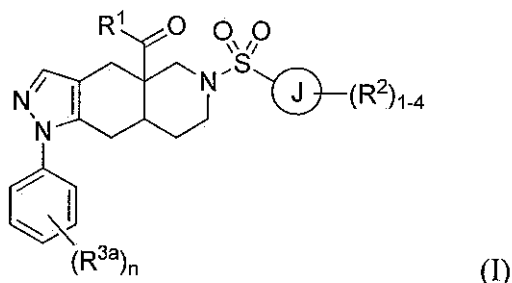


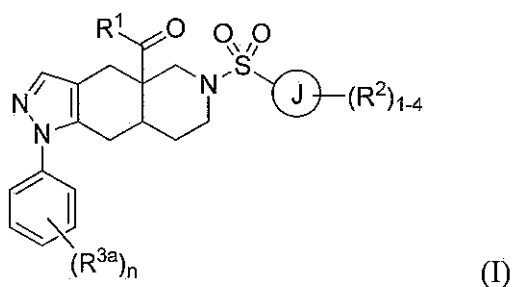
BRIEF SUMMARY

[0004] The present disclosure provides many fused azadecalin compounds. The present disclosure also provides compounds having the formula:



- 5 wherein R¹ of formula I is a heteroaryl ring having from 5 to 6 ring members and from 1 to 4 heteroatoms, which can each independently be N, O, or S, optionally substituted with 1-4 groups, which can each independently be R^{1a}. Each R^{1a} of formula I can independently be hydrogen, C₁₋₆ alkyl, halogen, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, N-oxide, or C₃₋₈ cycloalkyl. Ring J of formula I can be an aryl ring or a heteroaryl ring having from 5 to 6 ring members and
- 10 from 1 to 4 heteroatoms, which can each independently be N, O, or S. Each R² of formula I can independently be hydrogen, C₁₋₆ alkyl, halogen, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₁₋₆ alkyl-C₁₋₆ alkoxy, -CN, -OH, -NR^{2a}R^{2b}, -C(O)R^{2a}, -C(O)OR^{2a}, -C(O)NR^{2a}R^{2b}, -SR^{2a}, -S(O)R^{2a}, -S(O)₂R^{2a}, C₃₋₈ cycloalkyl, or C₃₋₈ heterocycloalkyl having from 1 to 3 heteroatoms wherein each can independently be N, O, or S. Alternatively, two R² groups on adjacent ring
- 15 atoms are combined to form a heterocycloalkyl ring having from 5 to 6 ring members and from 1 to 3 heteroatoms, which can each independently be N, O, or S, wherein the heterocycloalkyl ring is optionally substituted with from 1 to 3 R^{2c} groups. R^{2a}, R^{2b} and R^{2c} of formula I can each independently be hydrogen or C₁₋₆ alkyl. Each R^{3a} of formula I can independently be a halogen. Subscript n of formula I can be an integer from 0 to 3. The compounds of formula I can also be
- 20 the salts and isomers thereof.

[0004a] In one aspect of the present disclosure, there is provided a compound having the formula:



wherein

R^1 is a heteroaryl ring having from 5 to 6 ring members and from 1 to 4 heteroatoms each independently selected from the group consisting of N, O and S, optionally substituted with 1-4 groups each independently selected from R^{1a} ;

each R^{1a} is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, halogen, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, N-oxide, and C_{3-8} cycloalkyl;

ring J is selected from the group consisting of an aryl ring and a heteroaryl ring having from 5 to 6 ring members and from 1 to 4 heteroatoms each independently selected from the group consisting of N, O and S;

each R^2 is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, halogen, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{1-6} alkyl- C_{1-6} alkoxy, -CN, -OH, -NR^{2a}R^{2b}, -C(O)R^{2a}, -C(O)OR^{2a}, -C(O)NR^{2a}R^{2b}, -SR^{2a}, -S(O)R^{2a}, -S(O)₂R^{2a}, C_{3-8} cycloalkyl, and C_{3-8} heterocycloalkyl having from 1 to 3 heteroatoms each independently selected from the group consisting of N, O and S;

alternatively, two R^2 groups on adjacent ring atoms are combined to form a heterocycloalkyl ring having from 5 to 6 ring members and from 1 to 3 heteroatoms each independently selected from the group consisting of N, O and S, wherein the heterocycloalkyl ring is optionally substituted with from 1 to 3 R^{2c} groups;

R^{2a} , R^{2b} and R^{2c} are each independently selected from the group consisting of hydrogen and C_{1-6} alkyl;

each R^{3a} is independently halogen;

subscript n is an integer from 0 to 3;

or salts and isomers thereof.

[0005] In another aspect of the present disclosure, there is provided a pharmaceutical composition including a compound of the present disclosure, and a pharmaceutically acceptable excipient.

5 [0005a] In yet another aspect of the present disclosure, there is provided use of a compound as described herein, for the manufacture of a medicament for modulating a glucocorticoid receptor.

[0005b] In a further aspect of the present disclosure, there is provided use of a compound as described herein, for the manufacture of a medicament for treating a disorder through antagonizing a glucocorticoid receptor.

10 [0005c] In another aspect of the present disclosure, there is provided a compound as described herein, for use in modulating a glucocorticoid receptor.

[0005d] In yet another aspect of the present disclosure, there is provided a compound as described herein, for use in treating a disorder through antagonizing a glucocorticoid receptor.

15 [0006] In some embodiments, the present disclosure provides a method of modulating a glucocorticoid receptor including contacting a glucocorticoid receptor with a compound of the present disclosure, thereby modulating the glucocorticoid receptor.

((4aR,8aS)-1-(4-fluorophenyl)-6-((2-methyl-2H-1,2,3-triazol-4-yl)sulfonyl)-4,4a,5,6,7,8,8a,9-octahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(thiazol-4-yl)methanone,
 ((4aR,8aS)-1-(4-fluorophenyl)-6-((2-isopropyl-2H-1,2,3-triazol-4-yl)sulfonyl)-4,4a,5,6,7,8,8a,9-octahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(thiazol-4-yl)methanone, and
 ((4aR,8aS)-6-((2-ethyl-2H-1,2,3-triazol-4-yl)sulfonyl)-1-(4-fluorophenyl)-4,4a,5,6,7,8,8a,9-octahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(thiazol-4-yl)methanone.

17. A pharmaceutical composition comprising a compound of any one of claims 1 to 16 and a pharmaceutically acceptable excipient.

18. Use of a compound of any one of claims 1 to 16, for the manufacture of a medicament for modulating a glucocorticoid receptor.

19. Use of a compound of any one of claims 1 to 16, for the manufacture of a medicament for treating a disorder through antagonizing a glucocorticoid receptor.

20. The use of claim 19, wherein the disorder is selected from the group consisting of Cushing's Syndrome, obesity, diabetes, cardiovascular disease, hypertension, Syndrome X, depression, anxiety, glaucoma, human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS), neurodegeneration, Alzheimer's disease, Parkinson's disease, Huntington's disease, cognition enhancement, Addison's Disease, osteoporosis, frailty, muscle frailty, inflammatory diseases, osteoarthritis, rheumatoid arthritis, asthma and rhinitis, adrenal function-related ailments, viral infection, immunodeficiency, immunomodulation, autoimmune diseases, allergies, wound healing, compulsive behavior, multi-drug resistance,

addiction, psychosis, anorexia, cachexia, post traumatic stress disorder, postsurgical bone fracture, medical catabolism, major psychotic depression, mild cognitive impairment, dementia, hyperglycemia, central serous retinopathy, alcohol dependence, stress disorders, antipsychotic induced weight gain, delirium, cognitive impairment in depressed patients, cognitive deterioration in individuals with Down's syndrome, psychosis associated with interferon-alpha therapy, chronic pain, pain associated with gastroesophageal reflux disease, postpartum psychosis, postpartum depression, neurological disorders in premature infants, migraine headaches, and cancers such as ovarian, breast and prostate cancer.

21. A compound of any one of claims 1 to 16, for use in modulating a glucocorticoid receptor.

22. A compound of any one of claims 1 to 16, for use in treating a disorder through antagonizing a glucocorticoid receptor.