(c) **From the Bromohydrin Mixture.**—The crude mixture resulting from sodium borohydride reduction of 2 g. of methyl 4β-bromo-3-ketocholanate (II) was reduced directly as in (a) and the product (940 mg., 69%) m.p. 68–72°) purified by elution from alumina with petroleum ether–benzene.

Δ³-Cholenic Acid (L.F.F.)—The total Δ³-cholenate resulting from reduction of 320 mg. of the *cis*-bromohydrin acetate Vb was heated with alcoholic alkali and the solution diluted with water, when a sparingly soluble salt separated. This was filtered from a slightly yellowish mother liquor, dissolved in a large volume of water, and the solution acidified. The yield of pure white crude acid, m.p. 147–150°, was 220 mg. (quant.). The acid is readily soluble in hot methanol but crystallizes well at 25° in fibrous needles. m.p. 152–154°; recrystallized, m.p. 155–156°, α_D +18° Al.

Anal. Calcd. for $C_{24}H_{38}O_2$ (358.54): C, 80.39; H, 10.68. Found: C, 80.40; H, 10.58.

Bromination was conducted according to Wieland[15] and the product crystallized from ether–petroleum ether. The first crop formed prismatic needles, m.p. 228–229°; recrystallized, m.p. 232–233°. (Comparison with the Wieland samples was not possible since the latter were destroyed by fire in a bombing attack during the war.)

Methyl 3-Keto-Δ⁴-cholenate³ (III).—A solution of 500 mg. of methyl 4β-bromo-3-ketocholanate (II) in 50 cc. of pyridine (distilled over barium oxide) was refluxed for 12 hr., cooled, acidified with dilute hydrochloric acid, and the product extracted with ether. The solution was washed, dried, clarified with Norit and evaporated. On scratching an ice-cold methanol solution, crystals, m.p. 111–113°, were obtained. Several further crystallizations gave needles m.p. 123–125° (lit.[3] 124–125°), λ^{EtOH} 238 mμ (12,600).

Dehydrobromination in pyridine in a sealed tube at 136°[21] was tried but the starting material was recovered unchanged.

Methyl 3-Keto-Δ⁴-cholenate 2,4-Dinitrophenylhydrazone (a).—A solution of 200 mg. of methyl 4β-bromo-3-ketocholanate (97–99°) in 5 cc. of acetic acid was treated with 90 mg. of 2,4-dinitrophenylhydrazine and heated on a hot-plate under nitrogen for 4–5 min. The orange precipitate that separated was crystallized from chloroform–methanol to give orange-red microcrystals, m.p. 231–232°, yield 242 mg. (80%). A sample prepared from the ketone III melted at 232–233°.

Anal. Calcd. for $C_{31}H_{42}O_6N_4$ (566.68): C, 65.70; H, 7.47. Found: C, 65.70; H, 7.53.

(21) J. von Euw and T. Reichstein, *Helv. Chim. Acta*, **29**, 654 (1946).

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, HARVARD UNIVERSITY]

Configuration of Steroid Bromoketones. II. 4β-Bromotestane-17β-ol-3-one Acetate and 2β-Bromocholestane-3-one

BY LOUIS F. FIESER AND XORGE ALEJANDRO DOMINGUEZ[1]

RECEIVED NOVEMBER 3, 1952

Application of the method of diagnosis reported in paper I affords chemical evidence that the bromoketones listed in the titles have the configurations indicated. Discrepancies are noted between our conclusions and those based on analysis of molecular rotation data (Djerassi) and upon shifts in carbonyl absorption in the infrared (R. N. Jones) and the possibility is suggested that both methods of deducing configurations from physical constants may be invalidated by variations in the conformation of ring A depending upon the nature of the substituents in ring A and at C_{17}.

The method for determination of the configuration of α-bromoketones described in paper I[2] was applied to a further 3-ketone of the coprostane series, namely, Butenandt's[3] etiocholane-17β-ol-3-one acetate (I), for which we shall use the Ciba Conference[4] name testane-17β-ol-3-one acetate. The 4-bromo derivative (II), obtained in 60–70% yield, showed the usual resistance to dehydrohalogenation by pyridine. Reduction of II with sodium borohydride afforded only one bromohydrin (III) in 65% yield. This main product was identified as a *trans*-bromohydrin by its transformation on prolonged refluxing with alcoholic potassium hydroxide into the oxido alcohol IV, distinguished from a ketonic product by the absence of infrared carbonyl absorption. The hydroxyl group of the *trans*-bromohydrin (III) was shown to be α-oriented by hydrogenation in methanolic potassium hydroxide solution in the presence of palladium–charcoal to testane-3α,17β-diol (V); an identical product was obtained in 54% yield by the action of sodium borohydride on the starting ketone I. The 4-bromine substituent of the 4-bromo-3-ketone II is thus identified as β-oriented, as found in the analogous case in the bile acid series.[2] Also, the bromohydrin III was converted smoothly to an olefinic product (VI) on reaction with zinc and acetic acid.

The known 2-bromocholestane-3-one[5] (VIII) was obtained in high yield, and chromatography of the mother liquor afforded only more of the same product and a little of the 2,2-dibromoketone. Reduction of VIII with sodium borohydride gave a single bromohydrin, identified as *cis* because it gave cholestanone on dehydrohalogenation, and as having a 3β-hydroxyl group by debromination to cholestanol (which resulted in 76% yield by reduction of cholestanone with sodium borohydride). The evidence thus indicates that the halogen atom of 2-bromocholestane-3-one is β-oriented. The infrared spectrum of the bromohydrin acetate showed an undivided, strong band at 8.08 μ, which Jones[6] has shown to distinguish 3β-acetoxy allosteroids from the 3α-epimers. The bromohydrin IX on reduction with zinc and acetic acid gave a hydrocarbon corresponding in constants and in the properties of the dibromide with Mauthner's[7] Δ²-cholestene (X).

Djerassi[8] analyzed the molecular rotation data for seven 3-ketoallosteroids differently substituted at C_{17}, found that the M_D effect of introduction of the 3-keto group is constant (av. +70, range 58 to

(1) Fellow of the Camille and Henry Dreyfus Foundation.

(2) L. F. Fieser and R. Ettorre, THIS JOURNAL, **75**, 1700 (1953).

(3) A. Butenandt, K. Tscherning and H. Dannenburg, *Z. physiol. Chem.*, **248**, 205 (1937).

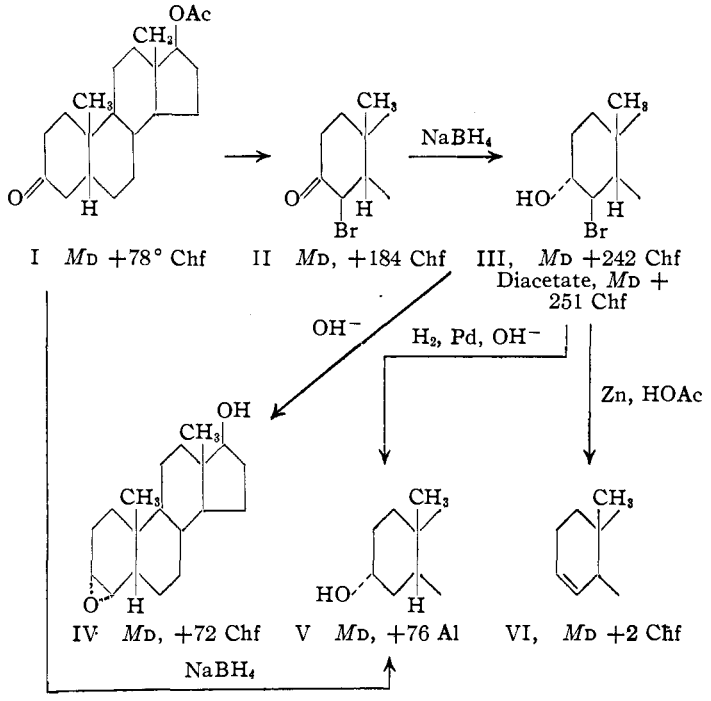
(4) *Chemistry and Industry*, SN1, June 23 (1951).

(5) A. Butenandt and A. Wolff, *Ber.*, **68**, 2091 (1935).

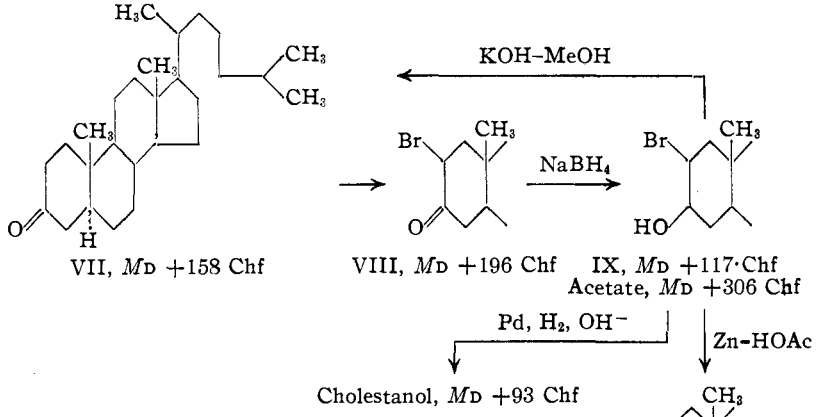
(6) R. N. Jones, P. Humphries, F. Herling and K. Dobriner, THIS JOURNAL, **73**, 3215 (1951).

(7) J. Mauthner, *Monatsh.*, **30**, 635 (1909).

(8) C. Djerassi, *J. Org. Chem.*, **12**, 823 (1947).



80), but made the surprising observation that the M_D effect of 2-bromination varies over the wide range +28 to +98. He tentatively suggested that the substances of high Δ^{Br} values (+92) are 2β-bromo-3-ketones and those of Δ^{Br} values around +30 are 2α-bromo-3-ketones, and that one compound of intermediate character (+58) is a 1:1 mixture of α- and β-epimers. Our finding that the halogen atom of 2-bromocholestanone is β-oriented and that it produces an M_D shift of +106 substantiates the first part of Djerassi's prediction. In a study of infrared absorption spectra, Jones, *et al.*,[9] deduced from theoretical considerations that a bromine atom should increase the frequency of carbonyl absorption of an adjacent keto group by 13–19 cm.$^{-1}$ if the bromine is equatorial but produce no shift if the C–Br bond is polar. Configurations deduced by this scheme for ring C bromoketones of three types, agreed with the configurations previously established by chemical means. In the ring A series Jones, *et al.*, predicted the configurations: 4β-bromocoprostanone and 2α-bromocholestanone.



(9) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

If, as seems likely from their behavior on dehydrohalogenation, the 4-bromo derivatives of coprostanone, methyl 3-ketocholanate and testane-17β-ol-3-one acetate all have the same configuration at C_4, the first prediction agrees with our chemical evidence. However, the configuration deduced for 2-bromocholestanone is the opposite of that indicated by chemical evidence. The deductions of both Djerassi and Jones, *et al.*, were based on the assumption that in both the 3-ketones and their bromo derivatives ring A exists preponderantly in the chair conformation, a qualification expressly stated in the Jones paper. Whereas in the ring C derivatives the rigidity of the ring fusion imposes a high barrier to conformation changes, no such barrier exists for ring A and we are inclined to think that the general assumption of chair conformation is not valid. The observation that the behavior on cathylation[10] of stanols epimeric at C_3 and C_5 does not conform accurately to predictions based on the concept of polar and equatorial bonds led us to suggest that ring A lacks the rigidity characteristic of the rest of the molecule. Perhaps the wide variation in Δ^{Br} values noted by Djerassi is due not to differences in composition of equilibrium mixtures but to variations in the contributions of chair and boat conformations. We plan to test this point experimentally. The hypothesis that the equilibrium conformation of ring A may vary according to the nature of the substituents in ring A and at C_{17} derives some support from comparison of the molecular rotations of methyl cholanate derivatives (a) and 17β-acetoxytestane derivatives (b). Values for M_D[a] Di − M_D[b] Chf are as follows: 3-ketones, +46; 4β-bromo-3-ketones, +71; 3α-hydroxy-4β-bromides, +22; 3α-acetoxy-4β-bromides, −65; 3α,-4α-oxides, −20; Δ^3-enes, +111. We see no explanation other than that suggested for the wide variation among pairs of compounds of comparable chemical behavior. The M_D increment for 4-bromination of methyl 3-ketocholanate (Δ = +131) does not differ much from that for 4-bromination of testane-17β-ol-3-one acetate (Δ = +106), but the M_D increment for conversion of coprostanone (M_D +139 Chf) to the 4-bromo derivative (M_D +187 Chf)[11] is only +48.

Experimental

4β-Bromotestane-17β-ol-3-one Acetate (II).—To a solution of 9 g. of testane-17β-ol-3-one 17-acetate (I), m.p. 146–147°, α_D +23.5° Chf, kindly supplied by Syntex S.A., in 45 cc. of acetic acid was added in 20 min. a solution of 4.4 g. of bromine and 10 drops of 48% hydrobromic acid solution

(10) L. F. Fieser, J. E. Herz, M. W. Klohs, M. A. Romero and T. Utne, *ibid.*, **74**, 3309 (1952).

(11) C. Djerassi and C. R. Scholz, *ibid.*, **70**, 417 (1948).

in 22 cc. of acetic acid.[12] Absorption of bromine was rapid, and 0.5 hour later 30 cc. of water was added and the mixture let stand at 5° for 10 hr. The precipitated product was collected, washed three times with 1:2 acetic acid–water and with water, and dried; 9.5 g., m.p. 170–175°. Crystallization from ethanol gave 7.2 g. (65%) of product, m.p. 174–175°, α_D +44.7 ± 2° Chf, λ^{Chf} 5.78 mμ.

Anal. Calcd. for $C_{21}H_{31}O_3Br$ (411.38): C, 61.31; H, 7.60; Br, 19.47. Found: C, 61.46; H, 7.81; Br, 19.70.

In two other runs the yields of recrystallized product were 60% and 73%. Processing of the mother liquors gave a small amount of substance, m.p. 183–185°.

Solutions of 600 mg. of the bromoketone and 1.2 cc. of γ-collidine in 15 cc. of xylene were refluxed for 2, 3 and 5 hr. and the solutions were washed with water and acid, dried and evaporated, and the residue crystallized from acetone. In each case the crystallizate was starting material (mixed m.p.), recovered in yields of 82.5, 61.5 and 78%; no other product could be isolated.

4β-Bromotestane-3α,17β-diol 17-Acetate (III).—A suspension of 3.2 g. of 4β-bromotestane-17β-ol-3-one acetate and 0.6 g. of sodium borohydride in 40 cc. of absolute ethanol was let stand at 25° for 12 hr., 40 cc. of water was added, and the resulting suspension was kept at 5° for 10 hr. and extracted three times with ether. Evaporation of the washed and dried extract gave a white residue, 2.9 g. m.p. 108–118°, α_D +52.7° Chf. Crystallization from ethanol gave 2.1 g. (65%) of plates, m.p. 138–139°; the mother liquor afforded amorphous material, m.p. 118–122°, α_D 55.5° Chf. A further crystallization of the bromohydrin gave plates, m.p. 138-139°, α_D +58.5 ± 2° Chf, λ^{Chf} 2.82, 5.80, 8.0 μ.

Anal. Calcd. for $C_{21}H_{33}O_3Br$ (413.39): C, 61.42; H, 8.05; Br, 19.33. Found: C, 61.26; H, 8.08; Br, 19.53.

The bromohydrin III was not precipitated by digitonin. Chromatography of the mother liquor material either as such or after acetylation failed to reveal the presence of another epimer.

4β-Bromotestane-3α,17β-diol 3,17-diacetate, prepared by acetylation of 261 mg. of the bromohydrin in pyridine at 25°, was crystallized twice from ethanol to give 178 mg. (61%) of long white needles, m.p. 161–162°, α_D +55.2° Chf, λ^{CS_2} 5.76, 8.02, 8.35 μ.

Anal. Calcd. for $C_{23}H_{35}O_4Br$ (455.43): C, 60.65; H, 7.74. Found: C, 60.61; H, 7.85.

3α,4α-Oxidotestane-17β-ol (IV).—A solution of 310 mg. of 4β-bromotestane-3α,17β-diol 17-acetate (m.p. 138–139°) in 30 cc. of methanol containing 0.3 g. of potassium hydroxide was refluxed for 46 hr., let cool, and diluted with 80 cc. of water. A yellowish product that separated was combined with an ether extract of the mother liquor and the solution washed, dried and evaporated. Three crystallizations of the residue from methanol gave 100 mg. (46%) of oxide, m.p. 186–188°, α_D +25 ± 3° Chf; infrared spectrum: no carbonyl or ester bands.

Anal. Calcd. for $C_{19}H_{30}O_2$ (290.43): C, 78.57; H, 10.41. Found: C, 78.41; H, 10.36.

Testane-3α,1-7β-diol[13] (V) (**a**).—A suspension of 1 g. of 4β-bromotestane-3α,17β-diol 17-acetate and 1 g. of 2% palladium–charcoal in a solution of 3 g. of potassium hydroxide in 60 cc. of methanol was shaken at 25° with hydrogen at 80 mm. pressure until absorption was complete. The filtered solution was acidified with 36% hydrochloric acid and left at 5° for 4 hr. and the inorganic crystals removed by filtration. The solution was made alkaline, diluted, and extracted with ether. Evaporation left 400 mg. (56%) of solid residue, that softened at about 165° and melted at 184–188°. Three crystallizations from ethanol gave small white needles, m.p. 228–229°, α_D +26 ± 2° Al, not precipitated by digitonin (lit.,[3] m.p. 232°, α_D +26.5° Al).

Anal. Calcd. for $C_{19}H_{32}O_2$ (292.45): C, 78.03; H, 11.03. Found: C, 77.96; H, 10.91.

(b) A suspension of 400 mg. of testane-17β-ol-3-one 17-acetate and 0.5 g. of sodium borohydride in 25 cc. of absolute ethanol was kept at 25° for 20 hr. and the solution was concentrated somewhat and diluted with 100 cc. of water. The resulting white precipitate was crystallized twice from ethanol–water and gave 218 mg. (54%) of small white needles, m.p. 228.5–229.5°, α_D +23.5 ± 2° Al, no depression in m.p. on admixture with sample (a).

Δ³-Testene-17β-ol 17-Acetate (VI).—A mixture of 200 mg. of 4β-bromotestane-3α,17β-diol 17-acetate, 0.8 g. of zinc dust and 22 cc. of acetic acid was refluxed for 2 hr. and the solution was filtered and concentrated to half the volume. On standing at 5° small white plates slowly separated, and recrystallization from acetic acid gave 89 mg. (57%) of plates, m.p. 142–143°, α_D +0.5 ± 1° Chf; Beilstein test negative; Liebermann–Burchard, tetranitromethane and bromine-absorption tests positive.

Anal. Calcd. for $C_{21}H_{32}O_2$ (316.47): C, 79.70; H, 10.19. Found: C, 79.33; H, 10.18.

2β-Bromocholestane-3-one[5] (VIII).—Hydrogenation of commercial cholesterol according to Hershberg, *et al.*,[14] gave **cholestanol**, m.p. 138–141°, in 70–87% yield. For oxidation,[15] a hot solution of 27 g. of sodium dichromate dihydrate in 170 cc. of acetic acid was added to a suspension of 26.1 g. of cholestanol in 155 cc. of acetic acid and the mixture was heated on the steam-bath for a few minutes to effect complete solution and then let stand overnight. The resulting paste was treated with 20 cc. of water and the precipitated cholestanone was collected, washed well with water and crystallized from 4:1 ethanol–acetone; yield 18–20.5 g. (67–78%), m.p. 127–128°, α_D +43° Chf. Bromination was conducted by slow addition (10 min.) of a solution of 4.5 g. of bromine and 6 drops of 48% hydrobromic acid in 20 cc. of acetic acid to a stirred solution of 10 g. of cholestanone in 300 cc. of acetic acid at 25°. The bromoketone crystallized promptly and was collected and washed. Two crystallizations from ethanol–acetone (5:1) gave 7.5–9.2 g. (62–76%) of **2β-bromocholestane-3-one**, as white needles, m.p. 168–169°, α_D +42° Chf.

2β-Bromocholestane-3β-ol (**IX**).—On addition of 0.6 g. of sodium borohydride to a suspension of 8.4 g. of 2β-bromocholestane-3-one in 350 cc. of ethanol at 25° reduction occurred promptly and the crystals all dissolved in 2 hr. The solution was let stand for another 20 hr. and then poured into 1.2 l. of water. After standing at 5° for 6 hr. the white precipitate was collected, washed thoroughly with water, and crystallized from ethanol. The substance formed small crystals, m.p. 104–105°, α_D +25 ± 2° Chf, yield 6.2–7.4 g. (73–87%).

Anal. Calcd. for $C_{27}H_{47}OBr$ (467.57): C, 69.35; H, 10.13; Br, 17.13. Found: C, 68.97; H, 10.18; Br, 17.33.

The acetate, prepared by acetylation of 4 g. of bromohydrin with pyridine–acetic anhydride (20 hr. at 25°), crystallized from ethanol–acetone (3:1) in long white needles; yield 3.4 g. (77%), m.p. 189–191°, α_D +60 ± 2° Chf, λ^{CS_2} 5.78, 8.08 μ.

Anal. Calcd. for $C_{29}H_{49}O_2Br$ (509.60): C, 68.35; H, 9.69. Found: C, 68.18; H, 9.60.

Sodium Borohydride Reduction of Cholestane-3-one.—Reduction of 800 mg. of cholestanone in 40 cc. of ethanol with 300 mg. of sodium borohydride at 25° as above and crystallization of the crude product (m.p. 134–136°) afforded 620 mg. (76%) of cholestane-3β-ol, m.p. 138–139.5° (undepressed).

Conversion of the Bromohydrin IX to Cholestanone.—A solution of 1.6 g. of 2β-bromocholestane-3β-ol and 1.6 g. of potassium hydroxide in 120 cc. of methanol was refluxed for 72 hr., cooled and acidified with 36% hydrochloric acid (4.5 cc.). The resulting suspension was let stand for 12 hr. and the solid was then filtered. The crude material melted at 104–108°, and the infrared spectrum indicated the presence of a ketone. Repeated crystallization afforded 0.1 g. of cholestanone, m.p. 126–127°, undepressed by admixture with authentic material. Fractionation of the mother liquor material gave 0.6 g. of unchanged 2β-bromocholestane-3β-ol. When refluxing was continued for periods of only 3 and 12 hr. pure starting material was recovered.

Δ²-Cholestene (**X**).—A mixture of 3 g. of 2β-bromocholestane-3β-ol and 6 g. of zinc dust in 150 cc. of acetic acid was

(12) This procedure was based on that described by B. A. Koechlin, T. H. Kritchevsky and T. F. Gallagher, *J. Biol. Chem.*, **184**, 393 (1950), for preparation of the d_2-11,12-derivative of II, α_D +45° Chf.

(13) Butenandt's epietiocholane-3,17-diol,[3] also known as etiocholane-3α,17β-diol.

(14) E. B. Hershberg, E. Oliveto, M. Rubin, H. Staeudle and L. Kuhlen, THIS JOURNAL, **73**, 1144 (1951).

(15) M. G. Vavon and B. Jakubowicz, *Bull. soc. chim.*, [4] **53**, 581 (1933).

refluxed for 0.5 hour and the solution filtered. On cooling, the reduction product separated in long white needles, m.p. 69–70°, α_D +63 ± 2° Chf (lit.[6] 68–69°, α_D +64° Chf), yield 1.3 g. (55%).

The dibromide, crystallized twice from ethanol–acetone (3:1), formed small plates, m.p. 123–124°, α_D +76° Chf (Mauthner,[6] 125°, α_D +75° Chf).

Anal. Calcd. for $C_{27}H_{46}Br_2$ (530.48): C, 61.34; H, 8.63; Br, 30.13. Found: C, 61.24; H, 8.66; Br, 30.13.

Hydrogenation of 2β-Bromocholestane-3β-ol.—A mixture of 300 mg. of 2β-bromocholestane-3β-ol, 150 mg. of 5% palladium–charcoal and a solution of 2 g. of potassium hydroxide in 40 cc. of absolute ethanol was shaken at 25° with hydrogen until absorption stopped (30 min.). The solution was filtered, acidified with dilute acid, and extracted with ether. The residue left on evaporation (m.p. 136°) on crystallization from ethyl acetate afforded 162 mg. (65%) of cholestane-3β-ol, m.p. 138–140°, α_D +22.2 ± 2° Chf, no depression in mixed m.p. determination.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

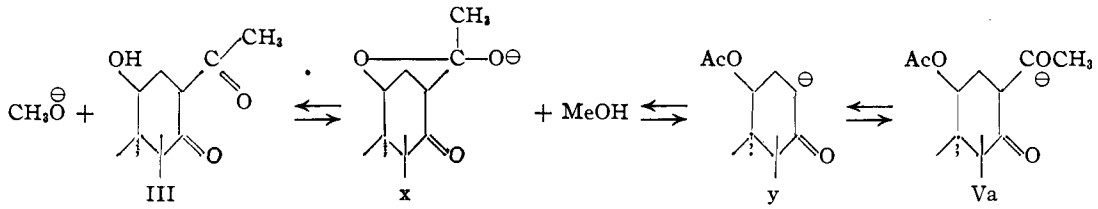
Approaches to the Total Synthesis of Adrenal Steroids. VI. 2,4b-Dimethyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one and Related Compounds

BY R. M. LUKES, G. I. POOS, R. E. BEYLER, W. F. JOHNS AND L. H. SARETT

RECEIVED NOVEMBER 24, 1952

Several methods for attaching a methyl group to the C-2 position of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,5,6,7,8,10,-10aβ-dodecahydrophenanthrene-4β-ol-1-one are described. Among these the most satisfactory was found to be the direct methylation with methyl iodide–potassium *t*-butoxide. The corresponding 2-methyl-1,4-diketone XIV could be smoothly prepared by hydrolysis of the 2-methyl-2-carbomethoxy derivative XII as well as by oxidation of the 2-methyl hydroxy ketones. The stereochemical configuration of the C-2 methyl group is discussed.

Methylation of the 4β-Hydroxy-1-ketone (I).—The attachment of a methyl group at the C-2 position of 4b-methyl-7-ethylenedioxy-1,2,3,4,4aα,4b,-5,6,7,8,10,10aβ-dodecahydrophenanthrene-4β-ol-1-one (I)[1] was a necessary preliminary to the final stages of construction of the steroid skeleton. A number of procedures yielded the desired 2-methyl derivative II. Among these the direct methylation of the hydroxy ketone with methyl iodide–potassium *t*-butoxide was the most productive.[2,3] Although an excess of these reagents led to the formation of considerable amounts of a dimethylated derivative, it was possible with a short reaction time and a limited amount of base to produce a mixture consisting chiefly, after removal of unreacted starting material, of the monomethylated ketone II. Separation of the methylation mixture could be accomplished quite easily by fractional crystallization. In view of the inaccessibility of the 4β-hydroxyl group, no 4β-methoxy derivative was expected nor was any found.



Another approach, consisting of acylation, methylation and cleavage, also afforded the desired monomethyl ketone. This reaction series served both to illumine the rather intricate internal reactions of ring C and to confirm the location of the methyl group of II at the C-2 position. The tricyclic ketone condensed with methyl acetate in the presence of sodium methoxide to give the 2-acetyl derivative III along with a second enolic substance in variable amount. Methylation of the former and alkaline cleavage of the resulting 2-methyl-2-acetyl derivative IV afforded the same monomethyl ketone II obtained by direct methylation.

The second enolic substance had no free hydroxyl group but instead possessed an ester linkage (5.80 μ band in the infrared) as well as the 1,3-diketone system (broad band at 6.18–6.30 μ). Analyses indicated an empirical formula in agreement with that of the 2-acetyl 4-acetate V. A corresponding 2-methyl derivative VI was obtained from the methylation of V. Confirmation of the structure of the acetyl acetate V could be obtained by subjecting the methyl derivative VI to vigorous saponification, thereby cleaving the 2-acetyl group and hydrolyzing the 4-acetate to give the 2-methyl ketone II described above. Of the two likeliest mechanisms leading to the appearance of an acetate at C-4, namely, the direct base-catalyzed transesterification of the hydroxyl group with methyl acetate or methyl acetoacetate[4] and the intramolecular shift shown below, the latter is probably to be preferred since 11β-hydroxyl groups in the steroids appear

(1) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

(2) The use of these reagents for the methylation of ketones was introduced by D. A. Peak and R. Robinson, *J. Chem. Soc.*, 1581 (1937). See also N. A. McGinnis and R. Robinson, *ibid.*, 404 (1941); A. Koebner and R. Robinson, *ibid.*, 566 (1941).

(3) The direct methylation of α-decalone has been investigated by W. S. Johnson and his students (W. S. Johnson, THIS JOURNAL, **65**, 1317 (1943); W. S. Johnson and H. Posvic, *ibid.*, **67**, 504 (1945); (see also R. Robinson (ref. 2)). They have shown that the methylene group is attacked in preference to the bridgehead methine. By analogy the C-2 position should be preferred over C-10a in the direct methylation of 1-ketopolyhydrophenanthrene.

(4) *Cf.* A. R. Bader, L. O. Cummings and H. A. Vogel, *ibid.*, **73**, 4195 (1951).