMS showed that the reaction was finished. The mixture was filtered through a pad of celite and the filter cake was washed with MeOH (50 mL×3). The combined filtrates were concentrated under reduced pressure to dryness to give compound **B2** (14.0 g, 86.9% yield) as a colorless oil.

**General procedure for the synthesis of B3**

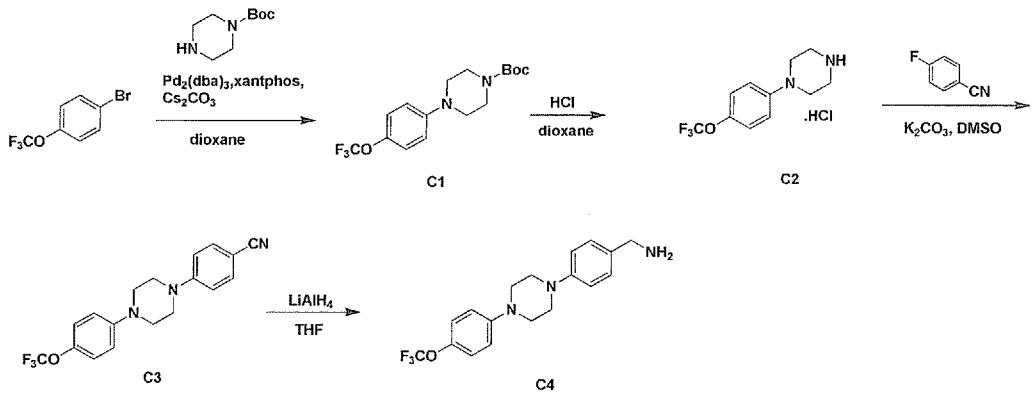
A solution of compound **B2** (14.0 g, 42.4 mmol) in HCl/dioxane (4N, 140 mL) was stirred at 25 °C for 3 hours. LCMS showed the reaction was finished. The reaction mixture was concentrated to dryness to give compound **B3** (14.0 g 92.1% yield) as a white solid.

**General procedure for the synthesis of B4**

To a solution of compound B3 (8.98 g, 39.0 mmol) and 4-fluorobenzonitrile (5.20 g, 43.0 mmol) in anhydrous DMSO (100 mL) was added $K_2CO_3$ (26.9 g, 195 mmol). The reaction mixture was stirred at 120 °C for 16 hours. LCMS indicated the reaction was finished. The mixture was poured into water (200 mL) and collected by filtration. The solid was dissolved in EtOAc (600 mL) which was washed with water (200 mL×3) and washed with brine (200 mL×3), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was triturated with n-hexane (100 mL) to afford compound **B4** (11.0 g, 85.5% yield) as a white solid.

**General procedure for the synthesis of B5**

To a suspension of compound **B4** (7.00 g, 21.2 mmol) in anhydrous THF (120 mL) was added $LiAlH_4$ (4.10 g, 108 mmol) at 0~10 °C. The reaction mixture was refluxed for 3 hours. TLC and LCMS showed the reaction was finished. The reaction mixture was cooled to 0 °C, and quenched with water (4.1 mL), NaOH (10%, 4.1 mL) and THF (120 mL) carefully. The mixture was filtered and the filtrate was dried over anhydrous $Na_2SO_4$, concentrated under reduced pressure. The residue was triturated with n-hexane (100 mL) to afford compound Y05 (5.60 g, crude) as white solid. To a solution of **B5** (5.60 g, crude), in MeOH (150 mL) was added $Boc_2O$ (9.42 g, 42.4 mmol). The mixture was stirred at about 18 °C for 2 hours. LCMS showed the reaction was finished. The solution was concentrated in *vacuo* and the residue was purified by combi flash (Eluents: THF/PE = 1/20) to give compound Y05_Boc (5.80 g, crude). A mixture of **B5**_Boc in HCl/dioxane (4N, 80 mL) was stirred at 18 °C for 3 hours. LCMS showed the reaction was finished. The reaction mixture was concentrated under reduced pressure to give compound **B5** (5.10 g 72.0% yield) as a white solid.




**Scheme 3**

**General procedure for the synthesis of C1**

To a suspension of 1-bromo-4-(trifluoromethoxy)benzene (20.0 g, 83.0 mmol), compound tert-butyl piperazine-1-carboxylate (18.6 g, 99.6 mmol) in dioxane (100 mL) was added $Cs_2CO_3$ (37.8 g, 166 mmol) and $Pd_2(dba)_3$ (1.20 g), Xantphos (1.20 g) under nitrogen. The reaction mixture was stirred at 120 °C under nitrogen for 16 hours. TLC and LCMS showed the reaction was finished. Water (200 mL) was added and the mixture was extracted with EtOAc (100 mL×3 ). The combined organic layers were washed with brine (100 mL×2), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was triturated with MTBE (50 mL) to afford compound **c1** (18.8 g, 65% yield) as a red solid.

**General procedure for the synthesis of C2**

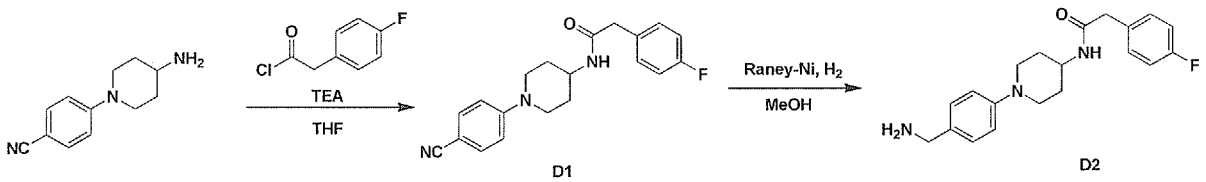
A solution of compound **C1** (18.8 g, 54.0 mmol) in HCl/dioxane (4N, 250 mmol) was stirred at 25 °C for 3 hours. LCMS showed the reaction was finished. The reaction mixture was concentrated to give compound **C2** (13.3 g, crude), which was used to next step directly.

**General procedure for the synthesis of C3**

To a solution of compound **C2** (13.3 g, 54.0 mmol) and 4-fluorobenzonitrile (7.20 g, 59.4 mmol) in anhydrous DMSO (150 mL) was added $K_2CO_3$ (30.0 g, 216 mmol). The reaction mixture was stirred at 120 °C for 16 hours. LCMS indicated the reaction was finished. The mixture was poured into water (600 mL) and collected by filtration. The solid was dissolved in EtOAc (500 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was triturated with n-Hexane/MTBE to afford compound **C3** (11.8 g, 62.9% yield) as brown solid.

**General procedure for the synthesis of C4**

To a suspension of compound **C3** (11.8 g, 34.0 mmol) in anhydrous THF (150 mL) was added $LiAlH_4$ (6.50 g, 170 mmol) at 0~10 °C. The reaction mixture was refluxed for 3 hours. TLC and LCMS showed the reaction was finished. The reaction mixture was cooled to 0 °C, and quenched with water (6.5 mL), NaOH (10%, 6.5 mL), and THF (100 mL) carefully. The mixture was filtered and the filtrate was dried over anhydrous $Na_2SO_4$, concentrated under reduced pressure. The residue was triturated with n-Hexane/MTBE to afford compound **C4** (5.37 g, 45 %yield) as yellow solid.



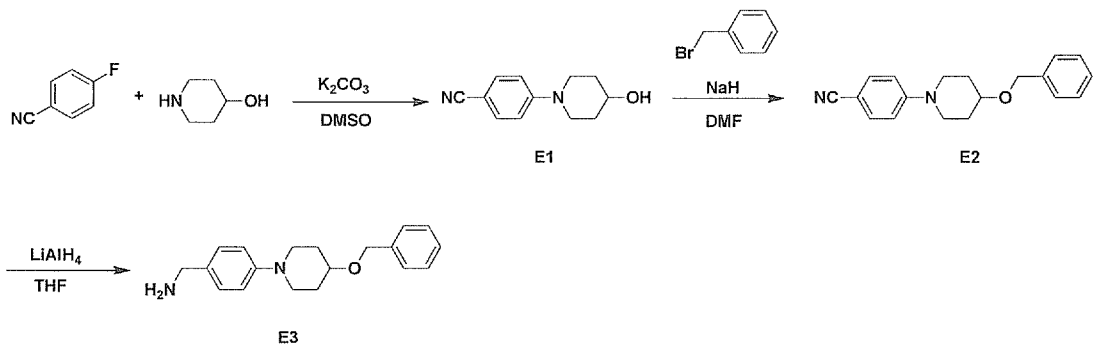

**Scheme 4**

**General procedure for the synthesis of D1**

To a solution of compound 4-(4-aminopiperidin-1-yl)benzonitrile (500 mg, 2.48 mmol) in anhydrous THF (5 mL) was added TEA (754 mg, 7.45 mmol) followed by (4-Fluoro-phenyl)-acetyl chloride (514 mg, 2.98 mmol) at 0 °C. After stirring at the temperature for 0.5 hour, the mixture was allowed to warm to 20 °C and stirred for 16 hours. The reaction mixture was diluted with water (100 mL), extracted with EtOAc (50 mL×3). The extracts was washed with brine, dried over $Na_2SO_4$ and concentrated to give a residue which was purified by silica gel column (eluent: PE/EA = 4/1 to 1/2) to afford 380 mg (yield: 45%) of **D1** as a white solid.

**General procedure for the synthesis of D2**

To a solution of compound **D1** (380 mg, 1.13 mmol) in MeOH (10 mL) was added Raney-Ni (50 mg). After stirring at 20 °C for 2 hours, the mixture was filtered and the filtrate was concentrated to give crude product which was purified by silica gel column (eluent: DCM/MeOH = 30/1 to 10/1) to afford 150 mg (yield: 39%) of **D2** as a white solid.




**Scheme 5**

**General procedure for the synthesis of E1**

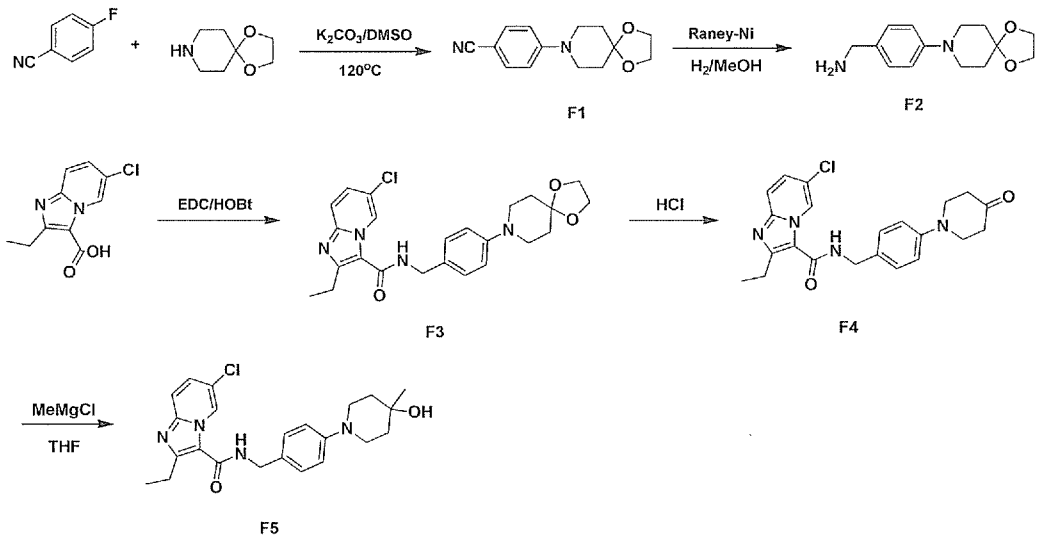
A mixture of 4-fluoro-benzonitrile (5.00 g, 41.3 mmol), piperidin-4-ol (8.35 g, 82.6 mmol) and $K_2CO_3$ (5.71 g, 41.3 mmol) in DMSO (50 mL) was stirred at 120 °C for 16 hours. The mixture was diluted with water (100 mL), extracted with EtOAc (100 mL×3). The combined extracts were washed with water (100 mL) and brine (100 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue was purified by silica gel column (eluent: PE/EtOAc = 5/1 to 1/1) to afford 4.70 g (yield: 57%) of **E1** as a white solid.

**General procedure for the synthesis of E2**

To a solution of compound **E1** (1.00 g, 4.94 mmol) in DMF (10 mL) was added NaH (60% dispersion in mineral oil, 237 mg, 5.93 mmol) at 0 °C. After stirring at 0 °C for 0.5 hour, Bromomethyl-benzene (930 mg, 5.4 mmol) was added to the mixture at 0 °C. Then the mixture was allowed to warm to 20°C and stirred for 16 hours. The reaction was quenched with water (100 mL) and extracted with EtOAc (50 mL×3). The combined extracts were washed with water (100 mL) and brine (100 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue was purified by silica gel column (eluent: PE/EtOAc = 4/1 to 1/1) to afford 1.10 g (yield: 78%) of **E2** as a white solid.

**General procedure for the synthesis of E3**

To a solution of compound **E2** (1.00 g, 3.42 mmol) in anhydrous THF (10 mL) was added $LiAlH_4$ (390 mg, 10.2 mmol) at 0 °C. After stirring at 0 °C for 0.5 hour, the mixture was allowed to warm to 20 °C and stirred for 0.5 hour. The reaction was quenched with NaOH solution (0.5 mL), diluted with water (50 mL), extracted with EtOAc (50 mL×3). The extracts was washed with brine, dried over $Na_2SO_4$ and concentrated to give a residue which was purified by silica gel column (eluent: DCM/MeOH = 20/1) to afford 350 mg (yield: 35%) of **E3** as a white solid.




**Scheme 6**

**General procedure for the synthesis of F1**

A mixture of 4-fluoro benzonitrile (10.0 g, 82.0 mmol), 1,4-dioxa-8-azaspiro[4.5]decane (11.8 g, 82.0 mmol) and $K_2CO_3$ (11.4 g, 82.0 mmol) in DMSO (100 mL) was stirred at 100 °C 16 hours. The mixture was diluted with water (200 mL), extracted with EtOAc (250 mL×3). The combined extracts were washed with water (200 mL) and brine (200 mL), dried over anhydrous $Na_2SO_4$ and concentrated to afford 18.0 g (yield: 90%) of **F1** as a yellow solid.

**General procedure for the synthesis of F2**

A solution of compound **F1** (5.00 g, 20.0 mmol) in MeOH (50 mL) was added Raney-Ni (1.0 g). After stirring at the temperature for 4 hours, the mixture was filtered and the filtrate was concentrated to afford **F2** (5.00 g, yield: 98%) as a yellow solid.

**General procedure for the synthesis of F3**

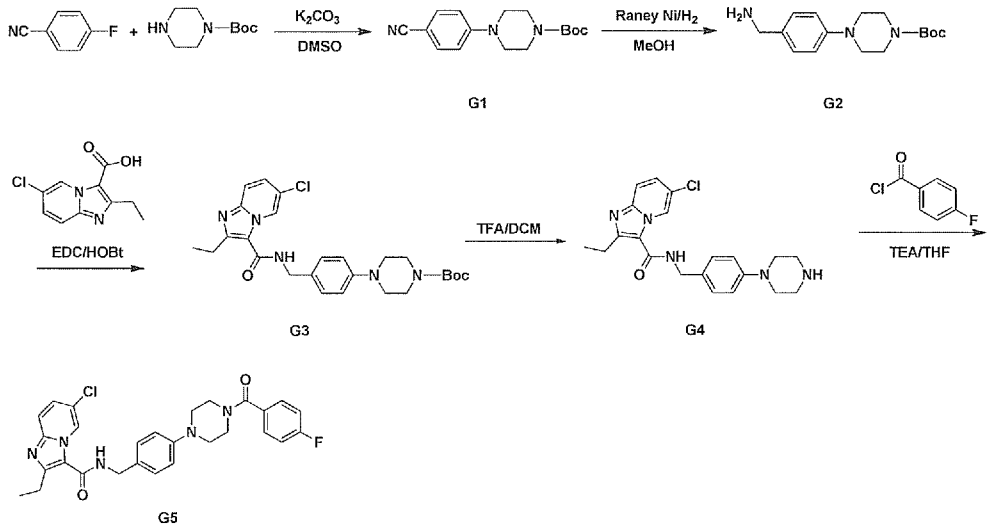
A mixture of compound **F2** (1.10 g, 4.50 mmol), 6-chloro-2-ethylimidazo[1,2-a]pyridine-3-carboxylic acid (1.00 g, 4.50 mmol), EDCI (955 mg, 4.90 mmol), HOBt (661 mg, 4.90 mmol) and TEA (1.30 g, 13.3 mmol) in THF (20 mL) was stirred at 20 °C for 16 hours. Then the mixture was diluted with water (50 mL) and extracted with EtOAc (50 mL×3). The extracts were combined, washed with brine, dried over $Na_2SO_4$ and concentrated to give a residue which was purified by silica gel column (eluent: DCM/MeOH = 20/1 to 15/1) to afford 1.50 g (yield: 75%) of **F3** as a yellow solid.

**General procedure for the synthesis of F4**

A solution of compound **F3** (1.40 g, 3.08 mmol) in THF/HCl (5 mL/5 mL, HCl: 2M) was refluxed for 16 hours. The mixture was diluted with water (80 mL) and basified with NaOH aqueous solution (2M, 5 mL) to pH = 8. Then the mixture was extracted with EtOAc (50 mL×3). The extracts were combined, washed with brine, dried over $Na_2SO_4$ and concentrated to give 1.00 g (yield: 79%) of compound **F4** as a brown solid.

## General procedure for the synthesis of F5

To a solution of compound **F4** (100 mg, 0.24 mmol) in anhydrous THF (5 mL) was added MeMgBr (0.16 mL, 0.48 mmol, 3.0 M in diethyl ether) dropwise at -78°C. The mixture was stirred at the temperature for 0.5 hour. The reaction mixture was quenched with MeOH (1 mL), diluted with water (30 mL), extracted with EtOAc (20 mL×3). The extracts were combined, washed with brine (30 mL), dried over $Na_2SO_4$ and concentrated to give a residue which was purified by Prep-HPLC (0.1% TFA as additive). Most of MeCN was removed under reduced pressure, the remaining solvent was removed by lyophilization to give 27 mg (as TFA salt, yield: 21%) of compound **F5** as pale yellow oil.




**Scheme 7**

## General procedure for the synthesis of G1

To a solution of 4-fluoro-benzonitrile (7.80 g, 63.9 mmol) and 1-Boc-piperazine (10.0 g, 53.7 mmol) in DMSO (200 mL) was added $K_2CO_3$ (14.8 g, 107 mmol). The resulting mixture was stirred at 100 °C for 16 hours. TLC and LCMS showed the reaction was finished. The DMSO solvent was removed in vacuum, and the residue was suspended in water (100 mL), extracted with EtOAc (100 mL×3). The combined extracts were washed with water (100 mL) and brine (100 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue

was purified by re-crystallization from MeOH (150 mL) to afford 7.08 g (yield: 43%) of compound **G1** as a white powder.

**General procedure for the synthesis of G2**

To a solution of **G1** (1.00 g, 3.50 mmol) in MeOH (50 mL) was added Raney-Ni (0.50 g). The suspension was degassed under vacuum and purged with $H_2$ for three times. The reaction mixture was stirred at 20 °C for 4 hours under $H_2$ atmosphere (45 psi). LCMS showed the reaction was completed. The reaction mixture was filtrated and the filtrate was concentrated under reduced pressure and purified by silica gel column (eluent: EtOAc/PE = 3/1 to EtOAc, 1% TEA as additive) to afford 1.00 g (yield: 100%) of compound **G2** as a white powder.

**General procedure for the synthesis of G3**

A mixture of compound 6-chloro-2-ethylimidazo[1,2-a]pyridine-3-carboxylic acid (140 mg, 0.48 mmol), **G2** (90 mg, 0.40 mmol), EDCI (234 mg, 1.20 mmol), HOBt (162 mg, 1.20 mmol) and TEA (121 mg, 2.00 mmol) in THF (10 mL) was stirred at 20 °C for 16 hours. LCMS showed the reaction was finished. The reaction mixture was poured into water (30 mL), extracted with EtOAc (20 mL×3). The combined extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue was purified by silica gel column (eluent: PE/EtOAc = 8/1 to 4/1) to afford 120 mg (yield: 47%) of compound **G3** as a white powder.

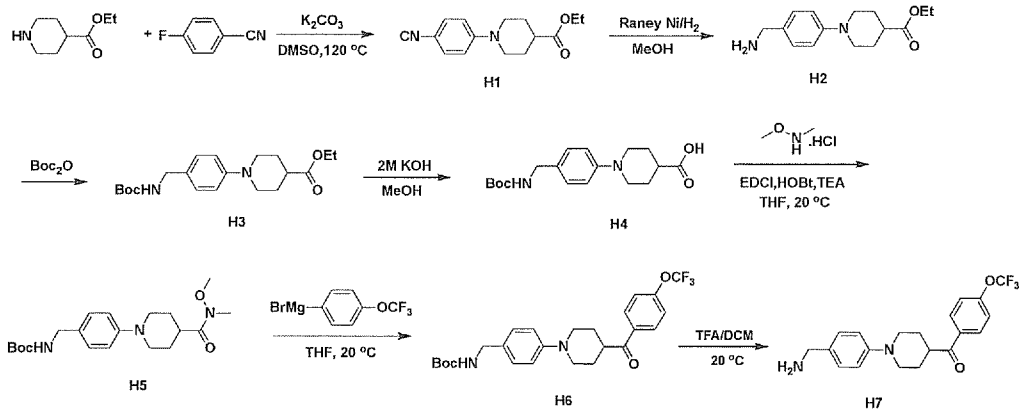
**General procedure for the synthesis of G4**

To a solution of **G3** (120 mg, 0.24 mmol) in DCM (5mL) was added TFA (1.5 mL). The resulting solution was stirred at 20 °C for 6 hours. LCMS showed the reaction was finished. The solvent was removed by concentration to afford 92 mg TFA Salt (yield: 87%) of compound **G4** as a white powder, without further purification for next step.

**General procedure for the synthesis of G5**

To a solution of compound **G4** (45 mg, 0.11 mmol) and TEA (40 mg, 0.55 mmol) in DCM (10 mL) was added dropwise 4-fluorobenzoyl chloride (21 mg, 0.13 mmol). The resulting mixture was stirred at 20 °C for 1.5 hours. LCMS showed the reaction was finished. The reaction mixture was concentrated to give a residue, which was purified by Prep-HPLC (0.1% TFA as additive), most of $CH_3CN$ was removed by evaporation under reduced pressure, and the remaining solvent was removed by lyophilization to afford 35 mg TFA salt (yield: 71%)

of **G5** as a white powder.




**Scheme 8**

**General procedure for the synthesis of H1**

A mixture of compound ethyl piperidine-4-carboxylate (10.0 g, 63.6 mmol), 4-fluorobenzonitrile (8.10 g, 65.5 mmol), $K_2CO_3$ (14.4 g, 104 mmol) in DMSO (150 mL) were stirred at 120 °C for 16 hours. LCMS showed the reaction was finished. After removal of solvent under vacuum, the residue was poured into water (100 mL), extracted with EtOAc (50 mL × 3), the combined extracts were washed with brine (50 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue, which was purified by silica gel column (eluent: PE/EtOAc = 4/1) to afford 9.50 g (yield: 51%) of compound **H1** as a dark oil.

**General procedure for the synthesis of H2**

A mixture of compound **H1** (8.50 g, 33.0 mmol), Raney Ni (1.00 g) in MeOH (300 mL) was stirred at 20 °C under $H_2$ ballon for 4 hours. LCMS showed the reaction was finished. After filtration, the filtrate was concentrated to give a residue, which was purified by silica gel column (eluent: EtOAc, 0.5% TEA as additive) to afford 6.08 g (yield: 71%) of compound **H2** as a white solid.

**General procedure for the synthesis of H3**

A mixture of compound **H2** (6.08 g, 26.0 mmol), $Boc_2O$ (6.83 g, 32.8 mmol) and TEA (2.55 g, 25.7 mmol) in THF (150 mL) was stirred at 20 °C for 16 hours. LCMS showed the reaction was finished. After removal of the solvent, the mixture was poured into water (100 mL), extracted with EtOAc (50 mL×3), the combined extracts were washed with brine (50 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue was purified by

silica gel column (eluent: PE/ EtOAc = 4/1) to afford 6.80 g of crude compound **H3** as a white solid, which was used for the next step without further purification.

**General procedure for the synthesis of H4**

A mixture of compound **H3** (crude, 6.80 g) and 2M KOH (20 mL) in MeOH (100 mL) was stirred at 30 °C for 3 hours. LCMS showed the reaction was finished. After removal of the solvent by concentration, the residue was poured into water (100 mL). The aqueous phase was extracted with EtOAc (30 mL×2) and discarded, the aqueous layer was acidified to pH = 4 with 2M HCl carefully and extracted with EtOAc (50 mL×3). The combined extracts were washed with brine (40 mL) and dried over anhydrous $Na_2SO_4$, concentrated to afford 5.50 g of crude compound **H4** as a white solid, which was used for the next step without further purification.

**General procedure for the synthesis of H5**

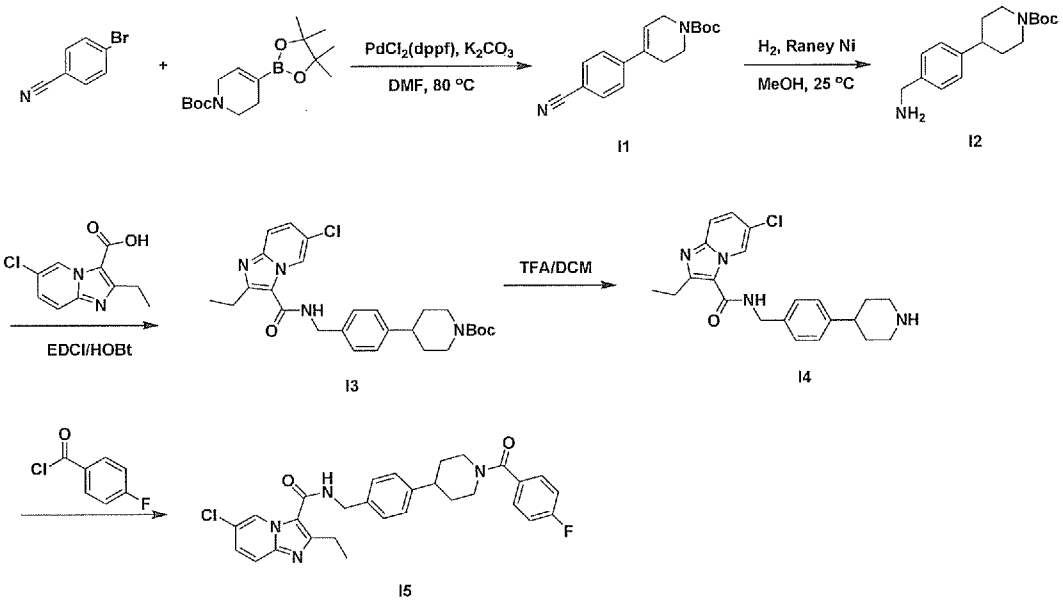
A mixture of compound **H4** (crude, 5.50 g), N,O-dimethylhydroxylamine hydrochloride (4.76 g, 49.0 mmol), EDCI (9.55 g, 49.0 mmol), HOBt (6.62 g, 49.0 mmol) and TEA (10.3 g, 82.0 mmol) in THF (150 mL) was stirred stirred at 20 °C for 12 hours. LCMS showed the reaction was finished. After removal of the solvent under reduced pressure, the mixture was poured into water (100 mL), extracted with EtOAc (70 mL×3). The combined extracts were washed with brine (50 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue, which was purified by silica gel column (eluent: PE/EtOAc = 4/1) to afford 5.80 g (3-step yield: 63%) of compound **H5** as a red solid.

**General procedure for the synthesis of H6**

A mixture of Mg (99.6 mg, 4.15 mmol) and 4-(trifluoromethoxy)-phenyl bromide (1.00 g, 4.15 mmol) in anhydrous THF (15 mL) was stirred at 50 °C until Mg almost disappeared. Then a solution of compound **H5** (400 mg, 1.06 mmol) in anhydrous THF (10 mL) was added into the above solution at 0 °C dropwise. The resulting mixture was stirred at 20 °C for another 3 hours. LCMS showed the reaction was finished. After the reaction was quenched with saturated $NH_4Cl$ aqueous solution (20 mL), the mixture was extracted with EtOAc (20 mL×3). The combined extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue, which was purified by silica gel column (eluent: PE/EtOAc = 4/1) to afford 100 mg (yield: 21%) of compound **H6** as a white solid.

**General procedure for the synthesis of H7**

To a solution of compound **H6** (100 mg, 0.21 mmol) in DCM (20 mL) was added TFA (4 mL), then the mixture was stirred at 20 °C for 5 hours. After removal of the solvent under vacuum, the mixture was poured into water (20 mL), extracted with EtOAc (10 mL), the extract was discarded. The aqueous layer was basified to pH = 9.0 with 1M NaOH aqueous solution, extracted with EtOAc (20 mL×3). The combined extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue, which was used directly in next step without further purification.




**Scheme 9**

**General procedure for the synthesis of I1**

A mixture of 4-bromobenzonitrile (1.40 g, 7.80 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (2.00 g, 6.48 mmol), anhydrous potassium carbonate (2.68 g, 19.5mmol) and $PdCl_2$(dppf) (0.95 g, 1.30 mmol) in anhydrous DMF (30 mL) was stirred at 80 °C under nitrogen atmosphere for 16 hours. The reaction mixture was poured into water (100 mL) and extracted with EtOAc (50 mL×3). The combined extracts were washed with water (50 mL) and brine (50 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue was purified by silica gel column (eluent: PE/EtOAc = 8/1) to afford 1.50 g (yield: 83%) of compound **I1** as a yellow oil.

**General procedure for the synthesis of I2**

A mixture of **I1** (1.50 g, 5.00 mmol) and Raney Ni (500 mg) in MeOH (40 mL) was hydrogenated at 25°C under 45 psi of hydrogen pressure for 3 hours. The mixture was filtered

and the **filtrate** was concentrated to give crude product. The crude product was purified by silica gel column (elutent: DCM/MeOH = 10/1, 1% TEA as additive) to afford 635 mg (yield: 42%) of **I2** as a yellow powder.

**General procedure for the synthesis of I3**

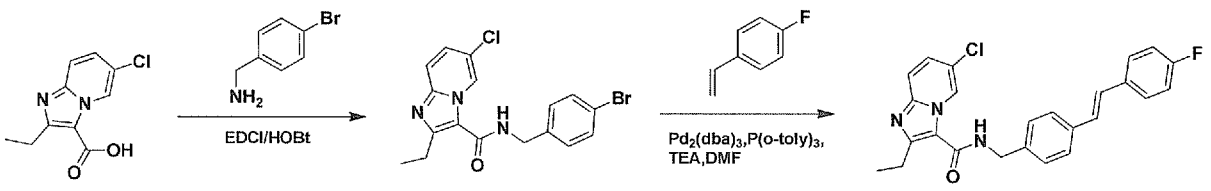
A mixture of compound 6-chloro-2-ethylimidazo[1,2-a]pyridine-3-carboxylic acid (278 mg, 1.24 mmol), **I2** (300 mg, 1.03 mmol), EDCI (242 mg, 3.10 mmol) and HOBT (167 mg, 3.10 mmol) in THF (15 mL) was stirred at 20 °C for 8 hours. The reaction mixture was poured into water (30 mL), extracted with EtOAc (20 mL×3). The combined extracts were washed with water (20 mL) and brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give a residue. The residue was purified by silica gel column (eluent: DCM/MeOH = 10/1, 0.5% TEA as additive) to afford 500 mg (yield: 97%) of **I3** as a yellow power.

**General procedure for the synthesis of I4**

To a solution of **I3** (500 mg, 1.00 mmol) in DCM (16 mL) was added TFA (4 mL) and the resulting mixture was stirred at 20 °C for 5 hours. TLC showed the reaction was finished. The reaction mixture was concentrated to afford 300 mg (as TFA salt, yield: 75%) of crude **I4** as yellow oil, which was used for next step without further purification.

**General procedure for the synthesis of I5**

To a mixture of **I4** (100 mg, 0.25 mmol) and $Et_3N$ (76 mg, 0.75 mmol) in anhydrous THF (10 mL) was added 4-fluorobenzoyl chloride (48 mg, 0.30 mmol) at 0 °C. The resulting mixture was stirred at 20 °C for 30 minutes. LCMS indicated the reaction was complete. The reaction mixture was poured into $H_2O$ (10 mL) extracted with EtOAc (10 mL×3). The combined extracts were washed with brine (10 mL), dried over anhydrous $Na_2SO_4$, and concentrated to give a residue. The residue was purified by Prep-HPLC (0.1% TFA as additive), most of MeCN was removed by concentration, then 0.5 mL conc. HCl was added and the water was removed by lyophilization to afford 26 mg (as HCl salt, yield: 20%) of **I5** as a white power.



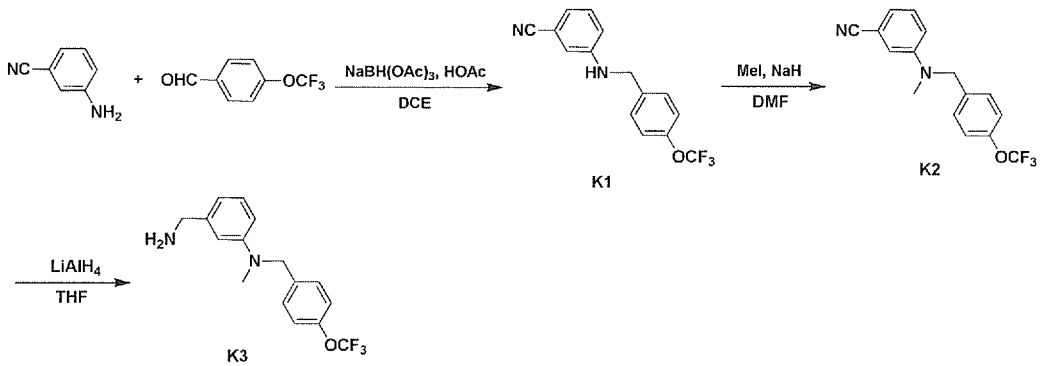

**Scheme 10**

**General procedure for the synthesis of J1**

A mixture of compound 6-chloro-2-ethylimidazo[1,2-a]pyridine-3-carboxylic acid (300 mg, 1.34 mmol, 4-Bromo-benzylamine (248 mg, 1.34 mmol), EDCI (286 mg, 1.47 mmol), HOBt (198 mg, 1.47 mmol) and TEA (405 mg, 4.01 mmol) in anhydrous THF (10 mL) was stirred at 20 °C for 16 hours. Then the mixture was diluted with water (50 mL) and extracted with EtOAc (40 mL×3). The combined extracts were washed with brine (100 mL), dried over anhydrous $Na_2SO_4$ and concentrated to afford 450 mg (yield: 86%) of compound **J1** which was used directly in next step.

**General procedure for the synthesis of J2**

A mixture of compound **J1** (100 mg, 0.25 mmol), 1-Fluoro-4-vinyl-benzene (46 mg, 0.38 mmol), $Pd_2(dba)_3$ (23 mg, 0.025 mmol), P(o-toly)$_3$ (8 mg, 0.025 mmol) and TEA (129 mg, 1.27 mmol) in DMF (2 mL) was stirred at 100 °C for 16 hours under $N_2$ atmosphere. The reaction mixture was diluted with water (50 mL) and extracted with EtOAc (40 mL×3). The combined extracts were washed with water (100 mL) and brine (100 mL), dried over anhydrous $Na_2SO_4$ and concentrated to give crude product which was purified by prep-HPLC (0.1% $NH_3{\cdot}H_2O$ as additive). Most of MeCN was removed under reduced pressure, the remaining solvent was removed by lyophilization to afford 14 mg (yield: 13%) of **J2** as a white amorphous.




**Scheme 11**

**General procedure for the synthesis of K1**

A solution of 3-aminobenzonitrile (4.12 g, 34.9 mmol), 4-(trifluoromethoxy)benzaldehyde (8.38 g, 44.1 mmol) and HOAc (2.43 g, 40.5 mmol) in DCE (100 mL) was stirred at 25 °C for 3 hours, then the $NaBH(OAc)_3$ (12.7 g, 60.0 mmol) was added into the reaction mixture and the resulting mixture was stirred at 25 °C for 16 hours, TLC showed the reaction was

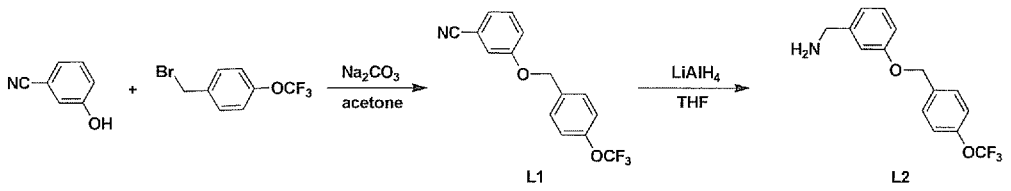
complete. The reaction mixture was basified with aqueous $NaHCO_3$ till pH = 8, extracted with EtOAc (30 mL × 3), the combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give 11.4 g (yield: 98%) of compound **K1** as a yellow solid. LCMS purity: 93%, without further purification for next step.

**General procedure for the synthesis of K2**

A solution of compound **K1** (2.00 g, 6.85 mmol ) in DMF (10 mL ) was added dropwise in portions into the suspension of NaH (0.328 g, 8.20 mmol, 60% dispersion in paraffin oil) in anhydrous DMF (5 mL) with syringe during a period of 10 minutes under $N_2$ while keeping inner temperature between 0 °C to 10 °C. The reaction mixture was allowed to stir at 25 °C for 10 minutes. Then MeI (1.06 g, 7.47 mmol) was added dropwise in portions into the reaction mixture during a period of 10 minutes with syringe while keeping inner temperature between 0 °C and 10 °C and then stirred at 25 °C for 14 hours. the reaction was quenched with saturated aqueous $NH_4Cl$ and extracted with EtOAc ( 30 mL × 3 ), The combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure, The residue was purified by silica gel column (eluent: PE/EtOAc = 12:1) to afford 350 mg (yield: 17%) of compound **K2** as a yellow oil.

**General procedure for the synthesis of K3**

A solution of $LiAlH_4$ (300 mg, 7.89 mmol) in anhydrous THF (10 mL) was stirred at 0 °C for 5 minutes, then a solution of compound **K2** (350 mg, 1.14 mmol) in anhydrous THF (10 mL) was added dropwise in portions into the mixture during a period of 10 minutes and the resulting mixture was refluxed for 3.5 hours, the reaction was quenched with $H_2O$ (5 mL) and 15% aqueous NaOH (3 mL) and $H_2O$ (10 mL) in turn, the mixture was extracted with EtOAc (15 mL × 3), the combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give 300 mg (yield: 85%) of compound **K3** as a colorless oil.



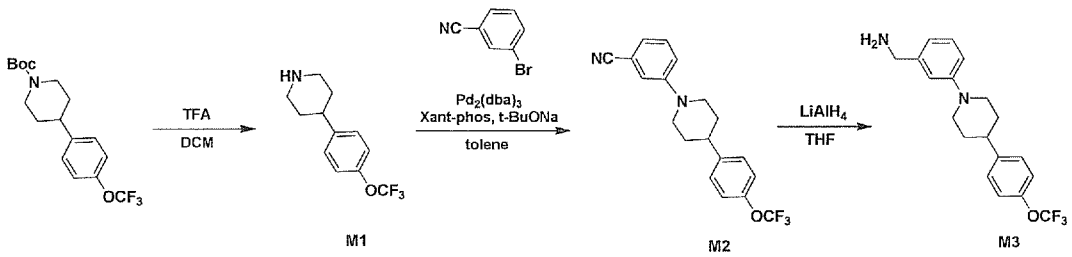

**Scheme 12**

**General procedure for the synthesis of L1**

A solution of 3-cyanophenol (1.40 g, 11.8 mmol), 4-(trifluoromethoxy)benzyl bromide (3.29 g , 13.0 mmol) and $Na_2CO_3$ (3.23 g , 23.4 mmol) in acetone (100 mL) was stirred while maintaining gentle reflux for 15 hours, the TLC showed that the reaction was completed. The reaction mixture was filtered to remove the precipitate. The solution was extracted with EtOAc (20 mL × 3), the combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to dryness, then the crude product was purified by silica gel column (eluent: PE/EtOAc = 12/1) to give 3.01 g ( yield: 87% ) of compound **L1** as a colourless oil.

**General procedure for the synthesis of L2**

A solution of $LiAlH_4$ (325 mg, 8.55 mmol) in THF (10 mL) was stirred at 0 °C for 5 minutes, then a solution of 3-3 (500 mg, 1.71 mmol) in THF (10 mL) was added dropwise in portions into the mixture during a period of 10 minutes, and the resulting mixture was refluxed for 3.5 hours, the TLC showed that the reaction was completed. The reaction was quenched with $H_2O$ (3 mL), 15% aqueous NaOH (3 mL) and $H_2O$ (9 mL) in turn, extracted with EtOAc (20 mL × 3), the combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give 480 mg (yield: 96%) of compound **L2** as a colourless oil.




**Scheme 13**

**General procedure for the synthesis of M1**

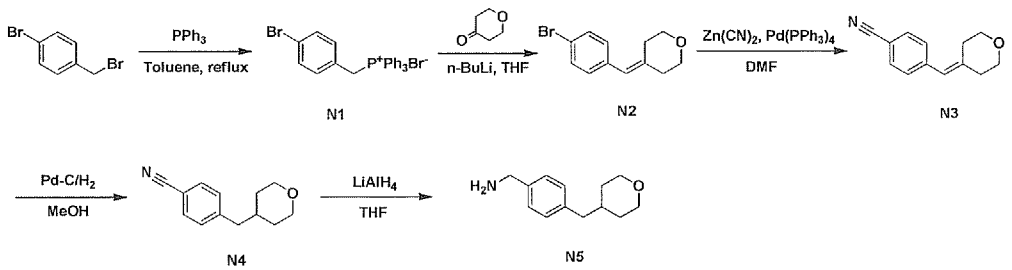
TFA (50 mL) was added dropwise into the solution of compound tert-butyl 4-(4-(trifluoromethoxy)phenyl)piperidine-1-carboxylate (12.5 g, 36.2 mmol) in DCM (100 mL) while keep inner temperature between 0 and 5 °C during a period of 30 minutes, then the reaction mixture was stirred at 25 °C for 17 hours. The reaction mixture was extracted with DCM (20 mL × 3), the combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give 8.50 g (yield: 96%) of compound **M1** as a yellow power.

**General procedure for the synthesis of M2**

A solution of compound **M1** (1.00 g, 4.08 mmol), compound 3-bromophenylisocyanide (890 mg, 4.92 mmol ), $Pd_2(dba)_3$ (750 mg, 0.819 mmol), Xantphos (720 mg, 1.24 mmol) and t-BuONa (1.70 g, 12.3 mmol) in toluene (30 mL) was stirred under $N_2$ at 110 °C for 18 hours. The reaction mixture was quenched with water (20 mL) at 0 °C, then filtered through celite pad. The mixture was extracted with EtOAc (20 mL × 3). The combined extracts was dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to obtain the crude product. The crude product was purified by silica gel chromatography (eluted: PE: EtOAc = 7 : 1) to give 1.00 g (yield: 69%) of compound **M2** as a yellow solid.

**General procedure for the synthesis of M3**

$LiAlH_4$ (280 mg, 7.36 mmol) was added into the THF (5 mL) and stirred under $N_2$ at 0 °C for 30 minutes. Then the solution of compound **M2** (500 mg, 1.44 mmol) in THF (5 mL) was added dropwise into the suspension while keep inner temperature between 0 and 5 °C during a period of 30 minutes. Then the reaction mixture was refluxed for 3.5 hours, TLC showed that the reaction was completed. The reaction was quenched with (3 mL) $H_2O$, 15% aqueous NaOH (3 mL) and $H_2O$ (9 mL) in turn. The mixture was extracted with EtOAc (20 mL × 3), the combined extracts were dried with anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give 390 mg (yield: 83%) of compound **M3** as a yellow oil.




N1 N2 N3 N4 N5

**Scheme 14**

**General procedure for the synthesis of N1**

A solution of 4-bromo benzyl bromide (10.0 g, 40.0 mmol) and $PPh_3$ (10.5 g, 40.0 mmol) in toluene (100 mL) was heated to reflux for 12 hours. After cooled to room temperature, the mixture was filtrated and the filter cake was washed with toluene (200 mL), dried over high vacuum to give compound **N1** (19.5 g, yield: 95%) as a white powder which was used to next step directly.

**General procedure for the synthesis of N2**

To a suspension of compound **N1** (14.4 g, 28.1 mmol) in anhydrous THF (120 mL) was dropwise added *n*-BuLi (11.8 mL, 29.5 mmol, 2.5 M in hexane) at -70 °C, the mixture was stirred at -70 °C for 30 minutes. Then the mixture was warmed to 0 °C, and a solution of tetrahydro-4H-pyran-4-one (2.95 g, 29.5 mmol) in anhydrous THF (10 mL) was dropwise added at 0 - 10 °C. Then the reaction mixture was stirred at 20 °C for 12 hours. Saturated $NH_4Cl$ (100 mL) was added at 0 - 10 °C, then diluted with water (200 mL), extracted with EtOAc (100 mL x 2). The combined organic layer was concentrated under reduced pressure to give the residue, which was purified by silica gel column (eluent: PE/EtOAc = 8/1) to give compound **N2** (4.90 g, yield: 69%) as a yellow oil.

**General procedure for the synthesis of N3**

A mixture of compound **N2** (4.90 g, 19.3 mmol), $Zn(CN)_2$ (2.38 g, 20.3 mmol) and $Pd(PPh_3)_4$ (2.24 g, 1.94 mmol) in DMF (20 mL) was heated to reflux for 1 hour under $N_2$. Then the reaction mixture was diluted with water (100 mL) and EtOAc (100 mL). After filtration, the organic layer was separated and washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure to give a crude oil, which was purified by silica gel column (eluent: PE/EtOAc = 10/1) to give compound **N3** (5.50 g, yield: 69%) as light yellow oil.

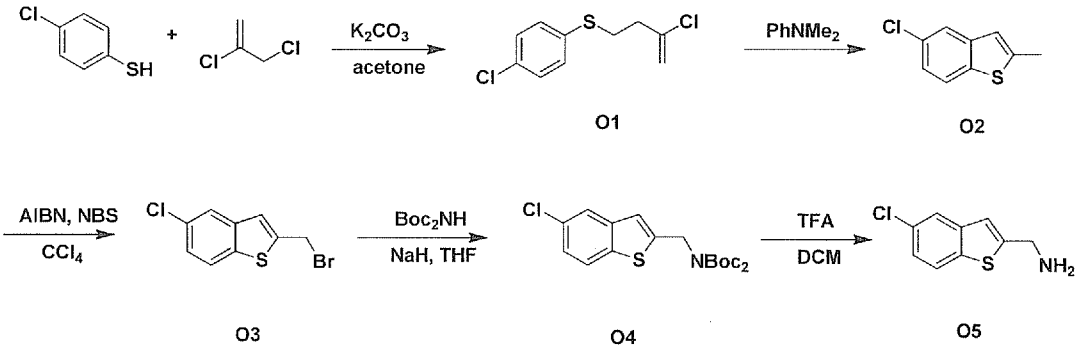
**General procedure for the synthesis of N4**

A mixture of compound **N3** (500 mg, 2.51 mmol) and Pd/C (100 mg, 10%) in MeOH (20 mL) was stirred under $H_2$ (balloon) at 20 °C for 24 hours. The mixture was filtrated and the filtrate was concentrated under reduced pressure to give the crude compound **N4** (420 mg) as a light yellow oil, which was used to next step directly

**General procedure for the synthesis of N5**

To a solution of compound **N4** (400 mg, from above) in anhydrous THF (10 mL) was added $LiAlH_4$ (378 mg, 9.94 mmol) at at 20 °C, the reaction mixture was heated at 70 °C for 12 hours. Water (0.4 mL) and 2M NaOH (0.4 mL) was dropwise added to the reaction mixture at 20 °C to quench the reaction. Then the mixture was filtrated and the cake was washed with THF (20 mL x 2). The combined filtrate was concentrated under reduced pressure to give the crude residue (440 mg) as a light yellow oil. The residue was dissolved in DCM (30 mL) and 1M HCl (30 mL), then extracted with DCM (30 mL x 2). The aqueous layer was adjust to pH = 8 by saturated $NaHCO_3$, then extracted with DCM (40 mL x 3), the combined organic phase

was dried over anhydrous $Na_2SO_4$ and concentrated to give compound **N5** (310 mg, 2 steps yield: 60%) as gum.




**Scheme 15**

**General procedure for the synthesis of O1**

To a mixture of 4-chlorothiophenol (10.0 g, 69.5 mmol) and $K_2CO_3$ (29.0 g, 210 mmol) in acetone (110 mL) was added 2,3-dichloro-1-propene (9.90 g, 90.0 mmol). The resulting mixture was stirred at 60 °C for 5 hours. After cooled to room temperature, the mixture was filtered and the filtrate was concentrated under reduced pressure to afford 10.0 g (yield: 65%) of compound **O1** as a yellow power.

**General procedure for the synthesis of O2**

A solution of compound **O1** (10.0 g, 45.9 mmol) in $PhNMe_2$ (50 mL) was stirred at 190 °C for 20 hours. After cooled to room temperature, the mixture was extracted with TBME (30 mL×3). The combined extracts was washed by brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by silica gel column (eluent: PE/EtOAc = 20/1) to afford 8.00 g (yield: 96%) of compound **O2** as a white power.

**General procedure for the synthesis of O3**

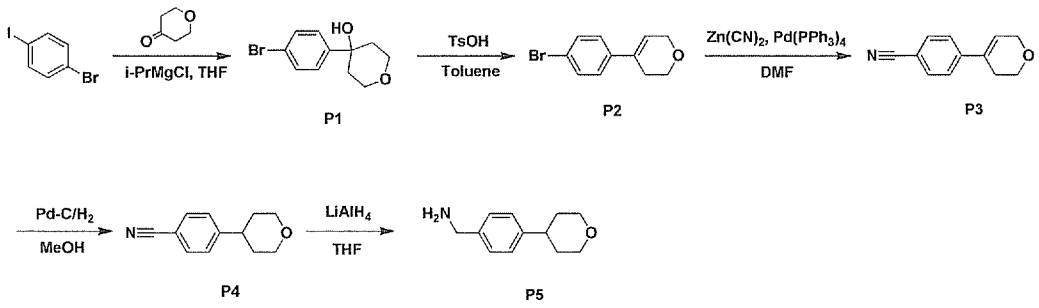
A solution of AIBN (300 mg, 1.83 mmol) and NBS (1.95 g, 11.0 mmol) in $CCl_4$ (10 mL) was stirred at 80 °C for 10 minutes, then a solution of compound **O2** (2.00 g, 11.0 mmol) in $CCl_4$ (20 mL) was added into the above solution. The resulting mixture was stirred at 80 °C for 17 hours. After cooling to room temperature, the mixture was filtered and the filtrate was concentrated under reduced pressure to give residue, which was purified by silica gel column (eluent: PE/EtOAc= 15/1) to afford 2.17 g (yield: 76%) of compound **O3** as a yellow power.

**General procedure for the synthesis of O4**

To a mixture of NaH (120 mg, 3.00 mmol, 60% dispersion in mineral oil) in anhydrous THF (10 mL) was added a solution of $Boc_2NH$ (454 mg, 1.09 mmol) in anhydrous THF (15 mL) at 0 °C under $N_2$ dropwise. After stirred at 0 °C for 30 minutes, a solution of compound **O3** (500 mg, 1.93 mmol) in anhydrous THF (10 mL) was added at 0 °C dropwise. The resulting mixture was allowed to stir at 25 °C for 15 hours. The reaction was quenched with water (30 mL) and extracted with EtOAc (30 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a yellow power, which was purified by silica gel column (eluent: PE/EtOAc= 12/1) to afford 400 mg (yield: 53%) of compound **O4** as a yellow power.

**General procedure for the synthesis of O5**

A solution of compound **O4** (400 mg, 1.05 mmol) and TFA (15 mL) in DCM (30 mL) was stirred at 25 °C for 15 hours. The mixture was concentrated under reduced pressure to give a residue, which was suspended in saturated aqueous $Na_2CO_3$ solution (20 mL) and extracted with EtOAc (20 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to afford 164 mg (yield: 79%) of compound **O5** as a yellow powder.




**Scheme 16**

**General procedure for the synthesis of P1**

To a solution of compound 1-bromo-4-iodobenzene (5.00 g, 17.7 mmol) in anhydrous THF (20 mL) was dropwise added *i*-PrMgCl (10 mL, 20.0 mmol, 2M in THF) at -40 °C. After being stirred at this temperature for 1 hour, a solution of tetrahydro-4H-pyran-4-one (1.77 g, 17.7 mmol) in anhydrous THF (2 mL) was dropwise added at -40 °C. Then the mixture was allowed to warm to 20 °C and stirred for 2 hours. Saturated $NH_4Cl$ (50 mL) was dropwise added at 10 - 25 °C, to quench the reaction followed by water (50 mL). The mixture was

extracted with EtOAc (50 mL x 2). The combined organic layer was concentrated and purified by silica gel column (eluent: PE/EtOAc = 20/1) to give compound **P1**(1.58 g, yield: 35%) as a white powder.

**General procedure for the synthesis of P2**

A solution of compound **P1** (1.57 g, 6.11 mmol) and *p*-toluenesulfonic acid monohydrate (5 mg) in toluene (40 mL) was heated to reflux for 8 hours. The reaction solution was concentrated under reduced pressure to give the crude compound **P2** (1.62 g, quant.) which was used to next step directly.

**General procedure for the synthesis of P3**

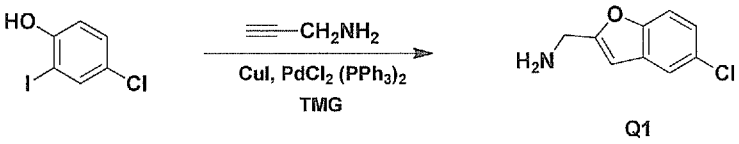
A mixture of compound **P2** (1.62 g, from above), $Zn(CN)_2$ (835 mg, 7.11 mmol) and $Pd(PPh_3)_4$ (783 mg, 0.678 mmol) in DMF (15 mL) was heated to reflux for 1 hour under $N_2$. Then the reaction mixture was diluted with water (50 mL) and EtOAc (30 mL x 3), the EtOAc layer was separated and washed with brine, dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a crude residue, which was purified by silica gel column (eluent: PE/EtOAc = 20/1) to give compound **P3** (930 mg, 2 steps yield: 82%) as a light yellow oil.

**General procedure for the synthesis of P4**

A mixture of compound **P3** (930 mg, 5.02 mmol) and Pd/C (150 mg, 10%) in MeOH (20 mL) was stirred at 20 °C under $H_2$ (1 atm) for 48 hours. The reaction mixture was filtrated, and the filtrate was concentrated to give a crude compound **P4** which was used to next step directly.

**General procedure for the synthesis of P5**

To a solution of compound **P4** (710 mg, 3.79 mmol) in anhydrous THF (30 mL) was added $LiAlH_4$ (720 mg, 19.0 mmol) at at 20 °C for 48 hours. Water (0.7 mL) and 2M NaOH (0.7 mL) was dropwise added to the reaction mixture at 20 °C to quench the reaction, then the mixture was filtrated and the filter cake was washed with THF (30 mL x 2). The combined filtrate was concentrated to give a crude residue, which was diluted with DCM (50 mL) and 1M HCl (40 mL), then extracted with DCM (30 mL x 2). The aqueous layer was adjust to pH = 8 by saturated $NaHCO_3$, then extracted with DCM (50 mL x 3), the combined DCM phase was dried over anhydrous $Na_2SO_4$ and concentrated to give compound **P5** (210 mg, yield: 29%) as light oil.

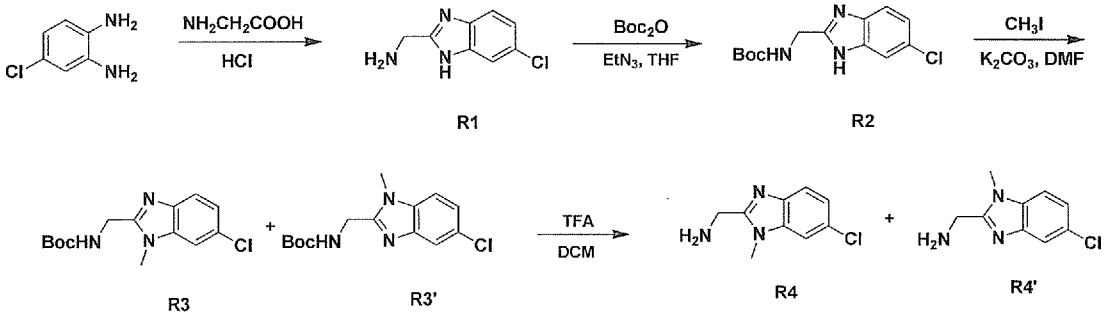



Q1

Scheme 17

**General procedure for the synthesis of R1**

A mixture of 4-chloro-2-iodophenol (1.00 g, 3.94 mmol), propargylamine (1.08 g, 19.6 mmol), CuI (75 mg, 0.40 mmol), $PdCl_2(PPh_3)_2$ (278 mg, 0.40 mmol) and TMG (4.21 g, 36.6 mmol) in anhydrous DMF (20 mL) was stirred at 50 °C under $N_2$ for 5 hours. After cooled to room temperature, the mixture was diluted with water (20 mL) and extracted with EtOAc (30 mL×3). The combined extracts were washed with brine (15 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by prep-HPLC (0.1% $NH_3.H_2O$). Most of $CH_3CN$ was removed by evaporation under reduced pressure, and the remaining solvent was removed by lyophilization to afford 300 mg (yield: 41%) of compound **R1** as a yellow powder.




R1 R2

R3 R3' R4 R4'

Scheme 18

**General procedure for the synthesis of R1**

A solution of 4-chloro-1,2-phenylenediamine (3.00 g, 21.1 mmol) and glycine (2.00 g, 26.0 mmol) in 6N HCl (16 mL) was stirred under $N_2$ at 100 °C for 72 hours. After cooled to room temperature, the mixture was suspended in concentrated $NH_3.H_2O$ solution (18 mL) and extracted with $CH_2Cl_2$ (30 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to afford 1.21 g (yield: 32%) of compound **R1** as a yellow powder.

**General procedure for the synthesis of R2**

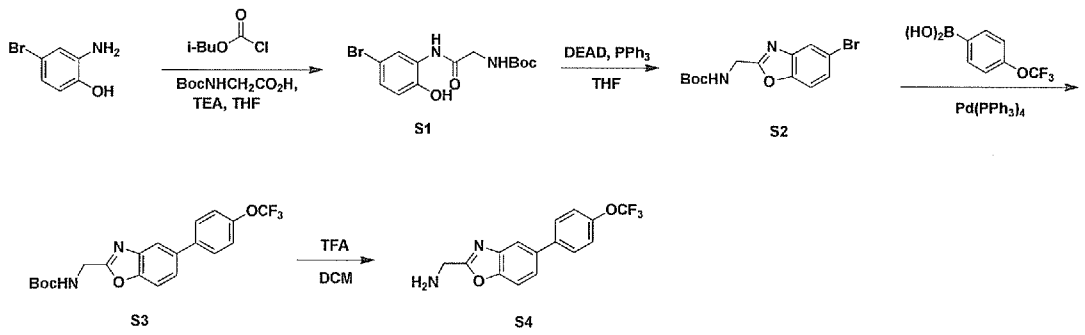
To a solution of compound **R1** (3.62 g, 20.0 mmol) and TEA (4.04 g, 40 mmol) in THF (70 mL) was added $Boc_2O$ (4.32 g, 20 mmol) at 0 °C dropwise and the resulting solution was stirred at 25 °C for 15 hours. The mixture was diluted with water (50 mL), extracted with EtOAc (30 mL×3). The combined extracts were dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by silica gel column (eluent: PE/ EtOAc= 1/5) to afford 900 mg (yield: 16%) of compound **R2** as a yellow powder.

**General procedure for the synthesis of R3 & R3'**

To a suspension of compound **R2** (600 mg, 2.14 mmol) and $K_2CO_3$ (588 mg, 4.26 mmol) in DMF (20 mL) was added $CH_3I$ (420 mg, 2.96 mmol) dropwise at 0 °C. The resulting mixture was stirred at 25 °C for 16 hours. The mixture was diluted with water (50 mL) and extracted with EtOAc (30 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give residue, which was purified by silica gel column (elutant: PE/EtOAc= 5/1) to afford 350 mg (yield: 56%) of a mixture compound **R3** and compound **R3'** as a yellow power.

**General procedure for the synthesis of R4 & R4'**

To a solution of compound **R3** and compound **R3'** (500 mg, 1.69 mmol) in DCM (25 mL) was added TFA (12 mL) dropwise at 0 °C. The resulting solution was stirred at 25 °C for 15 hours, the mixture was concentrated under reduced pressure to give a residue, which was suspended in saturated aqueous $Na_2CO_3$ (15 mL) and extracted with EtOAc (20 mL×3). The combined extracts were dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to afford 289 mg (yield: 88%) of a mixture of compound **R4** and compound **R4'** as a yellow power, used directly for next step without further purification.




**Scheme 19**

**General procedure for the synthesis of S1**

To a solution of Boc-GLY-OH (18.6 g, 106 mmol) and TEA (10.6 g, 105 mmol) in anhydrous THF (200 mL) was added isobutyl chloroformate (12.0 g, 87.9 mmol) at -20 °C dropwise. After the resulting solution was stirred at -20 °C for 1.5 hours, a solution of 2-amino-5-chlorophenol (20.0 g, 106 mmol) in anhydrous THF (50 mL) was added dropwise into above solution and the resulting mixture was stirred at 25 °C for 17 hours. The reaction was quenched with water (50 mL), and the mixture was suspended in saturated aqueous $Na_2CO_3$ (20 mL), extracted with EtOAc (50 mL×3). The combined extracts were washed with brine (30 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by silica gel column (elutent: PE/EtOAc= 4/1) to afford 12.0 g (yield: 32.6%) of compound S1 as a yellow powder.

**General procedure for the synthesis of S2**

A solution of compound **S1** (5.00 g , 14.5 mmol) and $PPh_3$ (8.45 g, 32.2 mmol) in anhydrous THF (70 mL) was stirred at 0 °C for 30 minutes, then DEAD (5.0 mL, 31.7 mmol) was added dropwise. The resulting solution was stirred at 25 °C for 15 hours. The reaction mixture was diluted with water (20 mL) and extracted with EtOAc (30 mL×3). The combined extracts were washed with brine (15 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by silica gel column (elutent: PE/EtOAc= 9/1) to afford 2.40 g (yield: 51%) of compound **S2** as a yellow powder

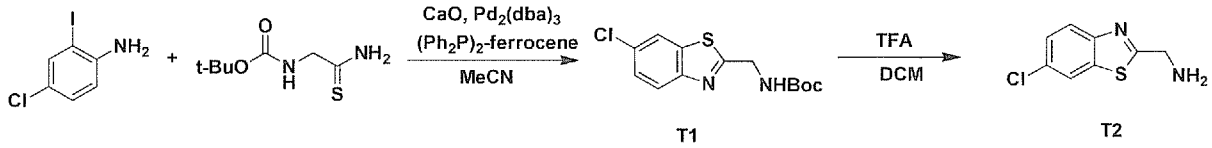
**General procedure for the synthesis of S3**

The solution of compound **S2** (1.00 g, 3.06 mmol), 4-( trifluoromethoxy) phenylboronic acid (800 mg, 3.88 mmol), $Pd(PPh_3)_4$, (600 mg, 0.519 mmol) and aqueous 2M $Na_2CO_3$ (10 mL) in DME (35 mL)was stirred at 80 °C for 17 hours. The mixture was diluted with water (20 mL), extracted with EtOAc (20 mL×3), washed with brine (10 mL). The combined extracts was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by column (elutent: PE/EtOAc= 9:1) to afford 1.00 g (yield: 80%) of compound **S3** as a white power.

**General procedure for the synthesis of S4**

A solution of compound **S3** (400 mg, 0.980 mmol) and TFA (7 mL) in DCM (12 mL) was stirred at 25 °C for 2.5 hours. The mixture was concentrated under reduced pressure to give a residue, the residue was suspended in saturated aqueous $Na_2CO_3$ (15 mL) and extracted with EtOAc (20 mL ×3). The combined extracts was washed with brine (15 mL), dried over

anhydrous $Na_2SO_4$ and concentrated under reduced pressure to afford 230 mg (yield: 76%) of compound **S4** as a yellow oil.



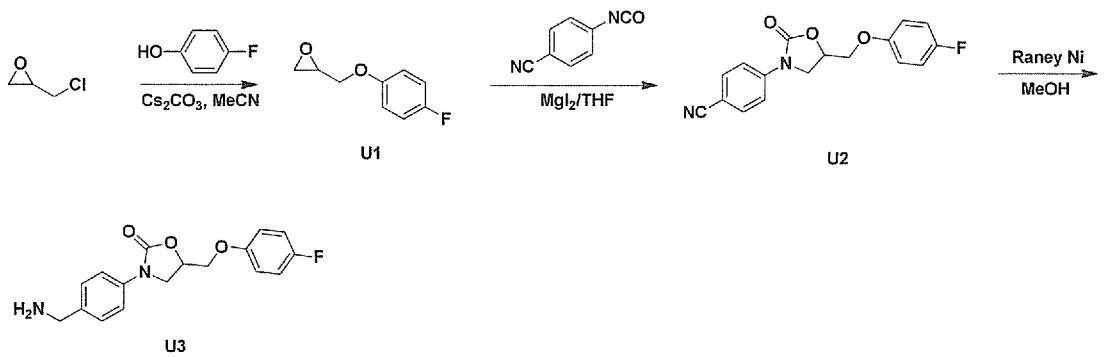

**Scheme 20**

**General procedure for the synthesis of T1**

To a mixture of tert-butyl-2-amino-2-thioxoethylcarbamate (450 mg, 2.37 mmol), CaO (165 mg, 2.94 mmol), $Pd_2(dba)_3$ (365 mg, 0.400 mmol) and dppf (885 mg, 1.60 mmol) in MeCN (7 mL) was added a mixture of 2-chloro-4-iodoaniline (500 mg, 1.97 mmol) in MeCN (3 mL) at 20 °C, the resulting mixture was stirred at 60 °C under $N_2$ atmosphere for 8 hours. After cooling to room temperature, the mixture was diluted with water (20 mL), extracted with EtOAc (30 mL × 3), washed with brine (10 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, which was purified by column (eluted: PE/EtOAc=6/1) to afford 500 mg (yield: 87%) of compound **T1** as a yellow powder.

**General procedure for the synthesis of T2**

A solution of compound **T1** (300 mg, 1.00 mmol) and TFA (5 mL) in DCM (8 mL) was stirred at 25 °C for 3 hours. The mixture was concentrated under reduced pressure to give a residue, which was suspended in saturated aqueous $Na_2CO_3$ solution (20 mL) and extracted with EtOAc (20 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to afford 182 mg (yield: 91%) of compound **T2** as a yellow powder.




**Scheme 21**

**General procedure for the synthesis of U1**

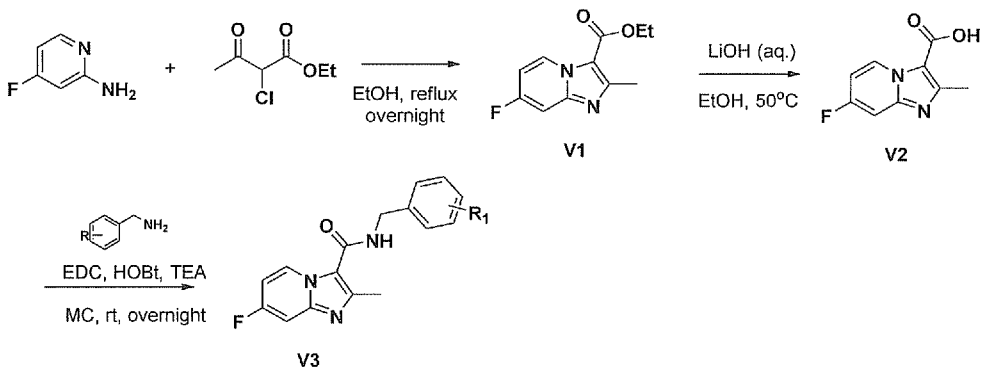
A mixture of epichlorohydrin (4.00 g, 43.2 mmol), 4-fluorophenol (5.34 g, 47.6 mmol) and $Cs_2CO_3$ (14.1 g, 43.3 mmol) in MeCN (50 mL) was stirred at 80 °C for 17 hours. After cooling to room temperature, the mixture was diluted with water (50 mL), extracted with EtOAc (50 mL x3), washed with brine (30 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, the residue was purified by silica gel column (eluted : EtOAc/PE =1: 10) to afford 2.10 g (yield: 29%) of compound **U1** as a colorless oil.

**General procedure for the synthesis of U2**

A mixture of compound **U1** (1.00 g, 5.95 mmol), 4-cyanophenyl isocyanate (1.03 g, 7.15 mmol) and $MgI_2$ (825 mg, 2.98 mmol) in anhydrous THF (25 mL) was stirred at 60 °C for 17 hours. After cooling to room temperature, the mixture was diluted with water (35 mL), extracted with EtOAc (30 mL x3), washed with brine (30 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure to give a residue, the residue was washed with EtOAc/PE (1/4, 15 mL) to afford 800 mg (yield: 43%) of compound **T2** as a dark powder.

**General procedure for the synthesis of U3**

The mixture of compound **U2** (400 mg, 1.28 mmol) and Raney Ni (100 mg) in MeOH (20 mL) was stirred under $H_2$ (50 psi) at 30 °C for 17 hours. The mixture was filtered and the filtration was concentrated under reduced pressure to afford 320 mg (yield: 78%) of compound **U3** as a yellow oil.




**Scheme 22**

**General procedure for the synthesis of V1**

A mixture of 2-amno-4-fluoropyridine (0.41 g, 3.66 mmol) and ethyl-2-chloroacetoacetate (0.66g, 4.02 mmol) in EtOH (7 mL) was stirred at reflux temperature for overnight. The

reaction mixture was concentrated under reduced pressure and the resulting residue was purified by column chromatography (n-hexane : ethyl acetate = 3 : 1 ratio) to give **V1**.

**General procedure for the synthesis of V2**

To a suspension of **V1** (0.20 g, 0.90 mmol) in MeOH (6 mL) was added aqueous LiOH (0.11 g, 4.5 mmol in 2mL $H_2O$) and then the resulting mixture was stirred at 50°C. After 2h, the organic solvent was removed under reduced pressure, the resulting aqueous suspension was acidified with 1M HCl (aq.) and then the resulting precipitate was filtered and dried in *vacuo* to give **V2** (0.10 g, 60 %) as a white solid.

**General procedure for the synthesis of V3**

To a stirred solution of **V2** (0.030 g, 0.16 mmol), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (0.044 g, 0.23 mmol), 1-hydroxybenzotriazole (0.010 g, 0.078 mmol) and triethylamine (0.043 mL, 0.31 mmol) in anhydrous DMF was added substituted benzylamine (0.17 mmol) and the resulting mixture was stirred for 4h at 80°C. The organic solvent was removed under reduced pressure and the resulting residue was purified by flash column chromatography (n-hexane : ethyl acetate = 2 : 1 ratio) to give **V3**.

Example 3: In vivo activity in a murine model

The effect of compounds 171 and 175 on the bacterial load of TB-infected mice was compared to that of the reference compound Isoniazid (INH). 8-week old female BalbC mice were infected with $8x10^6$ *M. tuberculosis* H37Rv via intranasal inoculation. Mice were sacrificed at day 1 to control the number of CFU in the lungs. In the acute model of infection, mice were treated for 3 days, starting at day 6. Compounds were freshly dissolved in a 20% *d*-α-tocopheryl polyethylene glycol 1000 succinate (ETPGS) solution and administered by oral gavage as single dose per day. Bacterial load was assessed in lungs after homogenizing the organs in 1X PBS. Serial dilutions of organs homogenates were spread on Middlebrook 7H11 plates and CFU were determined after 3 weeks incubation at 37°C under 5% CO2.

In the acute model of infection (after 3 days of treatment; Figure 3), a reduction of CFU compared to untreated mice was observed in the lungs of mice treated with 50 mg/kg of either compound 171 or compound 175 administered orally. Overall both compound 171 and compound 175, demonstrated effect in the acute mouse model of infection.

Investigation of bacillus growth inhibitors within macrophages has long been limited due to cumbersome CFU plating, slow bacillus growth, safety requirements and difficulties in setting-up appropriate infection conditions. As a consequence, this approach was always used as a secondary assay after the initial selection of compounds that are active on *in vitro* extracellular growth. With the advent of automated confocal microscopy, the above mentioned limitations could be readdressed and the methodology employed herein demonstrates the feasibility of large scale compound screening.

Obviously compounds tested to be active against *in vitro M. tuberculosis* growth are the most promising. The best inhibitors isolated from this library have an inhibitory activity. Further structure activity relationship studies will contribute to determine if their activity can be additionally improved. Taken together, the above results show that monitoring *M. tuberculosis* growth with automated fluorescence microscopy is highly robust and reliable and that this method enables fast selection of potent anti-TB compounds.

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Table 1

| # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) |
|---|---|---|---|---|---|
| 1 | +++ | 27 | ++ | 53 | +++ |
| 2 | +++ | 28 | +++ | 54 | +++ |
| 3 | +++ | 29 | +++ | 55 | +++ |
| 4 | +++ | 30 | +++ | 56 | +++ |
| 5 | +++ | 31 | +++ | 57 | +++ |
| 6 | +++ | 32 | +++ | 58 | ++ |
| 7 | +++ | 33 | +++ | 59 | +++ |
| 8 | +++ | 34 | ++ | 60 | +++ |
| 9 | +++ | 35 | +++ | 61 | +++ |
| 10 | +++ | 36 | +++ | 62 | +++ |
| 11 | +++ | 37 | +++ | 63 | +++ |
| 12 | +++ | 38 | +++ | 64 | +++ |
| 13 | +++ | 39 | +++ | 65 | +++ |
| 14 | +++ | 40 | +++ | 66 | +++ |
| 15 | +++ | 41 | +++ | 67 | +++ |
| 16 | +++ | 42 | +++ | 68 | +++ |
| 17 | +++ | 43 | +++ | 69 | +++ |
| 18 | +++ | 44 | +++ | 70 | +++ |
| 19 | +++ | 45 | +++ | 71 | +++ |
| 20 | +++ | 46 | +++ | 72 | +++ |
| 21 | +++ | 47 | +++ | 73 | +++ |
| 22 | ++ | 48 | +++ | 74 | +++ |
| 23 | +++ | 49 | +++ | 75 | +++ |
| 24 | +++ | 50 | +++ | 76 | +++ |
| 25 | ++ | 51 | +++ | 77 | +++ |
| 26 | +++ | 52 | +++ | 78 | ++ |

Activity range: +++ indicates < 1 uM, ++ indicates between 1-20 uM, + indicates > 20 uM

Table 1 continue

| # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) |
|---|---|---|---|---|---|
| 79 | +++ | 105 | ++ | 131 | +++ |
| 80 | +++ | 106 | +++ | 132 | +++ |
| 81 | +++ | 107 | +++ | 133 | +++ |
| 82 | +++ | 108 | +++ | 134 | +++ |
| 83 | +++ | 109 | +++ | 135 | +++ |
| 84 | ++ | 110 | +++ | 136 | +++ |
| 85 | +++ | 111 | +++ | 137 | +++ |
| 86 | +++ | 112 | ++ | 138 | +++ |
| 87 | +++ | 113 | +++ | 139 | +++ |
| 88 | ++ | 114 | +++ | 140 | +++ |
| 89 | ++ | 115 | +++ | 141 | +++ |
| 90 | +++ | 116 | +++ | 142 | +++ |
| 91 | +++ | 117 | ++ | 143 | ++ |
| 92 | +++ | 118 | +++ | 144 | +++ |
| 93 | +++ | 119 | +++ | 145 | +++ |
| 94 | +++ | 120 | +++ | 146 | +++ |
| 95 | +++ | 121 | +++ | 147 | +++ |
| 96 | +++ | 122 | +++ | 148 | +++ |
| 97 | +++ | 123 | +++ | 149 | +++ |
| 98 | +++ | 124 | +++ | 150 | +++ |
| 99 | ++ | 125 | ++ | 151 | ++ |
| 100 | +++ | 126 | +++ | 152 | ++ |
| 101 | +++ | 127 | +++ | 153 | +++ |
| 102 | +++ | 128 | +++ | 154 | ++ |
| 103 | ++ | 129 | ++ | 155 | +++ |
| 104 | ++ | 130 | +++ | 156 | +++ |

Activity range: +++ indicates < 1 uM, ++ indicates between 1-20 uM, + indicates > 20 uM

**Table 1 continue**

| # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) |
|---|---|---|---|---|---|
| 157 | +++ | 183 | +++ | 209 | ++ |
| 158 | +++ | 184 | +++ | 210 | +++ |
| 159 | +++ | 185 | ++ | 211 | +++ |
| 160 | +++ | 186 | +++ | 212 | ++ |
| 161 | +++ | 187 | +++ | 213 | +++ |
| 162 | +++ | 188 | +++ | 214 | +++ |
| 163 | +++ | 189 | ++ | 215 | ++ |
| 164 | +++ | 190 | +++ | 216 | +++ |
| 165 | +++ | 191 | +++ | 217 | ++ |
| 166 | +++ | 192 | +++ | 218 | +++ |
| 167 | +++ | 193 | +++ | 219 | +++ |
| 168 | ++ | 194 | +++ | 220 | +++ |
| 169 | +++ | 195 | +++ | 221 | +++ |
| 170 | +++ | 196 | +++ | 222 | +++ |
| 171 | +++ | 197 | +++ | 223 | +++ |
| 172 | +++ | 198 | ++ | 224 | +++ |
| 173 | +++ | 199 | +++ | 225 | +++ |
| 174 | +++ | 200 | ++ | 226 | +++ |
| 175 | +++ | 201 | +++ | 227 | +++ |
| 176 | +++ | 202 | ++ | 228 | +++ |
| 177 | +++ | 203 | +++ | 229 | +++ |
| 178 | +++ | 204 | +++ | 230 | +++ |
| 179 | +++ | 205 | +++ | 231 | +++ |
| 180 | +++ | 206 | +++ | 232 | + |
| 181 | +++ | 207 | +++ | 233 | +++ |
| 182 | +++ | 208 | +++ | 234 | + |

Activity range: +++ indicates < 1 uM, ++ indicates between 1-20 uM, + indicates > 20 uM

Table 1 continue

| # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) |
|---|---|---|---|---|---|
| 235 | +++ | 261 | +++ | 287 | +++ |
| 236 | +++ | 262 | + | 288 | +++ |
| 237 | +++ | 263 | + | 289 | +++ |
| 238 | +++ | 264 | ++ | 290 | +++ |
| 239 | +++ | 265 | ++ | 291 | +++ |
| 240 | +++ | 266 | ++ | 292 | +++ |
| 241 | +++ | 267 | +++ | 293 | +++ |
| 242 | +++ | 268 | +++ | 294 | +++ |
| 243 | +++ | 269 | +++ | 295 | +++ |
| 244 | +++ | 270 | +++ | 296 | +++ |
| 245 | +++ | 271 | ++ | 297 | +++ |
| 246 | +++ | 272 | ++ | 298 | +++ |
| 247 | ++ | 273 | +++ | 299 | +++ |
| 248 | ++ | 274 | ++ | 300 | +++ |
| 249 | + | 275 | + | 301 | +++ |
| 250 | + | 276 | + | 302 | +++ |
| 251 | ++ | 277 | + | 303 | +++ |
| 252 | +++ | 278 | ++ | 304 | ++ |
| 253 | +++ | 279 | +++ | 305 | ++ |
| 254 | +++ | 280 | +++ | 306 | ++ |
| 255 | + | 281 | ++ | 307 | +++ |
| 256 | +++ | 282 | ++ | 308 | +++ |
| 257 | +++ | 283 | ++ | 309 | +++ |
| 258 | +++ | 284 | +++ | 310 | +++ |
| 259 | +++ | 285 | +++ | 311 | +++ |
| 260 | + | 286 | +++ | 312 | +++ |

Activity range: +++ indicates < 1 uM, ++ indicates between 1-20 uM, + indicates > 20 uM

Table 1 continue

| # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) | # cpd | QUM ($MIC_{80}$, uM) |
|---|---|---|---|---|---|
| 313 | +++ | 328 | +++ | 343 | +++ |
| 314 | +++ | 329 | ++ | 344 | +++ |
| 315 | +++ | 330 | ++ | 345 | +++ |
| 316 | +++ | 331 | ++ | 346 | +++ |
| 317 | ++ | 332 | ++ | 347 | +++ |
| 318 | ++ | 333 | +++ | 348 | +++ |
| 319 | +++ | 334 | +++ | 349 | +++ |
| 320 | +++ | 335 | +++ | 350 | +++ |
| 321 | +++ | 336 | +++ | | |
| 322 | +++ | 337 | +++ | | |
| 323 | +++ | 338 | +++ | | |
| 324 | +++ | 339 | ++ | | |
| 325 | +++ | 340 | +++ | | |
| 326 | +++ | 341 | +++ | | |
| 327 | +++ | 342 | +++ | | |

Activity range: +++ indicates < 1 uM, ++ indicates between 1-20 uM, + indicates > 20 uM

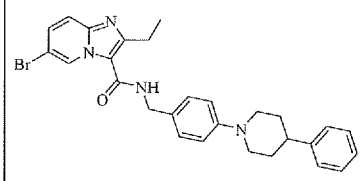
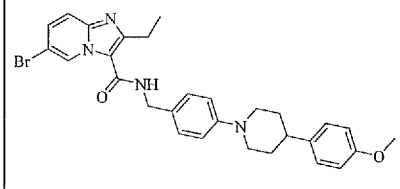
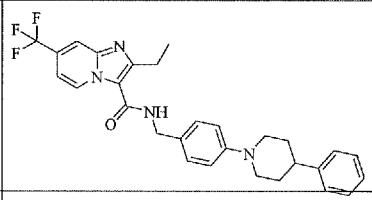
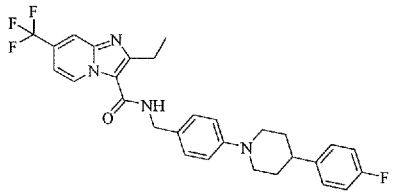
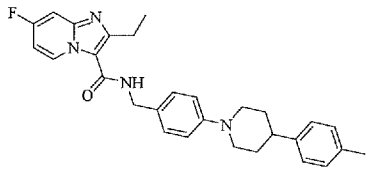
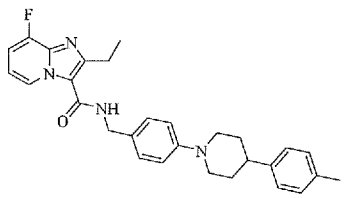
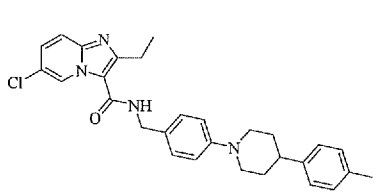
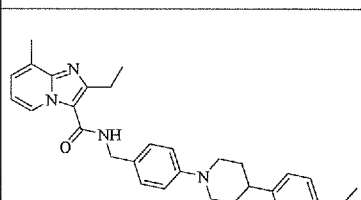
| cpd | Structure | Characterization Data |
|---|---|---|
| 1 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.66 (1H, d, $J$ = 1.2 Hz), 7.21-7.60 (9H, m), 7.02 (2H, d, $J$ = 8.4 Hz), 6.05 (1H, brs), 4.64 (2H, d, $J$ = 5.2 Hz), 3.79-3.93 (2H, m), 2.99 (2H, q, $J$ = 7.6 Hz), 2.80-2.94 (2H, m), 2.61-2.75 (1H, m), 1.87-2.05 (4H, m), 1.42 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 519.0[M+ H]+. |
| 2 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.65 (1H, s), 7.51 (1H, d, $J$ = 9.2 Hz ), 7.43 (1H, d, $J$ = 9.6 Hz), 7.27-7.33 (2H, m), 7.20 (2H, d, $J$ = 8.4 Hz), 7.01 (2H, d, $J$ = 8.4 Hz), 6.89 (2H. d, $J$ = 8.8 Hz), 6.05 (1H, brs), 4.64 (2H, d, $J$ = 5.2 Hz), 3.76-3.90 (5H, m), 2.98 (2H, q, $J$ = 7.6 Hz), 2.80-2.90 (2H, m), 2.60-2.73 (1H, m), 1.80-2.03 (4H, m), 1.42 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 549.1[M+ H]+. |
| 3 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, $J$ = 7.6 Hz), 7.93 (1H, s), 7.22-7.37 (10H, m), 7.11-7.13 (1H, m), 7.02 (2H, d, $J$ = 8.4 Hz), 6.09 (1H, brs), 4.65 (2H, d, $J$ = 5.2 Hz), 3.85 (2H, d, $J$ = 12.4 Hz), 3.02 (2H, q, $J$ = 7.6 Hz), 2.83-2.91 (2H, m), 2.66-2.70 (1H, m), 1.90-2.02 (4H, m), 1.44 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 507.1[M+ H]+. |
| 4 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, $J$ = 7.2 Hz), 8.04 (1H, s), 7.28-7.30 (3H, m), 7.20-7.24 (2H, m), 7.12 (1H, d, $J$ = 1.2 Hz), 7.00-7.10 (4H, m), 6.10 (1H, brs), 4.65 (2H, d, $J$ = 5.6 Hz), 3.84 (2H, d, $J$ = 12.4 Hz), 2.90-3.05 (2H, m), 2.82-2.89 (2H, m), 2.63-2.71 (1H, m), 1.82-1.99 (4H, m), 1.44 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 525.0[M+ H]+. |
| 5 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.44(1H, t, $J$= 7.2 Hz, 6.0 Hz), 7.28(2H, d, $J$= 8.8 Hz), 7.21-7.26(1H, m), 7.14-7.16.01(4H, m), 6.98(2H, d, $J$= 8.8 Hz), 6.77-6.81(1H, m), 5.99(1H, brs), 4.61(2H, d, $J$= 5.2 Hz), 3.80-3.87(2H, m), 2.92-2.98(2H, m), 2.80-2.86(2H, m), 2.59-2.67(2H, m), 2.92-2.98(1H, m), 2.34(3H, s), 1.83-1.97(2H, m), 1.39(3H, t, $J$= 7.2 Hz); LCMS: 98.2%, MS (ESI): m/z 493.0[M+ Na]+. |
| 6 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.20 (1H, d, $J$ = 6.8 Hz), 7.30 (2H, d, $J$ = 8.8 Hz), 7.20-7.10 (4H, m), 7.09-7.01 (3H, m), 6.86-6.81(1H, m), 6.08 (1H, brs), 4.63 (2H, d, $J$ = 5.2 Hz), 3.83-3.80 (2H, m), 3.00 (2H, q, $J$ = 7.6 Hz), 2.90-2.83 (2H, m), 2.68-2.60 (1H, m), 2.33 (1H, s), 1.97-1.86 (4H, m), 1.40 (3H, t, $J$ = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 471.1[M+ H]+. |
| 7 |  | white solid: $^1$H-NMR($CDCl_3$): δ 9.54 (1H, d, $J$ = 1.2 Hz), 7.54 (1H, d, $J$ = 9.6 Hz), 7.26-7.30 (3H, m), 7.12-7.17 (4H, m), 6.99 (2H, d, $J$ = 8.8 Hz), 6.02 (1H, brs), 4.62 (2H, d, $J$ = 5.2 Hz), 3.82 (2H, d, $J$ = 12 Hz), 2.96 (2H, q, $J$ = 7.6 Hz), 2.80-2.87 (2H, m), 2.60-2.66 (1H, m), 2.33 (3H, s), 1.83-1.97 (4H, m), 1.40 (3H, t, $J$ = 7.6 Hz); LCMS: 98.0%, MS (ESI): m/z 487.1[M+ H]+. |
| 8 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, $J$ = 7 Hz), 7.29 (2H, d, $J$ = 8.5 Hz), 7.17 (2H, d, $J$ = 8.8 Hz), 7.11 (1H, d, $J$ = 6.8 Hz), 6.98 (2H, d, $J$ = 8.5 Hz), 6.87 (2H, d, $J$ = 8.5 Hz), 6.82 (1H, t, $J$ = 6.9 Hz), 6.01 (1H, brs), 4.62 (2H, d, $J$ = 5.5 Hz), 3.81 (2H, d, $J$ = 12.2 Hz), 3.60 (3H, s), 2.99 (2H, q, $J$ = 7.5 Hz), 2.82 (2H, td, $J$ = 12.2, 2.5 Hz), 2.57-2.66 (1H, m), 2.61 (3H, s), 1.80-2.00 (4H, m), 1.37 (3H, t, $J$ = 7.7 Hz); LCMS: 100%, MS (ESI): m/z 483.1[M+ H]+. |

Table 2

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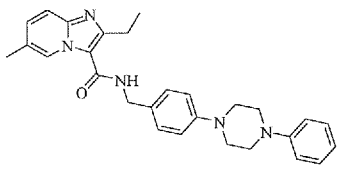
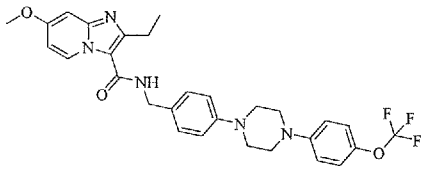
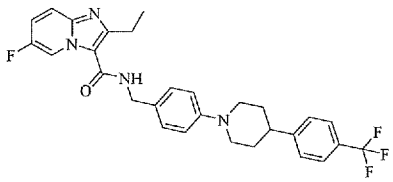
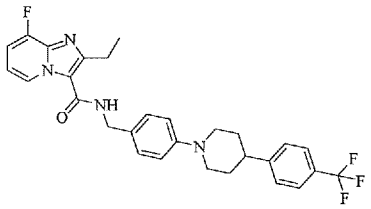
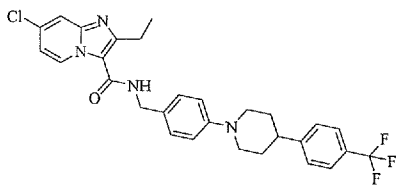
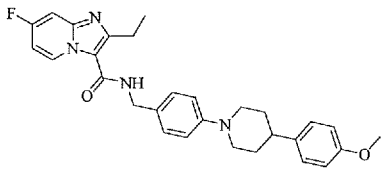
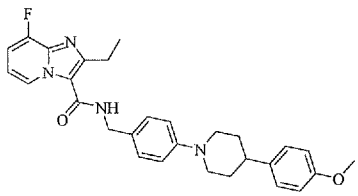
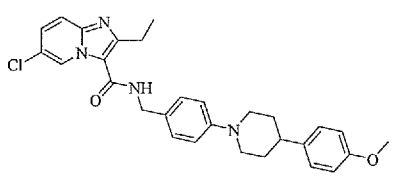
|---|---|---|
| 9 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.16 - 9.29 (1 H, m), 7.46 - 7.56 (1 H, m), 7.28 - 7.37 (4 H, m), 7.12 - 7.21 (1 H, m), 6.96 - 7.05 (4 H, m), 6.84 - 6.95 (1 H, m), 5.93 - 6.09 (1 H, m), 4.56 - 4.69 (2 H, m), 3.35 (8 H, s), 2.90 - 3.02 (2 H, m), 2.37 (3 H, s), 1.32 - 1.45 (3 H, m); LCMS:100%, MS (ESI): m/z 453.2[M+ H]+. |
| 10 |  | pink solid : $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, $J$ = 7.6 Hz), 7.31 (2H, d, $J$ = 8.4 Hz), 7.13 (2H, d, $J$ = 8.8 Hz), 6.91-7.01 (4H, m), 6.88 (1H, d, $J$ = 2.0 Hz), 6.61 (1H, dd, $J$ = 7.6 Hz, 2.4 Hz), 5.95 (1H, brs), 4.61 (2H, d, $J$ = 5.2 Hz), 3.86 (3H, s), 3.33 (8H, s), 2.91 (2H, q, $J$ = 7.6 Hz), 1.38 (3H, t, $J$ = 7.6 Hz); LCMS: 98.3%, MS (ESI): m/z 554.1[M+ H]+. |
| 11 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.47 (1H, dd, $J$ = 5.2, 2.4 Hz), 7.50-7.65 (3H, m), 7.37 (2H, d, $J$ = 8.4 Hz), 7.20-7.35 (3H, m overlap with $CDCl_3$ signal), 7.00 (2H, d, $J$ = 8.4 Hz), 6.04 (1H, bra), 4.63 (2H, d, $J$ = 5.6 Hz), 3.84 (2H, d, $J$ = 12.4 Hz), 2.98 (2H, q, $J$ = 7.6 Hz), 2.80-2.90 (2H, m), 2.65-2.80 (1H, m), 1.85-2.05 (4H, m), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 98.3%, MS (ESI): m/z 525.1[M+ H]+. |
| 12 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.21 (1H, d, $J$ = 6.8 Hz), 7.59 (2H, d, $J$ = 8.0 Hz), 7.37 (2H, d, $J$ = 8.0 Hz), 7.30 (2H, d, $J$ = 8.4 Hz), 7.06-6.99 (3H, m), 6.85-6.83 (1H, m), 6.07 (1H, brs), 4.63 (2H, d, $J$ = 5.6 Hz), 3.86-3.82 (2H, m), 3.01 (2H, q, $J$ = 7.6 Hz), 2.90-2.83 (2H, m), 2.80-2.67 (1H, m), 2.02-1.85 (4H, m), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 525.1[M+ H]+. |
| 13 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, d, $J$ = 7.6 Hz), 7.58 (2H, d, $J$ = 8.0 Hz), 7.37 (2H, d, $J$ = 8.0 Hz ), 7.25-7.35 (3H, m), 7.00 (2H, d, $J$ = 8.4 Hz), 6.91 (1H, dd, $J_1$ = 2.0 Hz, $J_2$ = 7.2 Hz), 6.03 (1H, brs), 4.62 (2H, d, $J$ = 5.2 Hz), 3.83 (2H, d, $J$ = 12 Hz), 2.96 (2H, q, $J$ = 7.6 Hz), 2.70-2.90 (2H, m), 2.65-2.79 (1H, m), 1.85-2.02 (4H, m), 1.39 (3H, t, $J$ = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 541.0 [M+ H]+. |
| 14 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.44(1H, t, $J$= 6.4 Hz), 7.17-7.30(6H, m), 6.99(2H, d, $J$= 8.8 Hz), 6.87(2H, d, J= 8.8 Hz), 6.87(1H, m), 6.00(1H, brs), 4.61(2H, d, $J$= 5.2 Hz), 3.81-3.87(5H, m), 2.93-2.98(2H, m), 2.80-2.86(2H, m), 2.54-2.57(1H, m), 1.18-1.97(4H, m), 1.40(3H, t, $J$= 7.2 Hz); LCMS: 98.2%, MS (ESI): m/z 487.1[M+ H]+. |
| 15 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.21 (1H, d, $J$ = 6.8 Hz), 7.29 (2H, d, $J$ = 8.4 Hz), 7.18 (2H, d, $J$ = 8.4 Hz), 7.04-6.98 (3H, m), 6.89-6.84 (3H, m), 6.07 (1H, brs), 4.63 (2H, d, $J$ = 5.2 Hz), 3.84-3.80 (5H, m), 3.00 (2H, q, $J$ = 7.6 Hz), 2.86-2.80 (2H, m), 2.64-2.56 (1H, m), 1.97-1.84 (4H, m), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 487.1[M+ H]+. |
| 16 |  | white solid: $^1$H-NMR($CDCl_3$): δ 9.54 (1H, d, $J$ = 1.2 Hz), 7.54 (1H, d, $J$ = 9.2 Hz), 7.27-7.31 (4H, m), 7.18 (2H, d, $J$ = 8.8 Hz), 6.99 (2H, d, $J$ = 8.8 Hz), 6.87 (2H, $J$ = 8.8 Hz), 6.03 (1H, brs), 4.62 (2H, d, $J$ = 5.6 Hz), 3.79-3.85 (5H, m), 2.97 (2H, q, $J$ = 7.6 Hz), 2.80-2.88 (2H , m), 2.58-2.68 (1H, m), 1.84-1.97 (4H, m), 1.40 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 525.1[M+ Na]+. |

Table 2

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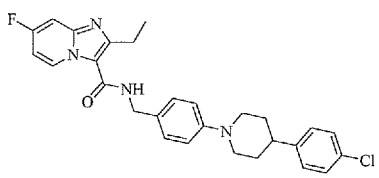
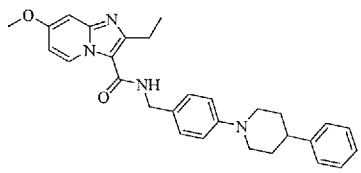
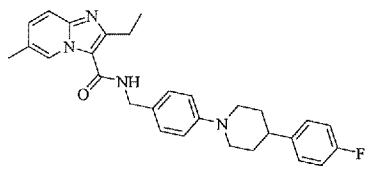
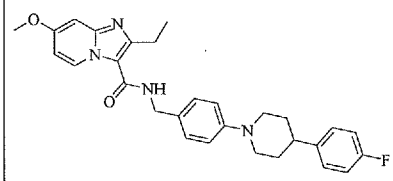
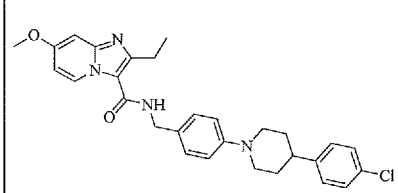
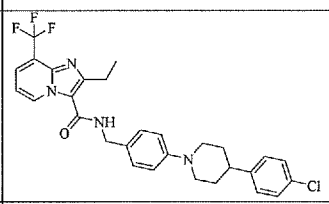
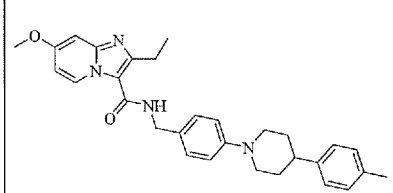
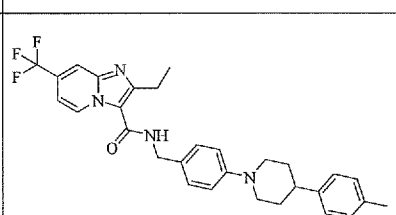
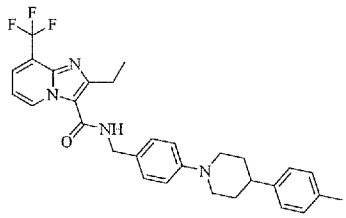
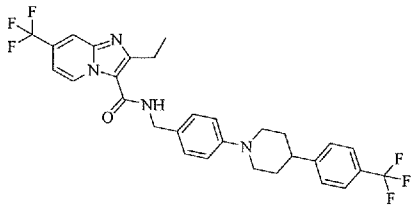
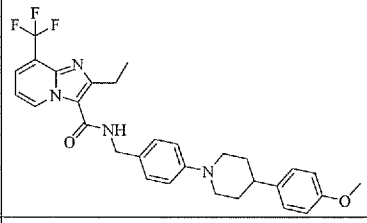
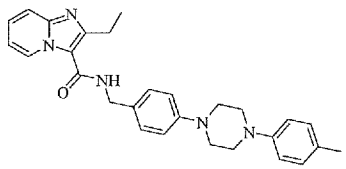
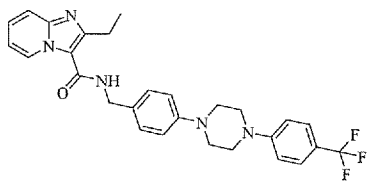
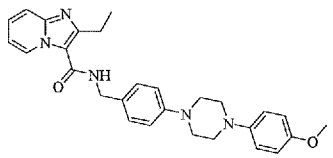
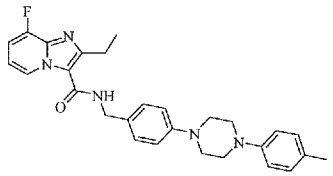
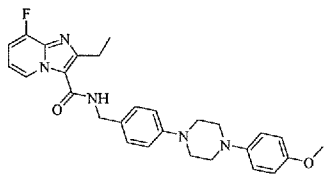
|---|---|---|
| 17 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.44(1H, t, *J*= 6.4 Hz, $J_2$= 6.8 Hz), 7.18-7.30(7H, m), 6.98(2H, d, *J*= 8 Hz), 6.78-6.80(1H, m), 6.01(1H, brs), 4.62(2H, d, *J*= 5.2 Hz), 3.81-3.84(2H, m), 2.93-2.98(2H, m), 2.80-2.86(2H, m), 2.52-2.55(1H, m), 1.84-1.96(4H, m), 1.40(3H, t, *J*=7.6 Hz); LCMS: 99.8%, MS (ESI): m/z 491.1[M+ H]+. |
| 18 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7.6 Hz), 7.15-7.36 (9H, m), 6.98 (2H, d, *J* = 8.8 Hz), 6.89 (1H, d, *J* = 2.4 Hz), 6.61 (1H, dd, *J* = 7.6 Hz, 2.4 Hz), 5.93 (1H, brs), 4.60 (2H, d, *J* = 5.2 Hz), 3.87 (3H, s), 3.82 (2H, d, *J* = 12.4 Hz), 2.75-2.95 (4H, m), 2.60-2.72 (1H, m), 1.80-2.02 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 469.1[M+ H]+. |
| 19 |  | pink solid: $^1$H-NMR ($CDCl_3$): δ 9.19 - 9.30 (1 H, m), 7.53 (1 H, d, *J*=9.03 Hz), 7.28 - 7.33 (2 H, t), 7.18 - 7.24 (3 H, m), 6.95 - 7.07 (4 H, m), 5.96 - 6.10 (1 H, m), 4.65 (2 H, d, *J*=5.52 Hz), 3.84 (2 H, d, *J*=12.30 Hz), 2.98 (2 H, q, *J*=7.57 Hz), 2.77 - 2.93 (2 H, m), 2.67 (1 H, s), 2.39 (3 H, s), 1.94 - 2.01 (2 H, m), 1.82 - 1.94 (2 H, m), 1.42 (3 H, t, *J*=7.59 Hz); LCMS: 98.0%, MS (ESI): m/z 471.1[M+ H]+. |
| 20 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 7.6 Hz), 7.15-7.35 (4H, m), 6.93-7.05 (4H, m), 6.89 (1H, d, *J* = 2.4 Hz), 6.61 (1H, dd, *J* = 7.6 Hz, 2.4 Hz),5.94 (1H, brs), 4.60 (2H, d, *J* = 5.2 Hz), 3.87 (3H, s), 3.81 (2H, d, *J* = 12.4 Hz), 2.92 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 12.4 Hz, 2.4 Hz), 2.55-2.70 (1H, m), 1.75-2.02 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 99.0%, MS (ESI): m/z 487.1[M+ H]+. |
| 21 |  | off-white solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 7.6 Hz), 7.22-7.35 (5H, m), 7.18 (2H, 2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.88 (1H, d, *J* = 2.4 Hz), 6.61 (1H, dd, *J* = 7.6 Hz, 2.4 Hz), 5.94 (1H, m), 4.60 (2H, d, *J* = 5.2 Hz), 3.87 (3H, s), 3.81 (2H, d, *J* = 12.4 Hz), 2.92 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 12.0 Hz, 2.4 Hz), 2.58-2.68 (1H, m), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 503.1[M+ H]+. |
| 22 |  | pink solid : $^1$H-NMR ($CDCl_3$): δ 9.60 (1H, d, *J* = 7.2 Hz), 7.68 (1H, d, *J* = 7.2 Hz), 7.20-7.40 (4H, m), 7.20 (2H, d, *J* = 8.4 Hz), 6.95-7.05 (3H, m), 6.12 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.80-3.90 (2H, m), 3.05 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.60-2.70 (1H, m), 1.80-2.00 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 541.0[M + H]+. |
| 23 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7.6 Hz), 7.28 (2H, d, *J* = 8.8 Hz), 7.08-7.20 (4H, m), 6.98 (2H, d, *J* = 8.8 Hz), 6.88 (1H, d, *J* = 2.4 Hz), 6.61 (1H, dd, *J* = 7.6 Hz, 2.4 Hz), 5.93 (1H, brs), 4.60 (2H, d, *J* = 5.2 Hz), 3.87 (3H, s), 3.80 (2H, d, *J* = 12.4 Hz), 2.92 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 12.0 Hz, 2.8 Hz), 2.55-2.68 (1H, m), 2.33 (3H, s), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 483.2[M+ H]+. |
| 24 |  | pink solid : $^1$H-NMR ($CDCl_3$): δ 9.52 (1H, d, *J* = 7.2 Hz), 7.90 (1H, s), 7.26-7.29 (2H, m), 7.10-7.15 (4H, m), 7.07 (1H, d, *J* = 2.0 Hz), 6.99 (2H, d, *J* = 8.8 Hz), 6.07 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.81 (2H, d, *J* = 12.0 Hz), 2.99 (2H, q, *J* = 7.6 Hz), 2.79-2.87 (2H, m), 2.60-2.68 (1H, m), 2.33 (3H, s), 1.85-1.96 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.6%, MS (ESI): m/z 521.1[M+ H]+. |

| | | |
|---|---|---|
| 25 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.61 (1H, d, *J* = 6.8 Hz), 7.68 (1H, d, *J* = 7.2 Hz), 7.20-7.40 (2H, m), 7.10-7.20 (4H, m), 6.95-7.05 (3H, m), 6.12 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.80-3.90 (2H, m), 3.05 (2H, q, *J* = 7.2 Hz), 2.80-2.90 (2H, m), 2.55-2.70 (1H, m), 2.36 (3H, s), 1.80-2.00 (4H, m), 1.40 (3H, t, *J* = 7.2 Hz); LCMS: 98.4%, MS (ESI): m/z 521.0[M + H]+. |
| 26 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, *J* = 7.2 Hz), 7.93 (1H, s), 7.60 (2H, d, *J* = 8.0 Hz), 7.38 (2H, d, *J* = 8.0 Hz), 7.28-7.34 (2H, m), 7.11 (1H, d, *J* = 7.2 Hz), 7.01 (2H, d, *J* = 8.4 Hz), 6.10 (1H, brs), 4.66 (2H, d, *J* = 5.2 Hz), 3.86 (2H, d, *J* = 12.4 Hz), 3.02 (2H, q, *J* = 7.6 Hz), 2.85-2.91 (2H, m), 2.72-2.79 (1H, m), 1.88-2.04 (4H, m), 1.44 (3H, t, *J* = 7.6Hz); LCMS: 99.2%, MS (ESI): m/z 575.0[M+ H]+. |
| 27 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.58 (1H, d, *J* = 6.8 Hz), 7.65 (1H, d, *J* = 7.2 Hz), 7.28 (2H, d, *J* = 8.8 Hz), 7.17 (2H, d, *J* = 8.8 Hz), 6.90-7.00 (3H, m), 6.86 (2H, d, *J* = 8.8 Hz), , 6.08 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.75-3.85 (2H, m), 3.80 (3H, s), 3.03 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.55-2.65 (1H, m), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 99.7%, MS (ESI): m/z 537.0[M + H]+. |
| 28 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.41 (1H, d, *J* = 7.2 Hz), 7.60 (1H, d, *J* = 8.8 Hz), 7.28-7.40 (3H, m), 7.10 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.80-6.95 (3H, m), 6.01 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.20-3.41 (8H, m), 2.97 (2H, q, *J* = 7.6 Hz), 2.28 (3H, s), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 99.7%, MS (ESI): m/z 454.0[M+ H]+. |
| 29 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.41 (1H, d, *J* = 6.8 Hz), 7.61 (1H, d, *J* = 9.2 Hz), 7.51 (2H, d, *J* = 8.8 Hz), 7.27-7.38 (3H, m), 6.95-7.04 (4H, m), 6.92 (1H, t, *J* = 6.8 Hz), 6.02 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.39-3.50 (4H, m), 3.29-3.39 (4H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 508.1 [M+ H]+. |
| 30 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.44 (1H, d, *J* = 6.8 Hz), 7.63 (1H, d, *J* = 9.2 Hz), 7.31-7.42 (2H, m, overlap with $CDCl_3$ signal), 6.85-7.08 (8H, m), 6.04 (1H, brs), 4.66 (2H, d, *J* = 5.2 Hz), 3.81 (3H, s), 3.38 (4H, t, *J* = 4.4 Hz), 3.26 (4H, t, *J* = 4.4 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 98.8%, MS (ESI): m/z 492.3 [M+ Na]+. |
| 31 |  | off-white solid: $^1$H-NMR ($CDCl_3$): δ 9.23 (1H, d, *J* = 7.2 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 7.08-6.99 (3H, m), 6.93 (2H, d, *J* = 8.4 Hz), 6.88-6.83 (1H, m), 6.08 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.39-3.30 (8H, m), 3.02 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 99.5%, MS (ESI): m/z 494.1[M+ Na]+. |
| 32 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.23 (1H, d, *J* = 7.2 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.08-6.96 (5H, m), 6.91-6.83 (3H, m), 6.08 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.81 (3H, s), 3.39-3.36 (4H, m), 3.27-3.24 (4H, m), 3.02 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 98.8%, MS (ESI): m/z 488.1[M+ H]+. |

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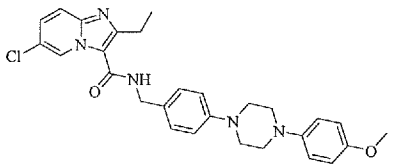
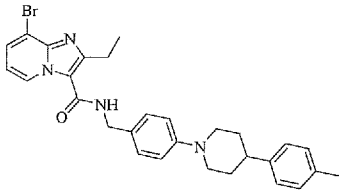
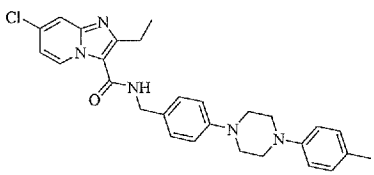
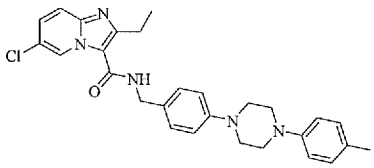
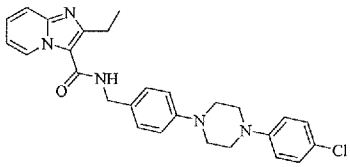
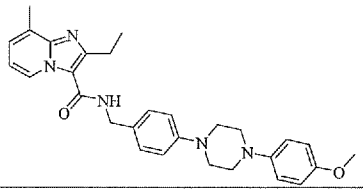
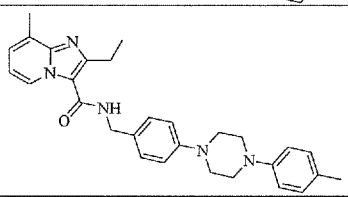
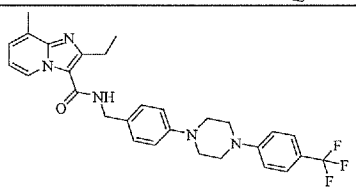
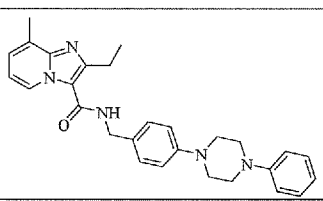
| 33 |  | white solid : $^1$H-NMR($CDCl_3$): δ 9.56 (1H, d, *J* = 1.2 Hz), 7.56 (1H, d, *J* = 9.6 Hz), 7.30-7.35 (3H, m), 6.97-7.05 (4H, m), 6.89 (2H, d, *J* = 8.8 Hz), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.81 (3H, s), 3.35-3.40 (4H, m), 3.23-3.29 (4H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 526.1[M+ Na]+. |
| 34 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.42 (1H, d, *J* = 6.8 Hz), 7.60 (1H, d, *J* = 6.8 Hz), 7.25-7.35 (2H, m), 7.12-7.20 (4H, m), 7.01 (2H, d, *J* = 8.8 Hz), 6.82 (1H, t, *J* = 7.2 Hz), 6.08 (1H, brs), 4.64 (2H, d, *J* = 5.6 Hz), 3.84 (2H, d, *J* = 12.0 Hz), 3.04 (2H, q, *J* = 7.6 Hz), 2.85 (2H, t, *J* = 12.0 Hz), 2.60-2.70 (1H, m), 1.85-2.00 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 531.1/533.1 [M+H]. |
| 35 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, *J* = 7.2 Hz), 7.61 (1H, s), 7.25-7.32 (2H, m), 7.13 (2H, d, *J* = 8.0 Hz), 6.90-7.05 (5H, m), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz ), 3.30-3.40 (8H, m), 2.97 (2H, q, *J* = 7.6 Hz), 2.31(1H, s), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 488.1 [M+ H]+. |
| 36 |  | off-white solid: $^1$H-NMR($CDCl_3$): δ 9.56 (1H, d, *J* = 1.2 Hz), 7.56 (1H, d, *J* = 9.6 Hz), 7.27-7.35 (3H, m), 7.13 (2H, d, *J* = 8.4 Hz), 7.01 (2H, d, *J* = 8.8 Hz), 6.93 (2H, d, *J* = 8.4 Hz), 6.06 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.29-3.40 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 510.1[M+ Na]+. |
| 37 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.43 (1H, d, *J* = 7.2 Hz), 7.63 (1H, d, *J* = 8.8 Hz), 7.31-7.42 (3H, m), 7.20-7.30 (2H, m, overlap with $CDCl_3$ signal), 7.00 (2H, d, *J* = 8.4 Hz), 6.85-6.98 (3H, m), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.20-3.45 (8H, m), 3.01 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 474.1[M+ H]+. |
| 38 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 6.8 Hz), 7.31 (2H, d, *J* = 8.5 Hz), 7.11 (1H, d, *J* = 6.9 Hz), 6.97 (4H, t, *J* = 8.7 Hz), 6.84-6.90 (2H, m), 6.82 (1H, t, *J* = 7.0 Hz), 6.02 (1H, brs), 4.63 (2H, d, *J* = 5.4 Hz), 3.78 (3H, s), 3.18-3.38 (8H, m), 3.00 (2H, q, *J* = 7.6 Hz), 2.61 (3H, s), 1.37 (3H, t, *J* = 7.7 Hz); LCMS: 100%, MS (ESI): m/z 484.1[M+ H]+. |
| 39 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 6.9 Hz), 7.31 (2H, d, *J* = 8.7 Hz), 7.07-7.15 (3H, m), 6.98 (2H, d, *J* = 8.7 Hz), 6.90 (2H, d, *J* = 8.5 Hz), 6.82 (1H, t, *J* = 7 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.5 Hz), 3.25-3.38 (8H, m), 3.00 (2H, q, *J* = 7.6 Hz), 2.61 (3H, s), 2.29 (3H, s), 1.37 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 490.1[M+ H]+. |
| 40 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7 Hz), 7.51 (2H, d, *J* = 8.7 Hz), 7.32 (2H, d, *J* = 8.5 Hz), 7.12 (1H, d, *J* = 7.5 Hz), 6.98 (4H, d, *J* = 8.5 Hz), 6.82 (1H, t, *J* = 6.9 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.5 Hz), 3.30-3.48 (8H, m), 3.00 (2H, q, *J* = 7.7 Hz), 2.62 (3H, s), 1.37 (3H, t, *J* = 7.7 Hz); LCMS: 98.5%, MS (ESI): m/z 522.1[M+ H]+. |
| 41 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7 Hz), 7.26-7.35 (4H, m), 7.11 (1H, d, *J* = 6.9 Hz), 6.96-7.03 (4H, m), 6.90 (1H, t, *J* = 7.3 Hz), 6.82 (1H, t, *J* = 7.0 Hz), 6.02 (1H, brs), 4.63 (2H, d, *J* = 5.4 Hz), 3.35 (8H, s), 3.00 (2H, q, *J* = 7.5 Hz), 2.61 (3H, s), 1.37 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 476.1[M+ H]+. |

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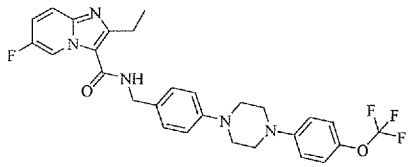
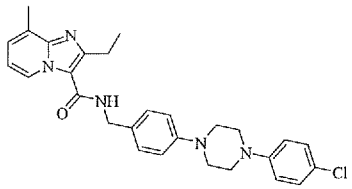
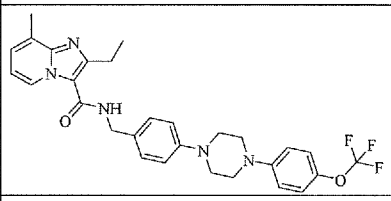
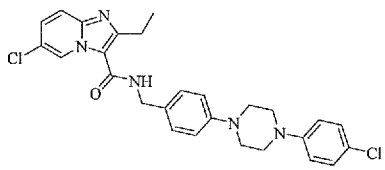
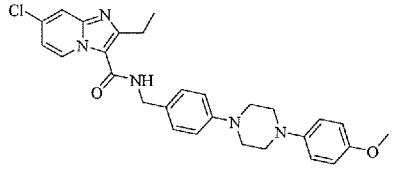
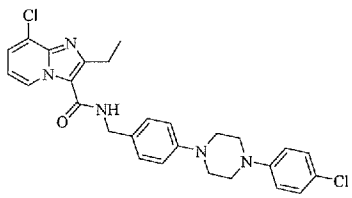
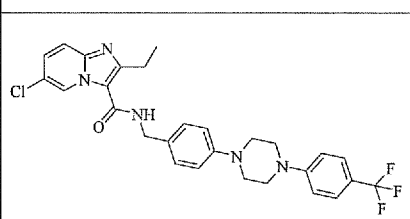
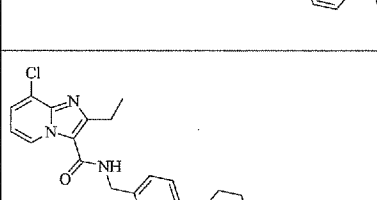
| 42 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.48 (1H, dd, *J* = 4.8, 2.0 Hz), 7.59 (1H, dd, *J* = 9.6, 5.2 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.24-7.30 (1H, m, overlap with $CDCl_3$ signal), 7.17 (2H, d, *J* = 8.8 Hz), 6.90-7.08 (4H, m), 6.06 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.36 (8H, s), 2.99 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 98.2%, MS(ESI): m/z 542.1 [M+H]+. |
| 43 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 6.9 Hz), 7.31 (2H, d, *J* = 8.5 Hz), 7.23 (2H, d, *J* = 8.9 Hz),7.12 (1H, d, *J* = 6.7 Hz), 6.98 (2H, d, *J* = 8.7 Hz), 6.90 (2H, d, *J* = 8.9 Hz), 6.82 (1H, t, *J* = 6.8 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.5 Hz), 3.28-3.38 (8H, m), 3.00 (2H, q, *J* = 7.7 Hz), 2.62 (3H, s), 1.37 (3H, t, *J* = 7.7 Hz); LCMS: 100%, MS (ESI): m/z 488.1[M+ H]+. |
| 44 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 6.9 Hz), 7.32 (2H, d, *J* = 8.7 Hz), 7.08-7.17 (3H, m), 6.91-7.03 (4H, m), 6.82 (1H, t, *J* = 6.9 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.5 Hz), 3.30-3.38 (8H, m), 3.00 (2H, q, *J* = 7.5 Hz), 2.62 (3H, s), 1.37 (3H, t, *J* = 7.7 Hz); LCMS: 98.3%, MS (ESI): m/z 538.1[M+ H]+. |
| 45 |  | white solid : $^1$H-NMR($CDCl_3$): δ 9.56 (1H, d, *J* = 1.2 Hz), 7.56 (1H, d, *J* = 9.2 Hz), 7.30-7.40 (3H, m), 7.23-7.29 (2H, m), 7.00 (2H, d, *J* = 8.4 Hz), 6.92 (2H, d, *J* = 8.8 Hz), 6.06 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.25-3.40 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 530.0[M+ Na]+. |
| 46 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.38 (1H, d, *J* = 7.2 Hz), 7.61 (1H, d, *J* = 1.6 Hz), 7.32 (2H, d, *J* = 8.4 Hz), 6.99 (4H, t, *J* = 8.8 Hz), 6.85-6.95 (3H, m), 6.03 (1H, brs), 4.64 (2H, d, *J* = 5.6 Hz ), 3.81 (3H, s), 3.20-3. 30 (4H, m), 3.32-3.40 (4H, m), 2.97 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 526.0 [M+ Na]+. |
| 47 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, d, *J* = 6.4 Hz） , 7.42 (1H, d, *J* = 7.2 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.25 (2H, d, *J* = 8.8 Hz), 7.00 (2H, d, *J* = 8.4 Hz), 6.82-6.93 (3H, m), 6.09 (1H, brs), 4.65 (2H, d, *J*= 5.2 Hz), 3.34 (8H, d, *J* = 6.8 Hz), 3.03 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 508.0[M+ H]+. |
| 48 |  | white solid : $^1$H-NMR($CDCl_3$): δ 9.56 (1H, d, *J* = 1.6 Hz), 7.53-7.59 (3H, m), 7.29-7.35 (3H, m), 7.00 (4H, d, *J* = 8.8 Hz), 6.07 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.43-3.49 (4H, m), 3.35-3.40 (4H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 542.0[M+ H]+. |
| 49 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, dd, *J1* = 0.8 Hz, *J2* = 7.2 Hz), 7.54 (2H, d, *J* = 8.8 Hz), 7.42 (1H, dd, *J1* = 0.8 Hz, *J2* = 7.6 Hz), 7.34 (2H, d, *J* = 8.8 Hz), 7.00 (4H, d, *J* = 8.4 Hz), 6.88 (1H, t, *J* = 7.2 Hz), 6.10 (1H, brs), 4.66 (2H, d, *J* = 5.6 Hz), 3.47 (4H, dd, *J1* = 4.4 Hz, *J2* =7.2 Hz), 3.38 (4H, dd, *J1* = 7.2 Hz, *J2* = 10 Hz), 3.04 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 542.0[M+ H]+. |

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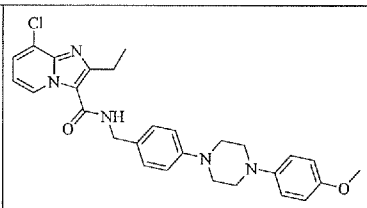
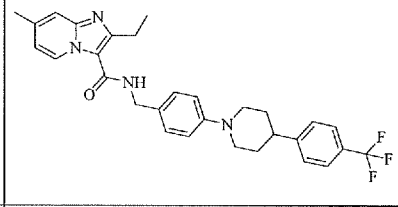
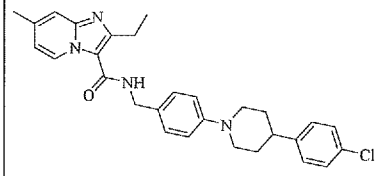
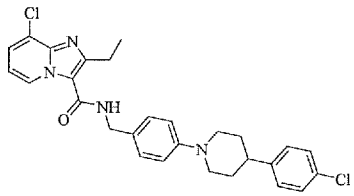
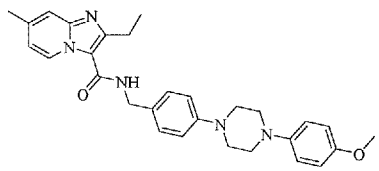
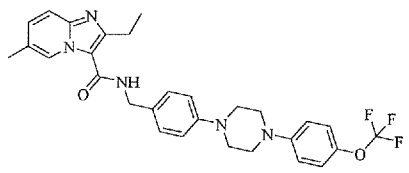
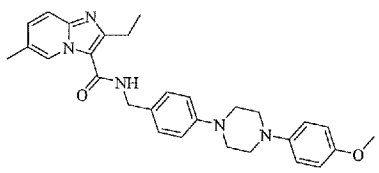
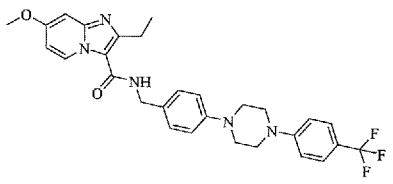
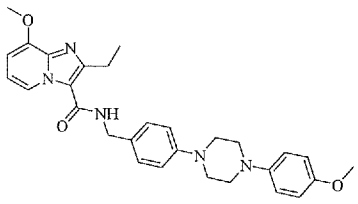
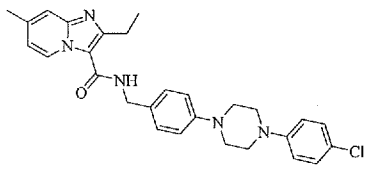
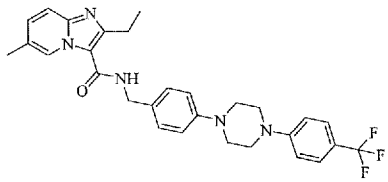
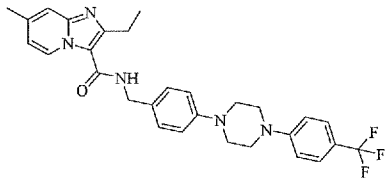
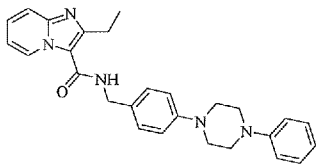
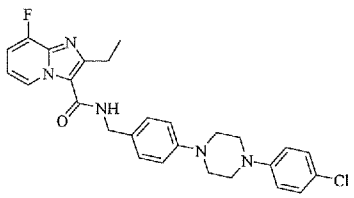
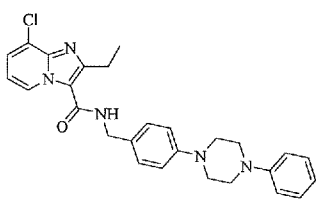
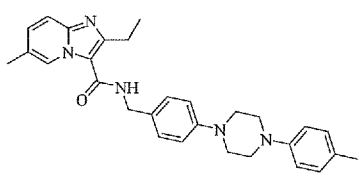
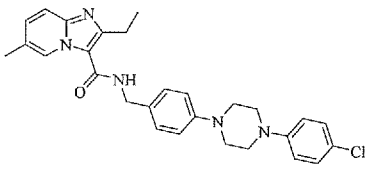
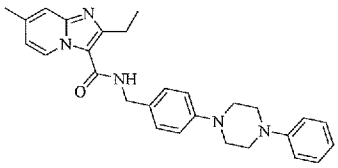
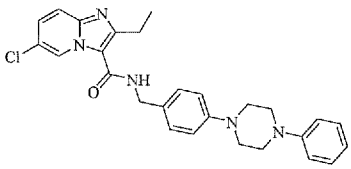
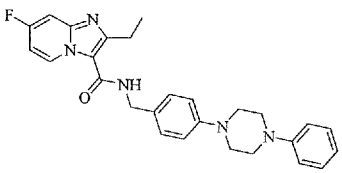
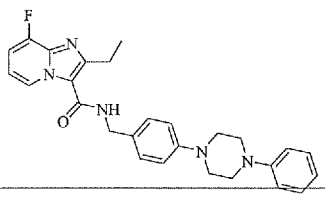
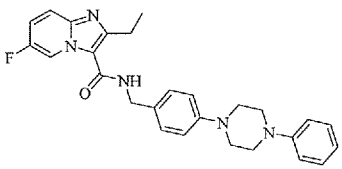
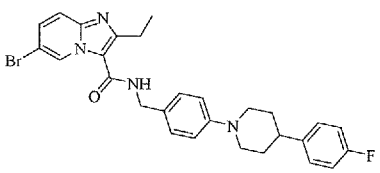
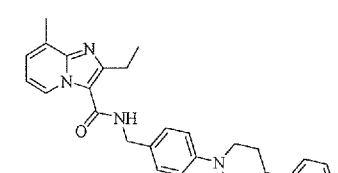
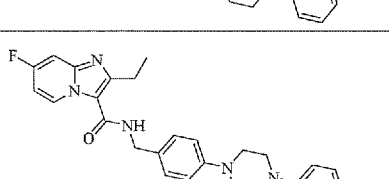
|---|---|---|
| 50 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, d, $J$ = 6.8 Hz), 7.42 (1H, d, $J$ = 6.4 Hz), 7.33 (2H, d, $J$ = 8.4 Hz), 7.00 (4H, t, $J$ = 9.2 Hz), 6.86-6.90 (3H, m), 6.10 (1H, brs), 4.65 (2H, d, $J$ = 5.6 Hz), 3.81 (3H, s), 3.38 (4H, t, $J$ = 5 Hz), 3.25 (4H, t, $J$ = 5 Hz), 3.04 (2H, q, $J$ = 7.6 Hz), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 526.1[M+ Na]+. |
| 51 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.31 (1H, d, $J$ = 7.2 Hz), 7.60 (2H, d, $J$ = 8.4 Hz), 7.38 (3H, d, $J$ = 8.0 Hz), 7.33-7.28 (2H, m), 7.01 (2H, d, $J$ = 8.8 Hz), 6.78 (1H, d, $J$ = 7.0 Hz), 6.01 (1H, brs), 4.64 (2H, d, $J$ = 5.2 Hz), 3.84 (2H, d, $J$ = 12.4 Hz), 2.96 (2H, q, $J$ = 7.2 Hz), 2.83 (2H, td, $J$ = 12 Hz, 2.4 Hz), 2.78-2.72 (1H, m), 2.45 (3H, s), 2.02-1.91 (4H, m), 1.28 (3H, t, $J$ = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 521.1[M+ H]+. |
| 52 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.30 (1H, d, $J$ = 7.2 Hz), 7.38 (1H, s), 7.32-7.29 (4H, m), 7.20 (2H, d, $J$ = 8.4 Hz), 7.00 (2H, d, $J$ = 8.4 Hz), 6.77 (1H, dd, $J$ = 7.2 Hz, 1.6 Hz), 6.0 (1H, brs), 4.64 (2H, d, $J$ = 5.6 Hz), 3.81 (2H, d, $J$ = 12.4 Hz), 2.97 (2H, q, $J$ = 7.2 Hz), 2.84 (2H, td, $J$ = 12 Hz, 2.4 Hz), 2.70-2.60 (1H, m), 2.42 (3H, s), 2.01-1.82 (4H, m), 1.39 (3H, t, $J$ = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 487.1[M+ H]+. |
| 53 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, dd, $J$ = 0.8 Hz, $J$ = 6.8 Hz), 7.42 (1H, dd, $J$ = 0.8 Hz, $J$ = 7.2 Hz), 7.31 (4H, d, $J$ = 8.4 Hz), 7.20 (2H, d, $J$ = 8.4 Hz), 7.00 (2H, d, $J$ = 8.8 Hz), 6.88 (1H, t, $J$ = 7.2 Hz), 6.09 (1H, brs), 4.64 (2H, d, $J$ = 5.2 Hz), 3.84 (2H, d, $J$ = 12.0 Hz), 3.04 (2H, q, $J$ = 7.6 Hz), 2.85 (2H, td, $J$ = 2.4, 12.4 Hz), 2.62-2.70 (1H, m), 1.83-1.98 (4H, m), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 507.0[M+ H]+. |
| 54 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, $J$ = 7.2 Hz), 7.35-7.29 (3H, m), 6.99-6.95 (4H, m), 6.86 (2H, d, $J$ = 8.8 Hz), 6.74 (1H, d, $J$ = 7.2 Hz), 5.99 (1H, brs), 4.62 (2H, d, $J$ = 5.6 Hz), 3.78 (3H, s), 3.36-3.22 (8H, m), 2.95 (2H, q, $J$ = 7.6 Hz), 2.17 (3H, s), 1.39 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 484.1[M+ H]+. |
| 55 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.14 - 9.31 (1H, m), 7.45 - 7.56 (1H, m), 7.29 - 7.38 (2H, m), 7.08 - 7.22 (3H, m), 6.96 (4H, s), 5.95 - 6.09 (1H, m), 4.57 - 4.73 (2H, m), 3.34 (8H, s), 2.89 - 3.04 (2H, m), 2.37 (3H, s), 1.40 (3H, s); LCMS: 98.2%, MS (ESI): m/z 538.1[M+ H]+. |
| 56 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.13 - 9.25 (1H, m), 7.46 - 7.54 (1H, m), 7.27 - 7.36 (2H, m), 7.09 - 7.21 (1H, m), 6.96 (4H, d, $J$=9.54 Hz), 6.88 (2H, s), 5.96 - 6.06 (1H, m), 4.59 - 4.67 (2H, m), 3.78 (3H, s), 3.35 (4H, d, $J$=5.27 Hz), 3.23 (4H, brs), 2.90 - 3.01 (2H, m), 2.36 (3H, s), 1.39 (3H, t, $J$=7.53 Hz); LCMS: 98.8%, MS (ESI): m/z 484.0[M+ H]+. |
| 57 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, $J$ = 7.6 Hz), 7.51 (2H, d, $J$ = 8.8 Hz), 7.31 (2H, d, $J$ = 8.4 Hz), 6.92-7.03 (4H, m),6.89 (1H, d, $J$ = 2.0 Hz) 6.61 (1H, dd, $J$ = 7.6 Hz, 2.4 Hz), 5.96 (1H, brs), 4.61 (2H, d, $J$ = 5.6 Hz), 3.87 (3H, s), 3.25-3.49 (8H, m), 2.92 (2H, q, $J$ = 7.6 Hz), 1.39 (3H, t, $J$ = 7.6 Hz); LCMS: 98.5%, MS (ESI): m/z 538.1[M+ H]+, 560.0 [M+Na]+. |

Table 2

| | | |
|---|---|---|
| 58 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 8.99 (1H, d, *J*= 6.8 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 6.97 (4H, t, *J* = 8.8 Hz), 6.87 (2H, d, *J* = 8.8 Hz), 6.81 (1H, t, *J* = 7.2 Hz), 6.62 (1H, d, *J* = 8.0 Hz), 6.05 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 4.02 (3H, s). 3.78 (3H, s), 3.35 (4H, t, *J* = 4.8 Hz), 3.23 (4H, t, *J* = 4.8 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 99.4%, MS (ESI): m/z 522.1[M+Na] +. |
| 59 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 7.2 Hz), 7.36 (1H, s), 7.31 (2H, d, *J* = 8.4 Hz), 7.23 (2H, d, *J* = 8.8 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.89 (2H, d, *J* = 8.8 Hz), 6.75 (1H, d, *J* = 6.4 Hz), 6.00 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.33-3.31 (8H, m), 2.95 (2H, q, *J* = 7.6 Hz), 2.42 (3H, s), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 488.1[M+ H]+. |
| 60 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.13 - 9.25 (1H, m), 7.46 - 7.54 (1H, m), 7.27 - 7.36 (2H, m), 7.09 - 7.21 (1H, m), 6.96 (4H, d, *J*=9.54 Hz), 6.88 (2H, s), 5.96 - 6.06 (1H, m), 4.59 - 4.67 (2H, m) ,3.78 (3H, s), 3.35 (4H, d, *J*=5.27 Hz), 3.23 (4H, brs), 2.90 - 3.01 (2H, m), 2.36 (3H, s), 1.39 (3H, t, *J*=7.53 Hz); LCMS: 99.0%, MS (ESI): m/z 522.1[M+ H]+. |
| 61 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 7.2 Hz), 7.51 (2H, d, *J* = 8.8 Hz), 7.36-7.30 (3H, m), 6.98 (4H, d, *J* = 8.4 Hz), 6.76 (1H, d, *J* = 7.2 Hz), 6.00 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.45-3.34 (8H, m), 2.94 (2H, q, *J* = 7.6 Hz), 2.42 (3H, s), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 99.3%, MS (ESI): m/z 522.1[M+ H]+. |
| 62 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.41 (1H, d, *J* = 7.2 Hz), 7.61 (1H, d, *J* = 8.8 Hz), 7.25-7.36 (5H, m, overlap with $CDCl_3$ signal), 6.95-7.04 (m, 4H), 6.86-6.94 (2H, m), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.35 (8H, s), 2.98 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 440.1 [M+ H]+. |
| 63 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.21 (1H, d, *J* = 6.8 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.24 (2H, d, *J* = 9.2 Hz), 7.06-6.97 (3H, m), 6.90 (2H, d, *J* = 9.2 Hz), 6.86-6.81 (1H, m), 6.07 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.35-3.30 (8H, m), 3.00 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 491.9[M+ Na]+. |
| 64 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.35 (1H, d, *J* =6.8 Hz） , 7.39 (1H, d, *J* = 7.2 Hz), 7.28-7.32 (4H, m), 6.99 (4H, d, *J* = 8 Hz), 6.83-6.92 (2H, m), 6.07 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.35 (8H, s), 3.01 (2H, q, *J* = 7.6 Hz), 1.39 (3H, t, *J* = 7.8 Hz); LCMS: 100.0%, MS (ESI): m/z474.0[M+ H]+. |
| 65 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.12 - 9.29 (1 H, m), 7.48 - 7.53 (1 H, m), 7.29 - 7.34 (2 H, m), 7.15 - 7.20 (1 H, m), 7.07 - 7.14 (2 H, m), 6.94 - 7.01 (2 H, m,), 6.85 - 6.94 (2 H, m), 5.95 - 6.04 (1 H, m), 4.63 (2 H, d, *J*=5.52 Hz,), 3.34 (4 H, d, *J*=5.77 Hz), 3.30 (4 H, d, *J*=5.77 Hz), 2.96 (2 H, d, *J*=7.53 Hz), 2.36 (3 H, s), 2.29 (3 H, s), 1.39 (3 H, t, *J*=7.53 Hz); LCMS: 100%, MS (ESI): m/z 467.2[M+ H]+. |

| | | |
|---|---|---|
| 66 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.14 - 9.31 (1 H, m), 7.45 - 7.56 (1 H, m), 7.28 - 7.40 (2 H, m), 7.19 - 7.30 (2 H, m), 7.15 - 7.20 (1 H, m), 6.94 - 7.02 (2 H, m), 6.85 - 6.94 (2 H, m), 5.97 - 6.06 (1 H, m), 4.63 (2 H, d, *J*=5.27 Hz), 3.32 (8 H, q, *J*=5.94 Hz), 2.96 (2 H, d, *J*=7.53 Hz), 2.36 (3 H, s), 1.39 (3 H, t, *J*=7.53 Hz); LCMS: 100%, MS (ESI): m/z 488.0[M+ H]+. |
| 67 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.30 (1H, d, *J* = 7.2 Hz), 7.38-7.28 (5H, m), 7.01 (4H, dd, *J* = 8.0 Hz, 1.6 Hz), 6.92 (1H, t, *J* = 7.2 Hz), 6.76 (1H, dd, *J* = 7.2 Hz, 1.6 Hz), 6.02 (1H, brs), 4.64 (2H, d, *J* = 5.6 Hz), 3.37 (8H, s), 2.97 (2H, q, *J* = 7.6 Hz), 2.44 (3H, s), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 476.1[M+ H]+. |
| 68 |  | white solid : $^1$H-NMR($CDCl_3$): δ 9.56 (1H, d, *J* = 1.2 Hz), 7.57 (1H, d, *J* = 9.2 Hz), 7.29-7.35 (5H, m), 7.01 (4H, d, *J* = 8.4 Hz), 6.93 (1H, t, *J* = 7.2 Hz), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.38 (8H, s), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 496.0[M+ Na]+. |
| 69 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.44-9.48(1H, m), 7.33-7.28(3H, m), 7.25-7.23(1H, m), 7.01(4H, d, *J*= 8.4 Hz), 6.92(4H, d, *J*=7.2Hz), 6.83-6.78(1H, m), 6.02(1H, brs), 4.64(2H, d, *J*=5.6Hz), 3.37(8H, s), 2.99-2.94(2H, m), 1.41(3H, t, *J*= 7.6 Hz); LCMS: 99.9%, MS (ESI): m/z 480.1[M+ Na]+. |
| 70 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.23 (1H, d, *J* = 6.8 Hz), 7.34-7.28 (4H, m), 7.08-7.00 (5H, m), 6.92 (1H, t, *J* = 7.2 Hz), 6.88-6.83 (1H, m), 6.10 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.38 (8H, s), 3.02 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.8%, MS (ESI): m/z 480.1[M+ Na]+. |
| 71 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.48 (1H, dd, *J* = 4.8, 2.0 Hz), 7.59 (1H, dd, *J* = 9.6, 5.2 Hz), 7.24-7.35 (5H, m, overlap with $CDCl_3$ signal), 7.01 (4H, d, *J* = 8.8 Hz), 6.93 (1H, t, *J* = 7.6 Hz), 6.06 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.38 (8H, s), 2.99 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 480.1[M+ Na]+. |
| 72 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.56 (1H, d, *J*= 1.6 Hz), 7.40-7.49 (1H, m), 7.29-7.37 (1H, m), 7.05-7.29 (4H. m), 6.84-7.01 (4H, m), 5.95 (1H, brs), 4.48-4.62 (2H, m), 3.65-3.81 (2H, m), 2.89 (2H, q, *J* = 7.6 Hz), 2.69-2.81 (2H, m), 2.50-2.61 (1H, m), 1.71-1.95 (4H, m), 1.33 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 535.0[M+ H]+. |
| 73 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 6.8 Hz), 7.18-7.36 (7H, m), 7.1 (1H, d, *J* = 6.8 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.81 (1H, t, *J* = 6.9 Hz), 6.03 (1H, brs), 4.62(2H, d, *J* = 5.5 Hz), 3.82 (2H, d, *J* = 12.3 Hz), 2.99 (2H, q, *J* = 7.7 Hz), 2.83 (2H, td, *J* = 12, 2.8 Hz), 2.62-2.71 (1H, m), 2.61 (3H, s), 1.83-2.01 (4H, m), 1.36 (3H, t, *J* = 7.5 Hz); LCMS: 100%, MS (ESI): m/z 475.2[M+ H]+. |
| 74 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.41-9.45(1H, m), 7.29(2H, d, J= 8.4 Hz), 7.20-7.22(1H, m), 6.93-6.99(4H, m), 6.85-6.88(2H, m), 6.75-6.80(1H, m), 5.99(1H, brs), 4.61(2H, d, *J*=5.2Hz), 3.78(3H, s), 3.33-3.36(4H, m), 3.21-3.24(4H, m), 2.91-2.97(2H, m), 1.38(3H, t, *J*= 7.2 Hz); LCMS: 98.0%, MS (ESI): m/z 488.1[M+ H]+, 510.1[M+ H]+ |

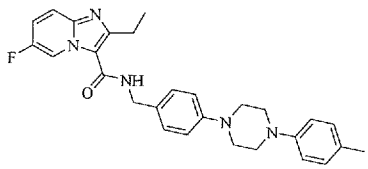
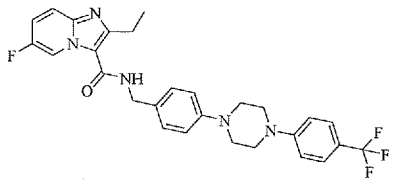
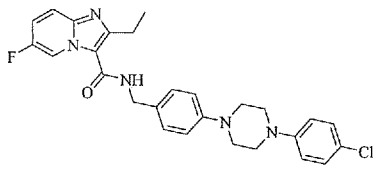
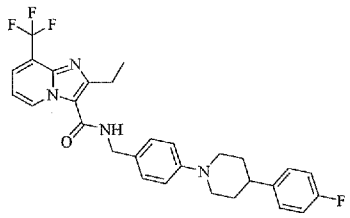
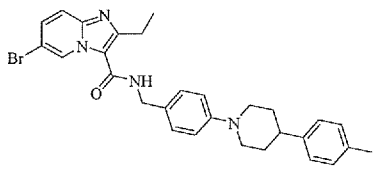
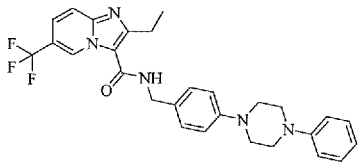
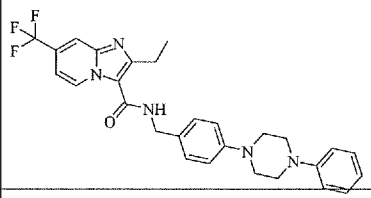
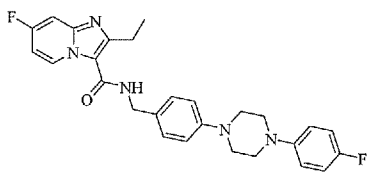
| | | |
|---|---|---|
| 75 |  | white solid :$^1$H-NMR ($CDCl_3$): δ 9.40-9.48 (1H, m), 7.52-7.60 (1H, m), 7.30 (2H, d, *J* = 8.8 Hz), 7.20-7.28 (1H, m, overlapped with $CDCl_3$), 7.10 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.90 (2H, d, *J* = 8.8 Hz), 6.02 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.20-3.40 (8H, m), 2.96 (2H, q, *J* = 7.6 Hz), 2.28 (3H, s), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 494.1[M+ Na]+. |
| 76 |  | white solid : $^1$H-NMR (DMSO-$d_6$): δ 9.40-9.51 (1H, m), 7.42-7.62 (3H, m), 7.26-7.40 (3H, m, overlap with $CDCl_3$ signal), 6.89-7.10 (4H, m), 6.04 (1H, brs), 4.63 (1H, d, *J* = 5.6 Hz), 3.20-3.50 (8H, m), 2.97 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 526.0[M+ H]+. |
| 77 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.40-9.52 (1H, m), 7.52-7.62 (1H, m), 7.31 (2H, d, *J* = 8.0 Hz), 7.15-7.28 (3H, m, overlapped with $CDCl_3$), 6.98 (2H, d, *J* = 8.0 Hz), 6.90 (2H, d, *J* = 8.4 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.20-3.45 (8H, m), 2.97 (2H, q, *J* = 7.2 Hz), 1.40 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 492.0[M+ H]+. |
| 78 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.60 (1H, d, *J* = 6.8 Hz), 7.65 (1H, d, *J* = 6.8 Hz), 7.25-7.40 (2H, m), 7.10-7.25 (2H, m), 6.90-7.10 (5H, m), 6.09 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.70-3.90 (2H, m), 3.02 (2H, q, *J* = 7.6 Hz), 2.75-2.90 (2H, m), 2.60-2.70 (1H, m), 1.80-2.05 (4H, m), 1.38 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 525.0[M + H]+. |
| 79 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.63 (1H, s), 7.49 (1H, d, *J* = 9.6 Hz ), 7.39 (1H, d, *J* = 9.6 Hz), 7.29-7.35 (2H, m), 7.05-7.20 (4H, m), 6.90-7.05 (2H, m), 6.03 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.71-3.91 (2H, m), 2.96 (2H, q, *J* = 7.6 Hz), 2.75-2.90 (2H, m), 2.55-2.70 (1H, m), 2.33 (3H, s), 1.80-2.05 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 98.1%, MS (ESI): m/z 531.1[M+ H]+. |
| 80 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, *J* = 8.8 Hz), 7.47 (1H, d, *J* = 9.2 Hz), 7.28-7.40 (4H, m), 6.95-7.10 (4H, m), 6.87-6.95 (1H, m), 6.07 (1H, s), 4.64 (2H, d, *J* = 5.2 Hz), 3.36 (8H, s), 2.99 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 530.1[M+ H]+. |
| 81 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.53 (1H, d, *J* = 7.2 Hz), 7.91 (1H, s), 7.26-7.33 (4H, m), 7.09 (2H, d, *J* = 7.6 Hz), 6.96-7.05 (4H,m), 6.89-6.92 (1H, m), 6.08 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.39-3.41 (8H, m), 3.00 (2H, q, *J*= 7.2 Hz), 1.42 (3H, t, *J* = 7.2 Hz); LCMS: 98.7%, MS (ESI): m/z 508.1[M+ H]+. |
| 82 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.42-9.46(1H, m), 7.31-7.13(3H, m), 7.01-6.86(6H, m), 6.80-6.77(1H, m), 6.00(1H, brs), 4.62(2H, d, *J*=5.2Hz), 3.35(4H, d, *J*=4.4Hz), 3.27(4H, d, *J*=4.4Hz),2.97-2.92(2H, m), 1.39(3H, t, *J*= 7.6 Hz); LCMS: 99.4%, MS (ESI): m/z 476.1[M+ H]+. |

Table 2

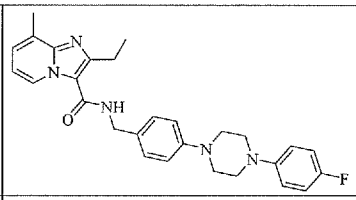
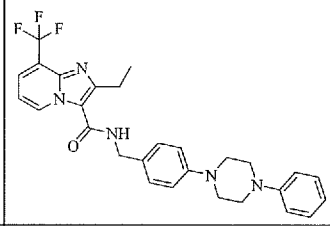
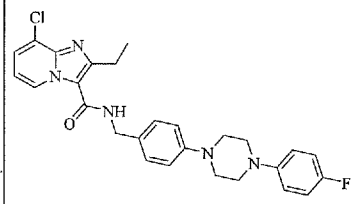
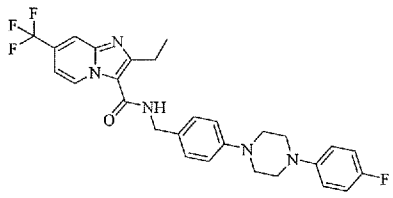
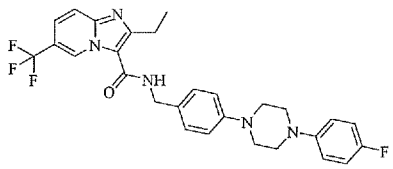
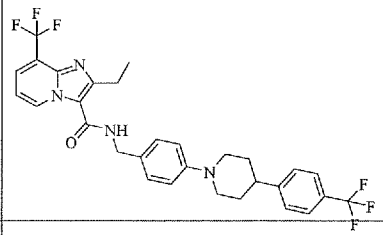
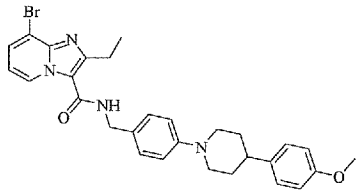
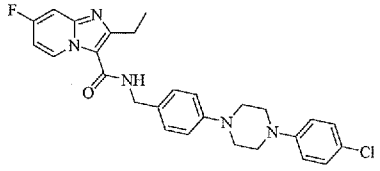
| | | |
|---|---|---|
| 83 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7 Hz), 7.31 (2H, d, *J* = 8.3 Hz), 7.12 (1H, d, *J* = 6.3 Hz), 6.89-7.04 (6H, m), 6.82 (1H, t, *J* = 6.8 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.3 Hz), 3.20-3.44 (8H, m), 3.00 (2H, q, *J* = 7.4 Hz), 2.62 (3H, s,), 1.37 (3H, t, *J* = 7.7 Hz); LCMS: 99.5%, MS (ESI): m/z 494.1[M+ H]+. |
| 84 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.58 (1H, d, *J* = 6.8 Hz), 7.66 (1H, d, *J* = 6.8 Hz), 7.25-7.35 (4H, m), 6.95-7.05 (5H, m), 6.91 (1H, t, *J* = 6.8 Hz), 6.10 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.36 (8H, s), 3.03 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 508.0[M + H]+. |
| 85 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.35 (1H, d, *J* =6.8 Hz), 7.39 (1H, d, *J* = 7.6 Hz), 7.30 (2H, d, *J* = 8 Hz), 6.89-7.19 (6H, m), 6.85 (1H, t, *J* = 7.2 Hz), 6.08 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.35 (2H, d, *J* = 5.6 Hz), 3.27 (2H, d, *J* = 5.6 Hz), 3.01 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS:100.0%, MS (ESI): m/z 492.0[M+ H]+. |
| 86 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.53 (1H, d, *J* = 7.2 Hz), 7.91 (1H, s), 7.45 (2H, d, *J* = 10.0 Hz), 7.09 (1H, d, *J* = 7.2 Hz), 6.94-7.00 (6H, m), 6.08 (1H, brs), 4.63 (2H, d, *J* = 4.8 Hz), 3.32-3.40 (4H, m), 3.27-3.30 (4H, m), 3.00 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.8%, MS (ESI): m/z 526.0[M+ H]+. |
| 87 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, *J* = 9.6 Hz), 7.48 (1H, d, *J* = 9.2 Hz), 7.28-7.41 (2H, m), 6.83-7.12 (6H, m), 6.08 (1H, s), 4.64 (2H, d, *J* = 5.2 Hz), 3.36 (4H, s), 3.26 (4H, s), 2.99 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 99.0%, MS (ESI): m/z 526.0[M+ H]+. |
| 88 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.60 (1H, d, *J* = 7.2 Hz), 7.66 (1H, d, *J* = 7.2 Hz), 7.58 (2H, d, *J* = 8.0 Hz), 7.36 (2H, d, *J* = 7.6 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 6.90-7.05 (3H, m), 6.10 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.75-3.90 (2H, m), 3.05 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.65-2.75 (1H, m), 1.80-2.05 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 575.0[M + H]+. |
| 89 |  | yellow solid : $^1$H-NMR (CDCl3): δ 9.39 (1H, d, *J* = 7.2 Hz), 7.58 (1H, d, *J* = 7.6 Hz), 7.20-7.40 (2H, m), 7.17 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* =8.0 Hz), 6.87 (2H, d, *J* = 7.2 Hz), 6.79 (1H, t, *J* = 7.2 Hz), 6.06 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.70-3.90 (5H, m), 3.01 (2H, q, *J* = 7.6 Hz), 2.83 (2H, t, *J* = 11.6 Hz), 2.61 (2H, t, *J* = 12.0 Hz), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 569.0/571.0 [M+23] |
| 90 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.43(1H, t, *J*= 7.6 Hz), 7.22-7.63(5H, m), 6.97(2H, d, *J*= 8.4 Hz), 6.89(2H, d, *J*= 8.4 Hz), 6.61-6.81(1H, m), 6.00(1H, brs), 4.61(2H, d, *J*= 4.8 Hz), 3.48-3.55(8H, m), 2.91-2.95(2H, m), 1.39(3H, d, *J*= 7.6 Hz); LCMS: 99.9%, MS (ESI): m/z 492.0[M+ H]+. |

Table 2

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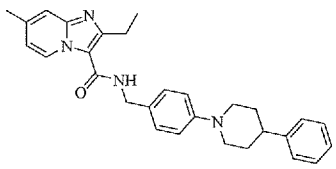
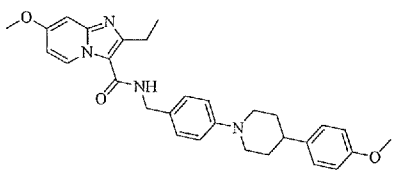
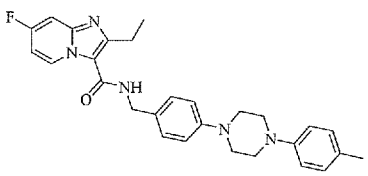
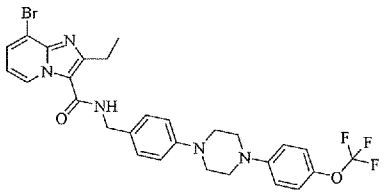
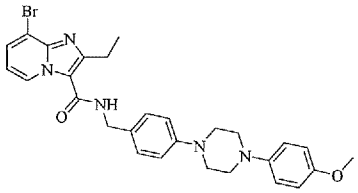
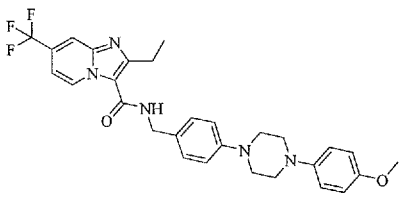
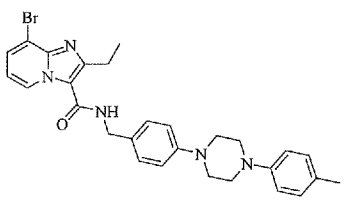
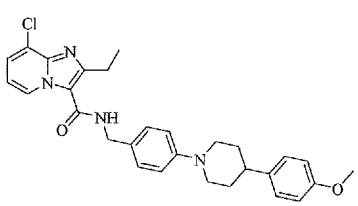
| 91 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 6.8 Hz), 7.35-7.22 (9H, m), 6.99 (2H, d, *J* = 7.6 Hz), 6.75 (1H, d, *J* = 6.8 Hz), 5.98 (1H, brs), 4.62 (2H, d, *J* = 4.4 Hz), 3.82 (2H, d, *J* = 11.2 Hz), 2.66 (1H, brs), 2.42 (3H, s), 1.95-1.83 (4H, m), 1.40-1.30 (3H, m); LCMS: 100%, MS (ESI): m/z 453.1[M+ H]+. |
| 92 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7.6 Hz), 7.28 (2H, d, *J* = 8.4 Hz), 7.17 (2H, d, *J* = 8.0 Hz), 6.98 (2H, d, *J* = 8.0 Hz), 6.80-6.90 (3H, m), 6.60 (1H, d, *J* = 6.4 Hz), 5.94 (1H, brs), 4.60 (2H, d, *J* = 5.2 Hz), 3.86 (3H, s), 3.70-3.82 (5H, m), 2.92 (2H, q, *J* = 7.6 Hz), 2.82 (2H, t, *J* = 12.0 Hz), 2.55-2.70 (1H, m), 1.85-2.02 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 499.1 [M+H]+, 521.1 [M+Na]+. |
| 93 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.44(1H, t, *J*= 7.2 Hz), 7.30(2H, d, *J*= 8 Hz), 7.21-7.24(1H, m), 7.10(2H, d, *J*= 7.6 Hz), 6.98(2H, d, *J*= 8.4 Hz), 6.90(2H, d, *J*= 8.0 Hz), 6.77-6.81(1H, m), 5.97(1H, brs), 4.61(2H, d, *J*= 5.2 Hz), 3.19-3.46(8H, m), 2.92-2.97(2H, m), 2.89(3H, s), 1.39(3H, t, *J*= 7.2 Hz); LCMS: 99.9%, MS (ESI): m/z 494.0[M+ Na]+. |
| 94 |  | white solid : $^1$H-NMR (CDCl3): δ 9.40 (1H, d, *J* = 6.8 Hz), 7.58 (1H, d, *J* = 7.6 Hz), 7.31 (2H, d, *J* = 8.0 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 7.05 (2H, d, *J* = 8.4 Hz), 6.85-7.05 (4H, m), 6.80 (1H, t, *J* = 7.2 Hz), 6.08 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.18-3.44 (8H, m), 3.02 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 98.2%, MS(ESI):m/z 601.8/603.8 [M+H]+ |
| 95 |  | white solid : $^1$H-NMR (CDCl3): δ 9.40 (1H, d, *J* = 6.8 Hz), 7.58 (1H, d, *J* = 6.8 Hz), 7.30 (2H, d, *J* = 8.4 Hz), 6.90-7.05 (4H, m), 6.87 (2H, d, *J* = 9.2 Hz), 6.79 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.96 (3H, s), 3.28-3.50 (4H, m), 3.15-3.28 (4H, m), 3.02 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 571.6/573.6 [M+23] |
| 96 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.53 (1H, d, *J* = 7.2 Hz), 7.91 (1H, s), 7.31 (2H, d, *J* = 8.4 Hz), 7.09 (1H, d, *J* = 6.8 Hz), 6.81-7.01 (4H, m), 6.87 (2H, d, *J* = 9.2 Hz), 6.11 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.79 (3H, s), 3.35-3.40 (4H, m), 3.28-3.32 (4H, m), 3.00 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 538.1[M+ H]+. |
| 97 |  | white solid : $^1$H-NMR (CDCl3): δ 9.40 (1H, d, *J* = 6.8 Hz), 7.58 (1H, d, *J* = 7.2 Hz), 7.31 (2H, d, *J* = 8.8 Hz), 7.11 (2H, d, *J* = 8.8 Hz), 6.99 (2H, d, *J* = 8.8 Hz), 6.90 (2H, d, *J* = 8.8 Hz), 6.80 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.20-3.40 (8H, m), 3.02 (2H, q, *J* = 7.6 Hz), 2.29 (3H, s), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 532.1/534.1 [M+H]+ |
| 98 |  | grey solid : $^1$H-NMR ($CDCl_3$): δ 9.34 (1H, d, *J* = 6.8 Hz） , 7.39 (1H, d, *J* = 7.2 Hz), 7.27 (2H, d, *J* = 8.4 Hz), 7.17 (2H, d, *J* = 8.4 Hz ), 6.99 (2H, d, *J* = 8.4 Hz), 6.83-6.87 (3H, m), 6.07 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.80-3.82 (5H, m), 3.02 (2H, q, *J* = 7.2 Hz), 2.82 (2H, t, *J* = 11.2 Hz), 2.61 (1H, t, *J* = 11.6 Hz), 1.81-1.95 (4H, m), 1.38 (3H, t, *J* = 7.2 Hz); LCMS: 100.0%, MS (ESI): m/z 525.1[M+ Na]+. |

Table 2

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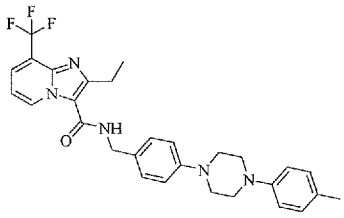
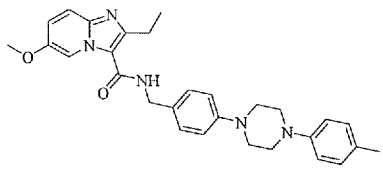
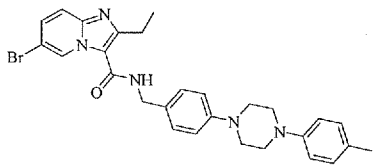
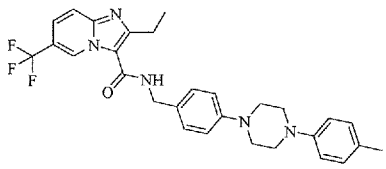
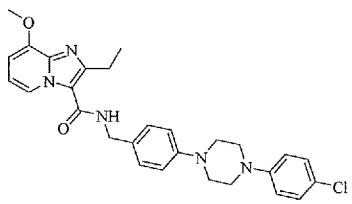
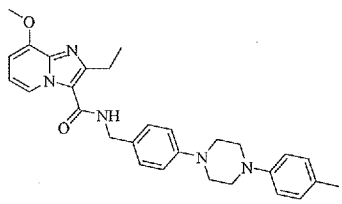
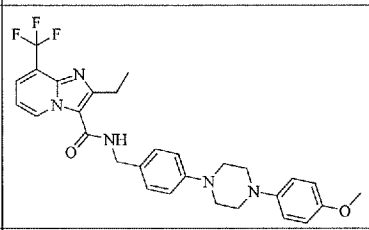
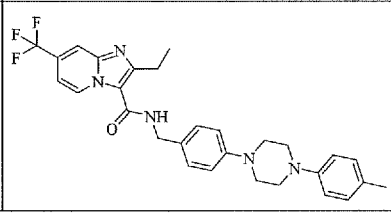
|---|---|---|
| 99 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.61 (1H, d, *J* = 6.8 Hz), 7.68 (1H, d, *J* = 6.8 Hz), 7.32 (2H, d, *J* = 8.8 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 6.98-7.03 (3H, m), 6.92 (2H, d, *J* = 8.4 Hz), 6.12 (1H, brs), 4.66 (2H, d, *J* = 5.2 Hz), 3.31-3.38 (8H, m), 3.05 (2H, q, *J* = 7.6 Hz), 2.31 (3H, s), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 522.1[M + H]+. |
| 100 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.13 (1H, d, *J* = 2.4 Hz), 7.52 (1H, d, *J* = 9.6 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.14 (2H, d, *J* =8.8 Hz), 7.01 (2H, d, *J* =8.4 Hz), 6.93 (2H, d, *J* = 8.4 Hz), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.90 (3H, s), 3.25-3.40 (8H, m), 2.97 (2H, q, *J* = 7.6 Hz), 2.31 (3H, s), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 484.1 [M+H]+ |
| 101 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.65 (1H, s), 7.51 (1H, d, *J* = 9.2 Hz ), 7.41 (1H, d, *J* = 9.6 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 7.01 (2H, d, *J* = 8.4 Hz), 6.93 (2H, d, *J* = 8.4 Hz), 6.07 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.26-3.42 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 534.0[M+ H]+. |
| 102 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.88 (1H, s), 7.71 (1H, d, *J* = 9.2 Hz), 7.49 (1H, dd, *J* = 7.6, 2.0 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.0 Hz), 7.01 (2H, d, *J* = 8.4 Hz), 6.93 (2H, d, *J* = 4.8 Hz), 6.09 (1H, s), 4.66 (2H, d, *J* = 5.2 Hz), 3.35-3.45 (4H, m), 3.25-3.35 (4H, m), 3.01 (2H, q, *J* = 7.6 Hz), 2.31 (3H, s), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 522.1[M+ H]+. |
| 103 |  | white solid : $^1$H-NMR (CDCl3): δ 9.01 (1H, d, *J*= 6.8 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 7.00 (2H, d, *J* = 8.4 Hz), 6.92 (2H, d, *J* = 9.2 Hz), 6.83 (1H, t, *J* = 7.4 Hz), 6.64 (1H, d, *J* = 7.6 Hz), 6.07 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 4.04 (3H, s). 3.36 (4H, d, *J* = 5.6 Hz), 3.33 (4H, d, *J* = 6.0 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 526.1[M+ Na]+. |
| 104 |  | yellow solid : $^1$H-NMR (CDCl3): δ 8.99 (1H, dd, *J*= 0.8 Hz, *J* = 7.2 Hz), 7.31 (2H, d, *J* = 8.8 Hz), 7.11 (2H, d, *J* = 8.0 Hz), 6.98 (2H, d, *J* = 8.8 Hz), 6.93 (2H, d, *J* = 10.0 Hz), 6.81 (1H, t, *J* = 7.4 Hz), 6.62 (1H, d, *J* = 7.2 Hz), 6.04 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 4.02 (3H, s). 3.28-3.84 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 2.29 (3H, s), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 484.1[M+ H]+. |
| 105 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.59 (1H, d, *J* = 7.2 Hz), 7.66 (1H, d, *J* = 6.8 Hz), 7.30 (2H, d, *J* = 8.4 Hz), 6.94-7.06 (5H, m), 6.85-6.90 (2H, m), 6.13 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.79 (3H, s), 3.34-3.37 (4H, m), 3.19-3.30 (4H, m), 3.03 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 99.4%, MS (ESI): m/z 538.1[M + H]+. |
| 106 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, *J* = 7.2 Hz), 7.93 (1H, s), 7.33 (2H, d, *J* = 8.4 Hz), 7.10-7.15 (3H, m), 7.01 (2H, d, *J* = 8.4 Hz), 6.92 (2H, d, *J* = 8.4 Hz), 6.10 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.36-3.40 (4H, m), 3.27-3.38 (4H, m), 3.01 (2H, q, *J* = 7.6 Hz), 2.31 (3H, s), 1.44 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 522.0[M+ H]+. |

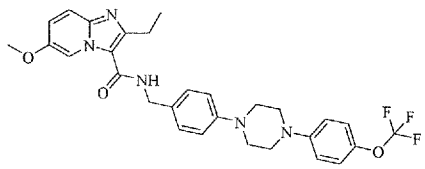
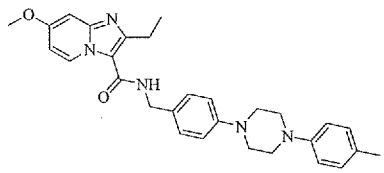
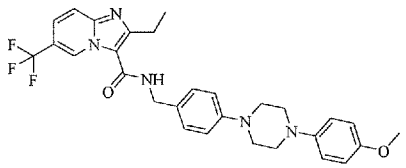
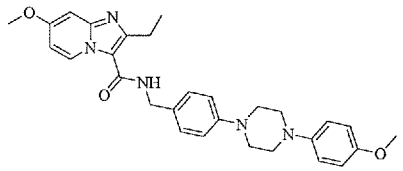
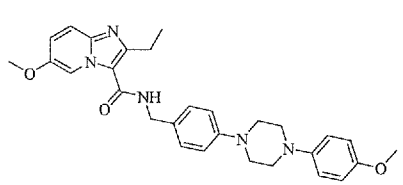
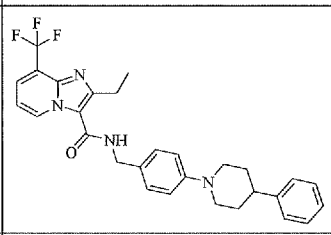
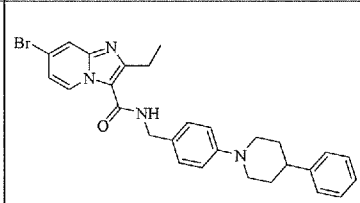
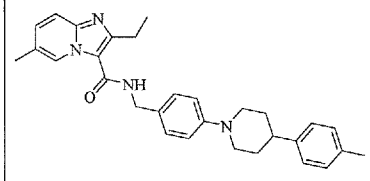
| | | |
|---|---|---|
| 107 |  | white solid : $^1$H-NMR (CDCl3): δ 9.13 (1H, d, *J* = 2.4 Hz), 7.52 (1H, d, *J* =9.6 Hz), 7.34 (2H, d, *J* = 8.8 Hz), 7.10-7.20 (3H, m), 6.92-7.04 (4H, m), 6.06 (1H, brs), 4.66 (2H, d, *J* = 5.6 Hz), 3.90 (3H, s), 3.26-3.40 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.0%, MS(ESI):m/z 554.1 [M+H]+ |
| 108 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7.6 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.11 (2H, d, *J* = 8.4 Hz),6.99 (2H, d, *J* = 8.4 Hz), 6.89-6.96 (3H, m), 6.61 (1H, dd, *J* = 7.6 Hz,2.4 Hz), 5.95 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.87 (3H, s), 3.52-3.71 (8H, m), 2.92 (2H, q, *J* = 7.6 Hz), 2.29 (3H, s), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 484.1[M+ H]+, 506.1 [M+Na]+. |
| 109 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.88 (1H, s), 7.72 (1H, d, *J* = 9.6 Hz), 7.50 (1H, dd, *J* = 8.0, 1.6 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 6.95-7.08 (4H, m), 6.89 (2H, d, *J* = 9.2 Hz), 6.10 (1H, s), 4.66 (2H, d, *J* = 5.6 Hz), 3.81 (3H, s), 3.35-3.52 (4H, m), 3.21-3.30 (4H, m), 3.01 (2H, q, *J* = 7.6 Hz), 1.44 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 538.1[M+ H]+. |
| 110 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.27 (1H, d, *J* = 7.6 Hz), 7.32 (2H, d, *J* = 8.4 Hz), 6.95-7.04 (4H, m), 6.85-6.94 (3H, m), 6.32 (1H, dd, *J* = 7.6, 2.4 Hz), 5.97 (1H, t, *J* = 4.4 Hz), 4.63 (2H, d, *J* = 5.6 Hz), 3.89 (3H, s), 3.81 (3H, s), 3.30-3.40 (4H, m), 3.20-3.29 (4H, m), 2.94 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 99.0%, MS (ESI): m/z 522.1[M+ Na]+. |
| 111 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.13 (1H, d, *J* = 2.0 Hz), 7.51 (1H, d, *J* =9.6 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.12 (2H, dd, *J* =9.6, 2.4 Hz), 6.92-7.08 (4H, m), 6.89 (2H, d, *J* =9.2 Hz), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.89 (3H, s), 3.30-3.40 (4H, m), 3.20-3.30 (4H, m), 2.97 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 522.1 [M+23]. |
| 112 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.61 (1H, d, *J* = 6.8 Hz), 7.68 (1H, d, *J* = 7.2 Hz), 7.20-7.40 (7H, m), 6.95-7.10 (3H, m), 6.12 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.80-3.90 (2H, m), 3.06 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.60-2.75 (1H, m), 1.85-2.05 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 507.0[M + H]+. |
| 113 |  | yellow solid : H-NMR ($CDCl_3$): δ 9.29 (1H, d, *J* = 7.6 Hz), 7.76 (1H, d, *J* = 2.0 Hz ), 7.15-7.36 (7H, m), 6.93-7.05 (3H, m), 6.05 (1H, brs), 4.60 (2H, d, *J* = 5.6 Hz), 4.52-4.63 (2H. m), 2.94 (2H, q, *J* = 7.6 Hz), 2.77-2.89 (2H, m), 2.60-2.71 (1H. m), 1.81-2.02 (4H. m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 98.3%, MS (ESI): m/z 517.0[M+ H]+. |
| 114 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.16 - 9.27 (1 H, m), 7.44 - 7.54 (1 H, m), 7.23 - 7.31 (3 H, m), 7.09 - 7.20 ( 4 H, m), 6.98 (2 H, d, *J*=8.60 Hz), 5.98 (1 H, br. s.), 4.61 (2 H, d, *J*=5.51 Hz), 3.80 (2 H, d, *J*=12.35 Hz), 2.95 (2 H, d, *J*=7.72 Hz), 2.77 - 2.86 (2 H, m), 2.62 (1 H, s), 2.34 (6 H, d, *J*=12.35 Hz), 1.81 - 1.98 (4 H, m), 1.38 (3 H, t, *J*=7.50 Hz,); LCMS: 98.0%, MS (ESI): m/z 453.0[M+ H]+. |

Table 2

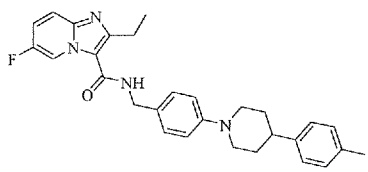
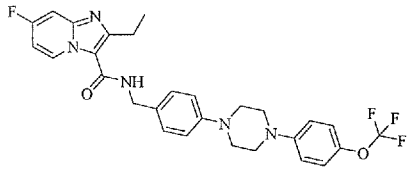
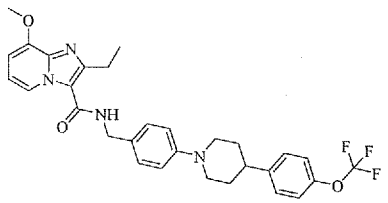
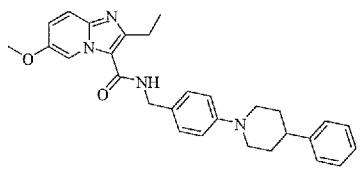
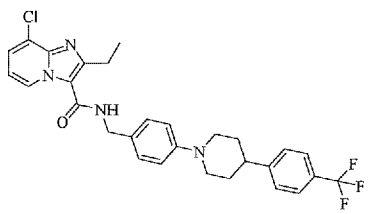
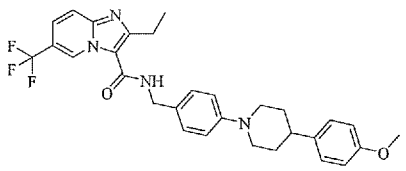
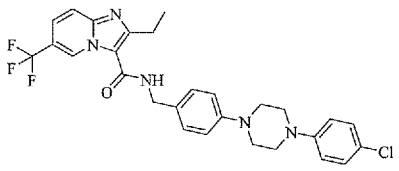
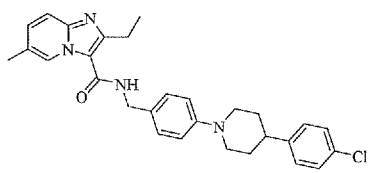
| | | |
|---|---|---|
| 115 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.45 (1H, dd, *J* = 5.2, 2.4 Hz), 7.55 (1H, dd, *J* = 10.0, 5.2 Hz), 7.20-7.30 (3H, m, overlap with $CDCl_3$ signa), 7.10-7.20 (4H, m), 6.98 (2H, d, *J* = 8.8 Hz), 6.01 (1H, brs), 4.55-4.65 (2H, m), 3.81 (2H, d, *J* = 12.0 Hz), 2.96 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 12.0, 2.8 Hz), 2.60-2.70 (1H, m), 2.32 (3H, s), 1.80-2.00 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 493.0[M+ Na]+. |
| 116 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.41-9.45(1H, m), 7.29(2H, d, *J*= 8.4 Hz), 7.19-7.22(1H, m), 7.12(2H, d, *J*= 8.4 Hz), 6.92-6.98(5H, m), 6.75-6.80(1H, m), 5.99(1H, brs), 4.60(2H, d, *J*=5.2Hz), 3.30-3.35(8H, m), 2.91-2.97(2H, m), 1.38(3H, t, *J*= 7.6 Hz); LCMS: 98.1%, MS (ESI): m/z 542.1[M+ H]+. |
| 117 |  | red solid: $^1$H-NMR ($CDCl_3$): δ 8.98 (1H, dd, *J*= 0.8 Hz, *J* = 6.8 Hz), 7.24-7.29 (4H, m), 7.15 (2H, d, *J* = 8.0 Hz), 6.97 (2H, d, *J* = 8.4 Hz), 6.80 (1H, t, *J* = 6.2 Hz), 6.60 (1H, d, *J* = 7.6 Hz), 6.03 (1H, brs), 4.61 (2H, d, *J* = 5.2 Hz), 4.01 (3H, s). 3.81 (2H, d, *J* = 12.4 Hz), 2.97 (2H, q, *J* = 7.6 Hz), 2.82 (2H, t, *J* = 11.4 Hz), 2.62-2.69 (1H, m), 1.82-1.96 (4H, m), 1.37 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 553.1[M+ H]+. |
| 118 |  | pink solid: $^1$H-NMR ($CDCl_3$): δ 9.10 (1H, d, *J* = 1.6 Hz), 7.48 (1H, d, *J* = 9.6 Hz), 7.17-7.35 (7H, m), 7.08 (1H, d, *J* = 7.2 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.02 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.86 (3H, s), 3.82 (2H, d, *J* = 12.4 Hz), 2.94 (2H, q, *J* = 7.6 Hz), 2.83 (2H, t, *J* = 12.0 Hz), 2.60-2.70 (1H, m), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 469.1 [M+H]+ |
| 119 |  | red solid: $^1$H-NMR ($CDCl_3$): δ 9.34 (1H, d, *J* = 6.8 Hz), 7.57 (2H, d, *J* = 8 Hz), 7.34-7.39 (3H, m), 7.28 (2H, d, *J* = 8. 8 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.85 (1H, t, *J* = 7.2 Hz), 6.06 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.82 (2H, d, *J* = 12.0 Hz), 3.01 (2H, q, *J* = 7.6 Hz), 2.84 (2H, td, *J* = 2.8, *J* = 12.4 Hz), 2.68-2.76 (1H, m), 1.84-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 98.5%, MS (ESI): m/z 541.1[M+ H]+. |
| 120 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.70-9.80 (1H, m), 7.68 (1H, d, *J* = 8.8 Hz), 7.46 (1H, dd, *J* = 7.6, 2.0 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 7.16 (2H, dd, *J* = 4.8 2.0 Hz), 6.98 (2H, d, *J* = 8.8 Hz), 6.86 (2H, dd, *J* = 4.8 2.0 Hz), 6.06 (1H, m), 4.62 (2H, d, *J* = 5.2 Hz), 3.82 (2H, s), 3.79 (3H, s), 2.99 (2H, q, *J* = 7.6 Hz), 2.75-2.89 (2H, m), 2.53-2.69 (1H, m), 1.78-2.01 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 537.0[M+ H]+. |
| 121 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.85 (1H, s), 7.69 (1H, d, *J* = 5.2 Hz), 7.47 (1H, dd, *J* = 7.6, 2.0 Hz), 7.30 (2H, d, *J* = 8.0 Hz), 7.18-7.24 (2H, m), 6.98 (2H, d, *J* = 8.4 Hz), 6.88 (2H, d, *J* = 5.2 Hz), 6.02-6.11 (1H, m), 4.63 (2H, d, *J* = 5.6 Hz), 3.30-3.35 (8H, m), 2.99 (2H, q, *J* = 8.4 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 541.8[M+ H]+. |
| 122 |  | red solid : $^1$H-NMR ($CDCl_3$): δ 9.15 - 9.27 (1 H, m), 7.49 (1 H, d, *J*=9.04 Hz), 7.22 - 7.33 (4 H, m), 7.17 (3 H, d, *J*=8.38 Hz), 6.97 (2 H, d, *J*=8.60 Hz), 5.94 - 6.06 (1 H, m), 4.61 (2 H, d, *J*=5.51 Hz), 3.80 ( 2 H, d, *J*=12.35 Hz), 2.95 (2 H, d, *J*=7.50 Hz), 2.81 (2 H, d, *J*=2.43 Hz), 2.57 - 2.69 (1 H, m), 2.35 (3 H, s), 1.92 (2 H, br. s.), 1.85 (2 H, dd, *J*=12.46, 3.42 Hz), 1.38 (3 H, t, *J*=7.50 Hz); LCMS: 100%, MS (ESI): m/z 487.0[M+ H]+. |

Table 2

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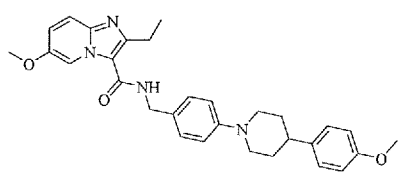
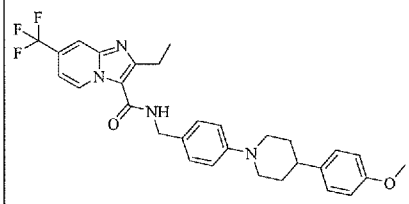
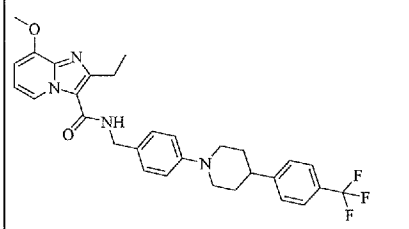
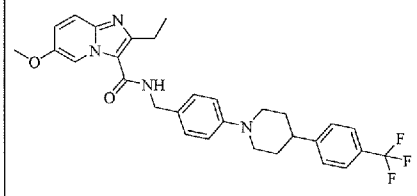
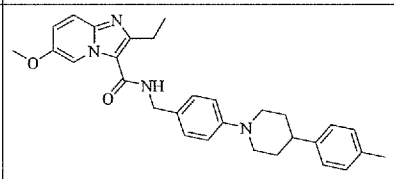
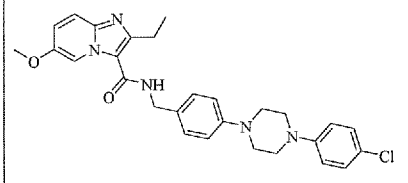
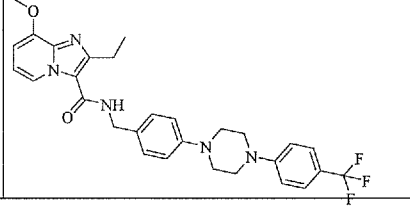
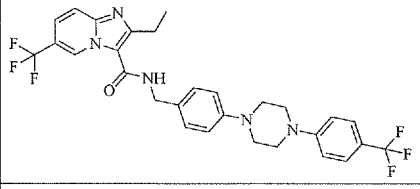
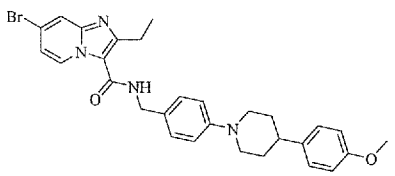
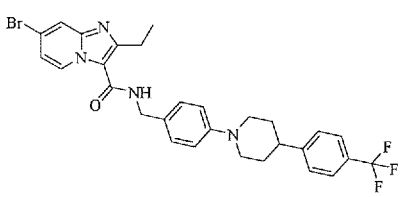
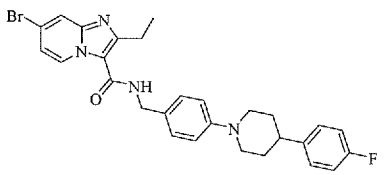
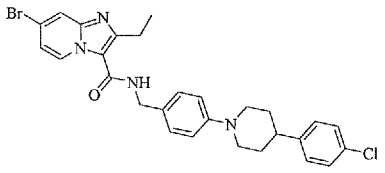
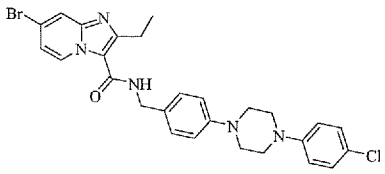
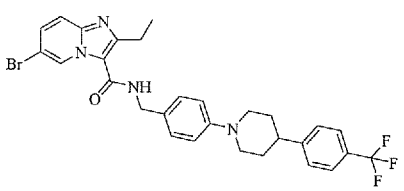
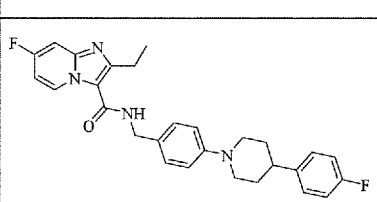
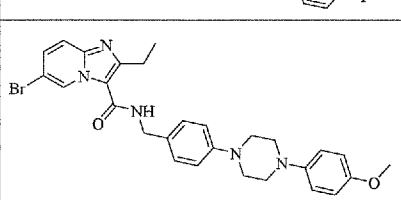
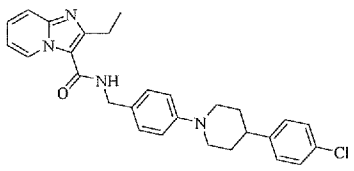
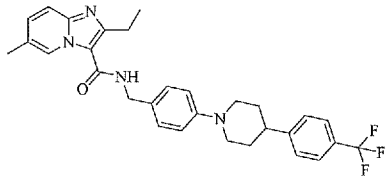
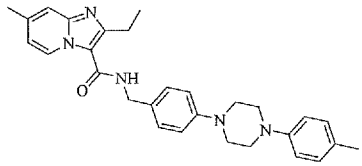
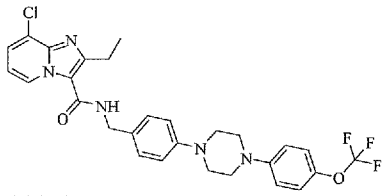
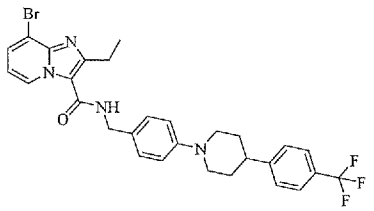
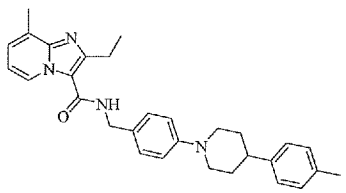
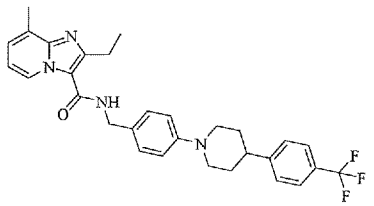
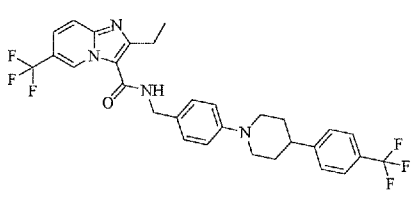
|---|---|---|
| 123 |  | pink solid : $^1$H-NMR (CDCl3): δ 9.13 (1H, d, *J* = 2.0 Hz), 7.52 (1H, d, *J* = 9.6 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.20 (2H, d, *J* = 8.4 Hz), 7.13 (1H, dd, *J* = 9.6, 2.4 Hz), 7.01 (2H, d, *J* = 8.8 Hz), 6.89 (2H, d, *J* = 8.8 Hz), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.90 (3H, s), 3.76-3.88 (5H, m), 2.97 (2H, q, *J* = 7.6 Hz), 2.87 (2H, td, *J* = 12.0, 2.4 Hz), 2.60-2.70 (1H, m), 1.80-2.00 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 521.1 [M+23] |
| 124 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, *J* = 7.2 Hz), 7.93 (1H, s), 7.30-7.32 (2H, m), 7.19 (2H, d, *J* = 8.4 Hz), 7.10 (1H, dd, *J* = 7.2, 1.6 Hz), 7.01 (2H, d, *J* = 8.8 Hz), 6.89 (2H, d, *J* = 8.4 Hz), 6.09 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.86 (2H, s), 3.82 (3H, s), 3.01 (2H, q, *J* = 7.6 Hz), 2.81-2.89 (2H, m), 2.61-2.67 (1H, m), 1.86-2.00 (4H, m), 1.44 (3H, t, *J* = 7.6 Hz); LCMS: 99.1%, MS (ESI): m/z 537.0[M+ H]+. |
| 125 |  | pink solid : $^1$H-NMR (CDCl3): δ 9.02 (1H, d, *J* = 6.8 Hz), 7.61 (2H, d, *J* = 8.0 Hz), 7.38 (2H, d, *J* = 8.0 Hz), 7.31 (2H, d, *J* =8.8 Hz), 7.00 (2H, d, *J* = 8.8 Hz), 6.83 (1 H, t, *J* = 7.6 Hz), 6.63 (1H, d, *J* = 7.6 Hz), 6.07 (1H, brs), 4.64 (2H, d, *J* = 5.6 Hz), 4.04 (3H, s), 3.85 (2H, d, *J* = 12.4 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 2.86 (2H, dt, *J* = 2.8 Hz, *J* = 12 Hz), 2.73 (1H, m), 1.87-2.00 (4H, m), 1.41 (3H, t, *J*= 7.6 Hz); LCMS: 99.1%, MS (ESI): m/z 537.1[M+ H]+. |
| 126 |  | red solid : $^1$H-NMR (CDCl3): δ 9.14 (1H, d, *J* = 2.0 Hz), 7.60 (1H, d, *J* = 8.4 Hz), 7.53 (2H, d, *J* = 9.6 Hz), 7.39 (2H, d, *J* = 8.4 Hz), 7.32 (2H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 9.6 Hz), 7.02 (2H, d, *J* = 8.8 Hz), 6.05 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.90 (3H, s), 3.86 (2H, d, *J* = 12.4 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 2.87 (2H, td, *J* = 12.0, 2.4 Hz), 2.70-2.80 (1H, m), 1.88-2.05 (4H, m), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.40%, MS(ESI):m/z 537.1 [M+H]+ |
| 127 |  | white solid : $^1$H-NMR (CDCl3): δ 9.13 (1H, d, *J* = 2.4 Hz), 7.52 (1H, d, *J* = 9.6 Hz), 7.31 (2H, d, *J* = 8.8 Hz),7.08-7.21 (5H, m), 7.02 (2H, d, *J* = 8.8 Hz), 6.04 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.90 (3H, s), 3.85 (2H, d, *J* = 12.0 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 2.85 (2H, td, *J* = 12.0, 2.8 Hz), 2.61-2.70 (1H, m), 2.36 (3H, m), 1.80-2.00 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 98.40%, MS(ESI):m/z 483.1 [M+H]+ |
| 128 |  | gray solid: $^1$H-NMR ($CDCl_3$): δ 9.13 (1H, d, *J* = 2.4 Hz), 7.51 (1H, d, *J* = 9.6 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.26 (2H, d, *J* = 9.2 Hz), 7.13 (1H, dd, *J* = 9.6, 2.4 Hz), 7.01 (2H, d, *J* = 7.6 Hz), 6.92 (2H, d, *J* = 8.8 Hz), 6.05 (1H, brs), 4.66 (2H, d, *J* = 5.6 Hz), 3.90 (3H, s), 3.25-3.40 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 504.1 [M+H]+ |
| 129 |  | yellow solid: $^1$H-NMR (CDCl3): δ 9.01 (1H, d, *J*= 6.8 Hz), 7.53 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.00 (4H, d, *J* = 8.4 Hz), 6.83 (1H, t, *J* = 7.4 Hz), 6.64 (1H, d, *J* = 7.6 Hz), 6.08 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 4.04 (3H, s). 3.36-3.47 (8H, m), 3.01 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 99.0%, MS (ESI): m/z 538.0[M+ H] +. |

Table 2

| | | |
|---|---|---|
| 130 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.88 (1H, s), 7.72 (1H, d, *J* = 9.2 Hz), 7.48-7.59 (3H, m), 7.34 (2H, d, *J* = 8.4 Hz), 6.95-7.08 (4H, m), 6.10 (1H, s), 4.67 (2H, d, *J* = 5.6 Hz), 3.41-3.52 (4H, m), 3.32-3.51 (4H, m), 3.02 (2H, q, *J* = 7.2 Hz), 1.44 (3H, t, *J* = 7.6 Hz); LCMS: 98.8%, MS (ESI): m/z 576.0[M+ H]+. |
| 131 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.32 (1H, d, *J* = 7.2 Hz), 7.79 (1H, d, *J* = 1.2 Hz ), 7.23-7.34 (2H, m), 6.95-7.08 (3H, m), 6.89 (2H, d, *J* = 8.8 Hz), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.78-3.89 (5H. m), 2.97 (2H, q, *J* = 7.6 Hz), 2.79-2.90 (2H, m), 2.56-2.69 (1H. m), 1.80-2.02 (4H. m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.5%, MS (ESI): m/z 517.0[M+ H]+. |
| 132 |  | red solid : $^1$H-NMR ($CDCl_3$): δ 9.33 (1H, d, *J* = 7.6 Hz), 7.80 (1H, d, *J* = 1.2 Hz ), 7.60 (2H, d, *J* = 8.0 Hz), 7.39 (2H, d, *J* = 8.0 Hz), 7.29-7.34 (2H, m), 6.97-7.09 (3H, m), 6.04 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 4.56-4.68 (2H. m), 2.98 (2H, q, *J* = 7.6 Hz), 2.80-2.93 (2H, m), 2.68-2.80 (1H. m), 1.83-2.02 (4H. m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.2%, MS (ESI): m/z 585.0[M+ H]+. |
| 133 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.32 (1H, d, *J* = 7.2 Hz), 7.80 (1H, d, *J* = 1.6 Hz ), 7.28-7.37 (2H, m), 7.20-7.26 (2H, m), 6.94-7.09 (5H. m), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 4.57-4.66 (2H. m), 2.98 (2H, q, *J* = 7.6 Hz), 2.79-2.90 (2H, m), 2.59-2.73 (1H. m), 1.80-2.01 (4H. m), 1.41 (3H, t, *J* = 7.6 Hz) |
| 134 |  | gray solid: $^1$H-NMR ($CDCl_3$): δ 9.33 (1H, d, *J* = 7.6 Hz), 7.80 (1H, d, *J* = 1.6 Hz ), 7.28-7.35 (6H, m), 7.17-7.25 (2H, m), 6.97-7.08 (3H. m), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 4.57-4.68 (2H. m), 2.98 (2H, q, *J* = 7.6 Hz), 2.78-2.89 (2H, m), 2.60-2.71 (1H. m), 1.81-2.00 (4H. m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 552.6[M+ H]+. |
| 135 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.33 (1H, d, *J* = 7.6 Hz), 7.80 (1H, d, *J* = 1.2 Hz ), 7.33 (2H, d, *J* = 8.8 Hz), 7.21-7.31 (2H, m), 6.96-7.08 (3H, m), 6.88-6.95 (2H, m), 6.05 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.27-3.41 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 99.0%, MS (ESI): m/z 553.6[M+ H]+. |
| 136 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.66 (1H, d, *J* = 1.2 Hz), 7.60 (2H, d, *J* = 8.0 Hz ), 7.52 (1H, d, *J* = 9.2 Hz), 7.35-7.45 (3H, m), 7.29-7.35 (2H, m), 7.02 (2H, d, *J* = 8.4 Hz), 6.06 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.80-3.91 (2H, m), 2.99 (2H, q, *J* = 7.6 Hz), 2.81-2.91 (2H, m), 2.70-2.80 (1H, m), 1.86-2.06 (4H, m), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 98.9%, MS (ESI): m/z 585.0[M+ H]+. |
| 137 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.43(1H, t, *J*= 6.4 Hz), 7.19-7.30(5H, m), 6.99-7.02(4H, m), 6.75-6.81(1H, m), 5.99(1H, brs), 4.61(2H, d, *J*= 5.6 Hz), 3.73-3.83(2H, m), 2.92-2.98(2H, m), 2.80-2.86(2H, m), 2.62-2.68(1H, m), 1.78-1.96(4H, m), 1.39(3H, t, *J*=7.6 Hz); LCMS: 99.9%, MS (ESI): m/z 475.0[M+ H]+. |
| 138 |  | gray solid : $^1$H-NMR ($CDCl_3$): δ 9.63 (1H, s), 7.49 (1H, d, *J* = 9.2 Hz ), 7.39 (1H, d, *J* = 9.6 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 6.90-7.17 (4H, m), 6.87 (2H, d, *J* = 8.8 Hz), 6.03 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.78 (3H, s), 3.14-3.45 (8H. m), 2.96 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 548.0[M+ H]+. |

| | | |
|---|---|---|
| 139 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.41 (1H, d, *J* = 7.2 Hz), 7.61 (1H, d, *J* = 8.8 Hz), 7.20-7.40 (5H, m, overlap with $CDCl_3$ signal), 7.18 (2H, d, *J* = 8.4 Hz), 6.82-7.05 (3H, m), 6.01 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.82 (2H, d, *J* = 12.0 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 2.83 (2H, t, *J* = 11.2 Hz), 2.53-2.70 (1H, m), 1.72-2.03 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 473.0[M+ H]+. |
| 140 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.16 - 9.29 (m, 1 H), 7.58 (br. s., 3 H), 7.12 - 7.41 (m, 6 H) 6.99 (br. s, 2 H), 5.94 - 6.10 (m, 1 H), 4.62 (br. s, 2 H), 3.83 (d, *J*=10.54 Hz, 2 H), 2.95 (d, *J*=6.53 Hz, 2 H), 2.84 (br. s, 2 H), 2.72 (br. s, 1 H), 2.36 (d, *J*=4.27 Hz, 3 H), 1.85 - 2.04 (m, 4 H), 1.31 - 1.47 (m, 3 H); LCMS: 99.1%, MS (ESI): m/z 521.0[M+ H]+. |
| 141 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 7.2 Hz), 7.35-7.29 (3H, m), 7.10 (2H, d, *J* = 8.0 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.75 (2H, d, *J* = 6.8 Hz), 5.99 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.35-3.29 (8H, m), 2.95 (2H, q, *J* = 7.6 Hz), 2.42 (3H, s), 2.29 (3H, s), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 490.1[M+ H]+. |
| 142 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.35 (1H, d, *J* = 6.4 Hz), 7.40 (1H, d, *J* = 7.2 Hz), 7.31 (2H, d, *J* = 6.8 Hz), 7.14 (2H, d, *J* = 7.2 Hz), 6.94-7.00 (4H, m), 6.86-6.88 (1H, m), 6.08 (1H, brs), 4.64 (2H, s), 3.34 (8H, s), 3.02 (2H, d, *J* = 7.2 Hz), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 97.9%, MS (ESI): m/z 474.0[M+ H]+. |
| 143 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.40 (1H, d, *J* = 6.8 Hz), 7.45-7.65 (3H, m), 7.30-7.45 (2H, m), 7.20-7.30 (2H, m), 7.00 (2H, d, *J* =7.6 Hz), 6.80 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.83 (2H, d, *J* = 12.0 Hz), 3.02 (2H, q, *J* = 7.6 Hz), 2.85 (2H, t, *J* = 12.0 Hz), 2.73 (2H, t, *J* = 7.6 Hz), 1.75-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 98.6%, MS(ESI):m/z 584.9/586.9 [M+H] |
| 144 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7 Hz), 7.29 (2H, d, *J* = 8.5 Hz), 7.07-7.20 (5H, m), 6.98 (2H, d, *J* = 8.5 Hz), 6.82 (1H, t, *J* = 6.9 Hz), 6.01 (1H, brs), 4.62 (2H, d, *J* = 5.3 Hz), 3.81 (2H, d, *J* = 12.0 Hz), 2.99 (2H, q, *J* = 7.5 Hz), 2.83 (2H, td, *J* = 11.7, 2.0 Hz), 2.55-2.68 (1H, m), 2.61 (3H, s), 2.33 (3H, s), 1.82-1.98 (4H, m), 1.37 (3H, t, *J* = 7.5 Hz); LCMS: 98.7%, MS (ESI): m/z 489.1[M+ H]+. |
| 145 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 6.8 Hz), 7.58 (2H, d, *J* = 8.2 Hz), 7.36 (2H, d, *J* = 8.2 Hz), 7.30 (2H, d, *J* = 8.6 Hz), 7.11 (1H, d, *J* = 6.6 Hz), 6.99 (2H, d, *J* = 8.6 Hz) 6.82 (1H, t, *J* = 6.9 Hz), 6.02 (1H, brs), 4.63 (2H, d, *J* = 5.5 Hz), 3.83 (2H, d, *J* = 12.3 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 2.84 (2H, td, *J* = 12, 2.5 Hz), 2.68-2.78 (1H, m), 2.61 (3H, s), 1.84-2.02 (4H, m), 1.37 (3H, t, *J* = 7.5 Hz); LCMS: 98.6%, MS (ESI): m/z 521.1[M+ H]+. |
| 146 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, d, *J* = 0.8 Hz), 7.68 (1H, d, *J* = 9.6 Hz), 7.56 (2H, d, *J* = 8.0 Hz), 7.46 (1H, d, *J* = 9.2 Hz), 7.35 (2H, d, *J* = 8.0 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.8 Hz), 6.06 (1H, m), 4.63 (2H, d, *J* = 5.2 Hz), 3.83 (2H, d, *J* = 12.4 Hz), 2.99 (2H, q, *J* = 7.6 Hz), 2.80-2.91 (2H, m), 2.57-2.79 (1H, m), 1.82-2.03 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 99.3%, MS (ESI): m/z 575.0[M+ H]+. |

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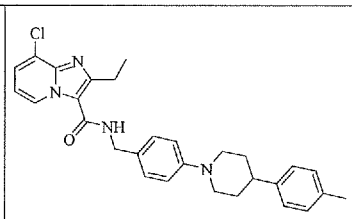
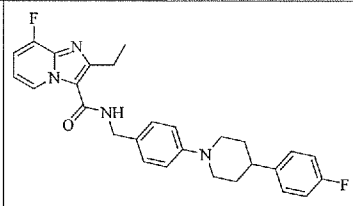
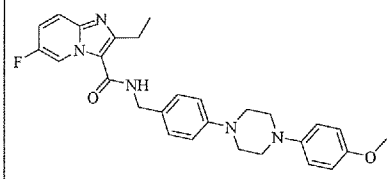
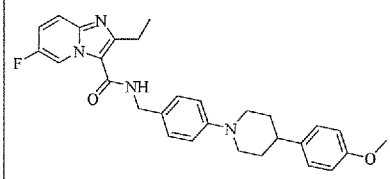
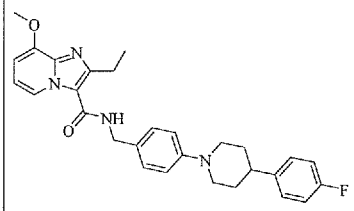
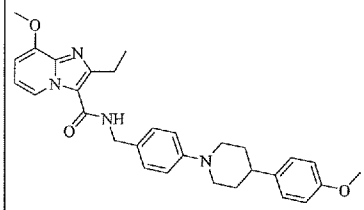
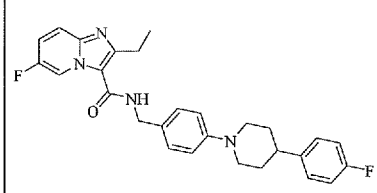
| 147 |  | red solid : $^1$H-NMR ($CDCl_3$): δ 9.34 (1H, dd, *J* = 8 Hz), 7.38 (1H, dd, *J* = 8 Hz), 7.27 (2H, m) 7.07-7.17 (4H, m), 6.98 (2H, d, *J* = 8.40 Hz), 6.84 (1H, t, *J* = 7.2 Hz), 6.05 (1H, brs), 4.61 (2H, d, *J* = 5.6 Hz), 3.81 (2H, d, *J* = 12.4 Hz), 3.01 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 2.8, *J* = 12.0 Hz), 2.62 (1H, m), 2.32 (3H, s), 1.85-1.96 (4H, m), 1.37 (3H, t, *J* = 8 Hz); LCMS:100.0%, MS (ESI): m/z 487.1[M+ H]+. |
| 148 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.20 (1H, d, *J* = 6.8 Hz), 7.29-7.17 (4H, m), 7.04-6.96 (5H, m), 6.85-6.80 (1H, m), 6.04 (1H, brs), 4.61 (2H, d, *J* = 5.6 Hz), 3.82-3.79 (2H, m), 2.98 (2H, q, *J* = 7.6 Hz), 2.85-2.78 (2H, m), 2.67-2.60 (1H, m), 1.95-1.79 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 475.0[M+ H]+. |
| 149 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.40-9.49 (1H, m), 7.55 (1H, dd, *J* = 9.6, 4.8 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 7.19-7.28 (2H, m, overlap with $CDCl_3$ signal), 6.90-7.00 (4H, m), 6.84 (2H, d, *J* = 8.4 Hz), 6.03 (1H, t, *J* = 4.4 Hz), 4.61 (2H, d, *J* = 5.6 Hz), 3.77 (3H, s), 3.30-3.40 (4H, m), 3.15-3.25 (4H, m), 2.96 (2H, q, *J* = 7.6 Hz), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 488.1[M+ H]+. |
| 150 |  | pink solid : $^1$H-NMR ($CDCl_3$): δ 9.45 (1H, dd, *J* = 4.8, 2.0 Hz), 7.56 (1H, dd, *J* = 10.0, 5.6 Hz), 7.20-7.31 (3H, m, overlap with $CDCl_3$ signal), 7.16 (2H, d, *J* = 8.8 Hz), 6.98 (2H, d, *J* = 8.8 Hz), 6.86 (2H, d, *J* = 8.8 Hz), 5.95-6.05 (1H, m), 4.61 (2H, d, *J* = 5.6 Hz), 3.76-3.88 (5H, m), 2.96 (2H, q, *J* = 7.2 Hz), 2.77-2.87 (2H, m), 2.53-2.66 (1H, m), 1.78-1.99 (4H, m), δ 1.39 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS(ESI): m/z 487.0 [M+H]+. |
| 151 |  | pink solid : $^1$H-NMR ($CDCl_3$): δ 8.97 (1H, dd, *J* = 0.4 Hz, *J* = 6.8 Hz) 7.25-7.29 (2H, m), 7.17-7.20 (2H, m), 6.96-7.01 (4H, m), 6.80 (1H, t, *J* = 7.6 Hz), 6.60 (1H, d, *J* = 7.6 Hz), 6.02 (1H , brs), 4.60 (2H, d, *J* = 5.6 Hz), 4.00 (3H, s), 3.80 (2H, d, *J* =12.4 Hz), 2.95 (2H, q, *J* = 8.0 Hz), 2.82 (2H, td, *J* = 2.4 Hz, *J* = 12.4 Hz), 2.66-2.60 (1H, m), 1.95-1.82 (4H, m), 1.37 (3H, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 487.1[M+ H]+. |
| 152 |  | pink solid : $^1$H-NMR ($CDCl_3$): δ 8.97 (1H, dd, *J* = 0.8 Hz, *J* = 7.2 Hz), 7.25-7.28 (2H, m), 7.17 (2H, d, *J* = 2.0 Hz), 7.15 (2H, d, *J* = 1.6 Hz), 6.96-6.98 (2H, m), 6.84-6.87 (2H, m), 6.80 (1H, t, *J* = 7.2 Hz), 6.60 (1H, d, *J* = 7.2 Hz), 6.02 (1H, brs), 4.60 (2H, d, *J* = 5.6 Hz), 4.0 (3H, s), 3.78-3.81 (5H, m), 2.96 (2H, q, *J* = 7.6 Hz), 2.80 (2H, td, *J* =2.4 Hz, *J* = 12Hz) 2.60 (1H, m), 1.82-1.99 (4H, m), 1.37 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 521.1[M+ Na]+. |
| 153 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.45 (1H, dd, *J* = 5.2, 2.4 Hz) , 7.56 (1H, dd, *J* = 9.6, 5.2 Hz) , 7.15-7.32 (5H, m, overlap with $CDCl_3$ signal) , 6.90-7.05 (4H, m) , 6.01 (1H, brs) , 4.60 (2H, d, *J* = 5.6 Hz) , 3.80 (2H, d, *J* = 12.4 Hz) , 2.95 (2H, q, *J* = 7.6 Hz) , 2.78-2.86 (2H, m) , 2.60-2.70 (1H, m) , 1.78-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 457.1[M+ H]+. |

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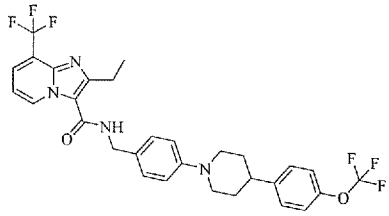
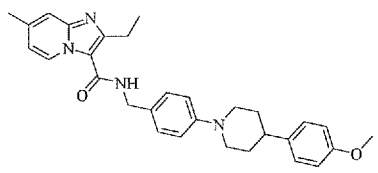
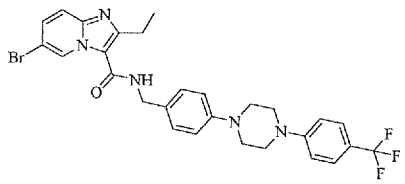
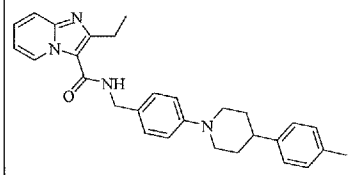
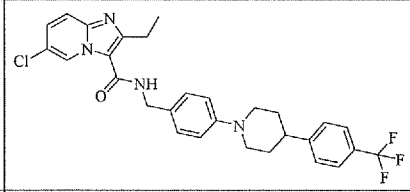
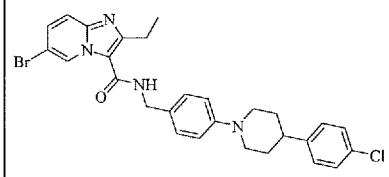
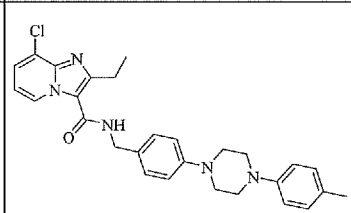
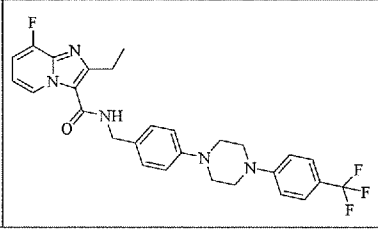
| 154 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.57 (1H, d, *J* = 7.6 Hz), 7.64 (1H, d, *J* = 7.2 Hz), 7.20-7.30 (4H, m), 7.15 (2H, d, *J* = 8.0 Hz), 6.95-7.00 (3H, m), , 6.08 (1H, brs), 4.62 (2H, d, *J* = 6.0 Hz), 3.68-3.85 (2H, m), 3.03 (2H, q, *J* = 7.6 Hz), 2.78-2.88 (2H, m), 2.65-2.72 (1H, m), 1.80-2.00 (4H, m), 1.37 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 591.0[M + H]+. |
| 155 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.27 (1H, d, *J* = 7.2 Hz), 7.35 (1H, s), 7.28 (2H, d, *J* = 8.4 Hz), 7.16 (2H, dd, *J* = 6.4 Hz, 2.0 Hz), 6.97 (2H, dd, *J* = 8.8 Hz, 2.0 Hz), 6.86 (2H, dd, *J* = 6.4 Hz, 2.0 Hz), 6.73 (1H, dd, *J* = 6.4 Hz, 2.0 Hz), 5.96 (1H, brs), 4.60 (2H, d, *J* = 2.8 Hz), 3.81-3.78 (5H, m), 2.93 (2H, q, *J* = 8.4 Hz), 2.83 (2H, td, *J* = 12 Hz, 2.4 Hz), 2.66-2.56 (1H, m), 2.41 (3H, d, *J* = 0.4 Hz), 1.98-1.82 (4H, m), 1.37 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 483.1[M+ H]+. |
| 156 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.56 (1H, s), 7.40-7.50 (3H, m), 7.29-7.37 (1H. m), 7.21-7.29 (2H, m), 6.81-6.97 (4H, m), 5.98 (1H, brs), 4.56 (2H, d, *J* = 5.6 Hz), 3.41-3.51 (4H, m), 3.22-3.41 (4H, m), 2.89 (2H, q, *J* = 7.6 Hz), 1.33 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 586.0[M+ H]+. |
| 157 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, *J* = 5.6 Hz), 7.59 (1H, d, *J* = 8.8 Hz), 7.26-7.35 (3H, m, overlap with $CDCl_3$ signal), 7.10-7.17 (4H, m), 6.95-7.03 (2H, m), 6.91 (1H, t, *J* = 6.8 Hz), 5.96-6.05 (1H, m), 4.61 (2H, d, *J* = 5.6 Hz), 3.75-3.85 (2H, m), 2.97 (2H, q, *J* = 7.6 Hz), 2.76-2.88 (2H, m), 2.56-2.68 (1H, m), 2.32 (3H, s), 1.80-1.99 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 475.1[M+ Na]+. |
| 158 |  | yellow solid : $^1$H-NMR($CDCl_3$): δ 9.54 (1H, dd, *J* = 2.0 Hz, *J* = 0.8 Hz), 7.50-7.60 (3H, m), 7.36-7.40 (2H, m), 7.27-7.32 (3H, m), 6.93-7.00 (2H, m), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.78-3.86 (2H, m), 2.98 (2H, q, *J* = 7.6 Hz), 2.82-2.89 (2H, m), 2.69-2.80 (1H, m), 1.82-2.00 (4H, m), 1.40 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 541.1[M+ H]+. |
| 159 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.65 (1H, d, *J* = 1.2 Hz), 7.51 (1H, d, *J* = 9.2 Hz ), 7.41 (1H, dd, *J* = 9.2, 2.0 Hz), 7.28-7.35 (4H, m), 7.20 (2H, d, *J* = 8.4 Hz), 7.01 (2H, d, *J* = 8.4 Hz), 6.05 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.76-3.90 (2H, m), 2.98 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.60-2.73 (1H, m), 1.80-2.03 (4H, m), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 553.0[M+ H]+. |
| 160 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, dd, *J1* = 0.8 Hz, *J2* = 6.8 Hz), 7.42 (1H, dd, *J1* = 0.8 Hz, *J2* = 7.6 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.0 Hz), 7.01 (2H, d, *J* = 8.8 Hz), 6.86-6.94 (3H, m), 6.09 (1H, brs), 4.65 (2H, d, *J* = 5.2 Hz), 3.37 (4H, dd, *J1* = 3.6 Hz, *J2* = 7.2 Hz), 3.31 (4H, dd, *J1* = 2.4 Hz, *J2* = 5.6 Hz), 3.04 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.4%, MS (ESI): m/z 488.1[M+ H]+. |
| 161 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.23 (1H, d, *J* = 6.8 Hz), 7.53 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.08-6.99 (5H, m), 6.88-6.83 (1H, m), 6.10 (1H, brs), 4.66 (2H, d, *J* = 5.6 Hz), 3.48-3.36 (8H, m), 3.01 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 99.5%, MS (ESI): m/z 526.1[M+ H]+. |

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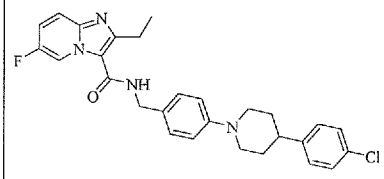
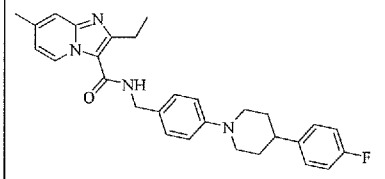
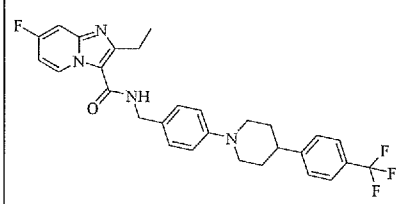
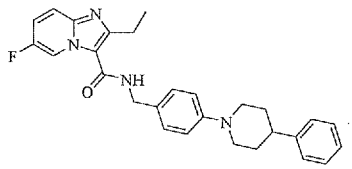
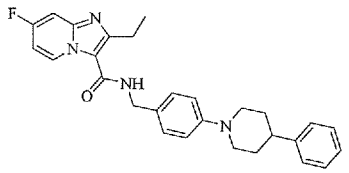
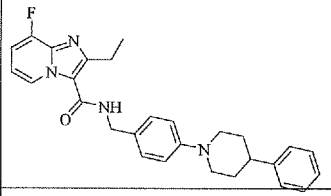
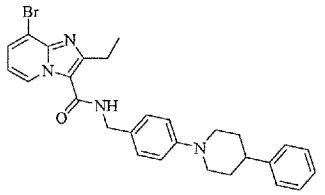
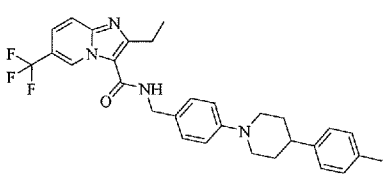
| 162 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.48 (1H, dd, $J$ = 4.8, 2.4 Hz), 7.59 (1H, dd, $J$ = 9.6, 5.2 Hz), 7.25-7.35 (5H, m, overlap with $CDCl_3$ signa), 7.20 (2H, d, $J$ = 8.4 Hz), 7.00 (2H, d, $J$ = 8.8 Hz), 6.05 (1H, brs), 4.64 (2H, d, $J$ = 5.6 Hz), 3.84 (2H, d, $J$ = 12.4 Hz), 2.99 (2H, q, $J$ = 7.6 Hz), 2.85 (2H, td, $J$ = 12.0, 2.4 Hz), 2.60-2.70 (1H, m), 1.80-2.00 (4H, m), 1.42 (3H, t, $J$ = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 491.0[M+ H]+. |
| 163 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, $J$ = 7.2 Hz), 7.35 (1H, s), 7.30-7.26 (2H, m), 7.21-7.18 (2H, m), 7.02-6.97 (4H, m), 6.75 (1H, dd, $J$ = 7.2 Hz, 1.6 Hz), 5.98 (1H, brs), 4.61 (2H, d, $J$ = 5.6 Hz), 3.80 (2H, d, $J$ = 12.4 Hz), 2.94 (2H, q, $J$ = 7.2 Hz), 2.82 (2H, td, $J$ = 12 Hz, 2.4 Hz), 2.68-2.61 (1H, m), 2.42 (3H, s), 1.98-1.80 (4H, m), 1.38 (3H, t, $J$ = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 471.1[M+ H]+. |
| 164 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.44(1H, t, $J_1$= 7.6 Hz, 6.0 Hz), 7.53(2H, d, $J$= 7.6 Hz), 7.34(2H, d, $J$= 8.8 Hz), 7.27(2H, d, $J$= 7.6 Hz), 7.21-7.23(1H, m), 7.95(2H, d, $J$= 8.8 Hz), 6.75-6.81(1H, m), 6.76-6.81(1H, m), 6.03(1H, brs), 4.61(2H, d, $J$= 5.6 Hz), 3.49-3.88(2H, m), 2.93-2.98(2H, m), 2.82-2.88(2H, m), 2.70-2.77(1H, m), 1.63-1.99(4H, m), 1.23(3H, t, $J$= 7.6 Hz); LCMS: 99.1%, MS (ESI): m/z 525.0[M+ H]+.490.1[M+ Na]+ |
| 165 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.45 (1H, dd, $J$ = 5.2, 2.4 Hz) , 7.56 (1H, dd, $J$ = 10.0, 5.2 Hz) , 7.18-7.40 (8H, m, overlap with $CDCl_3$ signal) , 7.00 (2H, d, $J$ = 8.4 Hz) , 6.02 (1H, brs) , 4.62 (2H, d, $J$ = 5.2 Hz) , 3.82 (2H, d, $J$ = 12.4 Hz) , 2.97 (2H, q, $J$ = 7.6 Hz) , 2.80-2.90 (2H, m) , 2.60-2.71 (1H, m) , 1.80-2.05 (4H, m), 1.40 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 457.0[M+ H]+ |
| 166 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.44(1H, t, $J$= 7.2 Hz), 7.21-7.35(7H, m), 7.00(2H, d, J= 8.4 Hz), 6.77-6.81(1H, m), 5.60(1H, brs), 4.61(2H, d, $J$= 5.6 Hz), 3.81-3.84(2H, m), 2.92-2.98(1H, m), 2.81-2.88(2H, m), 2.62-2.70(1H, m), 1.86-2.01(4H, m), 1.39(3H, t, $J$=7.6 Hz); LCMS: 99.9%, MS (ESI): m/z 457.0[M+ H]+. |
| 167 |  | red solid : $^1$H-NMR ($CDCl_3$): δ 9.20 (1H, d, $J$ = 6.8 Hz), 7.35-7.20 (6H, m), 7.05-6.98 (3H, m), 6.86-6.81 (1H, m), 6.06 (1H, brs), 4.62 (2H, d, $J$ = 5.6 Hz), 3.84-3.81 (2H, m), 3.00 (2H, q, $J$ = 7.6 Hz), 2.87-2.81 (2H, m), 2.71-2.63 (1H, m), 2.01-1.86 (4H, m), 1.40 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 457.0[M+ H]+. |
| 168 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, $J$ = 6.8 Hz), 7.58 (1H, d, $J$ = 7.2 Hz), 7.18-7.38 (8H, m), 6.99 (2H, d, $J$ = 7.6 Hz), 6.80 (1H, t, $J$ = 7.2 Hz), 6.07 (1H, brs), 4.62 (2H, d, $J$ = 5.6 Hz), 3.82 (2H, d, $J$ = 12.4 Hz), 3.02 (2H, q, $J$ = 7.6 Hz), 2.84 (2H, t, $J$ = 11.6 Hz), 2.60-2.75 (1H, m), 1.85-2.00 (4H, m), 1.38 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 516.8/518.8 [M+H]. |
| 169 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, $J$ = 9.2 Hz), 7.47 (1H, dd, $J$ = 7.6, 1.6 Hz), 7.28 (2H, t, $J$ = 8.4 Hz), 7.12 (4H, s), 6.99 (2H, d, $J$ = 8.0 Hz), 6.06 (1H, m), 4.63 (2H, d, $J$ = 5.2 Hz), 3.82 (2H, d, $J$ = 12.4 Hz), 2.99 (2H, q, $J$ = 7.2 Hz), 2.81-2.86 (2H, m), 2.58-2.70 (1H, m), 2.33 (3H, s), 1.82-2.02 (4H, m), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 521.0[M+ H]+. |

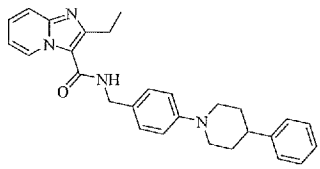
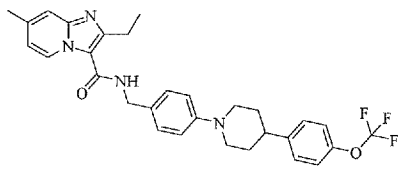
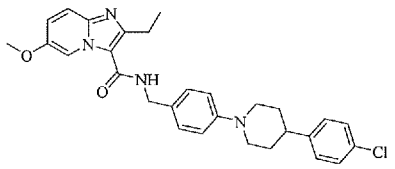
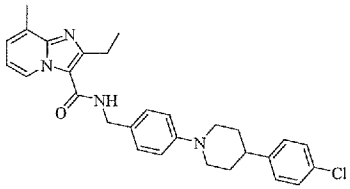
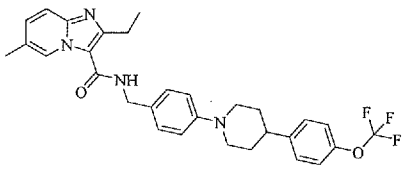
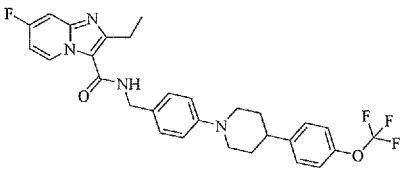
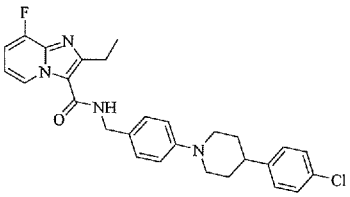
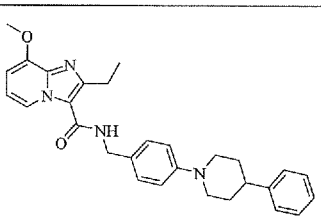
| | | |
|---|---|---|
| 170 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.41 (1H, d, *J* = 7.2 Hz), 7.61 (1H, d, *J* = 8.8 Hz), 7.15-7.36 (8H, m, overlap with $CDCl_3$ signal), 6.99 (2H, d, *J* = 8.8 Hz), 6.92 (1H, t, *J* = 7.2 Hz), 6.02 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.83 (2H, d, *J* = 12.0 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 2.72-2.90 (2H, m), 2.60-2.70 (1H, m), 1.81-2.04 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 99.3%, MS (ESI): m/z 439.1[M+ H]+. |
| 171 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 7.2 Hz), 7.38 (1H, s), 7.30-7.25 (3H, m), 7.17-7.15 (2H, m), 6.98 (2H, d, *J* = 8.4 Hz), 6.77 (1H, d, *J* = 6.0 Hz), 5.98 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 2.95 (2H, q, *J* = 7.6 Hz), 2.83 (2H, td, *J* = 10.8 Hz, 2.4 Hz), 2.70-2.62 (1H, m), 2.43 (3H, s), 2.03-1.75 (4H, m), 1.39 (3H, t, *J* = 8.4 Hz); LCMS: 100%, MS (ESI): m/z 537.1[M+ H]+. |
| 172 |  | white solid : $^1$H-NMR (CDCl3): δ 9.11 (1H, d, *J* = 2.4 Hz), 7.49 (1H, d, *J* = 9.6 Hz), 7.26-7.35 (4H, m), 7.18 (2H, d, *J* = 8.4 Hz), 7.11 (1H, dd, *J* = 9.6, 2.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.02 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.88 (3H, s), 3.82 (2H, d, *J* = 12.4 Hz), 2.95 (2H, q, *J* = 7.6 Hz), 2.85 (2H, td, *J* = 12.0, 2.4 Hz), 2.58-2.70 (1H, m), 1.80-2.00 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 503.0 [M+H]+ |
| 173 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 7 Hz), 7.26-7.31 (4H, m), 7.15-7.20 (2H, m), 7.11 (1H, d, *J* = 7 Hz), 6.98(2H, d, *J* = 8.5 Hz), 6.82 (1H, t, *J* = 6.9 Hz), 6.03 (1H, brs), 4.62(2H, d, *J* = 5.3 Hz), 3.81 (2H, d, *J* = 12.5 Hz), 2.99 (2H, q, *J* = 7.5 Hz), 2.83 (2H, td, *J* = 12.2, 2.5 Hz), 2.62-2.69 (1H, m), 2.61 (3H, s), 1.79-1.98 (4H, m), 1.37 (3H, t, *J* = 7.5 Hz); LCMS: 100%, MS (ESI): m/z 487.0[M+ H]+. |
| 174 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.19 - 9.27 (m, 1 H) 7.46 - 7.55 (m, 1 H), 7.25 - 7.32 (m, 4 H), 7.14 - 7.21 (m, 3 H), 6.92 - 7.07 (m, 2 H), 5.96 - 6.12 (m, 1 H), 4.59 - 4.65 (m, 2 H), 3.77 - 3.89 (m, 2 H), 2.91 - 3.00 (m, 2 H), 2.77 - 2.90 (m, 2 H), 2.61 - 2.75 (m, 1 H), 2.37 (s, 3 H), 1.80 - 2.00 (m, 4 H), 1.40 (s, 3 H); LCMS:100%, MS (ESI): m/z 537.0[M+ H]+. |
| 175 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.42-9.46 (1H, m), 7.30-7.21 (3H, m), 7.17-7.15 (2H, m), 6.99 (2H, d, *J*= 7.6 Hz), 6.81-6.77 (1H, m), 5.99 (1H, brs), 4.61 (2H, d, *J*= 5.2 Hz), 2.97-2.92 (2H, m), 2.86-2.80 (2H, m), 2.67 (1H, m), 1.97-1.89 (4H, m), 1.41-1.37 (3H, t, *J*= 7.6 Hz); LCMS: 99.9%, MS (ESI): m/z 541.0[M+ H]+. |
| 176 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.20 (1H, d, *J* = 6.8 Hz), 7.30-7.26 (4H, m), 7.18 (2H, d, *J* = 8.4 Hz), 7.06-6.97 (3H, m), 6.86-6.81(1H, m), 6.06 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.83-3.80 (2H, m), 3.00 (2H, q, *J* = 7.6 Hz), 2.86-2.80 (2H, m), 2.68-2.60 (1H, m), 1.96-1.83 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 491.0[M+ H]+. |
| 177 |  | yellow solid : $^1$H-NMR (CDCl3): δ 8.99 (1H, d, *J* = 6.8 Hz) 7.20-7.35 (7H, m), 6.99 (2H, d, *J* = 8.0 Hz), 6.81 (1H, t, *J* = 7.6 Hz), 6.61 (1H, d, *J* = 7.6 Hz), 6.04 (1H, brs), 4.61 (2H, d, *J* = 5.6 Hz), 4.01 (3H, s), 3.82 (2H, d, *J* = 12 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 2.83 (2H, t, *J* = 9.6 Hz), 2.63-2.69 (1H, m), 1.89-1.98 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 469.0[M+ H]+. |

Table 2

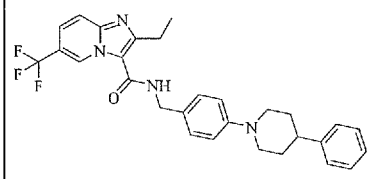
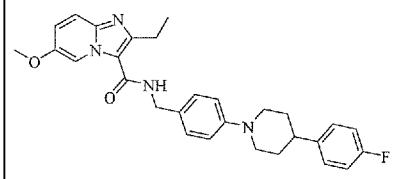
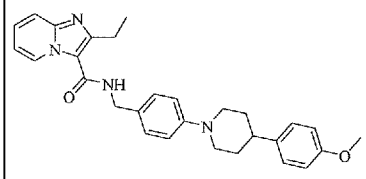
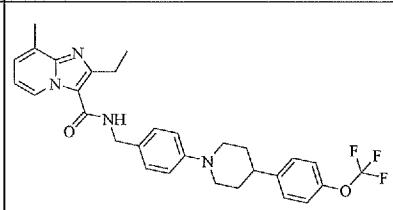
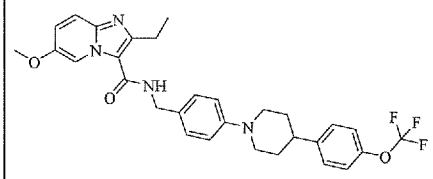
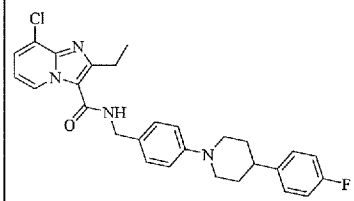
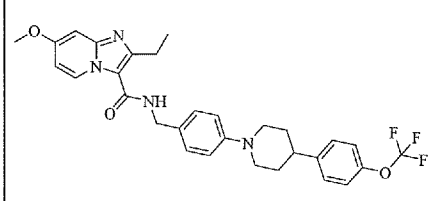
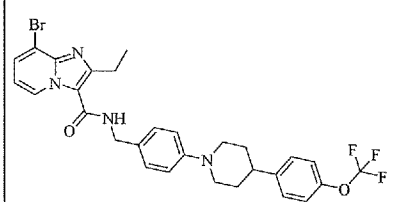
| | | |
|---|---|---|
| 178 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, *J* = 9.2 Hz), 7.47 (1H, dd, *J* = 7.6, 1.6 Hz), 7.18-7.36 (7H, m), 7.00 (2H, d, *J* = 8.0 Hz), 6.07 (1H, m), 4.63 (1H, d, *J* = 5.2 Hz), 3.83 (2H, d, *J* = 12 Hz), 2.97 (2H, q, *J* = 7.6 Hz), 2.71-2.88 (2 H, m), 2.57-2.63 (1H, m), 1.81-2.03 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 507.0[M+ H]+. |
| 179 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.10 (1H, d, *J* = 2.4 Hz), 7.49 (1H, d, *J* = 9.6 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 7.15-7.25 (2H, m), 7.11 (1H, dd, *J* = 8.4, 2.4 Hz), 7.00 (1H, t, *J* = 8.8 Hz), 6.03 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.87 (3H, s), 3.81 (2H, d, *J* = 12.4 Hz), 2.95 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 12.0, 2.4 Hz), 2.55-2.70 (1H, m), 1.80-2.00 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 487.0 [M+H]+. |
| 180 |  | red solid : $^1$H-NMR ($CDCl_3$): δ 9.40 (1H, d, *J* = 6.8 Hz), 7.60 (1H, d, *J* = 8.8 Hz), 7.25-7.35 (3H, m, overlap with $CDCl_3$ signal), 7.17 (2H, d, *J* = 8.4 Hz), 6.99 (2H, d, *J* = 8.8 Hz), 6.89-6.91 (1H, m), 6.87 (2H, d, *J* = 8.8 Hz), 6.02 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.72-3.84 (5H, m), 2.98 (2H, q, *J* = 7.6 Hz), 2.77-2.87 (2H, m), 2.56-2.67 (1H, m), 1.63-1.98 (4H, m), 1.40 (3H, t, *J* = 7.2 Hz); LCMS: 99.2%, MS (ESI): m/z 491.1 [M+ Na]+. |
| 181 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 6.8 Hz), 7.23-7.32 (4H, m), 7.16 (2H, d, *J* = 8.3 Hz), 7.11 (1H, d, *J* = 6.8 Hz), 6.98 (2H, d, *J* = 8.5 Hz), 6.82 (1H, t, *J* = 6.9 Hz), 6.02 (1H, brs), 4.62 (2H, d, *J* = 5.3 Hz), 3.82 (2H, d, *J* = 12.0 Hz), 2.99 (2H, q, *J* = 7.6 Hz), 2.84 (2H, td, *J* = 12.1, 2.4 Hz), 2.627-2.72 (1H, m), 2.61 (3H, s), 1.81-2.00 (4H, m), 1.37 (3H, t, *J* = 7.7 Hz); LCMS: 100%, MS (ESI): m/z 537.1[M+ H]+. |
| 182 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.11 (1H, d, *J* = 2.4 Hz), 7.50 (1H, d, *J* = 9.6 Hz), 7.22-7.32 (4H, m), 7.17 (2H, d, *J* = 8.4 Hz), 7.10 (1H, dd, *J* = 9.6, 2.4 Hz), 6.99 (2H, d, *J* = 8.8 Hz), 6.02 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.88 (3H, s), 3.82 (2H, q, *J* = 12.4 Hz), 2.95 (2H, q, *J* = 7.6 Hz), 2.83 (2H, td, *J* = 12.0, 2.4 Hz), 2.62-2.74 (1H, m), 1.80-2.00 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 553.1 [M+H]+. |
| 183 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.35 (1H, d, *J* = 6.8 Hz), 7.40 (1H, d, *J* = 7.2 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 7.20 (2H, dd, *J* = 8.8, *J* = 5.6 Hz), 6.98-7.03 (4H, m), 6.86 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.82 (2H, d, *J* = 12.4 Hz), 3.02 (2H, q, *J* = 7.6 Hz), 2.83 (2H, t, *J* = 11. 2 Hz), 2.64-2.65 (1H, m), 1.84-1.96 (4H, m), 1.39 (3H, t, *J* = 7.65 Hz); LCMS: 100.0%, MS (ESI): m/z491.0[M+ H]+. |
| 184 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7.6 Hz), 7.22-7.32 (4H, m), 7.16 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.89 (1H, d, *J* = 2.4 Hz), 6.60 (1H, dd, *J* = 6.4 Hz, 2.8 Hz), 5.94 (1H, brs), 4.60 (2H, d, *J* = 5.6 Hz), 3.87 (3H, s), 3.82 (2H, d, *J* = 12.4 Hz), 2.92 (2H, q, *J* = 7.6 Hz), 2.82 (2H, td, *J* = 12.0 Hz, 2.4 Hz), 2.60-2.72 (1H, m), 1.70-2.02 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 553.1 [M+H]+. |
| 185 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, *J* = 6.8 Hz), 7.58 (1H, d, *J* = 7.2 Hz), 7.20-7.32 (4H, m), 7.19 (2H, d, *J* = 8.0 Hz), 6.99 (2H, d, *J* =8.8 Hz), 6.79 (1H, t, *J* = 7.2 Hz), 6.08 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.83 (2H, d, *J* = 12.4 Hz), 3.04 (2H, q, *J* = 7.6 Hz), 2.83 (2H, td, *J* = 12.0, 2.4 Hz), 2.60-2.72 (1H, m), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 601.0/603.0 [M+H]+ |

Table 2

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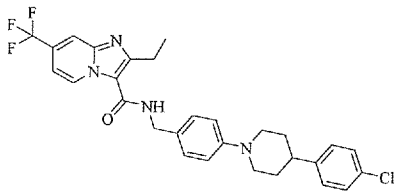
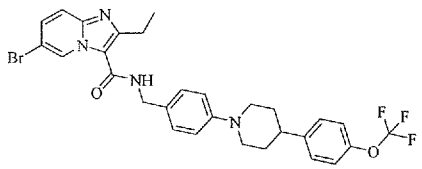
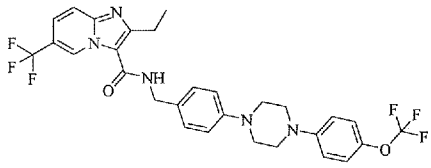
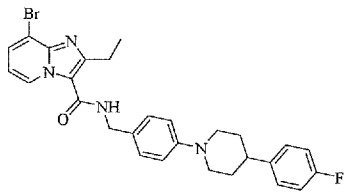
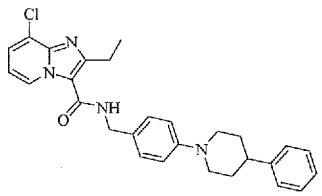
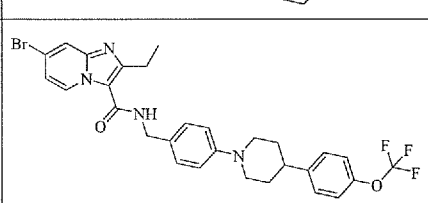
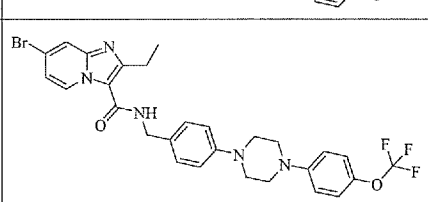
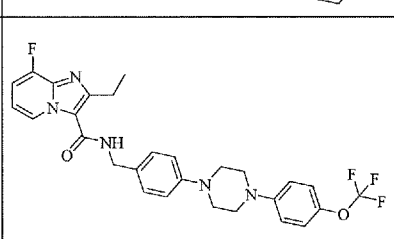
|---|---|---|
| 186 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.53 (1H, d, *J* = 7.2 Hz), 7.91 (1H, s), 7.24-7.38 (4H, m), 7.18 (2H, d, *J* = 8.0 Hz), 7.09 (1H, dd, *J* = 7.2, 1.6 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.11 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.81-3.86 (2H, m), 3.10 (2H, q, *J* = 7.6 Hz), 2.80-2.86 (2H, m), 2.61-2.68 (1H, m), 1.80-2.08 (4H, m), 1.44 (3H, t, *J* = 7.6Hz); LCMS: 100%, MS (ESI): m/z 541.1[M+ H]+. |
| 187 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.63 (1H, s), 7.49 (1H, d, *J* = 9.2 Hz ), 7.43 (1H, d, *J* = 7.6 Hz), 7.21-7.32 (3H, m), 7.13-7.20 (2H, m), 6.92-7.04 (2H, m), 6.04 (1H, brs), 4.54-4.67 (2H, m), 3.76-3.89 (2H, m), 2.94 (2H, q, *J* = 7.6 Hz), 2.76-2.89 (2H, m), 2.59-2.71 (1H, m), 1.77-2.00 (4H, m), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 602.8[M+ H]+. |
| 188 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.82 (1H, d, *J* = 15.2 Hz), 7.70 (1H, d, *J* = 9.2 Hz), 7.45-7.52 (2H, m), 7.32 (2H, d, *J* = 8.4 Hz), 7.14 (2H, d, *J* = 8.8 Hz), 6.88-7.08 (4H, m), 6.02-6.15 (1H, m), 4.64 (2H, d, *J* = 5.6 Hz), 3.23-3.42 (8H, m), 3.00 (2H, q, *J* = 7.6 Hz), 1.44 (3H, t, *J* = 7.2 Hz); LCMS: 98.0%, MS (ESI): m/z 592.0[M+ H]+. |
| 189 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, *J* = 6.4 Hz), 7.58 (1H, d, *J* = 6.8 Hz), 7.22-7.30 (2H, m), 7.15-7.21 (2H, m), 6.90-7.03 (4H, m), 6.80 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.82 (2H, d, *J* = 12.4 Hz), 3.12 (2H, q, *J* = 7.6 Hz), 2.83 (2H, td, *J* = 12.4, 2.8 Hz), 2.60-2.70 (1H, m), 1.80-2.00 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 99.0%, MS(ESI):m/z 535.0/537.0 [M+H] |
| 190 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.35 (1H, d, *J* = 6.8 Hz), 7.40 (1H, d, *J* = 6.8 Hz), 7.28-7.37 (4H, m), 7.21-7.25 (3H, m), 7.00 (2H, d, *J* = 8.4 Hz), 6.86 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.83 (2H, d, *J*=12 Hz), 3.02 (2H, q, *J* = 7.6 Hz), 2.82-2.87 (2H, m), 2.63-2.70 (1H, m), 1.86-2.01 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 99.6%, MS (ESI): m/z 473.0[M+ H]+. |
| 191 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.33 (1H, d, *J* = 7.6 Hz), 7.80 (1H, d, *J* = 1.6 Hz ), 7.28-7.36 (3H, m), 7.15-7.26 (2H, m), 6.97-7.12 (3H, m), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.73-3.92 (2H. m), 2.98 (2H, q, *J* = 7.6 Hz), 2.79-2.91 (2H, m), 2.63-2.78 (1H. m), 1.81-2.03 (4H. m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 603.0[M+ H]+. |
| 192 |  | yellow solid : $^1$H-NMR ($CDCl_3$): δ 9.30 (1H, d, *J* = 7.6 Hz), 7.78 (1H, d, *J* = 1.2 Hz ), 7.31 (2H, d, *J* = 8.4 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 6.87-7.05 (5H, m), 6.04 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.22-3.40 (8H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.3%, MS (ESI): m/z 602.0[M+ H]+. |
| 193 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.23 (1H, d, *J* = 7.2 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 7.17 (2H, d, *J* = 8.8 Hz), 7.08-6.96 (5H, m), 6.88-6.83 (1H, m), 6.09 (1H, brs), 4.66 (2H, d, *J* = 5.2 Hz), 3.40-3.30 (8H, m), 3.02 (2H, q, *J* = 7.6 Hz), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 96.5%, MS (ESI): m/z 542.1[M+ H]+. |

Table 2

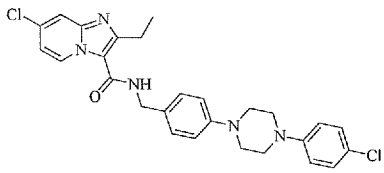
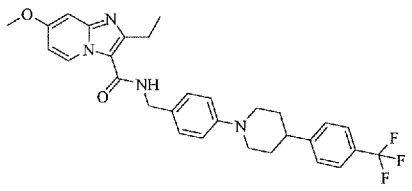
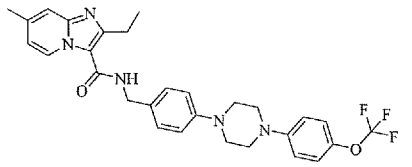
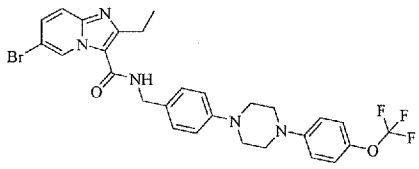
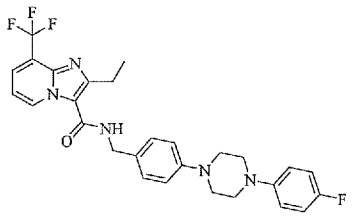
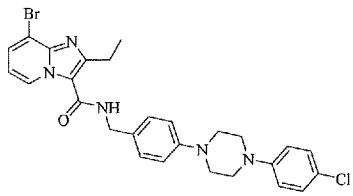
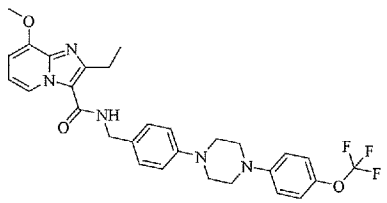
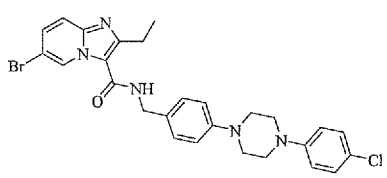
| | | |
|---|---|---|
| 194 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, *J* = 7.6 Hz), 7.61 (1H, d, *J* = 1.6 Hz), 7.32 (2H, d, *J* = 8.8 Hz), 7.26 (2H, d, *J* = 9.2 Hz), 7.00 (2H, d, *J* = 8.4 Hz), 6.88-9.95 (3H, m), 6.05 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.34 (8H, d, *J* = 6.8 Hz ), 2.98 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 97.6%, MS (ESI): m/z 507.9 [M+ H]+. |
| 195 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.25 (1H, d, *J* = 7.6 Hz), 7.57 (2H, d, *J* = 8.0 Hz), 7.37 (2H, d, *J* = 8.0 Hz), 7.29 (2H, d, *J* = 8.8 Hz), 6.99 (2H, d, *J* = 8.4 Hz), 6.89 (1H, d, *J* = 2.0 Hz), 6.61 (1H, dd, *J* = 7.6 Hz, 2.4 Hz), 5.95 (1H, brs), 4.61 (2H, d, *J* = 5.2 Hz), 3.87(3H, s),3.83 (2H, d, *J* = 12.4 Hz), 2.92 (2H, q, *J* = 7.6 Hz), 2.84 (2H, td, *J* = 12.0 Hz, 2.4 Hz), 2.55-2.70 (1H, m), 1.85-2.02 (4H, m), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 98.7%, MS (ESI): m/z 537.1 [M+H]+, 559.1 [M+Na]+. |
| 196 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 6.8 Hz), 7.36-7.31 (3H, m), 7.14 (2H, d, *J* = 8.8 Hz), 6.99-6.94 (4H, m), 6.75 (1H, d, *J* = 6.8 Hz), 5.30 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.34 (8H, brs), 2.95 (1H, q, *J* = 7.2 Hz), 2.42 (3H, s), 1.39 (3H, t, *J* = 7.6 Hz); LCMS: 97.9%, MS (ESI): m/z 454.1[M+ H]+. |
| 197 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.63 (1H, s), 7.49 (1H, d, *J* = 9.6 Hz ), 7.39 (1H, d, *J* = 9.2 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.14 (2H. d. *J* = 8.8 Hz), 6.87-7.05 (4H, m), 6.05 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.21-3.45 (8H. m), 2.96 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 95.9%, MS (ESI): m/z 603.8[M+ H]+. |
| 198 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.58 (1H, d, *J* = 6.8 Hz), 7.66 (1H, d, *J* = 6.8 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 6.90-7.10 (7H, m), 6.10 (1H, brs), 4.64 (2H, d, *J* = 5.6 Hz), 3.30-3.42 (4H, m), 3.20-3.30 (4H, m), 3.03 (2H, q, *J* = 7.2 Hz), 1.38 (3H, t, *J* = 7.2 Hz); LCMS: 97.5%, MS (ESI): m/z 526.0[M + H]+. |
| 199 |  | white solid : $^1$H-NMR (CDCl3): δ 9.40 (1H, d, *J* = 7.2 Hz), 7.58 (1H, d, *J* = 7.2 Hz), 7.42 (2H, d, *J* = 7.2 Hz), 7.24 (2H, d, *J* = 8.8 Hz), 6.98 (2H, d, *J* = 8.0 Hz), 6.90 (2H, d, *J* = 8.8 Hz), 6.80 (1H, t, *J* = 6.8 Hz), 6.08 (1H, brs), 4.63 (2H, d, *J* = 5.2 Hz), 3.20-3.40 (8H, m), 3.02 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 97.5%, MS(ESI):m/z 552.0/554.0 [M+H]+ |
| 200 |  | yellow solid : $^1$H-NMR (CDCl3): δ 8.99 (1H, d, *J*= 6.8 Hz), 7.32 (2H, d, *J* = 8.0 Hz), 7.14 (2H, d, *J* = 8.8 Hz), 6.94-6.99 (4H, m), 6.82 (1H, t, *J* = 7.2 Hz), 6.62 (1H, d, *J* = 7.6 Hz), 6.05 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 4.02 (3H, s). 3.34 (8H, s), 2.98 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 96.2%, MS (ESI): m/z 554.1[M+ H]+. |
| 201 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.63 (1H, s), 7.49 (1H, d, *J* = 9.6 Hz ), 7.39 (1H, d, *J* = 9.6 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.19-7.26 (2H, m), 6.98 (2H, d, *J* = 8.4 Hz), 6.90 (2H, d, *J* = 8.8 Hz), 6.04 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.15-3.40 (8H, m), 2.96 (2H, q, *J* = 7.6 Hz), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 97.8%, MS (ESI): m/z 552.0[M+ H]+. |

Table 2

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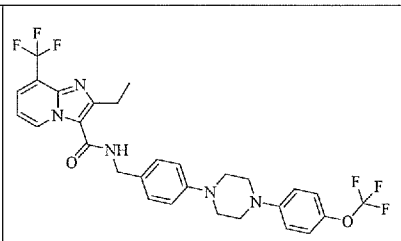
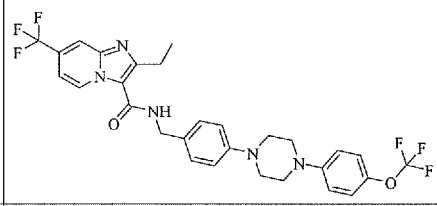
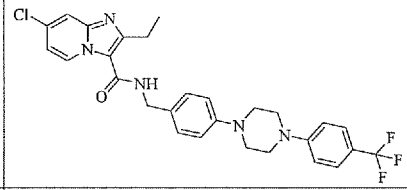
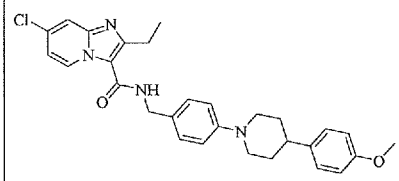
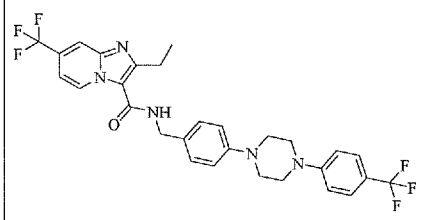
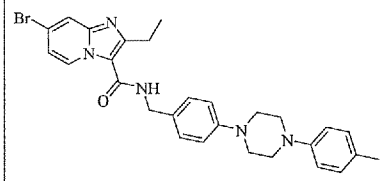
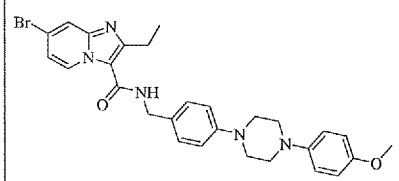
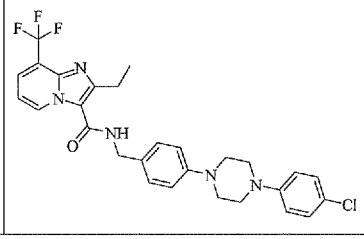
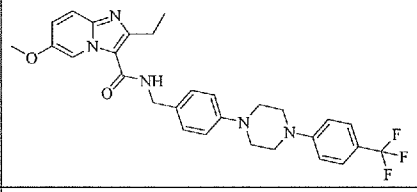
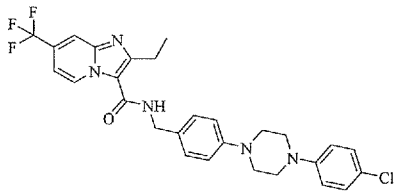
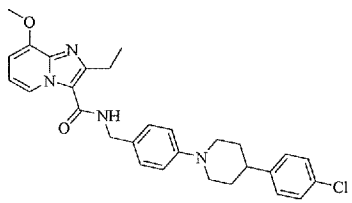
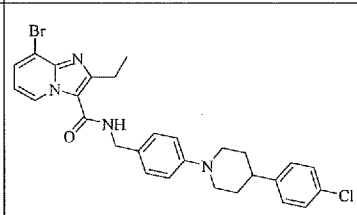
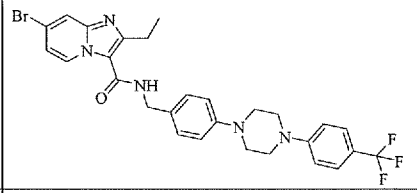
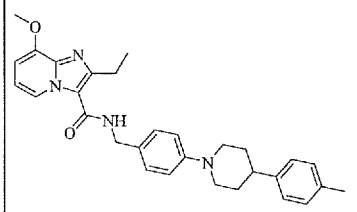
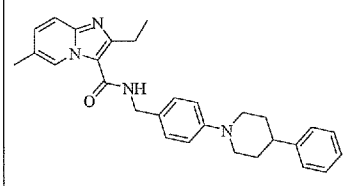
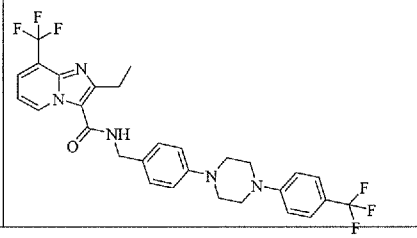
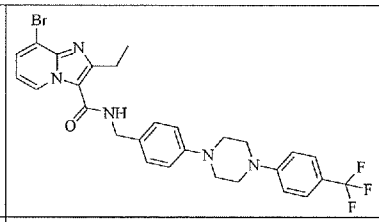
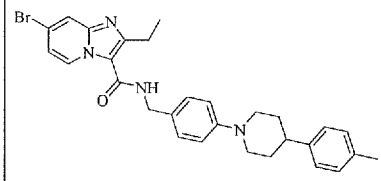
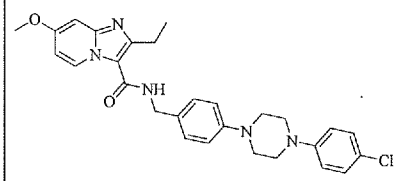
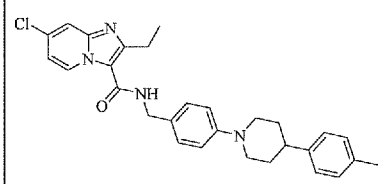
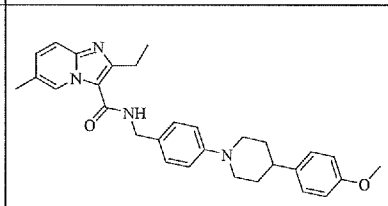
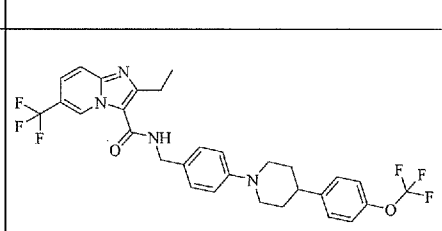
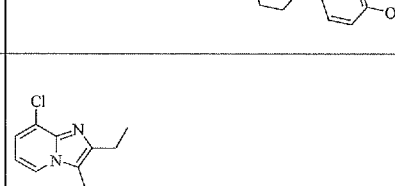
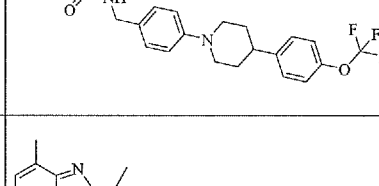
|---|---|---|
| 202 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.59 (1H, d, $J$ = 6.8 Hz), 7.66 (1H, d, $J$ = 7.2 Hz), 7.31 (2H, d, $J$ = 8.4 Hz), 7.14 (2H, d, $J$ = 8.4 Hz), 6.92-7.01 (5H, m), 6.12 (1H, brs), 4.64 (2H, d, $J$ = 5.6 Hz), 3.17-3.54 (8H, m), 3.03 (2H, q, $J$ = 7.6 Hz), 1.37 (3H, t, $J$ = 7.6 Hz); LCMS: 97.9%, MS (ESI): m/z 592.0[M + H]+. |
| 203 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, $J$ = 7.2 Hz), 7.93 (1H, s), 7.34 (2H, d, $J$ = 8.4 Hz), 7.16 (2H, d, $J$ = 8.4 Hz), 7.11 (1H, dd, $J$ = 7.6, 2.0 Hz), 6.96-7.03 (4H, m), 6.11 (1H, brs), 4.66 (2H, d, $J$ = 5.6 Hz), 3.29-3.38 (8H, m), 3.01 (2H, q, $J$ = 7.6 Hz), 1.44 (3H, t, $J$ = 7.6 Hz); LCMS: 97.7%, MS (ESI): m/z 592.0[M+ H]+. |
| 204 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, $J$ = 7.2 Hz), 7.62 (1H, s), 7.53 (2H, d, $J$ = 8.4 Hz), 7.33 (2H, d, $J$ = 8.0 Hz), 7.00 (4H, d, $J$ = 8.8 Hz), 6.93 (1H, dd, $J_1$ = 2.0 Hz, $J_2$ = 7.6 Hz), 6.04 (1H, brs), 4.64 (2H, d, $J$ = 5.6 Hz ), 3.30-3.50 (8H, m), 2.98 (2H, q, $J$ = 7.6 Hz), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 95.6%, MS (ESI): m/z 542.1 [M+ H]+. |
| 205 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.39 (1H, d, $J$ = 7.6 Hz), 7.61 (2H, d, $J$ = 1.6 Hz), 7.25-7.33 (2H, m), 7.20 (2H, d, $J$ = 8.8 Hz), 7.00 (2H, d, $J$ = 8.4 Hz), 6.85-6.95 (3H, m), 6.03 (1H, brs), 4.63 (2H, d, $J$ = 5.6 Hz), 3.75-3.90 (5H, m), 2.98 (2H, q, $J$ = 7.2 Hz), 2.80-2.90 (2H, m), 2.60-2.70 (1H, m), 1.83-2.02 (4H, m), 1.40 (3H, t, $J$ = 7.6 Hz); LCMS: 97.3%, MS (ESI): m/z 525.1 [M+ Na]+. |
| 206 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.55 (1H, d, $J$ = 7.2 Hz), 7.93 (1H, s), 7.53 (2H, d, $J$ = 8.8 Hz), 7.34 (2H, d, $J$ = 8.4 Hz), 7.11 (1H, dd, $J$ = 7.2, 1.6 Hz), 6.97-7.04 (4H, m), 6.11 (1H, brs), 4.66 (2H, d, $J$ = 5.2 Hz), 3.46-3.50 (4H, m), 3.31-3.40 (4H, m), 3.02 (2H, q, $J$ = 7.6 Hz), 1.44 (3H, t, $J$ = 7.6 Hz); LCMS: 97.2%, MS (ESI): m/z 576.0[M+ H]+. |
| 207 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.32 (1H, d, $J$ = 7.2 Hz), 7.79 (1H, d, $J$ = 2.0 Hz ), 7.32 (2H, d, $J$ = 8.8 Hz), 7.13 (2H. d. $J$ = 8.0 Hz), 6.97-7.10 (3H, m), 6.89-7.00 (2H. m), 6.05 (1H, brs), 4.64 (2H, d, $J$ = 5.2 Hz), 3.25-3.43 (8H, m), 2.98 (2H, q, $J$ = 7.6 Hz), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 97.1%, MS (ESI): m/z 532.0[M+ H]+. |
| 208 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.33 (1H, d, $J$ = 7.2 Hz), 7.80 (1H, d, $J$ = 1.6 Hz ), 7.32 (2H, d, $J$ = 8.8 Hz), 6.94-7.07 (5H, m), 6.90 (2H, d, $J$ = 8.8 Hz), 6.04 (1H, brs), 4.64 (2H, d, $J$ = 5.2 Hz), 3.90 (3H, s), 3.31-3.42 (4H, m), 3.20-3.30 (4H, m), 2.98 (2H, q, $J$ = 7.6 Hz), 1.41 (3H, t, $J$ = 7.6 Hz); LCMS: 95.4%, MS (ESI): m/z 548.0[M+ H]+. |
| 209 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.57 (1H, d, $J$ = 7.2 Hz), 7.64 (1H, d, $J$ = 7.2 Hz), 7.29 (2H, d, $J$ = 8.8 Hz), 7.20-7.26 (2H, m), 6.94-6.98 (3H, m), 6.86-6.91 (2H, m), 6.08 (1H, brs), 4.62 (2H, d, $J$ = 5.2 Hz), 3.28-3.35 (8H, m), 3.01 (2H, q, $J$ = 7.6 Hz), 1.37 (3H, t, $J$ = 7.6 Hz); LCMS: 97.4%, MS (ESI): m/z 542.0[M + H]+. |

Table 2

| | | |
|---|---|---|
| 210 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.13 (1H, s), 7.45-7.60 (3H, m), 7.34 (2H, d, *J* = 8.4 Hz), 7.14 (2H, d, *J* =8.8 Hz), 7.00 (4H, d, *J* =8.0 Hz), 6.06 (1H, brs), 4.66 (2H, d, *J* = 5.2 Hz), 3.90 (3H, s), 3.40-3.50 (4H, m), 3.30-3.40 (4H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.2%, MS(ESI):m/z 538.0 [M+H]+. |
| 211 |  | gray solid: $^1$H-NMR ($CDCl_3$): δ 9.51 (1H, d, *J* = 6.8 Hz), 7.89 (1H, s), 7.29 (2H, d, *J* = 15.2 Hz), 7.24-7.30 (2H, m), 7.07 (1H, d, *J* = 7.6 Hz), 7.00 (2H, dd, *J* = 12.0, 11.6 Hz), 6.89 (2H, m), 6.04 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 3.31-3.48 (4H, m), 3.25-3.30 (4H, m), 2.98 (2H, q, *J* = 7.6 Hz), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 97.4%, MS (ESI): m/z 541.8[M+ H]+. |
| 212 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 8.99 (1H, d, *J* = 6.8 Hz), 7.26-7.30 (4H, m), 7.17 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.81 (1H, t, *J* = 7.2 Hz), 6.61 (1H, d, *J* = 7.6 Hz), 6.04 (1H, brs), 4.61 (2H, d, *J* = 5.2 Hz), 4.02 (3H, s), 3.80 (2H, d, *J* = 12 Hz), 2.99 (2H ,q, *J* = 7.6 Hz), 2.83 (2H, td, *J* = 2.4 Hz, *J* = 12 Hz), 2.67-2.60 (1H, m), 2.01-1.80 (4H, m), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 99.3%, MS (ESI): m/z 503.0[M+ H]+. |
| 213 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.38 (1H, d, *J* = 6.8 Hz), 7.56 (1H, d, *J* = 7.2 Hz), 7.20-7.35 (4H, m), 7.16 (2H, d, *J* = 7.6 Hz), 6.97 (2H, d, *J* = 7.6 Hz), 6.78 (1H, t, *J* = 7.2 Hz), 6.07 (1H, brs), 4.60 (2H, d, *J* = 5.6 Hz), 3.80 (2H, d, *J* = 12.4 Hz), 3.02 (2H, q, *J* = 7.6 Hz), 2.81 (2H, td, *J* = 12.0, 2.4 Hz), 2.55-2.70 (1H, m), 1.75-2.00 (4H, m), 1.36 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 550.8/552.8 [M+H] |
| 214 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.31 (1H, d, *J* = 7.6 Hz), 7.78 (1H, s), 7.12 (2H, d, *J* = 6.8 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 6.81-7.09 (5H, m), 6.03 (1H, brs), 4.62 (2H, d, *J* = 5.2 Hz), 3.26-3.53 (8H, m), 2.87-3.05 (2H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.2%, MS (ESI): m/z 588.0[M+ H]+. |
| 215 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.01 (1H, d, *J* = 6.8 Hz), 7.28-7.32 (2H, m), 7.14-7.18 (4H, m), 7.00 (2H, d, *J* = 8.8 Hz), 6.83 (1H, t, *J* = 7.2 Hz), 6.63 (1H, d, *J* = 7.6 Hz), 6.06 (1H, brs), 4.62 (2H, d, *J* = 5.6 Hz), 4.04 (3H, s), 3.82 (2H, d, *J* = 12.4 Hz), 3.01 (2H ,q, *J* = 7.6 Hz), 2.85 (2H, td, *J* = 2.8 Hz, *J* = 12 Hz), 2.61-2.68 (1H, m), 2.35 (3H, s), 1.85-1.98 (4H, m), 1.40 (3H, t, *J* = 7.6 Hz); LCMS: 97.8%, MS (ESI): m/z 483.1[M+ H]+. |
| 216 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.19 - 9.29 (1 H, m), 7.52 (1 H, d, *J*=9.16 Hz), 7.14 - 7.41 (8 H, m), 7.01 (2 H, d, *J*=8.66 Hz), 5.97 - 6.11 (1 H, m), 4.64 (2 H, d, *J*=5.40 Hz), 3.85 (2 H, d, *J*=12.30 Hz), 2.91 - 3.04 (2 H, m), 2.86 (2 H, d, *J*=2.76 Hz), 2.60 - 2.73 (1 H, m), 2.39 ( 3 H, s), 1.98 (4 H, br. s.) , 1.41 (3 H, t, *J*=7.53 Hz); LCMS: 100%, MS (ESI): m/z 453.1[M+ H]+. |
| 217 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.61 (1H, d, *J* = 6.8 Hz), 7.68 (1H, d, *J* = 7.2 Hz), 7.53 (2H, d, *J* = 8.4 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 6.99-7.02 (5H, m), 6.13 (1H, brs), 4.66 (2H, d, *J* = 5.6 Hz), 3.31-3.49 (8H, m), 3.05 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 98.6%, MS (ESI): m/z 576.0[M + H]+. |

| | | |
|---|---|---|
| 218 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.42 (1H, d, *J* = 6.0 Hz), 7.61 (1H, d, *J* = 7.6 Hz), 7.53 (2H, d, *J* = 8.4 Hz), 7.34 (2H, d, *J* = 8.8 Hz), 7.00 (4H, d, *J* = 8.8 Hz), 6.82 (1H, t, *J* = 7.2 Hz), 6.10 (1H, brs), 4.65 (2H, d, *J* = 5.6 Hz), 3.30-3.50 (8H, m), 3.04 (2H, q, *J* = 7.6 Hz), 1.38 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS(ESI):m/z 585.8/587.8 [M+H]+ |
| 219 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.32 (1H, d, *J* = 7.6 Hz), 7.79 (1H, d, *J* = 1.6 Hz ), 7.28-7.33 (2H, m), 7.13-7.20 (4H, m), 6.93-7.06 (3H. m), 6.04 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 4.56-4.67 (2H. m), 2.98 (2H, q, *J* = 7.6 Hz), 2.76-2.92 (2H, m), 2.60-2.70 (1H. m), 1.83-2.02 (4H. m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 95.0%, MS (ESI): m/z 533.0[M+ H]+. |
| 220 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.27 (1H, d, *J* = 7.6 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 7.25 (2H, d, *J* = 8.8 Hz), 6.99 (2H, d, *J* = 8.8 Hz), 6.91 (3H, d, *J* = 8.8 Hz), 6.63 (1H, dd, *J* = 7.6 Hz, 2.4 Hz), 5.97 (1H, m), 4.63 (2H, d, *J* = 5.6 Hz), 3.89 (3H, s), 3.20-3.40 (8H, m), 2.94 (2H, q, *J* = 7.6 Hz), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100.0%, MS (ESI): m/z 504.0[M+ H]+. |
| 221 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.38 (1H, d, *J* = 7.6 Hz), 7.61 (1H, d, *J* = 1.6 Hz), 7.24-7.33 (2H, m), 7.13-7.20 (4H, m), 7.00 (2H, d, *J* = 8.4 Hz), 6.92 (1H, dd, $J_1$ = 2.4 Hz, $J_2$ = 7.6 Hz), 6.03 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.83 (2H, d, *J* = 12.4 Hz), 2.97 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.59-2.72 (1H, m), 2.35 (3H, s), 1.85-2.02 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 97.2%, MS (ESI): m/z 486.8 [M+ H]+. |
| 222 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.18 - 9.34 (m, 1 H), 7.48 - 7.58 (m, 1 H), 7.28 (s, 2 H) 7.17 - 7.23 (m, 3 H), 6.98 - 7.03 (m, 2 H), 6.90 (s, 2 H), 5.96 - 6.06 (m, 1 H), 4.64 (d, *J*=5.52 Hz, 2 H), 3.83 - 3.88 (m, 1 H), 3.82 (s, 4 H), 2.94 - 3.03 (m, 2 H), 2.79 - 2.90 (m, 2 H), 2.59 - 2.69 (m, 1 H), 2.39 (s, 3 H), 1.82 - 2.01 (m, 4 H), 1.42 (t, *J*=7.53 Hz, 3 H); LCMS: 100%, MS (ESI): m/z 483.0[M+ H]+. |
| 223 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, *J* = 9.2 Hz), 7.46 (1H, dd, *J* = 7.6, 1.6 Hz), 7.25-7.32 (4H, m), 7.16 (2H, d, *J* = 8.0 Hz), 7.00 (2H, d, *J* = 8.8 Hz), 6.00-6.16 (1H, m), 4.63 (2H, d, *J* = 5.2 Hz), 3.83 (2H, d, *J* = 12.4 Hz), 2.99 (2H, q, *J* = 7.6 Hz), 2.79-2.89 (2H, m), 2.51-2.73 (1H, m), 1.78-2.02 (4H, m), 1.42 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 591.0[M+ H]+. |
| 224 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.37 (1H, dd, $J_1$ = 0.8 Hz, $J_2$ = 6.8 Hz) , 7.41 (1H, dd, $J_1$ = 1.2 Hz, $J_2$ = 7.6 Hz), 7.27-7.32 (4H, m), 7.18(2H, d, *J* = 8 Hz ), 7.01 (2H, d, *J* = 8.4 Hz), 6.87 (1H, t, *J* = 7.2 Hz), 6.09 (1H, brs), 4.64 (2H, d, *J* = 5.2 Hz), 3.84 (2H, d, *J* = 12.4 Hz), 3.05 (2H, q, *J* = 7.6 Hz,), 2.86 (2H, t, *J* = 11.6 Hz), 2.70 (1H, t, *J* = 12 Hz), 1.88-1.99 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100.00%, MS (ESI): m/z 556.9[M+ H]+. |
| 225 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.24 (1H, d, *J* = 7 Hz), 7.29 (2H, d, *J* = 8.5 Hz), 7.16-7.23 (2H, m), 7.11 (1H, d, *J* = 7 Hz), 6.95-7.03 (4H, m), 6.81 (1H, t, *J* = 6.9 Hz), 6.03 (1H, brs), 4.62 (2H, d, *J* = 5.3 Hz), 3.81 (2H, d, *J* = 12.3 Hz), 2.99 (2H, q, *J* = 7.5 Hz), 2.83 (2H, td, *J* = 12.2, 2.6 Hz), 2.62-2.69 (1H, m), 2.61 (3H, s), 1.79-1.98 (4H, m), 1.36 (3H, t, *J* = 7.5 Hz); LCMS: 100%, MS (ESI): m/z 471.1[M+ H]+. |

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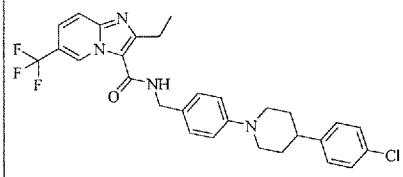
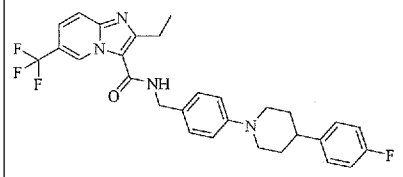
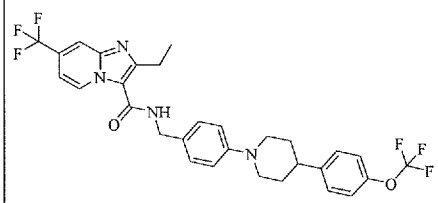
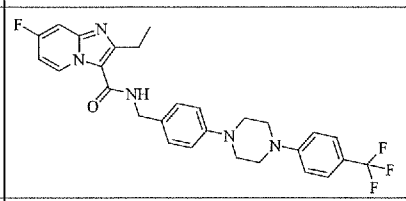
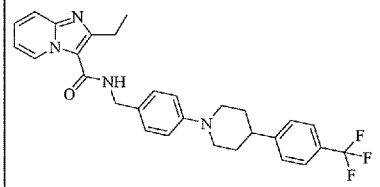
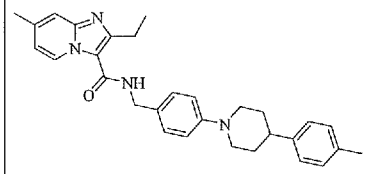
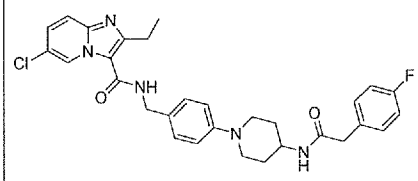
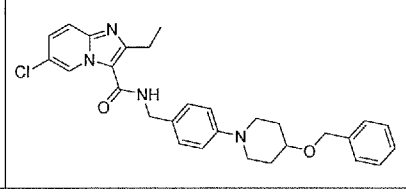
| 226 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, *J* = 9.2 Hz), 7.47 (1H, dd, *J* = 7.6, 2.0 Hz), 7.28-7.33 (4H, m), 7.18 (2H, d, *J* = 8.4 Hz), 6.99 (2H, d, *J* = 8.4 Hz), 6.07 (1H, m), 4.62 (2H, d, *J* = 5.6 Hz), 3.81 (2H, m), 2.99 (2H, q, *J* = 7.6 Hz), 2.77-2.90 (2H, m), 2.58-2.70 (1H, m), 1.79-2.00 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 541.0[M+ H]+. |
| 227 |  | yellow solid: $^1$H-NMR ($CDCl_3$): δ 9.86 (1H, s), 7.69 (1H, d, *J* = 9.2 Hz), 7.47 (1H, dd, *J* = 7.6, 2.0 Hz), 7.25-7.38 (2H, m), 7.15-7.25 (2H, m), 6.91-7.09 (4H, m), 6.13 (1H, m), 4.63 (1H, d, *J* = 5.2 Hz), 3.82 (2H, d, *J* = 12.4 Hz), 3.00 (2H, q, *J* = 7.8 Hz), 2.78-2.90 (2H, m), 2.49-2.73 (1H, m), 1.78-2.03 (4H, m), 1.43 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 525.0[M+ H]+. |
| 228 |  | white solid: $^1$H-NMR ($CDCl_3$): δ 9.53 (1H, d, *J* = 7.6 Hz), 7.91 (1H, s), 7.29-7.52 (3H, m), 7.28 (1H, s), 7.16 (2H, d, *J* = 8.0 Hz), 7.10 (1H, dd, *J* = 7.6, 1.6 Hz), 6.96 (2H, d, *J* = 22.0 Hz), 6.08 (1H, brs), 4.63 (2H, d, *J* = 5.6 Hz), 3.82 (2H, d, *J* = 12.4 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 2.79-2.82 (2H, m), 2.63-2.70 (1H, m), 1.84-1.89 (4H, m), 1.35 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 590.8[M+ H]+. |
| 229 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.46(1H, t, *J*= 7.2 Hz), 7.53(2H, d, *J*= 8.8 Hz), 7.33(2H, d, *J*= 8.4Hz), 7.23-7.25(1H, m), 6.99-7.01(4H, m), 6.79-6.83(1H, m), 6.04(1H, brs), 4.64(2H, d, *J*= 5.6 Hz), 3.36-3.48(8H, m), 2.94-3.00(2H, m), 1.41(3H, t, *J*= 7.6 Hz); LCMS: 99.9%, MS (ESI): m/z 526.0[M+ H]+. |
| 230 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.41 (1H, d, *J* = 7.2 Hz), 7.53-7.65 (3H, m), 7.28-7.40 (5H, m), 6.99 (2H, d, *J* = 8.4 Hz), 6.89-6.96 (1H, m), 5.97-6.09 (1H, m), 4.63 (2H, d, *J* = 5.6 Hz), 3.75-3.90 (2H, m), 2.98 (2H, q, *J* = 7.6 Hz), 2.80-2.90 (2H, m), 2.65-2.79 (1H, m), 1.85-2.01 (4H, m), 1.41 (3H, t, *J* = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 507.0[M+ H]+. |
| 231 |  | white solid : $^1$H-NMR ($CDCl_3$): δ 9.28 (1H, d, *J* = 7.2 Hz), 7.36 (1H, s), 7.30-7.26 (2H, m), 7.17-7.12 (4H, m), 6.98 (2H, d, *J* = 8.4 Hz), 6.75 (1H, dd, *J* = 7.2 Hz, 1.6 Hz), 4.61 (2H, d, *J* = 5.6 Hz), 3.73 (2H, d, *J* = 12.4 Hz), 2.94 (2H, q, *J* = 7.2 Hz), 2.81 (2H, td, *J* = 12 Hz, 2.4 Hz), 2.67-2.57 (1H, m), 2.42 (3H, s), 2.01-1.81 (4H, m), 1.39 (3H, t, *J* = 7.2 Hz). |
| 232 |  | white solid; $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.26 (3H, t, *J* = 7.6 Hz), 1.65-1.63 (2H, m), 1.92-1.89 (2H, m), 3.01 (2H, q, *J* = 7.6 Hz), 3.17 (1H, brs), 3.39 (2H, s), 3.62-3.59 (2H, m), 3.82 (1H, m), 4.49 (2H, d, *J* = 5.6 Hz), 7.10 (2H, t, *J* = 8.8 Hz), 7.29-7.25 (4H, m), 7.38-7.36 (2H, m), 7.65 (1H, dd, *J* = 9.2, 1.6 Hz), 7.78 (1H, d, *J* = 9.6 Hz), 8.19 (1H, d, *J* = 7.2 Hz), 8.70 (1H, t, *J* = 5.6 Hz), 9.11 (1H, s); LCMS: 99.7%, MS (ESI): m/z 548.2[M+ H]+. |
| 233 |  | yellow solid; $^1$H-NMR (MeOD, 300 MHz): δ1.37 (3H, t, *J* = 7.5 Hz), 2.15-2.23 (4H, m), 3.10 (2H, q, *J* = 7.5 Hz), 3.51-3.57 (2H, m), 3.77-3.87 (3H, m), 4.63 (2H, s), 4.68 (2H, s), 7.29-7.41 (5H, m), 7.57-7.64 (4H, m), 7.76-7.81 (2H, m), 9.22 (1H, d, *J* = 9.0 Hz); LCMS: 98.9%, MS (ESI): m/z 503.2[M+ H]+. |

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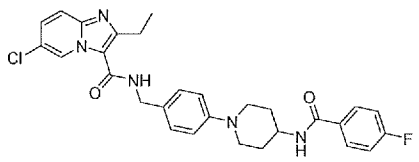
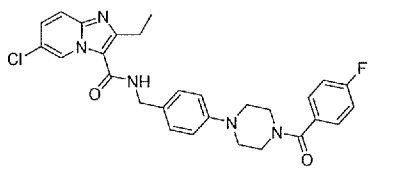
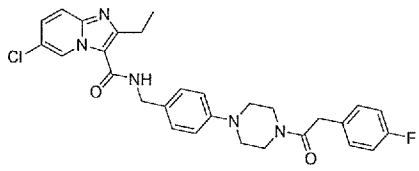
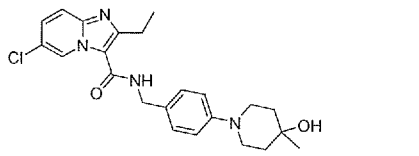
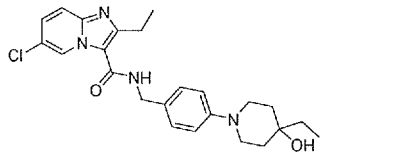
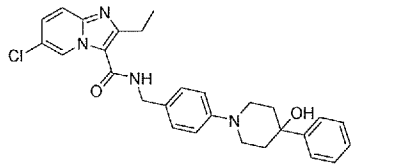
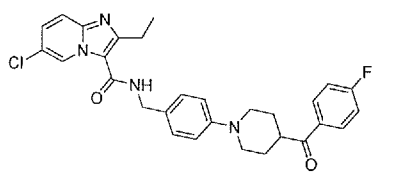
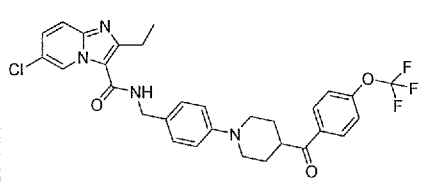
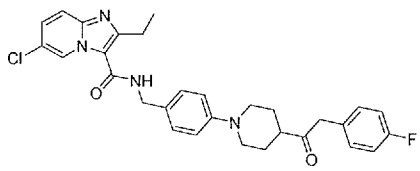
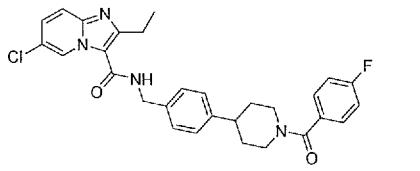
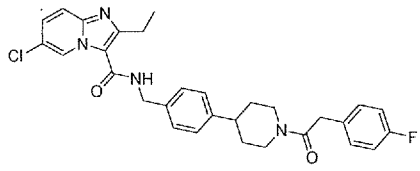
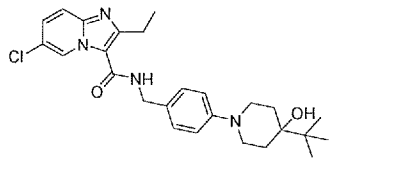
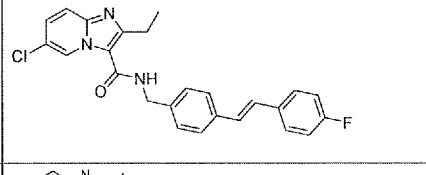
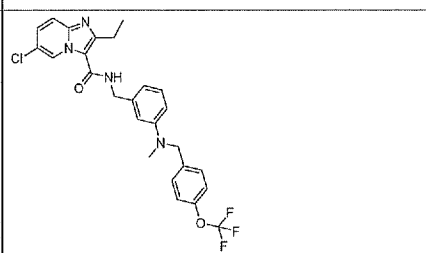
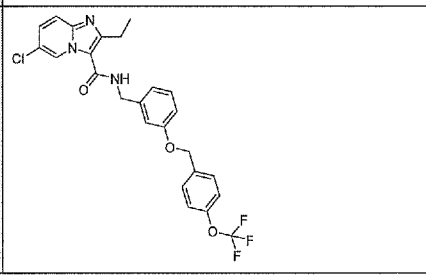
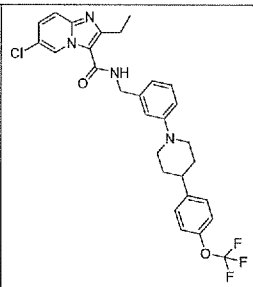
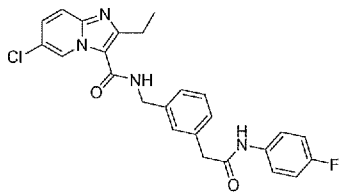
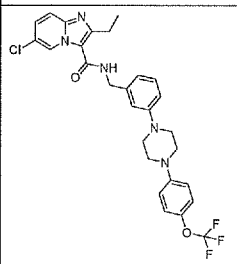
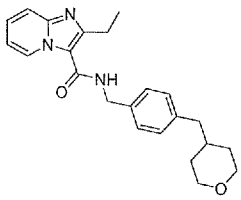
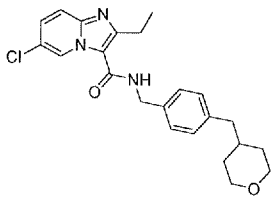
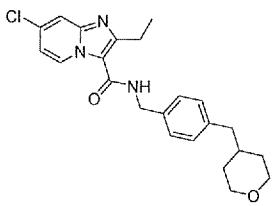
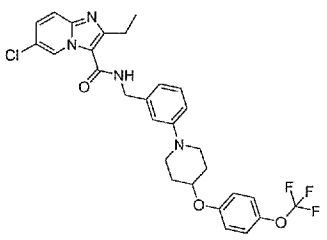
| 234 |  | white solid: $^1$H-NMR (DMSO-d6, 400 MHz): δ1.29 (3H, t, *J* = 7.6 Hz), 1.79-1.81 (2H, m), 1.97-1.99 (2H, m), 3.02 (2H, q, *J* = 7.6 Hz), 3.15 (1H, m), 3.70-3.73 (2H, m), 4.05 (1H, m), 4.50 (2H, d, *J* = 5.6 Hz), 7.25-7.33 (4H, m), 7.36-7.38 (2H, m), 7.64 (1H, dd, *J* = 1.6 Hz, 9.6 Hz), 7.78 (1H, d, *J* = 9.6 Hz), 7.92-7.96 (2H, m), 8.42 (1H, d, *J* = 7.2 Hz), 8.65 (1H, t, *J* = 5.6 Hz), 9.12 (1H, d, *J* = 1.6 Hz); LCMS: 100%, MS (ESI): m/z 534.1[M+ H]+. |
| 235 |  | white solid: $^1$H-NMR (DMSO-d6, Bruker Avance 300 MHz): δ 1.25 (3H, t, *J* = 7.5Hz), 3.00 (2H, q, *J* = 7.5Hz), 3.08-3.28 (4H, m), 3.31-3.91 (4H, m), 4.43 (2H, d, *J* = 5.7 Hz), 6.95 (2H, d, *J* = 8.7 Hz), 7.20-7.33 (4H, m), 7.49 (2H, dd, *J* = 8.4, 5.4 Hz), 7.70 (1H, dd, *J* = 9.2, 1.8 Hz), 7.80 (1H, d, *J* = 9.2 Hz), 8.70 (1H, t, *J* = 5.7 Hz), 9.10 (1H, s); LCMS: 100%, MS (ESI): m/z 520.0 [M+ H]+. |
| 236 |  | white solid: $^1$H-NMR (DMSO-d6, Bruker Advance 300 MHz): δ 1.24 (3H, t, J= 7.5Hz), 2.91-3.12 (6H, m), 3.51-3.65 (4H, m), 3.74 (2H, s), 4.42-4.44 (2H, m), 6.92 (2H, d, *J* = 8.7 Hz), 7.10 (2H, t, *J* = 8.8 Hz), 7.19-7.31 (4H, m), 7.69 (1H, dd, *J* = 9.6, 1.8 Hz), 7.78 (1H, d, *J* = 9.6 Hz), 8.66 (1H, t, *J* = 5.7 Hz), 9.10 (1H, s). LCMS: 100%, MS (ESI): m/z 534.0 [M+ H]+. |
| 237 |  | pale yellow oil; $^1$H-NMR (CD3OD, 300 MHz): δ1.32-1.41 (6H, m), 1.91-1.96 (2H, m), 2.02-2.13 (2H, m), 3.12 (2H, q, *J* = 7.5 Hz), 3.51-3.55 (2H, m), 3.82-3.91 (2H, m), 4.70 (2H, s), 7.66 (4H, s), 7.80-7.90 (2H, m), 9.24 (1H, s); LCMS: 98.4%, MS (ESI): m/z 427.1[M+ H]+. |
| 238 |  | pale yellow oil; $^1$H-NMR (CD3OD, 300 MHz): δ0.99 (3H, t, *J* = 7.5 Hz), 1.39 (3H, t, *J* = 7.5 Hz), 1.62 (2H, q, *J* = 7.5 Hz), 1.90-2.08 (4H, m), 3.12 (2H, q, *J* = 7.5 Hz), 3.53-3.59 (2H, m), 3.83-3.91 (2H, m), 4.70 (2H, s), 7.66 (4H, s), 7.80-7.90 (2H, m), 9.25 (1H, s); LCMS: 99.0%, MS (ESI): m/z 440.2[M+ H]+. |
| 239 |  | white solid; $^1$H-NMR (CD3OD, 400 MHz): δ1.40 (2H, t, *J* = 7.6 Hz), 2.11 (2H, d, *J* = 13.6 Hz), 2.50-2.61 (2H, m), 3.13 (2H, q, *J* = 7.6 Hz), 3.67 (2H, d, *J* = 12.4 Hz), 4.02-4.09 (2H, m), 4.72 (2H, s), 7.29 (1H, d, *J* = 7.6 Hz), 7.39 (2H, t, *J* = 8.0 Hz), 7.57 (2H, d, *J* = 7.2 Hz), 7.67-7.73 (4H, m), 7.81-7.89 (2H, m), 9.26 (1H, d, *J* = 0.8 Hz); LCMS: 99.9%, MS (ESI): m/z 489.2[M+ H]+. |
| 240 |  | white amorphous (powder); $^1$H-NMR (DMSO-d6, Bruker Avance 400 MHz): δ 1.33 (3H, t, *J* = 7.2 Hz), 2.00-2.12 (2H, m), 2.13-2.30 (2H, m), 3.11 (2H, q, *J* = 7.6 Hz), 3.55-3.70 (5H, m), 4.59 (2H, d, *J* = 5.6 Hz), 7.43 (2H, t, *J* = 8.8 Hz), 7.57 (2H, d, *J* = 7.6 Hz), 7.65-7.78 (2H, m), 7.88-7.95 (2H, m), 8.12 (2H, dd, *J* = 8.8, 5.6 Hz), 9.11 (1H, brs), 9.19 (1H, s); LCMS: 100%, MS (ESI): m/z 519 [M+H]+. |
| 241 |  | white amorphous (powder); $^1$H-NMR (MeOD, Bruker Avance 400 MHz): δ 1.43 (3H, t, *J* = 7.6 Hz), 2.16-2.38 (4H, m), 3.17 (2H, q, *J* = 7.6 Hz), 3.75-3.88 (4H, m), 3.90-4.01 (1H, m), 4.74 (2H, d, *J* = 4.4 Hz), 7.48 (2H, d, *J* = 8.4 Hz), 7.70 (4H, s), 7.89 (1H, d, *J* = 9.6 Hz), 8.00 (1H, dd, *J* = 9.6, 2.0 Hz), 8.22 (2H, d, *J* = 8.8 Hz), 8.95 (1H, t, *J* = 5.6 Hz), 9.31 (1H, s); LCMS: 100%, MS (ESI): m/z 584.8 [M+H]+. |

Table 2

| | | |
|---|---|---|
| 242 |  | white amorphous (powder); $^1$H-NMR (MeOD, Bruker Avance 400 MHz): δ 1.42 (3H, t, *J* = 7.6 Hz), 2.03-2.18 (2H, m), 2.25-2.35 (2H, m), 3.04-3.12 (1H, m), 3.18 (2H, q, *J* = 7.6 Hz), 3.68-3.70 (4H, m), 3.93 (2H, s), 4.72 (2H, d, *J* = 2.8 Hz), 7.06 (2H, t, *J* = 8.8 Hz), 7.23-7.30 (2H, dd, *J* = 8.4, 5.2 Hz), 7.67 (4H, s), 7.93 (1H, d, *J* = 9.6 Hz), 8.08 (1H, dd, *J* = 9.6, 2.0 Hz), 9.05 (1H, t, *J* = 6.0 Hz), 9.32 (1H, d, *J* = 1.2 Hz); LCMS: 100%, MS (ESI): m/z 533.0 [M+H]+. |
| 243 |  | white amorphous (gum); $^1$H-NMR (DMSO-d6, Bruker Avance 400 MHz): δ 1.32 (3H, t, *J* = 7.6 Hz), 1.52-1.91 (4H, m), 2.75-2.92 (2H, m), 3.08 (2H, q, *J* = 7.6 Hz), 3.10-3.25 (1H, m), 3.58-3.72 (1H, m), 4.53 (2H, d, *J* = 1.6 Hz), 7.26-7.38 (6H, m), 7.51 (2H, dd, *J* = 8.4, 5.6 Hz), 7.95 (2H, s), 9.09 (1H, t, *J* = 5.6 Hz), 9.19 (1H, s); LC-MS purity: 100%. MS (ESI): m/z 519.1 [M+H]+. |
| 244 |  | white solid(sticky powder); mp = 216.2-220.7℃: $^1$H-NMR (DMSO-d6, Bruker Avance 400 MHz): δ 1.32 (3H, t, *J* = 7.2 Hz), 1.37-1.50 (2H, m), 1.68-1.81 (2H, m), 2.58-2.82 (2H, m), 3.01-3.15 (3H, m), 3.74 (2H, s), 4.03-4.08 (1H, m), 4.51 (2H, d, *J* = 5.6 Hz), 4.54-4.58 (1H, m), 7.11-7.20 (4H, m), 7.24-7.40 (4H, m), 7.950 (2H, s), 9.06 (1H, brs), 9.19 (1H, s); LC-MS purity: 100%. MS (ESI): m/z 533.0 [M+H]+. |
| 245 |  | white solid (powder); mp = 221.5-221.8℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 0.85 (9H, s). 1.23 (3H, t, *J* = 7.6 Hz), 1.50 (2H, d, *J* = 12.4 Hz), 1.61-1.69 (2H, m), 2.86-2.98 (4H, m), 3.45 (2H, d, *J* = 9.6 Hz), 3.92 (1H, s), 4.40 (2H, d, *J* = 5.6 Hz), 6.89 (2H, d, *J* = 8.8 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 7.44 (1H, dd, *J* = 2.0 Hz, 9.2 Hz), 7.65 (1H, d, *J* = 9.6 Hz), 8.39 (1H, t, *J* = 5.6 Hz), 9.05 (1H, s); LCMS: 97.4%, MS (ESI): m/z 440.2[M+H]+. |
| 246 |  | white amorphous (powder); $^1$H-NMR (DMSO-d6, 300 MHz): δ 1.23 (3H, t, *J* = 7.5 Hz), 2.97 (2H, q, *J* = 7.5 Hz), 4.50 (2H, d, *J* = 5.7 Hz), 7.10-7.23 (4H, m), 7.34 (2H, d, *J* = 8.1 Hz), 7.43 (1H, dd, *J* = 9.6, 1.5 Hz), 7.50-7.70 (5H, m), 8.48 (1H, t, *J* = 5.7 Hz), 9.04 (1H, s); LCMS: 98.7%, MS (ESI): m/z 433.9 [M+ H]+. |
| 247 |  | white power; mp >142.3℃: decomposed; $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.23 (3H, t, *J* = 7.6 Hz), 2.94 (2H, q, *J* = 7.6 Hz), 2.97 (3H, s), 4.45 (2H, d, *J* = 6.0 Hz), 4.59 (2H, s), 6.60-6.70 (2H, m), 6.76 (1H, s), 7.12 (1H, t, *J* = 8.0 Hz), 7.24 (2H, d, *J* = 8.4 Hz), 7.29 (2H, d, *J* = 8.8 Hz), 7.45 (1H, dd, *J* = 9.2, 2.0 Hz), 7.66 (1H, d, *J* = 9.6 Hz), 8.43 (1H, t, *J* = 6.0 Hz), 9.04 (1H, d, *J* = 1.2 Hz); LCMS: 98.6%, MS (ESI): m/z 517.0 [M+ H]+. ℃ |
| 248 |  | white powder; mp >142.7℃: decomposed; $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.26 (3H, t, *J* = 7.6 Hz), 2.99 (2H, q, *J* = 7.6 Hz), 4.51 (2H, d, *J* = 5.6 Hz), 5.14 (2H, s), 6.90 (1H, dd, *J* = 8.4, 2.0 Hz), 6.94 (1H, d, *J* = 7.6 Hz), 7.03 (1H, s), 7.27 (1H, t, *J* = 8.0 Hz), 7.35 (2 H, d, *J* = 8.0 Hz), 7.45 (1H, dd, *J* = 9.2, 2.0 H, 7.56 (2H, d, *J* = 8.8 Hz), 7.67 (1H, d, *J* = 9.6 Hz), 8.47 (1H, t, *J* = 5.6 Hz), 9.07 (1H, d, *J* = 1.2 Hz); LCMS: 96.1%, MS (ESI): m/z 504.1[M+ H]+. |

| | | |
|---|---|---|
| 249 |  | white solid; mp = 135.5-136.4℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.26 (3H, t, *J* = 7.6 Hz), 1.69-1.79 (2H, m), 1.80-1.90 (2H, m), 2.70-2.80 (3H, m), 2.99 (2H, q, *J* = 7.6 Hz), 3.75-3.85 (2H, m), 4.49 (2H, d, *J* = 6.0 Hz), 6.78 (1H, d, *J* = 7.6 Hz), 6.88 (1H, d, *J* = 8.0 Hz), 7.01 (1H, s), 7.19 (1H, t, *J* = 8.0 Hz), 7.28 (2H, d, *J* = 8.0 Hz), 7.39-7.47 (3H, m), 7.66 (1H, d, *J* = 9.6 Hz), 8.51 (1H, t, *J* = 6.0 Hz), 9.03 (1H, d, *J* = 1.2 Hz); LCMS: 100%, MS (ESI): m/z 557.0 [M+ H]+. |
| 250 |  | white amorophous; mp >198.8℃: decomposed; $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.24 (3 H, t-*J* = 7.2 Hz), 2.98 (2H, q, *J* = 7.6 Hz), 3.62 (2H, s), 4.53 (2H, d, *J* = 6.0 Hz), 7.09 (2H, t, *J* = 9.2 Hz), 7.10-7.35 (4H, m), 7.46 (1H, dd, J= 9.2, 2.0 Hz), 7.58 (2H, dd , *J* = 9.5, 5.2 Hz), 7.66 (1H, d, *J* = 9.2 Hz), 8.50 (1H, brs, *J* = 6.0 Hz), 9.07(1H, d, *J* = 1.6 Hz), 10.21 (1H , brs); LCMS: 99%, MS (ESI): m/z 465.1 [M+ H]+. |
| 251 |  | white amorophous; mp >168.0℃: decomposed; $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.27 (3 H, t-*J* = 7.6 Hz), 3.00 (2H, q, *J* = 7.2 Hz), 3.20-3.30 (8H, m), 4.50 (2H, d, *J* = 6.0 Hz), 4.50 (2H, d, *J* = 6.0 Hz), 6.83 (1H, d, *J* = 7.6 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 7.02 (1 H, s), 7.07 (2H, d, *J* = 8.8 Hz), 7.20-7.26 (3H, m), 7.45 (1H, dd, *J* = 9.6, 2.0 Hz), 8.50 (1H, t, *J* = 6.0 Hz), 9.04 (1H, d, *J* = 1.6 Hz); LCMS: 95.2%, MS (ESI): m/z 580.1 [M+ Na]+. |
| 252 |  | Gum; $^1$H-NMR (CDCl3, 400 MHz): δ 1.20-1.40 (2H, m), 1.41 (3H, t, *J* = 7.2 Hz), 1.50-1.59 (2H, m), 1.68-1.82 (1H, m), 2.55 (2 H, d, *J* = 6.8 Hz), 2.99 (2H, q, *J* = 7.6 Hz), 3.28-3.38 (2H, m), 3.90-4.00 (2H, m), 4.68 (2 H, d, *J* = 5.2 Hz), 6.08 (1H, brs), 6.92 (1H, t, *J* = 6.8 Hz), 7.15 (2 H, d, *J* = 8.0 Hz), 7.26-7.40 (3H, m), 7.61 (1H, d, *J* = 8.8 Hz), 9.41 (1H, d, *J* = 6.8 Hz); LCMS: 98.96%, MS (ESI): m/z 377.8 [M+ H]+. |
| 253 |  | white solid; mp = 132.2-133.0℃: $^1$H-NMR (CDCl3, 400 MHz): δ 1.25-1.40 (2H, m), 1.44 (3H, t, *J* = 7.6 Hz), 1.52-1.59 (2H, m), 1.70-1.85 (1H, m), 2.57 (2H, d, *J* = 7.2 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 3.30-3.40 (2H, m), 3.90-4.00 (2H, m), 4.69 (2H, d, *J* = 5.6 Hz), 6.11 (1H, brs), 7.18 (2H, d, *J* = 8.0 Hz), 7.30-7.40 (3H, m), 7.57 (1H, d, *J* = 9.6 Hz), 9.56 (1H, d, *J* = 1.6 Hz); LCMS: 100%, MS (ESI): m/z 411.8 [M+ H]+. |
| 254 |  | white amorphous; mp >125.9℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.20-1.40 (2H, m), 1.40 (3H, t, *J* = 7.2 Hz), 1.50-1.60 (2H, m), 1.68-1.83 (1H, m), 2.56 (2H, d, *J* = 7.2 Hz), 2.97 (2H, q, *J* = 7.6 Hz), 3.28-3.40 (2H, m), 3.90-4.00 (2H, m), 4.67 (2H, d, *J* = 5.6 Hz), 6.08 (1H, brs), 6.91 (1H, dd, *J* = 7.6, 2.0 Hz), 7.15 (2H, d, *J* = 8.0 Hz), 7.26-7.38 (2H, m), 7.59 (1H, d, *J* = 1.6 Hz), 9.36 (1H, d, *J* = 7.2 Hz); LCMS: 99.86%, MS (ESI): m/z 411.7 [M+ H]+. |
| 255 |  | yellow solid; mp = 126.3-127.2℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.24 (3H, t, *J* = 7.6 Hz), 1.65-1.73 (2H, m), 1.95-2.05 (2H, m), 2.97 (2H, t, *J* = 7.2 Hz), 3.00-3.07 (2H, m), 3.45-3.55 (2H, m), 4.47 (2H, d, *J* = 6.0 Hz), 4.55-4.59 (1H, m), 6.76 (1H, d, *J* = 7.2 Hz), 6.84-6.86 (1H, m), 6.97 (1H, s), 7.06 (2H, d, *J* = 9.2 Hz), 7.17 (1H, t, *J* = 8.0 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 7.41-7.44 (1H, dd, *J* = 9.6, 2.0 Hz), 7.64 (1H, d, *J* = 9.2 Hz), 8.49 (1H, t, *J* = 5.6 Hz), 9.01 (1H, d, *J* = 1.6 Hz); LCMS: 96.4%, MS (ESI): m/z 573.1[M+ H]+. |

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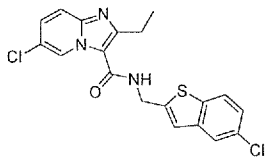
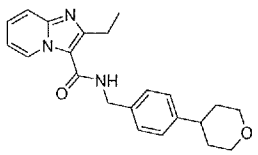
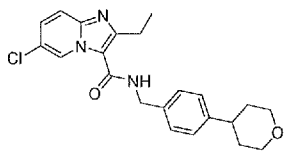
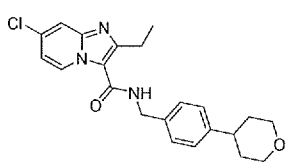
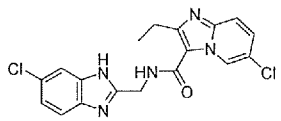
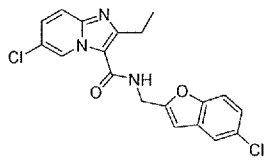
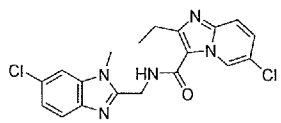
| 256 |  | white solid; mp >220℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.28 (3H, t, *J* = 7.6 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 4.79 (2H, d, *J* = 5.6 Hz), 7.33 (1H, dd, *J* = 8.4, 2.0 Hz), 7.37 (1H, s), 7.48 (1H, dd, *J* = 9.6, 2.0 Hz), 7.68 (1H, d, *J* = 9.2 Hz), 7.90 (1H, d, *J* = 2.0 Hz), 7.96(1H, d, *J* = 8.4 Hz), 8.70 (1H, t, *J* = 5.6 Hz), 9.12 (1H, d, *J* = 1.6 Hz); LCMS: 95.4%, MS (ESI): m/z 404.0 [M+ H]+. |
| 257 |  | White amorphous; mp >133.7℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.42 (3H, t, *J* = 7.6 Hz), 1.72-1.90 (4H, m), 2.70-2.82 (1H, m), 3.00 (2H, q, *J* = 7.6 Hz), 3.53 (2H, td, *J* = 11.6, 2.8 Hz), 3.93 (2H, dd, *J* = 10.8, 2.8 Hz), 4.68 (2H, d, *J* = 6.0 Hz), 6.09 (1H, brs), 6.90-6.95 (1H, m), 7.21-7.30 (2H, m), 7.30-7.40 (3H, m),7.61 (1H, d, *J* = 9.2 Hz), 9.41 (1H, d, *J* = 7.2 Hz); LCMS: 99.27%, MS (ESI): m/z 364.1 [M+ H]+. |
| 258 |  | White amorphous; mp >195.5℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.41 (3H, t, *J* = 7.6 Hz), 1.71-1.90 (4H, m), 2.72-2.84 (1H, m), 2.98 (2H, q, *J* = 7.2 Hz), 3.53 (2H, td, *J* = 11.6, 2.8 Hz), 4.08 (2H, dd, *J* = 11.2, 3.6 Hz), 4.68 (2 H, d, *J* = 5.6 Hz), 6.10 (1H, brs), 7.20-7.28 (2H, m), 7.28-7.49 (3H, m), 7.54 (1H, d, *J* = 9.6 Hz), 9.54 (1H, d, *J* = 1.6 Hz); LCMS: 100%, MS (ESI): m/z 398.1 [M+ H]+. |
| 259 |  | White amorphous; mp >156.6℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.40 (3H, t, *J* = 7.6 Hz), 1.71-1.90 (4H, m), 2.72-2.84 (1H, m), 2.97 (2H, q, *J* = 7.6 Hz), 3.53 (2H, td, *J* = 11.6, 2.8 Hz), 4.05-4.15 (2H, m), 4.67 (2H, d, *J* = 6.0 Hz), 6.09 (1H, brs), 6.91 (1H, dd, *J* = 7.6, 2.4 Hz), 7.23-7.26 (2H, m), 7.33 (2H, ,d, *J* = 8.0 Hz), 7.59 (1H, d, *J* = 2.0 Hz), 9.36 (1H, d, *J* = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 398.1 [M+ H]+. |
| 260 |  | yellow amorphous; $^1$H-NMR (DMSO-d6, 400 MH℃z): δ 1.31 (3H, t, *J* = 7.6 Hz), 3.03 (2H, q, *J* = 7.6 Hz), 4.76 (2H, s), 7.18 (1H, dd, *J* = 8.4, 2.0 Hz), 7.45-7.55 (2H, m), 7.56 (1H, d, *J* = 2.0 Hz), 7.68-7.70 (1H, m), 8.57 (1H, brs), 9.24 (1H, d, *J* = 1.6 Hz); LCMS: 100%, MS (ESI): m/z 388.1[M+ H]+. |
| 261 |  | white solid; mp = 223.5-225.6℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.27 (3H, t, *J* = 7.6 Hz), 3.00 (2H, q, *J* = 7.2 Hz), 4.70 (2H, d, *J* = 5.6 Hz), 6.81 (1H, s), 7.29 (1H, dd, *J* = 8.8, 2.4 Hz), 7.47 (1H, dd, *J* = 9.6, 2.0 Hz), 7.58 (1H, d, *J* = 8.4 Hz), 7.68 (2H, dd, *J* = 5.6, 3.6 Hz), 8.59 (1H, t, *J* = 5.2 Hz), 9.08 (1H, d, *J* = 1.6 Hz); LCMS: 99.3%, MS (ESI): m/z 387.8[M+ H]+. |
| 262 |  | white solid; mp >220℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.29 (3H, t, *J* = 7.6 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 3.85 (3H, s), 4.84 (2H, d, *J* = 5.6 Hz), 7.21 (1H, dd, *J* = 8.4, 2.0 Hz), 7.47 (1H, dd, *J* = 9.2, 2.0 Hz), 7.59 (1H, d, *J* = 8.8 Hz), 7.68 (1H, d, *J* = 9.6 Hz), 7.74 (1H, d, *J* = 2.0 Hz), 8.65 (1H, t, *J* = 5.6 Hz), 9.26 (1H, d, *J* = 1.6 Hz); LCMS: 100%, MS (ESI): m/z 402.0[M+ H]+. |

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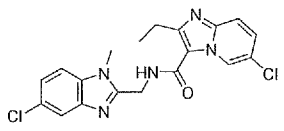
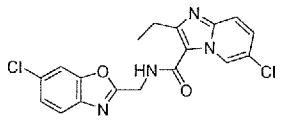
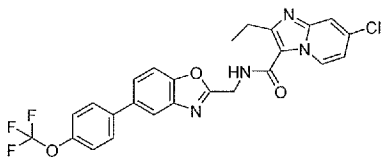
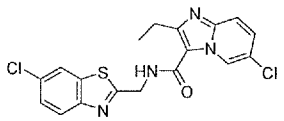
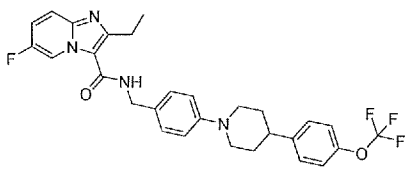
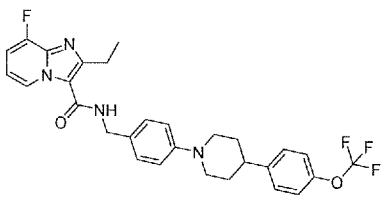
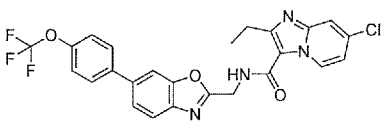
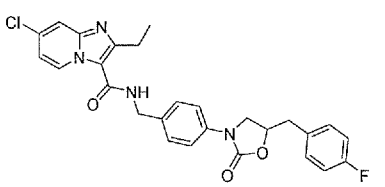
|---|---|---|
| 263 |  | white solid; mp >220℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.28 (3H, t, *J* = 7.6 Hz), 3.01 (2H, q, *J* = 7.6 Hz), 3.86 (3H, s), 4.84 (2H, d, *J* = 5.6 Hz), 7.28 (1H, dd, *J* = 8.4, 2.0 Hz), 7.47 (1H, dd, *J* = 9.2, 2.0 Hz), 7.59-7.71 (3H, m), 8.66 (1H, t, *J* = 5.6 Hz), 9.24 (1H, d, *J* = 1.6 Hz); LCMS: 98.7%, MS (ESI): m/z 401.9[M+ H]+. |
| 264 |  | white solid; mp = 201.1-201.8℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.31 (3H, t, *J* = 7.2 Hz), 3.05 (2H, q, *J* = 7.2 Hz), 4.84 (2H, d, *J* = 5.6 Hz), 7.43 (1H, dd, *J* = 8.4, 2.0 Hz), 7.49 (1H, dd, *J* = 9.6, 2.0 Hz), 7.69 (1H, d, *J* = 5.6 Hz), 7.71 (1H, d, *J* = 9.6 Hz), 7.74 (1H, d, *J* = 8.8 Hz), 7.95 (1H, d, *J* = 2.0 Hz), 8.68 (1H, t, *J* = 5.6 Hz), 9.13 (1H, d, *J* = 1.6 Hz); LCMS: 98.6%, MS (ESI): m/z 389.0[M+ H]+. |
| 265 |  | white solid; mp >220℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.32 (3H, t, *J* = 7.6 Hz), 3.06 (2H, q, *J* = 7.6 Hz), 4.86 (2H, d, *J* = 4.4 Hz), 7.12 (1H, dd, *J* = 7.6, 2.4 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.69 (1H, dd, *J* = 8.4, 1.6 Hz), 7.79-7.86 (4H, m), 8.02 (1H, d, *J* = 1.2 Hz), 8.70 (1H, brs), 9.01 (1H, d, *J* = 7.6 Hz); LCMS: 98.2%, MS (ESI): m/z 515.1[M+ H]+. |
| 266 |  | white solid; mp >220℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.33 (3H, t, *J* = 7.6 Hz), 3.07 (2H, q, *J* = 7.6 Hz), 4.93 (2H, d, *J* = 6.0 Hz), 7.50 (1H, dd, *J* = 9.6, 2.0 Hz), 7.55 (1H, dd, *J* = 8.8, 2.4 Hz), 7.70 (1H, dd, *J* = 9.6, 0.8 Hz), 7.97 (1H, d, *J* = 8.8 Hz), 8.24 (1H, d, *J* = 2.0 Hz), 8.88 (1H, t, *J* = 6.0 Hz), 9.15 (1H, dd, *J* = 2.4, 0.8 Hz); LCMS: 100%, MS (ESI): m/z 405.0 [M+ H]+. |
| 267 |  | yellow amorphous; mp >167.9℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.40 (3H, t, *J* = 7.6 Hz), 1.80-1.99 (4H, m), 2.65-2.72 (1H, m), 2.75-2.87 (2H, m), 2.97 (2H, q, *J* = 7.6 Hz), 3.75-3.85 (2H, m), 4.62 (2H, d, *J* = 5.2 Hz), 6.03 (1H, brs), 6.99 (2H, d, *J* = 8.8 Hz), 7.16 (2H, d, *J* = 8.4 Hz), 7.25-7.32 (5H, m), 7.56 (1H, dd, *J* = 10.0, 5.2 Hz), 9.46 (1H, dd, *J* = 5.2, 2.4 Hz); LCMS: 98.7%, MS (ESI): m/z 541.3 [M+ H]+. |
| 268 |  | white amorphous; mp >177.7℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.39 (3H, t, *J* = 7.6 Hz), 1.83-1.96 (4H, m), 2.63-2.69 (1H, m), 2.70-2.90 (2H, m), 2.97 (2H, q, *J* = 7.6 Hz), 3.75-3.85 (2H, m), 4.60 (2H, d, *J* = 5.2 Hz), 6.04 (1H, brs), 6.78-6.84 (1H, m), 6.95-6.99 (3H, m), 7.14 (2H, d, *J* = 8.8 Hz), 7.23-7.29 (4H, m), 9.18 (1H, dd, *J* = 6.8, 0.8 Hz); LCMS: 99.5%, MS (ESI): m/z 541.3 [M+ H]+. |
| 269 |  | white solid; mp >220℃: $^1$H-NMR (DMSO-d6, 400 MHz): δ 1.32 (3H, t, *J* = 7.2 Hz), 3.07 (2H, q, *J* = 7.2 Hz), 4.86 (2H, d, *J* = 5.6 Hz), 7.12 (1H, dd, *J* = 7.6, 2.4 Hz), 7.46-7.50 (2H, m), 7.69 (1H, dd, *J* = 8.4, 0.8 Hz), 7.79-7.80 (4H, m), 8.06(1H, d, *J* = 1.2 Hz ), 8.69 (1H, t, *J* = 6.0 Hz ), 9.01 (1H, dd, *J* = 7.6, 0.8 Hz ); LCMS: 99.4%, MS (ESI): m/z 515.2 [M+ H]+. |
| 270 |  | white amorphous; mp > 96.9℃: decomposed; $^1$H-NMR (CDCl3, 400 MHz): δ 1.38 (3H, t, *J* = 7.6 Hz), 2.95 (2H, q, *J* = 7.6 Hz), 3.02 (1H, dd, *J* = 14.4, 6.4 Hz), 3.15 (1H, dd, *J* = 14.0, 6.0 Hz), 3.70 (1H, dd, *J* = 8.8, 6.8 Hz), 4.02 (1H, t, *J* = 8.8 Hz), 4.65 (2H, d, *J* = 5.6 Hz), 4.82-4.90 (1H, m), 6.05 (1H, t, *J* = 2.8 Hz), 6.89 (1H, dd, *J* = 7.6, 2.4 Hz), 6.99-7.05 (2H, m), 7.21-7.26 (2H, m), 7.36 (2H, dd, *J* = 6.8, 2.0 Hz), 7.46 (2H, dd, *J* = 6.4, 2.0 Hz), 7.58 (1H, dd, *J* = 2.0, 0.8 Hz), 9.36 (1H, d, *J* = 0.8 Hz); |

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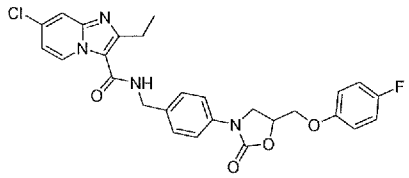
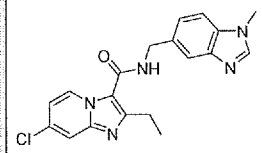
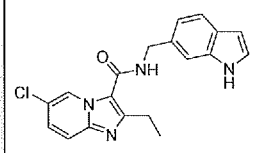
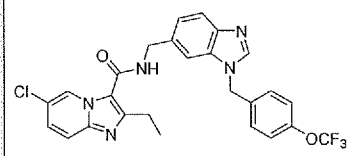
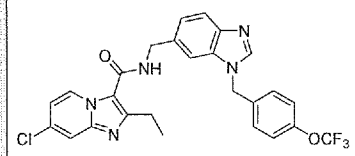
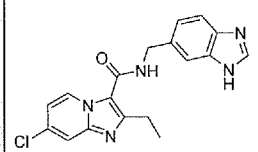
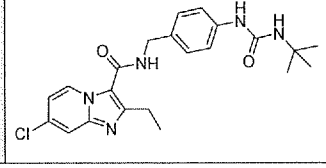
| | | LCMS: 100%, MS (ESI): m/z 507.0 [M+ H]+. |
| 271 |  | white amorphous; mp > 97.10℃: $^1$H-NMR (CDCl3, 400 MHz): δ 1.27 (3H, t, *J* = 7.6 Hz), 3.00 (2H, q, *J* = 7.6 Hz), 3.89-3.94 (1H, m), 4.19-4.30 (3H, m), 4.51 (2H, d, *J* = 6.0 Hz), 5.01-.06 (1H, m), 6.95-7.00 (2H, m), 7.08-7.22 (3H, m), 7.40 (2H, d, *J* = 8.8 Hz), 7.56 (2H, d, *J* = 8.8 Hz), 7.85 (1H, s), 8.58 (1H, t, *J* = 7.2 Hz), 8.97 (1H, dd, *J* = 7.2, 0.4 Hz); LCMS: 97.1%, MS (ESI): m/z 523.3 [M+ H]+. |
| 272 |  | Brown solid: $^1$H-NMR (400 MHz, DMSO): δ 8.96 (d, *J* = 7.6 Hz, 1H), 8.56 - 8.50 (m, 1H), 8.15 (s, 1H), 7.78 (s, 1H), 7.62 (t, *J* = 5.2 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.33 - 7.24 (m, 1H), 7.10 - 7.07 (m, 1H), 4.65 (dd, *J* = 13.2, 6.4 Hz, 2H), 3.82 (s, 3H), 3.02 - 2.94 (m, 2H), 1.28 - 1.23 (m, 3H); LCMS (electrospray) m/z (M+H)+ |
| 273 |  | Brown solid: $^1$H-NMR (400 MHz, DMSO): δ 11.03 (s, 1H), 9.08 (d, *J* = 2.0 Hz, 1H), 8.50 (t, *J* = 6.0 Hz, 1H), 7.67 (d, *J* = 9.2 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.45 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.39 (s, 1H), 7.30 (t, *J* = 2.8 Hz, 1H), 7.03 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.38 (t, *J* = 2.4 Hz, 1H), 4.61 (d, *J* = 6.0 Hz, 2H), 2.99 (q, *J* = 14.4, 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ |
| 274 |  | White solid: $^1$H-NMR (400 MHz, DMSO): δ 9.06 (d, *J* = 2.0 Hz, 1H), 8.51 -8.43 (m, 1H), 8.40 (s, 1H), 7.68 - 7.63 (m, 2H), 7.50 -7.43 (m, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.34 (t, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 1H), 5.34 (s, 2H), 4.62 (d, *J* = 5.6 Hz, 2H), 3.00 -2.93 (m, 2H), 1.26 -1.19 (m, 3H); LCMS (electrospray) m/z (M+H)+ 528.26 |
| 275 |  | White solid: $^1$H-NMR (400 MHz, DMSO): δ 8.95 (d, *J* = 7.2 Hz, 1H), 8.60 -8.41 (m, 1H), 8.40 (s, 1H), 7.78 (t, *J* = 5.2 Hz, 1H), 7.66 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.37 -7.31 (m, 1H), 7.29 -7.25 (m, 2H), 7.09 -7.06 (m, 1H), 5.34 (s, 2H), 4.61 (d, *J* = 5.6 Hz, 2H), 2.99 -2.91 (m, 2H), 1.25 -1.09 (m, 3H); LCMS (electrospray) m/z (M+H)+ 528.26 |
| 276 |  | Brown solid: $^1$H-NMR (400 MHz, DMSO): δ 12.40 (s, 1H), 8.96 (d, *J* = 7.2 Hz, 1H), 8.52 (t, *J* = 5.3 Hz, 1H), 8.17 (s, 1H), 7.78 (d, *J* = 1.6 Hz, 1H), 7.57 (brs, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.09 (dd, *J* = 7.6, 2.0 Hz, 1H), 4.63 (d, *J* = 5.6 Hz, 2H), 2.98 (q, *J* = 15.2, 7.6 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H), ; LCMS (electrospray) m/z (M+H)+ 354.16. |
| 277 |  | White solid: $^1$H-NMR (400 MHz, DMSO): δ 8.94 (d, *J* = 7.2, 1H), 8.41 (t, *J* = 6.0 Hz, 1H), 8.30 (brs, 1H), 7.78 (d, *J* = 2.0 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.08 (dd, *J* = 7.2, 2.0 Hz, 1H), 6.03 (brs, 1H), 4.43 (d, *J* = 6.0 Hz, 2H), 2.96 (q, *J* = 14.8, 7.2 Hz, 2H), 1.25 (t, *J* = 7.6 Hz, 3H), ; LCMS (electrospray) m/z (M+H)+ 428.15 |

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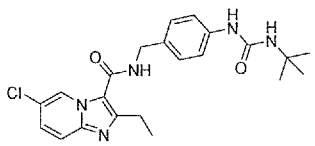
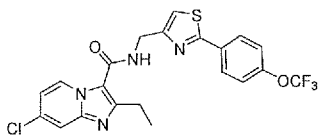
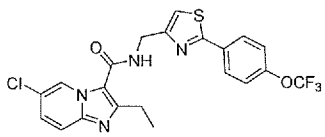
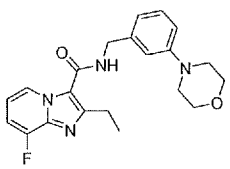
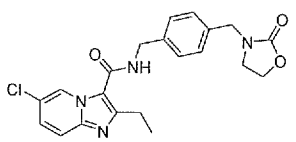
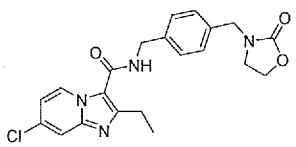
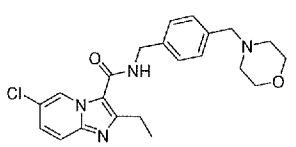
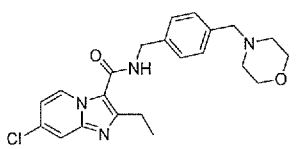
| 278 |  | White solid: $^1$H-NMR (400 MHz, DMSO): δ 9.06 (d, *J* = 2.0, 1H), 8.42 (t, *J* = 6.0 Hz, 1H), 8.20 (s, 1H), 7.66 (d, *J* = 9.6 Hz, 1H), 7.45 (dd, *J* = 9.6, 2.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 5.95 (s, 1H), 4.44 (d, *J* = 6.0 Hz, 2H), 2.97 (q, *J* = 15.2, 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H), ; LCMS (electrospray) m/z (M+H)+ 428.24 |
| 279 |  | Brown solid: $^1$H-NMR (400 MHz, DMSO): δ 8.98 (d, *J* = 7.2, 1H), 8.55 (t, *J* = 5.6 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 2.4 Hz, 1H), 7.58 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.11 (dd, *J* = 7.2, 2.0 Hz, 1H), 4.69 (d, *J* = 5.6 Hz, 2H), 3.03 (q, *J* = 15.2, 7.6 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 481.09 |
| 280 |  | Brown solid: $^1$H-NMR (400 MHz, DMSO): δ 9.09 (d, *J* = 7.2 Hz, 1H), 8.58 (t, *J* = 5.6 Hz, 1H), 8.07 (d, *J* = 9.6 Hz, 2H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.61 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.46 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.69 (d, *J* = 5.6 Hz, 2H), 3.03 (q, *J* = 14.8, 7.2 Hz, 2H), 1.29 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 481.08 |
| 281 |  | White solid: $^1$H-NMR (400 MHz, DMSO): δ 8.74 (d, *J* = 6.8 Hz, 1H), 8.57 (t, *J* = 6.0 Hz, 1H), 7.28 (dd, *J* = 10.8, 7.6 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.00 -6.97 (m, 1H), 6.95 (s, 1H), 6.83 (t, *J* = 8.0 Hz, 2H), 4.49 (d, *J* = 6.0 Hz, 2H), 3.73 (t, *J* = 4.4 Hz,, 4H), 3.09 (t, *J* = 4.7 Hz,, 4H), 3.00 (q, *J* = 14.8, 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 383.31 |
| 282 |  | White solid; mp = 179℃: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.25 (t, *J* = 7.6 Hz, 3H), 2.98 (q, *J* = 7.6 Hz, 2H), 3.39 (t, *J* = 8.0 Hz, 2H), 4.24 (t, *J* = 8.0 Hz, 2H), 4.31 (s, 2H), 4.51 (d, *J* = 5.6 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.65 (d, *J* = 9.2 Hz, 1H), 8.46 (t, *J* = 5.6 Hz, 1H, NH), 9.06 (s, 1H); LCMS (electrospray) m/z (M+H) + 413. |
| 283 |  | White solid; mp = 172℃: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.25 (t, *J* = 7.6 Hz, 3H), 2.97 (q, *J* = 7.6 Hz, 2H), 3.39 (t, *J* = 8.0 Hz, 2H), 4.24 (t, *J* = 8.0 Hz, 2H), 4.32 (s, 2H), 4.51 (d, *J* = 5.6 Hz, 2H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.77 (s, 1H), 8.46 (t, *J* = 5.6 Hz, 1H, NH), 8.95 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 413. |
| 284 |  | White solid; mp = 133℃: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.24 (t, *J* = 7.6 Hz, 3H), 2.31 (brs, 4H), 2.97 (q, *J* = 7.6 Hz, 2H), 3.42 (s, 2H), 3.54 (brs, 4H), 4.50 (d, *J* = 5.6 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 9.2 Hz, 1H), 7.65 (d, *J* = 9.2 Hz, 1H), 8.46 (t, *J* = 5.6 Hz, 1H, NH), 9.06 (s, 1H) ; LCMS (electrospray) m/z (M+H) + 413. |
| 285 |  | White solid; mp = 107℃: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.25 (t, *J* = 7.6 Hz, 3H), 2.32 (brs, 4H), 2.97 (q, *J* = 7.6 Hz, 2H), 3.43 (s, 2H), 3.55 (brs, 4H), 4.50 (d, *J* = 5.6 Hz, 2H), 7.08 (d, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.78 (s, 1H), 8.45 (t, *J* = 5.6 Hz, 1H, NH), 8.95 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z (M+H) + 413. |

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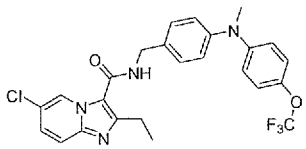
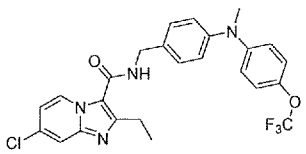
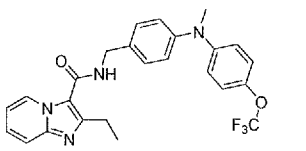
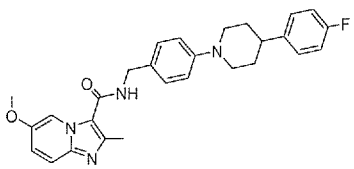
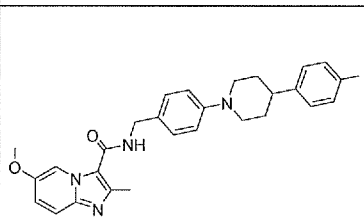
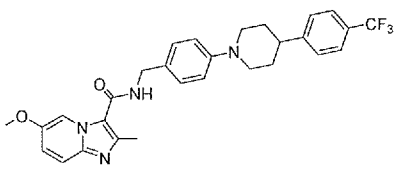
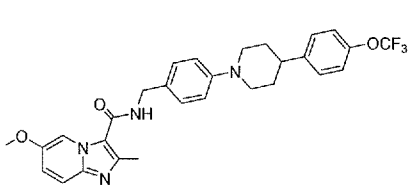
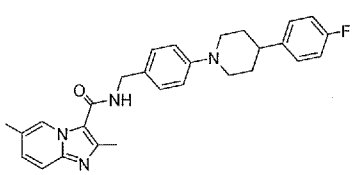
| 286 |  | White solid; mp = 138 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.26 (t, *J* = 7.6 Hz, 3H), 3.00 (q, *J* = 7.6 Hz, 2H), 3.25 (s, 3H), 4.50 (d, *J* = 6.0 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 9.2 Hz, 1H), 7.66 (d, *J* = 9.2 Hz, 1H), 8.46 (t, *J* = 6.0 Hz, 1H, NH), 9.09 (s, 1H); LCMS (electrospray) m/z (M+H) + 503. |
| 287 |  | White solid; mp = 134 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.26 (t, *J* = 7.6 Hz, 3H), 2.97 (q, *J* = 7.6 Hz, 2H), 3.24 (s, 3H), 4.50 (d, *J* = 6.0 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 7.08-7.10 (m, 3H), 7.19 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 7.78 (s, 1H), 8.45 (t, *J* = 6.0 Hz, 1H, NH), 8.97 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z (M+H) + 503. |
| 288 |  | White solid; mp = 120 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.27 (t, *J* = 7.6 Hz, 3H), 2.99 (q, *J* = 7.6 Hz, 2H), 3.25 (s, 3H), 4.50 (d, *J* = 5.6 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.98-7.02 (m, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.34-7.39 (m, 3H), 7.59 (d, *J* = 6.8 Hz, 1H), 8.38 (t, *J* = 5.6 Hz, 1H, NH), 8.98 (d, *J* = 6.8 Hz, 1H); LCMS (electrospray) m/z (M+H) + 469. |
| 289 |  | Ivory solid; mp = 192 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.69-1.76 (m, 2H), 1.81-1.84 (m, 2H), 2.54 (s, 3H), 2.63-2.74 (m, 3H), 3.74-3.78 (m, 5H), 4.42 (d, *J* = 5.6 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.07-7.12 (m, 2H), 7.16 (dd, *J* = 2.4 Hz, 9.6 Hz, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.27-7.31 (m, 2H), 7.48 (d, *J* = 9.6 Hz, 1H), 8.17 (t, *J* = 5.6 Hz, 1H, NH), 8.70 (d, *J* = 2.4 Hz, 1H); LCMS (electrospray) m/z (M+H) + 473. |
| 290 |  | Ivory solid; mp = 178 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.68-1.75 (m, 2H), 1.79-1.82 (m, 2H), 2.24 (s, 3H), 2.54 (s, 3H), 2.56-2.62 (m, 1H), 2.67-2.74 (m, 2H), 3.73-3.77 (m, 5H), 4.42 (d, *J* = 6.0 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 2H), 7.16 (dd, *J* = 2.4 Hz, 9.6 Hz, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 9.6 Hz, 1H), 8.18 (t, *J* = 6.0 Hz, 1H, NH), 8.70 (d, *J* = 2.4 Hz, 1H); LCMS (electrospray) m/z (M+H) + 469. |
| 291 |  | Ivory solid; mp = 207 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.74-1.81 (m, 2H), 1.85-1.88 (m, 2H), 2.56 (s, 3H), 2.70-2.78 (m, 3H), 3.77-3.80 (m, 5H), 4.42 (d, *J* = 5.6 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.16 (dd, *J* = 2.4 Hz, 9.6 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 9.6 Hz, 1H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 8.18 (t, *J* = 5.6 Hz, 1H, NH), 8.70 (d, *J* = 2.4 Hz, 1H); LCMS (electrospray) m/z (M+H) + 523. |
| 292 |  | White solid; mp = 183 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.71-1.77 (m, 2H), 1.84-1.87 (m, 2H), 2.54 (s, 3H), 2.69-2.75 (m, 3H), 3.75-3.79 (m, 5H), 4.42 (d, *J* = 6.0 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.16 (dd, *J* = 2.4 Hz, 9.6 Hz, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 9.6 Hz, 1H), 8.17 (t, *J* = 6.0 Hz, 1H, NH), 8.70 (d, *J* = 2.4 Hz, 1H); LCMS (electrospray) m/z (M+H) + 539. |
| 293 |  | Ivory solid; mp = 181 °C: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.69-1.76 (m, 2H), 1.81-1.84 (m, 2H), 2.29 (s, 3H), 2.53 (s, 3H), 2.64-2.74 (m, 3H), 3.74-3.77 (m, 2H), 4.41 (d, *J* = 6.0 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.07-7.12 (m, 2H), 7.20-7.23 (m, 3H), 7.27-7.30 (m, 2H), 7.45 (d, *J* = 9.2 Hz, 1H), 8.21 (t, *J* = 6.0 Hz, 1H, NH), 8.83 (s, 1H); LCMS (electrospray) m/z (M+H) + 457. |

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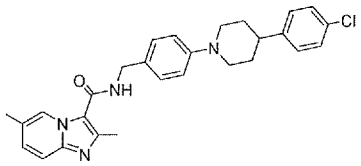
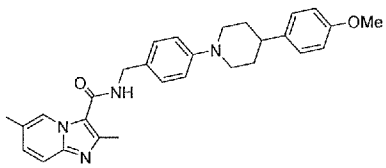
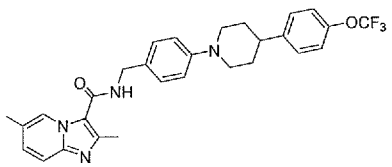
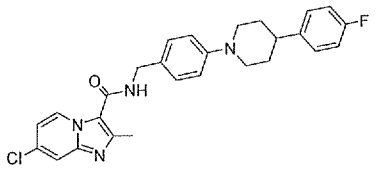
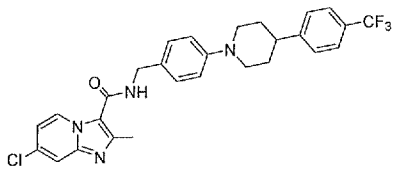
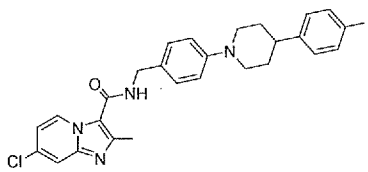
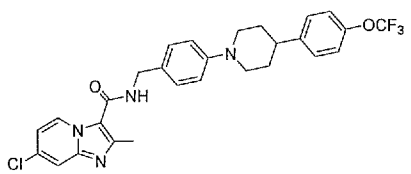
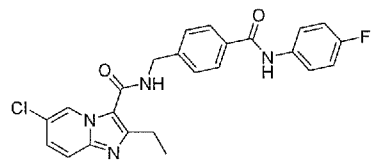
| 294 |  | Ivory solid; mp = 188℃ $^1$H-NMR (400 MHz, DMSO-d6): δ 1.68-1.75 (m, 2H), 1.81-1.84 (m, 2H), 2.29 (s, 3H), 2.53 (s, 3H), 2.63-2.74 (m, 3H), 3.75-3.78 (m, 2H), 4.41 (d, *J* = 6.0 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.21-7.24 (m, 3H), 7.28 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 1H), 8.21 (t, *J* = 6.0 Hz, 1H, NH), 8.82 (d, *J* = 1.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 473. |
| 295 |  | Ivory solid; mp = 184℃: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.67-1.74 (m, 2H), 1.79-1.82 (m, 2H), 2.29 (s, 3H), 2.53 (s, 3H), 2.54-2.59 (m, 1H), 2.67-2.73 (m, 2H), 3.70 (s, 3H), 3.74-3.77 (m, 2H), 4.41 (d, *J* = 6.0 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.21-7.23 (m, 3H), 7.45 (d, *J* = 9.6 Hz, 1H), 8.21 (t, *J* = 6.0 Hz, 1H, NH), 8.82 (d, *J* = 0.8 Hz, 1H); LCMS (electrospray) m/z (M+H) + 469. |
| 296 |  | Ivory solid; mp = 184℃: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.71-1.78 (m, 2H), 1.83-1.86 (m, 2H), 2.29 (s, 3H), 2.53 (s, 3H), 2.69-2.75 (m, 3H), 3.76-3.79 (m, 2H), 4.41 (d, *J* = 6.0 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.21-7.23 (m, 3H), 7.27 (d, *J* = 8.8 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 1H), 8.21 (t, *J* = 6.0 Hz, 1H, NH), 8.82 (s, 1H); LCMS (electrospray) m/z (M+H) + 523. |
| 297 |  | Pale yellow solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.69-1.76(m, 2H), 1.82-1.85(m, 2H), 2.56 (s, 3H), 2.61-2.75(m, 3H), 3.75-3.78 (m, 2H), 4.43 (d, *J* = 6.0 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 7.08-7.13 (m, 3H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.28-7.32 (m, 2H), 7.74 (d, *J* = 1.2 Hz, 1H), 8.35 (t, *J* = 5.8 Hz, 1H), 9.00 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 477. |
| 298 |  | Pale yellow solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.75-1.81 (m, 2H), 1.86-1.89 (m, 2H), 2.56 (s, 3H), 2.72-2.82 (m, 3H), 3.79 (d, *J* = 11.6 Hz, 2H), 4.43 (d, *J* = 6.0 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 7.6, 2.0, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 1.6 Hz, 1H), 8.35 (t, *J* = 5.8 Hz), 9.00 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 527. |
| 299 |  | Yellow solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.67-1.74 (m, 2H), 1.79-1.81 (m, 2H), 2.24(s, 3H), 2.54 (s, 3H), 2.56-2.62 (m, 1H), 2.67-2.73 (m, 2H), 3.75 (d, *J* =12.4 Hz, 2H), 4.41(d, *J* = 6.0 Hz, 2H), 6.93(d, *J* = 8.8 Hz, 2H), 7.07(dd, *J* = 7.6, 2.0 Hz, 3H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.72(d, *J* = 2.0 Hz, 1H), 8.33 (t, *J* = 6.0 Hz, 1H), 8.98 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 473. |
| 300 |  | Pale pink solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.70-1.74(m, 2H), 1.83-1.86 (m, 2H), 2.55 (s, 3H), 2.68-2.74(m, 3H), 3.76 (d, *J* = 12.4 Hz, 2H), 4.41 (d, *J* = 6.0 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.07 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 1.2 Hz, 1H), 8.32(t, *J* = 5.8 Hz, 1H), 8.99 (d, *J* = 7.2 Hz, 1H) ; LCMS (electrospray) m/z (M+H) + 543 |
| 301 |  | $^1$H-NMR (400 MHz, CDCl3 + CD3OD): δ 9.22 -9.23 (m, 1H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.59 -7.63 (m, 2H), 7.50 (dd, *J* = 9.6, 2.0 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.33 (dd, *J* = 9.6, 2.0 Hz, 1H), 7.02 (dd, *J* = 9.6, 8.4 Hz, 1H), 4.68 (s, 2H), 2.98 (q, *J* = 7.6 Hz, 2H), 1.33 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 451. |

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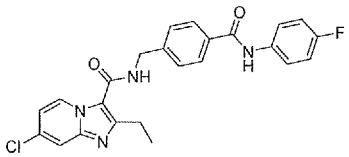
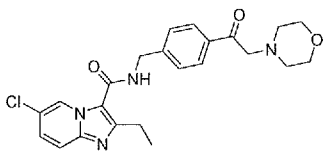
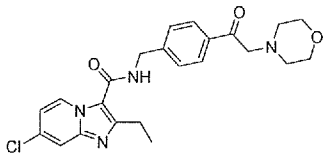
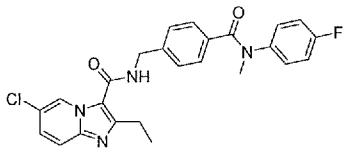
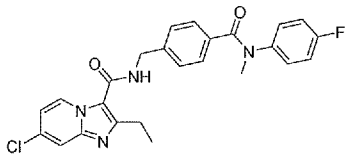
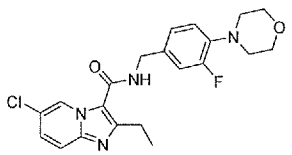
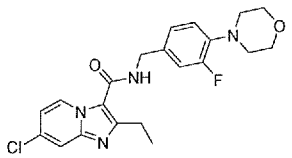
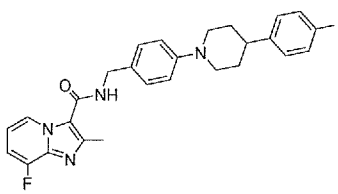
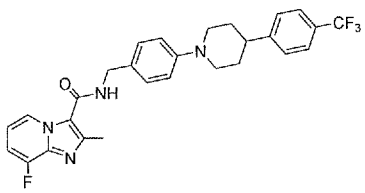
| 302 |  | $^1$H-NMR (400 MHz, CDCl3 + CD3OD): δ 9.06 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.60 -7.62 (m, 2H), 7.54 (d, *J* = 2.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.02 (dd, *J* = 8.8, 8.8 Hz, 2H), 6.93 (dd, *J* = 7.6, 2.0 Hz, 1H), 4.68 (s, 2H), 2.7 (q, *J* = 7.6 Hz, 2H), 1.33 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 451. |
| 303 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.51 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 9.6 Hz, 1H), 7.31 -7.41 (m, 4H), 7.29 (dd, *J* = 9.6, 2.0 Hz, 1H), 6.12 (t, *J* = 5.2 Hz, 1H), 4.68 (d, *J* = 5.6 Hz, 2H), 3.68 -3.80 (m, 4H), 2.97 (q, *J* = 7.6 Hz, 2H), 2.42 -2.52 (m, 4H), 1.39 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 441 |
| 304 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.35 (d, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.33 -7.38 (m, 4H), 6.90 (dd, *J* = 7.4, 2.0 Hz, 1H), 6.09 (t, *J* = 5.0 Hz, 1H), 4.68 (d, *J* = 5.6 Hz, 2H), 3.68 -3.80 (m, 4H), 2.96 (q, *J* = 7.6 Hz, 2H), 2.42 -2.52 (m, 4H), 1.39 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 441. |
| 305 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.48 -9.49 (m, 1H), 7.53 (d, *J* = 8.8 Hz, 1H), 7.28 -7.31 (m, 3H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.00 -7.03 (m, 2H), 6.92 (dd, *J* = 8.8, 8.0 Hz, 2H), 6.07 (m, 1H), 4.62 (d, *J* = 5.6 Hz, 2H), 3.46 (s, 3H), 2.93 (q, *J* = 7.6 Hz, 2H), 1.36 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 465. |
| 306 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.28 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.98 -7.01 (m, 2H), 6.86 -6.93 (m, 3H), 6.92 (dd, *J* = 8.8, 8.0 Hz, 2H), 6.15 (t, *J* = 5.6 Hz, 1H), 4.60 (d, *J* = 5.6 Hz, 2H), 3.43 (s, 3H), 2.89 (q, *J* = 7.6 Hz, 2H), 1.34 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 465. |
| 307 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.53 (d, *J* = 2.0 Hz, 1H (m, 1H), 7.55 (d, *J* = 9.6 Hz, 1H), 7.31 (dd, *J* = 9.6, 2.0 Hz, 1H), 7.05 -7.10 (m, 2H), 6.93 (dd, *J* = 9.2, 8.0 Hz, 2H), 6.08 (t, *J* = 5.6 Hz, 1H), 4.62 (d, *J* = 5.6 Hz, 2H), 3.85 -3.88 (m, 4H), 3.07 -3.10 (m, 4H), 2.98 (q, *J* = 7.6 Hz, 2H), 1.42 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 417. |
| 308 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.36 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 7.05 -7.10 (m, 2H), 6.90 -6.95 (m, 2H), 6.07 (t, *J* = 5.6 Hz, 1H), 4.62 (d, *J* = 5.6 Hz, 2H), 3.85 -3.88 (m, 4H), 3.08 -3.09 (m, 4H), 3.00 (q, *J* = 7.6 Hz, 2H), 1.41 (t, *J* = 7.6 Hz, 3H); LCMS (electrospray) m/z (M+H)+ 417. |
| 309 |  | $^1$H-NMR (400 MHz, DMSO-d6): δ 8.80 (d, *J* = 6.8 Hz, 1H), 8.42 (t, *J* = 6.0 Hz, 1H), 7.27 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.95 -6.98 (m, 4H), 6.94 (d, *J* = 8.8 Hz, 2H), 4.41 (d, *J* = 6.0 Hz, 2H), 3.70 -3.80 (m, 2H), 3.40 -3.48 (m, 3H), 2.67 -2.73 (m, 2H), 2.57 (s, 3H), 2.24 (s, 3H), 1.78 -1.84 (m, 2H), 1.50 -1.76 (m, 2H); LCMS (electrospray) m/z (M+H)+ 457. |
| 310 |  | $^1$H-NMR (400 MHz, DMSO-d6): δ 8.80 (d, *J* = 6.8 Hz, 1H), 8.42 (t, *J* = 6.0 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.27 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 2H), 6.96 -6.99 (m, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 4.42 (d, *J* = 6.0 Hz, 2H), 3.70 -3.80 (m, 2H), 3.30 -3.40 (m, 3H), 2.70 -2.80 (m, 2H), 2.57 (s, 3H), 1.84 -1.90 (m, 2H), 1.70 -1.80 (m, 2H); LCMS (electrospray) m/z (M+H)+ 511. |

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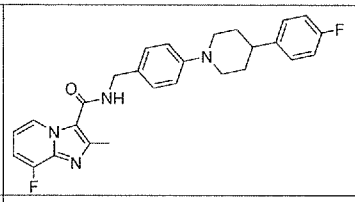
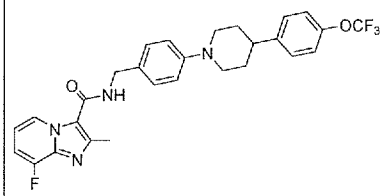
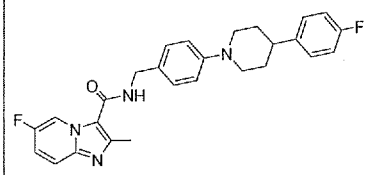
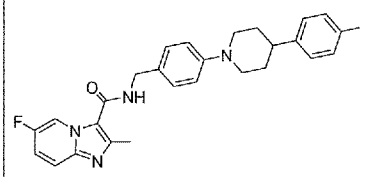
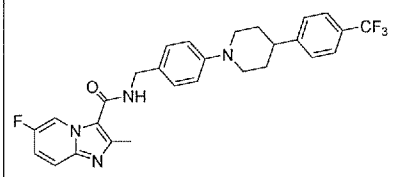
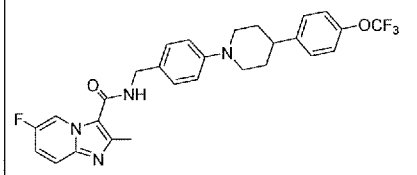
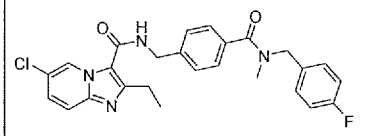
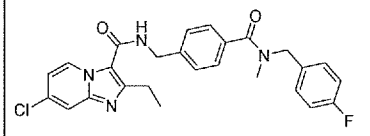
|---|---|---|
| 311 |  | $^1$H-NMR (400 MHz, CDCl3): δ 9.24 (d, *J* = 6.8 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.15 -7.24 (m, 3H), 6.97 -7.06 (m, 4H), 6.81 -6.97 (m, 1H), 6.05 (br s, 1H), 4.62 (d, *J* = 5.2 Hz, 2H), 3.76 -3.85 (m, 2H), 2.80 -2.90 (m, 2H), 2.69 (s, 3H),2.60 -2.68 (m, 1H), 1.60 -2.00 (m, 4H); LCMS (electrospray) m/z (M+H)+ 461. |
| 312 |  | $^1$H-NMR (400 MHz, DMSO-d6): δ 8.80 (d, *J* = 6.8 Hz, 1H), 8.43 (t, *J* = 6.0 Hz, 1H), 7.39 (d, *J* = 8.8 Hz, 2H), 7.24 -7.29 (m, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 6.96 -6.99 (m, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 4.42 (d, *J* = 6.0 Hz, 2H), 3.70 -3.80 (m, 2H), 3.30 -3.40 (m, 3H), 2.70 -2.80 (m, 2H), 2.57 (s, 3H), 1.82 -1.90 (m, 2H), 1.68 -1.80 (m, 2H); LCMS (electrospray) m/z (M+H)+ 527. |
| 313 |  | $^1$H-NMR (400 MHz, DMSO-d6): δ-1.68 -1.75 (m, 2H), 1.79 -1.85 (m, 2H), 2.56 (s, 3H), 2.62 -2.73 (m, 3H), 3.74 -3.77 (m, 2H), 4.43 (d, *J* = 5.6 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 7.04 -7.11 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.27 -7.30 (m, 2H), 7.44 -7.49 (m, 1H), 7.61 -7.64 (m, 1H), 8.28 (t, *J* = 5.6 Hz, 1H, NH), 9.06 -9.07 (m, 1H), ; LCMS (electrospray) m/z (M+H)+ 461. |
| 314 |  | $^1$H-NMR (400 MHz, DMSO-d6): δ-1.68 -1.75 (m, 2H), 1.79 -1.83 (m, 2H), 2.56 (s, 3H), 2.58 -2.62 (m, 1H), 2.68 -2.73 (m, 1H), 3.74 -3.77 (m, 2H), 4.42 (d, *J* = 6.0 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.07 -7.13 (m, 4H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.44 -7.49 (m, 2H), 7.61 -7.64 (m, 1H), 8.27 (t, *J* = 6.0 Hz, 1H, NH), 9.05 -9.07 (m, 1H) ; LCMS (electrospray) m/z (M+H)+ 456. |
| 315 |  | $^1$H-NMR (400 MHz, DMSO-d6): δ-1.71 -1.80 (m, 2H), 1.83 -1.88 (m, 2H), 2.56 (s, 3H), 2.71 -2.80 (m, 3H), 3.77 -3.80 (m, 2H), 4.43 (d, *J* = 6.0 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.44 -7.50 (m, 3H), 7.61 -7.65 (m, 3H), 8.28 (t, *J* = 6.0 Hz, 1H, NH), 9.05 -9.07 (m, 1H) ; LCMS (electrospray) m/z (M+H)+ 511. |
| 316 |  | $^1$H-NMR (400 MHz, Acetone-d6): δ-1.82 -1.89 (m, 2H), 1.92 -1.96 (m, 2H), 2.66 (s, 3H), 2.76 -2.84 (m, 3H), 3.82 -3.86 (m, 2H), 4.58 (d, *J* = 5.6 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.26 -7.31 (m, 4H), 7.37 -7.44 (m, 4H), 7.55 -7.59 (m, 1H), 9.34 -9.36 (m, 1H) ; LCMS (electrospray) m/z (M+H)+ 527. |
| 317 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.40 (t, *J* = 7.6 Hz, 3H), 2.86 -3.00 (m, 5H), 4.70 -4.47 (m, 4H), 6.20 (brs, 1H), 7.45 -7.01 (m, 9H), 7.53 (d, *J* = 9.6 Hz, 1H), 9.50 (s, 1H). |
| 318 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.39 (t, *J* = 7.6 Hz, 3H), 2.86 -2.99 (m, 5H), 4.48 (m, 2H), 4.71 -4.69 (m, 2H), 6.16 (brs, 1H), 6.89 (dd, *J* = 7.2Hz, 2.0 Hz, 1H), 7.01 -7.45 (m, 8H), 7.59 (d, *J* = 2.0 Hz, 1H), 9.34 (d, *J* = 7.2 Hz, 1H) |

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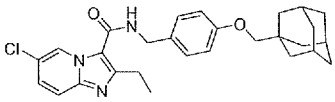
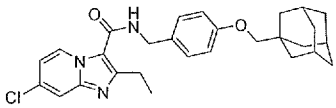
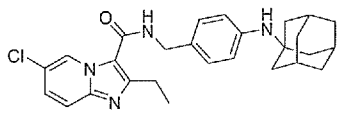
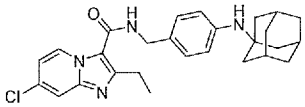
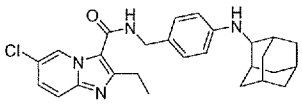
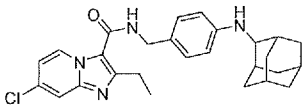
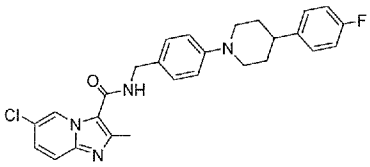
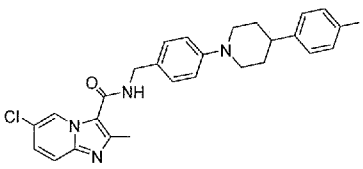
| 319 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.37 (t, *J* = 7.6 Hz, 3H), 2.02 -1.64 (m, 15H), 2.93 (q, *J* = 7.6 Hz, 2H), 3.48 (s, 2H), 4.60 (d, *J* = 5.2 Hz, 2H), 6.05 (brs, 1H), 6.88 (d, *J* = 8.0 Hz, 2H), 7.25 -7.27 (m, 3H), 7.51 (d, *J* = 9.6 Hz, 1H), 9.50 (s, 1H); ); 13C NMR (100 MHz, CDCl3) d 13.4, 23.6, 28.4, 28.5, 34.0, 37.3, 39.7, 43.4, 76.9, 77.2, 77.5, 78.6, 115.1, 117.0, 121.6, 126.3, 128.3, 129.2, 129.7, 144.6, 151.5, 159.6, 161.2, 199.8 |
| 320 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.36 (t, *J* = 7.6 Hz, 3H), 2.00 -1.64 (m, 15H), 2.92 (q, *J* = 7.6 Hz, 2H), 3.48 (s, 2H), 4.59 (d, *J* = 5.6 Hz, 2H), 6.05 (brs, 1H), 6.89 -6.85 (m, 3H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 2.0 Hz, 1H), 9.32 (d, *J* = 7.6 Hz, 1H); 13C NMR (100 MHz, CDCl3) d 13.4, 23.6, 28.4, 28.6, 34.0, 37.3, 39.7, 43.4, 76.9, 77.2, 77.5, 78.6, 114.7, 115.1, 115.8, 128.6, 129.2, 129.7, 133.6, 146.2, 151.7, 159.6, 161.2, 199.8 |
| 321 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.36 (t, *J* = 7.6 Hz, 3H), 2.10 -1.63 (m, 15H), 2.94 (q, *J* = 7.6 Hz, 2H), 4.56 (d, *J* = 5.2 Hz, 2H), 5.99 (brs, 1H), 6.77 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.20 -7.29 (m, 1H), 7.52 (d, *J* = 9.6 Hz, 1H), 9.51 (d, *J* = 1.6 Hz, 1H); ; LCMS (electrospray) m/z (M+H)+ 463. |
| 322 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.37 (t, *J* = 7.6 Hz, 3H), 2.10 -1.63 (m, 15H), 2.94 (q, *J* = 7.6 Hz, 2H), 4.54 (d, *J* = 5.2 Hz, 2H), 5.95 (brs, 1H), 6.59 (d, *J* = 8.8 Hz, 2H), 6.88 (dd, *J* = 2.4 Hz, 7.6 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.58(d, *J* = 2.0 Hz, 1H), 9.35 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z (M+H)+ 463 |
| 323 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.38 (t, *J* = 7.6 Hz, 3H), 2.04 -1.61 (m, 15H), 2.94 (q, *J* = 7.6 Hz, 2H), 4.54 (d, *J* = 5.2 Hz, 2H), 5.98 (brs, 1H), 6.59 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.8, 1H), 7.27 (dd, *J* = 2.4 Hz, 9.6 Hz, 1H), 7.52 (d, *J* = 9.2 Hz, 1H), 9.51 (d, *J* = 1.2 Hz, 1H); LCMS (electrospray) m/z (M+H)+ 463. |
| 324 |  | $^1$H-NMR (400 MHz, CDCl3): δ 1.37 (t, *J* = 7.6 Hz, 3H), 2.02 -1.61 (m, 15H), 2.93 (q, *J* = 7.6 Hz, 2H), 4.56 (d, *J* = 5.2 Hz, 2H), 5.97 (brs, 1H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.88 (dd, *J* = 2.0 Hz, 7.0 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.58(d, *J* = 2.0 Hz, 1H), 9.34 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z (M+H)+ 463. |
| 325 |  | White solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.78-1.95 (m, 4H), 2.60 (s, 3H), 2.72-2.82 (m, 1H), 2.92-3.08 (m, 2H), 3.73-3.76 (m, 2H), 4.48 (d, *J* = 6.0 Hz, 2H), 7.11-7.22 (m, 4H), 7.29-7.35 (m, 4H), 7.54 (dd, *J* = 9.6, 1.6 Hz, 1H), 7.68 (d, *J* = 9.6 Hz, 1H), 8.48 (t, *J* = 6.0 Hz, 1H, NH), 9.15 (d, *J* = 1.2 Hz, 1H); LCMS (electrospray) m/z (M+H) + 477. |
| 326 |  | Beige solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.66-1.86 (m, 4H), 2.60 (s, 3H), 2.70-2.75 (m, 3H), 3.76-3.79 (m, 2H), 4.43 (d, *J* = 5.6 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.09-7.15 (m, 4H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.46 (dd, *J* = 9.6, 2.4 Hz, 1H), 7.63 (d, *J* = 9.6 Hz, 1H), 8.36 (t, *J* = 5.6 Hz, 1H, NH), 9.12 (d, *J* = 1.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 473. |

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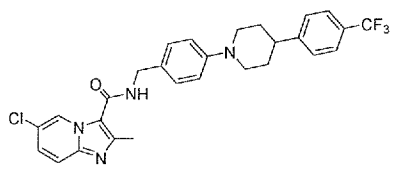
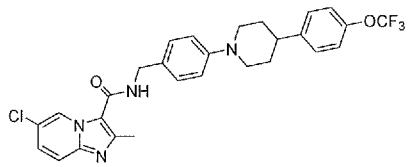
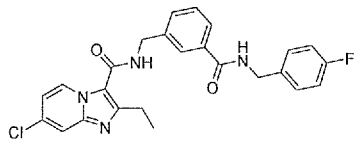
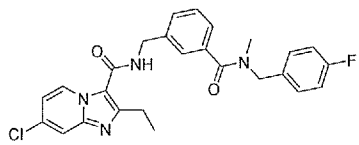
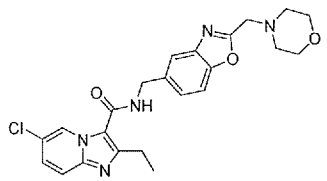
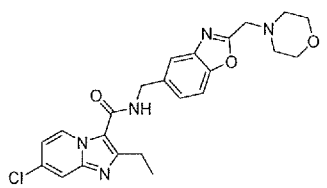
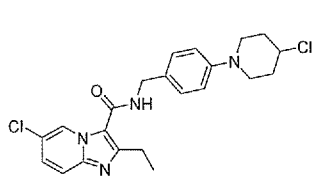
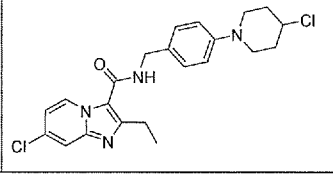
| 327 |  | Beige solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.72-1.92 (m, 4H), 2.59 (s, 3H), 2.73-2.79 (m, 3H), 3.79-3.82 (m, 2H), 4.44 (d, *J* = 6.0 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.46 (dd, *J* = 9.4, 2.2 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.62-7.67 (m, 3H), 8.37 (t, *J* = 6.0 Hz, 1H, NH), 9.13 (d, *J* = 2.0 Hz, 1H) ); LCMS (electrospray) m/z (M+H) + 527. |
| 328 |  | Beige solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.78-1.90 (m, 4H), 2.58 (s, 3H), 2.71-2.76 (m, 3H), 3.77-3.81 (m, 2H), 4.44 (d, *J* = 6.0 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.46 (dd, *J* = 9.6, 2.0 Hz, 1H), 7.63 (d, *J* = 9.6 Hz, 1H), 8.36 (t, *J* = 6.0 Hz, 1H, NH), 9.13 (d, *J* = 1.6 Hz, 1H); LCMS (electrospray) m/z (M+H) + 543. |
| 329 |  | White solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.38 (t, *J* = 7.6 Hz, 3H), 2.95 (q, *J* = 7.6 Hz, 2H), 4.61 (d, *J* = 6.0 Hz, 2H), 4.73 (d, *J* = 6.0 Hz, 2H), 6.16 (brs, 1H), 6.37 (brs, 1H), 6.89 (dd, *J* = 2.0, 7.6 Hz, 1H), 6.99 -7.06 (m, 2H), 7.30 -7.36 (m, 2H), 7.42 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.51 -7.55 (m, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.66 -7.68 (m, 1H), 7.84 (s, 1H), 9.33 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z 465, 467 (M+H)+, Cl-isotope pattern. |
| 330 |  | Pale brown solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.35 (t, *J* = 7.6Hz, 3H), 2.76 -2.97 (m, 2H), 2.86 & 2.94 (s, 3H), 4.45 & 4.68 (s, 2H), 6.31 (brs, 1H), 6.87 (dd, *J* = 2.0, 7.2 Hz, 1H), 7.00 -7.08 (m, 3H), 7.26 -7.43 (m, 5H), 7.57 (d, *J* = 2.0 Hz, 1H), 9.28 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z 479, 481 (M+H)+, Cl- isotope pattern. |
| 331 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.37 (t, *J* = 7.6 Hz, 3H), 2.62 -2.64 (m, 4H), 2.94 (q, *J* = 7.6 Hz, 2H), 3.74 -3.76 (m, 4H), 3.85 (s, 2H), 4.78 (d, *J* = 5.6 Hz, 2H), 6.18 (brt, *J* = 5.6 Hz, 1H), 7.28 (dd, *J* = 2.0, 9.6 Hz, 1H), 7.37 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.51 -7.54 (m, 2H), 7.70 (d, *J* = 1.2 Hz, 1H), 9.51 (d, *J* = 2.0 Hz, 1H); LCMS (electrospray) m/z 454, 456 (M+H)+, Cl- isotope pattern. |
| 332 |  | Pale brown solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.37 (t, *J* = 7.6 Hz, 3H), 2.63 -2.65 (m, 4H), 2.94 (q, *J* = 7.6 Hz, 2H), 3.75 -3.77 (m, 4H), 3.86 (s, 2H), 4.79 (d, *J* = 6.0 Hz, 2H), 6.13 (brt, *J* = 6.0 Hz, 1H), 6.90 (dd, *J* = 2.0, 7.2 Hz, 1H), 7.37 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 1H), 9.36 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z 454, 456 (M+H)+, Cl- isotope pattern. |
| 333 |  | Pale red solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.37 (t, *J* = 7.6 Hz, 3H), 1.98 -2.04 (m, 2H), 2.18 -2.29 (m, 2H), 2.93 (q, *J* = 7.6 Hz, 2H), 3.05 -3.11 (m, 2H), 3.49 -3.55 (m, 2H), 4.19 -4.24 (m, 1H), 4.60 (d, *J* = 5.2 Hz, 2H), 6.01 (brs, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 7.26 -7.31 (m, 3H), 7.52 (d, *J* = 9.6 Hz, 1H), 9.53 (d, *J* = 2.1 Hz, 1H); LCMS (electrospray) m/z 431 (M+H)+. |
| 334 |  | Pale red solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.36(t, *J* = 7.2 Hz, 3H), 1.99 -2.04 (m, 2H), 2.17 -2.20 (m, 2H), 2.92 (q, *J* = 7.2 Hz, 2H), 3.05 -3.10 (m, 2H), 3.50 -3.52 (m, 2H), 4.20 -4.23 (m, 1H), 4.59 (d, *J* = 5.6 Hz, 2H), 5.99 (brs, 1H), 6.89 -6.94 (m, 3H), 7.26 -7.27 (m, 2H), 7.58 (s, 1H), 9.35 (d, *J* = 6.8 Hz, 1H); LCMS (electrospray) m/z 431 (M+H)+. |

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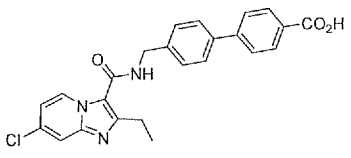
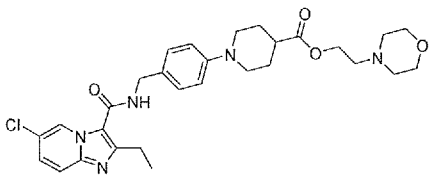
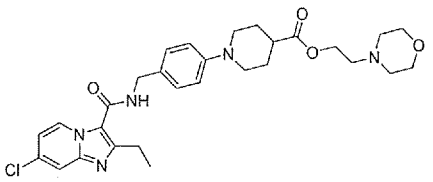
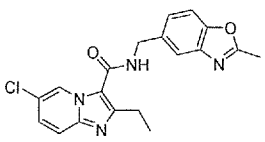
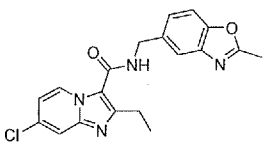
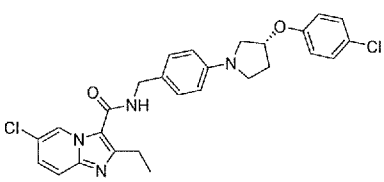
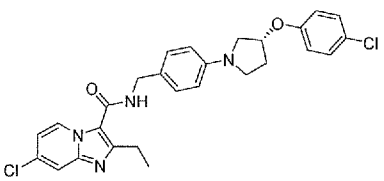
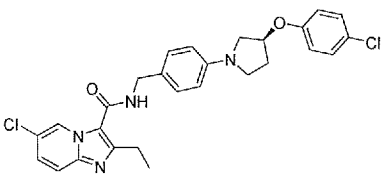
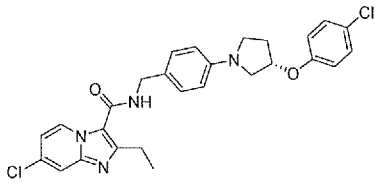
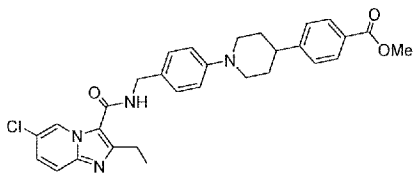
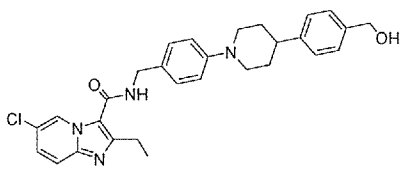
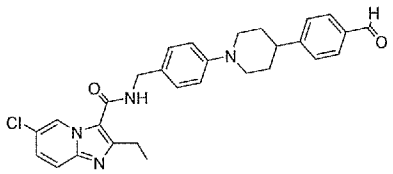
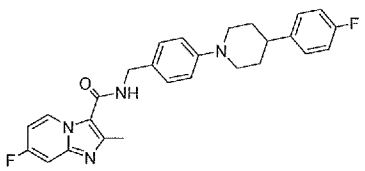
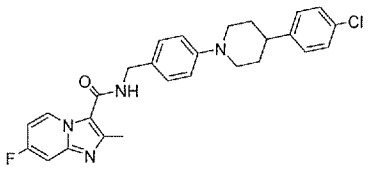
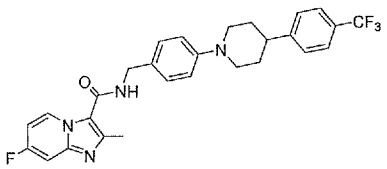
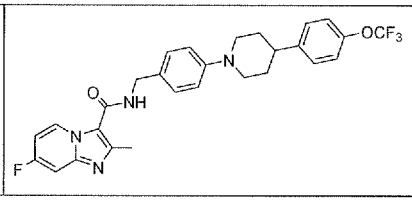
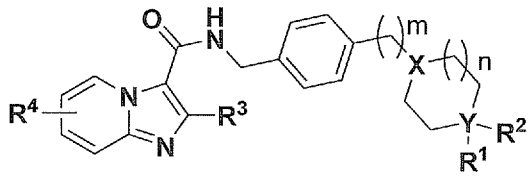
| 335 |  | White solid: $^1$H-NMR (400 MHz, DMSO-d6): δ 1.26 (t, *J* = 7.6 Hz, 3H), 2.98 (q, *J* = 7.6 Hz, 2H), 4.58 (d, *J* = 6.0 Hz, 2H), 7.08 (dd, *J* = 2.4, 7.2 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.78 -7.80 (m, 3H), 8.00 (d, *J* = 8.4 Hz, 2H), 8.51 (brt, *J* = 5.6 Hz, 1H), 8.97 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z 434, 436 (M+H)+, Cl- isotope pattern. |
| 336 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.36 (t, *J* = 7.6 Hz, 3H), 1.71 -2.03 (m, 8H), 2.47 -2.55 (m, 2H), 2.62 -2.65 (m, 1H), 2.72 -2.84 (m, 2H), 2.87 -2.97 (m, 3H), 3.30 -3.40 (m, 2H), 3.62 -3.77 (m, 4H), 4.23 -4.26 (m, 1H), 4.58 (d, *J* = 5.2 Hz, 2H), 6.02 (brs, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 7.24 -7.29 (m, 3H), 7.51 (d, *J* = 9.6 Hz, 1H), 9.51 (d, *J* = 1.2 Hz, 1H); LCMS (electrospray) m/z 554, 556 (M+H)+, Cl- isotope pattern. |
| 337 |  | Pale pink solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.36 (t, *J* = 7.6 Hz, 3H), 1.82 -1.92 (m, 2H), 2.00 -2.04 (m, 2H), 2.44 -2.51 (m, 5H), 2.61 (t, *J* = 5.6 Hz, 2H), 2.77 -2.84 (m, 2H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.91 -2.97 (m, 1H), 3.62 -3.70 (m, 5H), 4.22 (t, *J* = 5.6 Hz, 2H), 4.58 (d, *J* = 5.6 Hz, 2H), 5.97 (brt, *J* = 5.6 Hz, 1H), 6.88 -6.94 (m, 3H), 7.25 -7.27 (m, 2H), 7.58 -7.59 (m, 1H), 9.35 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z 554, 556 (M+H)+, Cl- isotope pattern. |
| 338 |  | White solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.38 (t, *J* = 7.6 Hz, 3H), 2.64 (s, 3H), 2.95 (q, *J* = 7.6 Hz, 2H), 4.78 (d, *J* = 5.6 Hz, 2H), 6.15 (brt, *J* = 5.6 Hz, 1H), 7.31 -7.35 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 9.2 Hz, 1H), 7.65 (s, 1H), 9.54 (s, 1H); LCMS (electrospray) m/z 369, 371 (M+H)+, Cl- isotope pattern. |
| 339 |  | White solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.36 (t, *J* = 7.6 Hz, 3H), 2.64 (s, 3H), 2.93 (q, *J* = 7.6 Hz, 2H), 4.77 (d, *J* = 6.0 Hz, 2H), 6.14 (brt, *J* = 6.0 Hz, 1H), 6.90 (dd, *J* = 2.4, 7.6 Hz, 1H), 7.31 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 9.36 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z 369, 371 (M+H)+, Cl- isotope pattern. |
| 340 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3 + CD3OD): δ 1.24 (t, *J* = 7.6 Hz, 3H), 2.19 -2.25 (m, 2H), 2.81 (q, *J* = 7.6 Hz, 2H), 3.33 -3.45 (m, 3H), 3.58 -3.62 (m, 1H), 4.46 (d, *J* = 5.2 Hz, 2H), 4.93 -4.94 (m, 1H), 6.34 (brs, 1H), 6.48 (d, *J* = 8.2 Hz, 2H), 6.72 -6.75 (m, 2H), 7.13 -7.17 (m, 4H), 7.23 -7.26 (m, 1H), 7.42 -7.44 (m, 1H), 9.30 -9.31 (m, 1H); LCMS (electrospray) m/z 509, 511 (M+H)+, Cl- isotope pattern. |
| 341 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.35 (t, *J* = 7.6Hz, 3H), 2.27 -2.33 (m, 2H), 2.90 (q, *J* = 7.6 Hz, 2H), 3.41 -3.54 (m, 3H), 3.66 -3.70 (m, 1H), 4.56 (d, *J* = 5.2 Hz, 2H), 4.99 -5.02 (m, 1H), 5.95 (brs, 1H), 6.56 (d, *J* = 8.4 Hz, 2H), 6.79 -6.83 (m, 2H), 6.88 (dd, *J* = 2.0, 7.2 Hz, 1H), 7.21 -7.25 (m, 4H), 7.58 (d, *J* = 2.0 Hz, 1H), 9.34 (d, *J* = 7.2 Hz, 1H); LCMS (electrospray) m/z 509, 511 (M+H)+, Cl- isotope pattern. |
| 342 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3 + CD3OD): δ 1.28 (t, *J* = 7.6 Hz, 3H), 2.23 -2.28 (m, 2H), 2.85 (q, *J* = 7.6 Hz, 2H), 3.37 -3.49 (m, 3H), 3.61 -3.65 (m, 1H), 4.50 (d, *J* = 5.2 Hz, 2H), 4.96 -4.97 (m, 1H), 6.22 (brs, 1H), 6.52 (d, *J* = 8.8 Hz, 2H), 6.75 -6.79 (m, 2H), 7.17 -7.20 (m, 4H), 7.28 (d, *J* = 1.6 Hz, 1H), 7.46 (d, *J* = 9.6 Hz, 1H), 9.37 -9.38 (m, 1H); LCMS (electrospray) m/z 509, 511 (M+H)+, Cl- isotope pattern. |

| | | |
|---|---|---|
| 343 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.34 (t, *J* = 7.6 Hz, 3H), 2.26 -2.33 (m, 2H), 2.89 (q, *J* = 7.6 Hz, 2H), 3.41 -3.53 (m, 3H), 3.66 -3.70 (m, 1H), 4.56 (d, *J* = 5.2 Hz, 2H), 4.99 -5.01 (m, 1H), 5.97 (brt, *J* = 5.2 Hz, 1H), 6.56 (d, *J* = 8.4 Hz, 2H), 6.78 -6.82 (m, 2H), 6.87 (dd, *J* = 2.0, 7.6 Hz, 1H), 7.21 -7.25 (m, 4H), 7.57 (d, *J* = 2.0 Hz, 1H), 9.34 (d, *J* = 7.6 Hz, 1H); LCMS (electrospray) m/z 509, 511 (M+H)+, Cl-isotope pattern. |
| 344 |  | Pale yellow solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.39 (t, *J* = 7.6 Hz, 3H), 1.99 -2.19 (m, 4H), 2.77 -2.80 (m, 1H), 2.95 -3.05 (m, 4H), 3.79 -3.82 (m, 2H), 3.90 (s, 3H), 4.64 (d, *J* = 5.6 Hz, 2H), 6.41 (brs, 1H), 7.31 -7.39 (m, 7H), 7.61 (d, *J* = 9.6 Hz, 1H), 7.97 -8.00 (m, 2H), 9.49 (d, *J* = 1.2 Hz, 1H); LCMS (electrospray) m/z 531, 533 (M+H)+ , Cl- isotope pattern. |
| 345 |  | Yellow solid: $^1$H-NMR (400 MHz, CDCl3 + CD3OD): δ 1.32 (t, *J* = 7.6 Hz, 3H), 1.97 -2.03 (m, 2H), 2.65 -2.80 (m, 1H), 2.95 -3.01 (m, 6H), 3.71 -3.74 (m, 2H), 4.57 (s, 2H), 4.57 (d, *J* = 6.4 Hz, 2H), 7.21 -7.28 (m, 6H), 7.40 -7.43 (m, 3H), 7.62 (d, *J* = 9.2 Hz, 1H), 9.28 (d, *J* = 1.6 Hz, 1H); LCMS (electrospray) m/z 503, 505 (M+H)+ , Cl- isotope pattern. |
| 346 |  | Violet solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.39 (t, *J* = 7.6 Hz, 3H), 1.99 -2.09 (m, 4H), 2.79 -3.02 (m, 4H), 3.47 -3.50 (m, 1H), 3.81 -3.84 (m, 2H), 4.63 (s, 2H), 6.16 (brs, 1H), 7.00 -7.10 (m, 2H), 7.27 -7.45 (m, 5H), 7.57 -7.59 (m, 1H), 7.84 -7.85 (m, 2H), 9.52 (s, 1H), 9.99 (s, 1H); LCMS (electrospray) m/z 501, 503 (M+H)+, Cl- isotope pattern. |
| 347 |  | Pale pink solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.94 -2.04 (m, 4H), 2.61 -2.71 (m, 1H), 2.66 (s, 3H), 3.78 -3.81 (m, 2H), 4.61 (d, *J* = 5.6 Hz, 2H), 6.15 (brs, 1H), 6.79 -6.83 (m, 1H), 6.98 -7.16 (m, 4H), 7.19 -7.24 (m, 3H), 7.31 -7.33 (m, 2H), 9.43 -9.47 (m, 1H); LCMS (electrospray) m/z 461 (M+H)+. |
| 348 |  | White solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.96 -2.02 (m, 4H), 2.65 -2.75 (m, 1H), 2.70 (s, 3H), 2.95 -2.99 (m, 2H), 3.77 -3.80 (m, 2H), 4.63 (d, *J* = 5.6 Hz, 2H), 6.42 (brs, 1H), 6.84 -6.88 (m, 1H), 7.19 -7.24 (m, 2H), 7.26 -7.33 (m, 5H), 7.37 -7.41 (m, 2H), 9.42 -9.45 (m, 1H); LCMS (electrospray) m/z 477, 479 (M+H)+, Cl- isotope pattern . |
| 349 |  | Pale pink solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.97 -2.05 (m, 4H), 2.68 (s, 3H), 2.73 -2.82 (m, 1H), 2.83 -2.96 (m, 2H), 3.80 -3.83 (m, 2H), 4.62 (d, *J* = 5.6 Hz, 2H), 6.25 (brs, 1H), 6.81 -6.85 (m, 1H), 7.00 -7.18 (m, 2H), 7.24 -7.27 (m, 1H), 7.31 -7.41 (m, 4H), 7.56 -7.58 (m, 2H), 9.43 -9.47 (m, 1H); LCMS (electrospray) m/z 511 (M+H)+. |

| | | |
|---|---|---|
| 350 |  | White solid: $^1$H-NMR (400 MHz, CDCl3): δ 1.96 -2.05 (m, 4H), 2.69 (s, 3H), 2.69 -2.74 (m, 1H), 2.85 -2.96 (m, 2H), 3.78 -3.81 (m, 2H), 4.62 (d, *J* = 5.6 Hz, 2H), 6.31 (brs, 1H), 6.82 -6.87 (m, 1H), 7.15 -7.17 (m, 2H), 7.20 -7.30 (m, 5H), 7.35 -7.41 (m, 2H), 9.43 -9.46 (m, 1H); LCMS (electrospray) m/z 527 (M+H)+. |

## Claims

1. A compound having the general formula I:



I

wherein

X is CH or N;

Y is CH, O or N;

m is 0 or 1;

n is 0 or 1;

$R^1$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, ethyl, t-butyl, phenyl, $-NC(O)R^5$, $-OR^5$, $-C(O)R^5$, $-C(O)OR^5$, any of which is optionally substituted;

$R^2$ is, at each occurrence, independently selected from the group consisting of hydrogen and hydroxyl;

$R^3$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^4$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^5$ is, at each occurrence, independently selected from the group consisting of $C_1$-$C_3$ alkylhetorocycle, phenyl and benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof;

wherein, if m is 0, n is 1, X is N, Y is O and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro, 6-methyl, 6-methoxy, 6-bromo, 6-trifluoromethyl, 6-fluoro, 7-chloro, 7-methyl, 7-methoxy, 7-trifluoromethyl, 7-bromo, 8-fluoro, 8-trifluoromethyl, 8-methoxy, or 8-bromo;

wherein, if m is 0, n is 1, X is N and Y is C, $R^1$ is H, $R^2$ is H, $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N and Y is N, $R^1$ is methyl, $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^2$ is hydroxyl, $R^3$ is ethyl and $R^4$ is 7-chloro, then $R^1$ is not hydrogen;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-fluorobenzyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-chlorophenyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-fluorophenyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-(trifluoromethyl)phenyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is $OR^5$, $R^2$ is hydrogen, $R^3$ is ethyl and $R^5$ is 4-(trifluoromethoxy)phenyl, then $R^4$ is not 6-chloro, 6-trifluoromethyl or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is methyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not 6- chloro or 7-chloro;

wherein, if m is 0, n is 0, X is N, Y is C, $R^1$ is methyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not 6- chloro or 7-chloro;

wherein, if m is 1, n is 1, X is N, Y is N, $R^1$ is 4-(butyramidomethyl)phenyl and $R^3$ is ethyl, then $R^4$ is not 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is N, $R^1$ is 4-fluorophenyl and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-fluoro, 6-chloro, 6-methyl, 6-methoxy, 6-bromo, 7-bromo, 7-chloro, 7-methyl, 7-methoxy , 8-methoxy, 8-bromo or 8-fluoro;

wherein, if m is 0, n is 1, X is N, Y is N, $R^1$ is 4-(trifluoromethoxy)phenyl and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-fluorophenyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-(trifluoromethoxy)phenyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-chlorophenyl, $R^2$ is hydrogen and $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is 4-fluorophenyl, $R^2$ is hydroxy and $R^3$ is ethyl, then $R^4$ is not 6-chloro or 7-chloro;

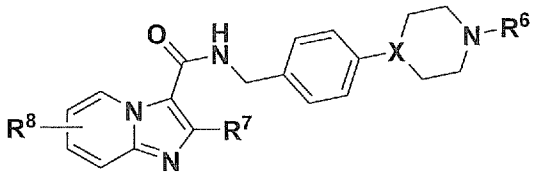
wherein, if m is 0, n is 1, X is N, Y is C, $R^1$ is phenyl, $R^2$ is hydroxy and $R^3$ is ethyl, then $R^4$ is not 7-chloro;

wherein, if m is 0, n is 1, X is N, Y is N, $R^1$ is phenyl and $R^3$ is ethyl, then $R^4$ is not 7-chloro.

2. The Compound according to claim 1, wherein m = 0.

3. The compound according to any of claims 1 and 2, wherein m = 0 and $R^1$ is, at each occurrence, independently selected from the group consisting of halogen, methyl, ethyl, t-butyl, phenyl, $-NC(O)R^5$, $-OR^5$, $-C(O)R^5$, $-C(O)OR^5$, any of which is optionally substituted.

4. A compound having the general formula II:



II

wherein

X is CH or N

$R^6$ is, at each occurrence, independently selected from the group consisting of phenyl and $C(O)R^9$ , any of which is optionally substituted;

$R^7$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^8$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^9$ is, at each occurrence, independently selected from the group consisting of phenyl, benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof;

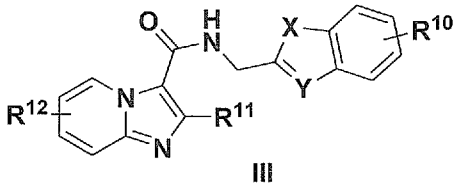
wherein, if X is N, $R^6$ is phenyl and $R^7$ is ethyl, then $R^8$ is not 7-chloro;

wherein, if X is N, $R^6$ is 4-fluorophenyl and $R^7$ is ethyl, then $R^8$ is not hydrogen, 6-fluoro, 6-chloro, 6-methyl, 6-methoxy, 6-bromo, 7-bromo, 7-chloro, 7-methyl, 7-methoxy , 8-methoxy, 8-bromo or 8-fluoro;

wherein, if X is N, $R^6$ is 4-(butyramidomethyl)phenyl and $R^7$ is ethyl, then $R^8$ is not 7-chloro;

wherein, if X is N, $R^6$ is 4-(trifluoromethoxy)phenyl and $R^7$ is ethyl, then $R^8$ is not hydrogen, 6-chloro or 7-chloro.

5. A compound having the general formula III:



III

wherein
X is S, O or $NR^{13}$
Y is CH or N

$R^{10}$ is, at each occurrence, independently selected from the group consisting of halogen and phenyl, any of which is optionally substituted;

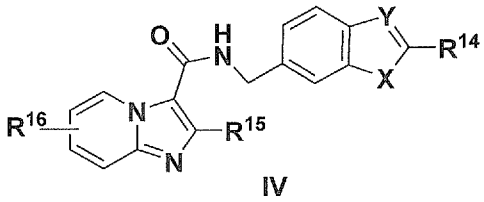
$R^{11}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{12}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^{13}$ is, at each occurrence, independently selected from the group consisting of hydrogen, methyl and benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof.

6. A compound having the general formula IV:



IV

wherein

X is S, O or $NR^{17}$

Y is CH or N

$R^{14}$ is, at each occurrence, independently selected from the group consisting of hydrogen, $C_1$-$C_3$ alkyl, $C_1$-$C_3$ alkylheterocycle, phenyl, any of which is optionally substituted;

$R^{15}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{16}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

$R^{17}$ is, at each occurrence, independently selected from the group consisting of hydrogen, methyl and benzyl, any of which is optionally substituted;

and pharmaceutically acceptable salts thereof;

wherein, if X is $NR^{17}$, Y is N, $R^{14}$ is 4-(trifluoromethoxy)phenyl, $R^{15}$ is ethyl and $R^{17}$ is hydrogen, then $R^{16}$ is not 6-chloro or 7-chloro;

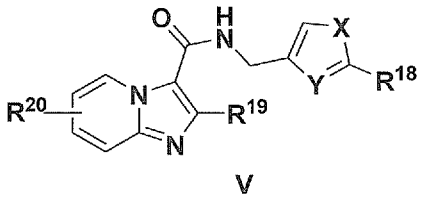
wherein, if X is $NR^{17}$, Y is N, $R^{14}$ is morpholinomethyl, $R^{15}$ is ethyl and $R^{17}$ is hydrogen, then $R^{16}$ is not 7-chloro;

wherein, if X is O, Y is N, $R^{14}$ is 4-(trifluoromethoxy)phenyl, and $R^{15}$ is ethyl, then $R^{16}$ is not 6-chloro or 7-chloro;

wherein, if X is O, Y is N, $R^{14}$ is 4-fluorophenyl, and $R^{15}$ is ethyl, then $R^{16}$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if X is O, Y is N, $R^{14}$ is cyclohexyl, and $R^{15}$ is ethyl, then $R^{16}$ is not 6-chloro or 7-chloro.

7. A compound having the general formula V:



V

wherein

X is S, O or NH

Y is CH or N

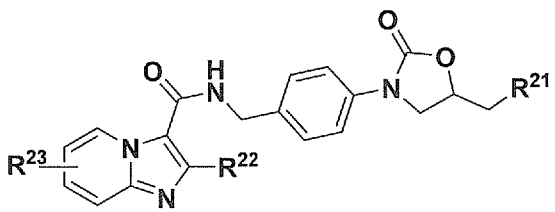
$R^{18}$ is, at each occurrence, independently selected from the group consisting of $C_1$-$C_3$ alkylheterocycle, phenyl and benzyl, any of which is optionally substituted;

$R^{19}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{20}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

8. A compound having the general formula VI:



VI

wherein

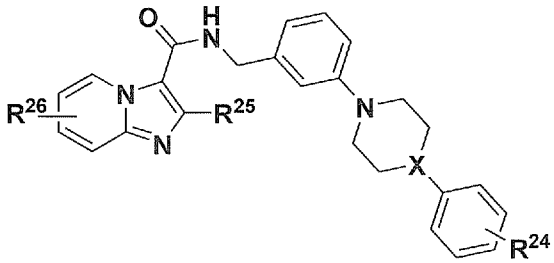
$R^{21}$ is, at each occurrence, independently selected from the group consisting of phenyl and O-phenyl, any of which is optionally substituted;

$R^{22}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{23}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

9. A compound having the general formula VII:



VII

wherein
X is CH or N

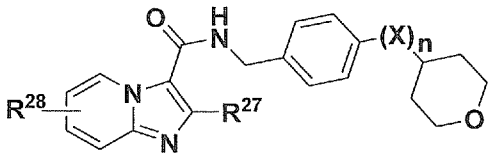
$R^{24}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, $C_1$-$C_2$ alkyl, -methoxy, $-CF_3$ and $-OCF_3$;

$R^{25}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{26}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, –methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

10. A compound having the general formula VIII:



VIII

wherein

X is $CH_2$ or NH

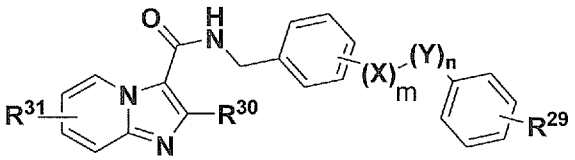
n is 0 or 1

$R^{27}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{28}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogen, methyl, -methoxy and $-CF_3$;

and pharmaceutically acceptable salts thereof.

11. A compound having the general formula IX:



IX

wherein

X is $CH_2$, $NR^{32}$, O, C(O)NH or –HC=CH-

Y is $CH_2$, or C(O)NH,

m is 0 or 1

n is 0 or 1

$R^{29}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogens, $C_1$-$C_2$ alkyl, -methoxy, COOH, $-CF_3$ and $-OCF_3$;

$R^{30}$ is, at each occurrence, independently selected from the group consisting of methyl and ethyl;

$R^{31}$ is, at each occurrence, independently selected from the group consisting of hydrogen, halogens, methyl, -methoxy and $-CF_3$;

$R^{32}$ is, at each occurrence, independently selected from the group consisting of hydrogen and methyl;

and pharmaceutically acceptable salts thereof;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is methyl, then $R^{31}$ is not hydrogen;

wherein, if X is *para*-C, m is 0, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is methyl, then $R^{31}$ is not hydrogen, 6-chloro or 7-chloro;

wherein, if X is *para*-C, m is 0, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-chloro or 6-methyl;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is hydrogen and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-methyl or 6-chloro;

wherein, if X is *para*-C, m is 0, n is 0, $R^{30}$ is ethyl and $R^{31}$ is 6-chloro, then $R^{29}$ is not 2-chloro, 4-chloro, 2-methyl, 3-methyl, 2-trifluoromethyl or 4-methyl;

wherein, if X is *para*-C, m is 0, n is 0, $R^{30}$ is ethyl, $R^{31}$ is 7-chloro, then $R^{29}$ is not hydrogen, 2-chloro, 4-chloro, 2-methyl, 3-methyl, 4-methyl, 4-fluoro, 4-methoxy, 4-trifluoromethoxy, 4-trifluoromethyl or 2-trifluoromethyl;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is 4-trifluoromethoxy and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-chloro or 7-chloro, 6-fluoro, 6-bromo, 6-methyl, 7-methyl or 8-fluoro;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is 4-fluoro and $R^{30}$ is ethyl, then $R^{31}$ is not 6-chloro, 6-bromo or 7-chloro;

wherein, if X is *para*-O, m is 1, n is 0, $R^{29}$ is 4-chloro and $R^{30}$ is ethyl, then $R^{31}$ is not 6-chloro or 7-chloro;

wherein, if X is *para*-N, Y is C, m is 1, $R^{29}$ is 4-trifluoromethoxy, $R^{30}$ is ethyl, $R^{31}$ is 7-chloro and $R^{32}$ is hydrogen, then n is not 0 or 1;

wherein, if X is *para*-O, Y is C, m is 1, n is 1, $R^{29}$ is 4-trifluoromethoxy and $R^{30}$ is ethyl, then $R^{31}$ is not hydrogen, 6-chloro, 6-fluoro, 6-bormo or 7-chloro;

wherein, if X is *para*-O, Y is C, m is 1, n is 1, $R^{29}$ is 4-fluoro and $R^{30}$ is ethyl, then $R^{31}$ is not 6-chloro or 7-chloro;

wherein, if X is *meta*-C, m is 0, n is 0, $R^{30}$ is ethyl and $R^{31}$ is 7-chloro, then $R^{29}$ is not 4-trifluoromethoxy;

wherein, if X is *para*-N, Y is C, m is 1, n is 1, $R^{29}$ is 4-trifluoromethoxy, $R^{30}$ is ethyl and $R^{31}$ is hydrogen, then $R^{32}$ is not methyl.

12. The compound according to any of claims 1-11, having one of the formulae 1-350 as shown in Tables 1 and 2, preferably one of the formulae 1-21, 23-24, 26, 28-33, 35-57, 59-77, 79-83, 85-87, 90-98, 100-102, 106-111, 113-116 118-124, 126-128, 130-142, 144-150, 153, 155-167, 169-184, 186-188, 190-197, 199, 201, 203-208, 210-211, 213-214, 216, 218-231, 233, 235-246, 252-254, 256-259, 261, 267-270, 273, 279-280, 284-303, 307-316, 319-328, 333-338, 340-350 as shown in Tables 1 and 2.

13. The compound according to any of claims 1 – 12, having one of the formulae 55, 171, 175 and 325 as shown in Tables 1 and 2,

and pharmaceutically acceptable salts thereof.

14. The compound according to any of claims 1 – 13, for use in the treatment of a bacterial infection.

15. The compound according to claim 14, wherein said bacterial infection is Tuberculosis.

16. A pharmaceutical composition comprising a compound according to any of claims 1 – 15, and a pharmaceutically acceptable carrier.

17. A method of treatment of a bacterial infection, in particular Tuberculosis, comprising the application of a suitable amount of a compound according to any of claims 1 – 15 or a pharmaceutical composition according to claim 16, to a person in need thereof.

18. A compound that competitively inhibits the specific binding of a compound according to any of claims 1 – 15.

19. A method of treatment of a bacterial infection, in particular Tuberculosis, comprising the application of a suitable amount of a compound, which compound is characterized by an ability to competitively inhibit the specific binding of a compound according to any of claims 1 – 15 or a pharmaceutical composition according to claim 18, to its target protein, to a person in need thereof.

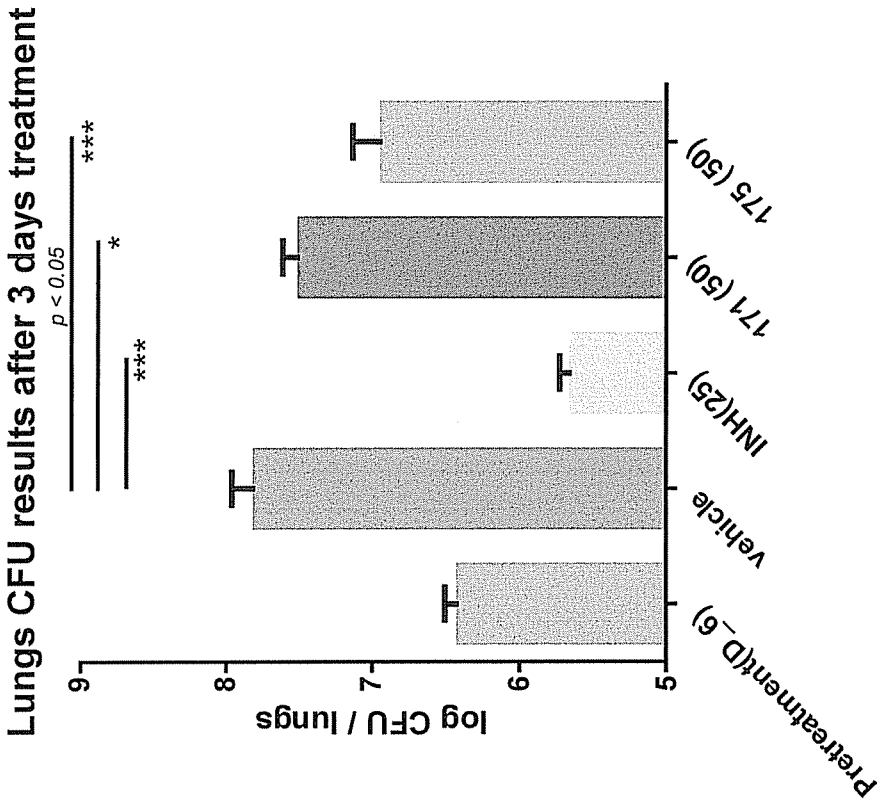

Lungs CFU results after 3 days treatment
p < 0.05
***
*
***
log CFU / lungs
9
8
7
6
5
Pretreatment(D_6)
Vehicle
INH(25)
1T1 (50)
1T5 (50)

Figure 1