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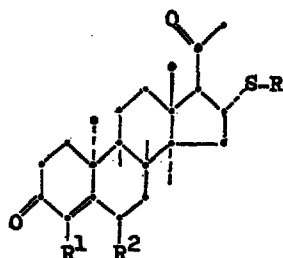
COMPLETE SPECIFICATION

Novel 9 β ,10 α -Steroids and a process for the manufacture thereof

We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESELLSCHAFT, a Swiss Company of 124—184 Grenzacherstrasse, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is concerned with novel 9 β ,10 α -steroids and a process for the manufacture thereof.

The novel 9 β ,10 α -steroids provided by the present invention are compounds of the general formula



(I)

wherein R represents a hydrogen atom or an alkyl, hydroxy-alkyl, alkoxy-alkyl, mercapto-alkyl, alkylthio-alkyl, akenyl, alkynyl, aryl, aralkyl, alkanoyl or cyano group, a 5-membered or 6-membered heterocyclic group (which may be hydroxysubstituted) or a 5-membered or 6-membered heterocyclyl-methyl group and R¹ and R² each represent a hydrogen or halogen atom or an alkyl group, and Δ^1 -dehydro, Δ^6 -dehydro and $\Delta^{1,6}$ -bisdehydro derivatives thereof. They are endocrinologically useful. They are useful as progestational agents. In particular they influence the physiological processes which are controlled by sex hormones. For instance, the compound 16 α -ethylthio-9 β ,10 α -pregna-4,6-dien-3,20-dione shows a

definite stimulating effect on the thickening of the cervical mucus. Compounds exhibiting such activity can be used, for example, as contraceptive agents.

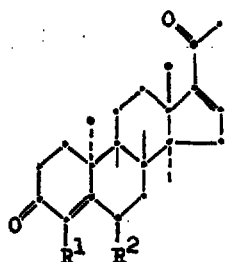
One interesting class of novel 9 β ,10 α -steroids provided by the present invention comprises those compounds of formula I in which R represents a hydrogen atom or an alkyl, hydroxy-alkyl, alkoxy-alkyl, mercapto-alkyl, alkylthio-alkyl, alkenyl, alkynyl, aryl, aralkyl, alkanoyl or cyano group, and Δ^1 -dehydro, Δ^6 -dehydro and $\Delta^{1,6}$ -bisdehydro derivatives thereof. The Δ^6 -dehydro derivatives of the compounds of formula I represent a preferred class of novel 9 β ,10 α -steroids provided by the invention.

It will be appreciated that the term 'alkyl' is used in this description and in the claims appended hereto to mean both straight-chain and branched-chain saturated hydrocarbon groups such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, octyl, decyl, dodecyl and octadecyl. Examples of alkenyl groups are vinyl, allyl and methallyl and examples of alkynyl groups are ethynyl and propargyl. Examples of alkanoyl groups are acetyl, propionyl, butyryl, valeryl and capryl. The phenyl and tolyl groups are the preferred aryl groups. The benzyl group is an example of an aralkyl group. The term 'halogen' includes fluorine, chlorine, bromine and iodine. Examples of 5-membered heterocyclic groups are thienyl, imidazolyl-(2) and 1H-1,2,4-triazolyl-(3). An example of a hydroxy-substituted 6-membered heterocyclic group is the 4-hydroxy-pyrimidyl-(2) group. Examples of 5-membered heterocyclyl-methyl groups are thenyl and furfuryl. Any alkyl, alkenyl, alkynyl or alkanoyl groups which may be present preferably contain up to 6 carbon atoms.

According to the process provided by the invention, the novel 9 β ,10 α -steroids aforesaid are manufactured by reacting a compound of the general formula

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(II)

wherein R^1 and R^2 have the significance given earlier, or a Δ^6 -dehydro derivative thereof, with a compound of the general formula



(III)

wherein R has the significance given earlier, and, if desired, introducing a double-bond into the 6,7-position of the reaction product if not already present in the starting material and/or into the 1,2-position.

The starting compounds of formula II hereinbefore, insofar as they are not known, can be prepared in a manner known *per se*. The compounds of formula II in which at least one of R^1 and R^2 represents a halogen atom or an alkyl group and their 6-dehydro derivatives are claimed *per se* in the specification of our co-pending Application for Letters Patent No. 1418/69 (now Serial No. 1154407) and may be prepared as described therein.

The reaction of a compound of formula II with a compound of formula III can be brought about by mixing the two reaction partners in a suitable solvent. An excess of the thio compound of formula III can serve as the solvent if desired. The reaction can be carried out at room temperature or a temperature below room temperature or the reaction mixture can also be heated if necessary. The reaction is preferably carried out in the presence of an acid or a base which will function as a catalyst and which can also function as the solvent. Organic bases such as piperidine, pyridine or collidine are suitable bases for this purpose. Suitable acids are, for example, mineral acids such as hydrochloric acid or organic acids, especially sulphonic acids such as *paratoluene*-sulphonic acid.

When a 6-dehydro derivative of a compound of formula II is used as the starting material, after the introduction of the substituent $-S-R$ into the 16-position, an addition of the compound $R-SH$ at the 6,7-double bond can also occur. In this case, in order to obtain optimum yields, the course of the reaction is conveniently followed in a suitable manner (e.g. by analysis of the reaction mixture such as by means of thin layer chromatography) and the reaction is discontinued as soon as the analysis shows the presence of a 7,16-disubstitution product.

Insofar as they are not already present, double bonds can be introduced at the 1- and/or 6-position of the compounds of formula I. This can be achieved according to methods which are known for this operation in steroids of the normal (i.e. $9\alpha,10\beta$) series. A suitable method for the introduction of a Δ^6 -double bond is, for example, treatment with chloranil in amyl alcohol. A Δ^1 -double bond can be introduced for example, by treatment with dichloro-dicyano-benzoquinone in the presence of a small amount of *paratoluene*-sulphonic acid or a small amount of hydrochloric acid.

The novel $9\beta,10\alpha$ -steroids provided by the invention can be administered internally (for example, orally or parenterally) in the form of conventional pharmaceutical preparations which contain them in admixture with conventional pharmaceutical organic or inorganic carrier materials suitable for enteral or parenteral administration such as, for example, water, gelatin, lactose, starch, magnesium stearate, talc, vegetable oils, gums, polyalkylene glycols and petroleum jelly. The pharmaceutical preparations can be administered in conventional solid forms such as tablets, dragées, suppositories or capsules, or in conventional liquid forms such as solutions, suspensions or emulsions. They can be submitted to conventional pharmaceutical processes such as sterilization and/or can contain conventional pharmaceutical additives such as preservatives, stabilizing agents, wetting agents, emulsifying agents, salts for the adjustment of osmotic pressure or buffers. They can also contain other pharmaceutically valuable ingredients.

The following Examples illustrate the process provided by the invention:

EXAMPLE 1

A mixture of 70.0 g of $9\beta,10\alpha$ -pregna-4,6,16-triene-3,20-dione, 700 ml of ethyl mercaptan and 140 ml of piperidine is heated to reflux for 0.25 hour. The resulting solution is subsequently evaporated to dryness in water-jet vacuum and the residue chromatographed on silica gel. Elution with (petroleum ether)/ether (1:1) yields 55 g of 16α -ethylthio- $9\beta,10\alpha$ -pregna-4,6-diene-3,20-dione of melting point $117^\circ-118^\circ\text{C}$ (from acetone/hexane); $n_{D,25}^{25}=26,500$; $[\alpha]_D^{25}=-534^\circ$ (in dioxan).

A solution of 2.8 g of 16α -ethylthio- $9\beta,10\alpha$ -pregna-4,6-diene-3,20-dione and 2.8 g of 2,3-dichloro-5,6-dicyano-benzoquinone in 120 ml of absolute dioxan is heated to reflux for 10 hours. 100 ml of benzene are then added and the mixture is filtered through a column of 60 g of aluminium oxide (activity II). The crude product obtained by complete elution with benzene and evaporation of the solvent from the eluate is chromatographed on silica gel with (petroleum ether)/ether. The fractions which are uniform according to thin layer chromatography are

combined and recrystallized from acetone/hexane to yield 16α - ethylthio - $9\beta,10\alpha$ - pregna - 1,4,6 - triene - 3,20 - dione of melting point 112° — 113°C ; $\epsilon_{222}=14,000$; $\epsilon_{250}=10,200$; $\epsilon_{302}=13,200$; $[\alpha]_D^{25}=388^\circ$ (in dioxan).

EXAMPLE 2

A solution of 4.0 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione in 50 ml of methyl mercaptan and 2 ml of piperidine is stirred at 0°C for 5 minutes. The resulting mixture is concentrated to dryness *in vacuo*. The residue is dissolved in (petroleum ether)/ether (1:1) and the solution is filtered through silica gel to yield 4.0 g of chromatographically pure 16α - methylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione which, after recrystallization from (methylene chloride)/(isopropyl ether), melts at 136° — 137°C ; $\epsilon_{284}=27,400$; $[\alpha]_D^{15}=-534^\circ$ (in dioxan).

EXAMPLE 3

According to the method described in the first paragraph of Example 1, from $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione and *iso*-propyl mercaptan there is obtained 16α - *iso*-propylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 119° — 120°C (from acetone/hexane); $\epsilon_{284}=27,200$; $[\alpha]_D^{15}=-532^\circ$ (in dioxan).

EXAMPLE 4

In accordance with the procedure described in the first paragraph of Example 1, from $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione and propyl mercaptan there is obtained 16α - propylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 122° — 125°C ; $\epsilon_{284.5}=25,600$; $[\alpha]_D^{25}=-440^\circ$ (in chloroform).

EXAMPLE 5

In accordance with the procedure described in the first paragraph of Example 1, from $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione and butyl mercaptan there is obtained 16α - butylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 141° — 143°C ; $\epsilon_{284}=26,400$ $[\alpha]_D^{25}=-540^\circ$ (in chloroform).

EXAMPLE 6

A mixture of 2.0 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione, 60 ml of benzene, 4 ml of allyl mercaptan and 1 ml of piperidine is stirred at room temperature for 3.5 hours. A further 10 ml of allyl mercaptan are then added and the mixture is stirred for a further 5 hours. After standing at 0°C for several hours, the resulting mixture is concentrated to dryness *in vacuo* and the residue chromatographed on silica gel. Elution with (methylene chloride)/acetone (99:1) yields 1.9 g of 16α - allylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 98° — 100°C (from ether/hexane); $\epsilon_{285}=26,100$ $[\alpha]_D^{25}=-522^\circ$ (in dioxan).

EXAMPLE 7

A solution of 3.0 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione in 60 ml of benzyl mercaptan and 3 ml of piperidine is

heated at 50°C for 0.25 hour. The resulting mixture is worked up according to the procedure described in the first paragraph of Example 1 to yield 2.7 g of 16α - benzylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 158° — 160°C (from ether); $\epsilon_{284}=25,000$; $[\alpha]_D^{25}=-487^\circ$ (in dioxan).

EXAMPLE 8

A mixture of 3.0 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione, 300 ml of benzene, 12 ml of thiophenol and 1.5 ml of piperidine is stirred at room temperature for 1.25 hours. The resulting mixture is diluted with 200 ml of petroleum ether and chromatographed on silica gel. The (petroleum ether)/ether (2:1) eluates yield 16α - phenylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 198° — 200°C ; $\epsilon_{283}=26,500$; $[\alpha]_D^{25}=-587^\circ$ (in dioxan).

EXAMPLE 9

A stream of hydrogen sulphide is passed for 1.5 hours through a solution of 2.30 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione and 6 drops of piperidine in 60 ml of pyridine. The resulting mixture is concentrated *in vacuo* and the residue chromatographed on silica gel. The ether/(petroleum ether) (1:1) eluates yield 16α - mercapto - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione which, after recrystallization from ether, has a melting point of 130° — 135°C (with 0.5 mol of ether); $\epsilon_{283}=24,200$; $[\alpha]_D^{25}=-453^\circ$ (in dioxan).

EXAMPLE 10

A solution of 1.5 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione in 15 ml of 2-mercapto - ethanol is held at 0°C for 2 hours. It is then poured on ice-water and the resulting mixture is extracted with methylene chloride. The extract is washed neutral with water, dried with sodium sulphate and evaporated to dryness to yield 2.2 g of crude product which is chromatographed on silica gel. Elution with ether then gives 16α - (2 - hydroxy - ethylthio) - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 171° — 172°C [from (methylene chloride)/(isopropyl ether)], $\epsilon_{284}=27,200$; $[\alpha]_D^{25}=-514^\circ$ (in dioxan).

EXAMPLE 11

A solution of 1.0 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione in 20 ml of thioacetic acid is held at 5°C for 0.25 hour. The resulting mixture is poured on ice-water and extracted with ether. The ether extract is washed with dilute sodium hydroxide solution and then several times with water, dried with sodium sulphate and evaporated to dryness. The residue is chromatographed on 50 g of silica gel. The ether eluates yield 16α - acetylthio - $9\beta,10\alpha$ - pregna - 4,6 - diene - 3,20 - dione of melting point 135°C (from acetone/hexane); $\epsilon_{284}=27,400$; $\epsilon_{283}=6,800$; $[\alpha]_D^{25}=-617^\circ$ (in dioxan).

EXAMPLE 12

A mixture of 2.0 g of $9\beta,10\alpha$ - pregna - 4,6,16 - triene - 3,20 - dione, 120 ml of glacial

acetic acid, 4.0 g of potassium thiocyanate and 4.0 ml of concentrated hydrochloric acid is stirred at room temperature for 3 hours. It is then poured on ice-water and extracted with methylene chloride. The extracts, after washing neutral with sodium bicarbonate solution and water, yield 2.3 g of crystalline crude product which, for purification, is chromatographed on silica gel. The ether/(petroleum ether) (3:2) fractions yield 1.2 g of 16 α -cyanothio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione of melting point 222°—223°C (from acetone/hexane); ϵ_{284} =26,500; $[\alpha]_D^{25}$ =-622° (in dioxan).

EXAMPLE 13

1 g of 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione is dissolved in 5 ml of dioxan and the solution is treated with 5 ml of dithioglycol monomethyl ether. After 20 minutes at 25°C, starting material can no longer be detected by thin layer chromatogram and the solution is then taken up in 150 ml of ethyl acetate, extracted twice with 2 - N sodium hydroxide solution and washed neutral with water. There are obtained 1.58 g of crude product which is chromatographed on 30 g of silica gel in the system (methylene chloride)/(ethyl acetate). 5 ml fractions were collected. Fractions 85—137 yield 0.5 g of an oil which is obtained from isopropyl ether, on addition of pentane, as a semi-crystalline precipitate. This precipitate consists of 16 α - (2 - methylthio - ethylthio) - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione of melting point 125°C; ϵ_{284} =20,700; $[\alpha]_D^{25}$ =-342°.

EXAMPLE 14

A mixture of 375 mg of 6 - chloro - 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione [prepared as described in the specification of our copending Application No. 1418/69 (now Serial No.), 20 ml of ethyl mercaptan and 0.3 ml of piperidine is stirred at 5°C for 1 hour. The resulting mixture is worked up according to the procedure described in the first paragraph of Example 1 to give 6 - chloro - 16 α - ethylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione of melting point 157°—158°C (from ether); ϵ_{287} =22,200; $[\alpha]_D^{25}$ =-384° (in dioxan).

EXAMPLE 15

A solution of 3.45 g of 4 - chloro - 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione [prepared as described in the specification of our copending Application for Letters Patent No. 1418/69 (now Serial No. 1154407)] in a mixture of 35 ml of benzene and 56 ml of ethyl mercaptan is treated with 1 ml of piperidine. The resulting mixture is allowed to stand at 15°C for 48 hours and is then diluted with ether, washed with dilute hydrochloric acid, sodium bicarbonate solution and water, and evaporated. The residue is chromatographed

on silica gel to yield 1.87 g of chromatographically pure 4 - chloro - 16 α - ethylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione which is recrystallized from ether; melting point=159°—162°C; ϵ_{286} =23,100; $[\alpha]_D^{25}$ =-502° (in chloroform).

EXAMPLE 16

A mixture of 5.0 g of 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione, 100 ml of benzene, 30 ml of propargyl mercaptan and 2.5 ml of piperidine is stirred at 0°C under nitrogen for 3.5 hours. The resulting mixture is evaporated to dryness *in vacuo* and the residue is chromatographed on silica gel. Elution with (petroleum ether)/ether (1:1) yields 3.9 g of 16 α - [propyn - (2) - ylthio] - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione of melting point 188°—190°C [from acetone/(isopropyl ether)], ϵ_{284} =25,500; $[\alpha]_D^{25}$ =-536° (in dioxan).

EXAMPLE 17

In accordance with the procedure described in the first paragraph of Example 1, from 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione and octyl mercaptan there is obtained the oily 16 α - octylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione; ϵ_{284} =27,100; $[\alpha]_D^{25}$ =-453° (in dioxan).

EXAMPLE 18

In accordance with the procedure described in the first paragraph of Example 1, from 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione and octadecyl mercaptan there is obtained 16 α - octadecylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione; ϵ_{284} =26,800; $[\alpha]_D^{25}$ =-343° (in dioxan).

EXAMPLE 19

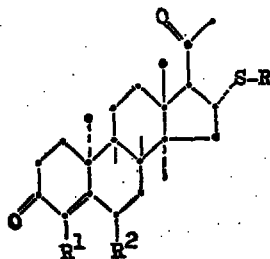
A mixture of 2.0 g of 9 β ,10 α - pregna - 4,6,16 - triene - 3,20 - dione, 40 ml of benzene, 10 ml of furfuryl mercaptan and 0.8 ml of piperidine is stirred at room temperature in a nitrogen atmosphere for 1 hour. The resulting solution is subsequently evaporated to dryness in water-jet vacuum and the residue is chromatographed on silica gel. Elution with ether/hexane (1:1) yields 2.2 g of 16 α - furfurylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione of melting point 144°—145°C (from acetone/hexane); ϵ_{222} =12,100; $[\alpha]_D^{25}$ =-481° (in dioxan).

The following Example illustrates the manner in which the novel 9 β ,10 α -steroids provided by the invention may be made up into pharmaceutical preparations:

Tablets each containing 5 mg of 16 α - ethylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione, 71 mg of lactose, 71 mg of corn starch, 2.7 mg of talc and 0.3 mg of magnesium stearate are prepared by mixing the ingredients together and forming the mixture into tablets.

WHAT WE CLAIM IS:—

1. A compound of the general formula



(I)

wherein R represents a hydrogen atom or an alkyl, hydroxy-alkyl, alkoxy-alkyl, mercapto-alkyl, alkylthio-alkyl, akenyl, alkynyl, aryl, aralkyl, alkanoyl or cyano group, a 5-membered or 6-membered heterocyclic group (which may be hydroxysubstituted) or a 5-membered or 6-membered heterocyclyl-methyl group and R¹ and R² each represent a hydrogen or halogen atom or an alkyl group, or a Δ^1 -dehydro, a Δ^6 -dehydro or a $\Delta^{1,6}$ -bisdehydro derivative thereof.

2. A compound as formulated in claim 1, wherein R represents a hydrogen atom or an alkyl, hydroxy-alkyl, alkoxy-alkyl, mercapto-alkyl, alkylthio-alkyl, alkenyl, alkynyl, aryl, aralkyl, alkanoyl or cyano group, or a Δ^1 -dehydro, a Δ^6 -dehydro or a $\Delta^{1,6}$ -bisdehydro derivative thereof.

3. A Δ^6 -dehydro derivative of a compound as formulated in claim 1 or as set forth in claim 2.

4. A compound or derivative as set forth in any one of the preceding claims, wherein any alkyl, alkenyl, alkynyl or alkanoyl groups which may be present contain up to 6 carbon atoms.

5. 16 α - Methylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

6. 16 α - Ethylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

7. 16 α - Propylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

8. 16 α - Isopropylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

9. 16 α - Octylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

10. 16 α - Octadecylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

11. 16 α - Butylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

12. 16 α - Phenylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

13. 16 α - Benzylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

14. 16 α - Mercapto - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

15. 16 α - Cyanothio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

16. 16 α - Allylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

17. 16 α - (2 - methylthio - ethylthio) - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

18. 16 α - (2 - hydroxy - ethylthio) - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

19. 16 α - Acetylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

20. 16 α - Ethylthio - 6 - chloro - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

21. 16 α - Ethylthio - 4 - chloro - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

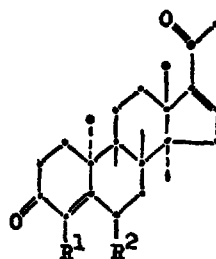
22. 16 α - [propyn - (2) - ylthio] - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

23. 16 α - Furfurylthio - 9 β ,10 α - pregna - 4,6 - diene - 3,20 - dione.

24. 16 α - Ethylthio - 9 β ,10 α - pregna - 1,4,6 - triene - 3,20 - dione.

25. A pharmaceutical preparation comprising a 9 β ,10 α -steroid as set forth in any one of the preceding claims in association with a compatible pharmaceutical carrier.

26. A process for the manufacture of the 9 β ,10 α -steroids claimed in claim 1, which process comprises reacting a compound of the general formula



(II)

wherein R¹ and R² have the significance given in claim 1, or a Δ^6 -dehydro derivative thereof, with a compound of the general formula



wherein R has the significance given in claim 1, and, if desired, introducing a double-bond into the 6,7-position of the reaction product if not already present in the starting material and/or into the 1,2-position.

27. A process as set forth in claim 26, wherein a compound of the formula first written in that claim or a Δ^6 -dehydro derivative thereof is reacted with a compound of the formula second written in that claim in which R represents a hydrogen atom or an alkyl, hydroxyl-alkyl, alkoxy-alkyl, mercapto-alkyl, alkylthio-alkyl, alkenyl, alkynyl, aryl, aralkyl, alkanoyl or cyano group.

28. A process as set forth in claim 26 or claim 27, wherein a Δ^6 -dehydro derivative of a compound of the formula first written in claim 26 is used as the starting material.

29. A process as set forth in any one of claims 26 to 28 inclusive, wherein any alkyl, alkenyl, alkynyl or alkanoyl groups which may be present in the starting materials contain up to 6 carbon atoms.



5 30. A process as set forth in any one of claims 26 to 29 inclusive insofar as a Δ^6 -dehydro derivative of a compound of the formula first written in claim 26 is used, wherein the reaction is discontinued as soon as analysis shows the presence of a 7,16-disubstitution product.

10 31. A process as set forth in any one of claims 26 to 30 inclusive, wherein the reaction is carried out in the presence of an organic base.

32. A process as set forth in claim 31, wherein said organic base is piperidine or collidine.

33. A process for the manufacture of the 9 β ,10 α -steroids claimed in claim 1, substantially as described with reference to Examples 1 to 19.

34. 9 β ,10 α -Steroids as claimed in claim 1, when manufactured by the process claimed in any one of claims 26 to 33 inclusive.

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