

L103,988



PATENT SPECIFICATION

NO DRAWINGS

L103,988

Date of Application and filing Complete Specification: March 29, 1965.
No. 36706/67.

Application made in United States of America (No. 400206) on Sept. 29, 1964.
(Divided out of No. 1103574).

Complete Specification Published: Feb. 21, 1968.

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Index at acceptance: —C2 C(3A8A3, 3A8A4, 3A8B2, 3A8C1, 3A8K, 3A12A3, 3A12A4B, 3A12B1, 3A12C6, 3A13A3A3, 3A13A3B2, 3A13A3L, 3A14A3C, 3A14A7B, 3A14A8D, 3A14B2A2, 3A14B3C, 3A14B7A, 3A14B8D, 3A19A3, 3A19B2, 3A19C1, 3A19D1)

Int. Cl.: —C 07 c 49/38

COMPLETE SPECIFICATION

A Process for the Preparation of Des-A-Steroids

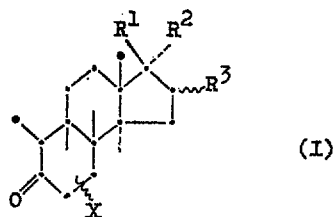
We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESELLSCHAFT, a Swiss Company of 124—184 Grenzacherstrasse, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following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

The present invention relates to a process for the preparation of des-A-steroids. More particularly, the invention is concerned with a process for the preparation of 9 β ,10 β -des-A-androstan(or pregnan)-5-ones and with certain novel 9 β ,10 β - desA - androstan(or pregnan) - 5 - ones.

9 β ,10 β - desA - androstan(or pregnan)-5-ones are valuable intermediates for the manufacture of 9 β ,10 α -steroids of the androstane or pregnane series; for example, they can be condensed with a lower-alkyl vinyl ketone or a lower-alkyl ethynyl ketone in accordance with the process described and claimed in the specification of our copending Application for Letters Patent no: 13173/65 (now serial no: 1103574).

Useful desA-steroids obtained by carrying out the present process are:

a) 9 β ,10 β - desA - androstan - 5 - ones of the formula

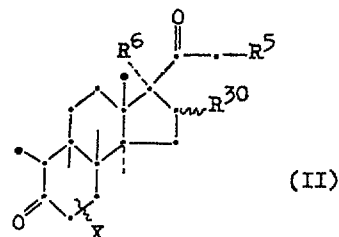


wherein R¹ represents a hydroxy or lower-

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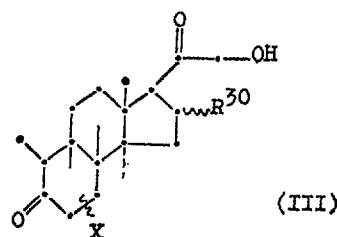
alkanoyloxy group, R² represents a hydrogen atom or a lower-alkyl group or R¹ together with R² represents an oxo or 17 β - hydroxy-17 α - (lower alkanolic acid) lactone group, R³ represents a hydrogen atom or a lower-alkyl, hydroxy or lower-alkanoyloxy group and X represents a hydrogen or halogen atom or a lower-alkyl, lower-alkylthio or lower-alkanoylthio group in the 6- or 7-position.

b) 9 β ,10 β - desA - pregnan - 5 - ones of the formula



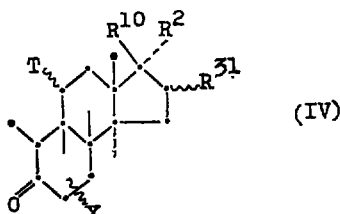
wherein X has the significance earlier, R³⁰ represents a hydrogen or fluorine atom or a lower-alkyl, hydroxy or lower-alkanoyloxy group, R⁵ represents a hydrogen or halogen atom and R⁶ represents a hydrogen or halogen atom or a lower-alkyl or hydroxy group.

c) 9 β ,10 β - desA - pregnan - 5 - ones of the formula



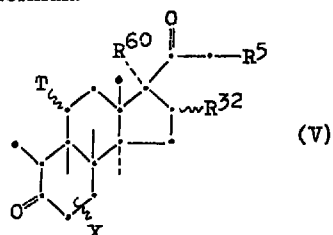
wherein R^{30} and X have the significance given earlier. Especially useful desA-steroids obtained by carrying out the present process are:

- d) $9\beta,10\beta$ - desA - androstan - 5 - ones of the formula



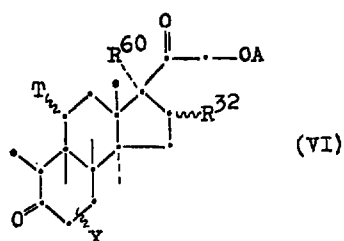
wherein R^{10} represents a hydrogen atom or an esterified hydroxy group, R^2 has the significance given earlier or R^{10} together with R^2 represents an oxo, lower-alkylenedioxy or 17β -hydroxy- 17α -(lower alkanolic acid) lactone group, R^{31} represents a hydrogen atom or a lower-alkyl, hydroxy or esterified hydroxy group, T represents a hydrogen atom or a hydroxy or esterified hydroxy group and X has the significance given earlier.

- e) $9\beta,10\beta$ - desA - pregnan - 5 - ones of the formula



- wherein R^5 , T and X have the significance given earlier, R^{32} represents a hydrogen or fluorine atom or a lower-alkyl, hydroxy or esterified hydroxy group and R^{60} represents a hydrogen or halogen atom or a lower-alkyl, hydroxy or esterified hydroxy group, as well as 20-ketals thereof, $16\alpha,17\alpha$ -ketals and acetals of those compounds in which R^{32} and R^{60} each represent a hydroxy group, derivatives of those compounds in which the 20-oxo group is reduced to a 20-hydroxy group and the corresponding derivatives in which said 20-hydroxy group is esterified.

- f) $9\beta,10\beta$ - desA - pregnan - 5 - ones of the formula



wherein R^{32} , R^{60} , T and X have the significance given earlier and OA represents a hydroxy or esterified hydroxy group, $17\alpha,20$; $20,21$ -bis(methylenedioxy) derivatives of those compounds in which OA and R^{60} each represent a hydroxy group, $17\alpha,21$ -ketals and acetals of those compounds in which OA and R^{60} each represent a hydroxy group, $16\alpha,17\alpha$ -ketals and acetals of those compounds in which OA and R^{32} each represent a hydroxy group, derivatives of those compounds in which the 20-keto group is reduced to a 20-hydroxy group and the corresponding derivatives in which said 20-hydroxy group is esterified.

According to the process of the present invention, $9\beta,10\beta$ - desA - androstan(or pregnan) - 5 - ones are prepared by catalytically hydrogenating a desA - androst(or pregn) - 9-en - 5 - one.

A process for the preparation of desA-androst(or pregn) - 9 - en - 5 - ones is described and claimed in the specification of our copending Application for Letters Patent no: 36705/67 (now serial no: 1103987) where certain of the desA - androst(or pregn) - 9-en - 5 - ones are claimed *per se*. Further, certain intermediates useful in the production of these desA - androst(or pregn) - 9 - en - 5 - ones are claimed *per se* in the specifications of our copending Applications for Letters Patent nos: 36700/67, 36701/67, 36702/67, 36703/67 and 36704/67, (now serial nos: 1103982, 1103983, 1103984, 1103985 and 1103986 respectively).

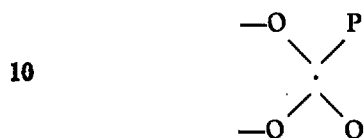
It will be appreciated that it may be necessary or desirable to protect certain of the substituents in the molecule prior to the catalytic hydrogenation. It will further be appreciated that the starting materials may contain substituents which are present in protected form. The protecting groups can be inserted and split off by methods known *per se*. The various substituents which are susceptible to being protected are exemplified by the 16-hydroxy group, the 17β -hydroxy group, the 17α -hydroxy group, the 21-hydroxy group, the 20-oxo group or the 17-oxo group.

The 17-oxo or 20-oxo group is suitably protected by ketalisation (e.g. by reaction with an alkanediol containing not more than 6 carbon atoms) to yield a 17 - (lower alkylenedioxy) or 20 - (lower alkylenedioxy) compound (i.e. a 17-ketal or a 20-ketal).

The 16-hydroxy, 17α -hydroxy, 17β -hydroxy or 21-hydroxy groups can be protected by esterification and/or etherification. Any available acid which will form an ester than can subsequently be hydrolysed to regenerate the hydroxy group is suitable. Examples of acids which are useful for this purpose are alkanolic acids containing not more than 6 carbon atoms (e.g. acetic acid), caproic acid, benzoic acid,

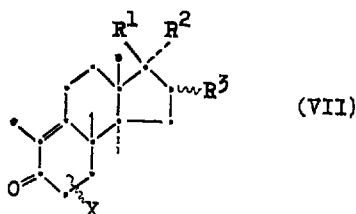
- phosphoric acid and alkane dicarboxylic acids containing not more than 6 carbon atoms (e.g. succinic acid). Also, protection for the 16 α -hydroxy, 17 α -hydroxy or 21-hydroxy groups can be effected by forming the lower-alkyl *ortho*esters thereof; that is, 16 α ,17 α - or 17 α ,21-(lower alkyl) *ortho*esters. A suitable ether protecting group is, for example, the tetrahydro-pyranyl ether group.
- 10 In compounds containing the dihydroxy-acetone side chain at the 17-carbon atom (for example, compounds of formula V in which R⁶ is a hydroxy group), this side chain can be protected by forming the 17,20;20,21-bis(methylenedioxy) group or by forming a 17,21-acetal or ketal group or by forming a 17,21-diester. The 17,21-acetal or ketal and 17,21-diester hinder the 20-ketone group and minimise the possibility of its participating in unwanted side-reactions. On the other hand, the 17,20;20,21-bis(methylenedioxy) derivatives actually convert the ketone to a non-reactive derivative. When both a 16 α -hydroxy and 17 α -hydroxy group are present, these groups can be protected by the formation of a 16 α ,17 α -acetal or ketal. The various protecting groups mentioned earlier can be removed by methods known *per se*; for example, by mild acid hydrolysis.
- 30 In compounds which contain a 20-oxo group but no 17 α -hydroxy or 21-hydroxy group, the 20-oxo group can be protected by reduction to the hydroxy group (i.e. reduction to the corresponding carbinol). Thus, for example, the 17-acetal side chain can be protected by conversion to a 17-(α -hydroxy-ethyl) side chain. Regeneration of the 17-acetyl side chain can be simply effected by conventional oxidation means; for example, by oxidation with chromium trioxide in an organic solvent such as glacial acetic acid. Similarly, in compounds containing a 17-oxo group, this group can be protected by reduction to the hydroxy group (i.e. reduction to the corresponding carbinol). Thus, the 17-oxo group can be reduced to a 17 β -hydroxy, 17 α -hydrogen moiety, from which, when desired, the 17-oxo moiety can be regenerated by oxidation as described earlier.
- 50 Furthermore, a 20-hydroxy or 17 β -hydroxy group can itself be protected by esterification; for example, with an alkanolic acid containing not more than 6 carbon atoms (such as acetic acid) or caproic acid.
- 55 The 16 α ,17 α or 17 α ,21-acetals and ketals discussed hereinbefore can be formed by reacting 16 α ,17 α -bis(hydroxy) or 17 α ,21-bis(hydroxy) compounds with an aldehyde or a ketone. This is preferably effected by reacting a simple acetal or ketal (e.g. an alkylene-glycol acetal or ketal of a suitable aldehyde or ketone containing not more than 6 carbon atoms) with the groups sought to be protected.
- Suitable aldehydes and ketones include lower-alkanals (i.e. alkanals containing from 2 to 6 carbon atoms) (such as paraldehyde, propanal and hexanal), di(lower alkyl) ketones (such as acetone, diethyl ketone, dibutyl ketone, methyl ethyl ketone and methyl *iso*-butyl ketone), *cyclo*alkanones (such as *cyclo*-butanone, *cyclopentanone* and *cyclohexanone*), *cyclo*alkyl-(lower alkanals) (such as *cyclopentyl* carboxaldehyde and *cyclohexyl* carboxaldehyde), *cyclo*alkyl (lower alkyl ketones (such as *cyclopentyl* propyl ketone, *cyclohexylmethyl* ethyl ketone), *dicyclo*alkyl ketones (such as *dicyclopentyl* ketone, *dicyclohexyl* ketone and *cyclopentyl cyclohexyl* ketone), *cyclo*alkyl monocyclic aromatic ketones (such as *cyclohexyl p* - chloro - phenyl ketone, *cyclopentyl o* - methoxy - phenyl ketone, *cyclopentyl o,p* - dihydroxy - phenyl ketone and *cyclohexyl m*-tolyl ketone), *cyclo*alkyl (lower alkyl) monocyclic aromatic ketones (such as *cyclopentylmethyl* phenyl ketone) *cyclo*alkyl monocyclic aromatic-(lower alkyl) ketones (such as *cyclopentyl* benzyl ketone and *cyclohexyl* phenylethyl ketone), *cyclo*alkyl-(lower alkyl) monocyclic aromatic-(lower alkyl ketones (such as *cyclopentylmethyl* benzyl ketone), halo-(lower alkanals) such as chloral hydrate, trifluoro-acetaldehyde hemiacetal and heptafluoro-butanal ethyl hemiacetal), halo-(lower alkanones) (such as 1,1,1-trifluoro-acetone), monocyclic carbocyclic aromatic aldehydes (such as benzaldehyde, halobenzaldehydes, for example *p* - chloro - benzaldehyde and *p* - fluoro - benzaldehyde), lower alkoxy-benzaldehydes (such as *o*-anisaldehyde), di-(lower alkoxy)-benzaldehydes (such as veratraldehyde), hydroxy-benzaldehydes (such as salicylaldehyde), lower alkyl-benzaldehydes (such as *m*-tolualdehyde and *p* - ethyl - benzaldehyde), di(lower alkyl)-benzaldehydes (such as *o,p* - dimethyl - benzaldehyde), monocyclic carboxylic aromatic lower alkanals (such as phenylacetaldehyde, α - phenyl - propionaldehyde, β - phenyl - propionaldehyde, 4-phenyl - butyraldehyde) and aromatically-substituted halo-, lower alkoxy-, hydroxy-, lower alkyl- and cyano-derivatives thereof, monocyclic carbocyclic aromatic ketones (such as acetophenone, α,α,α - trifluoro - acetophenone, propiophenone, butyrophenone, valerophenone), halo-phenyl lower-alkyl ketones (e.g. *p*-chloro-acetophenone and *p* - chloro - propiophenone, (lower alkoxy) - phenyl lower - alkyl ketones (such as *p*-anisyl methyl ketone), di(lower alkoxy)-phenyl lower-alkyl ketones, hydroxy-phenyl lower-alkyl ketones (lower alkyl)-phenyl lower-alkyl ketones (such as methyl *p*-tolyl ketone), di(lower alkyl)-phenyl lower-alkyl ketones (such as *o,p*-xylyl methyl ketone) benzophenone and mono- or bis-substituted halo, lower-alkoxy, hydroxy and lower-alkyl derivatives thereof and monocyclic carbocyclic aromatic lower-alkanones (such as 1 - phenyl-butanone-(3) and 1 - phenyl - pentanone - (4))

and aromatically substituted derivatives thereof. The terms 'lower alkoxy' and 'lower alkanone' are used herein to mean alkoxy groups and alkanones respectively which contain not more than 6 carbon atoms. Especially suitable are those aldehydes or ketones which, with the 16 α ,17 α - or 17 α ,21-bis(hydroxy) grouping form an acetal or ketal grouping of the formula

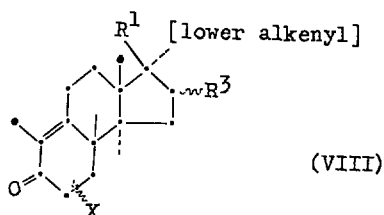


wherein P represents a hydrogen atom or a lower-alkyl group, Q represents a lower-alkyl or aryl group or P and Q together represent a lower-alkylene group such as tetramethylene or pentamethylene.

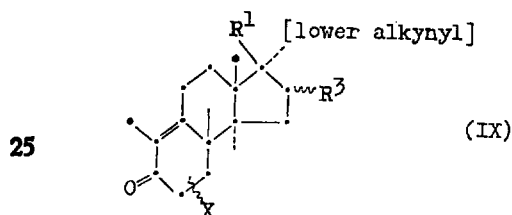
15 According to one embodiment of the present process, the 9 β ,10 β - desA - androstan - 5-ones of formula I can be prepared by hydrogenating a desA - androst - 9 - en - 5-
20 one of the formula



or

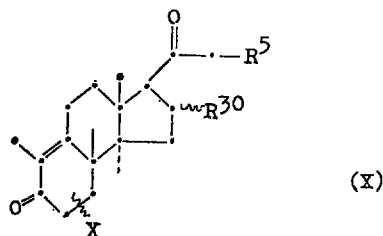


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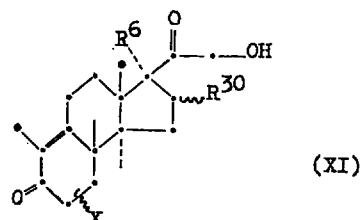


in which formulae, R¹, R², R³ and X have the significance given earlier. Also, the 9 β ,10 β - desA - pregnan - 5 - ones of formulae

II and III can be prepared by hydrogenating a desA - pregn - 9 - en - 5 - one of the
30 formula



or



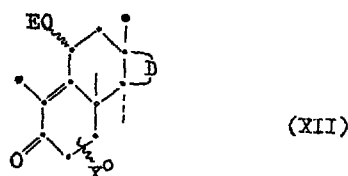
in which formulae, R³⁰, R⁵, R⁶ and X have the same significance given earlier. Prior to hydrogenation, the C-20 keto group in desA-steroids of formulae X and XI or the C-17 keto group in the desA-steroids of formula VII should be protected either by conversion to the corresponding carbinol or by ketalisation as described earlier.

Moreover, it should be noted that the hydrogenation, besides inserting a hydrogen atom at each of the 9- and 10-positions can also simultaneously bring about hydrogenation of other groups in the molecule. For example, the C-20 keto group can be hydrogenated to the corresponding carbinol or the C-17 (lower alkenyl) group in compounds of formula VIII or the C-17 (lower alkynyl) group in compounds of formula IX can be hydrogenated to the corresponding C-17 (lower alkyl) group. Compounds of formula VIII and IX can, in turn, be prepared from compounds of formula VII in which R¹ and R² together represent an oxo group by reaction with a lower-alkenyl or lower-alkynyl GRIGNARD reagent (with prior protection of the 5-keto group); for example, by forming 5-ketals without concurrent blocking of the 17-keto group.

The hydrogenation of the desA - androst-9 - en - 5 - ones of formulae VII to IX and of the desA - pregn - 9 - en - 5 - ones of formulae X and XI is effected by catalytic means, suitably using a precious metal catalyst. Especially preferred precious metal catalysts are palladium, platinum and rhodium. It is particularly advantageous to use rhodium; for example, rhodium-on-charcoal or rhodium-on-alumina. In contrast to what would be expected, it has been found that such a cata-
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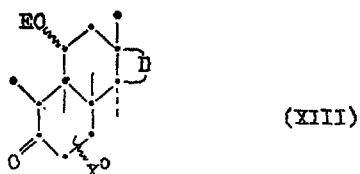
lytic hydrogenation of a compound of formula VII to XI gives a substantial yield of a compound of formulae I to III respectively. In fact, it has been found that such catalytic hydrogenation gives a major proportion of a compound of the formula I, II or III. This catalytic hydrogenation is suitably effected in an inert organic solvent; for example, an alkaneol containing not more than six carbon atoms (such as methanol or ethanol), an ether (such as dioxan or diglyme) or a hydrocarbon (such as cyclohexane or hexane). Moreover, the catalytic hydrogenation is suitable conducted in the presence of an acidic or basic catalyst; for example, an alkali-metal or alkaline-earth-metal hydroxide (such as sodium hydroxide) or a mineral acid. Examples of suitable acids are the hydrohalic acids (such as hydrochloric acid). The catalytic hydrogenation can be conducted at, above or below room temperature; for example from about -5°C to 100°C . However, it is preferably conducted at a temperature between about 0°C and 35°C .

A further embodiment of the present process comprises the catalytic hydrogenation of a compound of the general formula



wherein D represents the remainder of the D-ring present in compounds of formula I, II or III hereinbefore, X° represents a hydrogen atom or a lower-alkyl, lower-alkylthio or lower-alkanoylthio group in the 6-position or a halogen atom or a lower-alkyl, lower alkylthio or lower-alkanoylthio group in the 7-position and EO is an esterified hydroxy group. These compounds of formula XII are claimed *per se* in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987) and may be prepared as described therein.

The catalytic hydrogenation of the compounds of formula XII yields an 11-(esterified hydroxy) - desA - $9\beta,10\beta$ - androstan - 5-one or 11 - (esterified hydroxy) - desA - $9\beta,10\beta$ - pregnan - 5 - one of the formula

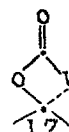


wherein X° , D and EO have the significance given earlier. This hydrogenation can be carried

out in the same manner as described earlier for the hydrogenation of compounds of formulae VII to XI to compounds of formulae I, II or III. Also, compounds of formula XII containing a 17-oxo group can be converted into a corresponding compound containing a 17β -hydroxy, 17α -(lower alkenyl) or 17α -(lower alkynyl) group by the methods described earlier. Also, compounds of formula XIII can be hydrolysed to yield the corresponding 11-hydroxy compounds.

The compounds of formula XIIIa as well as the corresponding 17β -hydroxy, 17α -(lower alkenyl) or 17α -(lower alkynyl) compounds are of value for the manufacture of $9\beta,10\alpha$ -steroids which contain an 11-(esterified hydroxy) group.

It will be appreciated that the term 'lower alkyl' is used in this description and in the claims appended hereto to mean both straight-chain and branched-chain alkyl groups containing not more than 6 carbon atoms (e.g. methyl, ethyl, propyl and isopropyl). Similarly, the term 'lower-alkanoyl' means alkanoyl groups containing not more than 6 carbon atoms (e.g. acetyl) and the term 'lower alkanoyloxy' means alkanoyloxy groups containing not more than 6 carbon atoms (e.g. acetoxy). Again, the term 'lower alkenyl' means alkenyl groups containing not more than 6 carbon atoms (e.g. vinyl) and the term 'lower alkynyl' means alkynyl groups containing not more than 6 carbon atoms (e.g. ethynyl). The term 'halogen' means iodine, bromine, chlorine and fluorine. The expression '17 β - hydroxy - 17α - (lower alkanoyl acid) lactone' refers to a configuration at the C-17 carbon atom illustrated as follows



wherein W is a lower-alkylene group such as ethylene or propylene. The term 'lower alkylene' is used to mean an alkylene containing not more than 6 carbon atoms. With regard to X, the preferred compounds are those in which it represents a hydrogen atom or lower-alkyl group in the 6- or 7-position or a halogen atom in the 7-position.

The following Examples illustrate the invention:

EXAMPLE 1

A suspension of 262 mg of 5 per cent rhodium on alumina catalyst in a mixture of 26 ml of 95 per cent ethanol and 5.25 ml of 2-N sodium hydroxide solution was pre-reduced (i.e. hydrogenated at room temperature and atmospheric pressure). To this

was added a solution of 262 mg of 17 α -ethyl - 17 β - hydroxy - desA - androst - 9-en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] in 15 ml of 95% ethanol and the mixture was then hydrogenated at atmospheric pressure and room temperature. After one mol equivalent of hydrogen had been absorbed the reaction was stopped, the catalyst separated by filtration, and the filtrate evaporated *in vacuo*. 1 ml of glacial acetic acid was added to the residue, which was then dissolved in 1 litre of ether. The cloudy solution which resulted was washed with 2-N sodium carbonate solution and then with water, dried and evaporated to dryness *in vacuo*.

The reaction was repeated three more times and the combined products were chromatographed on a column of activated magnesium silicate adsorbent. The eluates with 1 per cent ethyl acetate in benzene first gave crystalline fractions, which were followed by non-crystalline fractions. The non-crystalline fractions were dissolved in 100 ml of methylene chloride and, after the addition of 2.5 ml of 2 per cent chromium trioxide in 90 per cent acetic acid, were stirred overnight. The excess of chromic acid was removed by washing the methylene chloride solution with 10 ml of 10 per cent sodium hydrogen sulphite solution, followed by washing with 2-N sodium carbonate solution and then with water. The solution was then dried and evaporated *in vacuo*. The residue was dissolved in 50 ml of anhydrous ethanol containing 172 mg of sodium ethoxide and left overnight. The next day, after addition of 0.5 ml of glacial acetic acid, the solution was evaporated *in vacuo* and the residue was taken up in 1 litre of ether. The ether solution was washed with 2-N sodium carbonate solution and then with water, dried and evaporated. The residue was chromatographed on a column of activated magnesium silicate adsorbent and gave crystalline 17 α - ethyl - 17 β - hydroxy - desA - 9 β ,10 β - androstan - 5 - one, which was shown by thin layer chromatography to be identical with the crystalline material obtained in the first chromatographic separation. After two recrystallizations from ether it melted at 142°—144°C; $[\alpha]_D^{25} = -11.65^\circ$ (c=1.245 per cent in methanol).

EXAMPLE 2

(i) A suspension of 262 mg of 5 per cent rhodium on alumina catalyst in a mixture of 26 ml of 95 per cent ethanol and 5.25 ml of 2-N aqueous sodium hydroxide was hydrogenated at room temperature and atmospheric pressure. A solution of 262 mg of 20 β - hydroxy - desA - pregn - 9 - en - 5-one [obtained as described in the specification of our copending application for Letters Patent No: 36705/67 (now serial No:

1103987)] in 15 ml of 95 per cent ethanol was added to the mixture, and the reaction mixture was then hydrogenated at room temperature and atmospheric pressure. After one mol equivalent of hydrogen had been absorbed, the reaction was stopped and the catalyst was separated by filtration. After standing overnight the filtrate was concentrated *in vacuo*. 1 ml of glacial acetic acid was added to the residue and the mixture was then dissolved in 1 litre of ether. The cloudy solution was washed with 2-N aqueous sodium carbonate solution and then with water, dried over anhydrous sodium sulphate and evaporated to dryness *in vacuo*. It yielded a colourless oil which was chromatographed on a silica gel column using 1 per cent ethyl acetate in benzene as the eluant. First eluted was 20 β - hydroxy - 10 α - desA - pregnan-5-one of melting point 107°—108°C after recrystallization from (methylene chloride)/(petroleum ether). Rotatory dispersion (in methanol): $[\alpha]_{500} = -25.3^\circ$; $[\alpha]_{400} = -89^\circ$; $[\alpha]_{350} = -274^\circ$; $[\alpha]_{305} = -1335^\circ$; $[\alpha]_{300} = -1165^\circ$.

Further elution yielded 20 β - hydroxy-9 β ,10 β - desA - pregnan - 5 - one as a colourless oil. Rotatory dispersion (in methanol): $[\alpha]_{500} = -14.8^\circ$; $[\alpha]_{400} = -4.4^\circ$; $[\alpha]_{350} = +22.2^\circ$; $[\alpha]_{310} = +2148^\circ$.

(ii) A suspension of 262 mg of 5 per cent rhodium on alumina catalyst in a mixture of 2 ml of 3-N aqueous hydrochloric acid and 18 ml of 95 per cent ethanol was hydrogenated at room temperature and atmospheric pressure. A solution of 262 mg of 20 β -hydroxy - desA - pregn - 9 - en - 5 - one in 5 ml of absolute ethanol was introduced into the hydrogenation flask and the reaction mixture was hydrogenated at room temperature and atmospheric pressure. After one mol equivalent of hydrogen had been absorbed the reaction was stopped, the catalyst separated by filtration, and the filtrate neutralized with 2-N aqueous sodium hydroxide solution. An excess of 5 ml of 2-N aqueous sodium hydroxide was added and the solution allowed to stand overnight. Ethanol was then removed by evaporation at reduced pressure and, after the addition of 1 ml of glacial acetic acid, the residue was extracted with 1 litre of ether. The extract was washed with 2-N aqueous sodium carbonate solution and then with water, dried and concentrated *in vacuo*. It gave a colourless oil, which was chromatographed on a silica gel column using 2 per cent ethyl acetate in benzene as the eluant. On concentration, the first fractions of the eluate yielded 20 β -hydroxy - 10 α - desA - pregnan - 5 - one. 20 β - Hydroxy - 9 β ,10 β - desA - pregnan-5 - one was obtained from the immediately subsequent fraction. Both products were identical with the same compounds obtained in part (i) of this Example.

EXAMPLE 3

17 α - Acetoxy - 20 β - hydroxy - 9 β ,10 β -desA - pregnan - 5 - one was prepared from 17 α - acetoxy - 20 β - hydroxy - desA - pregn-9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation under acidic conditions in the presence of a rhodium catalyst according to the procedure of Example 2(ii).

EXAMPLE 4

A solution of 236 mg of 17 β - hydroxy-desA - androst - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] in 40 ml of 95 per cent ethanol and 5.25 ml of 2-N aqueous sodium hydroxide solution was hydrogenated with one mol equivalent of hydrogen over 236 mg of prereduced 5 per cent rhodium on alumina catalyst. After separation of the catalyst, the solution was concentrated to dryness *in vacuo* and the residue was taken up in one litre of ether. The ether solution was washed with water, dried over anhydrous sodium sulphate and evaporated to dryness *in vacuo*. 17 β - Hydroxy-9 β ,10 β - desA - androstan - 5 - one was obtained from the residue by crystallization; melting point 144.5°—145°C; $[\alpha]_D^{25} = -22^\circ$ (c=0.103 in dioxan).

17 β - Hydroxy - 9 β ,10 β - desA - androstan - 5 - one was converted into 5,5-ethylenedioxy - 17 β - hydroxy - 9 β ,10 β - desA - androstane as follows:

A solution of 238 mg of 17 β - hydroxy-9 β ,10 β - desA - androstan - 5 - one, 1 ml of ethylene glycol and a catalytic amount of *paratoluene-sulphonic acid* in 100 ml of anhydrous benzene was slowly distilled until no more water was coming over. The solution was then concentrated to a small volume *in vacuo* and 5,5 - ethylenedioxy - 17 β -hydroxy - 9 β ,10 β - desA - androstane was obtained from the residue by crystallization; melting point 115°—116°C, $[\alpha]_D^{25} = -9^\circ$ (c=0.0987 in dioxan).

5,5 - Ethylenedioxy - 17 β - hydroxy - 9 β ,10 β - desA - androstane was oxidized to 5,5-ethylenedioxy - 9 β ,10 β - desA - androstan-17-one as follows:

1 equivalent of 2 per cent chromic acid in pyridine was added to a solution of 282 mg of 5,5 - ethylenedioxy - 17 β - hydroxy-9 β ,10 β - desA - androstane in 50 ml of methylene chloride and the reaction mixture stirred overnight. The reaction mixture was then washed with 10 per cent aqueous sodium hydrogen sulphite, 2-N aqueous sodium carbonate and water, then dried over anhydrous sodium sulphate and concentrated to dryness *in vacuo*. Crystallization of the residue gave

5,5 - ethylenedioxy - 9 β ,10 β - desA - androstan - 17 - one.

Splitting of the ketal in acetone solution in the presence of a catalytic amount of *paratoluene-sulphonic acid* gave 9 β ,10 β - desA - androstane - 5,17 - dione which melted at 77.5°—78°C; $[\alpha]_D^{25} = +55^\circ$ (c=0.107 in dioxan).

9 β ,10 β - DesA - androstane - 5,17 - dione was also obtained as follows:

1 ml of JONES reagent (0.004 mol CrO₃) was added to 200 mg of 17 β - hydroxy-9 β ,10 β - desA - androstan - 5 - one in 20 ml of acetone at -10°C. The mixture was left for 15 minutes at room temperature and 5 ml of ethanol were then added. The resulting suspension was evaporated to dryness *in vacuo*, water was added to the residue and the undissolved portion taken up in ether. The ether phase was washed with a solution of sodium bicarbonate and then with water, dried over sodium sulphate and evaporated to dryness. There was thus obtained an oil which crystallized upon the addition of a small portion of petroleum ether. The so-obtained crystals of 9 β ,10 β - desA - androstane - 5,17 - dione melted at 77.5°—78°C after recrystallization from *cyclohexane*; $[\alpha]_{589}^{25} = +55^\circ$ (c=0.107 in dioxan); rotatory dispersion in dioxan (c=0.107%): $[\alpha]_{550} = +70^\circ$; $[\alpha]_{500} = +297^\circ$; $[\alpha]_{436} = +798^\circ$; $[\alpha]_{420} = +2968^\circ$ (max); $[\alpha]_{300} = +467^\circ$; $[\alpha]_{290} = 0^\circ$; $[\alpha]_{200} = -1890^\circ$.

5,5 - Ethylenedioxy - 9 β ,10 β - desA - androstan - 17 - one was converted to 17 α -[propyn - (1) - yl] - (1)] - 17 β - hydroxy-9 β ,10 β - desA - androstan - 5 - one as follows:

A tetrahydro-furan solution of 200 mg of 5,5 - ethylenedioxy - 9 β ,10 β - desA - androstan - 17 - one was added to a preformed solution of one mol equivalent of propyn-(1) - yl - (1) lithium in 100 ml of anhydrous liquid ammonia and the reaction mixture was stirred for 2 hours. After addition of 1 g of ammonium chloride, cooling was discontinued and the reaction mixture was allowed to evaporate. The residue was extracted with methylene chloride, the extract washed with water, dried over anhydrous sodium sulphate and evaporated. The residue was dissolved in 20 ml of acetone and the catalytic amount of *paratoluene-sulphonic acid* added. The solution was heated at reflux for 2 hours, then poured in water and extracted with methylene chloride. The methylene chloride extract was washed with water, dried over anhydrous sodium sulphate and evaporated to dryness *in vacuo*. Crystallization of the residue gave 17 α - [propyn - (1) - yl - (1)] - 17 α - hydroxy - 9 β ,10 β - desA - androstan - 5 - one.

5,5 - Ethylenedioxy - 9 β ,10 β - desA - androstan - 17 - one was converted to 17 α -[2 - methyl - propen - (2) - yl - (1)] - 17 β -

hydroxy - 9 β ,10 β - desA - androstan - 5-one as follows:

A solution of 280 mg of 5,5 - ethylenedioxy - 9 β ,10 β - desA - androstan - 17-one in 100 ml of tetrahydro-furan was added dropwise to a stirred solution of one mol equivalent of 2 - methyl - propen - (2) - yl - (1) magnesium bromide in 100 ml of ether of room temperature. The reaction mixture was heated at reflux for 1 hour. After cooling in an ice-salt bath, a saturated solution of sodium sulphate was slowly added in order to decompose the GRIGNARD complex. This was followed by addition of anhydrous sodium sulphate. The solution was separated by filtration and concentrated to dryness *in vacuo*. The solution of the residue and of a catalytic amount of *paratoluene*-sulphonic acid in 20 ml of acetone was heated at reflux for 2 hours, then poured in water and extracted with methylene chloride. The methylene chloride extract was washed with water, dried over anhydrous sodium sulphate and evaporated to dryness. 17 α - [2 - methylpropen - (2) - yl - (1)] - 17 β - hydroxy-9 β ,10 β - desA - androstan - 5 - one was obtained from the residue.

EXAMPLE 5

17 β - Acetoxy - 9 β ,10 β - desA - androstan - 5 - one was obtained by reduction of 17 β - acetoxy - desA - androst - 9 - en - 5 - one [obtained by acetylation of testosterone followed by ozonolysis, pyrolysis, and bromination and dehydrobromination according to the methods described in our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] according to the method of the first paragraph of Example 4, and melted at 118°—119°C; $[\alpha]_D^{25} = -28^\circ$ (c=0.103 in dioxan).

17 β - Acetoxy - 9 β ,10 β - desA - androstan - 5 - one was also obtained as follows:

A solution of 250 mg of 17 β - hydroxy-9 β ,10 β - desA - androstan - 5 - one in 2.5 ml of pyridine and 2.5 ml of acetic anhydride was left at room temperature for 18 hours. The mixture was then evaporated to dryness at 80°C/11 mm., the residue was taken up in ether, and the ether phase washed with 1-N hydrochloric acid, sodium bicarbonate and water, and then dried over sodium sulphate. After filtration and evaporation of the ether, the residue was treated with a small quantity of petroleum ether to yield crystals of 17 β - acetoxy - 9 β ,10 β - desA - androstan - 5 - one which melted at 118—119°C after recrystallization from methanol; $[\alpha]_{589}^{25} = -28^\circ$ (c=0.103% in dioxan). Rotatory dispersion in dioxan (c=0.103%); $[\alpha]_{400} = -30^\circ$; $[\alpha]_{356} = 0^\circ$; $[\alpha]_{350} = +10^\circ$; $[\alpha]_{313} = +449^\circ(\text{max})$; $[\alpha]_{307} = +374^\circ(\text{min})$; $[\alpha]_{305} = +380^\circ(\text{max})$; $[\alpha]_{300} = +224^\circ$; $[\alpha]_{293} = 0^\circ$; $[\alpha]_{280} = -652^\circ$.

17 β - Acetoxy - 9 β ,10 β - desA - andro-

stan - 5 - one was hydrolysed to 17 β -hydroxy-9 β ,10 β - desA - androstan - 5 - one as follows:

A solution of 250 mg of 17 β - acetoxy-9 β ,10 β - desA - androstan - 5 - one in 60 ml of 95 per cent methanol containing 144 mg of potassium hydroxide was heated at reflux for 1 hour. The resulting mixture was evaporated to dryness *in vacuo*, water was added to the residue and the suspension extracted with ether. The ether phase was washed with water, dried over sodium sulphate, filtered, the solvent removed and the crystalline residue then crystallized from a small volume of cyclohexane to yield crystals of 17 β - hydroxy - 9 β ,10 β - desA - androstan - 5 - one which melted at 144.5°—145°C after recrystallization from ethyl acetate; $[\alpha]_{589}^{25} = -22^\circ$ (c=0.103 in dioxan). Rotatory dispersion in dioxan (c=0.103): $[\alpha]_{400} = -7^\circ$; $[\alpha]_{390} = 0^\circ$; $[\alpha]_{350} = +52^\circ$; $[\alpha]_{313} = +571^\circ(\text{max})$; $[\alpha]_{307} = +492^\circ(\text{min})$; $[\alpha]_{305} = +504^\circ(\text{max})$; $[\alpha]_{300} = +324^\circ$; $[\alpha]_{293} = 0^\circ$; $[\alpha]_{280} = -202^\circ$.

EXAMPLE 6

16 α - Acetoxy - 20,20 - ethylenedioxy-9 β ,10 β - desA - pregnan - 5 - one was prepared from 16 α - acetoxy - 20,20 - ethylenedioxy - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation under basic conditions in the presence of a rhodium catalyst according to the procedure of Example 2(i).

EXAMPLE 7

16 α - Methyl - 20,20 - ethylenedioxy - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 16 α - methyl - 20,20 - ethylenedioxy - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation under basic conditions in the presence of a rhodium catalyst according to the procedure of Example 2(i).

EXAMPLE 8

21 - Acetoxy - 20,20 - ethylenedioxy - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 21 - acetoxy - 20,20 - ethylenedioxy - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation under acidic conditions in the presence of a rhodium catalyst according to the procedure of Example 2(ii).

EXAMPLE 9

20 β - Hydroxy - 16 α ,17 α - isopropylidenedioxy - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 20 β - hydroxy - 16 α ,17 α -

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isopropylidenedioxy - desA - pregn - 9 - en - 5-one [obtained as described in the specification of our copending application for Letters Patent no. 36705/67 (now serial no: 1103987)] by hydrogenation according to the procedure of Example 2(i).

EXAMPLE 10

7 α ,17 α - Dimethyl - 17 β - hydroxy - desA - 9 β ,10 β - androstan - 5 - one was prepared from 7 α ,17 α - dimethyl - 17 β - hydroxy - desA - androst - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation in the presence of a rhodium catalyst according to the procedure of Example 1.

EXAMPLE 11

20 β - Hydroxy - 17 α - methyl - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 17 α - methyl - 20 β - hydroxy - desA - pregnan - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] according to the procedure of Example 2(ii).

EXAMPLE 12

17 α - Methyl - 17 β - hydroxy - desA - 9 β ,10 β - androstan - 5 - one was prepared from 17 α - methyl - 17 β - hydroxy - desA - androst - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation of the latter according to the procedure of Example 1. On recrystallization from (ethyl acetate)/(petroleum ether), the product melted at 94.5°—95.5°C; $[\alpha]_D^{25} = -36^\circ$ (c=0.0998 in dioxan).

EXAMPLE 13

Hydrogenation of 11 α ,20 β - diacetoxy - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no. 1103987)] in ethanolic hydrochloric acid over 5 per cent rhodium-on-alumina catalyst at room temperature and atmospheric pressure according to the procedure of Example 2(ii) gave 11 α ,20 β - diacetoxy - 9 β ,10 β - desA - pregnan - 5 - one.

11 α ,20 β - Diacetoxy - 9 β ,10 β - desA - pregnan - 5 - one was hydrolysed in methanol solution with one mol equivalent of potassium carbonate to give 11 α ,20 β - dihydroxy - 9 β ,10 β - desA - pregnan - 5 - one.

EXAMPLE 14

3 - (17 β - hydroxy - 5 - oxo - 9 β ,10 β - desA - androstan - 17 α - yl) - propionic acid lactone was prepared from 3-(17 β -hydroxy-

5 - oxo - desA - androst - 9 - en - 17 α - yl) - propionic acid lactone [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation in the presence of a rhodium catalyst according to the procedure of Example 1.

EXAMPLE 15

17 α , 20;20,21 - bis(methylenedioxy) - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 17 α ,20;20,21 - bis(methylenedioxy) - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 110398)] by hydrogenation in the presence of a rhodium catalyst according to the procedure of Example 2(i).

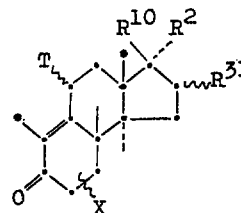
The activated magnesium silicate adsorbent used in the foregoing examples is a synthetic magnesia-silica gel marketed by the Floridin Company, Tallahassee, Florida. 100—200 mesh material was used. It will be appreciated that when compounds of the pregnane series are referred to in this specification these compounds are of the 17 β -pregnane series unless specifically indicated to the contrary.

It will be appreciated that in the formulae given in this description and accompanying claims the dots denote carbon atoms or CH, CH₂ or CH₃ groups, the residual valencies being satisfied by hydrogen atoms; such valencies only being shown to indicate hydrogen atoms when configuration is of significance, and then as untermiated solid or broken lines. Valencies shown as solid lines denote β -configuration and those shown as broken lines denote α -configuration. The dots representing angular methyl groups are enlarged solely for reasons of clarity.

WHAT WE CLAIM IS:—

1) A process for the preparation of 9 β ,10 β - desA - androstan(or pregnan) - 5-ones, which process comprises catalytically hydrogenating a desA - androst(or pregn) - 9 - en - 5 - one.

2) A process at set forth in claim 1, wherein a compound of the formula



wherein R¹⁰ represents a hydroxy or esterified hydroxy group, R² represents a hydrogen atom or a lower-alkyl group or R¹⁰ together with R² represents an oxo, lower-alkylenedioxy or 17 β - hydroxy - 17 α - lower alkanolic acid) lactone group, R³¹ represents a hydrogen atom or a lower-alkyl, hydroxy or esterified



isopropylidenedioxy - desA - pregn - 9 - en - 5-one [obtained as described in the specification of our copending application for Letters Patent no. 36705/67 (now serial no: 1103987)] by hydrogenation according to the procedure of Example 2(i).

EXAMPLE 10

7 α ,17 α - Dimethyl - 17 β - hydroxy - desA - 9 β ,10 β - androstan - 5 - one was prepared from 7 α ,17 α - dimethyl - 17 β - hydroxy - desA - androst - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation in the presence of a rhodium catalyst according to the procedure of Example 1.

EXAMPLE 11

20 β - Hydroxy - 17 α - methyl - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 17 α - methyl - 20 β - hydroxy - desA - pregnan - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] according to the procedure of Example 2(ii).

EXAMPLE 12

17 α - Methyl - 17 β - hydroxy - desA - 9 β ,10 β - androstan - 5 - one was prepared from 17 α - methyl - 17 β - hydroxy - desA - androst - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation of the latter according to the procedure of Example 1. On recrystallization from (ethyl acetate)/(petroleum ether), the product melted at 94.5°—95.5°C; $[\alpha]_D^{25} = -36^\circ$ (c=0.0998 in dioxan).

EXAMPLE 13

Hydrogenation of 11 α ,20 β - diacetoxy - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] in ethanolic hydrochloric acid over 5 per cent rhodium-on-alumina catalyst at room temperature and atmospheric pressure according to the procedure of Example 2(ii) gave 11 α ,20 β - diacetoxy - 9 β ,10 β - desA - pregnan - 5 - one.

11 α ,20 β - Diacetoxy - 9 β ,10 β - desA - pregnan - 5 - one was hydrolysed in methanol solution with one mol equivalent of potassium carbonate to give 11 α ,20 β - dihydroxy - 9 β ,10 β - desA - pregnan - 5 - one.

EXAMPLE 14

3 - (17 β - hydroxy - 5 - oxo - 9 β ,10 β - desA - androstan - 17 α - yl) - propionic acid lactone was prepared from 3-(17 β -hydroxy-

5 - oxo - desA - androst - 9 - en - 17 α - yl)-propionic acid lactone [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation in the presence of a rhodium catalyst according to the procedure of Example 1.

EXAMPLE 15

17 α , 20;20,21 - bis(methylenedioxy) - 9 β ,10 β - desA - pregnan - 5 - one was prepared from 17 α ,20;20,21 - bis(methylenedioxy) - desA - pregn - 9 - en - 5 - one [obtained as described in the specification of our copending application for Letters Patent no: 36705/67 (now serial no: 1103987)] by hydrogenation in the presence of a rhodium catalyst according to the procedure of Example 2(i).

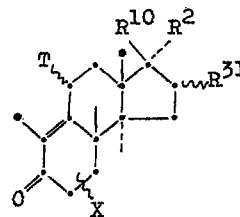
The activated magnesium silicate adsorbent used in the foregoing examples is a synthetic magnesia-silica gel marketed by the Floridin Company, Tallahassee, Florida. 100—200 mesh material was used. It will be appreciated that when compounds of the pregnane series are referred to in this specification these compounds are of the 17 β -pregnane series unless specifically indicated to the contrary.

It will be appreciated that in the formulae given in this description and accompanying claims the dots denote carbon atoms or CH, CH₂ or CH₃ groups, the residual valencies being satisfied by hydrogen atoms; such valencies only being shown to indicate hydrogen atoms when configuration is of significance, and then as untruncated solid or broken lines. Valencies shown as solid lines denote β -configuration and those shown as broken lines denote α -configuration. The dots representing angular methyl groups are enlarged solely for reasons of clarity.

WHAT WE CLAIM IS:—

1) A process for the preparation of 9 β ,10 β - desA - androstan(or pregnan) - 5-ones, which process comprises catalytically hydrogenating a desA - androst(or pregn) - 9 - en - 5 - one.

2) A process as set forth in claim 1, wherein a compound of the formula



wherein R¹⁰ represents a hydroxy or esterified hydroxy group, R² represents a hydrogen atom or a lower-alkyl group or R¹⁰ together with R² represents an oxo, lower-alkylenedioxy or 17 β - hydroxy - 17 α - lower alkanolic acid) lactone group, R³¹ represents a hydrogen atom or a lower-alkyl, hydroxy or esterified

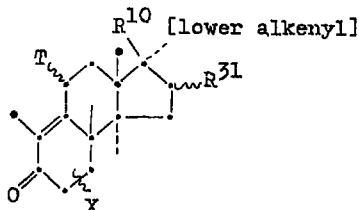


hydroxy group, X represents a hydrogen or halogen atom or a lower-alkyl, lower-alkylthio or lower-alkanoylthio group in the 6- or 7-position and T represents a hydrogen atom or a hydroxy or esterified hydroxy group, is catalytically hydrogenated.

3) A process as set forth in claim 2, wherein a 17α - (lower alkyl) - 17β - hydroxy - desA - androst - 9 - en - 5 - one is catalytically hydrogenated.

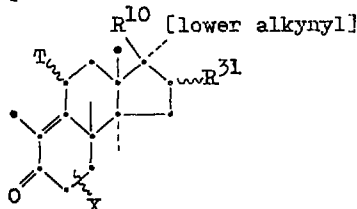
4) A process as set forth in claim 3, wherein 17α - ethyl - 17β - hydroxy - desA - androst - 9 - en - 5 - one is catalytically hydrogenated.

5) A process as set forth in claim 1, wherein a compound of the formula



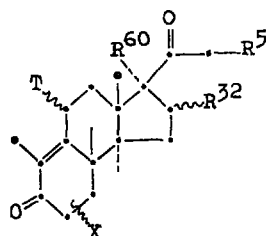
, wherein R^{10} , R^{31} , T and X have the significance given in claim 2, is catalytically hydrogenated.

6) A process as set forth in claim 1, wherein a compound of the formula



, wherein R^{10} , R^{31} , T and X have the significance in claim 2, is catalytically hydrogenated.

7) A process as set forth in claim 1, wherein a compound of the formula

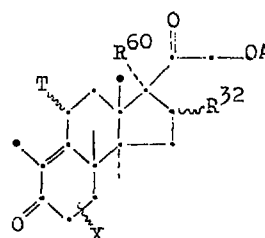


, wherein R^{32} represents a hydrogen or fluorine atom or a lower-alkyl, hydroxy or esterified hydroxy group, R^5 represents a hydrogen or halogen atom, R^{60} represents a hydrogen or halogen atom or a lower-alkyl, hydroxy or esterified hydroxy group and T and X have the significance given in claim 2, or a 20-ketal thereof, a $16\alpha,17\alpha$ -ketal or acetal of such a compound in which R^{32} and

R^{60} each represent a hydroxy group, a derivative of such a compound in which the 20-oxo group is reduced to a 20-hydroxy group or a corresponding derivative in which said 20-hydroxy group is esterified, is catalytically hydrogenated.

8) A process as set forth in claim 7, wherein 20 - hydroxy - desA - pregn - 9 - en - 5 - one is catalytically hydrogenated.

9) A process as set forth in claim 1, wherein a compound of the formula



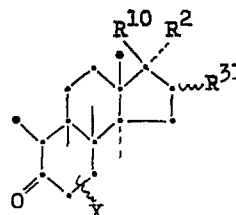
, wherein T and X have the significance given in claim 2, R^{32} and R^{60} have the significance given in claim 7 and OA represents a hydroxy or esterified hydroxy group, or a $17\alpha,20$; $20,21$ -bis(methylene dioxy) derivative of such a compound in which OA and R^{60} each represent a hydroxy group, a $17\alpha,21$ -ketal or acetal of such a compound in which OA and R^{60} each represent a hydroxy group, a $16\alpha,17\alpha$ -ketal or acetal of such a compound in which R^{32} and R^{60} each represent a hydroxy group, a derivative of such a compound in which the 20-keto group is reduced to a 20-hydroxy group or a corresponding derivative in which said 20-hydroxy group is esterified, is catalytically hydrogenated.

10) A process as set forth in any one of claims 1 to 9 inclusive, wherein rhodium is used as the hydrogenation catalyst.

11) A process for the preparation of $9\beta,10\beta$ - desA - androstan(or pregnan) - 5 - ones, substantially as described with reference to the foregoing examples.

12) $9\beta,10\beta$ - desA - androstan(or pregnan) - 5 - ones, when manufactured by the process claimed in any one of claims 1 to 11 inclusive.

13) Compounds of the formula



, wherein R^{10} , R^2 , R^{31} and X have the significance given in claim 2.

14) A 17α - (lower alkyl) - 17β - hydroxy - desA - $9\beta,10\beta$ - androstan - 5 - one.

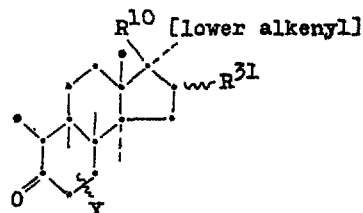
15) 17α - (Methyl or ethyl) - 17β -

hydroxy - desA - $9\beta,10\beta$ - androstan - 5 - one.

16) DesA - $9\beta,10\beta$ - androstan - 5,17 - dione.

5 17) 17β - Hydroxy - desA - $9\beta,10\beta$ - androstan - 5 - one.

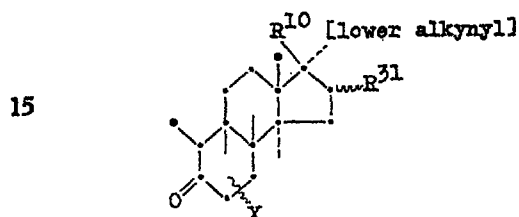
18) Compounds of the formula



10 wherein R^{10} , R^{31} and X have the significance in claim 2.

19) 17α - [2 - methyl - propen - (2) - yl - (1)] - 17β - hydroxy - desA - $9\beta,10\beta$ - androstan - 5 - one.

20) Compounds of the formula

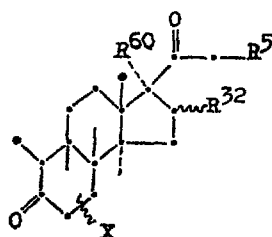


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wherein R^{10} , R^{31} and X have the significance given in claim 2.

20 21) 17α - [propyn - (1) - yl - (1)] - 17β - hydroxy - desA - $9\beta,10\beta$ - androstan - 5 - one.

22) Compounds of the formula



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, wherein R^{32} , R^5 and R^{60} have the significance given in claim 7 and X has the significance given in claim 2, 20-ketals thereof, $16\alpha,17\alpha$ -ketals and acetals of those compounds in which R^{32} and R^{60} each represent a hydroxy group, derivatives thereof in which the 20-oxo group is reduced to a 20-hydroxy group and the corresponding derivatives in which said 20-hydroxy group is esterified.

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23) A 20 - hydroxy - $9\beta,10\beta$ - desA - pregnan - 5 - one.

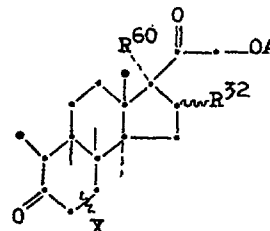
35 24) 20β - Hydroxy - $9\beta,10\beta$ - desA - pregnan - 5 - one.

25) A 20 - (lower alkylenedioxy) - $9\beta,10\beta$ - desA - pregnan - 5 - one.

26) 20 - Ethylenedioxy - $9\beta,10\beta$ - desA - pregnan - 5 - one.

27) Compounds of the formula

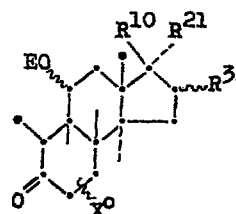
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, wherein R^{32} and R^{60} have the significance given in claim 7, OA has the significance given in claim 9 and X has the significance given in claim 2, $17\alpha,20;20,21$ - bis (methylenedioxy) derivatives of those compounds in which OA and R^{60} each represent a hydroxy group, $17\alpha,21$ -ketals and acetals of those compounds in which OA and R^{60} each represent a hydroxy group, $16\alpha,17\alpha$ -ketals and acetals of those compounds in which R^{32} and R^{60} each represent a hydroxy group, derivatives thereof in which the 20-keto group is reduced to a 20-hydroxy group and the corresponding derivatives in which 20-hydroxy group is esterified.

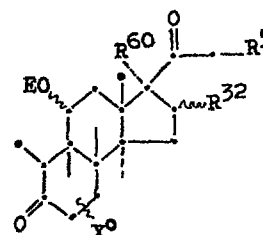
28) $17\alpha,20;20,21$ - bis(methylenedioxy) - $9\beta,10\beta$ - desA - pregnan - 5 - one.

29) Compounds of the formula



wherein R^{10} and R^{31} have the significance given in claim 2, X^o represents a hydrogen atom or a lower-alkyl, lower-alkylthio or lower-alkanoylthio group in the 6- or 7-position or a halogen atom in the 7-position, EO represents a hydroxy or esterified hydroxy group and R^{21} represents a hydrogen atom or a lower-alkyl, lower-alkenyl or lower-alkynyl group.

30) Compounds of the formula

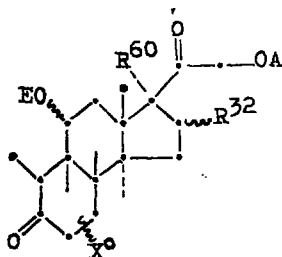


, wherein R^{32} , R^5 and R^{60} have the significance given in claim 7 and X^o and EO have the significance given in claim 29, 20-ketals

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thereof, 16 α ,17 α -ketals and acetals of those compounds in which R³² and R⁶⁰ each represent a hydroxy group, derivatives thereof in which the 20-oxo group is reduced to a 20-hydroxy group and the corresponding derivatives in which said 20-hydroxy group is esterified.

31) Compounds of the formula



, wherein R³² and R⁶⁰ have the significance given in claim 7, OA has the significance given in claim 9 and X^o and EO have the significance given in claim 29, 17 α ,20;20,21-bis(methylenedioxy) derivatives of those compounds in which OA and R⁶⁰ each represent a hydroxy group, 17 α ,21-ketals and acetals of those compounds in which R⁶⁰ and OA each represent a hydroxy group, 16 α ,17 α -ketals and acetals of those compounds in which R³² and R⁶⁰ each represent a hydroxy group, derivatives of those compounds in which the 20-keto group is reduced to a 20-hydroxy group and the corresponding derivatives in which said 20-hydroxy group is esterified.

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Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1968.

Published by the Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.



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