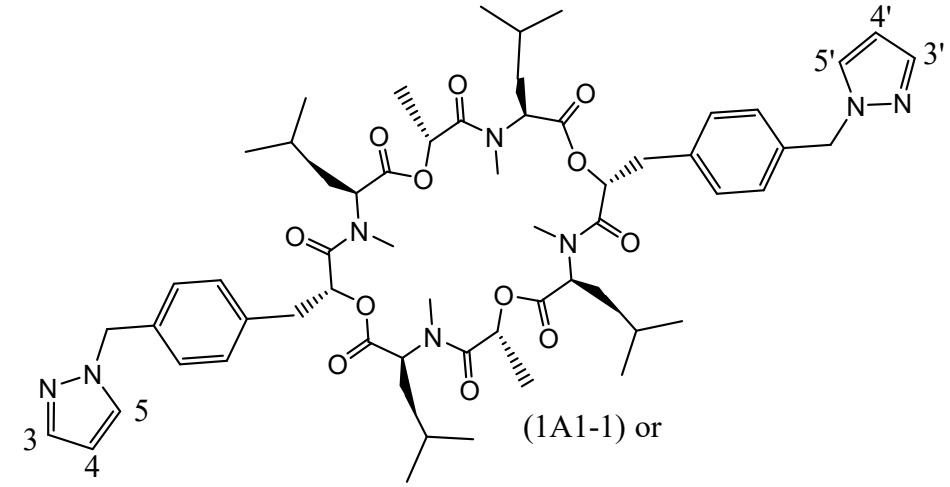
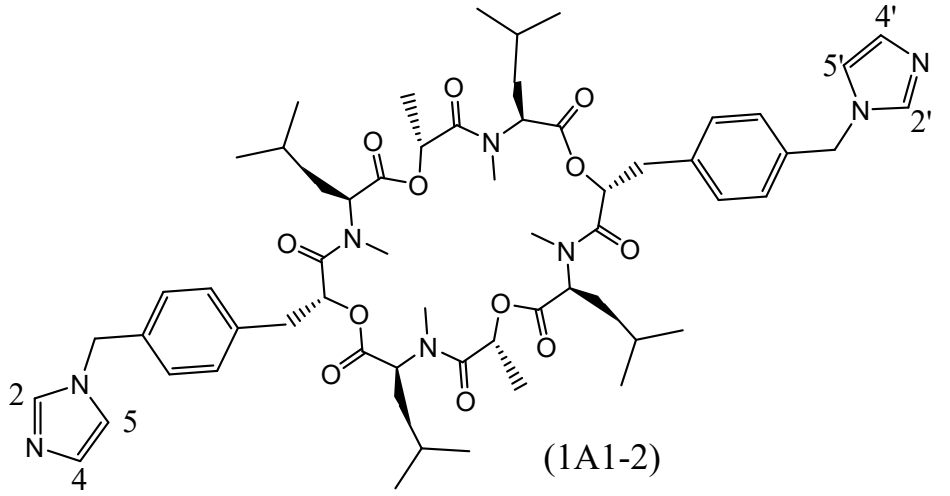
Claims

1. A compound of Formula (1A1-1) or Formula (1A1-2)



(1A1-1) or



(1A1-2)

wherein the pyrazole and imidazole heteroaryl moieties are each independently and separately optionally substituted with at least one substituent selected from C_1-C_6alkyl, halo, cyano, C_1-C_6haloalkyl, C_3-C_6cycloalkyl optionally substituted with at least one substituent selected from fluoro, chloro, methyl, and methoxy; C_1-C_6alkoxy, phenyl optionally substituted with at least one substituent selected from halo and methoxy; -C_1-cyclopropyl, and C_2-C_6alkynl optionally substituted with cyclopropyl or phenyl; stereoisomers thereof, and veterinary acceptable salts thereof.

2. A compound of Claim 1 that is a Formula (1A1-1) compound, stereoisomers thereof, and veterinary acceptable salts thereof.

3. A compound of Claim 2 that is a Formula (1A1-1) compound described in Table 1b, stereoisomers thereof, and veterinary acceptable salts thereof.

4. A compound of Claim 3 wherein each pyrazole is independently and separately optionally substituted with at least one substituent selected from methyl, ethyl, propyl, isopropyl, t-butyl, isobutyl, sec-butyl, cyano, bromo, fluoro, chloro, iodo, $-CH_2F$, $-CHF_2$, $-CF_3$; cyclopropyl, cylobutyl, cyclopentyl, each optionally substituted with at least substituent selected from fluoro, chloro, methyl, and methoxy; methoxy, ethoxy, isopropoxy, isobutoxy; phenyl optionanlly substituted with at least one substituent selected from halo and methoxy; C_2-C_6alkynl optionally substituted with cyclopropyl or phenyl; pyrrole optionally substituted with at least one substituent selected from cyano and methyl.

5. A compound of Claim 4 that is a compound selected from:
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis({4-[(3,5-dicyclopropyl-1H-pyrazol-1-yl)methyl]phenyl}methyl)-4,10,12,16,22,24-hexamethyl-3,9,15,21-tetrakis(2-methylpropyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis[(4-{[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]methyl}phenyl)methyl]-4,10,12,16,22,24-hexamethyl-3,9,15,21-tetrakis(2-methylpropyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-chloro-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-iodo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;

(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-chloro-3,5-dimethyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((3-phenyl-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((3-(trifluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((3,5-bis(difluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((3-chloro-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-cyclopropyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((4-(3-methylbut-1-yn-1-yl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-(cyclopropylethynyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;

(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-(but-1-yn-1-yl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((5-isopropyl-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(tert-butyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((5-phenyl-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-cyclobutyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((5-(4-methoxyphenyl)-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((3-isopropoxy-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(4-chlorophenyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-cyclopentyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;

(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-(2-(4-ethoxy-1H-pyrazol-1-yl)propan-2-yl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-isobutoxy-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-ethoxy-3-phenyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(4-((5-ethyl-3-methyl-1H-pyrazol-1-yl)methyl)benzyl)-18-(4-((3-ethyl-5-methyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(cyclopropylmethyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((5-isobutyl-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(sec-butyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(1-fluorocyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(2,2-difluorocyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-

1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(1-chlorocyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((5-(1-methylcyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((5-(2-methylcyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
((3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis[[4-[(4-ethoxypyrazol-1-yl)methyl]phenyl]methyl]-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetrazacyclotetracosane-2,5,8,11,14,17,20,23-octaone);
((3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis[[4-(pyrazol-1-ylmethyl)phenyl]methyl]-1,7,13,19-tetraoxa-4,10,16,22-tetrazacyclotetracosane-2,5,8,11,14,17,20,23-octaone); and
((3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(difluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone);
stereoisomers thereof, and veterinary acceptable salts thereof.

6. A composition comprising a compound of any one of the preceding Claims, and further comprising a veterinary acceptable excipient.

7. The composition of Claim 6, further comprising at least one additional antiparasitic agent.

8. Use of an effective amount of a compound from any one of Claims 1-5 in the manufacture of a medicament for treating a parasitic infection in an animal in need thereof, wherein the said medicament is to be administered, and wherein the parasitic infection is heartworm.

9. The use of Claim 8 wherein the effective amount of the compound is to be administered to the animal in need thereof by oral, injectable, or topical administration.

10. The use of Claim 9 wherein the animal is canine.

11. Use of a compound of any one of Claims 1-5 to prepare a medicament for treating an endoparasitic infection in an animal in need thereof; wherein said endoparasitic infection is heartworm infection and the animal is canine.

12. A compound selected from the group consisting of:
1-(4-(((2R,5S,8R,11S,14R,17S,20R,23S)-14-(4-((4-bromo-3-cyano-1H-pyrazol-1-yl)methyl)benzyl)-5,11,17,23-tetraisobutyl-4,8,10,16,20,22-hexamethyl-3,6,9,12,15,18,21,24-octaoxo-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2-yl)methyl)benzyl)-1H-pyrazole-3,5-dicarbonitrile;
1-(4-(((2R,5S,8R,11S,14R,17S,20R,23S)-5,11,17,23-tetraisobutyl-4,8,10,16,20,22-hexamethyl-3,6,9,12,15,18,21,24-octaoxo-14-(4-((5-phenyl-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2-yl)methyl)benzyl)-1H-pyrazole-3,5-dicarbonitrile;
1-(4-(((2R,5S,8R,11S,14R,17S,20R,23S)-14-(4-((3,5-dicyclopropyl-1H-pyrazol-1-yl)methyl)benzyl)-5,11,17,23-tetraisobutyl-4,8,10,16,20,22-hexamethyl-3,6,9,12,15,18,21,24-octaoxo-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2-yl)methyl)benzyl)-1H-pyrazole-3,5-dicarbonitrile;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(4-((4-iodo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-18-(4-((4-methyl-1H-

pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12-(4-((3-(trifluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-24-(4-((5-(trifluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(4-((3-bromo-1H-pyrazol-1-yl)methyl)benzyl)-18-(4-((5-bromo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(4-((3-cyclopentyl-1H-pyrazol-1-yl)methyl)benzyl)-18-(4-((5-cyclopentyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis({4-[(3,5-dicyclopropyl-1H-pyrazol-1-yl)methyl]phenyl}methyl)-4,10,12,16,22,24-hexamethyl-3,9,15,21-tetrakis(2-methylpropyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-chloro-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-iodo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((3-(trifluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((3,5-bis(difluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-

1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((3-chloro-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-cyclopropyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-(cyclopropylethynyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((5-isopropyl-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(tert-butyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((5-phenyl-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-cyclobutyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((5-(4-methoxyphenyl)-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((3-isopropoxy-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-

1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-(2-(4-ethoxy-1H-pyrazol-1-yl)propan-2-yl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-isobutoxy-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(4-((5-ethyl-3-methyl-1H-pyrazol-1-yl)methyl)benzyl)-18-(4-((3-ethyl-5-methyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(cyclopropylmethyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-((5-isobutyl-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(1b-215). (3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(1-fluorocyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(2,2-difluorocyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((5-(1-chlorocyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-

1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis(4-((5-(1-methylcyclopropyl)-1H-pyrazol-1-yl)methyl)benzyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-(cyclopropyl(4-isopropoxy-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-(2-(4-cyclopropyl-1H-pyrazol-1-yl)propan-2-yl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-6,18-bis(4-(2-(4-isopropoxy-1H-pyrazol-1-yl)propan-2-yl)benzyl)-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-(2-(4-bromo-1H-pyrazol-1-yl)propan-2-yl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-benzyl-18-(4-((4-iodo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-benzyl-18-(4-((3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-benzyl-3,9,15,21-tetraisobutyl-18-(4-((5-isopropyl-1H-pyrazol-1-yl)methyl)benzyl)-4,10,12,16,22,24-hexamethyl-

1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-[[3-[(4-bromopyrazol-1-yl)methyl]phenyl]methyl]-18-[[4-[(4-bromopyrazol-1-yl)methyl]phenyl]methyl]-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetrazacyclotetracosane-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(3-((4-cyclopropyl-1H-pyrazol-1-yl)methyl)benzyl)-18-(4-((4-cyclopropyl-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6-(3-((4-iodo-1H-pyrazol-1-yl)methyl)benzyl)-18-(4-((4-iodo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(3-((4-bromo-1H-pyrazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-bis(4-((4-bromo-1H-imidazol-1-yl)methyl)benzyl)-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosan-2,5,8,11,14,17,20,23-octaone;
1-[[4-[[(2R,5S,8R,11S,14R,17S,20R,23S)-14-[[4-[(2-cyanopyrrol-1-yl)methyl]phenyl]methyl]-5,11,17,23-tetraisobutyl-4,8,10,16,20,22-hexamethyl-3,6,9,12,15,18,21,24-octaoxo-1,7,13,19-tetraoxa-4,10,16,22-tetrazacyclotetracos-2-yl]methyl]phenyl]methyl]pyrrole-2-carbonitrile;
(3S,6R,9S,12R,15S,18R,21S,24R)-3,9,15,21-tetraisobutyl-4,6,10,16,18,22-hexamethyl-12,24-bis[[4-[(3-oxopyrido[3,2-b][1,4]thiazin-4-yl)methyl]phenyl]methyl]-1,7,13,19-tetraoxa-4,10,16,22-tetrazacyclotetracosane-2,5,8,11,14,17,20,23-octaone;
1-(4-(((2R,5S,8R,11S,14R,17S,20R,23S)-14-benzyl-5,11,17,23-tetraisobutyl-4,8,10,16,20,22-hexamethyl-3,6,9,12,15,18,21,24-octaoxo-1,7,13,19-tetraoxa-

4,10,16,22-tetraazacyclotetracosan-2-yl)methyl)benzyl)-1H-pyrrole-2,5-dicarbonitrile; and (3S,6R,9S,12R,15S,18R,21S,24R)-6-benzyl-18-[[4-(2,3-dihydropyrido[2,3-b][1,4]oxazin-1-ylmethyl)phenyl]methyl]-3,9,15,21-tetraisobutyl-4,10,12,16,22,24-hexamethyl-1,7,13,19-tetraoxa-4,10,16,22-tetrazacyclotetracosane-2,5,8,11,14,17,20,23-octaone.