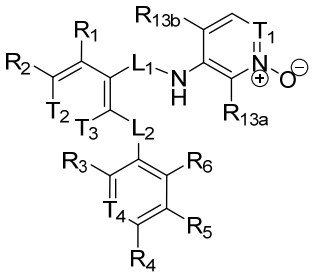
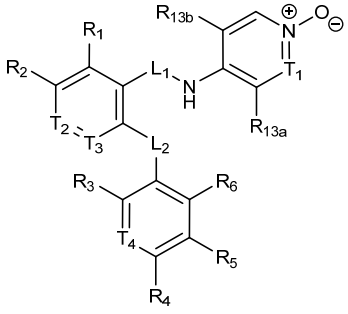
Claims

1. A compound, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein the compound is selected from



(I-1) and 

(I-2),

wherein,

T_1 is selected from N and C(R_7);

T_2 is selected from N and C(R_8);

T_3 is selected from N and C(R_9);

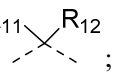
T_4 is selected from N and C(R_{10});

R_1, R_2, R_8, R_9 are each independently selected from H, halogen, OH, NH_2, CN, SF_5, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, vinyl-C_{1-6} alkyl-, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl-, 3-6 membered heterocycloalkyl-C_{1-6} alkyl-, 3-6 membered heterocycloalkyl-C_{1-6} alkyl-O-, phenyl-C_{1-3} alkyl-, C_{3-6} cycloalkyl-C_{1-3} alkyl-O-, 3-6 membered heterocycloalkyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-NH-, 5-6 membered heteroaryl-C_{1-3} alkyl-, 5-6 membered heteroaryl-C_{1-3} alkyl-O- and 5-6 membered heteroaryl-C_{1-3} alkyl-NH-, the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylamino, vinyl-C_{1-6} alkyl-, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl-, 3-6 membered heterocycloalkyl-C_{1-6} alkyl-, 3-6 membered heterocycloalkyl-C_{1-6} alkyl-O-, phenyl-C_{1-3} alkyl-, C_{3-6} cycloalkyl-C_{1-3} alkyl-O-, 3-6 membered heterocycloalkyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-NH-, 5-6 membered heteroaryl-C_{1-3} alkyl-, 5-6 membered heteroaryl-C_{1-3} alkyl-O- or 5-6 membered heteroaryl-C_{1-3} alkyl-NH- is optionally substituted by 1, 2 or 3 R;

and, when T_3 is selected from N, R_1 is not H;

R_3, R_4, R_5, R_6, R_{10} are each independently selected from H, halogen, OH, NH_2, SF_5, CN, C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkoxy, C_{3-6} cycloalkayl, -O-C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl- and 3-6 membered heterocycloalkyl-C_{1-6} alkyl-, the C_{1-6} alkyl, C_{1-6} alkylamino, C_{1-6} alkoxy, C_{3-6} cycloalkayl, -O-C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-6} alkyl- or 3-6 membered heterocycloalkyl-C_{1-6} alkyl- is optionally substituted by 1, 2 or 3 R;

R_7 is selected from H, F, Cl, Br, I, C_{1-6} alkyl, C_{1-6} alkoxy and C_{1-6} alkylamino, the C_{1-6} alkyl, C_{1-6} alkoxy or C_{1-6} alkylamino is optionally substituted by 1, 2 or 3 R;

L_1 is selected from C(=O), NH and 

;

L_2 is selected from O, S, NH and CH_2, the CH_2 is optionally substituted by 1 or 2 R, and NH is optionally

substituted by R;

R_{11} and R_{12} are each independently selected from H, halogen, OH, NH_2 and C_{1-6} alkyl, the C_{1-6} alkyl is optionally substituted by 1, 2 or 3 R; or, R_{11} and R_{12} are connected together to form a 3-6 membered ring;

R_{13a}, R_{13b} are each independently selected from H, halogen and C_{1-6} alkyl, the C_{1-6} alkyl is optionally substituted by 1, 2 or 3 R

each of R is independently selected from H, D, halogen, OH, NH_2, CN, , C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio and C_{1-6} alkylamino, the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio or C_{1-6} alkylamino is optionally substituted by 1, 2 or 3 R';

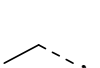
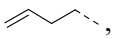
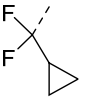
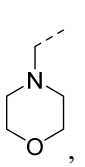
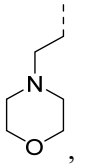
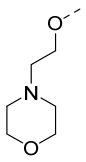
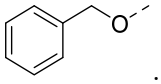
R' is selected from F, Cl, Br, I, OH, NH_2 and CH_3;

the 3-6 membered heterocycloalkyl or 5-6 membered heteroaryl contains 1, 2 or 3 heteroatoms or heteroatom groups independently selected from -O-, -NH-, -S-, -C(=O)-, -C(=O)O-, -S(=O)-, -S(=O)$_2$- and N.

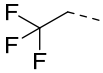
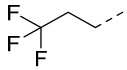
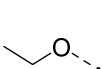
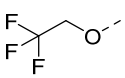
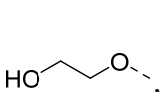
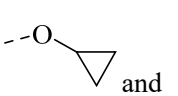
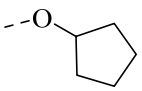
2. The compound as defined in claim 1, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R is selected from H, D, F, Cl, Br, I, OH, NH_2, , Me, CF_3, CHF_2, CH_2F, ,  and .

3. The compound as defined in claim 1 or 2, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R_1, R_2, R_8, R_9 are each independently selected from H, halogen, OH, NH_2, CN, SF_5, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkylamino, vinyl-C_{1-3} alkyl-, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-3} alkyl-, 3-6 membered heterocycloalkyl-C_{1-3} alkyl-, 3-6 membered heterocycloalkyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-, phenyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-NH-, pyridyl-C_{1-3} alkyl-, pyrimidinyl-C_{1-3} alkyl-, thiophenyl-C_{1-3} alkyl-, thiazolyl-C_{1-3} alkyl-, pyrazolyl-C_{1-3} alkyl-, imidazolyl-C_{1-3} alkyl-, pyridyl-C_{1-3} alkyl-O-, pyrimidinyl-C_{1-3} alkyl-O-, thiophenyl-C_{1-3} alkyl-O-, thiazolyl-C_{1-3} alkyl-O-, pyrazolyl-C_{1-3} alkyl-O-, imidazolyl-C_{1-3} alkyl-O-, pyridyl-C_{1-3} alkyl -NH-, pyrimidinyl-C_{1-3} alkyl-NH-, thiophenyl-C_{1-3} alkyl-NH-, thiazolyl-C_{1-3} alkyl-NH-, pyrazolyl-C_{1-3} alkyl-NH- and imidazolyl-C_{1-3} alkyl-NH-, the C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkylamino, vinyl-C_{1-3} alkyl-, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-3} alkyl-, 3-6 membered heterocycloalkyl- C_{1-3} alkyl-, 3-6 membered heterocycloalkyl-C_{1-3} alkyl-O-, phenyl-C_{1-3} alkyl-, phenyl-C_{1-3} alkyl-O-, phenyl- C_{1-3} alkyl-NH-, pyridyl-C_{1-3} alkyl-, pyrimidinyl-C_{1-3} alkyl-, thiophenyl-C_{1-3} alkyl-, thiazolyl-C_{1-3} alkyl-, pyrazolyl-C_{1-3} alkyl-, imidazolyl-C_{1-3} alkyl-, pyridyl-C_{1-3} alkyl-O-, pyrimidinyl-C_{1-3} alkyl-O-, thiophenyl-C_{1-3} alkyl-O-, thiazolyl-C_{1-3} alkyl-O-, pyrazolyl-C_{1-3} alkyl-O-, imidazolyl-C_{1-3} alkyl-O-, pyridyl-C_{1-3} alkyl -NH-, pyrimidinyl-C_{1-3} alkyl-NH-, thiophenyl-C_{1-3} alkyl-NH-, thiazolyl-C_{1-3} alkyl-NH-, pyrazolyl-C_{1-3} alkyl-NH- or imidazolyl-C_{1-3} alkyl-NH- is optionally substituted by 1, 2 or 3 R.

4. The compound as defined in claim 3, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R_1, R_2, R_8, R_9 are each independently selected from H, F, Cl, Br, I, OH, NH_2, CN, SF_5, Me,

CF_3, CHF_2, CF_3CF_2, CH_2F, OCF_3, $HOCH_2CH_2O$, $CH_3NHCH_2CH_2O$, $(CH_3)_2NCH_2CH_2O$, , , , , , , , , , , , , , , , , , and .

5. The compound as defined in claim 1 or 2, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R_3, R_4, R_5, R_6, R_{10} are each independently selected from H, halogen, OH, NH_2, SF_5, CN, C_{1-3} alkyl, C_{1-3} alkylamino, C_{1-3} alkoxy, C_{3-6} cycloalkayl, -O-C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-3} alkyl- and 3-6 membered heterocycloalkyl-C_{1-3} alkyl-, the C_{1-3} alkyl, C_{1-3} alkylamino, C_{1-3} alkoxy, C_{3-6} cycloalkayl, -O-C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, C_{3-6} cycloalkyl-C_{1-3} alkyl- or 3-6 membered heterocycloalkyl-C_{1-3} alkyl- is optionally substituted by 1, 2 or 3 R.

6. The compound as defined in claim 5, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R_3, R_4, R_5, R_6, R_{10} are each independently selected from H, F, Cl, Br, I, OH, NH_2, SF_5, Me, CF_3, CHF_2, CH_2F, CN, $CH(F_2)CH_3$, CD_3, OCD_3, , , , , , , , , , , , , , , and .

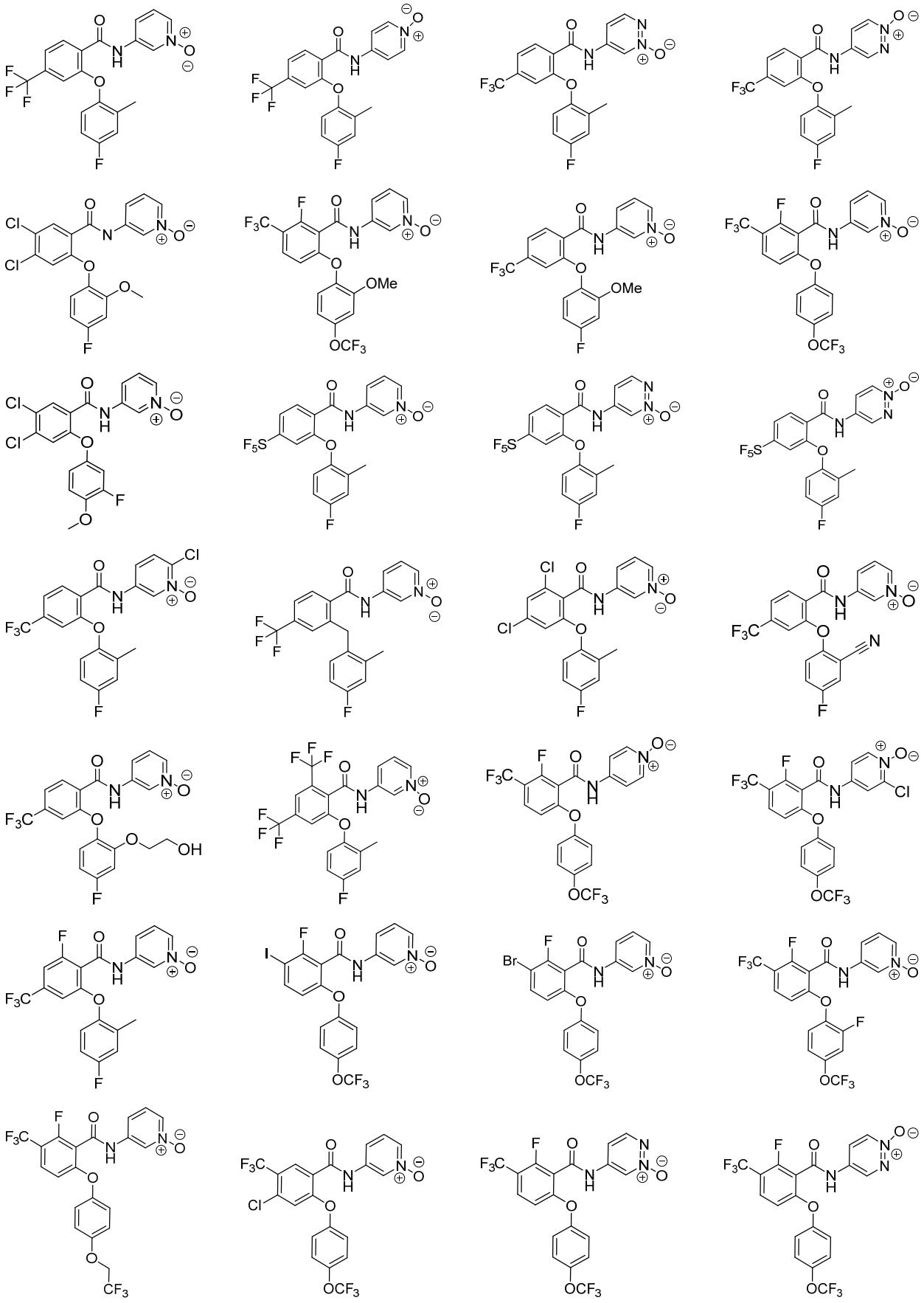
7. The compound as defined in claim 1, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R_{11}, R_{12} are each independently selected from H, F, Cl, Br, I, OH, NH_2, Me, CHF_2, CF_3,  and .

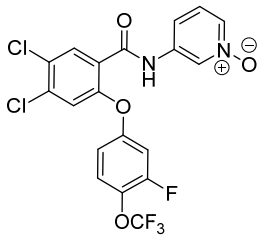
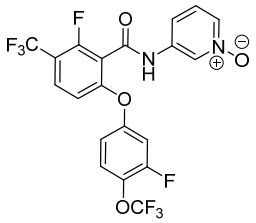
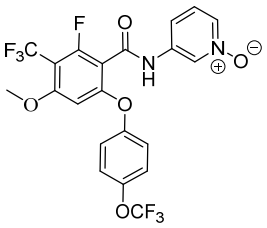
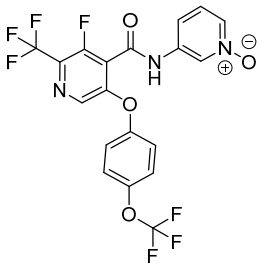
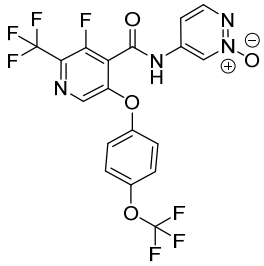
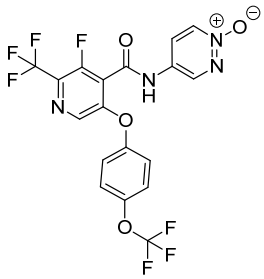
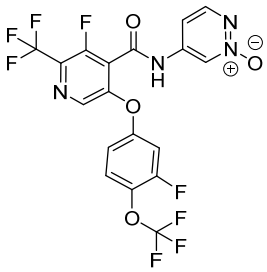
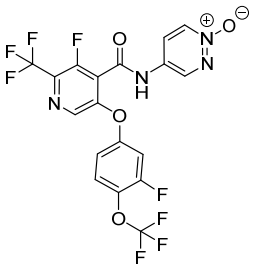
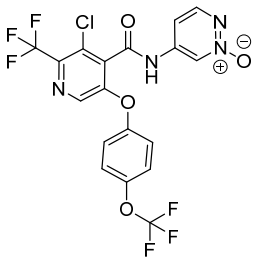
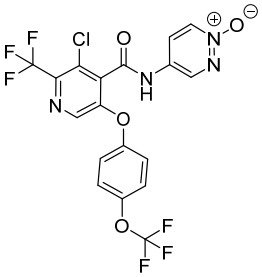
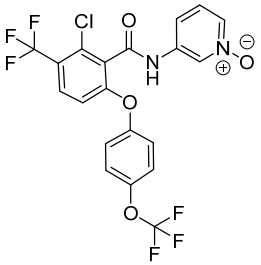
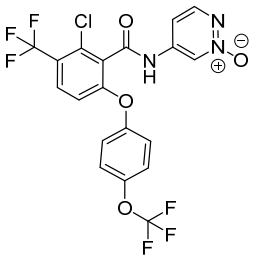
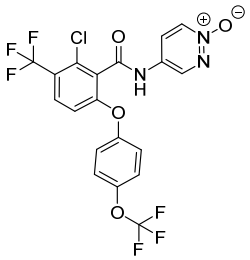
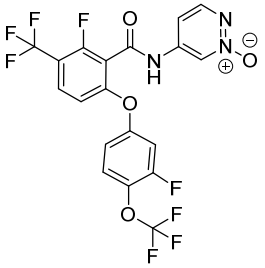
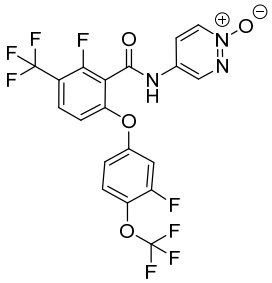
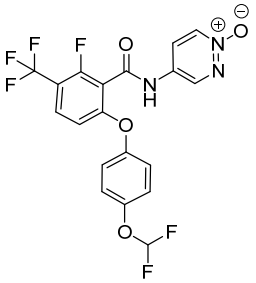
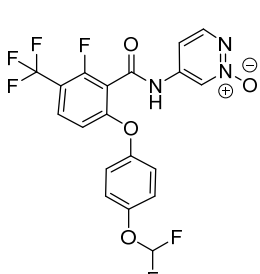
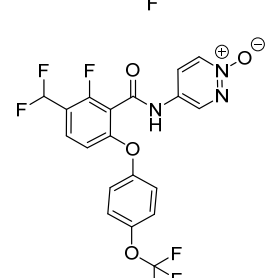
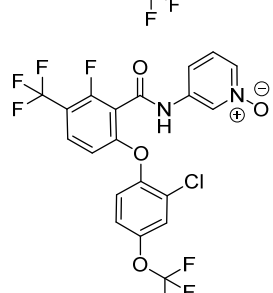
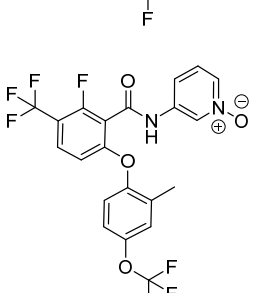
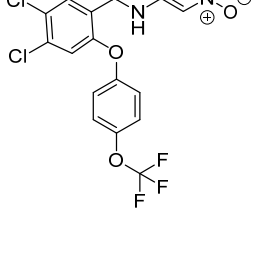
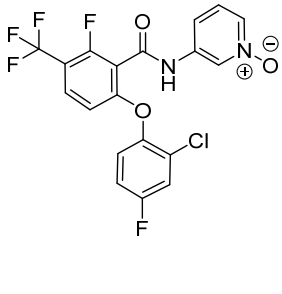
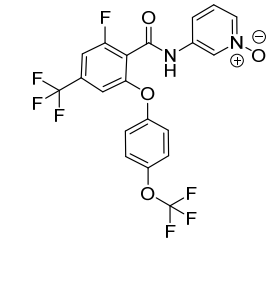
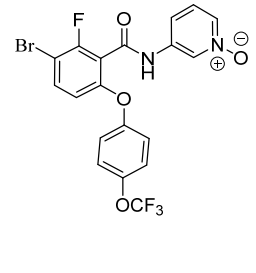
8. The compound as defined in claim 1, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, R_{11} and R_{12} are connected together to form a cyclopropyl, oxetanyl, azetidinyl or cyclopentanonyl.

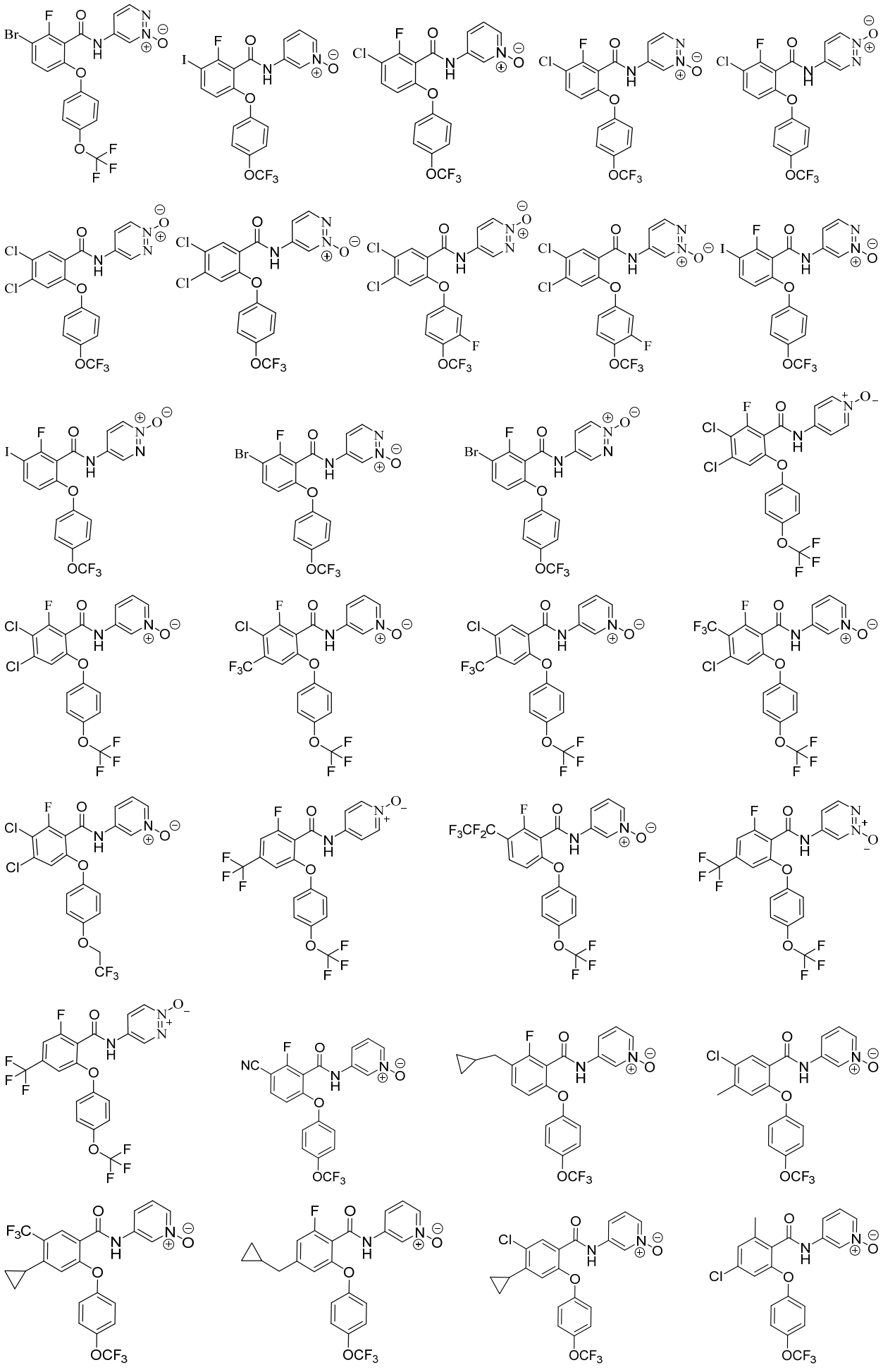
9. The compound as defined in claim 7 or 8, the optical isomer thereof or the pharmaceutically acceptable salt thereof, wherein, L_1 is selected from C(=O), CH_2, NH, $CH(CH_3)$, CHF, CF_2, $CHCHF_2$, $CHCF_3$, ,  and .

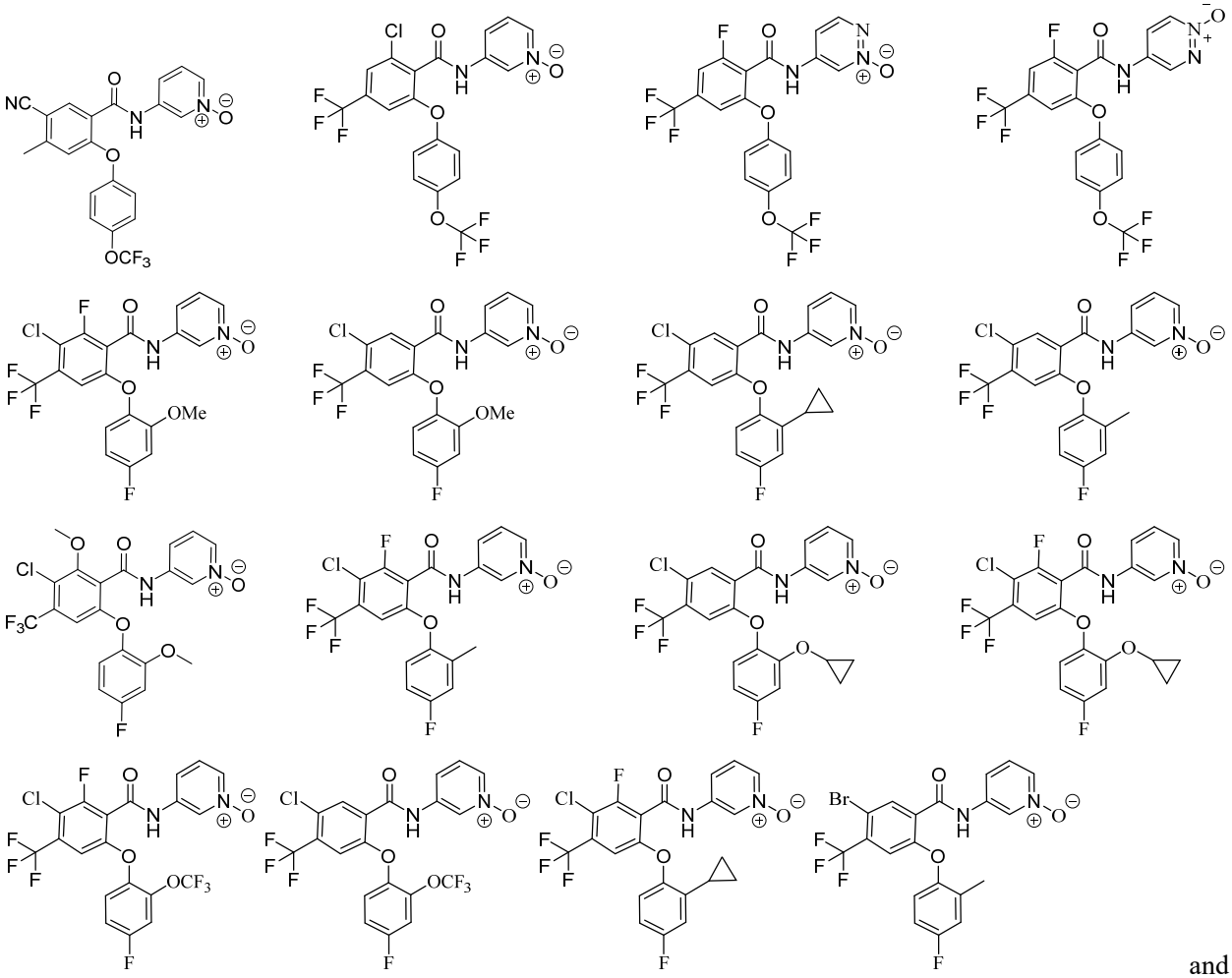
10. A compound as shown in the formula below, an optical isomer thereof or a pharmaceutically acceptable

salt thereof selected from

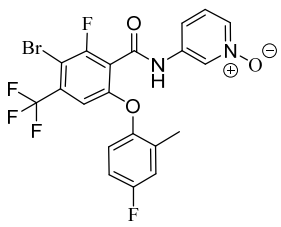




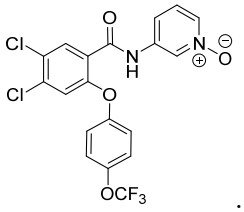


and



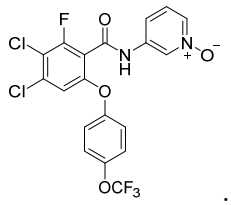
.

11. The compound as defined in claim 1, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



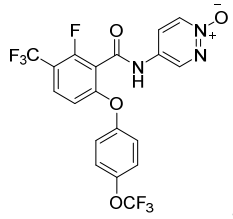
.

12. The compound as defined in claim 1, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



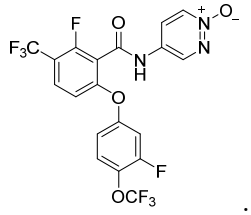
.

13. The compound as defined in claim 1, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



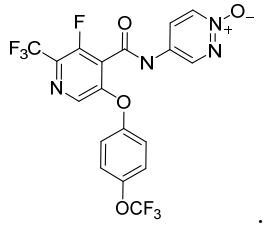
.

14. The compound as defined in claim 1, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



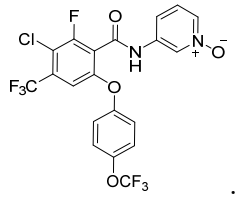
.

15. The compound as defined in claim 1, , an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



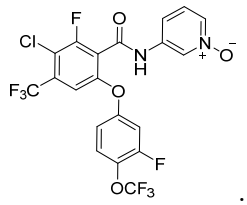
.

16. The compound as defined in claim 1, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



.

17. The compound as defined in claim 1, an optical isomer thereof or a pharmaceutically acceptable salt thereof, wherein, the compound is



.

18. A pharmaceutical composition, wherein, the pharmaceutical composition comprises the compound as defined in any one of claims 1-17, the optical isomer thereof or the pharmaceutically acceptable salt thereof.

19. The pharmaceutical composition as defined in claim 18, wherein, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier or excipient.

20. A use of the compound as defined in any one of claims 1-17, the optical isomer thereof or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition as defined in claim 18 or 19 in the manufacture of a medicament for treating and/or preventing pain or cough, or relieving the severity of pain or cough in an individual.

21. The use as defined in claim 20, wherein, the pain is selected from chronic pain, intestinal pain, neuropathic pain, musculoskeletal pain, acute pain, inflammatory pain, cancer pain, primary pain, postoperative pain, visceral pain, multiple sclerosis, Charcot, Marfan and Down syndrome, incontinence and arrhythmia.