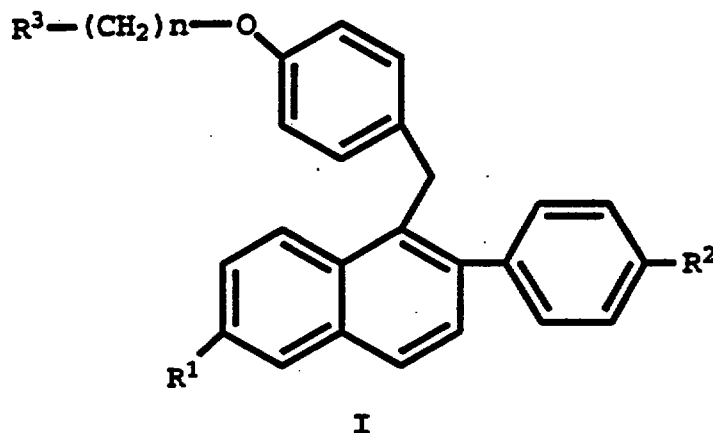


Claims

1. A compound of formula I



wherein

10 R^1 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₄-C₆ alkyl);

R^2 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl) or -OSO₂(C₄-C₆ alkyl);

n is 2 or 3; and

15 R^3 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; or a pharmaceutically acceptable salt thereof.

20 2. A compound according to Claim 1 wherein n is 2, or a pharmaceutically acceptable salt thereof.

3. A compound according to Claim 2 wherein R^3 is 1-piperidinyl, or a pharmaceutically acceptable salt thereof.

25 4. A compound according to Claim 3 wherein R^1 and R^2 each are -OH, or a pharmaceutically acceptable salt thereof.

5. A compound according to Claim 3 wherein R^1 and R^2 each are -OCH₃, or a pharmaceutically acceptable salt thereof.

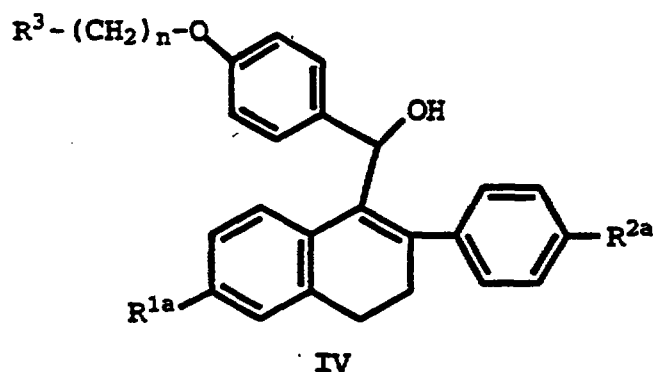
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6. A compound according to Claim 3 wherein R^1 and R^2 each are $-\text{OSO}_2(\text{C}_4\text{-C}_6 \text{ alkyl})$, or a pharmaceutically acceptable salt thereof.

7. A compound according to Claim 6 wherein R^1 and R^2 each are $-\text{OSO}_2(\text{CH}_2)_4\text{CH}_3$, or a pharmaceutically acceptable salt thereof.

8. A compound as claimed in any one of Claims 1 to 7 wherein said salt thereof is the hydrochloride salt.

9. A compound of formula IV



wherein

R^{1a} is $-\text{H}$, $-\text{OH}$, or $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$;

R^{2a} is $-\text{H}$, $-\text{OH}$, or $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$;

R^3 is 1-piperidinyl, 1-pyrrolidinyl, dimethylamino, diethylamino, or 1-hexamethyleneimino; and

n is 2 or 3;

or a pharmaceutically acceptable salt thereof.

10. A compound according to Claim 9 wherein R^3 is 1-piperidinyl and n is 2, or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 10 wherein R^{1a} and R^{2a} each are $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, or a pharmaceutically acceptable salt thereof.

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12. A compound according to Claim 11 wherein R^{1a} and R^{2a} each are -OCH₃, or a pharmaceutically acceptable salt thereof.

5 13. A compound according to Claim 10 wherein R^{1a} and R^{2a} each are -OH, or a pharmaceutically acceptable salt thereof.

14. A compound as claimed in any one ^{of} Claims 9 to 13 wherein said salt thereof is the hydrochloride salt.

10 15. A pharmaceutical composition comprising a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, and, optionally, an effective amount of estrogen or progestin, in combination with a
15 pharmaceutically acceptable carrier, diluent or excipient.

16. A pharmaceutical composition according to Claim 15 wherein said salt thereof is the hydrochloride salt thereof.

20 17. A pharmaceutical composition comprising a compound as claimed in any one of Claims 9 to 13, or a pharmaceutically acceptable salt thereof, and, optionally, an effective amount of estrogen or progestin, in combination with a
25 pharmaceutically acceptable carrier, diluent or excipient.

18. A pharmaceutical composition according to Claim 17 wherein said salt thereof is the hydrochloride salt thereof.

~~19. A method for alleviating the symptoms of post-~~
30 ~~menopausal syndrome comprising administering to a woman in need of such treatment an effective amount of a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof.~~

~~20. A method according to Claim 19 wherein the post-~~
35 ~~menopausal syndrome pathological condition is osteoporosis.~~

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~~21. A method according to Claim 19 wherein the post-menopausal syndrome pathological condition is related to a cardiovascular disease.~~

5 22. A method according to Claim 21 wherein the cardiovascular disease is hyperlipidemia.

10 23. A method according to Claim 19 wherein said post-menopausal syndrome pathological condition is estrogen-dependent cancer.

 24. A method according to Claim 23 wherein the estrogen-dependent cancer is breast or uterine cancer.

15 25. A method for inhibiting uterine fibroid disease comprising administering to a woman in need of such treatment an effective amount of a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof.

20 26. A method for inhibiting endometriosis comprising administering to a woman in need of such treatment an effective amount of a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof.

 27. A method for inhibiting aortal smooth muscle cell proliferation comprising administering to a human in need of such treatment an effective amount of a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof.

30 28. A method for inhibiting restenosis comprising administering to a human in need of such treatment an effective amount of a compound as claimed in any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof.

35 29. A method for alleviating the symptoms of post-menopausal syndrome comprising the method of Claim 19, and

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~~further comprising administering to said woman an effective amount of estrogen.~~

5 30. A method for alleviating the symptoms of post-menopausal syndrome comprising the method of Claim 19, and further comprising administering to said woman an effective amount of progestin.

10 31. A method as claimed in any one of Claims 19 to 30 wherein said salt thereof is the hydrochloride salt.

15 19 32. A compound as claimed in any of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, and, optionally, estrogen or progestin, for use as an agent for alleviating the symptoms of post-menopausal syndrome, particularly osteoporosis, cardiovascular disease including hyperlipidemia, and estrogen-dependent cancer including breast and uterine cancer.

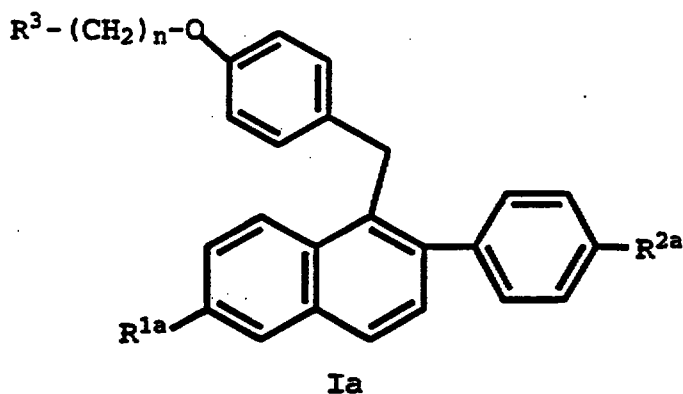
20 19 20 33. A compound according to Claim 32 wherein said salt thereof is the hydrochloride salt.

25 21 34. A compound as claimed in any of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, and optionally, estrogen or progestin, for use as an agent for inhibiting uterine fibroid disease, endometriosis, aortal smooth muscle cell proliferation and restenosis.

30 21 22 35. A compound according to Claim 34 wherein said salt thereof is the hydrochloride salt.

23 36. A process for preparing a compound of formula Ia

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wherein

R^{1a} is -H, -OH, or -O(C₁-C₄ alkyl);

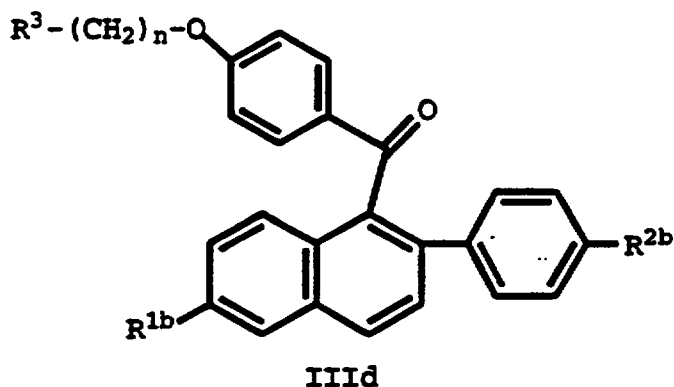
R^{2a} is -H, -OH, or -O(C₁-C₄ alkyl);

R³ is 1-piperidinyl, 1-pyrrolidinyl, dimethylamino, diethylamino, or 1-hexamethyleneimino; and

n is 2 or 3;

or a pharmaceutically acceptable salt thereof, which comprises

a) reacting a compound of formula IIIId



wherein

R^{1b} is -H or -O(C₁-C₄ alkyl);

R^{2b} is -H or -O(C₁-C₄ alkyl); and

R³ and n are as defined above, with a reducing agent in the presence of a solvent having a boiling point in the range from about 150° C to about 200° C, and heating the mixture to reflux;

b) when R^{1b} and/or R^{2b} is -O(C₁-C₄ alkyl), optionally removing the R^{1b} and/or R^{2b} hydroxy protecting groups; and

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c) optionally salifying the reaction product from step a) or b).

5 ²³
24 37. A process according to Claim 36 wherein said process is carried out in a single same vessel.

10 ²⁴
25 38. A process according to Claim 37 wherein the formula Ia compound is a compound wherein

R^{1a} and R^{2a} each are methoxy;

R³ is 1-piperidinyl; and

n is 2;

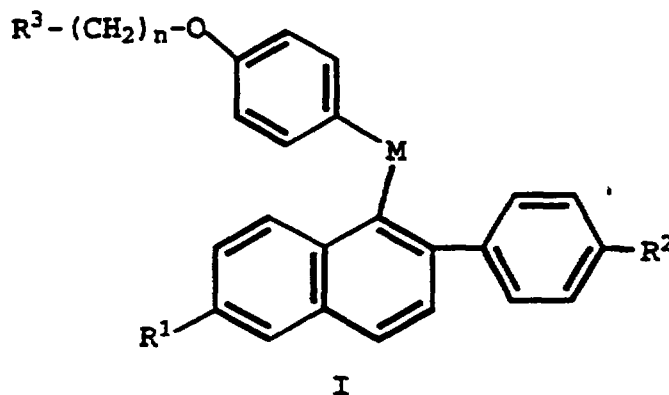
or a pharmaceutically acceptable salt thereof.

15 ²⁵
26 39. A process according to Claim 38 wherein the salt of a compound of formula Ia is the hydrochloride salt.

20 ²⁶
27 40. A process according to Claim 39 wherein said reducing agent is lithium aluminum hydride.

25 ²⁷
28 41. A process according to Claim 40 wherein said solvent having a boiling point from about 150° C to about 200° C is n-propylbenzene.

29 42. A process for preparing a compound of formula I



wherein

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R^1 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₄-C₆ alkyl);

R^2 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl) or -OSO₂(C₄-C₆ alkyl);

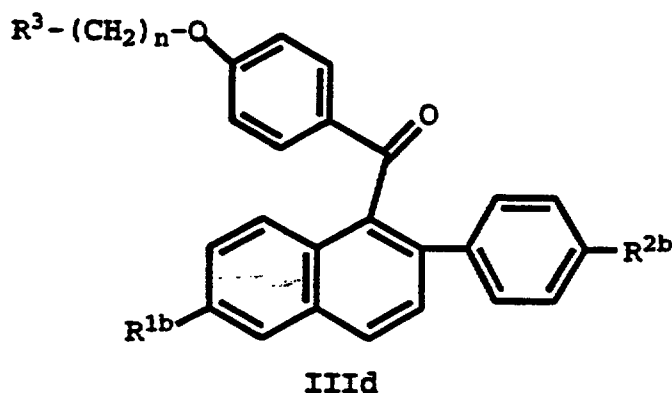
R^3 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino;

M is -CH(OH)- or -CH₂-; and

n is 2 or 3;

or a pharmaceutically acceptable salt thereof, which comprises

a) reacting a compound of formula IIIId



wherein

R^{1b} is -H or -O(C₁-C₄ alkyl);

R^{2b} is -H or -O(C₁-C₄ alkyl); and

R^3 and n are as defined above, with a reducing agent;

b) when R^{1b} and/or R^{2b} is -O(C₁-C₄ alkyl), optionally removing the R^{1b} and/or R^{2b} hydroxy protecting groups;

c) when R^1 and R^2 are -OH, optionally replacing said hydroxy groups with a substituent of the formula -O(C₁-C₄ alkyl), -COC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₄-C₆ alkyl); and

d) optionally salifying the reaction product from step a), b), or c.

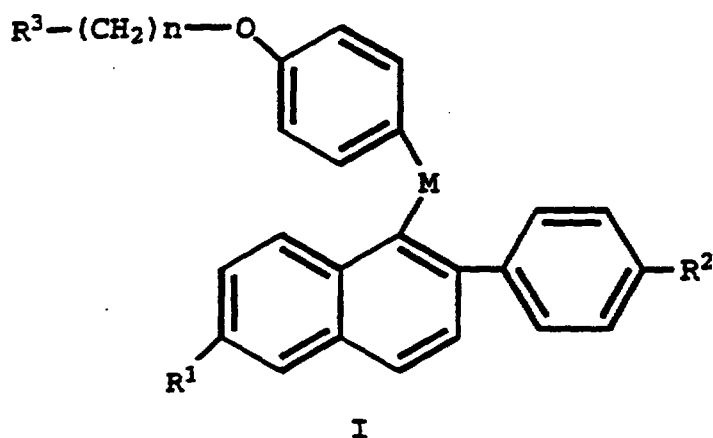
30 43. A process according to Claim ²⁹42 wherein said reaction product is a compound of formula I wherein R^1 and R^2

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each are -OH, R^3 is 1 piperidinyl, M is -CH₂-, and n is 2, or a pharmaceutically acceptable salt thereof.

³⁰ 31 ~~44~~. A process as claimed in any one of Claims ²⁹ ~~42~~ to ~~43~~ wherein said salt of a compound of formula I is the hydrochloride salt.

32 ~~45~~. A process for preparing a compound of formula I



wherein

R^1 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₄-C₆ alkyl);

R^2 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl) or -OSO₂(C₄-C₆ alkyl);

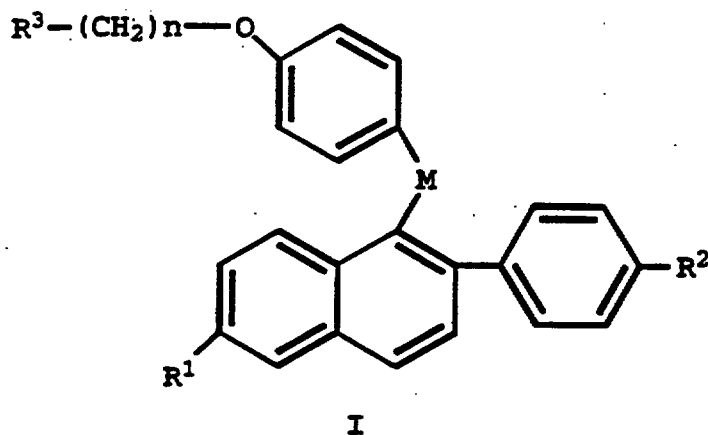
M is -CH(OH)- or -CH₂-;

n is 2 or 3; and

R^3 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; or a pharmaceutically acceptable salt thereof, substantially as hereinbefore described with reference to any of the examples.

33 ~~46~~. A compound of formula I

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wherein

R^1 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl), or -OSO₂(C₄-C₆ alkyl);

R^2 is -H, -OH, -O(C₁-C₄ alkyl), -OCOC₆H₅, -OCO(C₁-C₆ alkyl) or -OSO₂(C₄-C₆ alkyl);

M is -CH(OH)- or -CH₂-;

n is 2 or 3; and

10 R^3 is 1-piperidinyl, 1-pyrrolidinyl, methyl-1-pyrrolidinyl, dimethyl-1-pyrrolidinyl, 4-morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; or a pharmaceutically acceptable salt thereof, substantially as hereinbefore described with reference to any of the examples.

→
Add claims 34 to 44.