1.5990, mp 45.5–50°,[4] 10 g 0.05 mol) in 20 ml of ether was added together with a few drops of boron trifluoride etherate. The reaction mixture was refluxed for 30 hr and then was decomposed with dilute hydrochloric acid. The organic layer was separated, washed several times with aqueous sodium thiosulfate, and dried over anhydrous sodium sulfate. After removal of ether, the residue was ozonized in carbon tetrachloride solution to remove the unreacted olefin. After usual work-up of the ozonide, the neutral fraction was chromatographed on a neutral alumina column (3 × 210 cm) to give pure (−)-(*R*)-1,1-diphenyl-2-methylcyclopropane (**7**), completely free from (−)-menthol and benzophenone as indicated by the ir spectrum and vpc analysis. The ir spectrum was identical in every respect with that of the authentic specimen: bp 104–105° (0.1 mm); $n^{25}D$ 1.5764;[5] $[\alpha]^{25}D$ −0.28° (neat) on a Yanagimoto spectropolarimeter, Model ORD-3; yield 1.2 g.

**Registry No.**—**4**, 16118-44-8; **5**, 10488-06-9; **6**, 3471-09-8; **7**, 14275-48-0.

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## Steroids. CCCXI.[1] The Degradation of Stigmasterol to 3β,5α,6β-Trihydroxy-23,24-bisnorcholan-22-oic Acid

FRANCISCO S. ALVAREZ AND ALEXANDER N. WATT

*Institute of Steroid Chemistry,*
*Syntex Research,*
*Palo Alto, California*

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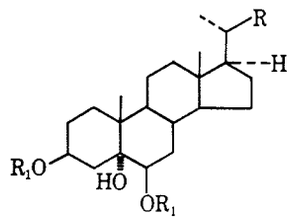
In connection with the synthesis of the insect moulting hormone Ecdysone, recently reported from these laboratories,[2] the preparation of large quantities of 3β,5α,6β-trihydroxy-23,24-bisnorcholan-22-oic acid (**1d**) became necessary.

The degradation of the stigmasterol side chain reported by Fernholz[3a] *via* selective bromination of the nuclear double bond affords 3-hydroxy-23,24-bisnorchol-5-en-22-oic acid in only 20% yield. A modified procedure reported by Smith and Wallis,[3b] which uses iodobenzene dichloride as the selective chlorinating agent, proved to be unsatisfactory for large-scale operation. Thus the approach outlined below was investigated.

Selective epoxidation of the nuclear double bond of stigmasterol acetate was achieved in high yield with *m*-chloroperbenzoic acid in chloroform solution at −80°. The total crude products, consisting mainly of 5α,6α and 5β,6β oxides, were heated on the steam bath with formic acid to yield, after saponification and purification, 72.5% of 24-ethyl-cholest-22-ene-3β,5α,6β-triol[3c] (**1a**). Acetylation of this compound with acetic anhydride in pyridine yielded the diacetate **1b**. Ozonolysis of this diacetate in ethyl acetate solution at




**1a**, $R_1$ = H; R = $C_8H_{15}$
**b**, $R_1$ = Ac; R = $C_8H_{15}$
**c**, $R_1$ = Ac; R = $CO_2H$
**d**, $R_1$ = H; R = $CO_2H$
**e**, $R_1$ = H; R = $CO_2CH_3$

−80° followed by peracetic acid oxidation afforded 3β,5α,6β-trihydroxy-23,24-bisnorcholan-22-oic acid 3,6-diacetate (**1c**). The crude product was saponified to the triol (**1d**) in an over-all yield of 52% from stigmasterol. Formation of the methyl ester (**1e**) of this acid with diazomethane proceeds in quantitative yield.[2a] However, for large scale preparations, other procedures were examined. Esterification of the acid **1d** in the presence of methanol containing 2% w/w of sulfuric acid yielded the methyl ester (**1e**) in only 53.6% yield.

A brief report[4] describing the use of methyl iodide in dimethyl acetamide with sodium bicarbonate as a superior method to esterify acids, prompted us to try these conditions. The reaction proceeds slowly at room temperature, but the transformation is practically quantitative.

### Experimental Section[5]

**24-Ethylcholest-22-ene-3β,5α,6β-triol** (**1a**).—A suspension of 2 kg of stigmasterol in a mixture of 4 l. of pyridine and 2 l. of acetic anhydride was heated under anhydrous conditions with mechanical stirring on the steam bath for 2 hr. The resulting solution of stigmasterol acetate that began to crystallize on cooling, was poured into 60 l. of water and stirred for *ca.* 1 hr to hydrolize the excess acetic anhydride. The crude stigmasterol acetate was collected by filtration, washed with water, and dried at 80° *in vacuo* to yield 2.392 kg of crude product. This material was dissolved in 24 l. of chloroform, cooled to −80° with an external acetone–Dry Ice bath under anhydrous conditions. The mixture was stirred mechanically while a solution of 1.115 kg of *m*-chloroperbenzoic acid in 9 l. of chloroform was added over a period of 3 hr. The reaction temperature was kept at −80° for an additional 3 hr. The acetone–Dry Ice bath was removed and the mixture was allowed to come to room temperature in 24 hr. Stirring was continued for 72 hr and the reaction mixture was washed with a 5% sodium bicarbonate solution until alkaline and then with water until neutral.

The resulting solution was distilled to dryness under reduced pressure, and the residue was heated with 17 l. of 85% aqueous formic acid for 2 hr on the steam bath and then stirred without heating overnight. The crystalline product thus obtained was collected by filtration, washed with formic acid and then with water, and sucked as dry as possible on the filter.

This solid was dissolved in 20 l. of methanol under reflux and a solution of 1.2 kg of potassium hydroxide in 4 l. of methanol was added. The reaction mixture was kept under reflux and with mechanical stirring for 2 hr, cooled to room temperature and poured into 150 l. of water. The crystalline precipitate thus obtained was collected by filtration, washed with water, and dried

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at 80° *in vacuo*. This crude product was purified by stirring with 10 l. of methylene chloride for 2 hr at room temperature, filtration, and repetition of this treatment. Drying of the product at 80° *in vacuo* afforded 1.577 kg of triol (**1a**). The analytical sample was obtained by recrystallization from methanol: mp 256–257°; $[\alpha]D$ −8°; $\nu_{max}$ 3440, 2870, 2940, 2960, 960–970 $cm^{-1}$; nmr, 5.13 (22, 23-H), 4.32–4.42 (3α-OH and 6α-H and 3α-H), 1.05 (19-H), 0.642 ppm (18-H).

*Anal.* Calcd for $C_{27}H_{50}O_3$: C, 77.97; H, 11.28; O, 10.75. Found: C, 77.88; H, 11.31; O, 10.78.

**24-Ethylcholest-22-ene-3β,5α,6β-triol 3,6-Diacetate (1b).**—A mixture of 1.530 kg of the triol **1b**, 3 l. of pyridine, and 1.5 l. of acetic anhydride was heated with stirring and under anhydrous conditions for 4 hr on the steam bath, and the resulting solution was left at room temperature overnight.

The reaction mixture was poured into 50 l. of water and stirred for 1 hr to hydrolize the excess acetic anhydride. The mixture was acidified with dilute hydrochloric acid, then extracted with methylene chloride; the extracts were washed with water until neutral, dried with anhydrous sodium sulfate, and concentrated to dryness *in vacuo* to yield an amorphous residue of crude 24-ethylcholest-22-ene-3β,5α,6β-triol 3,6-diacetate (**1b**). A pure specimen was obtained after filtration of the crude product through a column of silica gel, eluting with methylene chloride. The material resisted all attempts at crystallization but was shown to be homogeneous by thin layer chromatography: $[\alpha]D$ −61°; $\nu_{max}$ 3847, 2875, 2960, 3600, 1730, 1215, 960–970 $cm^{-1}$; nmr 5.16 (22, 23-H), 4.83–5.5 (3α-H), 4.78 (6α-H), 3.25 (OH), 2.31, 2.08 (2AcO), 0.704, (18-H), 0.988 ppm (19-H).

*Anal.* Calcd for $C_{33}H_{54}O_5 \cdot H_2O$: C, 74.39; H, 10.59; O, 15.02. Found: C, 74.56; H, 10.12; O, 15.17.

**3β,5α,6β-Trihydroxy-23,24-bisnorcholan-22-oic Acid 3,6-Diacetate (1c).**—The total crude residue from the above concentration was dissolved in 25 l. of ethyl acetate, cooled to −80° by means of an external acetone–Dry Ice bath and a stream of oxygen containing 6% of ozone[6] was bubbled in at a rate of 6.5 l. per minute for a total of 18 hr. The reaction vessel was removed from the cooling bath and a mixture of 1.08 l. of 40% peracetic acid[7] in 1.08 l. of water was added. The mixture was allowed to reach room temperature overnight under continuous mechanical stirring.

The mixture was washed with 10% aqueous sodium iodide solution, 10% aqueous sodium thiosulfate solution, and finally with water. The ethyl acetate layer was concentrated to dryness under reduced pressure. The residue was dissolved in ether and extracted with 5% aqueous potassium carbonate solution. The aqueous layer was washed several times with ether to eliminate neutral components and then acidified with concentrated aqueous hydrochloric acid. The mixture was extracted with methylene chloride, the extracts were washed with water until neutral, then d[illegible] anhydrous sodium sulfate, and distilled to dryness under reduced pressure to yield a crystalline residue of 3β,5α,6β-trihydroxy-23,24-bisnorcholan-22-oic acid 3,6-diacetate (**1c**). The pure specimen was prepared by several crystallizations from acetone–hexane: mp 193–194°; $[\alpha]D$ −58°; $\nu_{max}$ 3460, 1740, 1715, 1250 $cm^{-1}$; nmr 5.35–5.1 (3α-H), 4.7 (6α-H), 2.06 and 2.00 (2AcO), 1.28 (21-H), 1.15 (19-H), 0.71 ppm (18-H).

*Anal.* Calcd for $C_{26}H_{40}O_7$: C, 67.21; H, 8.68; O, 24.11. Found: C, 67.58; H, 8.72; O, 23.82.

**3β,5α,6β-Trihydroxy-23,24-bisnorcholan-22-oic Acid (1d).**—The total crude diacetate (**1c**) from the above operation was dissolved in 8 l. of methanol under reflux, then a solution of 520 g of potassium hydroxide in 500 ml of water was added slowly and the mixture was allowed to reflux for 4 hr, then was left overnight at room temperature. The solution was then concentrated to *ca.* 2.8 l. and carefully acidified with dilute hydrochloric acid. The mixture was then diluted to *ca.* 28 l. with 5% aqueous sodium chloride solution. The crystalline precipitate of 3β,5α,6β-trihydroxy-23,24-bisnorcholan-22-oic acid (**1d**) was collected by filtration, washed with water, and dried at 80° *in vacuo* to afford 940 g of **1d** (51.2% over-all from stigmasterol). The pure specimen was obtained by recrystallization from methanol: mp 275°; $[\alpha]D$ −20° (dioxane); $\nu_{max}$ 3840, 3450, 1710 $cm^{-1}$; nmr (in DMSO) 3.72–3.42 (OH), 3.3 (MeOH), 1.14 (21-H), 1.01 (19-H), 0.63 ppm (18-H).

(6) A Welsbach Ozonator style T-816 was used. (The Welsbach Corporation, Ozone Products Division, Philadelphia, Pa.

(7) 40% Peracetic acid in acetic acid, Becco peracetic acid, F.M.C. Corp., Inorganic Chemical Division, Buffalo, N. Y.

*Anal.* Calcd for $C_{22}H_{36}O_5 \cdot CH_3OH$: C, 64.83; H, 9.98; O, 25.19. Found: C, 65.82; H, 9.20; O, 24.95.

**3β,5α,6β-Trihydroxy-23,24-bisnorcholan-22-oic Acid Methyl Ester (1e). A. By Esterification with Methanol–Sulfuric Acid.**—A solution of 5 g of the carboxylic acid **1d** in 50 ml of methanol containing 2% (w/w) of concentrated sulfuric acid was heated under reflux for 2 hr on the steam bath. The reaction mixture was poured into 500 ml of 1% aqueous potassium hydroxide solution. The material that precipitated was collected by filtration and crystallized from ethyl acetate to yield 2.3 g of the methyl ester **1e**, (mp 228–230°, $[\alpha]D$ −18°) identical in all respects with an authentic specimen.[2a]

**B. By Treatment with Methyl Iodide and Sodium Bicarbonate in Dimethyl Acetamide.**—A solution of 872 g of crude carboxylic acid (**1d**) from the last reaction in 4.5 l. of dimethyl acetamide was treated with 450 g of sodium bicarbonate and 945 g of methyl iodide under anhydrous conditions. The mixture was stirred at room temperature in the dark for 48 hr, then poured into 90 l. of 10% aqueous sodium chloride solution. The crystalline material thus obtained was collected by filtration; washed with water, and dried *in vacuo* at 80° to afford 826 g of the methyl ester **1e**: mp 227–230°; $[\alpha]D$ −17°. This material did not depress the melting point of the authentic sample.[2a] It also exhibited similar ir and nmr spectra.

**Registry No.**—**1a**, 16118-24-4; **1b**, 16214-82-7; **1c**, 16176-01-5; **1d**, 16118-25-5; **1e**, 5241-14-5; stigmasterol, 83-48-7.

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## α,α-Di-*t*-butyl-β-propiolactone and Methyldi-*t*-butylacetic Acid from Di-*t*-butylketene[1]

MELVIN S. NEWMAN AND ARIE LEEGWATER[2]

*Evans Chemistry Laboratory of The Ohio State University, Columbus, Ohio 43210*

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In earlier work, the preparation of di-*t*-butylketene (I) and its unreactivity was reported.[3] Herein we describe attempts to effect the reaction of I with a number of reagents which normally react with olefinic and carbonyl groups.

The first series of reactions involved attempts to add carbenes to the olefinic function of I. Di-*t*-butylketene was recovered almost quantitatively from the following treatments: (1) a mixture of I, methylene iodide, and Zn–Cu alloy in ether under reflux for 24 hr;[4] (2) a mixture of I, ethyl trichloroacetate, and sodium methoxide in pentane at 0° for 6 hr;[5] (3) a solution of I and phenyltrichloromethylmercury in benzene at 75° for 18 hr;[6] (4) a mixture of I, phenyltrichloromethylmercury, and sodium iodide in 1,2-dimethoxyethane (glyme) at room temperature for 15 hr;[7] and (5) a solution of I, bromomalononitrile,

(1) This work was supported by Grant GP-5552 of the National Science Foundation.

(2) Details of this work can be found in the Ph.D. thesis of A. Leegwater presented to The Ohio State University in 1967.

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