944. *Calciferol and its Relatives. Part VII.*[1] *An Alternative Route from Cholesterol to Des-AB-cholestane Derivatives.*

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A method of degrading the 3-methyl ether of Westphalen's diol to 9β-hydroxy-des-AB-cholestan-8α-carboxylic acid is described.

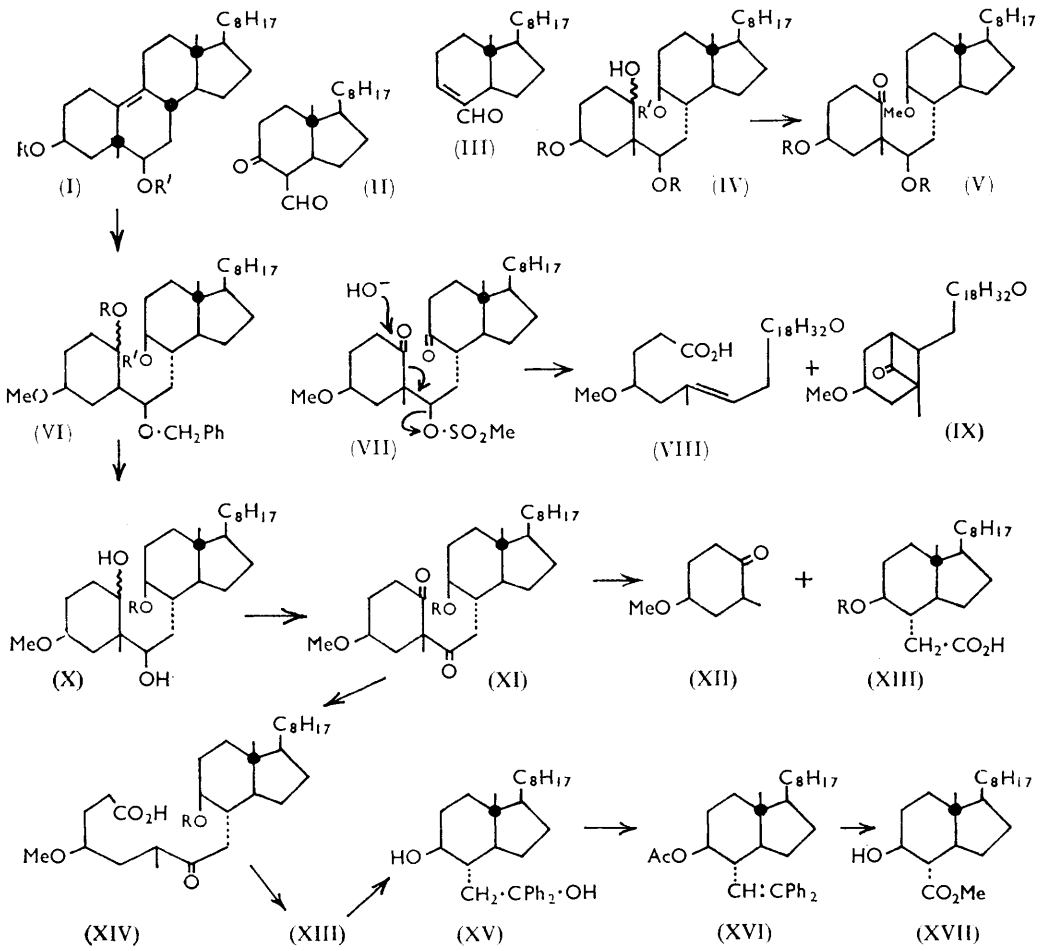
In parallel with the work described in the preceding Paper,[1] studies on an alternative route from cholesterol to des-AB-cholestane derivatives were put in hand. The double bond in Westphalen's diol (I; R = R′ = H) has been shown [2] to join positions 9 and 10, whilst the presence of an oxygen function at position 6 appears to offer opportunities for cleaving the molecule at the 6,7- or 5,6-positions. Thus, rapid access to the β-keto-aldehyde (II), and thence to the unsaturated aldehyde (III), seemed possible. We first attempted to achieve these aims by elimination reactions using suitable derivatives of the methyl ether [3] (I; R = Me, R′ = H), but could obtain no homogeneous 6,9-diene. The 6-keto compound obtained [3] by oxidising the methyl ether (I; R = Me, R′ = H) was then used in attempts to introduce a second oxygen function at position 7, but these attempts too were unsuccessful. Ultimately a method of removing ring A from the methyl ether (I; R = Me, R′ = Ac) was found which, although considerably less direct than we had hoped, gave access to the hydroxy-ester [1] (XVII). The experiments by which this was effected are described in the present Paper.

The first step in the degradation was the cleavage of the double bond; it was studied using the readily available diacetate (I; R = R′ = Ac). Ozonolysis gave a syrupy seco-diketone in which one of the two keto groups (that at position 10) was, due to steric hindrance, considerably less reactive than the other; thus the compound formed a mono-semicarbazone. Reduction of the diketone with sodium borohydride gave a crystalline diol (IV; R = Ac, R′ = H); the β-configuration is assigned to the hydroxyl group at position 9 in this compound on the basis of experiments described below. The hindered nature [4] of the hydroxyl group at position 10 was shown by mild acetylation of the diol (IV; R = Ac, R′ = H), which appeared to introduce only one further acetate group; similarly, reaction with methyl iodide and silver oxide gave a syrupy monomethyl ether (IV; R = Ac, R′ = Me), hydrolysis of which with alkali provided the crystalline triol (IV; R = H, R′ = Me). Reaction with *p*-nitrobenzoyl chloride in pyridine converted

[1] Part VI, Davidson, Günther, Waddington-Feather, and Lythgoe, preceding Paper.
[2] Bladon, Henbest, and Wood, *J.*, 1952, 2737; Ellis and Petrow, *J.*, 1952, 2246.
[3] Davis and Petrow, *J.*, 1951, 2211.
[4] The C(5) hydroxyl group in 5,6-secocholestan-3β,5,6-triol is similarly hindered: Lettré and Jahn, *Annalen*, 1957, **608**, 43.

this into the di-*p*-nitrobenzoate (IV; R = CO·C_6H_4·NO_2, R′ = Me), which was oxidised with chromic oxide to the ketone (V; R = CO·C_6H_4·NO_2). We expected that the alkaline hydrolysis of this compound might be accompanied by retroaldolisation; this would have been of interest as a possible means of detaching ring A. However, none occurred, and the diol (V; R = H) was obtained from the reaction in good yield.

Operations with the diol (IV; R = Ac, R′ = H) were made difficult by the inconveniently large number of reactive oxygen functions, so we investigated the ozonolysis of the monomethyl ether (I; R = Me, R′ = Ac). The resulting seco-diketone, and also the diol obtained by reducing it, were non-crystalline, but the monomethyl monobenzyl ether (I; R = Me, R′ = CH_2Ph) gave a crystalline diol (VI; R = R′ = H). As seen below, one of the hydroxyl groups in this diol was, as expected, relatively unreactive, but by using as the reagent acetic anhydride containing toluene-*p*-sulphonic acid a syrupy diacetate (VI; R = R′ = Ac) was obtained. The benzyl group was removed from it by hydrogenation with palladium, giving the 6-hydroxy compound. This was used as the starting material in experiments designed to introduce, by elimination reactions, a



6,7-double bond. It was also used in attempts to prepare the 6-keto-compound and to introduce into it an oxygen function at position 7. These attempts provided no well-defined products, and we gave up the plan of cleaving the molecule at the 6,7-position in favour of a cleavage between positions 5 and 6.

With this aim, the 3-methyl ether 6-methanesulphonate (I; R = Me, R′ = SO_2Me) was ozonised to obtain the crude seco-diketone (VII). It seemed possible that this might react with sodium hydroxide (as shown by the arrows) to give the olefin (VIII). Some acidic material was indeed formed in the reaction, but the major product was a crystalline diketone which showed $\nu_{max.}$ 1705 and 1767 $cm.^{-1}$. It was therefore assigned [5] the cyclobutanone structure (IX). Similar decompositions of simple 2-hydroxyalkyl-2-methylcyclohexanone toluene-*p*-sulphonates to give cyclobutanone derivatives have recently [6] been recorded.

Methylation with methyl iodide and silver oxide converted the benzyl ether (VI; R = R′ = H) into the ether (VI; R = H, R′ = Me). After catalytic hydrogenolysis of the benzyl group the resulting 6,10-diol (X; R = Me) was oxidised to the β-diketone (XI; R = Me). In theory, this might react with alkali in two ways; cleavage of the 5,6-link would give the ketone (XII) and the acid (XIII; R = Me), whilst cleavage of the 5,10-link would give the keto-acid (XIV; R = Me). Reaction with aqueous alcoholic potassium hydroxide gave, in fact, a mixture of acidic and neutral substances. This, and the neutralisation equivalent of the acidic material, which was intermediate between the values expected for the acids (XIII; R = Me) and (XIV; R = Me), suggested that both modes of cleavage were taking place side by side. The occurrence of the first mode was proved by the isolation of 4-methoxy-2-methylcyclohexanone from the neutral material, and later the acid (XIII; R = Me) was prepared from the acidic fraction.

This method of removing ring A was then modified by using the ester (X; R = CO_2Et) in place of the methyl ether (X; R = Me). The diol (VI; R = R′ = H) reacted with ethyl chloroformate [7] in pyridine giving the ester (VI; R = H, R′ = CO_2Et). Removal of the benzyl group gave the crystalline diol (X; R = CO_2Et), oxidation of which provided the β-diketone (XI; R = CO_2Et). This was subjected to alkaline cleavage, and the resulting acidic material was separated by means of Girard's reagent T into ketonic and non-ketonic fractions. From the latter 9β-hydroxy-des-AB-cholestane-8α-acetic acid (XIII; R = H) was isolated, first as the methyl ester *p*-nitrobenzoate, and later, after hydrolysis, as the free hydroxy-acid. The ketonic acidic material appeared to consist mainly of the acid (XIV; R = H). Its methyl ester was acetylated and then subjected to Baeyer-Villiger oxidation with trifluoroperacetic [8] acid. Hydrolysis then provided a further small amount of the acid (XIII; R = H).

Barbier-Wieland degradation of the latter acid gave successively the diphenylcarbinol (XV), the diphenylethylene (XVI), and the methyl ester (XVII) of 9β-hydroxy-des-AB-cholestan-8α-carboxylic acid. The conversion of this ester into the αβ-unsaturated aldehyde (III) has already been described.[1]

From the standpoint of preparative convenience, the present route to the ester (XVII) is inferior to that [1] which used 7-oxocholesteryl acetate as the starting material. We think it likely that some improvement could be made by degrading the acid (XIV; R = H) directly to the ester (XVII) instead of to the homologous acid (XIII; R = H), but we have not investigated this, because the route to the ester (XVII) described in the preceding paper removed the need to do so. It is of interest that the present work provides conclusive proof of the structure now accepted [2] for Westphalen's diol.

Experimental

Ozonolysis of the Diacetate (I; R = R′ = Ac) *of Westphalen's Diol.*—Ozonised oxygen (*ca.* 5% w/w) was passed into a solution of the diacetate (I; R = R′ = Ac) (5 g.) in light petroleum (b. p. 60—80°) at −70° until the solution became blue. After the solution had

[5] Gell, Ph.D. Thesis, Leeds, 1958.
[6] Wenkert and Strike, *J. Org. Chem.*, 1962, **27**, 1883; Nerdel, Frank, and Marschall, *Angew. Chem. Int. Ed.*, 1962, **1**, 457.
[7] Fieser, Herz, Kloho, Romero, and Utne, *J. Amer. Chem. Soc.*, 1952, **74**, 3309.
[8] Emmons and Lucas, *J. Amer. Chem. Soc.*, 1955, **77**, 2287.

warmed to room temperature the solvent was removed under reduced pressure, glacial acetic acid (50 c.c.) was added, and the solution was shaken with zinc dust (5 g.) for 45 min.; tests then showed the absence of peroxides. The mixture was diluted with ether (200 c.c.), filtered, and the filtrate washed with water, sodium hydrogen carbonate solution, and water, and then dried and evaporated to a colourless syrup (5·2 g.) which showed $\nu_{max.}$ (in $CHCl_3$) 1730 and 1710 $cm.^{-1}$. When a portion (500 mg.) of this ketone was warmed with aqueous ethanolic semicarbazide acetate (from 1 g. semicarbazide hydrochloride), the diketone *monosemicarbazone* (500 mg.) was obtained. It formed needles (from ethanol) m. p. 128—130°, $[\alpha]_D^{20}$ −53° (*c* 2·0 in $CHCl_3$) (Found: C, 67·0; H, 9·65; N, 6·95. $C_{32}H_{53}N_3O_6$ requires C, 66·75; H, 9·3; N, 7·3%).

The Diol (IV; R = Ac, R′ = H).—The above diketone (5 g.) in methanol (50 c.c.) was cooled to −10° and methanolic sodium borohydride added with stirring so as to keep the temperature below 5°. After standing for a further 8 min. at 3° the solution was acidified with acetic acid and poured into water (300 c.c.) with stirring. The crystalline precipitate was collected, washed with water, combined with material from three similar reductions, and recrystallised from dilute ethanol. The *diol* (9·9 g.) formed needles, m. p. 177—178°, $[\alpha]_D^{16}$ +26° (*c* 1·0 in $CHCl_3$) (Found: C, 71·5; H, 10·3. $C_{31}H_{54}O_6$ requires C, 71·25; H, 10·35%).

Methylation of the Diol (IV; R = Ac, R′ = H).—The diol (10 g.), methyl iodide (70 c.c.) and silver oxide [9] (13·5 g.) were heated together under reflux in the dark for 6 hr. after which further methyl iodide (10 c.c.) and silver oxide (6·5 g.) were added; after a further 10 hr. reaction these additions were repeated. After a total time of 26 hr., ether (200 c.c.) was added, and the mixture was filtered and evaporated. The crude monomethyl ether (10 g.) was heated under reflux with 5% methanolic potassium hydroxide (100 c.c.). The hydrolysis product, isolated in the usual manner, crystallised from aqueous acetone in needles (7 g.), m. p. 92—93°, $[\alpha]_D^{16}$ +60° (*c* 1·0 in $CHCl_3$); it was a *monohydrate* of the *methyl ether* (IV; R = H, R′ = Me) (Found: C, 71·55; H, 11·2; OMe, 6·8; H_2O lost at 65°/0·1 mm., 3·5. $C_{28}H_{52}O_4,H_2O$ requires C, 71·5; H, 11·5; OMe, 6·6; H_2O, 3·8%).

Reaction of a portion (1·95 g.) with *p*-nitrobenzoyl chloride (2·5 g.) in pyridine (15 c.c.) gave the *di*-p-*nitrobenzoate* (from chloroform-methanol) as needles (2·5 g.), m. p. 192—193°, $[\alpha]_D^{20}$ +67·5° (*c* 2·0 in $CHCl_3$) (Found: C, 67·05; H, 7·6; N, 3·7. $C_{42}H_{58}N_2O_{10}$ requires C, 67·15; H, 7·8; N, 3·75%).

The Monoketone (V; R = H).—The above di-*p*-nitrobenzoate (2·05 g.) in glacial acetic acid (80 c.c.) and chromic oxide (0·3 g.) in water (0·5 c.c.) and glacial acetic acid (20 c.c.) were mixed, kept for 20 min., and then diluted with water. The precipitated *ketone di*-p-*nitrobenzoate* separated from chloroform–methanol as plates (1·5 g.), m. p. 216—217°, $[\alpha]_D^{20}$ +61° (*c* 2·0 in $CHCl_3$) (Found: C, 67·45; H, 7·35; N, 4·0. $C_{42}H_{56}N_2O_{10}$ requires C, 67·35; H, 7·55; N, 3·75%).

Hydrolysis of the di-*p*-nitrobenzoate (7·5 g.) with methanolic potassium hydroxide under reflux gave the *ketone* (V; R = H) as plates (3·85 g.) (from aqueous acetone), m. p. 95—96°, $[\alpha]_D^{21}$ +34° (*c* 2·0 in $CHCl_3$). A second crystalline form, m. p. 78—80°, more stable than the above, was also obtained (Found: C, 74·45; H, 11·1. $C_{28}H_{50}O_4$ requires C, 74·6; H, 11·2%).

The Benzyl Ether (I; R = Me, R′ = CH_2Ph).—The acetate (I; R = Me, R′ = Ac) (20·6 g.) in toluene (300 c.c.) containing benzyl chloride (25 c.c.) and finely powdered potassium hydroxide (120 g.) was heated under reflux with vigorous stirring for 7 hr. The mixture was then cooled, treated with water (250 c.c.) and steam distilled. The cooled residue was extracted with ether, removal of which afforded the *benzyl ether* as an oil (22·1 g.), $[\alpha]_D^{20}$ +72° (*c* 1·0 in $CHCl_3$) (Found: C, 82·65; H, 10·45. $C_{35}H_{54}O_2$ requires C, 82·95; H, 10·75%).

The Diol (VI; R = R′ = H).—The above benzyl ether (11 g.) in ethyl acetate (175 c.c.), light petroleum (175 c.c.; b. p. 60—80°) and ethanol (10 c.c.) was cooled to −70° and ozonised for 76 min. with 5·3% (w/w) ozonised oxygen at 0·4 l./min. The solution was allowed to warm to room temperature, the solvents were removed under reduced pressure, and the residue, in glacial acetic acid (100 c.c.), was shaken for 1 hr. with zinc dust (8 g.). After the mixture had been diluted with light petroleum (200 c.c.; b. p. 40—60°) and filtered, the filtrate was washed with water, then sodium carbonate solution, and water. Removal of the solvents gave the crude seco-diketone as a syrup (11·2 g.).

To the diketone (22·6 g.) in ethanol (400 c.c.) sodium borohydride (4 g.) was added during 15 min., and after a further 45 min. the solution was made acid with acetic acid, poured into

[9] Helferich and Klein, *Annalen*, 1926, **450**, 219.

water, and the product isolated with ether. Crystallisation from dilute ethanol gave the *diol* as needles (10·5 g.), m. p. 129—131°, $[\alpha]_D^{19}$ +55° (*c* 2·0 in $CHCl_3$) (Found: C, 77·45; H, 10·85. $C_{35}H_{58}O_4$ requires C, 77·45; H, 10·75%).

The above diol (4 g.) was kept with acetic anhydride (70 c.c.) containing toluene-*p*-sulphonic acid (0·75 g.) for 16 hr. at 18°. The product was isolated in the usual way and chromatographed on neutral alumina (Grade 2). Elution with light petroleum (b. p. 40—60°) -benzene (1 : 1) gave the *diacetate* (4 g.) as a gum, $[\alpha]_D^{20}$ +35° (*c* 1·9 in $CHCl_3$) (Found: C, 74·45; H, 10·2. $C_{39}H_{62}O_6$ requires C, 74·7; H, 9·9%). It showed no hydroxylic absorption near 3 μ.

Interaction of the Methanesulphonate (VII) *with Alkali.*—The methanesulphonate [10] (I; R = Me, R′ = SO_2Me) (2 g.) in ethyl acetate (40 c.c.) containing ethanol (3 c.c.) was ozonised at −70° until the solution became blue. The solvents were then removed under reduced pressure, and the crystalline residue was shaken with acetic acid (40 c.c.) and zinc dust (2 g.) for 45 min. Ether (200 c.c.) was added, the inorganic material was removed by filtration, and the solution was then washed successively with water, aqueous sodium hydrogen carbonate, and water, and finally dried and evaporated. The crude syrupy seco-diketone (2 g.) showed bands near 1710, 1357, and 1172 $cm.^{-1}$. It was kept under nitrogen at reflux temperature for 2 hr. with N-methanolic sodium hydroxide (uptake, 1·25 mol.). The cooled mixture was diluted with water, and the neutral product isolated with ether. Thereafter, the aqueous phase was acidified and the syrupy acidic fraction (290 mg.) was isolated.

Crystallisation of the neutral product (1·3 g.) from light petroleum (b. p. 40—60°) gave the *diketone* (IX) as needles (500 mg.), m. p. 138°, $[\alpha]_D^{18}$ +27·5° (*c* 2·0 in $CHCl_3$) (Found: C, 77·8; H, 10·65; OMe, 7·55. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·75; OMe, 7·2%).

It formed a *furfurylidene* derivative which separated from aqueous methanol in needles, m. p. 106—107°, $[\alpha]_D^{19}$ −11·5° (*c* 2·0 in $CHCl_3$) (Found: C, 77·85; H, 9·25. $C_{33}H_{48}O_4$ requires C, 77·9; H, 9·5%). This had $\lambda_{max.}$ (in EtOH) 324 mμ (log ε 4·33).

The Diketone (XI; R = Me).—The diol (VI; R = R′ = H) (5 g.) was methylated with methyl iodide and silver oxide in the manner described for the diol (IV; R = Ac, R′ = H). Chromatography of the product on alumina (Grade 2) and elution with benzene–ether (3 : 1) gave the *dimethyl ether* (VI; R = H, R′ = Me) (4·1 g.) as a gum, $[\alpha]_D^{20}$ +41° (*c* 1·0 in $CHCl_3$) (Found: C, 77·55; H, 10·7. $C_{36}H_{60}O_4$ requires C, 77·7; H, 10·8%).

The dimethyl ether (4·1 g.) in ethyl acetate (40 c.c.) containing a trace of concentrated hydrochloric acid was hydrogenated with 5% palladised charcoal for 1½ hr. (hydrogen uptake, 0·96 mol.). The filtered solution was diluted with ether and washed with aqueous sodium carbonate and then with water. Evaporation gave the *diol* (X; R = Me) as a gum (3·34 g.). A chromatographically purified sample had $[\alpha]_D^{24}$ = 74° (*c* 1·0 in $CHCl_3$) (Found: C, 74·25; H, 11·4; OMe, 13·7. $C_{29}H_{54}O_4$ requires C, 74·65; H, 11·6; OMe, 13·3%). The *dibenzoate* separated from aqueous ethanol in needles, m. p. 128—129·5°, $[\alpha]_D^{20}$ = 57° (*c* 2·0 in $CHCl_3$) (Found: C, 76·4; H, 9·1. $C_{43}H_{62}O_6$ requires C, 76·5; H, 9·2%).

Oxidation of the diol (X; R = Me) (1·8 g.) in acetone (200 c.c.) with Djerassi's [11] chromic acid reagent (2 c.c.) for 5 min. followed by dilution with water and extraction with ether, gave the *diketone* (XI; R = Me) as a colourless gum (1·75 g.). It was purified by chromatography on alumina and elution with benzene-ether (1 : 1) (Found: C, 75·4; H, 11·05. $C_{29}H_{50}O_4$ requires C, 75·3; H, 10·8%).

Alkaline Cleavage of the Diketone (XI; R = Me).—The diketone (1·75 g.) was kept under nitrogen with 10% aqueous ethanolic potassium hydroxide (50 c.c.) for 16 hr., then diluted and acidified and the product isolated with ether. It was separated into a neutral fraction (285 mg.) and an acidic fraction (1·46 g.) in the usual way. The neutral material was distilled under reduced pressure and the distillate treated with 2,4-dinitrophenylhydrazine phosphate, when the 2,4-dinitrophenylhydrazone of 4-methoxy-2-methylcyclohexanone, m. p. 138—139° (lit.,[12] 138°) was obtained (Found: C, 51·7; H, 5·35. Calc. for $C_{14}H_{18}N_4O_5$: C, 51·2; H, 5·6%).

The acidic fraction had a titration equivalent of 442; calc. for the acid (XIII; R = Me), 338; calc. for the acid (XIV; R = Me), 480. Reaction with diazomethane gave the neutral methyl ester mixture (1·4 g.). Its solution in methylene chloride (75 c.c.) was stirred with powdered anhydrous disodium hydrogen phosphate (15 g.) whilst a solution of trifluoroperacetic acid, prepared from trifluoroacetic anhydride (5 c.c.), methylene chloride (10 c.c.) and 90%

[10] Shealy and Dodson, *J. Org. Chem.*, 1951, **16**, 1427.
[11] Djerassi, Engle, and Bowers, *J. Org. Chem.*, 1956, **21**, 1547.
[12] Acheson, *J.*, 1956, 4232.

hydrogen peroxide (0·75 c.c.), was added during 10 min. The mixture was heated under reflux for 2 hr., cooled, and filtered, and the filtrate was washed, first with aqueous sodium carbonate and then with water, and evaporated. The residual gum (1·46 g.) was heated under nitrogen for 2 hr. with 10% aqueous ethanolic potassium hydroxide. The cooled mixture was diluted and extracted with light petroleum, the extracts being discarded. Acidification, followed by extraction with light petroleum (b. p. 40—60°) gave an acidic gum (600 mg.). Crystallisation from aqueous alcohol gave the *methoxy-acid* (XIII; R = Me) (210 mg.), m. p. 109·5—110·5°, $[\alpha]_D^{20}$ +56° (in $CHCl_3$) (Found: C, 74·35; H, 11·2; Equiv., 335. $C_{21}H_{38}O_3$ requires C, 74·6; H, 11·2; Equiv., 338).

The Diketone (XI; R = CO_2Et).—To the diol (VI; R = R′ = H) (10·5 g.) in pyridine (50 c.c.), ethyl chloroformate (13 c.c.) was added cautiously and the mixture was kept at 18° for 16 hr.; it was then treated with water (10 c.c.) and kept a further ½ hr., and then diluted with ether (200 c.c.). The ethereal solution was washed successively with water, dilute sulphuric acid, aqueous sodium carbonate and water, and then dried and evaporated. Chromatographic purification on alumina gave the ethoxycarbonyloxy compound (VI; R = H, R′ = COOEt) (11·65 g.) as a syrup (Found: C, 74·05; H, 10·0. $C_{38}H_{62}O_6$ requires C, 74·2; H, 10·1%). It showed a strong band near 2·9 μ. A portion (6·3 g.) was dissolved in ethyl acetate (200 c.c.) containing a trace of concentrated hydrochloric acid, and hydrogenated with 5% palladised charcoal (1 g.) (uptake, 0·93 mol.). The product, isolated in the usual manner, was a syrup (5·03 g.). Crystallisation from light petroleum (b. p. 60—80°) gave the *diol* (X; R = CO_2Et), m. p. 104—105·5°, $[\alpha]_D^{20}$ +56° (*c* 1·2 in $CHCl_3$) (Found: C, 70·75; H, 10·75. $C_{31}H_{56}O_6$ requires C, 70·95; H, 10·8%).

A solution of this material (8·75 g.) in acetic acid (50 c.c.) was stirred and cooled to 15° during the slow addition of a solution of chromic oxide (3·35 g.) in water (3 c.c.) and acetic acid (50 c.c.). It was stirred for 16 hr. and then cooled whilst methanol (10 c.c.) was added. After a few minutes ether (250 c.c.) was added, and the solution was washed with water, then aqueous sodium carbonate, and finally with water, and then dried and evaporated. The diketone (XI; R = COOEt) formed a syrup (8·58 g.) which showed absorption bands at 1700 and 1730 $cm.^{-1}$.

Alkaline Cleavage of the Diketone (XI; R = CO_2Et).—The diketone (9·2 g.) was kept at room temperature under nitrogen with 10% aqueous ethanolic potassium hydroxide (200 c.c.) for 16 hr., and the acidic material so formed isolated in the usual manner. It formed a syrup (7·0 g.). A portion (3·0 g.) was kept under reflux for 1 hr. with 95% ethanol (40 c.c.), glacial acetic acid (4 c.c.) and Girard's reagent T (4·0 g.). Ether (250 c.c.) was added to the cooled mixture, and the solution was washed thoroughly with water; the aqueous washings were kept for recovery of the ketonic acidic fraction. Evaporation of the dried ethereal solution gave the non-ketonic acidic fraction as a gum (1·6 g.). By use of diazomethane in the usual manner it was converted into the methyl ester (1·59 g.), which was esterified in pyridine (10 c.c.) with *p*-nitrobenzoyl chloride (1·7 g.). Isolation in the usual manner and chromatographic purification on alumina gave the *methyl ester* of the acid (XIII; R = $CO{\cdot}C_6H_4{\cdot}NO_2$) as pale yellow needles (1·04 g.) (from methanol), m. p. 109·5—110·5°, $[\alpha]_D^{20}$ +67° (*c* 1·0 in $CHCl_3$) (Found: C, 69·15; H, 8·55; N, 2·95. $C_{28}H_{41}NO_6$ requires C, 69·0; H, 8·4; N, 2·91%). The corresponding *hydroxy-acid* (XIII; R = H) separated from ethyl acetate–light petroleum (b. p. 40—60°) as colourless needles, m. p. 127—128°, $[\alpha]_D^{20}$ +26° (*c* 1·0 in $CHCl_3$) (Found: C, 74·4; H, 11·1. $C_{20}H_{36}O_3$ requires C, 74·1; H, 11·1%).

The aqueous layer (450 c.c.) from the Girard separation was decomposed by heating for 40 min. with concentrated hydrochloric acid (50 c.c.). Isolation with ether gave the ketonic acidic material (1·32 g.), neutralisation Equiv. 456. The acid (XIV; R = H) requires Equiv. 466. Its methyl ester was acetylated with acetic anhydride in pyridine, and the crude product subjected to Baeyer–Villiger oxidation with trifluoroperacetic acid in methylene chloride containing suspended disodium hydrogen phosphate. Hydrolysis of the product gave an acid from which a further amount (170 mg.) of the methyl ester *p*-nitrobenzoate of the acid (XIII; R = H) was isolated.

Degradation of the Acid (XIII; R = H) *to the Ester* (XVII).—Reaction of the acid (XIII; R = H) (0·51 g.) with diazomethane in the normal way gave the methyl ester as a gum (0·55 g.). Its solution in benzene (8 c.c.) was added to a solution of phenylmagnesium bromide, prepared from bromobenzene (4·5 g.), magnesium (0·68 g.) and ether (20 c.c.). The mixture was heated under reflux for 3 hr., after which the ether was evaporated, and replaced by

benzene (40 c.c.), and refluxing was continued for 16 hr. The cooled solution was decomposed with ice and ammonium chloride, and the filtered benzene solution was evaporated. The residue was first hydrolysed with aqueous ethanolic sodium hydroxide to remove any unchanged ester, and the product was then distilled in steam to remove diphenyl. The non-volatile material, isolated with ether, separated from light petroleum (b. p. 60—80°) giving needles (0·51 g.) of the *alcohol* (XV), m. p. 186—187° (Found: C, 82·75; H, 10·15. $C_{32}H_{46}O_2$ requires C, 83·1; H, 10·0%).

This diphenylcarbinol (0·35 g.) was kept for 16 hr. with pyridine (0·5 c.c.) and acetic anhydride (0·3 c.c.); excess reagent was then decomposed with ethanol, and the acetoxycarbinol (0·38 g.) isolated in the usual way; it formed a syrup which showed absorption near 3470 $cm.^{-1}$. It was heated under reflux with glacial acetic acid (10 c.c.) for 16 hr.; most of the acetic acid was then removed under reduced pressure, the remainder by washing an ethereal solution of the product with aqueous sodium carbonate and then with water. Evaporation and purification by chromatography on alumina gave the diphenylethylene (XVI) as a syrup (0·32 g.); it showed no absorption band near 3 μ, but had $\lambda_{max.}$ (in hexane) 248 mμ (ε 15,000).

Into a solution of the diphenylethylene (0·30 g.) in ethyl acetate (10 c.c.) at −70°, 5% (w/w) ozonised oxygen was passed for 3 min. The solvent were then removed under reduced pressure, and the residue was kept at 100° for 1 hr. with acetic acid (15 c.c.) containing 8% hydrogen peroxide (2 c.c.), and then for a further 16 hr. at 18°. The solvents were removed under reduced pressure, and to the residue was added 2N-sodium hydroxide solution (10 c.c.); the mixture was then extracted with ether to remove neutral matter. After the addition of ethanol (5 c.c.), the aqueous phase was heated under reflux for 2 hr., and then cooled and acidified with dilute hydrochloric acid. The acidic product was isolated with ether, and converted into the methyl ester by reaction with diazomethane. Crystallisation from ether gave the methyl ester (XVII), m. p. 123—123·5°, undepressed on admixture with authentic material;[1] it had $[\alpha]_D^{21}$ +36·7° (*c* 1·0 in EtOH).

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