TITLE OF THE INVENTION

BICYCLOHEPTANE PYRROLIDINE OREXIN RECEPTOR AGONISTS

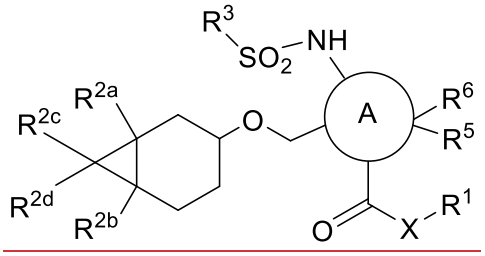
BACKGROUND OF THE INVENTION

The orexins (hypocretins) comprise two neuropeptides produced in the hypothalamus: orexin A (OX-A) (a 33 amino acid peptide) and the orexin B (OX-B) (a 28 amino acid peptide) (Sakurai T. et al., Cell, 1998, 92, 573-585). Orexins regulate states of sleep and wakefulness opening potentially novel therapeutic approaches for narcolepsy, idiopathic hypersomnia, excessive daytime sleepiness, shift work disorder, obstructive sleep apnea and insomnia (Chemelli R.M. et al., Cell, 1999, 98, 437-451). Orexins are found to stimulate food consumption in rats suggesting a physiological role for these peptides as mediators in the central feedback mechanism that regulates feeding behavior (Sakurai T. et al., Cell, 1998, 92, 573-585). Orexins have also been indicated as playing a role in arousal, emotion, energy homeostasis, reward, learning and memory (Peyron, et al., Journal Neurosci., 1998,18(23):9996-100150, Harris, et al., Trends Neurosci., 2006, 29 (10), 571-577). Two orexin receptors have been cloned and characterized in mammals. They belong to the super family of G-protein coupled receptors (Sakurai T. et al., Cell, 1998, 92, 573-585): the orexin-1 receptor (OX or OX1R) is partially selective for OX-A and the orexin-2 receptor (OX2 or OX2R) is capable of binding OX-A as well as OX-B with similar affinity. The physiological actions in which orexins are presumed to participate are thought to be expressed via one or both of OX1 receptor and OX2 receptor as the two subtypes of orexin receptors.

SUMMARY ~~OF THE INVENTION~~

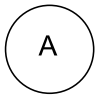
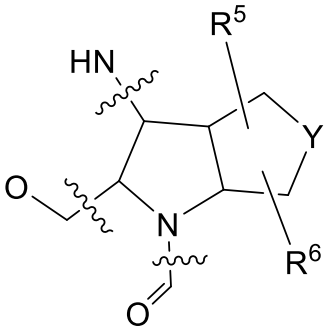
The present ~~invention~~ disclosure is directed to bicyclo[4.1.0]heptane pyrrolidine compounds which are agonists of orexin receptors. The present disclosure ~~invention~~ is also directed to uses of the compounds described herein in the potential treatment or prevention of neurological and psychiatric disorders and diseases in which orexin receptors are involved. The present disclosure ~~invention~~ is also directed to compositions comprising these compounds. The present disclosure ~~invention~~ is also directed to uses of these compositions in the potential prevention or treatment of such diseases in which orexin receptors are involved.

In one aspect, there is provided a compound of the formula I:



I

wherein:

A is  or , wherein n is 0 or 1;

X is -O- or -NH-, or X may be a direct bond to R^1;

Y is O or CH_2;

R^1 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,; and

(3) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^4;

R^{2a} and R^{2b} are selected from:

(1) hydrogen,

(2) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(3) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(4) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4, and

(5) -heteroaryl, where the heteroaryl is selected from: pyridyl, pyrimidinyl, benzothiazolyl, thiazolyl and pyrazinyl, and the heteroaryl is unsubstituted or substituted with one to three substituents independently selected from R^4,

provided that at least one of R^{2a} and R^{2b} is hydrogen;

R^{2c} and R^{2d} are independently selected from:

(1) hydrogen, and

(2) fluoro;

R^3 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(3) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4,

(4) -$NR^{10}R^{11}$, wherein R^{10} and R^{11} are independently selected from:

(a) hydrogen, and

(b) C_{1-6}alkyl, which is unsubstituted or substituted with one to six R^4,

(5) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^4,

(6) -CHF_2, and

(7) -CF_3;

R^4 is independently selected from:

(1) hydroxyl,

(2) halogen,

(3) C_{1-6}alkyl, which is unsubstituted or substituted with one to six substituents independently selected from R^7,

(4) C_{2-4}alkenyl,

(5) C_{2-4}alkynyl,

(6) -C_{3-6}cycloalkyl, which is unsubstituted or substituted with one to six substituents independently selected from R^7,

(7) -O-C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^7,

(8) -O(C=O)-C_{1-6}alkyl,

(9) -NH_2,

(10) -NH-C_{1-6}alkyl,

(11) -NO_2,

(12) phenyl,

(13) -CO_2H,

(14) -SO_2-C_{1-6}alkyl,

(15) -C_{3-5}cycloalkyl(SO_2),

(16) -CN,

(17) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^7,

(18) -CHF_2, and

(19) -CF_3;

R^5 and R^6 are independently selected from:

(1) hydrogen,

(2) C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4, and

(3) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

or R^5 and R^6 are joined together with the carbon atoms to which they are attached to form a -C_{3-6}cycloalkyl ring, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4;

R^7 is independently selected from:

(1) halogen,

(2) C_{1-6}alkyl, which is unsubstituted or substituted with one to six substituents independently selected from halo, phenyl or cycloalkyl,

(3) -CHF_2, and

(4) -CF_3;

or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided a compound which is selected from Methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-phenylbicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(Ex No. 1 & 2)**

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(3-fluorophenyl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**3**) ;

methyl (2R,3S,5R)-2-(((6-(3,5-difluorophenyl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((N,N-dimethylsulfamoyl)amino)-5-methylpyrrolidine-1-carboxylate; (**4**)

methyl (2R,3S,5R)-2-(((6-(4-cyanophenyl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((N,N-dimethylsulfamoyl)amino)-5-methylpyrrolidine-1-carboxylate; (**5**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate ; (**6**)

methyl (2R,3S,5R)-2-(((7,7-difluoro-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((N,N-dimethylsulfamoyl)amino)-5-methylpyrrolidine-1-carboxylate ; (**7**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**8**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyridin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**9**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**10**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**11**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**13**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**14**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**16**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**17**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**19**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**20**)

methyl (2R,3S)-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate;**(21)**;
methyl (2R,3S)-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(24)**
methyl (2R,3S)-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(25)**
isopropyl (2R,3S,5R)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate;**(26)**;
isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(28)**
isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(29)**
methyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(30)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((trifluoromethyl)sulfonamido)pyrrolidine-1-carboxylate; **(31)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((2,2,2-trifluoroethyl)sulfonamido)pyrrolidine-1-carboxylate; **(32)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(propylsulfonamido)pyrrolidine-1-carboxylate; **(33)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((phenylmethyl)sulfonamido)pyrrolidine-1-carboxylate; **(34)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((2-methylpropyl)sulfonamido)pyrrolidine-1-carboxylate; **(35)**
methyl (2R,3S,5R)-3-(ethylsulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(36)**
methyl (2R,3S,5R)-3-((chloromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(37)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((1-methylethyl)sulfonamido)pyrrolidine-1-carboxylate; **(38)**
methyl (2R,3S,5R)-3-(azetidine-1-sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(39)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(oxetane-3-sulfonamido)pyrrolidine-1-carboxylate; **(40)**

methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((1-methylpropyl)sulfonamido)pyrrolidine-1-carboxylate; **(41)**
methyl (2R,3S,5R)-3-(cyclopropanesulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(42)**
methyl (2R,3S,5R)-3-(azetidine-1-sulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(43)**
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((trifluoromethyl)sulfonamido)pyrrolidine-1-carboxylate; **(44)**
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((phenylmethyl)sulfonamido)pyrrolidine-1-carboxylate; **(45)**
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((1-methylethyl)sulfonamido)pyrrolidine-1-carboxylate; **(46)**
methyl (2R,3S,5R)-3-(ethylsulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(47)**
methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(48)**
(3-fluorocyclobutyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(49)**
1,1-difluorobutan-2-yl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(50)**
((1R,2R)-2-fluorocyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(51)**
3,3-difluoropropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(52)**
(1-fluorocyclobutyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(53)**
2-cyclobutyl-2-fluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(54)**

((1R,3S)-2,2-difluoro-3-methylcyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(55)**
(3S,4S)-4-fluorotetrahydrofuran-3-yl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(56)**
(2,2-difluoro-1-methylcyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(57)**
2-fluoropropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(58)**
(2,2-difluorocyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(59)**
2,2-difluorobutyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(60)**
(1-fluorocyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(61)**
2-Fluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(62)**
1,1-Difluoropropan-2-yl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(63)**
2,2-difluoropropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fl uoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(64)**
2,2,2-trifluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(65)**
2,2-difluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(65)**
methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate;(**67**);
methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-5-methyl-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**68**);

methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-5-methyl-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**69**);
methyl (2R,3S,5R)-2-(((6-(5-chloro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(70)**;
methyl (2R,3S,5R)-2-(((6-(4,7-difluorobenzo[d]thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(71)**
methyl (2R,3S,5R)-2-(((6-(5-chloro-4-(trifluoromethyl)pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(72)**
methyl (2R,3S,5R)-2-(((6-(4-(difluoromethyl)-5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(73)**
methyl (2R,3S,5R)-2-(((6-(4-cyclopropyl-5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(74)**
methyl (2R,3S,5R)-2-(((6-(5-(difluoromethoxy)-4-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(75)**
methyl (2R,3S,5R)-2-(((6-(5-fluoro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(76)**
methyl (2R,3S,5R)-2-(((6-(5-fluoro-4-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(77)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((difluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(78)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(79)**
isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((difluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate**;** (**81**)
isopropyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((difluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate**; (82)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(83)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate;**(84)**
methyl (2R,3S,5R)-2-(((6-(5-fluoro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(85)**
methyl (2R,3S,5R)-2-(((6-(5-chloro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(86)**

methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; (**87**)
methyl (2R,3S,5R)-2-(((6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(89)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(90)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(91)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(92)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(93)**
methyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(94)**
isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(95)**
isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(96)**
isopropyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(99)**
isopropyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(100)**
isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(103)**
isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(104)**
isopropyl (2R,3S,5R)-2-(((6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(105)**
isopropyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(107)**
isopropyl (2R,3S,5R)-2-(((6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(108)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(109)**

isopropyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(111)**
methyl (2R,3S,5S)-5-(difluoromethyl)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(112)**
methyl (2R,3S,5S)-5-(difluoromethyl)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(113)**
methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-(difluoromethyl)-3-(ethylsulfonamido)pyrrolidine-1-carboxylate; **(114)**
methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-(difluoromethyl)-3-((fluoromethyl)sulfonamido)pyrrolidine-1-carboxylate; **(115)**
methyl (2R,3S,5S)-3-(cyclopropanesulfonamido)-5-(difluoromethyl)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(116)**
methyl (2R,3S,5S)-5-(difluoromethyl)-3-(ethylsulfonamido)-2-(((6-(5-fluoropyrimidin-2-l)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(117)**
isopropyl (2R,3S,5S)-5-(difluoromethyl)-3-(ethylsulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(118)**
isopropyl (2R,3S,5S)-5-(difluoromethyl)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(119)**
methyl (2R,3S,5S)-5-(difluoromethyl)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((1-methylethyl)sulfonamido)pyrrolidine-1-carboxylate; **(120)**
isopropyl (2R,3S)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(121)**
isopropyl (2R,3S)-3-(cyclopropanesulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(122)**
isopropyl (2R,3S)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((trifluoromethyl)sulfonamido)piperidine-1-carboxylate; **(123)**
isopropyl (2R,3S)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(124)**
isopropyl (2R,3S)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)piperidine-1-carboxylate; **(125)**
isopropyl (2R,3S)-3-(ethylsulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(126)**

methyl (2R,3S,5S)-5-(difluoromethyl)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(127)**

methyl (2R,3S,3aS,6aR)-3-(cyclopropanesulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(128)**

methyl (2R,3S,3aS,6aR)-3-(ethylsulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(129)**

methyl (2R,3S,3aS,6aR)-3-((fluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(130)**

methyl (2R,3S,3aS,6aR)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(131)**

methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-(methoxymethyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(132)**

methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)-5-(trifluoromethyl)pyrrolidine-1-carboxylate; **(133)**

Methyl (2R,3aS,6aS)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)hexahydro-1H-furo[3,4-b]pyrrole-1-carboxylate; **(134)**

methyl (2R,3S,5R)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**135**)

methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**136**)

methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate (**137**)

methyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**140**)

methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**141**)

methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**142**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**145**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**146**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**149**)

isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**150**)

isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**151**)

isopropyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**154**)

methyl (2R,3S,5R)-5-methyl-2-((((1R,3R,6S)-6-(5-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**155**)

methyl (2R,3S,5R)-5-methyl-2-((((1S,3S,6R)-6-(5-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**156**)

methyl (2R,3S,5R)-5-methyl-2-(((6-(5-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**159**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**160**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**161**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**164**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**165**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**166**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**167**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**169**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**170**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**171**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**174**)

methyl (2R,3S,3aS,6aR)-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; (**175**)

methyl (2R,3S)-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**176**)

methyl (2R,3S)-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**177**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**180**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**181**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**184**)

methyl (2R,3S)-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**185**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**186**)

methyl (2R,3S,5R)-2-(((6-(5-cyanopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**188**)

methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-cyanopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate (**190**)

or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided a pharmaceutical composition which comprises an inert carrier and a compound as provided herein or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided a compound as provided herein or a pharmaceutically acceptable salt thereof for use in therapy.

In another aspect, there is provided a compound as provided herein, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of a sleep disorder.

In another aspect, there is provided use of the compound as provided herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of narcolepsy.

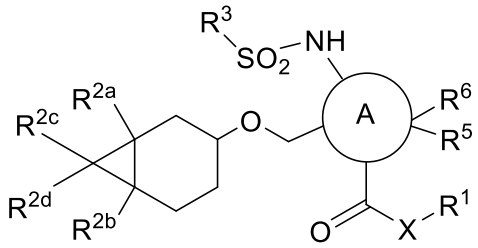
In another aspect, there is provided use of the compound as provided herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of hypersomnia.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to compounds of the formula I:

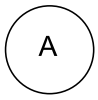
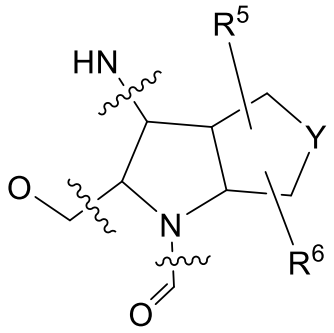
WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

A is  or , wherein n is 0 or 1;

X is -O- or -NH-, or X may be a direct bond to R^1;

Y is O or CH_2;

R^1 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,; and

(3) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^4;

R^{2a} and R^{2b} are selected from:

(1) hydrogen,

(2) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(3) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(4) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4, and

(5) -heteroaryl, where the heteroaryl is selected from: pyridyl, pyrimidinyl, benzothiazolyl, thiazolyl and pyrazinyl, and the heteroaryl is unsubstituted or substituted with one to three substituents independently selected from R^4,

~~Provided~~ provided that at least one of R^{2a} and R^{2b} is hydrogen;

R^{2c} and R^{2d} are independently selected from:

(1) hydrogen, and

(2) fluoro;

R^3 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(3) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4,

(4) -$NR^{10}R^{11}$, wherein R^{10} and R^{11} are independently selected from:

(a) hydrogen, and

(b) C_{1-6}alkyl, which is unsubstituted or substituted with one to six R^4,

(5) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^4,

(6) -CHF_2, and

(7) -CF_3;

R^4 is independently selected from:

(1) hydroxyl,

(2) halogen,

(3) C_{1-6}alkyl, which is unsubstituted or substituted with one to six substituents independently selected from R^7,

(4) C_{2-4}alkenyl,

(5) C_{2-4}alkynyl,

(6) -C_{3-6}cycloalkyl, which is unsubstituted or substituted with one to six substituents independently selected from R^7,

(7) -O-C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^7,

(8) -O(C=O)-C_{1-6}alkyl,

(9) -NH_2,

(10) -NH-C_{1-6}alkyl,

(11) -NO_2,

(12) phenyl,

(13) -CO_2H,

(14) -SO_2-C_{1-6}alkyl,

(15) -C_{3-5}cycloalkyl(SO_2),

(16) -CN,

(17) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^7,

(18) -CHF_2, and

(19) -CF_3;

R^5 and R^6 are independently selected from:

(1) hydrogen,

(2) C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4, and

(3) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

or R^5 and R^6 are joined together with the carbon atoms to which they are attached to form a -C_{3-6}cycloalkyl ring, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4;

R^7 is independently selected from:

(1) halogen,

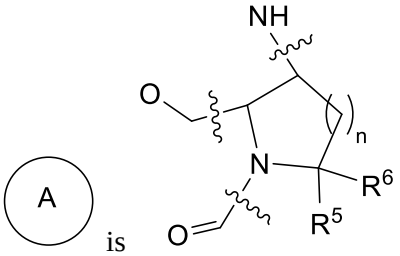
(2) C_{1-6}alkyl, which is unsubstituted or substituted with one to six substituents independently selected from halo, phenyl or cycloalkyl,

(3) -CHF_2, and

(4) -CF_3;

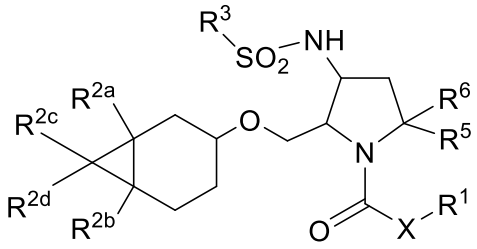
or a pharmaceutically acceptable salt thereof.

2. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein

A is 

, wherein n is 0 or 1.

3. The compound of any Claim 1 or 2, according to formula IA:



IA

wherein:

X is -O- or -NH-, or X may be a direct bond to R^1;

R^1 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4, and

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4;

R^{2a} and R^{2b} are selected from:

(1) hydrogen,

(2) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(3) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(4) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4, and

(5) -heteroaryl, where the heteroaryl is selected from: pyridyl, pyrimidinyl, and pyrazinyl, and the heteroaryl is unsubstituted or substituted with one to three substituents independently selected from R^4;

Provided that at least one of R^{2a} and R^{2b} is hydrogen;

R^{2c} and R^{2d} are independently selected from:

(1) hydrogen, and

(2) fluoro;

R^3 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

(3) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4, and

(4) -$NR^{10}R^{11}$, wherein R^{10} and R^{11} are independently selected from:

(a) hydrogen, and

(b) C_{1-6}alkyl, which is unsubstituted or substituted with one to six R^4;

R^4 is independently selected from:

(1) hydroxyl,

(2) halogen,

(3) C_{1-6}alkyl, which is unsubstituted or substituted with one to six substituents independently selected from R^7,

(4) C_{2-4}alkenyl,

(5) C_{2-4}alkynyl,

(6) -C_{3-6}cycloalkyl, which is unsubstituted or substituted with one to six substituents independently selected from R^7,

(7) -O-C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^7,

(8) -O(C=O)-C_{1-6}alkyl,

(9) -NH_2,

(10) -NH-C_{1-6}alkyl,

(11) -NO_2,

(12) phenyl,

(13) -CO_2H,

(14) -SO_2-C_{1-6}alkyl,

(15) -C_{3-5}cycloalkyl(SO_2),

(16) -CN,

(17) -heterocyclyl, where the heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from R^7,

(18) -CHF_2, and

(19) -CF_3;

R^5 and R^6 are independently selected from:

(1) hydrogen,

(2) C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4, and

(3) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4,

or R^5 and R^6 are joined together with the carbon atoms to which they are attached to form a -C_{3-6}cycloalkyl ring, where the cycloalkyl is unsubstituted or substituted with one to six substituents independently selected from R^4;

R^7 is independently selected from:

(1) halogen,

(2) C_{1-6}alkyl, which is unsubstituted or substituted with one to six substituents independently selected from halo, phenyl or cycloalkyl,

(3) -CHF_2, and

(4) -CF_3;

or a pharmaceutically acceptable salt thereof.

4. The compound of any of Claims 1-3 or a pharmaceutically acceptable salt thereof wherein R^1 is selected from:

(1) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to three substituents independently selected from hydroxyl, halo, -C_{3-6}cycloalkyl, -O-C_{1-6}alkyl, -O(C=O)-C_{1-6}alkyl, and

(2) -C_{3-6}cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from R^4.

5. The compound any of Claims 1-4 or a pharmaceutically acceptable salt thereof wherein R^{2a} and R^{2b} are selected from:

(1) hydrogen,

(2) -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to three fluoro,

(3) phenyl, which is unsubstituted or substituted with one to three fluoro, -CN, or -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to three fluoro, and

(4) heteroaryl, where the heteroaryl is selected from: pyridyl, pyrimidinyl, benzothiazolyl, thiazolyl and pyrazinyl, and the heteroaryl is unsubstituted or substituted with one to three substituents selected from halo, -C_{3-6}cycloalkyl, -O-C_{1-6}alkyl, CN, or -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to three fluoro;

Provided that at least one of R^{2a} and R^{2b} is hydrogen.

6. The compound of any of Claims 1-5 or a pharmaceutically acceptable salt thereof wherein R^{2a} and R^{2b} are selected from:

(1) hydrogen,

(2) $-CH_2(CH_3)_2$,

(3) $-CF_3$,

(4) $-CH_2CHF_2$,

(5) $-CH_2CF_3$,

(6) pyridyl,

(7) pyrimidinyl,

(8) pyrazinyl,

(9) phenyl,

(10) benzothiazolyl, and

(11) thiazolyl;

Wherein said pyridyl, pyrimidinyl, pyrazinyl, phenyl, benzothiazolyl or thiazolyl is unsubstituted or substituted with halo, $-C_{3-6}$cycloalkyl, $-O-C_{1-6}$alkyl, CN, or $-C_{1-6}$alkyl, where the alkyl is unsubstituted or substituted with one to three fluoro;

Provided that at least one of R^{2a} and R^{2b} is hydrogen.

7. The compound of any of Claims 1-6 or a pharmaceutically acceptable salt thereof wherein R^3 is selected from:

(1) $-C_{1-6}$alkyl, where the alkyl is unsubstituted or substituted with one to four substituents independently selected from R^4,

(2) $-C_{3-6}$cycloalkyl, where the cycloalkyl is unsubstituted or substituted with one to four substituents independently selected from R^4,

(3) -phenyl, where the phenyl is unsubstituted or substituted with one to three substituents independently selected from R^4,

(4) $-NR^{10}R^{11}$, wherein R^{10} and R^{11} are independently selected from:

(a) hydrogen, and

(b) C_{1-6}alkyl, which is unsubstituted or substituted with one to four R^4,

(5) -heterocyclyl, where the heterocyclyl is azetidinyl or oxetanyl and is unsubstituted or substituted with one to three substituents independently selected from R^4,

(6) $-CHF_2$, and

(7) $-CF_3$.

8. The compound of any of Claims 1-7 or a pharmaceutically acceptable salt thereof wherein R^3 is -C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to three fluoro.

9. The compound of any of Claims 1-8 or a pharmaceutically acceptable salt thereof wherein R^5 and R^6 are independently selected from:

(1) hydrogen,
(2) methyl,
(3) ethyl,
(4) -CHF_2,
(5) -CF_3,
(6) -CH_2OH,
(7) -CH_2OCH_3, and
(8) cyclopropyl.

10. The compound of any of Claims 1-9 or a pharmaceutically acceptable salt thereof wherein R^5 is C_{1-6}alkyl, where the alkyl is unsubstituted or substituted with one to six substituents independently selected from R^4, and R^6 is hydrogen.

11. A compound which is selected from
Methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-phenylbicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(Ex No. 1 & 2)**
methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(3-fluorophenyl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**3)** ;
methyl (2R,3S,5R)-2-(((6-(3,5-difluorophenyl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((N,N-dimethylsulfamoyl)amino)-5-methylpyrrolidine-1-carboxylate; (**4)**
methyl (2R,3S,5R)-2-(((6-(4-cyanophenyl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((N,N-dimethylsulfamoyl)amino)-5-methylpyrrolidine-1-carboxylate; (**5)**
methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate ; (**6)**
methyl (2R,3S,5R)-2-(((7,7-difluoro-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((N,N-dimethylsulfamoyl)amino)-5-methylpyrrolidine-1-carboxylate ; (**7)**

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**8)**

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyridin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**9)**

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**10)**

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**11)**

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**13)**

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrazin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**14)**

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**16)**

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**17)**

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**19**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**20**)

methyl (2R,3S)-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate;(**21**);

methyl (2R,3S)-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**24**)

methyl (2R,3S)-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**25**)

isopropyl (2R,3S,5R)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate;(**26**);

isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**28**)

isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**29**)

methyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(30)**

methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((trifluoromethyl)sulfonamido)pyrrolidine-1-carboxylate; **(31)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((2,2,2-trifluoroethyl)sulfonamido)pyrrolidine-1-carboxylate; **(32)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(propylsulfonamido)pyrrolidine-1-carboxylate; **(33)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((phenylmethyl)sulfonamido)pyrrolidine-1-carboxylate; **(34)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((2-methylpropyl)sulfonamido)pyrrolidine-1-carboxylate; **(35)**
methyl (2R,3S,5R)-3-(ethylsulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(36)**
methyl (2R,3S,5R)-3-((chloromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(37)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((1-methylethyl)sulfonamido)pyrrolidine-1-carboxylate; **(38)**
methyl (2R,3S,5R)-3-(azetidine-1-sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(39)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(oxetane-3-sulfonamido)pyrrolidine-1-carboxylate; **(40)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((1-methylpropyl)sulfonamido)pyrrolidine-1-carboxylate; **(41)**
methyl (2R,3S,5R)-3-(cyclopropanesulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(42)**
methyl (2R,3S,5R)-3-(azetidine-1-sulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(43)**
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((trifluoromethyl)sulfonamido)pyrrolidine-1-carboxylate; **(44)**
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((phenylmethyl)sulfonamido)pyrrolidine-1-carboxylate; **(45)**
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-((1-methylethyl)sulfonamido)pyrrolidine-1-carboxylate; **(46)**
methyl (2R,3S,5R)-3-(ethylsulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(47)**

methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(48)**
(3-fluorocyclobutyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(49)**
1,1-difluorobutan-2-yl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(50)**
((1R,2R)-2-fluorocyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(51)**
3,3-difluoropropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(52)**
(1-fluorocyclobutyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(53)**
2-cyclobutyl-2-fluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(54)**
((1R,3S)-2,2-difluoro-3-methylcyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(55)**
(3S,4S)-4-fluorotetrahydrofuran-3-yl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(56)**
(2,2-difluoro-1-methylcyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(57)**
2-fluoropropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(58)**
(2,2-difluorocyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(59)**

2,2-difluorobutyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(60)**
(1-fluorocyclopropyl)methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(61)**
2-Fluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(62)**
1,1-Difluoropropan-2-yl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(63)**
2,2-difluoropropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fl uoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(64)**
2,2,2-trifluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(65)**
2,2-difluoroethyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(65)**
methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate;(**67**);
methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-5-methyl-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**68**);
methyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-5-methyl-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**69**);
methyl (2R,3S,5R)-2-(((6-(5-chloro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(70)**;
methyl (2R,3S,5R)-2-(((6-(4,7-difluorobenzo[d]thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(71)**
methyl (2R,3S,5R)-2-(((6-(5-chloro-4-(trifluoromethyl)pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(72)**
methyl (2R,3S,5R)-2-(((6-(4-(difluoromethyl)-5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(73)**
methyl (2R,3S,5R)-2-(((6-(4-cyclopropyl-5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(74)**
methyl (2R,3S,5R)-2-(((6-(5-(difluoromethoxy)-4-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(75)**

methyl (2R,3S,5R)-2-(((6-(5-fluoro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(76)**
methyl (2R,3S,5R)-2-(((6-(5-fluoro-4-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(77)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((difluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(78)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; (**79**)
isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((difluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate**;** (**81**)
isopropyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((difluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate**; (82)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; (**83)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate;(**84)**
methyl (2R,3S,5R)-2-(((6-(5-fluoro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(85)**
methyl (2R,3S,5R)-2-(((6-(5-chloro-4-methoxypyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(86)**
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; (**87**)
methyl (2R,3S,5R)-2-(((6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(89)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(90)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(91)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(92)**
isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(93)**
methyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(94)**

isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(95)**

isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(96)**

isopropyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(99)**

isopropyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(100)**

isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(103)**

isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(104)**

isopropyl (2R,3S,5R)-2-(((6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(105)**

isopropyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(107)**

isopropyl (2R,3S,5R)-2-(((6-(5-bromopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((fluoromethyl)sulfonamido)-5-methylpyrrolidine-1-carboxylate; **(108)**

isopropyl (2R,3S,5R)-3-((difluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(109)**

isopropyl (2R,3S,5R)-3-((fluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; **(111)**

methyl (2R,3S,5S)-5-(difluoromethyl)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(112)**

methyl (2R,3S,5S)-5-(difluoromethyl)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(113)**

methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-(difluoromethyl)-3-(ethylsulfonamido)pyrrolidine-1-carboxylate; **(114)**

methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-(difluoromethyl)-3-((fluoromethyl)sulfonamido)pyrrolidine-1-carboxylate; **(115)**

methyl (2R,3S,5S)-3-(cyclopropanesulfonamido)-5-(difluoromethyl)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(116)**

methyl (2R,3S,5S)-5-(difluoromethyl)-3-(ethylsulfonamido)-2-(((6-(5-fluoropyrimidin-2-l)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(117)**

isopropyl (2R,3S,5S)-5-(difluoromethyl)-3-(ethylsulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; **(118)**

isopropyl (2R,3S,5S)-5-(difluoromethyl)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(119)**

methyl (2R,3S,5S)-5-(difluoromethyl)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((1-methylethyl)sulfonamido)pyrrolidine-1-carboxylate; **(120)**

isopropyl (2R,3S)-3-((difluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(121)**

isopropyl (2R,3S)-3-(cyclopropanesulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(122)**

isopropyl (2R,3S)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-((trifluoromethyl)sulfonamido)piperidine-1-carboxylate; **(123)**

isopropyl (2R,3S)-3-((fluoromethyl)sulfonamido)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(124)**

isopropyl (2R,3S)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)piperidine-1-carboxylate; **(125)**

isopropyl (2R,3S)-3-(ethylsulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)piperidine-1-carboxylate; **(126)**

methyl (2R,3S,5S)-5-(difluoromethyl)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(127)**

methyl (2R,3S,3aS,6aR)-3-(cyclopropanesulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(128)**

methyl (2R,3S,3aS,6aR)-3-(ethylsulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(129)**

methyl (2R,3S,3aS,6aR)-3-((fluoromethyl)sulfonamido)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(130)**

methyl (2R,3S,3aS,6aR)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; **(131)**
methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-(methoxymethyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; **(132)**
methyl (2R,3S,5S)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)-5-(trifluoromethyl)pyrrolidine-1-carboxylate; **(133)**
Methyl (2R,3aS,6aS)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)hexahydro-1H-furo[3,4-b]pyrrole-1-carboxylate; **(134)**
methyl (2R,3S,5R)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**135**)
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**136**)
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate (**137**)
methyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**140**)
methyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**141**)
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**142**)
methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**145**)
methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**146**)
methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(thiazol-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**149**)
isopropyl (2R,3S,5R)-2-((((1R,3R,6S)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**150**)
isopropyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**151**)
isopropyl (2R,3S,5R)-2-(((6-(5-chloropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**154**)
methyl (2R,3S,5R)-5-methyl-2-((((1R,3R,6S)-6-(5-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**155**)

methyl (2R,3S,5R)-5-methyl-2-((((1S,3S,6R)-6-(5-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**156**)

methyl (2R,3S,5R)-5-methyl-2-(((6-(5-methylpyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**159**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**160**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**161**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**164**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1R,3R,6S)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**165**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-((((1S,3S,6R)-6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**166**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**167**)

methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-2-(((6-(5-fluoropyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methylpyrrolidine-1-carboxylate; (**169**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**170**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**171**)

isopropyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**174**)

methyl (2R,3S,3aS,6aR)-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)hexahydrocyclopenta[b]pyrrole-1(2H)-carboxylate; (**175**)

methyl (2R,3S)-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**176**)

methyl (2R,3S)-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**177**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1R,3R,6S)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**180**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-((((1S,3S,6R)-6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**181**)

methyl (2R,3S,5R)-5-methyl-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**184**)
methyl (2R,3S)-3-(methylsulfonamido)-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**185**)
methyl (2R,3S,5R)-3-((N,N-dimethylsulfamoyl)amino)-5-methyl-2-(((6-(pyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)pyrrolidine-1-carboxylate; (**186)**
methyl (2R,3S,5R)-2-(((6-(5-cyanopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate; (**188**)
methyl (2R,3S,5R)-2-((((1S,3S,6R)-6-(5-cyanopyrimidin-2-yl)bicyclo[4.1.0]heptan-3-yl)oxy)methyl)-5-methyl-3-(methylsulfonamido)pyrrolidine-1-carboxylate (**190**)
or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition which comprises an inert carrier and a compound of any of Claims 1-11 or a pharmaceutically acceptable salt thereof.

13. A compound of any of Claims 1-11 or a pharmaceutically acceptable salt thereof for use in therapy.

14. A compound of any of Claims 1-11, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of a sleep disorder.

15. Use of ~~A method for treating narcolepsy in a mammalian subject which comprises administering to the patient an effective amount of~~ the compound of any of Claims 1-11 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of narcolepsy.

16. Use of ~~A method for treating hypersomnia in a mammalian subject which comprises administering to the patient an effective amount of~~ the compound of any of Claims 1-11 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of hypersomnia.