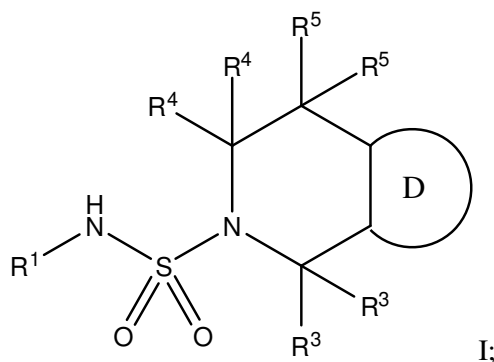


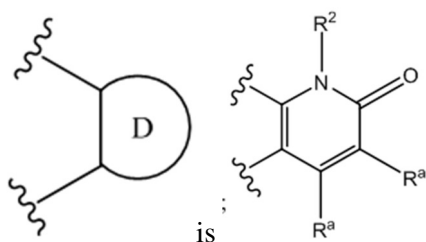
CLAIMS

What is claimed is:

1. A compound of Formula (I), an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof,



Wherein the group:



R^1 is a 5- or 6-membered heteroaryl, wherein the heteroaryl group can have from 1 to 3 heteroatoms independently selected from O, N or S, and the heteroaryl group is substituted with 0, 1, 2, 3, or 4 substituents independently selected from halo, -CN, -C₁₋₆alkyl, haloC₁₋₆alkyl, -OH, -O-C₁₋₆alkyl, -O-haloC₁₋₆alkyl, -C(=O)OR^a, or -(CR^bR^b)_nNR^aR^a;

R^2 is a 5- or 6-membered aryl or heteroaryl, where the heteroaryl group can have from 1 to 3 heteroatoms independently selected from O, N or S, and the aryl or heteroaryl group is optionally substituted with from 1 to 5 R⁶ substituents independently selected from halo, -CN, -C₁₋₆alkyl, haloC₁₋₆alkyl, -OH, -O-C₁₋₆alkyl, -O-haloC₁₋₆alkyl, -(CR^bR^b)_mA, -C₂₋₆alkenyl-A, -C₂₋₆alkynyl-A, or -O(CR^bR^b)_m-A;

each R³ is independently selected from H, -C₁₋₆alkyl;

each R⁴ is independently selected from H, -C₁₋₆alkyl;

each R⁵ is H;

A is a 4 to 9 membered aryl, heteroaryl, or heterocycloalkyl group, or a 3-, 4-, 5-, 6-, 7-, 8-, 9-, or 10- membered cycloalkyl group, where the heteroaryl or heterocycloalkyl group can have from 1 to 3 heteroatoms independently selected from O, N or S;

and the aryl, heteroaryl, heterocycloalkyl, or cycloalkyl group is substituted with 0, 1, 2, 3, or 4 R^7 substituents independently selected from halo, $-NR^aR^a$, $-C_{1-6}alkyl$, $-O-C_{1-6}alkyl$, $-(CR^bR^b)_mOH$, hydroxy $C_{1-6}alkyl$, halo $C_{1-6}alkyl$, $-O-haloC_{1-6}alkyl$, $-CN$, $-C(=O)NR^aR^a$, $-O-(CR^bR^b)_mB$ or $-(CR^bR^b)_mB$;

B is a 5 to 6 membered aryl, heteroaryl, or heterocycloalkyl group, or a 3 to 5 membered cycloalkyl group, where the heteroaryl or heterocycloalkyl group can have from 1 to 3 heteroatoms independently selected from O, N or S; and the aryl, heteroaryl, cycloalkyl or heterocycloalkyl group is substituted with 0, 1, 2, 3, or 4 R^8 substituents independently selected from halo, $-NR^aR^a$, $-C_{1-6}alkyl$, $-OC_{1-6}alkyl$, hydroxy $C_{1-6}alkyl$, $-CF_3$, $-CHF_2$, $-CH_2F$, $-OCF_3$, $-OCHF_2$, $-OCH_2F$, $-CN$ or $-C(=O)NR^aR^a$;

each R^a is independently H, halo, $-CN$, $-NR^cR^c$, $-OH$, $-C_{1-6}alkyl$, $-C_{1-6}haloalkyl$, $-OC_{1-6}haloalkyl$, or $-OC_{1-6}alkyl$;

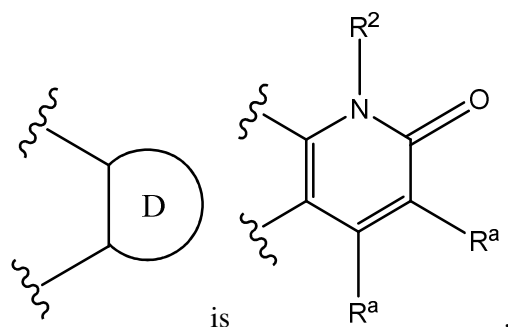
each R^b is independently H, halo, $-CN$, $-NR^cR^c$, $-OH$, $-C_{1-6}alkyl$, $-C_{1-6}haloalkyl$, $-OC_{1-6}haloalkyl$, or $-OC_{1-6}alkyl$;

each R^c is independently H or $-C_{1-6}alkyl$;

each n is independently 0, 1, 2, 3 or 4; and

each m is independently 0.

2. The compound in accordance with claim 1, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein the group



3. The compound in accordance with claim 1 or 2, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R^2 is a 6 membered aryl or a 6 membered heteroaryl group.

4. The compound in accordance with claim 1 or 2, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R^2 is phenyl.

5. The compound in accordance with any one of claims 1-4, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R² is substituted with from 1 to 3 R⁶ substituents independently selected from -OC₁₋₆alkyl, halo, -C₁₋₆alkyl, haloC₁₋₆alkyl, -(CR^bR^b)_m-A, or -C₂₋₆alkynyl-A.

6. The compound in accordance with claim 5, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein in said R⁶ - (CR^bR^b)_m-A group, A is a ring selected from phenyl, pyridyl, or pyrimidinyl, wherein the ring is substituted with 0, 1, 2, 3, or 4 R⁷ substituents independently selected from chloro, fluoro, methyl, methoxy, -CF₃, -CHF₂, -CH₂F, -OCF₃, -OCHF₂, -OCH₂F, -OCH₂CF₃, or -CN; each R^b is independently H or -C₁₋₆alkyl; and m is 0 or 1.

7. The compound in accordance with claim 5, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein in said R⁶ -C₂₋₆alkynyl-A group, A is a C₃₋₈cycloalkyl ring substituted with 0, 1, 2, 3, or 4 R⁷ substituents selected from chloro, fluoro, methyl, methoxy, -CF₃, -CHF₂, -CH₂F, -OCF₃, -OCHF₂, -OCH₂F, or -CN.

8. The compound in accordance with any one of claims 1-7, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R² is phenyl or pyridinyl ring substituted with 3 R⁶ substituents comprising:

- (a) *ortho* to ring D: R⁶ is selected from methyl, methoxy or ethoxy;
- (b) *meta* to ring D: R⁶ is selected from absent, methyl, F, or Cl; and
- (c) *para* to ring D: R⁶ is selected from halo, phenyl ring, or pyridyl ring; wherein each of said phenyl ring or pyridyl ring is substituted with 0, 1, 2, 3, or 4 R⁷ substituents selected from F, Cl, methyl, cyclopropyl, methoxy, ethoxy, -CF₃, -CHF₂, -CH₂F, -OCF₃, -OCHF₂, -OCH₂F, or -CN.

9. The compound in accordance with Claim 8, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein said R² is phenyl ring.

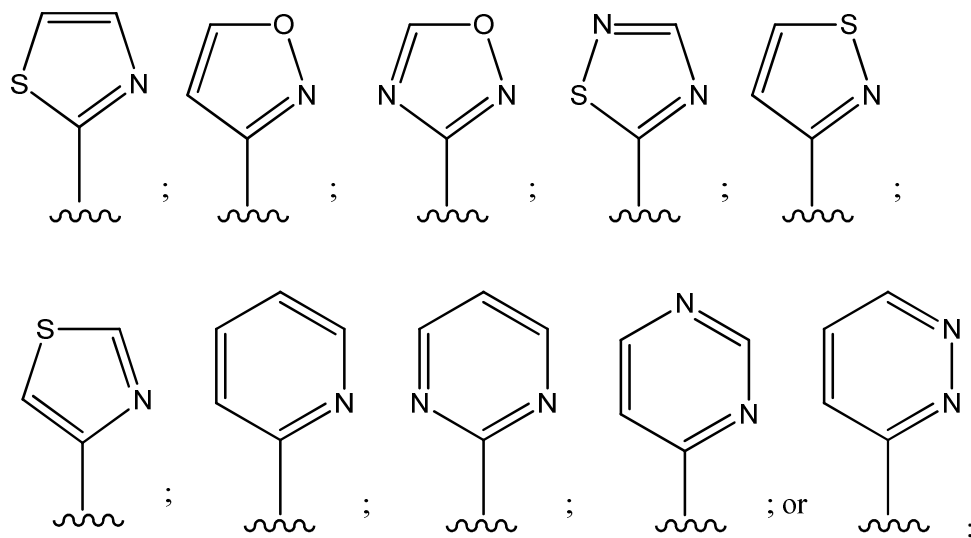
10. The compound in accordance with any one of claims 1-9, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein each of R³, R⁴, and R⁵ is independently selected from H or methyl.

11. The compound in accordance with any one of claims 1-10, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R¹ is a 5 to 6 membered heteroaryl group.

12. The compound in accordance with any one of claims 1-11, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R¹ is isoxazolyl, thiazolyl, thiadiazolyl, pyridazinyl, pyridyl, or pyrimidinyl ring, wherein the

ring is unsubstituted or is substituted with 0, 1, 2, 3, or 4 substituents independently selected from halo or -C₁₋₆alkyl.

13. The compound in accordance with any one of claims 1-12, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, wherein R¹ is:



wherein the ring is unsubstituted or is substituted with 0, 1, 2, 3, or 4 substituents independently selected from halo or -C₁₋₆alkyl.

14. The compound in accordance with any one of claims 1-13, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, selected from:

1-(4'-chloro-2-fluoro-3',5-dimethoxy-4-biphenyl)-2-oxo-N-3-pyridazinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(4'-chloro-2-fluoro-3',5-dimethoxy-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(2-fluoro-5-methoxy-3'-(trifluoromethyl)-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(3'-chloro-2,5'-difluoro-5-methoxy-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(5-fluoro-2-methoxy-4-(2-methoxy-5-(trifluoromethyl)-3-pyridinyl)phenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(4'-chloro-2-fluoro-5-methoxy-3'-methyl-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(4'-chloro-2-fluoro-5-methoxy-3'-methyl-4-biphenyl)-2-oxo-N-2-pyrimidinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

2-oxo-N-3-pyridazinyl-1-(2,3',4'-trifluoro-5-methoxy-4-biphenyl)-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(4'-chloro-2-fluoro-5-methoxy-3'-methyl-4-biphenyl)-2-oxo-N-3-pyridazinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(3'-chloro-2,5'-difluoro-5-methoxy-4-biphenyl)-2-oxo-N-3-pyridazinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(4'-chloro-2-fluoro-5-methoxy-3'-methyl-4-biphenyl)-2-oxo-N-1,3-thiazol-2-yl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(2,3'-difluoro-5-methoxy-5'-(trifluoromethyl)-4-biphenyl)-2-oxo-N-3-pyridazinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(3'-cyclopropyl-2-fluoro-5-methoxy-4-biphenyl)-2-oxo-N-3-pyridazinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(2-fluoro-5-methoxy-3'-(trifluoromethyl)-4-biphenyl)-2-oxo-N-3-pyridazinyl-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

2-oxo-N-3-pyridazinyl-1-(2,3',4',5'-tetrafluoro-5-methoxy-4-biphenyl)-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(2,4'-dichloro-3',5'-dimethoxy-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(2,3'-dichloro-5'-fluoro-5-methoxy-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide;

1-(2-chloro-5-methoxy-3'-(trifluoromethyl)-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide; and

1-(2-fluoro-3',5'-dimethoxy-4'-methyl-4-biphenyl)-N-3-isoxazolyl-2-oxo-1,5,7,8-tetrahydro-1,6-naphthyridine-6(2H)-sulfonamide.

15. The compound in accordance with Claim 14, wherein the compound is a P atropisomer.

16. A pharmaceutical composition comprising the compound in accordance with any one of claims 1 to 15, an enantiomer, diastereomer, atropisomer thereof, or a mixture thereof, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

17. Use of the compound in accordance with any one of claims 1-15, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating pain, cough, or itch, wherein the pain is selected from chronic pain, acute pain, neuropathic pain, pain associated with rheumatoid arthritis, pain associated with osteoarthritis, pain associated with cancer, or pain associated with diabetes; wherein the cough is selected from post viral cough, viral cough, or acute viral cough; and wherein the itch is selected from a) psoriatic pruritis, itch due to hemodialysis, allergic pruritis, and itching caused by skin disorders, systemic disorders, neuropathy, psychogenic factors or a mixture thereof, b) itch caused by allergic reactions, insect bites, hypersensitivity,

inflammatory conditions or injury, c) itch associated with vulvar vestibulitis, d) skin irritation or inflammatory effect from administration of another therapeutic selected from antibiotics, antivirals, or antihistamines, or e) itch due to activation of PAR-2 G-protein coupled receptors.