alumina. From the crystalline benzene–20% chloroform fractions single-spot XXVII was obtained (50 mg.) which on crystallization from acetone–ether gave pure XXVII, m.p. 231–234°.

The mobile fractions from the original chromatogram (40 mg.) were separated by chromatography on Whatman No. 3 filter paper (benzene–cyclohexane 4:1, saturated with formamide, system). From the more polar band (9 mg.) was obtained on crystallization from acetone–ether nearly pure $\Delta^{1,4,14,16}$-tetraene XXXII (see above): m.p. 270–278° dec.; λ_{max} 306 mμ (ε 12,600) and 236 (16,800). Crystallization of material eluted from the more mobil band (17 mg.) from acetone–ether gave **15α-chloro-9α-fluoro-16-methyl-$\Delta^{1,4,16}$-pregnatriene-11β,21-diol-3,20-dione 21-acetate (XXXI)**: sintering at 200°, m.p. 272–275° dec.; λ_{max} 241 mμ (ε 20,800); $\lambda_{max}^{CHCl_3}$ 2.77, 2.90–2.95, 5.74, 6.00, 6.12, 6.18 and 11.16 μ.

9α-Fluoro-Δ^{15}-16-methylprednisolone 21-Acetate (XXVIII).—To a solution of 850 mg. of 16α, 17α-oxide XXVI in 10 ml. of acetic acid at 15° was added 10 ml. of 7% hydrogen chloride in acetic acid. After 15 min. at 15°, water was added and the mixture was extracted with chloroform. The chloroform extract was washed with water, 5% potassium bicarbonate solution, and brine, dried over magnesium sulfate, and concentrated to dryness to give a crystalline residue (850 mg.). Paper chromatography (benzene–chloroform 9:1 saturated with formamide) showed the latter to consist of two components of nearly similar mobility, the more polar XXVII (major) and the less polar XXVIII (minor) which by n.m.r. analysis was 80–85% XXVII and 15–20% XXVIII. The mixture could not be separated by column chromatography on alumina or by partition chromatography on celite. A 400-mg. portion was resolved, however, by preparative paper chromatography (40 mg. per 15 × 45 cm. sheet of Whatman No. 3 paper, benzene–chloroform 9:1, saturated with formamide). The desired Δ^{15}-16-methyl compound (XXVIII, 40 mg.) was obtained as single-spot material from the lower band and on crystallization from acetone–ether gave the analytical sample: m.p. 242–247°; $[\alpha]^{acetone}_D$ +45°; λ_{max} 238 mμ (ε 15,100); λ_{max}^{Nujol} 2.91, 3.05, 5.75, 5.81, 6.01, 6.15, 6.19, and 11.25 μ; n.m.r., τ 8.07 (C-16 $-CH_3$).

Anal. Calcd. for $C_{24}H_{29}FO_6$: C, 66.65; H, 6.76. Found: C, 66.72; H, 7.08.

From the upper band, 300 mg. of mixed fractions was recovered.

When 100 mg. of the 16α,17α-oxide XXVI in 3 ml. of acetone was treated with 1 ml. of concentrated hydrochloric acid at 0° for 1.5 hr., the product was a ~1:1 mixture of XXVII and XXVIII (n.m.r. and paper chromatography).

When 100 mg. of the 16α,17α-oxide XXVI was refluxed in 6 ml. of benzene and 7 mg. of *p*-toluenesulfonic acid for 1 hr., the product contained a ~5:1 mixture of XXVII and XXVIII.

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The Reaction of Various Steroid α-Bromo Ketones with Dimethyl Sulfoxide[1]

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The reaction of methyl 4β-bromo-3-keto-5β-cholanate with dimethyl sulfoxide gave methyl 3,4-diketo-5β-cholanate and methyl-3-ketochol-4-enate, while the corresponding acid gave 3-ketochol-4-enic acid and 3-keto-5β-chol-1-enic acid. Similarly, 5-bromo-5α-cholestan-3β-ol-6-one acetate gave cholest-4-en-3β-ol-6-one acetate; 6β-bromo-5α-cholestan-3β-ol-7-one acetate gave cholest-5-en-3β-ol-7-one acetate and cholesta-3,5-dien-7-one; and 7α-bromo-5α-cholestan-3β-ol-6-one acetate gave cholest-5-ene-3β,6-diol-7-one 3-acetate.

In an accompanying paper[3] the reaction of 2α-bromo-5α-cholestan-3-one with dimethyl sulfoxide is described. The reaction gave a complex mixture of products, including the expected 3-hydroxy-5α-cholest-3-en-2-one and 5α-cholest-1-en-3-one, and was of little synthetic utility. In this paper reactions of other steroid α-bromo ketones (Chart I) are described which proceeded in a more straightforward manner and are of synthetic utility.

The first compound studied was methyl 4β-bromo-3-keto-5β-cholanate (Ia), which has the bromine atom in the equatorial conformation and an adjacent 5-axial hydrogen atom. When this compound was heated in dimethyl sulfoxide at 125–130°, starting material was recovered (32%) and methyl 3,4-diketo-5β-cholanate (II, 25%) and methyl 3-ketochol-4-enate (IIIa, 28%) were formed (the latter two yields are based on recovered starting material). The diketone gave a positive enol test with ferric chloride and therefore probably exists as a diosphenol, but no attempt was made to determine which isomer was present. It also gave a typical diosphenol ultraviolet absorption spectrum (λ_{max} 271 mμ). Although this bromo ketone had the same stereochemistry as 2α-bromo-5α-cholestan-3-one (bromine atom equatorial, hydrogen atom axial), its reaction with dimethyl sulfoxide was much less complex and the products were readily separable by column chromatography, thus providing a useful route to the previously unreported diosphenol.

When 4β-bromo-3-keto-5β-cholanic acid (Ib), instead of the methyl ester (Ia), was heated in dimethyl sulfoxide at 125–130° with sodium bicarbonate, the reaction, surprisingly and anomalously, resulted in elimination products only. Two olefins were formed, 3-ketochol-4-enic acid (IIIb, 80%) and what appeared to be 3-keto-5β-chol-1-enic acid (IV, 20%) (these yields are crude estimates from the ultraviolet spectrum), and no evidence could be obtained for the presence of any diosphenol. A possible explanation for this result is that the cholanic acid was present in the reaction mixture as the anion, owing to reaction with sodium bicarbonate. Thus, this anion, a stronger base than dimethyl sulfoxide or bicarbonate ion, was present to promote elimination at a more rapid rate than it took place with the methyl ester, where no base of comparable strength was present.

The next bromo ketone studied was 5-bromo-5α-cholestan-3β-ol-6-one acetate (VI). This compound

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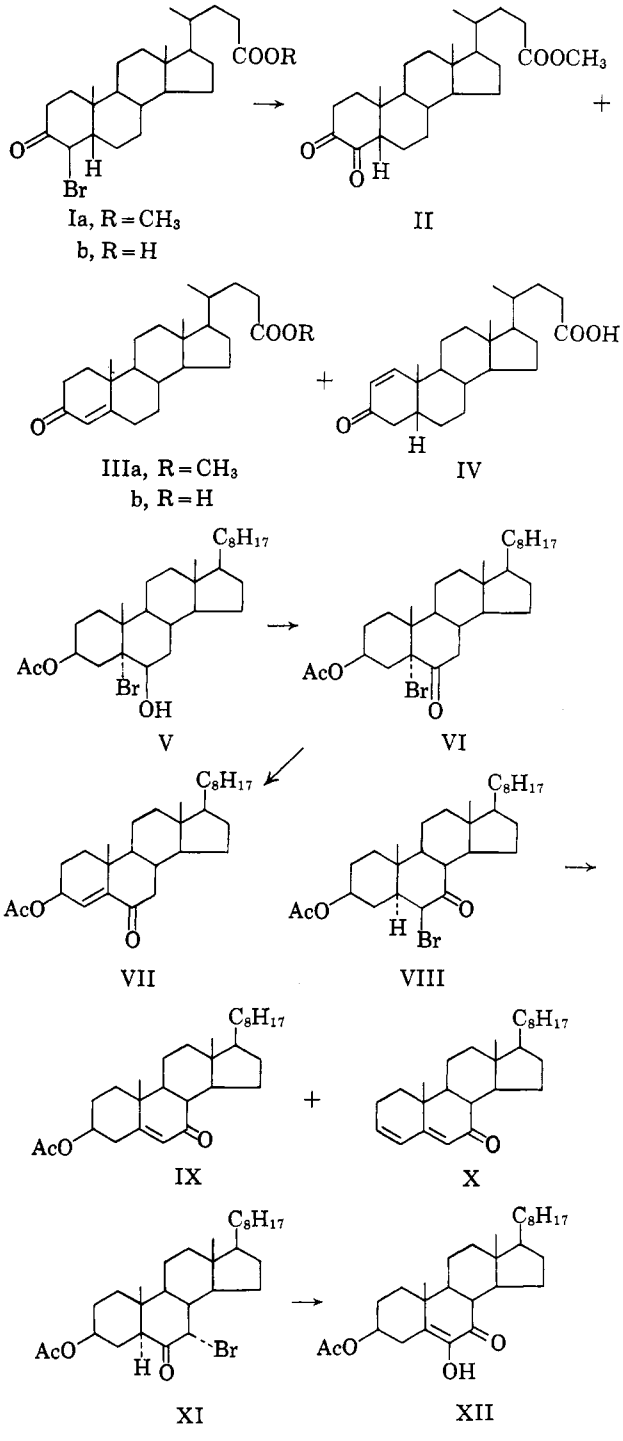
(2) The major portion of this work is abstracted from the Ph.D. Thesis of R. N. I., Brown University, 1963. Brown University Fellow, 1959–1961. Holder of the Shell Oil Co. Fundamental Research Grant in Chemistry, 1961–1962.

(3) H. R. Nace and R. N. Iacona, *J. Org. Chem.*, **29**, 3498 (1964).

CHART I

REACTION OF VARIOUS α-BROMO KETONES WITH DIMETHYL SULFOXIDE



was prepared by Jones oxidation of 5-bromo-5α-cholestane-3β,6β-diol 3-acetate (V), which in turn was prepared in 98% yield (crude) by application of the method used by Grenville, *et al.*,[4] for the preparation of bromohydrins in the androst-5-ene series. This bromo ketone VI, in contrast to the previous ones, possesses an axial bromine atom and an axial hydrogen atom at C-4. When it was heated in dimethyl sulfoxide at 125–130° with sodium bicarbonate, a single product, cholest-4-en-3β-ol-6-one 3-acetate (VII) was formed in 70% yield. Because the bromine atom is on a tertiary carbon atom, no oxidation to a diosphenol is possible and elimination is the only reaction to be expected.

The next compound studied, 6β-bromo-5α-cholestan-3β-ol-7-one 3-acetate (VIII), also has the bromine atom axial and an adjacent axial hydrogen atom, but in this case oxidation to a diosphenol is possible. When this bromo ketone was heated in dimethyl sulfoxide at 125–130° with sodium bicarbonate, two products were obtained, cholest-5-en-3β-ol-7-one 3-acetate (IX, 73%) and cholesta-3,5-dien-7-one (X, 12%), and no evidence for the presence of a diosphenol could be obtained. Thus again elimination was the only reaction to take place.

The last compound studied was 7α-bromo-5α-cholestan-3β-ol-6-one 3-acetate (XI) which also has an axial bromine atom and an adjacent axial hydrogen atom. After heating this compound in dimethyl sulfoxide at 125–130° with sodium bicarbonate (a nitrogen atmosphere was necessary to prevent decomposition), the only product which could be isolated was cholest-5-ene-3β,6-diol-7-one 3-acetate (XII) in 55% yield. In this case only oxidation occurred, which is not surprising in view of the fact that 7-enes are well known to be extremely difficult to form. The yield of diosphenol obtained by this method is considerably higher than the one obtained by treating the bromo ketone with silver nitrate in pyridine[5] and thus makes this compound relatively accessible for the first time.

Several observations on the mechanism of reaction of α-halo ketones with dimethyl sulfoxide can be made on the basis of the data reported here. Thus, it appears that when the halogen atom and adjacent hydrogen atom have a *trans* equatorial–axial relationship [2α-bromo-5α-cholestan-3-one[3] and methyl 4β-bromo-3-keto-5β-cholanate (Ia)] elimination to form the α,β-unsaturated ketone is relatively difficult, and oxidation to the diosphenol becomes an important competing reaction. Conversely, when the halogen atom and adjacent hydrogen atom have a *trans* diaxial relationship, elimination is the predominant reaction, unless other factors intervene, as in the case of 7α-bromo-5α-cholestan-3β-ol-6-one acetate (XI).

If, as postulated in the accompanying paper,[3] the diosphenol is formed by displacement of the halogen by dimethyl sulfoxide to give a sulfoxonium intermediate, the elimination reactions must be proceeding by a different pathway. This appears to be necessary because the sulfoxonium intermediate, if formed by nucleophilic displacement with inversion, has a changed conformational relationship of the hydrogen atom and the halogen atom. As a consequence, where a favorable configuration for elimination originally existed, a less favorable one is formed. In fact, however, in the cases studied elimination is the predominant reaction (VI and VIII). It is hoped that the mechanism studies now in progress will shed further light on this question.

Experimental[6]

Reaction of Methyl 4β-Bromo-3-keto-5β-cholanate (Ia) with Dimethyl Sulfoxide.—A mixture of 720 mg. (1.54 mmoles) of

(4) V. Grenville, D. K. Patel, V. Petrow, I. A. Stuart-Webb, and D. M. Williamson, *J. Chem. Soc.*, 4105 (1957).

(5) I. M. Heilbron, E. R. H. Jones, and F. S. Spring, *ibid.*, 334 (1938).

(6) The experimental details and procedures are the same as those given in the accompanying paper,[3] except that 3:1 benzene–ether containing 1% of acetic acid was used for thin layer chromatography of the bile acid derivatives and their methyl esters.

the bromo ester Ia, 720 mg. (8.55 mmoles) of sodium bicarbonate, and 15 ml. of dimethyl sulfoxide was stirred and heated at 125–130° for 75 min., and then was cooled to room temperature, diluted with 250 ml. of cold, saturated brine (the odor of dimethyl sulfide was apparent), and extracted with three 30-ml. portions of ether. The extract was washed with ten 25-ml. portions of water, dried over anhydrous magnesium sulfate, and evaporated to dryness to give 560 mg. of a pale yellow solid. T.l.c. of this gave three spots, R_f 0.70, 0.57, and 0.41. The solid was dissolved in 10 ml. of 1:10 benzene–petroleum ether (b.p. 30–60°) and chromatographed on a column (25 mm. in diameter) of 50 g. of silica gel. Elution with 175 ml. of 1.5% ether in benzene solvent gave 230 mg. of a colorless oil which was recrystallized from methanol and had m.p. 104–104.5°, $[\alpha]_D$ +50°; lit.[7] m.p. 99–100°, $[\alpha]_D$ +54.6° (dioxane). This represents a 32% recovery of starting material.

Elution with 200 ml. of 2% ether in benzene and 200 ml. of 2.5% ether in benzene gave 110 mg. (25%) of methyl 3,4-diketo-5β-cholanate (II), which was recrystallized from aqueous methanol: m.p. 109.5–112.5°; λ_{max}^{KBr} 2.93, 5.75, and 6.00 μ; λ_{max}^{EtOH} 271 mμ (ε 6850); deep violet color with ferric chloride. Three more recrystallizations from aqueous methanol and drying at 55° (5 mm.) for 3 hr. gave an analytical sample, m.p. 112–114°, $[\alpha]_D$ +25°.

Anal. Calcd. for $C_{25}H_{38}O_4$: C, 74.58; H, 9.51. Found: C, 74.73; H, 9.64.

Finally, elution with 300 ml. of 4% ether in benzene gave 115 mg. (28%) of methyl 3-ketochol-4-enate (IIIa): λ_{max}^{KBr} 5.76, 5.98, and 6.20 μ, spectrum identical with that of authentic material. Recrystallization from aqueous methanol gave needles: m.p. 127–128° (no depression on admixture with authentic material); $[\alpha]_D$ +82°; λ_{max}^{EtOH} 241 mμ (ε 14,800); lit.[8] m.p. 126–127°; $[\alpha]_D$ +87° ($CHCl_3$); $\lambda_{max}^{CHCl_3}$ 5.77, 6.01, 6.19, and 11.55 μ; λ_{max}^{MeOH} 241 mμ (ε 16,800).

Reaction of 4β-Bromo-3-keto-5β-cholanic Acid (Ib) with Dimethyl Sulfoxide.—A mixture of 250 mg. (0.55 mmole) of 4β-bromo-3-keto-5β-cholanic acid, 250 mg. (2.98 mmoles) of sodium bicarbonate, and 5 ml. of dimethyl sulfoxide was stirred and heated at 125–130° for 30 min. The odor of dimethyl sulfide was evident; a yellow color developed and grew darker as the heating was continued. The reaction mixture was then cooled to room temperature, diluted with 200 ml. of cold, saturated brine containing 20 ml. of dilute hydrochloric acid, and extracted with three 20-ml. portions of ether. The extract was washed with saturated brine and with water, dried over anhydrous magnesium sulfate, and evaporated to give 205 mg. of an orange, bromine-free solid which had λ_{max}^{KBr} 2.90–3.30, 5.76, and 5.98 μ; λ_{max}^{EtOH} 242 mμ (absorbance = 0.46) for a sample obtained by 1:25 dilution of a stock solution containing 15 mg. of crude product in 25 ml. of ethanol. T.l.c. gave two spots, R_f 0.43 and 0.35, attributed to 3-ketochol-4-enic acid (IIIb) and 3-keto-5β-chol-1-enic acid (IV), respectively (see below). From the ultraviolet absorption data the yield of the two compounds was estimated as 80 and 20%, respectively. The value of ε 9000 for the methyl ester of IV[8] was used for this crude estimate.

A 190-mg. sample of the crude product in 8 ml. of 1:1 petroleum ether–benzene was chromatographed on a column (15 mm. in diameter) of 25 g. of silica gel. Elution with 150 ml. of 15% ether in benzene gave 25 mg. of a clear oil which by t.l.c. showed two spots, R_f 0.43 (strong) and 0.35 (faint). Crystallization from aqueous acetic acid gave white crystals of what appeared to be 3-keto-5β-chol-1-enic acid (IV): m.p. 120–135°; λ_{max}^{KBr} 2.90–3.30, 5.76, 5.98, and 12.80 μ (the latter is characteristic of 3-keto-1-enes)[9]; λ_{max}^{EtOH} 237 mμ. There was insufficient material for purification and positive identification. Continued elution with the same solvent gave 120 mg. of 3-ketochol-4-enic acid (IIIb, R_f 0.35, strong), contaminated by the 1-ene (R_f 0.43, weak). Recrystallization from aqueous acetic acid gave white crystals: m.p. 158–168°; λ_{max}^{KBr} 2.90–3.30, 5.75, 5.98, 6.20, and 11.50 μ (the latter is characteristic of 3-keto-4-enes[9]); λ_{max}^{EtOH} 242 mμ. The infrared spectrum was almost identical with that of authentic 3-ketochol-4-enic acid, prepared as described below.

3-Ketochol-4-enic Acid (IIIb).—A sample of 4β-bromo-3-keto-5β-cholanic acid was converted to the 2,4-dinitrophenylhydrazone of 3-ketochol-4-enic acid by the method of Djerassi[10] and was hydrolyzed, without characterization, to 3-ketochol-4-enic acid by the method of DeMaecker and Martin.[11] After several recrystallizations from aqueous acetic acid the acid had m.p. 185–187.5°; λ_{max}^{KBr} 2.95–3.35, 5.80, 6.10, and 6.24 μ; λ_{max}^{EtOH} 242 mμ (ε 15,400); R_f 0.35; lit. m.p. 178°[12] and 185–186°.[13]

5-Bromo-5α-cholestane-3β,6β-diol 3-Acetate (V).—This compound was prepared by the method used by Grenville, *et. al.*,[14] for the preparation of bromohydrins in the androst-5-ene series. To a solution of 5.0 g. (11.7 mmoles) of 3β-acetoxycholest-5-ene in 60 ml. of dioxane was added 10 ml. of an aqueous solution containing 1.62 g. (11.7 mmoles) of N-bromoacetamide and 0.58 ml. of 70% perchloric acid. The mixture was stirred at room temperature for 2.25 hr., then diluted with 500 ml. of saturated brine and extracted with three 50-ml. portions of ether. The ether extract was washed successively with 50-ml. portions of 10% sodium iodide solution, 10% sodium thiosulfate solution, 5% sodium carbonate solution, and water, and then was dried over anhydrous sodium sulfate and evaporated to give 6 g. (98%) of the crude bromohydrin V. After several recrystallizations from petroleum ether (b.p. 60–70°) it had m.p. 179–182°, $[\alpha]_D$ −38°, λ_{max}^{KBr} 2.90 and 5.86 μ; lit.[15] m.p. 177–179°, $[\alpha]_D$ −37°.

Reaction of 5-Bromo-5α-cholestan-3β-ol-6-one 3-Acetate (VI) with Dimethyl Sulfoxide.—A mixture of 1.50 g. (2.88 mmoles) of the bromo ketone (prepared by Jones oxidation of the bromohydrin V, or by bromination of 5α-cholestan-3β-ol-6-one 3-acetate[16]), 1.50 g. (17.9 mmoles) of sodium bicarbonate, and 15 ml. of dimethyl sulfoxide was heated at 125–130° for 1.5 hr. Carbon dioxide was evolved and a yellow color developed which darkened as the reaction proceeded. The mixture was cooled to room temperature, diluted with 250 ml. of saturated brine, and extracted with five 40-ml. portions of ether. The extract was dried over anhydrous sodium sulfate and evaporated to give 1.30 g. of bromine-free solid. This was dissolved in 5 ml. of 5:1 petroleum ether–benzene and chromatographed on a column (20 mm. in diameter) of 20 g. of silica gel. Elution with petroleum ether gave 340 mg. of a dark red oil which was not investigated. Elution with 1:1 benzene–ether gave 890 mg. (70%) of cholest-4-en-3β-ol-6-one 3-acetate (VII) as a pale yellow solid. Two recrystallizations from methanol (charcoal) gave white scales: m.p. 108–109.5°, $[\alpha]_D$ −61°, λ_{max}^{EtOH} 236 mμ (ε 6800), R_f 0.62, mixture melting point 107.5–109.5° with an authentic sample, infrared spectra identical (chromatography of the crude material on alumina resulted in extensive decomposition of the product); lit.[16] m.p. 110°, $[\alpha]_D$ −50.5°, λ_{max}^{EtOH} 236 mμ (ε 6300).

Reaction of 6β-Bromo-5α-cholestan-3β-ol-7-one 3-Acetate (VIII) with Dimethyl Sulfoxide.—A mixture of 300 mg. (0.57 mmole) of the bromo ketone VIII, 300 mg. of sodium bicarbonate, and 10 ml. of dimethyl sulfoxide was stirred and heated at 125–130° for 30 min. No odor of dimethyl sulfide was apparent and no color developed; however, carbon dioxide was evolved. The mixture was cooled to room temperature, diluted with 250 ml. of cold saturated brine, and extracted with three 25-ml. portions of ether. The extract was washed with five 25-ml. portions of water, dried over anhydrous magnesium sulfate, and evaporated to give 260 mg. of a white, bromine-free solid which gave a negative test for diosphenols with alcoholic ferric chloride. The solid had λ_{max}^{KBr} 5.78, 5.98, and 6.10 μ, nearly identical with the spectrum of cholest-5-en-3β-ol-7-one 3-acetate. However, the ultraviolet spectrum showed λ_{max}^{EtOH} 235 (absorbance = 0.47) and 278 mμ (absorbance = 0.20) for a sample obtained by 1:25 dilution of a stock solution containing 15.5 mg. in 25 ml. of ethanol. T.l.c. showed two components, R_f 0.53 (intense) and 0.67 (faint). By comparison with authentic samples these were attributed to cholest-5-en-3β-ol-7-one 3-acetate and cholesta-3,5-dien-7-one. From the ultraviolet absorption data the yields of the two compounds were estimated to be 73 and 12%, respectively.

A sample of the crude material was chromatographed on silica gel and elution with 5% ether in benzene gave cholest-5-en-3β-ol-7-one 3-acetate (IX), which had m.p. 153–154° after recrystal-

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(12) E. Dane, Y. Wang, and W. Schulte, Z. *Physiol. Chem.*, **245**, 80 (1936).

(13) R. Shoenhiemer and F. Berliner, *J. Biol. Chem.*, **115**, 9 (1936).

(14) V. Grenville, D. K. Patel, V. Petrow, I. A. Stuart-Webb, and D. M. Williamson, *J. Chem. Soc.*, 4105 (1957).

(15) D. R. James and C. W. Shoppee, *ibid.*, 4224 (1954).

(16) I. M. Heilbron, E. R. H. Jones, and F. S. Spring, *ibid.*, 801 (1937).

lization from methanol; mixture melting point was undepressed with an authentic sample; infrared spectra were superimposable.

An authentic sample of cholesta-3,5-dien-7-one was obtained from the cholest-5-en-3β-ol-7-one 3-acetate in the manner described by Turner, Meador, and Winkler[17] and had m.p. 112–113°, λ_{max}^{EtOH} 278 mμ (ε 22,400), and R_f 0.66.

Reaction of 7α-Bromo-5α-cholestan-3β-ol-6-one 3-Acetate (XI) with Dimethyl Sulfoxide.—A stream of nitrogen was bubbled for several minutes through a mixture of 500 mg. (0.95 mmole) of the bromo ketone XI, 500 mg. (5.95 mmoles) of sodium bicarbonate, and 10 ml. of dimethyl sulfoxide, and then the mixture was stirred and heated at 125–130° under 1 atm. of nitrogen for 1 hr. The odor of dimethyl sulfide was evident and a yellow color developed. The mixture was then cooled to room temperature, diluted with 250 ml. of cold saturated brine, and extracted with three 25-ml. portions of ether. The extract was washed with ten 20-ml. portions of water, dried over anhydrous magnesium sulfate, and evaporated to give 400 mg. of a bromine-free, yellow, crystalline residue which gave a deep violet-red color with alcoholic ferric chloride. When the reaction was not carried out under a nitrogen atmosphere, a bromine-containing, dark-red intractible oil was obtained as the only product.

(17) R. B. Turner, W. R. Meador, and R. E. Winkler, *J. Am. Chem. Soc.*, **79**, 4122 (1957).

The yellow residue had λ_{max}^{KBr} 2.92, 5.76, 5.98, 6.07, and 8.10 μ, similar to the spectrum of 5α-cholestan-3β-ol-6,7-dione 3-acetate (XII). The ultraviolet spectrum had λ_{max}^{EtOH} 275 mμ (absorbance = 0.69) with a shoulder at 310 mμ (absorbance = 0.13) for a sample obtained by 7:100 dilution of a stock solution containing 18.7 mg. in 25 ml. of ethanol. It was estimated from the absorbance at 275 mμ that the mixture contained 60 ± 5% of the diosphenol XII, corresponding to a yield of about 55%. T.l.c. showed a spot, R_f 0.60, attributed to the diosphenol by comparison with an authentic sample, and spots, R_f 0.65, 0.54, and 0.47, which were not identified.

A 200-mg. sample of the mixture was chromatographed on a column (15 mm. in diameter) of 15 g. of silica gel and elution with 400 ml. of benzene gave 80 mg. of a white solid: λ_{max}^{KBr} 2.92, 5.76, 5.98, 6.08, and 8.10 μ (identical with the spectrum of authentic diosphenol XII); λ_{max}^{EtOH} 273 mμ (ε 7000); R_f 0.61. The material gave a deep violet-red color with alcoholic ferric chloride. Recrystallization from methanol gave white crystals, m.p. 155–157°, undepressed on admixture with authentic material, lit.[5] m.p. 156–157°, λ_{max}^{EtOH} 274 mμ (ε 10,800).

Further elution of the column with more polar solvents gave 60 mg. of a yellow, intractible oil, which by t.l.c. gave three spots, R_f 0.65, 0.53, and 0.46. The oil was not investigated further.

The Reaction of 2α-Bromo-5α-cholestan-3-one with Dimethyl Sulfoxide

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The reaction of 2α-bromo-5α-cholestan-3-one with dimethyl sulfoxide has been shown to give 3-hydroxy-5α-cholest-3-en-2-one, 2,3-seco-5α-cholestane-2,3-dioic acid, 5α-cholestan-3-one, 5α-cholest-1-en-3-one, cholest-4-en-3-one, 2α-hydroxy-5α-cholestan-3-one, dimethyl sulfide, and other, unidentified products. The reaction of 2,2-dibromo-5α-cholestan-3-one with dimethyl sulfoxide gave 2-bromo-5α-cholest-1-en-3-one. The reaction of 2α-bromo-5α-cholestan-3-one with collidine and with lithium chloride in dimethylformamide was reinvestigated.

In recent years a number of reactions have been discovered in which dimethyl sulfoxide, commonly used as a solvent, behaved in an unusual manner as one of the reactants. Among the first of these reactions to be discovered was the conversion of α-bromo ketones to the corresponding α-diketones.[2] It was also found that secondary halides and sulfonate esters of secondary alcohols could be converted to olefins in high yield by dimethyl sulfoxide.[3] The third reaction of interest here is the conversion of primary alkyl halides and sulfonate esters of primary alcohols to the corresponding aldehydes.[4]

It is important to note the distinction between the behavior of the primary and the secondary alkyl derivatives in these reactions, the former reacting to give oxidation products, the corresponding aldehyde, and the latter reacting to give elimination products, olefins, Also of interest is the behavior of the α-halo ketones, which, while secondary halides, were of the type aryl–CO–CHBr–aryl or aryl–CO–CH_2Br where an elimination reaction would be impossible. These compounds also gave oxidation products. The question then arises as to whether α-halo ketones, structurally constituted so as to allow elimination, will give diketones or unsaturated ketones, or both, when allowed to react with dimethyl sulfoxide.

Steroid halo ketones were chosen for a study of this reaction because they were readily available, the conformation of the halogen atom was known, and, in most cases, the expected products were well-characterized compounds. In addition it was hoped that the study would result in the development of good synthetic routes to either α,β-unsaturated ketones or α-diketones in the steroid series.

The first compound chosen for study was 2α-bromo-5α-cholestan-3-one (I). Since this compound contains an equatorial bromine atom and undergoes elimination with difficulty,[5] it was anticipated that the major product would be the diketone, in the form of its diosphenol, 3-hydroxy-5α-cholest-3-en-2-one (II). Infact, when the bromo ketone was heated with dimethyl sulfoxide at 125–130° a complex mixture of products was obtained (Chart I). Sodium bicarbonate was used as an acid acceptor, since it is known that hydrogen bromide reacts with dimethyl sulfoxide to produce

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