WO2004/085457 discloses steroidal compounds capable of inhibiting 17β-hydroxysteroid dehydrogenase. WO2006/003012 discloses 2-substituted D-homo-estriene derivatives suitable for the treatment of estrogen-dependent diseases that can be influenced by the inhibition of the 17β-hydroxysteroid dehydrogenase type 1. Similarly WO2006/003013 presents 2-substituted estratrienones usable for preventing and treating estrogen-dependent diseases influenced by inhibiting 17β-hydroxysteroid dehydrogenase type 1.

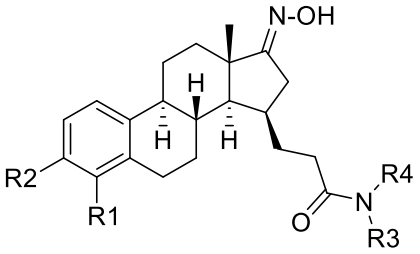
15-substituted estradiol analogues acting as locally active estrogens are presented in WO2004/085345. WO2006/027347 discloses 15b-substituted estradiol derivatives having selective estrogenic activity for the treatment or prevention of estrogen receptor-related diseases and physiological conditions. Further, WO2005/047303 discloses 3, 15 substituted estrone derivatives capable of inhibiting the 17β-hydroxysteroid dehydrogenase type 1.

International application WO2008/034796 relates to estratrien triazoles suitable for use in treatment and prevention of steroid hormone dependent diseases or disorders requiring the inhibition of a 17β-hydroxysteroid dehydrogenases such as 17β-HSD type 1, type 2 or type 3 enzyme. Inhibitors of 17β-HSD type 3 enzyme have been disclosed in WO99/46279.

International applications WO2014/207309, WO2014/207310 and WO2014/207311 relate to estrone C-15 thiazole derivatives, estrone C-17 ketimine C-15 thiazole derivatives and estradiol C-15 thiazole derivatives, respectively, as well as their use in therapy.

SUMMARY

In an aspect of the present disclosure, there is provided a compound of formula (I)



(I)

wherein R1 and R2 are each independently selected from the group consisting of H and halogen;

(i) R3 is selected from the group consisting of H and C1-3-alkyl; and

R4 is selected from the group consisting of

C1-3-alkyl,

4 to 6 membered unsubstituted saturated heterocycle comprising 1 heteroatom selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered partially unsaturated heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituents selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy,

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

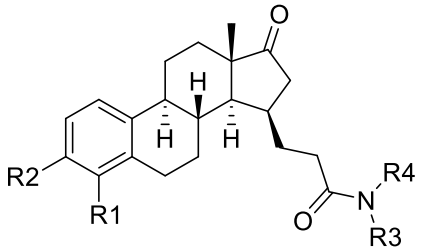
6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring;

or

(ii) R3 and R4 form together with the nitrogen atom they are attached to form a group selected from a 5 to 6 membered saturated heterocycle comprising said nitrogen atom and being optionally substituted with a substituent selected from the group consisting of halogen, CN, methyl, C1-3-(per)haloalkyl, OH, and methoxy; and an unsubstituted bicyclic spirocyclic or fused heterocycle containing said nitrogen atom and optionally 1 or 2 further heteroatom(s) selected from a group consisting of nitrogen, oxygen and sulfur;

or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a compound of formula (II)



(II)

wherein R1 and R2 are each independently selected from the group consisting of H and halogen;

(i) R3 is selected from the group consisting of H and C1-3-alkyl; and

R4 is selected from the group consisting of

C1-3-alkyl,

4 to 6 membered unsubstituted saturated heterocycle comprising 1 heteroatom selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered partially unsaturated heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituents selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, $C(O)N(C1\text{-}3\text{-}alkyl)_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy,

5 membered unsubstituted unsaturated or aromatic heterocycle comprising 1 nitrogen atom and 1 to 2 further heteroatom(s) independently se-

lected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, $C(O)N(C1\text{-}3\text{-}alkyl)_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, $C(O)N(C1\text{-}3\text{-}alkyl)_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring;

or

(ii) R3 and R4 form together with the nitrogen atom they are attached to form a group selected from a 5 to 6 membered saturated heterocycle comprising said nitrogen atom and being optionally substituted with a substituent selected from the group consisting of halogen, CN, methyl, C1-3-(per)haloalkyl, OH, and methoxy; and an unsubstituted bicyclic spirocyclic or fused heterocycle containing said nitrogen atom and optionally 1 or 2 further heteroatom(s) selected from a group consisting of nitrogen, oxygen and sulfur.

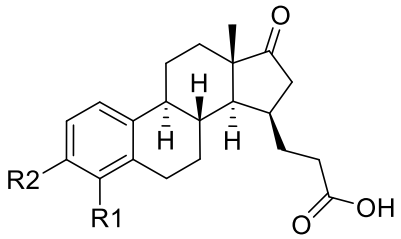
In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising an effective amount of one or more compounds or pharmaceutically acceptable salts as disclosed herein, together with one or more pharmaceutically acceptable excipient(s).

In a further aspect of the present disclosure, there is provided a

method for the preparation of a compound of formula (I) as disclosed herein,

comprising the steps of:

reacting a compound of formula (III)



(III)

wherein R1 and R2 are each independently selected from the group consisting of H and halogen;

with compound of formula (IV)

NR3R4 (IV)

wherein R3 and R4 are as defined for compound of formula (I),

in the presence of amide bond forming reagents, in particular T_3P and a base, preferably pyridine,

to obtain a compound of formula (II), and reacting the obtained compound with

NH_2-OH (V)

or hydrogen halide thereof,

in the presence of a base, preferably pyridine,

to obtain a compound of formula (I); and optionally converting the compound of formula (I) to a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of a compound or pharmaceutically acceptable salt as disclosed herein, or a pharmaceutical composition also disclosed herein, in the manufacture of a medicament for the treatment or prevention of a disease selected from a group consisting of breast cancer, prostate carcinoma, ovarian cancer, uterine cancer, endometrial cancer, endometrial hyperplasia, endometriosis, uterine fibroids, adenomyosis, polycystic ovarian syndrome, dysmenorrhea, menorrhagia, metrorrhagia, contraception, prostadynia, benign prostatic hyperplasia, urinary dysfunction, lower urinary tract symptoms, chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), systemic lupus erythematosus (SLE), multiple sclerosis, obesity, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), lung cancer, colon cancer, tissue wounds, skin wrinkles and

cataracts,

wherein said disease is associated with increased level of estradiol and/or treatable by inhibition of 17β-HSD1 enzyme.

In a further aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salt as as disclosed herein, or a pharmaceutical composition also disclosed herein, for use in the treatment or prevention of a disease selected from a group consisting of breast cancer, prostate carcinoma, ovarian cancer, uterine cancer, endometrial cancer, endometrial hyperplasia, endometriosis, uterine fibroids, adenomyosis, polycystic ovarian syndrome, dysmenorrhea, menorrhagia, metrorrhagia, contraception, prostadynia, benign prostatic hyperplasia, urinary dysfunction, lower urinary tract symptoms, chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), systemic lupus erythematosus (SLE), multiple sclerosis, obesity, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), lung cancer, colon cancer, tissue wounds, skin wrinkles and cataracts,

wherein said disease is associated with increased level of estradiol and/or treatable by inhibition of 17β-HSD1 enzyme.

BRIEF DESCRIPTION OF THE INVENTION

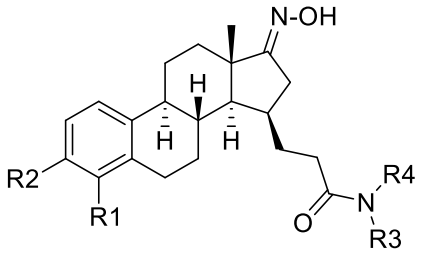
An object of the present invention is to provide compounds useful in treating disorders and diseases associated with increased level of estradiol and/or treatable by inhibition of 17β-HSD1 enzyme. It is further an object of the present invention to provide compounds that show little or no inhibitory effect on 17β-HSD2 enzyme.

One of the problems associated with the known 17β-HSD1 inhibitors is the disposition, in particular the metabolic stability, of the compounds. It is therefore yet a further object of the present invention to provide compounds with improved metabolic stability.

One further problem associated with the known 17β-HSD1 inhibitors is the formation of conjugative metabolites and species selectivity of the compounds. It is therefore yet a further object of the present invention to provide

CLAIMS

1. A compound of formula (I)



(I)

wherein R1 and R2 are each independently selected from the group consisting of H and halogen;

(i) R3 is selected from the group consisting of H and C1-3-alkyl; and

R4 is selected from the group consisting of

C1-3-alkyl,

4 to 6 membered unsubstituted saturated heterocycle comprising 1 heteroatom selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered partially unsaturated heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituents selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy,

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

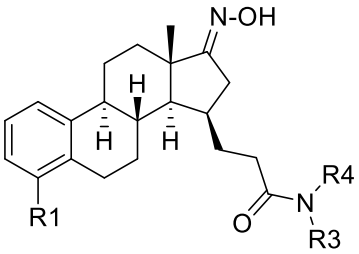
6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring;

or

(ii) R3 and R4 form together with the nitrogen atom they are attached to form a group selected from a 5 to 6 membered saturated heterocycle comprising said nitrogen atom and being optionally substituted with a substituent selected from the group consisting of halogen, CN, methyl, C1-3-(per)haloalkyl, OH, and methoxy; and an unsubstituted bicyclic spirocyclic or fused heterocycle containing said nitrogen atom and optionally 1 or 2 further heteroatom(s) selected from a group consisting of nitrogen, oxygen and sulfur;

or a pharmaceutically acceptable salt thereof.

2. The compound as claimed in claim 1, having formula (Ia)



(Ia)

wherein R1 is selected from the group consisting of H and halogen;

(i) R3 is selected from the group consisting of H and C1-3-alkyl; and

R4 is selected from the group consisting of

C1-3-alkyl,

4 to 6 membered unsubstituted saturated heterocycle comprising 1 heteroatom selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered partially unsaturated heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with

one or two substituents selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy,

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring;

or

(ii) R3 and R4 form together with the nitrogen atom they are attached to form a group selected from a 5 to 6 membered saturated heterocycle comprising said nitrogen atom and being optionally substituted with a substituent selected from the group consisting of halogen, CN, methyl, C1-3-(per)haloalkyl, OH, and methoxy; and an unsubstituted bicyclic spirocyclic or fused heterocycle containing said nitrogen atom and optionally 1 or 2 further heteroatom(s) selected from a group consisting of nitrogen, oxygen and sulfur;

or a pharmaceutically acceptable salt thereof.

3. The compound or pharmaceutically acceptable salt as claimed in claim 2, wherein R1 is selected from the group consisting of H, F and Cl, preferably F and Cl.

4. The compound or pharmaceutically acceptable salt as claimed in any one of claims 1 to 3, wherein R3 is H or methyl.

5. The compound or pharmaceutically acceptable salt as claimed in claim 4, wherein R3 is H.

6. The compound or pharmaceutically acceptable salt as claimed in any one of claims 1 to 5, wherein R4 is selected from a group consisting of

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

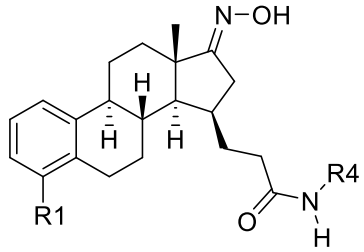
6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring.

7. The compound or pharmaceutically acceptable salt as claimed in any one of claims 1 to 5, wherein R4 is selected from the group consisting of oxetanyl, pyrrolidinyl, piperidinyl, tetrahydropyranyl, dihydrothiazolyl, pyridinyl, fluoropyridinyl, cyanopyridinyl, methylpyridinyl, dimethylpyridinyl, isopropylpyridinyl, hydroxypyridinyl, methoxypyridinyl, morpholinopyridinyl, methylpiperazi-

nylpyridinyl, pyrazinyl, methylpyridazinyl, and methoxypyridazinyl; in particular from the group consisting of oxetanyl and tetrahydropyranyl, dihydrothiazolyl, fluoropyridinyl, methoxypyridinyl, methylpyridazinyl, and methoxypyridazinyl.

8. The compound or pharmaceutically acceptable salt as claimed in any one of claims 1 to 4, wherein R3 and R4 form together with the nitrogen they are attached to a ring selected from the group consisiting of pyrrolidinyl, methoxymethylpyrrolidinyl, and oxaazaspiro[4.5]decanyl.

9. The compound as claimed in claim 1, wherein the compound has formula (Ib)



(Ib)

wherein R1 is selected from the group consisting of H and halogen; and

R4 is selected from the group consisting of

C1-3-alkyl,

4 to 6 membered unsubstituted saturated heterocycle comprising 1 heteroatom selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered partially unsaturated heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituents selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy,

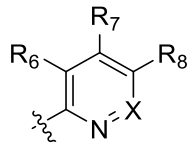
5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s)

independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring;

or a pharmaceutically acceptable salt thereof.

10. The compound or pharmaceutically acceptable salt as claimed in claim 9, wherein R4 is a 6 membered aromatic heterocycle of formula (A)



(A)

wherein

X is CR9 or N;

one of R6, R7, R8 is H, and the others are independently selected from a group consisting of H, halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, and morpholine ring; and

R9 is H or C1-3-alkyl.

11. The compound as claimed in claim 1 selected from the group consisting of:

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methoxypyridazin-3-yl)propanamide;

3-((13*S*,15*R,E*)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-15-yl)-N-(5-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(oxetan-3-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-methyl-(oxetan-3-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-1-(pyrrolidin-1-yl)propan-1-one;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methylpyridazin-3-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(1,3,4-thiadiazol-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyamino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridazine-3-yl)propanamide;

N-(4,5-dihydrothiazol-2-yl)-3-((13S,15R,E)-4-fluoro-17-(hydroxylamino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N,N-diethyl-3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methoxypyridazin-3-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methylpyridazin-3-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridazin-3-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-methyl-N-(oxetan-3-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(1,3,4-thiadiazol-2-yl)propanamide;

N,N-diethyl-3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-isopropylpyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridazine-3-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)- N-(4,5-dihydrothiazol-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-1-(8-oxa-2-azaspiro[4.5]decan-2-yl)propan-1-one;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)- N-(6-methoxypyridazin-3-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N,N-diethylpropanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-methylpyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)- N-(5-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)- N-(pyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)- N-(4-methylpyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)- N-(5-cyanopyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyrazin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methylpyridazin-3-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-morpholinopyridin-2-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridazin-3-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyamino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-(4-methylpiperazin-1-yl)pyridin-2-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methylpyridin-2-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-morpholinopyridin-2-yl)propanamide;

6-(3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamido)-N,N-dimethylnicotinamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-isopropylpyridin-2-yl)propanamide;

N-(5-fluoropyridin-2-yl)-3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(5-cyanopyridin-2-yl)-3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-hydroxypyridin-2-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridin-2-yl)propanamide;

3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-isopropylpyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-morpholinopyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-(4-methylpiperazin-1-yl)pyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-methylpropanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N,N-dimethylpropanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(tetrahydro-2H-pyran-4-yl)propanamide;

N-Cyclohexyl-3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyrazin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-1-(8-oxa-2-azaspiro[4.5]decan-2-yl)propan-1-one;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methylpyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-1-morpholinopropan-1-one;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-fluoropyridin-2-yl)propanamide;

N-(3,5-difluoropyridin-2-yl)-3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(5-cyanopyridin-2-yl)-3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

N-(3,5-difluoropyridin-2-yl)-3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-3-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-morpholinopyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-fluoropyridin-2-yl)propanamide;

N-(4-fluoropyridin-2-yl)-3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(3-fluoropyridin-2-yl)-3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3,5-difluoropyridin-2-yl)propanamide;

N-(3,5-difluoropyridin-2-yl)-3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(6-fluoropyridin-2-yl)-3-((13S,15R,E)-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-fluoropyridin-2-yl)propanamide;

6-(3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamido)-N,N-dimethylnicotinamide;

3-((13S,15R,E)-3-chloro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl)propanamide;

6-(3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamido)-N,N-dimethylnicotinamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl)propanamide;

or a pharmaceutically acceptable salt thereof.

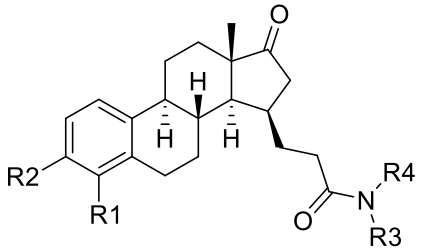
12. The compound as claimed in claim 11 selected from the group consisting of:

3-((13S,15*R*,*E*)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-15-yl)-N-(5-methoxypyridin-2-yl)propanamide;

3-((13S,15R,E)-4-fluoro-17-(hydroxyimino)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-fluoropyridin-2-yl)propanamide;

or a pharmaceutically acceptable salt thereof.

13. A compound of formula (II)



(II)

wherein R1 and R2 are each independently selected from the group consisting of H and halogen;

(i) R3 is selected from the group consisting of H and C1-3-alkyl; and

R4 is selected from the group consisting of

C1-3-alkyl,

4 to 6 membered unsubstituted saturated heterocycle comprising 1 heteroatom selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered partially unsaturated heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituents selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy,

5 membered unsubstituted unsaturated or aromatic heterocycle comprising 1 nitrogen atom and 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substitu-

ent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring;

or

(ii) R3 and R4 form together with the nitrogen atom they are attached to form a group selected from a 5 to 6 membered saturated heterocycle comprising said nitrogen atom and being optionally substituted with a substituent selected from the group consisting of halogen, CN, methyl, C1-3-(per)haloalkyl, OH, and methoxy; and an unsubstituted bicyclic spirocyclic or fused heterocycle containing said nitrogen atom and optionally 1 or 2 further heteroatom(s) selected from a group consisting of nitrogen, oxygen and sulfur.

14. The compound as claimed in claim 13, wherein R1 and R2 are each independently selected from the group consisting of H and halogen, preferably F and Cl.

15. The compound as claimed in claim 13 or 14, wherein R3 is H or methyl.

16. The compound as claimed in any one of claims 13 to 15, wherein R4 is selected from a group consisting of

5 membered unsubstituted unsaturated or aromatic heterocycle comprising 1 nitrogen atom and 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen,

5 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, C1-3-alkoxy,

C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle containing 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, and

6 membered unsaturated or aromatic heterocycle comprising 1 nitrogen atom and optionally 1 to 2 further heteroatom(s) independently selected from the group consisting of nitrogen, sulfur, and oxygen, and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, oxo, C1-3-alkoxy, C(O)N(C1-3-alkyl)$_2$, and 6 membered saturated heterocycle comprising 1 to 2 heteroatom(s) independently selected from the group consisting of nitrogen, oxygen and sulfur and being optionally substituted with one or two substituent(s) independently selected from the group consisting of halogen, CN, C1-3-alkyl, C1-3-(per)haloalkyl, OH, and C1-3-alkoxy, or two adjacent substituents may form a 5 or 6 membered saturated fused ring.

17. The compound as claimed in any one of claims 13 to 16, wherein R4 is selected from the group consisting of oxetanyl, pyrrolidinyl, piperidinyl, tetrahydropyranyl, dihydrothiazolyl, thiadiazolyl, oxazolyl, methyloxazolyl, pyridinyl, fluoropyridinyl, cyanopyridinyl, methylpyridinyl, dimethylpyridinyl, isopropylpyridinyl, hydroxypyridinyl, methoxypyridinyl, morpholinopyridinyl, methylpiperazinylpyridinyl, pyrazinyl, methylpyridazinyl, and methoxypyridazinyl; in particular from the group consisting of oxetanyl and tetrahydropyranyl, dihydrothiazolyl, thiadiazolyl, oxazolyl, methyloxazolyl, fluoropyridinyl, methoxypyridinyl, methylpyridazinyl, and methoxypyridazinyl.

18. The compound as claimed in claim 13 or 14, wherein R3 and R4 form together with the nitrogen they are attached to a ring selected from the group consisiting of pyrrolidinyl, methoxymethylpyrrolidinyl, and oxaazaspiro[4.5]decanyl.

19. The compound as claimed in claim 13 selected from the group consisting of:

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-methylisoxazol-3-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methoxypyridazin-3-yl)propanamide;

3-((13*S*,15*R*)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-15-yl)-N-(5-methoxypyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-fluoropyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(oxetan-3-yl)propanamide

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-methyl-(oxetan-3-yl)propanamide;

(13S,15R)-4-fluoro-13-methyl-15-(3-oxo-3-(pyrrolidin-1-yl)propyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-methylpyridazin-3-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(1,3,4-thiadiazol-2-yl)propanamide;

N-(4,5-dihydrothiazol-2-yl)-3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N,N-diethyl-3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-isopropylpyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-morpholinopyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-(4-methylpiperazin-1-yl)pyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-methylpropanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N,N-dimethylpropanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(tetrahydro-2H-pyran-4-yl)propanamide;

N-cyclohexyl-3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyrazin-2-yl)propanamide;

(13S,15R)-4-fluoro-13-methyl-15-(3-oxo-3-(8-oxa-2-azaspiro[4.5]decan-2-yl)propyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methylpyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-methoxypyridin-2-yl)propanamide;

3-((13S,15R)-3-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-methylisoxazol-3-yl)propanamide;

(13S,15R)-4-fluoro-13-methyl-15-(3-morpholino-3-oxopropyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(pyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-fluoropyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-fluoropyridin-2-yl)propanamide;

N-(3,5-difluoropyridin-2-yl)-3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(5-cyanopyridin-2-yl)-3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R)-3-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

N-(3,5-difluoropyridin-2-yl)-3-((13S,15R)-3-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R)-3-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(5-morpholinopyridin-2-yl)propanamide;

3-((13S,15R)-3-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(4-fluoropyridin-2-yl)propanamide;

N-(4-fluoropyridin-2-yl)-3-((13S,15R)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(3-fluoropyridin-2-yl)-3-((13S,15R)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R)-3-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3-fluoropyridin-2-yl)propanamide;

3-((13S,15R)-3-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(3,5-difluoropyridin-2-yl)propanamide;

N-(3,5-difluoropyridin-2-yl)-3-((13S,15R)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

N-(6-fluoropyridin-2-yl)-3-((13S,15R)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamide;

3-((13S,15R)-3-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(6-fluoropyridin-2-yl)propanamide;

6-(3-((13S,15R)-3-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamido)-N,N-dimethylnicotinamide;

3-((13S,15R)-3-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl)propanamide;

6-(3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)propanamido)-N,N-dimethylnicotinamide, and

3-((13S,15R)-4-fluoro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-15-yl)-N-(2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl)propanamide.

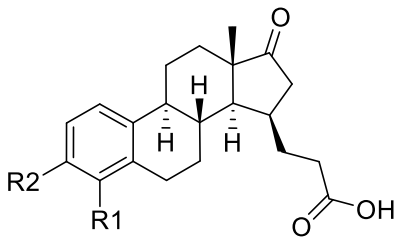
20. A pharmaceutical composition comprising an effective amount of one or more compounds or pharmaceutically acceptable salts as claimed in any one of claims 1 to 12, together with one or more pharmaceutically acceptable excipient(s).

21. A pharmaceutical composition as claimed in claim 20 comprising one or more compounds or pharmaceutically acceptable salts as claimed in any one of claims 1 to 12 in combination with one or more other active ingredients.

22. A method for the preparation of a compound of formula (I) as defined in any one of claims 1 to 12,

comprising the steps of:

reacting a compound of formula (III)



(III)

wherein R1 and R2 are each independently selected from the group consisting of H and halogen;

with compound of formula (IV)

NR3R4 (IV)

wherein R3 and R4 are as defined for compound of formula (I),

in the presence of amide bond forming reagents, in particular T_3P and a base, preferably pyridine,

to obtain a compound of formula (II), and reacting the obtained compound with

NH_2-OH (V)

or hydrogen halide thereof,

in the presence of a base, preferably pyridine,

to obtain a compound of formula (I); and optionally converting the compound of formula (I) to a pharmaceutically acceptable salt thereof.

23. Use of a compound or pharmaceutically acceptable salt as claimed in any one of claims 1 to 12 or a pharmaceutical composition as claimed in claim 20 or 21 in the manufacture of a medicament for the treatment or prevention of a disease selected from a group consisting of breast cancer, prostate carcinoma, ovarian cancer, uterine cancer, endometrial cancer, endometrial hyperplasia, endometriosis, uterine fibroids, adenomyosis, polycystic ovarian syndrome, dysmenorrhea, menorrhagia, metrorrhagia, contraception, prostadynia, benign prostatic hyperplasia, urinary dysfunction, lower urinary tract symptoms, chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), systemic lupus erythematosus (SLE), multiple sclerosis, obesity, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), lung cancer, colon cancer, tissue wounds, skin wrinkles and cataracts,

wherein said disease is associated with increased level of estradiol and/or treatable by inhibition of 17β-HSD1 enzyme.

24. A compound or pharmaceutically acceptable salt as claimed in

any one of claims 1 to 12, or a pharmaceutical composition as claimed in claim 20 or 21, for use in the treatment or prevention of a disease selected from a group consisting of breast cancer, prostate carcinoma, ovarian cancer, uterine cancer, endometrial cancer, endometrial hyperplasia, endometriosis, uterine fibroids, adenomyosis, polycystic ovarian syndrome, dysmenorrhea, menorrhagia, metrorrhagia, contraception, prostadynia, benign prostatic hyperplasia, urinary dysfunction, lower urinary tract symptoms, chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), systemic lupus erythematosus (SLE), multiple sclerosis, obesity, rheumatoid arthritis, chronic obstructive pulmonary disease (COPD), lung cancer, colon cancer, tissue wounds, skin wrinkles and cataracts,

wherein said disease is associated with increased level of estradiol and/or treatable by inhibition of 17β-HSD1 enzyme.