



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic

R^1 and R^2 are independently selected from H and lower alkyl;

R^3 is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R^4 and R^5 are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R^6 and R^7 are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or R^6 and R^7 taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

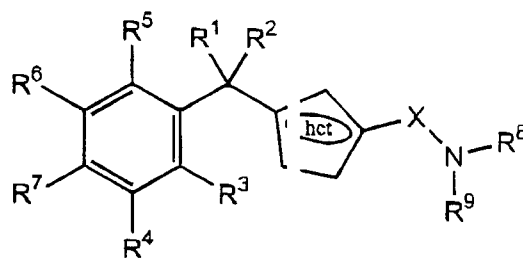
wherein at least one of R^3 , R^4 , R^5 , R^6 , and R^7 is other than hydrogen;

R^8 is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20; and

R^9 is selected from H and substituted and unsubstituted alkyl;

or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

10. A compound of Formula I:



where X is selected from C=O, C=S, S=O, and S(O)₂;



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic;

R¹ and R² are independently selected from H and lower alkyl;

R³ is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH₂OR, OR, and C(O)OR, where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R⁴ and R⁵ are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH₂OR, OR, and C(O)OR, where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R⁶ and R⁷ are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH₂OR, OR, and C(O)OR; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or R⁶ and R⁷ taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

wherein at least one of R³, R⁴, R⁵, R⁶, and R⁷ is other than hydrogen;

R⁸ is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH₂OR, OR, and C(O)OR,

where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20; and

R^9 is selected from H and substituted and unsubstituted alkyl;

or R^1 or R^2 can be -OH or =O; and/or R^8 can also be hydrogen;

and/or R can be COR or hydrogen; and/or R^8 can have any desired number of carbon atoms;

and/or R^8 and R^9 can also form a ring; and/or any adjacent R groups, such as R^5 and R^6 or R^3 and R^4 can form a ring, such as those described for R^6 and R^7 ;

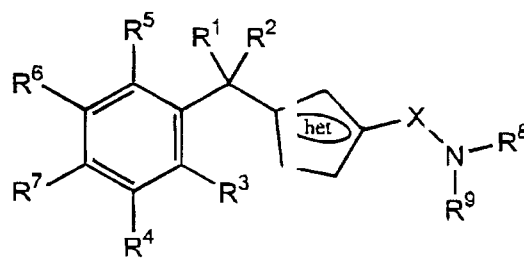
and/or R^6 can be COR; and/or the (het) group can be substituted or unsubstituted.

or R^8 and/or R^9 can be selected from heterocyclic groups or any compound that forms an amide bond with the nitrogen of Formula I;

or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

11. A pharmaceutical composition comprising:

(a) therapeutically effective amount of a compound of the Formula I:



where X is selected from C=O, C=S, S=O, and S(O)₂;



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic

R^1 and R^2 are independently selected from H and lower alkyl;

R^3 is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclo, aryl, heteroaryl, CH₂OR, OR, and C(O)OR, where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl,

cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R^4 and R^5 are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

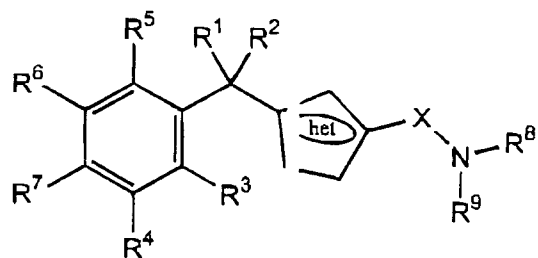
R^6 and R^7 are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or R^6 and R^7 taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

R^8 is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20;

R^9 is selected from H and substituted and unsubstituted alkyl; or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof; and

(b) a pharmaceutically acceptable carrier or diluent.

12. A method for regulating the secretion of gonadotropins in mammals, comprising administering to a mammal in need of such regulation, a therapeutically effective amount of a compound of the formula I:



where X is selected from $C=O$, $C=S$, $S=O$, and $S(O)_2$;



is a 5-membered heterocyclic ring containing from 1 to 4 heteroatoms selected from N, O, and S, wherein the ring may be saturated, partially unsaturated, or fully unsaturated, and may be aromatic;

R^1 and R^2 are independently selected from H and lower alkyl;

R^3 is selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, and heteroaryl, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R^4 and R^5 are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is as defined above; and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12;

R^6 and R^7 are independently selected from H, halogen, and substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$; where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 1 to 12; or R^6 and R^7 taken together with the atoms to which they are bonded form an optionally substituted 5- or 6-membered ring optionally having up to four heteroatoms selected from O, N, and S;

R^8 is a lipophilic moiety selected from substituted and unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocycle, aryl, heteroaryl, CH_2OR , OR, and $C(O)OR$, where R is as defined above, and where the total number of carbon atoms present (not including any optional substituents) ranges from 6 to 20;

R^9 is selected from H and substituted and unsubstituted alkyl; or

a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

STATEMENT UNDER ARTICLE 19

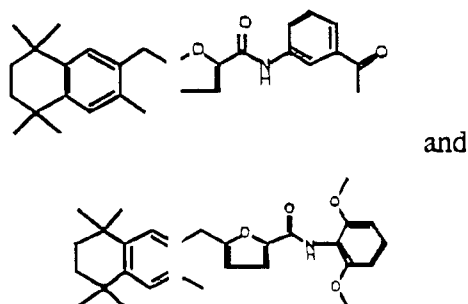
Replacement sheets with amended claims 9 and 10, and new claims 11 and 12 (pages 436, 437, 438, 439, 440, 441 and 442) are provided herewith. Please note that claims 6-8 and the abstract remain unchanged. Claims 9 and 10 have been amended to clarify that at least one of R^3 , R^4 , R^5 , R^6 , and R^7 is other than hydrogen. This clarification more clearly distinguishes the claimed subject matter over the references cited in the International Search Report. Claims 9 and 10 have also been amended to clarify that they also cover pharmaceutically acceptable salts, polymers, prodrugs, and active metabolites of the compound. Claims 11 and 12 have been added. Claims 11 and 12 are parallel to claims 7 and 8, but define the compound as in original claim 9. It is submitted that the claims as amended herein do not extend beyond the disclosure of the international application as originally filed.

An Amendment under Article 19 must be filed within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. Applicants submit that this amendment is timely, being due on or before October 21, 2000 (the later of the two time limits), and that no fee is due. However, in the event any extensions of time or additional fees are required to prevent withdrawal of this application, then such extensions of time are hereby requested and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-0622.

AMENDED CLAIMS

[received by the International Bureau on 20 October 2000 (20.10.00);
original claims 9 and 10 amended; new claims 11 and 12 added;
remaining claims unchanged (6 pages)]

6. A compound having a formula selected from the group consisting of:

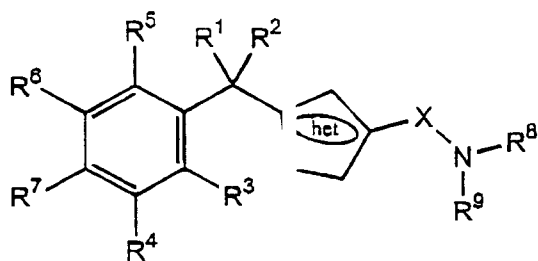


or a pharmaceutically acceptable salt, multimer, prodrug, or active metabolite thereof.

7. A pharmaceutical composition comprising: a therapeutically effective amount of a compound, pharmaceutically acceptable salt, multimer, prodrug, or active metabolite as defined in any of claims 1-6; and a pharmaceutically acceptable carrier or diluent.

8. A method for regulating the secretion of gonadotropins in mammals, comprising administering a therapeutically effective amount of a compound, pharmaceutically acceptable salt, multimer, prodrug, or active metabolite as defined in any of claims 1-6.

9. A compound of the Formula I:



I

where X is selected from C=O, C=S, S=O, and S(O)₂;