tribromide, 34.6 g. (0.13 mol.) (Eastman), was added to 200 ml. of absolute ether and cooled to −12°. 1-Phenyl-1-(1-phenylcyclopropyl)propane-1,3-diol, 23.8 g. (0.09 mol.), in 125 ml. of anhydrous ether was added over a period of 2 hr. at −5 to 0°. Following stirring for 48 hr. the solution was poured into ice water, the ether layer was separated and neutralized with saturated sodium bicarbonate and dried over sodium sulfate. Upon removal of the ether under vacuum there remained 16.1 g. of dark, partly crystalline product. Attempted recrystallization from absolute methanol yielded 0.7 g. of fine needles, m.p. 141.8–143.8°, which gave a negative test with alcoholic silver nitrate; the methanol-soluble portion after many treatments with charcoal, in acetone solution, yielded a brown solid. A sample of this material, after six recrystallizations from absolute alcohol, melted at 75.3–75.7° and gave a positive test with alcoholic silver nitrate.

*Anal.* Calcd. for $C_{18}H_{18}Br_2$: C, 54.84; H, 4.60; Br, 40.55. Found: C, 54.66; H, 4.43; Br, 40.5.

*B. Using phosphorus tribromide in methylene chloride.* A solution of 5 g. (0.019 mol.) of diol in 25 ml. of methylene chloride was cooled to −12°, and 5.4 g. (0.02 mol.) of phosphorus tribromide was added during 10 min.. maintaining the temperature below 10°. After standing for 10 days, the mixture was poured over ice and the methylene chloride layer was separated, neutralized, and dried. Removal of the solvent under vacuum gave 7.3 g. of an oil which solidified rapidly. Recrystallization from absolute alcohol using charcoal yielded 1.7 g. (23%) of material, m.p. 69.7–71.0°, with an additional 2.2 g. (30%) isolated from the mother liquors. Subsequent work with this material showed it to be impure, containing some of the higher melting dibromide, m.p. 145.7–146.1°.

One experiment using 5.0 g. (0.019 mol.) of diol and 10.8 g. (0.04 mol.) of phosphorus tribromide was allowed to stand for 1 week. On removal of the methylene chloride, 3.0 g. of an oil was obtained which solidified upon the addition of absolute methanol. Recrystallization from methanol yielded a dibromide, m.p. 144.3–144.9°, which gave a negative test with alcoholic silver nitrate and whose mixed melting point with the higher melting dibromide previously obtained showed no depression.

*Anal.* Calcd. for $C_{18}H_{18}Br_2$: C, 54.84; H, 4.60. Found: C, 54.88, 55.19; H, 4.90, 5.22.

*1,1′-Diphenylbicyclopropyl* (XVI). The cyclization procedure is that of Bartleson, Burk, and Lankelma.[32] *n*-Propyl alcohol (100 ml.) and 13.08 g. (0.2 mol.) of zinc dust were cooled to −5° and the crude product from the reaction of 32.5 g. (0.12 mol.) of diol with phosphorus tribromide in ether was added in 90 min. at −3° to −5°. After stirring for 3 days, water was added, the alcohol distilled from the reaction mixture, and the mixture extracted with ether. The ether was washed with saturated sodium bicarbonate and dried over sodium sulfate. Upon removal of the ether, the residue was distilled at 0.1 mm.; 3.5 g. of material distilled between 124–130° and a large amount of tar remained in the distilling flask. The distilled material gave a negative test for halogens using the sodium fusion method. Its infrared spectrum agreed qualitatively with that expected for 1,1′-diphenylbicyclopropyl; it could not be induced to crystallize upon long standing.

Treatment of 2.0 g. of crude 1,1′-diphenylbicyclopropyl with a mixture of 10 ml. of acetic anhydride, 7 ml. of glacial acetic acid, and 7 ml. of nitric acid (*d* 1.5) at −15° gave a small amount of material which could not be recrystallized satisfactorily.

*Acknowledgment.* The authors wish to express their appreciation for the support of this work by research grant C-3113 from the National Cancer Institute of the National Institutes of Health. Support of the junior author, J.G.B., by the Sterling-Winthrop Research Institute in July and August, 1958 is also gratefully acknowledged.

TROY, N. Y.

(32) J. D. Bartleson, R. E. Burk, and H. P. Lankelma, *J. Am. Chem. Soc.*, **68**, 2513 (1946).

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[CONTRIBUTION NO. 1566 FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

# 20-Methylpregnane and Derivatives[1,2]

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*Received July 9, 1959*

20-Methylpregnane and several of its significant derivatives have been prepared by the Wittig reaction and by other methods.

In calculating the contributions of side chains to the optical rotations of sterols,[4] the molecular rotations of the respective sterols are generally compared with those of corresponding derivatives of pregnane. Pregnane, however, is not an ideal reference compound for such purposes. It has its C-17 attached to a β-oriented, secondary C-20 atom, while in the natural sterols C-17 is joined to β-oriented, tertiary C-20 atom. 20-Methylpregnane and its derivatives would therefore be more suitable reference compounds. At the beginning of this investigation, however, surprisingly little was known about this series of compounds or of others with relatively short alkyl side chains.

A number of derivatives of 20-methylpregnane have now been prepared by several methods. In one approach, 3β-acetoxydinor-5-cholenic acid (I), which possesses the desired carbon skeleton, was reduced to the known diol (IIa). This was converted

(1) The material presented in this paper constitutes part of a dissertation submitted by John P. Dusza in partial fulfillment of the requirements for the Ph.D. degree, Yale University, 1958.

(2) The investigation was in part supported by a research grant, Nonr 253(00), from the Office of Naval Research.

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(4) W. M. Stokes and W. Bergmann, *J. Org. Chem.*, **16**, 1817 (1951).

*Deceased.

to 20-methyl-5-pregnen-3β-ol (IIIa) by reductive cleavage of the monotosylate (IIb). A selective, direct monotosylation of the primary alcohol function of IIa was unsuccessful. The desired derivative was obtained only by selective hydrolysis of the ditosylate (IIc) with a dilute aqueous solution of sulfuric acid in acetone. This method had previously been used in the preparation of 3β,17-diol-17-monotosylates.[5] The monotosylate (IIb) was then reduced with lithium aluminum hydride in boiling dioxane. Some diol,[6] IIa, was obtained along with the desired product, IIIa.[7]

Hydrogenation of 20-methyl-5-pregnen-3β-ol (IIIa) smoothly afforded the stanol (IVa) which has become the reference compound of this series. It was oxidized with a chromic anhydride-pyridine complex to the stanone (V) which was reduced to 20-methyl-5α-pregnane (VI). Treatment of IIIa with thionyl chloride gave the 3-chloro-derivative (VII) which was reduced with sodium in amyl alcohol to 20-methyl-5-pregnene (VIII). Oxidation of IIIa with chromic anhydride gave the ketone, (IX).

In another series of experiments 5-pregnen-20-on-3β-ol (Xa) was converted by way of its tetrahydropyranyl ether (Xc) into XIa by means of the Wittig reaction. A preparation of this dienol by a very similar procedure has since been reported.[8] We have also obtained this compound by the dehydrotosylation of IIb with boiling collidine. Attempts to reduce selectively XIa to IIIa were unsuccessful. Even under mild conditions the hydrogenation proceeded rapidly, and only the stanol (IVa) was obtained. 20-Methyl-5,20-pregnadien-3β-ol (XIa) resisted all attempts to isomerize the exocyclic bone to give the known 20-methyl-5,17-pregnadien-3β-ol. Thus treatment of the acetate (XIc) with anhydrous hydrogen chloride in chloroform, a typical isomerization procedure for terminal double bonds in terpenes,[9] afforded a chloride which was reconverted to the starting material on treatment with base. The dienol (XIa) also did not react with maleic anhydride to give a 2-substituted succinic acid.[10] It appears therefore that the 20,22-double bond offers considerable resistance to rearrangement into the 17, 20-position. Oxidation of XIa with chromic anhydride leads to the methylene derivative of progesterone (XII) which had previously been prepared by a dehydrotosylation reaction.[11]

20-Methyl-5α-pregnan-3β-ol (IVa) was also prepared from the readily available 16-dehydropregnenolone acetate (XIIIb). The latter was converted by way of the pyranyl ether (XIIIc)[12] to the methylene derivative (XIVc) from which 20-methyl-5,16,20-pregnatrien-3β-ol (XIVa) was obtained. Since this work was completed a preparation of the acetate (XIVb) by way of the Wittig reaction has been reported.[8] The formulation of the trienol as XIV may be questioned. It is known that the Wittig reaction with α,β-unsaturated ketones may entail 1,4-rather than 1,2-additions.[13] In the present case therefore, structure XVI may not *a priori* be excluded. On the contrary a 1,4- addition might also be expected because of the particular susceptibility of 16-dehydropregnenolone (XIII) to base attack at C-16.[14] The problem was easily solved in favor of structure XIVa by the catalytic reduction of the trienol. It afforded 20-methyl- (IVa) rather than 16-methyl-5α-pregnan-3β-ol. Partial reduction of the trienol (XIVa) with sodium in ethanol gave a new pregnadienol. Its spectrum lacked absorption characteristics of a conjugated diene and of a terminal methylene group. Since its physical properties are different from those of 20-methyl-5,17-pregnadien-3β-ol, the new compound must be 20-methyl-5,16-pregnadien-3β-ol (XVa).

TABLE I

MOLECULAR ROTATIONS OF DERIVATIVES OF 20-METHYLPREGNANE

| Compound | $M_D$ |
|---|---|
| 20-Methyl-5α-pregnane (VI) | +27 |
| 20-Methyl-5α-pregnan-3β-ol (IVa) | +30 |
| 20-Methyl-5α-pregnan-3β-ol acetate (IVb) | −7 |
| 20-Methyl-5α-pregan-3-one (V) | +96 |
| 20-Methyl-5-pregnene (VIII) | −270 |
| 20-Methyl-5-pregnen-3β-ol (IIIa) | −208 |
| 20-Methyl-5-pregnen-3β-ol acetate (IIIb) | −248 |
| 20-Methyl-5,16-pregnadien-3β-ol (XVa) | −185 |
| 20-Methyl-5,16-pregnadien-3β-ol acetate (XVb) | −232 |
| 20-Methyl-4-pregnen-3-one (IX) | +355 |

(5) M. N. Huffman, M. H. Lott, and A. Tillotson, *J. Biol. Chem.*, **222**, 447 (1956).

(6) This anomalous cleavage of the tosyl group to the alcohol is not without parallel in the steroid literature. Thus the reduction of cholestan-3β-ol tosylate gave both cholestane and cholestan-3β-ol and that of cholestan-6α-ol tosylate gave both cholestane (38%) and cholestan-6α-ol (57%) [P. Karrer, H. Asmis, K. N. Sareen, and R. Schwyzer, *Helv. Chim. Acta*, **34**, 1022 (1951); **35**, 427 (1952)]. Under similar conditions moradiol 28-monotosylate, a primary tosylate, afforded only the diol [D. H. R. Barton and C. J. W. Brooks, *J. Chem. Soc.*, 257 (1951)].

(7) The new compound is not identical with a "20-methyl-5-pregnen-3β-ol" mentioned in the older literature. The assignment of structure IIIa to this compound is contraindicated by the strongly positive rotation of 69°, and has already been questioned [*Elseviers Encyclopaedia of Organic Chemistry*, Elsevier Publishing Company, New York, Vol. **14**, p. 1600s].

(8) F. Sondheimer and R. Mechoulam, *J. Am. Chem. Soc.*, **79**, 5029 (1957).

(9) A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 2548 (1953); J. S. E. Holker, A. D. G. Powell, A. Robertson, J. J. H. Simes, R. S. Wright, and R. M. Gascoque, *J. Chem. Soc.*, 2422 (1953).

(10) R. T. Arnold and J. S. Showell, *J. Am. Chem. Soc.*, **79**, 419 (1957).

(11) C. Meystre and K. Miescher, *Helv. Chim. Acta*, **32**, 1758 (1949).

(12) W. Bergmann and J. P. Dusza, *J. Org. Chem.*, **23**, 459 (1958).

(13) H. H. Inhoffen, K. Bruchner, D. K. Domagk, and H. Erdmann, *Ber.*, **88**, 1415 (1955).

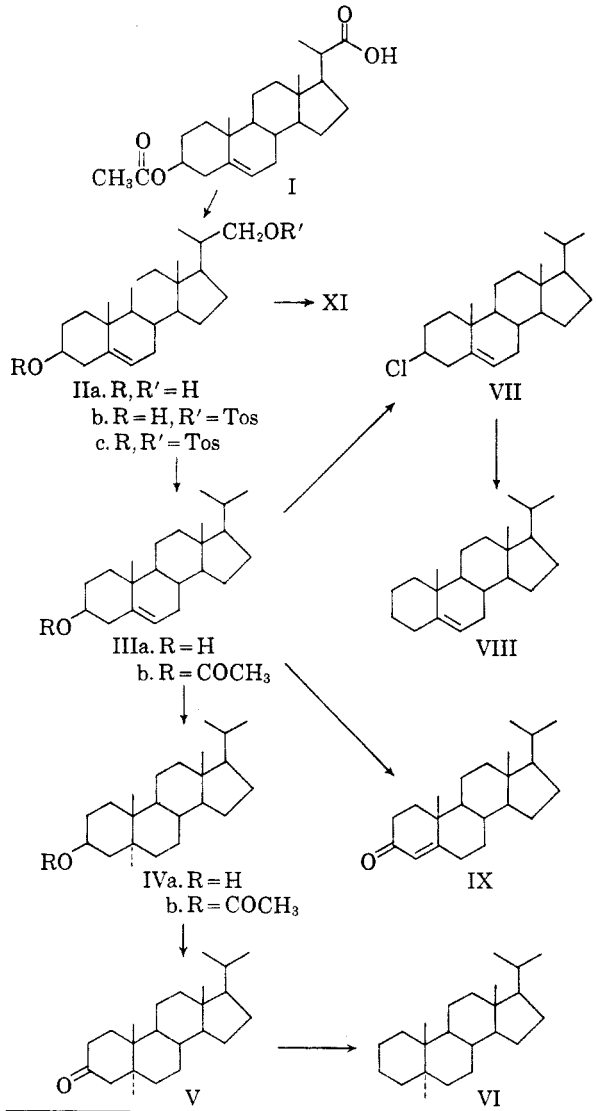
(14) D. K. Fukushima and T. G. Gallagher, *J. Am. Chem. Soc.*, **73**, 196 (1951).

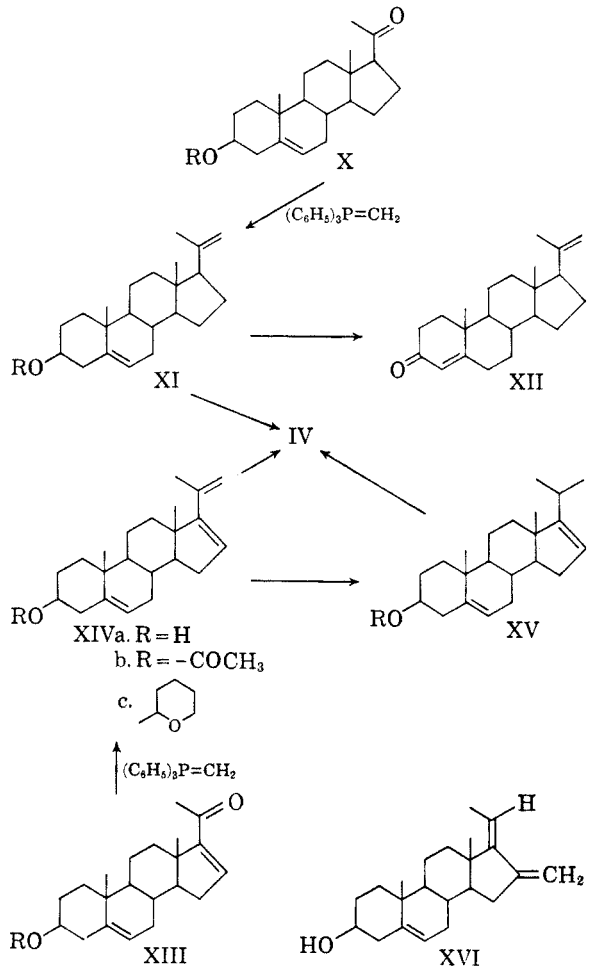
Catalytic hydrogenation of this dienol gave the expected stanol (IVa). Table I lists the molecular rotations of the new compounds which may be used as references.

## EXPERIMENTAL

*Dinor-5-cholene-3β,22-diol* (IIa). A solution of 3β-acetoxydinor-5-cholenic acid (I) (6.0 g.) in dry tetrahydrofuran[15] (50 ml.) was added dropwise to a suspension of lithium aluminum hydride (2.2 g.) in tetrahydrofuran.[15] The solution was then stirred vigorously and refluxed for 5 hr. After cooling, ethyl formate was added to decompose the excess hydride, and the mixture poured into 2*N* sulfuric acid (500 ml.). The precipitated diol was collected and recrystallized several times from methanol; long needles, m.p. 204–206° (rep.[16] 202–206°); $[\alpha]_D^{25}$ −47.0° (c 0.35 in $CHCl_3$). The material was probably the hemihydrate.

The diacetate, prepared in the usual manner, was recrystallized from dilute methanol; needles, m.p. 128–129° (rep.[16] 127–129°); $[\alpha]_D^{25}$ −51.6° (c 1.30 in $CHCl_3$).




*Dinor-5-cholene-3β,22-diol 22-tosylate* (IIb). *p*-Toluenesulfonyl chloride (6.4 g.) was added to a solution of dinor-5-cholene-3β,22-diol (IIa) (2.0 g.) in pyridine (50 ml.) at a rate which did not let the temperature of the mixture exceed 20° (ice bath). The mixture was allowed to stand at room temperature for 24 hr. when it was poured into ice water (100 ml.) and kept at 5° for another 24 hr. The supernatant liquid was then decanted, and the sticky precipitate dissolved in ether. The ether extract was washed with cold 2*N* hydrochloric acid and then thoroughly with water. Evaporation of the dried extract left a glassy residue. It was dissolved in alcohol-free acetone (200 ml.) to which was added water (60 ml.) and 10 drops of concentrated sulfuric acid. The solution was then refluxed for 4 hr., diluted with water (40 ml.), and concentrated until it became turbid. The monotosylate (IIb) obtained on cooling was recrystallized twice from dilute acetone; 1.82 g.; m.p. 115–118°; $[\alpha]_D^{25}$ −37.2° (*c* 1.00, $CHCl_3$).

*Anal.* Calcd. for $C_{29}H_{42}O_4S$: C, 71.56; H, 8.69. Found: C, 71.23; H, 8.72.

*20-Methyl-5-pregnen-3β-ol* (IIIa). Lithium aluminum hydride (500 mg.) was added to a solution of the tosylate (IIb) (1.01 g.) in dry dioxane (150 ml.).[17] The mixture was refluxed for 4 hr., and the excess hydride was decomposed with ethyl acetate and hydrochloric acid. The solution was then poured into water and extracted with ether. The ether extract was washed with water, dried and evaporated to dryness. The amorphous residue was taken up in benzene and chromatographed over neutral aluminum oxide (II–III). Elution with benzene-ether (5:1) gave the product which was crystallized from dilute methanol; yield: 0.59

(15) The solvent had been stored over sodium hydroxide pellets and distilled from lithium aluminum hydride.

(16) A. V. McIntosh, Jr., E. M. Meinzer, and R. H. Levin, *J. Am. Chem. Soc.*, **70**, 2955 (1948); H. L. Herzog, C. C. Payne, and E. B. Hershberg, *J. Am. Chem. Soc.*, **77**, 5324 (1955).

(17) The solvent had been passed over active aluminum oxide and distilled over lithium aluminum hydride.

g.; m.p. 131–133° (hydrate). After drying *in vacuo*, m.p. 136–137°; $[\alpha]_D^{25}$ −65.8° (c 1.30 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{36}O$: C, 83.45; H, 11.47. Found: C, 83.35; H, 11.52.

Elution with benzene-ether (1:1) gave some dinor-5-cholen-3β,22-diol (IIa), m.p. 203–205°.

The *acetate* (IIIb) was prepared by refluxing the alcohol (IIIa) with acetatic anhydride. It was recrystallized several times from methanol; large plates, m.p. 121–121.5°; $[\alpha]_D^{26}$ −69.2° (c 1.37 in $CHCl_3$).

*Anal.* Calcd. for $C_{24}H_{28}O_2$: C, 80.39; H, 10.68. Found: C, 80.65; H, 10.67.

*20-Methyl-5α-pregnan-3β-ol* (IVa). Platinum oxide (35 mg.) was added to a solution of 20-methyl-5-pregnen-3β-ol (IIIa) (75 mg.) in acetic acid (30 ml.) and ethyl acetate (30 ml.). The solution was shaken for 2 hr. under hydrogen at 14 lb. pressure. The catalyst was filtered, the solvent removed *in vacuo*, and the residue recrystallized twice from methanol. The stanol melted at 145–146°; $[\alpha]_D^{25}$ +9.3° (c 1.31 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{38}O$: C, 82.95; H, 12.03. Found: C, 82.98; H, 11.96.

The *acetate* formed long needles, m.p. 122–123°; $[\alpha]_D^{25}$ −1.9° (c 1.31 in $CHCl_3$).

*Anal.* Calcd. for $C_{24}H_{40}O_2$: C, 79.94; H, 11.18. Found: C, 80.29; H, 11.30.

*20-Methyl-5α-pregnan-3-one* (V). A solution of 20-methyl-5α-pregnan-3β-ol (IVa) (110 mg.) in pyridine (3 ml.) was added to a suspension of chromic anhydride complex[18] prepared from chromic anhydride (0.1 g.) and pyridine (5 ml.). The solution was allowed to stand for 17 hr. and was then poured into dilute hydrochloric acid and extracted with ether. The extract was washed with sodium carbonate solution and water, dried, and evaporated to dryness. The residue was dissolved in hexane and chromatographed on neutral alumina (VI). The material eluted with benzene-hexane (1:1) was recrystallized from dilute methanol. The ketone (87 mg.) melted at 144–145°; $[\alpha]_D^{25}$ +30.2° (c 1.18 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{36}O$: C, 83.48; H, 11.47. Found: C, 83.48; H, 11.53.

*20-Methyl-5α-pregnane* (VI). A solution of 20-methyl-5α-pregnan-3-one (V) (100 mg.) in acetic acid (10 ml.) was refluxed with amalgamated zinc (3.5 g.). Over a 7-hr. period a solution of acetic acid (5 ml.), concentrated hydrochloric acid (20 ml.), and xylene (0.5 ml.) was added. The reaction mixture was refluxed during this time and an additional 30 min. After cooling, the solution was poured into water, extracted with ether, and the extract washed with 2*N* sodium hydroxide, water, and dried. The residue obtained upon evaporation of the ether was taken up in hexane and passed through neutral alumina (I). The hexane eluate was evaporated, and the residue crystallized twice from methanol and then sublimed. The hydrocarbon melted at 111–112°; $[\alpha]_D^{25}$ +8.90° (c 1.53 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{38}$: C, 87.34; H, 12.66. Found: C, 87.12; H, 12.69.

*20-Methyl-4-pregnen-3-one* (IX). To a solution of 20-methyl-5-pregnen-3β-ol (IIIa) (120 mg.) in alcohol-free acetone (30 ml.) was added 0.18 ml. of a standard chromic anhydride–sulfuric acid solution[19] (2.67 g. of chromic anhydride, 2.3 ml. of concentrated sulfuric acid, total volume brought to 10 ml. with water). This mixture was swirled for 5 min. until the characteristic light green precipitate was formed. The mixture was diluted with water and immediately extracted with ether. The residue obtained upon evaporation of the ether was refluxed with 2% alcoholic potassium hydroxide solution (25 ml.) for 10 min. and most of the methanol was then removed *in vacuo*. Water was added to the reaction mixture which was then extracted with ether. Evaporation of the ether gave a brown viscous oil which was chromatographed on neutral alumina (II). The fraction eluted with hexane-benzene (1:1) was crystallized from methanol-water (5:1) to give 30 mg. of long needles of the enone, m.p. 143–144°; $[\alpha]_D^{27}$ +113° (c 0.41 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{34}$: C, 84.01; H, 10.90. Found: C, 84.17; H, 11.08.

*3β-Chloro-20-methyl-5-pregnene* (VII). To a solution of 20-methyl-5-pregnen-3β-ol (IIIa) (0.8 g.) in dry benzene (25 ml.) was added 1.0 ml. of thionyl chloride. The mixture was allowed to stand at room temperature for 30 min. and then kept for 90 min. at 50–60°. The benzene and excess thionyl chloride was removed at reduced pressure and the residue taken up in hexane. The hexane solution was passed through a neutral alumina (VI) column. The solvent was evaporated and the residue crystallized from methanol; long needles; (0.78 g.) m.p. 147.5–148°; $[\alpha]_D$ −52.4° (c 1.30 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{35}Cl$: C, 78.88; H, 10.53. Found: C, 78.78; H, 10.63.

*20-Methyl-5-pregnene* (VIII). 3β-Chloro-20-methyl-5-pregnene (VII) (0.56 g.) was refluxed with 20 ml. of distilled isoamyl alcohol. To the refluxing solution were added small cubes of sodium. The addition of sodium was continued until the color of the solution had changed from yellow to colorless. This required approximately 1 g. of sodium and covered a period of 90 min.[20] Water was added, the mixture extracted with ether, and the extract thoroughly washed with water and dried. The residue was recrystallized three times from methanol-ether; very long needles (0.25 g.); m.p. 104.5–105°; $[\alpha]_D^{26}$ −89.7° (c 1.27 in $CHCl_3$).

*Anal.* Calcd. for $C_{22}H_{36}$: C, 87.92; H, 12.08. Found: C, 88.03; H, 12.17.

*5-Pregnen-20-one-3β-(2¹-tetrahydropyranyl)-ether* (Xc). 5-Pregnen-20-one-3β-ol (Xa) (2 g.) 2-methoxytetrahydropyran (15 ml.) and Doxex-50 (2 g.) (H form, dried at 70° for 24 hr.) were heated on an oil bath at 95° for 10 hr. The resin was filtered and the excess 2-methoxytetrahydropyran was evaporated *in vacuo*. The slightly yellow, crystalline residue was dissolved in hexane and chromatographed on neutral alumina (VI) (60 g.). The hexane eluate was evaporated, and the residue crystallized from methanol; yield 1.81 g., m.p. 126–128°; $[\alpha]_D^{25}$ +16.5° (c 1.45 in $CHCl_3$), rep.[21] m.p. 129–131°, $[\alpha]_D^{25}$ +17.7°.

*20-Methyl-5,20-pregnadiene-3β-(2¹-tetrahydropyranyl)-ether* (XIb). This compound was prepared from 5-pregnen-20-one-3β (2¹-tetrahydropyranyl)-ether (Xc) (2.44 g.) and triphenylphosphonium methylene, obtained from 2.16 g. of triphenylphosphonium bromide, by the Wittig reaction, using the procedures previously described.[12] The ether thus obtained (2.01 g.) showed a great tendency to gel. Thus, crystallization from ethanol always gave a gel which slowly turned into crystalline material, a process which was somewhat hastened by successive warming and cooling of the solution. The crystalline ether melted at 110–112°; $[\alpha]_D^{24}$ −39.6° (c 1.25 in $CHCl_3$).

(18) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(19) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

(20) This reduction could not be carried out with lithium aluminum hydride in boiling tetrahydrofuran. Similar conditions were used by H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 3289 (1956) to reduce 3β-chloro-1-cholestene to 1-cholestene. In this case, however, the chlorine atom was in the more reactive allylic position. In contrast M. Gut and M. Vskokovic [133rd Meeting, ACS, San Francisco, Calif., April 1958, Abstract of Papers, p. 99N] reduced the sulfite function in bis(3β-chloro-androst-5-en-17β-yl) sulfite with lithium aluminum hydride selectively to 3β-chloroandrost-5-en-17-ol without touching the homoallylic chlorine.

(21) A. C. Ott, M. F. Murray, and R. L. Pederson, *J. Am. Chem. Soc.*, **74**, 1239 (1952).

*Anal.* Calcd. for $C_{27}H_{42}O_2$: C, 81.35; H, 10.62. Found: C, 81.55; H, 10.66.

*20-Methyl-5,20-pregnadien-3β-ol* (XIa). To a solution of 20-methyl-5,20-pregnadien-3β-(2¹-tetrahydropyranyl)-ether (2 g.) in hexane (100 ml.) was added 100 ml. of methanol containing 5 drops of concentrated hydrochloric acid. After standing at room temperature for 1 hr. the solution was evaporated to dryness and the residue crystallized from methanol-water (5:1); 1.23 g., m.p. 120–125°. An analytical sample after drying *in vacuo* exhibited the following properties: m.p. 133.5–134°; $[\alpha]_D^{25}$ −66.4° (c 0.55 in $CHCl_3$); rep.[8] m.p. 133–134°; $[\alpha]_D$ −59°.

*Anal.* Calcd. for $C_{22}H_{34}O$: C, 84.01; H, 10.90. Found: C, 84.23; H, 11.08.

The acetate (Xc) was recrystallized from methanol; long needles of m.p. 128.5–129°; $[\alpha]_D^{27}$ −72° (c 1.62 in $CHCl_3$).

*Anal.* Calcd. for $C_{24}H_{36}O_2$: C, 80.85; H, 10.18. Found: C, 80.55; H, 10.45.

*20-Methyl-5,20-pregnadien-3β-ol* (Xa) *by dehydrotosylation.* Dinor-5-cholene-3β,22-diol 22-tolsylate (IIb) (0.7 g.) was refluxed with 10 ml. of dry, freshly distilled collidine for 3 hr. After cooling, the mixture was extracted with ether and the extract washed with dilute hydrochloric acid and dried. The residue obtained upon evaporation of the ether was taken up in hexane and chromatographed on neutral alumina (II). The material eluted with benzene-ether was crystallized several times from methanol to give 50 mg. of a product of m.p. 115–117°. It was somewhat impure 20-methyl-5,20-pregnadien-3β-ol. Its infrared spectrum was nearly identical to that of the pure product mentioned above.

*20-Methyl-4,20-pregnadien-3-one* (XII). This compound was prepared by the oxidation of 20-methyl-5,20-pregnadien-3β-ol (XIa) (0.2 g.) with a standard chromic anhydride–sulfuric acid solution according to the procedure outlined in the preparation of 20-methyl-4-pregnen-3-one (IX). The crude ketone was chromatographed on neutral alumina (III). The material eluted with hexane-benzene (9:1) was crystallized from methanol-water (5:1). It gave 97 mg. of long needles, m.p. 152–154°; $[\alpha]_D^{27}$ +112° (c 1.35 in $CHCl_3$); lit.[12] m.p. 155–160°, $[\alpha]_D^{23}$ +105°.

*Hydrogenation of 20-methyl-5,20-pregnadiene-3β-ol* (XIa). 20-Methyl-5,20-pregnadien-3β-ol (0.4 g.) was dissolved in 150 ml. of absolute ethanol and was hydrogenated using a 5% palladium-on-carbon catalyst (0.2 g.) under 14 lb. pressure of hydrogen for 1 hr. After filtration of the catalyst the solvent was evaporated to dryness and the residue crystallized from methanol-water (5:1). There was obtained 0.29 g. of 20-methyl-5α-pregnan-3β-ol, m.p. 144–145°. This was identical to the material previously prepared from the hydrogenation of 20-methyl-5-pregnen-3β-ol (IIIa).

*5,16-Pregnadien-20-one-3β (2¹-tetrahydropyranyl)-ether* (XIIIc). 5,16-Pregnadiene-20-one-3β-ol, (XIIIa) (5 g.), 2-methoxytetrahydropyran (50 ml.), and Dowex-50 (3 g.) (H-form dried at 70° for 24 hr.) were heated at 90° for 6 hr. with stirring and under nitrogen with exclusion of moisture. The resin was filtered and the excess 2-methoxytetrahydropyran removed under reduced pressure. The crystalline residue was taken up in hexane and passed through a neutral alumina (VI) column. The hexane eluate was evaporated to dryness and the residue crystallized from ether to give 4.2 g. of pyranyl ether, m.p. 165–167°. The mother liquor was evaporated and the residue crystallized from a minimum amount of ether to give 1.2 g. of additional product, m.p. 163–165°; $[\alpha]_D^{27}$ +49.7° (c 0.95 in $CHCl_3$).

*Anal.* Calcd. for $C_{26}H_{38}O_3$: C, 78.35; H, 9.61. Found: C, 78.50; H, 9.66.

*20-Methyl-5,16,20-pregnatriene-3β-(2¹-tetrahydropyranyl)-ether* (XIV). This compound (1.5 g.) was prepared from the pyranyl ether (XIIIc) (2.2 g.) and triphenylphosphonium methylene by the procedure previously described.[12] It crystallizes from acetone in large plates, m.p. 155–156°; $[\alpha]_D^{27}$ −56.0° (c 0.82 in $CHCl_3$). $\lambda_{max}$ 239 mμ (ε 16,500); shoulder 234 mμ (ε 15,600); inflection 247 mμ (ε 11,200); $\lambda_{max}$ 6.17, 6.35, 11.41, 11.55, 12.43, and 12.56μ.

*Anal.* Calcd. for $C_{27}H_{40}O_2$: C, 81.76; H, 10.17. Found: C, 81.95; H, 10.27.

*20-Methyl-5,16-20-pregnatrien-3β-ol* (XIVa). A solution of 20-methyl-5,16,20-pregnatriene-3β-(2¹-tetrahydropyranyl)-ether (XIVb) (0.26 g.) in hexane (25 ml.) was added to a solution of two drops of concentrated hydrochloric acid in methanol (25 ml.). The solution was allowed to stand at room temperature for 1 hr. with occasional stirring. The unhomogeneous mixture was evaporated to dryness *in vacuo* and the residue crystallized from methanol-water (5:1) to give the sterol (0.165 g.) of m.p. 149–161° dec. The infrared spectrum showed this material to be strongly hydrated. After subsequent recrystallizations from methanol the melting point was constant at 162–164°, $[\alpha]_D^{27}$ −69.0° (c 1.39 in $CHCl_3$). $\lambda_{max}$ 239 mμ (ε 15,600); $\lambda_{max}$ 2.95, 3.32, 5.67, 6.00, 6.12, 6.35, 11.38, 12.42, and 12.53μ.

*Anal.* Calcd. for $C_{29}H_{32}O$: C, 84.56; H, 10.32. Found: C, 84.55; H, 10.32.

The acetate was recrystallized from methanol; very long needles, m.p. 125–125.5°; $[\alpha]_D^{27}$ −75.3° (c 1.17 in $CHCl_3$); $\lambda_{max}$ 239 mμ (ε 16,700); rep. m.p.[8] 124.5–126°, $[\alpha]_D$ −76°; $\lambda_{max}$ 239 mμ (log ε: 4.21).

*Hydrogenation of 20-methyl-5,16,20-pregnatrien-3β-ol* (XIVa). Catalytic hydrogenation of XIVa in glacial acetic acid with a platinum oxide catalyst gave 20-methyl-5α-pregnan-3β-ol (IVa), m.p. 145–146°. The infrared spectra of this compound and of an authentic sample were identical.

*20-Methyl-5,16-pregnadien-3β-ol* (XVa). A solution of 20-methyl-5,16,20-pregnatriene-3β-ol (XIVa) (0.53 g.) in absolute ethanol (75 ml.) was refluxed vigorously. Cubes of sodium metal were added over a 90-min. period. After approximately 7 g. had been added, the solution was refluxed an additional 0.5 hr. It was then poured into water, extracted with ether, and the extract washed with a saturated salt solution until neutral and dried.

The ether was evaporated and the residue crystallized three times from methanol-water (5:1). The dienol (0.17 g.) melted at 130–132°; $[\alpha]_D^{27}$ −58.6° (*c* 1.40); $\lambda_{max}$ 3.05, 6.00, 7.30, 7.37 (sh), and 12.43μ.

*Anal.* Calcd. for $C_{29}H_{34}O$: C, 84.01; H, 10.90. Found: C, 84.20; H, 11.17.

The acetate, (XVb), was recrystallized from methanol; m.p. 136–138°, $[\alpha]_D^{27}$ −65.5° (*c* 1.87 in $CHCl_3$). $\lambda_{max}$ 5.75, 6.00, 8.06, and 12.53μ.

*Anal.* Calcd. for $C_{24}H_{36}O_2$: C, 80.85; H, 10.18. Found: C, 80.85; H, 10.18.

*Hydrogenation of 20-methyl-5,16-pregnadien-3β-ol* (XVa). Hydrogenation of XVa in glacial acetic acid with a platinum oxide catalyst under 14 lb. pressure gave 20-methyl-5α-pregnan-3β-ol (IVa); short needles, m.p. 145–146°. This was identical in all respects with the previously prepared reference compound.

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