Selective Oxidation of Allylic Alcohols with Active N-Halogen Compounds. II[1]

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It was shown in the previous paper[1] that active *N*-halogen compounds are effective reagents for the selective oxidation of allylic alcohols[2]. This article presents examples of selective oxidation of dihydroxylic compounds, each carrying an allylic and a primary or equatorial hydroxyl group, to α,β-unsaturated ketones with the unaffected primary or equatorial hydroxyl group, which may be difficult when manganese dioxide is employed[4,5], and of an allylic alcohol with an isolated ethylenic linkage to an α,β-unsaturated ketone without affecting the isolated double bond.

Reduction of methyl 3-keto-23,24-dinorchol-4-en-22-oate[6] (I) with lithium aluminum hydride gave a product which is presumed a mixture consisting essentially of 23,24-dinorchol-4-en-3β,22-diol and its 3α-epimeride. Oxidation of the mixture III by means of *N*-bromoacetamide in benzene-pyridine gave 23,24-dinorchol-4-en-22-ol-3-one (IVa)[7] in an overall yield of 78% from keto ester I. Similarly, reduction[8] of 3-keto-23,24-dinorchol-4-en-22-al[9] (II) with sodium borohydride to diol mixture III followed by oxidation with *N*-bromoacetamide or with isocyanur bromide[10] yielded 23,24-dinorchol-4-en-22-ol-3-one (IVa)[11].

The lithium aluminum hydride reduction of methyl 3-keto-20-*iso*-23,24-dinorchol-4-en-22-oate (V)[6] to diol mixture VII and the succeeding oxidation with *N*-bromoacetamide furnished 20-*iso*-23,24-dinorchol-4-en-22-ol-3-one (VIIIa) in an overall yield of 72%. The same compound VIIIa was also obtained from 3-keto-20-*iso*-23,24-dinorchol-4-en-22-al[6] (VI) by sodium borohydride reduction followed by the selective oxidation with *N*-bromoacetamide.

Treatment of methyl 3-keto-23,24-dinorchol-4-en-22-oate (I) with ethylene glycol in benzene solution in the presence of *p*-toluenesulfonic acid furnished methyl 3-ethylenedioxy-23,24-dinorchol-5-en-22-oate (IX), m. p. 188~189°C, α_D −46°. The rotatory dispersion curve[14] of this compound (negative plain) is consistent with a 5-ene-ketal. Djerassi et al.[15] have shown that 5-ene-steroids give negative plain dispersion curves. Acid hydrolysis of ketal ester IX regenerated methyl 3-keto-23,24-dinorchol-4-en-22-oate (I). Reduction of ketal ester IX with lithium aluminum hydride gave 3-ethylenedioxy-23,24-dinorchol-5-en-22-ol (Xa), m. p. 181~182°C, α_D −33°. Hydrolysis of ketal alcohol Xa gave 23,24-dinorchol-4-en-22-ol-3-one (IVa), which was identical with the sample derived from compound I or II through diols III.

Addition of hypobromous acid to 3-ethylenedioxy-cholest-5-ene (XI) by means of *N*-bromoacetamide in dioxane containing

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1) Part I. K. Morita, This Bulletin, **31**, 450 (1958). (Steroids Part XXIV; Part XXIII, Idem., ibid., **31**, 379 (1958)).

2) Though Romero[3] recently reported that the reaction of cholest-4-ene-3β,6β-diol with *N*-bromosuccinimide in aqueous dioxane furnished cholest-4-en-6β-ol-3-one only in a low yield, it should be noted that the presence of water markedly decreases the yield of the reaction[1].

3) M. A. Romero, *J. Org. Chem.*, **22**, 1267 (1957).

4) H. Bruderer, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **39**, 858 (1956).

5) C. Amendolla, G. Rosenkranz and F. Somdheimer, *J. Chem. Soc.*, **1954**, 1226.

6) M. E. Herr and F. W. Heyl, *J. Am. Chem. Soc.*, **74**, 3627 (1952).

7) C. Meystre and K. Miescher, *Helv. Chim. Acta*, **31**, 211 (1949). Identity was established by a direct comparison with the sample kindly provided by Dr. C. Meystre of CIBA Ltd. The author wishes to express his hearty thanks to him.

8) Partial reduction of keto aldehyde II to corresponding keto alcohol IVa may be probable. cf. E. H. Jensen and W. A. Struck, *Anal. Chem.*, **27**, 271 (1955).

9) G. Slomp, Jr. and L. J. Johnson, *J. Am. Chem. Soc.*, **80**, 915 (1958); cf. D. A. Shepherd et al., ibid., **77**, 1212 (1955).

10) K. Morita, This Bulletin, **31**, 347 (1958).

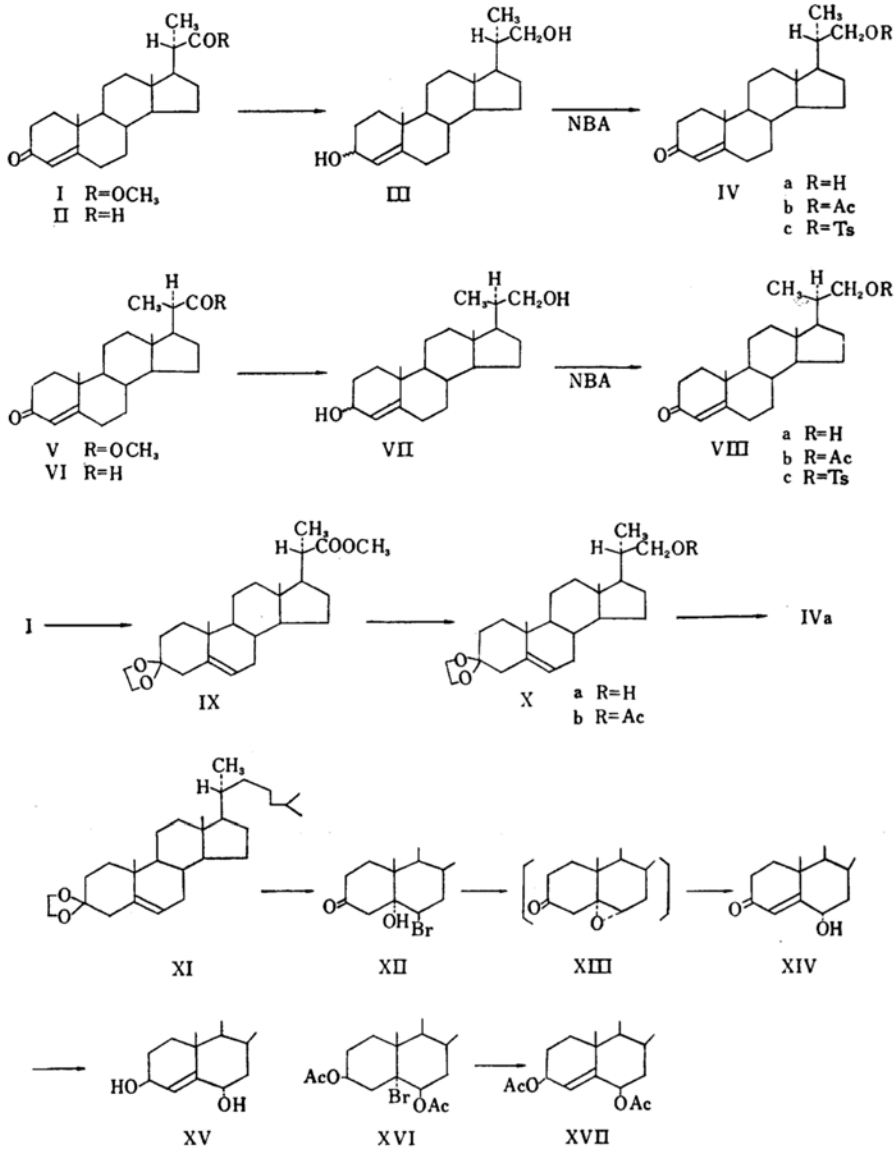
11) In this case the yield was lower than that of the reduction by means of lithium aluminum hydride, probably owing to the formation of a small amount of by-products (saturated compound[12], etc.[13]) during the reduction with sodium borohydride.

12) F. Sondheimer et al., *Chem. & Ind.*, **1954**, 1482; J. K. Normberski and G. F. Woods, *J. Chem. Soc.*, **1955**, 3426; C. Djerassi et al., *J. Am. Chem. Soc.*, **79**, 3528 (1957).

13) W. W. Zorbach, ibid., **75**, 6344 (1953).

14) Determination of the rotatory dispersion curve was kindly carried out by Professor Carl Djerassi of Wayne State University. The author wishes to express his hearty thanks to him.

15) C. Djerassi, W. Closson and A. E. Lippman, *J. Am. Chem. Soc.*, **78**, 3163 (1956).



dilute perchloric acid yielded 6β-bromocholestan-5α-ol-3-one (XII) in 50% yield[16]. Treatment of compound XII with sodium hydroxide in methylenechloride-methanol at room temperature gave 6α-hydroxycholest-4-en-3-one (XIV), which was converted into cholest-4-ene-3β,6α-diol (XV)[17] by lithium aluminum hydride reduction. Dehydrobromination of 5α-bromocholestane-3β,6β-diol diacetate (XVI)[18] with boiling pyridine gave cholest-4-ene-3β,6β-diol diacetate (XVII).

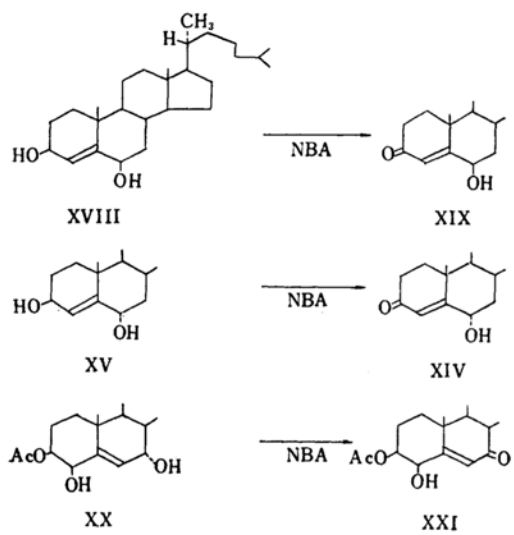
Oxidation of cholest-4-ene-3β,6β-diol (XVIII) and cholest-4-ene-3β,6α-diol (XV) by means of about one equivalent of *N*-bromoacetamide gave cholest-4-en-6β-ol-3-one (XIX) and cholest-4-en-6α-ol-3-one (XIV) in good yields, respectively. Proofs for these structures were obtained from their conversion into acetates and into 5α-cholestane-3,6-dione by a reaction with hydrochloric acid[19]. The method may be applica-

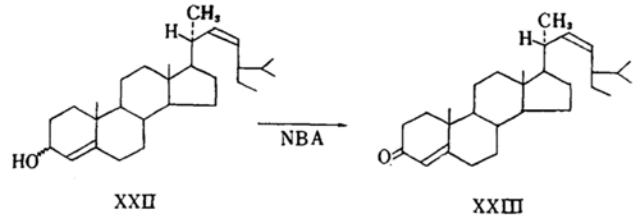
16) Cf. S. Mori, K. Morita and F. Mukawa, *Proc. Japan Acad.*, **32**, 585 (1956).

17) Y. Urushibara and K. Mori, *Abstract of the 10th Annual Meeting of the Chemical Society of Japan*, p. 204 (1957).
Detail of the experimental for preparation of cholest-4-ene-3β, 6α-diol (XV) from cholest-4-ene-3β-ol-6-one by hydride reduction was informed by Miss K. Mori to whom author's thanks are due.

18) Y. Ueno, *J. Pharm. Soc. Japan* (*Yakugaku Zasshi*), **71**, 1626 (1952).

19) B. E. Ellis and V. A. Petrow, *J. Chem. Soc.*, **1939**, 1078.





ble to a general synthesis of 6β-hydroxy-3-keto-4-ene-steroids[20,21] and of 6α-hydroxy-3-keto-4-ene-steroids[20,22]. Amendolla et al.[5], reported that manganese dioxide oxidation of cholest-4-ene-3β,6β-diol (XVIII) gave cholest-4-en-6β-ol-3-one (XIX) in a good yield while the oxidation of cholest-4-ene-3β,6α-diol (XV), in which $C_{(6)}$-hydroxyl group is equatorial, gave cholest-4-ene-3,6-dione even under mild conditions.

It is noteworthy that on the *N*-bromoacetamide oxidation of compound XVIII 3β-hydroxy group (quassi equatorial) was selectively oxidized whereas 6β-hydroxy group (axial) remained unaffected. This fact is contrary to the general rule for the oxidation by means of *N*-bromoacetamide to the effect that axial hydroxyl groups are more readily oxidized than equatorial ones. Lieberman and Fukushima[23] reported the selective oxidation of cholest-5-ene-3β,4β,7α-triol 3-monoacetate (XX) to cholest-5-ene-3β,4β-diol-7-one 3-monoacetate (XXI), in which quassi axial hydroxyl group 7α was selectively oxidized and axial hydroxyl group 4β remained unaffected. It might be expected that *N*-bromoacetamide oxidation of allylic hydroxyl groups to give s-trans α,β-unsaturated ketones is easier than that of allylic hydroxyl groups to give s-*cis* α,β-unsaturated ketones.

Reduction of stigmasta-4,22-dien-3-one (XXIII)[24] with lithium aluminum hydride gave a mixture of stigmasta-4,22-dien-3β-ol and the corresponding 3α-ol. Oxidation of the mixture XXII by means of about one equivalent of *N*-bromoacetamide gave stigmasta-4,22-dien-3-one (XXIII) in 80% yield. *N*-Halogen compounds may also be effective for the selective oxidation of allylic alcohols containing isolated ethylenic double bonds to α,β-unsaturated ketones without affecting the isolated double bonds.

Experimental[25]

23,24-Dinorchol-4-en-22-ol-3-one (IVa).—*a) From Methyl 3-Keto-23,24-dinorchol-4-en-22-oate (I).*—A mixture of 165 mg. of ketoester I[6] and 100 mg. of lithium aluminum hydride in 15 ml. of anhydrous tetrahydrofuran was heated under reflux for 5 hours. After careful decomposition of excessive lithium aluminum hydride with a small amount of water, tetrahydrofuran was evaporated under a reduced pressure. The solid was collected, dried, and washed well with dioxane. Evaporation of the solvent under a reduced pressure yielded a solid, m. p. 187~204°C, in a quantitative yield.

A solution of the above solid (162.3 mg.) in 2 ml. of benzene and 4 ml. of pyridine was treated with 82 mg. of *N*-bromoacetamide at room temperature (17~18°C) for two and a half hours in the dark. The solution was diluted with benzene and washed successively with 10% aqueous sodium bisulfite, with 10% aqueous sodium hydroxide, with water, with dilute sulfuric acid, and again with water, and dried over anhydrous sodium sulfate. The solvent was evaporated under a reduced pressure, and 165 mg. of a crystalline solid was obtained. The solid was dissolved in 10 ml. of benzene and adsorbed on a column of alumina (5 g.). Elution with ether gave 129 mg. (78% from I) of IVa with m. p. 135~136°C. Recrystallization from aqueous acetone yielded pure IVa, m. p. 137~138°C, $[\alpha]_D^{18}$ +94 (C, 1.125), λ_{max} 241 mμ, log ε, 4.20, ν_{max}^{Nujol} 2.90 (OH), 6.09 (C=O), 6.18 μ (C=C). The melting point was not depressed on admixture with an authentic sample (m. p. 137.5~138°C) kindly provided by Dr. C. Meystre[7].

20) M. Ehrenstein et al., *J. Org. Chem.*, **16**, 1051 (1951); **17**, 1587 (1952); **19**, 1331 (1954). L. F. Fieser, *J. Am. Chem. Soc.*, **75**, 4377 (1953).
21) F. Sondheimer et al., *J. Chem. Soc.*, **1954**, 1226; *J. Am. Chem. Soc.*, **76**, 5020 (1954).
22) K. Morita, *Proc. Japan Academy.*, **32**, 588 (1956).
23) S. Lieberman and D. K. Fukushima, *J. Am. Chem. Soc.*, **72**, 5211 (1950).
24) G. Slomp, Jr., et al., ibid., **77**, 1216 (1955). Cf. D. A. Shepherd et al., ibid., **77**, 1212 (1955).
25) All melting points are uncorrected. Rotations are all measured in chloroform solution.

Anal. Found: C, 79.51; H, 10.42. Calcd. for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37%.

b) From 3-Keto-23, 24-dinorchol-4-en-22-al (II) by use of N-Bromoacetamide.—To a suspension of 1.5 g. of keto aldehyde II[9] in 90 ml. of methanol, a solution of 0.3 g. of sodium borohydride in 0.7 ml. of water and 15 ml. of methanol was added with stirring at room temperature. After standing for 2 hours at room temperature excessive sodium borohydride was decomposed by careful addition of a small amount of dilute acetic acid. Then the solution was poured into an excess of water. The solid was collected and well washed with water. The solid melted at 175~190°C. Yield, 1.4 g.

The mixture, dissolved in 15 ml. of benzene and 30 ml. of pyridine, was treated with 700 mg. of *N*-bromoacetamide as described above, and 870 mg. of compound IVa with m. p. 135~138°C was obtained. Identity was established by a mixed melting point determination.

c) From 3-Keto-23, 24-dinorchol-4-en-22-al (II) by use of Isocyanur Bromide[10].—To a solution of 5 g. of keto aldehyde II in 100 ml. of tetrahydrofuran, 2 g. of sodium borohydride in 10 ml. of water was added at room temperature. After allowed to stand overnight at room temperature the solution was poured into an excess of water. The solid was collected by filtration. The solid melted at 196~205°C. Yield, 4.8 g.

A mixture of 404 mg. of the above solid, 25 ml. of *tert*-butyl alcohol, 1 ml. of pyridine and 205 mg. of 83% isocyanur bromide[10] was treated as usual, and 260 mg. of compound IVa with m. p. 134~138°C was obtained.

d) From 3-Ethylenedioxy-23, 24-dinorchol-5-en-22-ol (Xa).—To a suspension of 128 mg. of ketal alcohol Xa in 13 ml. of methanol, 1.3 ml. of 8% (by volume) sulfuric acid was added, and the mixture was refluxed for one hour. A few drops of water were added and the precipitated needles were collected by filtration and recrystallized from aqueous acetone to give 72 mg. of IVa in needles, m. p. 137~138°C. The melting point was not depressed on admixture with the above samples.

23, 24-Dinorchol-4-en-22-ol-3-one acetate (IVb).—The substance was obtained in a usual way, and recrystallized from *n*-hexane, m. p. 131~132°C, $[\alpha]_D^{22}$ +95 (c, 1.248).

Anal. Found: C, 76.89, H, 9.91. Calcd. for $C_{24}H_{36}O_3$: C, 77.37, H, 9.74%.

When a mixture of 21 mg. of the acetate IVb, 3 ml. of methanol and 0.3 ml. of 0.8% (by volume) sulfuric acid was heated under reflux for 45 minutes, compound IVa was obtained.

23, 24-Dinorchol-4-en-22-ol-3-one tosylate (IVc).—To 249 mg. of compound IVa in 2 ml. of pyridine, 0.19 g. of *p*-toluenesulfonyl chloride was added and the mixture was allowed to stand overnight at room temperature. The mixture was poured into an excess of water. The solid was collected, washed with dilute hydrochloric acid and with water, dried, and recrystallized from acetone to give IVc in plates, m. p. 175~177°C (dec.), ν_{max}^{Nujol} 5.99 (C=O), 6.17, 6.24 (C=C), 7.30, 8.51 μ (—O—SO_2—).

Anal. Found: C, 72.66, H, 7.05. Calcd. for $C_{29}H_{36}SO_4$: C, 72.46, H, 7.55%.

Methyl 3-Keto-23,24-dinorchol-4-en-22-oate (I).—To a suspension of 50 mg. of ketal ester IX in 4 ml. of methanol, 0.4 ml. of 8% (by volume) sulfuric acid was added and the mixture was refluxed for 40 minutes. The solid soon disappeared and in about 10 minutes a new crystalline substance began to separate out. The suspension was diluted with water and the solid (m. p. 170~172°C; 45 mg.) was collected and recrystallized from acetone to give I in crystals with m. p. 178~180°C. The identity was established by a mixed[6] melting point determination.

Methyl 3-Keto-20-*iso*-23, 24-dinorchol-4-en-22-oate (V).—3-Keto-20-*iso*-23, 24-dinorchol-4-en-22-al (II)[6] (391 mg.) (m. p. 142~143°C from methylene chloride-isopropyl alcohol; reported m. p. 140~142°C[6], 137.5~139°C[26]), dissolved in 8 ml. of benzene and 8 ml. of glacial acetic acid, was oxidized with 118 mg. of chromic acid in 0.25 ml. of water and 8 ml. of acetic acid according to Herr and Heyl[6].

The ethereal extract was washed twice with 10% sodium carbonate. The sodium salt was collected centrifugally, and washed with ether. Treatment of the salt with 20% sulfuric acid gave 135 mg. of 3-keto-23, 24-dinorchol-4-en-22-oic acid with m. p. 233~243°C, which gave a pure sample, m. p. 265~268°C, on recrystallization from methylene chloride-methanol.

The alkaline solution was neutralized with 20% sulfuric acid and 262 mg. of crude 3-keto-20-*iso*-23, 24- dinorchol-4-en-22-oic acid with m. p. 201~204°C was obtained. Methylation of the crude acid with diazomethane yielded 123 mg. of V with m. p. 118~121°C. Reported m. p. 119~121°C[6].

20-*Iso*-23, 24-dinorchol-4-en-22-ol-3-one (VIIIa).—*a) From Methyl 3-Keto-20-iso-23, 24-dinorchol-4-en-22-oate (V).*—A mixture of 73.7 mg. of keto ester V and 52 mg. of lithium aluminum hydride in 2 ml. of tetrahydrofuran was treated in the same way as described above (reflux for 5 hours) to give 73.4 mg. of a mixture (VII) with m. p. 188~205°C.

The above solid was dissolved in a mixture of 1 ml. of benzene and 3 ml. of pyridine and the solution was treated with 37 mg. of *N*-bromoacetamide (standing for 3 hours at room temperature). After being treated as usual, the crystalline residue (73.6 mg.; m. p. 120~138°C) was dissolved in 10 ml. of benzene and adsorbed on a column of alumina (3 g.). Elution with ether and recrystallization from aqueous acetone gave 53 mg. of VIIIa, m. p. 147~148°C, $[\alpha]_D^{21.5}$ +96 (c, 0.532), λ_{max} 241 mμ, log ε, 4.24, ν_{max}^{Nujol} 2.89 (OH), 6.03 (C=O) 6.20 μ (C=C).

Anal. Found: C, 79.90, H, 10.48. Calcd. for $C_{22}H_{34}O_2$: C, 79.95, H. 10.37%.

b) From 3-Keto-20-iso-23, 24-dinorchol-4-en-22-al (VI).—To a mixture of 1 g. of compound VI[6] in 60 ml. of methanol, a solution of 0.2 g. of sodium borohydride in 1 ml. of water and 5 ml. of methanol was added with stirring at the room

26) K. Tsuda. R. Hayatsu, Y. Kishida and S. Akagi, *J. Am. Chem. Soc.*, 80, 921 (1958).

temperature. After one hour the reaction mixture was diluted with water and the solid (m. p. 175～195°C) was collected by filtration. Yield, 1 g.

A mixture of 203.7 mg. of the above solid, 2 ml. of benzene, 5 ml. of pyridine and 108.2 mg. of *N*-bromoacetamide was treated in the same way as described above to give 135 mg. of compound VIIIa with m. p. 145～147°C. The melting point was not depressed on admixture with the sample obtained above.

20-*Iso*-23,24-dinorchol-4-en-22-ol-3-one acetate (VIIIb). — The substance was prepared in the usual way from 34 mg. of compound VIIIa. The crude substance showed m. p. 85～91°C, $[\alpha]_D^{22}$ +94 (c, 0.726). No attempt was made to purify it further, because only a few mg. of this substance which is crystallized with difficulty was available.

20-*Iso*-23,24-dinorchol-4-en-22-ol-3-one tosylate (VIIIc).—To 138 mg. of compound VIIIa in 3 ml. of pyridine, 87 mg. of *p*-toluenesulfonyl chloride was added and the mixture was left to stand overnight. Treatment in the usual way gave VIIIc in plates with m. p. 176～178°C (dec.), ν_{max}^{Nujol} 5.99 (C=O), 6.20, 6.26 (C=C), 7.31, 8.51 μ (—O—SO_2—).

Anal. Found: C, 72.35, H, 7.08. Calcd. for $C_{25}H_{36}SO_4$: C, 72.46, H, 7.55%.

Methyl 3-Ethylenedioxy-23,24-dinorchol-5-en-22-oate (IX).—A mixture of 2 g. of compound I[6], 140 ml. of dry benzene, 10 ml. of ethylene glycol and 0.2 g. of *p*-toluenesulfonic acid monohydrate was distilled until 30 ml. of the distillate was azeotropically removed in about 1 hour, and the mixture was refluxed for further 8 hours[27]. After cooling, the mixture was extracted with benzene, and the extract was washed with 10% aqueous potassium carbonate and with water, and dried over anhydrous sodium sulfate. The solvent was evaporated under a reduced pressure, and the crystalline residue was recrystallized from acetone to give 1.4 g. of IX in needles, m. p. 188～189°C, $[\alpha]_D^{20}$ −46 (c, 1.410), ν_{max}^{Nujol} 5.80 (C=O). 7.95 (O=C—O—C), 9.25 μ (ketal)[28].

Anal. Found: C, 74.64, H, 9.86. Calcd for $C_{25}H_{38}O_4$: C, 74.58, H, 9.51%.

3-Ethylenedioxy-23,24-dinorchol-5-en-22-ol (Xa).—A mixture of 748 mg. of ketal ester IX, 170 mg. of lithium aluminum hydride and 20 ml. of anhydrous tetrahydrofuran was treated in the same way as described above (reflux for 4 hours), and recrystallization of the product from methanol gave 610 mg. of Xa in fine needles, m. p. 181～182°C, $[\alpha]_D^{16.5}$ −33 (c, 1.28).

Anal. Found: C, 77.07, H, 9.93. Calcd for $C_{24}H_{38}O_3$: C, 76.96, H, 10.23%.

3-Ethylenedioxy-23,24-dinorchol-5-en-22-ol acetate (Xb). — The substance was prepared in the usual way. Recrystallization from aqueous ethanol gave Xb in long needles, m. p. 122～123°C, $[\alpha]_D^{21.5}$ −32 (c, 1.75).

Anal. Found: C, 74.89, H, 10.00. Calcd. for $C_{26}H_{40}O_4$: C, 74.96, H, 9.68%.

A mixture of 9 mg. of acetate XIb, 3 ml. of methanol and 0.3 ml. of 0.8% (by volume) sulfuric acid was treated in the same way as described above (reflux for 50 min.) to give IVa, m. p. and mixed m. p. 137～138°C.

6β-Bromocholestan-5α-ol-3-one (XII). — A suspension of 1 g. of 3-ethylenedioxy-cholest-5-ene (XI) in 50 ml. of dioxane and 3 ml. of water was mixed with 1 ml. of 60% perchloric acid and 350 mg. of *N*-bromoacetamide, and the mixture was shaken occasionally at room temperature. The whole solid soon went into solution and in a few hours a new solid appeared. After being kept overnight the suspension was diluted with 10 ml. of water and left to stand in a refrigerator for two hours, and the solid was collected, dried, and triturated with hot acetone to give 520 mg. of XII melting at 176～178°C. Recrystallization from acetone raised the melting point to 181～182°C (dec.), which was not depressed on admixture with an authentic sample of XII[29].

Cholest-4-en-6α-ol-3-one (XIV).—To a solution of 59 mg. of bromohydrin XII in 5 ml. of methylene chloride and 10 ml. of methanol, 17 mg. of potassium hydroxide in 8.5 ml. of methanol was added. After being kept at room temperature overnight, the solution was neutralized with acetic acid and concentrated to half the volume under a reduced pressure. Water was added and crystals were collected by filtration to obtain 51 mg. of XIV, m. p. 152～156°C. The melting point was raised to 160～161°C on recrystallization from aqueous ethanol. Identity was established by a mixed[22] melting point determination.

It was shown in a previous paper[22] that sodium bicarbonate hydrolysis of 6β-chlorocholestan-5α-ol-3-one furnished compound XIV in a good yield while sodium bicarbonate hydrolysis of bromohydrin XII in the same manner as described previously furnished compound XIV only in a low yield. When a mixture of bromohydrin XII (0.4 g.) in ethanol (30 ml.) and potassium bicarbonate (0.2 g.) in water (3 ml.) was heated under reflux for 5 hours, 0.35 g. of 5α-cholestane-3,6-dione was obtained, m. p. 169～170°C, $[\alpha]_D^{25}$ +5 (c, 2.50).

Cholest-4-en-3β,6α-diol (XV).—A mixture of 108 mg. of XIV and 50 mg. of lithium aluminum hydride in 3 ml. of tetrahydrofuran was treated in the same manner as described above (reflux for 1 hour). The residue (107 mg.) exhibited m. p. 126～148°C, $[\alpha]_D^{24}$ +47 (c, 1.07). Two recrystallizations from methanol gave 48 mg. of XV in needles, m. p. 178～179°C, $[\alpha]_D^{25}$ +31 (c, 0.388). Reported m. p. 175～178°C, $[\alpha]_D$ +29[30], 176～177°C[17], 178～179°C[31]. Identity was established

27) cf R. Antonucci, S. Bernstein, R. Littel, K. J. Sac and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952).
28) S. Bernstein, R. H. Lenhard and T. B. Williams, ibid., **19**, 41 (1954).
29) S. Mori and F. Mukawa, *Proc. Japan Acad.*, **31**, 31 (1955). cf. D. H. R. Barton and E. Miller, *J. Am. Chem. Soc.*, **72**, 1066 (1950).
30) V. Prelog and E. Tagmann, *Helv. Chim. Acta*, **27**, 1867 (1944).
31) Y. Urushibara, This Bulletin, **16**, 184 (1941).

by a mixed[17] melting point determination.

Cholest-4-ene-3β,6β-diol (XVIII).—5α-Bromocholestan-3β, 6β-diol diacetate[18] (2 g.) in dry pyridine (15 ml.) was heated under reflux for 8 hours. The mixture was diluted with ice-cold water and extracted with ether. The extract was washed with diluted hydrochloric acid and with water, dried over anhydrous sodium sulfate, and evaporated. Recrystallizations (twice) from methanol gave 1.2 g. of cholest-4-ene-3β, 6β-diol diacetate, m. p. 132~135°C.

Hydrolysis of the diacetate (1 g.) in methanol (20 ml.) with potassium hydroxide (0.3 g.) in methanol (3 ml.) at room temperature gave 0.7 g. of diol XVIII, m. p. 255~258°C. Identity was established by a mixed[32] melting point determination.

Cholest-4-en-6β-ol-3-one (XIX).—A solution of 200 mg. of 3β, 6β-diol XVIII in 3 ml. of benzene and 4 ml. of pyridine was treated with 72 mg. (1.05 equiv.) of *N*-bromoacetamide at room temperature for 18 hours. After being treated as usual, the crystalline residue was recrystallized from acetone—*n*-hexane to give 155mg. of XIX in needles, m. p. 185~189°C. The melting point was raised to 190~191°C by recrystallizations (twice) from acetone—*n*-hexane and was not depressed when mixed with an authentic sample of XIX[22].

The identity was further established by conversion into the acetate, m. p. and mixed m. p. 101~102°C, and into 5α-cholestan-3, 6-dione, m. p. and mixed m. p. 170~171°C, on treating with hydrochloric acid in ethanol.

Cholest-4-en-6α-ol-3-one (XIV).—A solution of 157 mg. of 3β, 6α-diol XV in 3 ml. of benzene and 4 ml. of pyridine was treated with 57 mg. of *N*-bromoacetamide at room temperature overnight. After being treated as usual, the crystalline residue was recrystallized from acetone-*n*-hexane to give 121 mg. of XIV in needles, m. p. 150~155°C. The melting point was raised to 160~161°C when recrystallized from aqueous ethanol. Identity was established by a mixed[22] melting point determination.

The identity was further established by conversion into the acetate, m. p. and mixed[33] m. p. 103~104°C, and into 5α-cholestane-3, 6-dione, m. p. and mixed m. p. 170~171°C, on treating with hydrochloric acid in ethanol.

Stigmasta-4, 22-dien-3-ol (XXII).—A mixture of 0.5 g. of stigmasta-4, 22-dien-3-one (XXIII)[24], m. p. 123~125°C, and 0.2 g. of lithium aluminum hydride in 15 ml. of anhydrous tetrahydrofuran was treated in the same manner as described above (reflux for 1.5 hours) to give a mixture, m. p. 134~163°C, $[\alpha]_D^{24}$ +32 (c, 1.57). It is presumed that the mixture consists essentially of stigmasta-4, 22-dien-3β-ol and the corresponding 3α-ol.

Stigmasta-4, 22-dien-3-one (XXIII).—A solution of 200 mg. of the above mixture (XXII) in 3 ml. of benzene and 4 ml. of pyridine was treated with 70 mg. (1.05 equiv.) of *N*-bromoacetamide at room temperature for 2 hours. After being treated as usual, the crystalline residue was recrystallized from acetone to give 162 mg. of XXIII in needles, m. p. 118~122°C. The melting point was raised to 126~127°C by three recrystallizations from acetone and was not depressed when admixed with an authentic sample of XXIII[24].

Ultraviolet and Infrared Absorption Spectra.—They were measured by use of Hitachi Photoelectric Spectrophotometer Model EPU-2 and ŌYŌ-KŌKEN instrument, respectively. Samples for ultraviolet spectra were dissolved in 95% ethanol. Infrared spectra were kindly measured at Institute of Physical and Chemical Research.

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