The crude product (13.8 g., m.p. 123.6–126.5°) was recrystallized several times from methanol and acetone to give XI, m.p. 124.5–127.2°, $[\alpha]^{21}\mathrm{D}$ +82.0° (2% in $CHCl_3$).

Anal. Calcd. for $C_{28}H_{46}O_2$: C, 81.10; H, 11.18. Found: C, 81.07; H, 10.92.

25-Hydroxy-Δ⁴-cholestene-3-one (**XII**).—25-Hydroxycholesterol[4] (25 g.) was oxidized by the procedure used for the preparation of 25-hydroxy-Δ⁴-norcholestene-3-one (IX). The crude product (20.5 g., m.p. 145.2–146.4°) was recrystallized from acetone and methanol to give XII (plates) melting 147.8–148.4°, $[\alpha]^{20}\mathrm{D}$ +88.4° (2% in $CHCl_3$).

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.80; H, 11.00.

25-Chloro-Δ⁵-norcholestene-3β-ol-acetate (**XIII**).—To a solution of 40 g. of 25-hydroxynorcholesteryl acetate (II) in 1200 ml. of dry pyridine was added 40 ml. of freshly distilled phosphorus oxychloride. The mixture was refluxed for 0.5 hour, cooled to 10° and poured into a mixture of ice and water. The precipitated product was filtered and washed neutral with water. The dried crude product was dissolved in hot benzene and filtered to remove a brown insoluble substance. The filtrate, after treatment with decolorizing charcoal, was concentrated to dryness and the residue recrystallized from methanol and acetone to give 20.7 g. of XIII (needles), m.p. 116.2–117.0°, $[\alpha]^{23}\mathrm{D}$ −35.4° (2% in $CHCl_3$).

Anal. Calcd. for $C_{28}H_{45}O_2Cl$: C, 74.88; H, 10.10; Cl, 7.89. Found: C, 74.71; H, 10.32; Cl, 8.44.

25-Chloro-Δ⁵-norcholestene-3β-ol (**XIV**).—A solution of 15 g. of the 25-chloroacetate (XIII) was hydrolyzed by refluxing for two hours with ethanolic potassium hydroxide. The crude product (13.5 g.), after recrystallization from methanol and from acetone, gave XIV (fine needles) melting at 132.0–133.0°, $[\alpha]^{29}\mathrm{D}$ −38.6° (2% in $CHCl_3$).

Anal. Calcd. for $C_{26}H_{43}OCl$: C, 76.71; H, 10.65; Cl, 8.71. Found: C, 76.92; H, 10.24; Cl, 8.38.

25-Chloro-Δ⁴-norcholestene-3-one (**XV**).—A 10.5-g. sample of 25-chloro-5-norcholestene-3β-ol (XIV) was oxidized by the procedure used for the preparation of 25-hydroxy-Δ⁴-norcholestene-3-one (IX). The crude product (8.0 g.), after successive recrystallizations from methanol and acetone, gave XV (needles) melting at 119.0–119.9°, $[\alpha]^{20}\mathrm{D}$ +101.6° (2% in $CHCl_3$).

Anal. Calcd. for $C_{26}H_{41}OCl$: C, 77.09; H, 10.20, Cl, 8.75. Found: C, 77.05; H, 9.97; Cl, 9.04.

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3α-Carboxylic Acids of 5-Sitostene and Stigmastane

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Previous work has dealt with the introduction of the carboxylic acid group in the 3α-position of the 5-cholestene, cholestane and 5-androstene nuclei.[1,2] The present work deals with the insertion of the carboxylic acid group at the 3α-positions of 5-sitostene and stigmastane nuclei.

Sitosteryl chloride was prepared in good yield by treatment of β-sitosterol with thionyl chloride. A high melting side product has been isolated in this preparation. Conversion to sitosterylmagnesium chloride followed by carbonation yields 5-sitostene-3α-carboxylic acid which has been characterized by transformation to its methyl ester. β-Sitosteryl is a probable by-product from the preparation of the Grignard reagent. Catalytic low pressure hydrogenation of the 5-sitostene-3α-carboxylic acid gives the stigmastane-3-carboxylic acid which is characterized through its methyl ester.

The low pressure hydrogenations of 5-cholestene-3α-carboxylic acid and 5-sitostene-3α-carboxylic acid catalyzed by platinum oxide are interesting because of the completeness of the reaction; *i.e.*, the resulting acids do not give a Liebermann–Burchard reaction nor a yellow color with tetranitromethane. In this Laboratory similarly hydrogenated products of cholesteryl chloride, cholesteryl acetate and cholesterol all give positive Liebermann–Burchard reactions and yellow coloration with tetranitromethane, indicating small amounts of unsaturated materials in the product.

Experimental[3]

3α-Chloro-5-sitostene.—Purified β-sitosterol[4] was converted to the chloro compound as described by Shoppee.[5] In some of these preparations of sitosteryl chloride, a petroleum ether-insoluble substance was isolated and is presumably bis-sitosteryl sulfite.[6] Recrystallization of this material from ethyl ether gave colorless crystals, m.p. 197–200°, $[\alpha]^{25}\mathrm{D}$ −29.4°, *c* 1.175 in chloroform, Rast molecular weight was abnormally high (1.1 × 10^3), Liebermann–Burchard reaction was positive, bromine in carbon tetrachloride was absorbed, alkaline or acid hydrolysis in ethanol gives β-sitosterol, m.p. 140–141°, $[\alpha]^{25}\mathrm{D}$ −34°, *c* 1.69 in chloroform.

5-Sitostene-3α-carboxylic Acid.—Methylmagnesium iodide was prepared from 6.0 (42.3 mmoles) of methyl iodide and 3.0 g. (123 mg. atoms) of magnesium in 50 ml. of dry ethyl ether. To this there was added 15.7 g. (36.2 mmoles) of sitosteryl chloride in 50 ml. of dry ether. The solution was then refluxed for 48 hours under the usual conditions; carbon dioxide gas at 1 atm. was passed into the reaction mixture at room temperature for 40 hours. The entire reaction mixture was poured onto 500 ml. of 1:5 hydrochloric acid and stirred well. The two layers were transferred to a separatory funnel and *ca.* 200 ml. of ether added. After separation of the acid layer, an ether-insoluble fraction, 1.76 g., m.p. > 270° dec., was filtered from the ether. The ether layer was then extracted alternately with 10% sodium hydroxide and water to yield the sodium 5-sitostene-3-carboxylate in the aqueous layer; the remainder of the sodium salt was secured by filtration of the ether layer in which it was suspended. The solid salt was added to the aqueous layer which was acidified with hydrochloric acid to congo red and allowed to stand overnight on the steam-bath prior to filtration, which gave 7.5 g. of the crude acid, m.p. 195–202°. This was taken up in *ca.* 200 ml. of refluxing benzene and crystallization was allowed to proceed during slow evaporation of the solvent to yield 5-sitostene-3α-carboxylic acid as colorless platelets, m.p. 206–208°, $[\alpha]^{24}\mathrm{D}$ −15.1°, *c* 1.79 in chloroform.

Anal. Calcd. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.39. Found: C, 81.39, 81.18; H, 11.18, 11.31.

Crystallization of the high melting side product from benzene gave colorless crystals, m.p. 302–306°. This probably is bisitosteryl which was formed in the same manner as bicholesteryl.[2]

3α-Carbomethoxy-5-sitostene.—To 100 ml. of absolute methanol containing 2 ml. of concd. sulfuric acid there was added 0.690 g. of 5-sitostene-3α-carboxylic acid. The solution was heated at reflux temperature for 3 hours and then poured onto *ca.* 100 g. of ice. The insoluble ester was filtered and washed well with cold water until neutral to litmus. It was then taken up in 60 ml. of hot methanol and upon standing 0.575 g. of colorless platelets were secured, m.p. 85°, $[\alpha]^{22}\mathrm{D}$ −19.4°, *c* 2.78 in chloroform.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.48. Found: C, 81.7; H, 11.40.

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(1) The 3α-designation is based upon the work of R. H. Baker and Q. R. Petersen, THIS JOURNAL, **73**, 4080 (1951).

(2) R. E. Marker, T. S. Oakwood and H. M. Crooks, *ibid.*, **58**, 481 (1936); R. H. Baker and E. N. Squire, *ibid.*, **70**, 1487 (1948); R. H. Baker and E. N. Squire, *ibid.*, **71**, 1383 (1949).

(3) Microanalyses by Dr. Carl Tiedke.

(4) We are indebted to Dr. Howard L. Gerhardt of the Pittsburgh Paint and Glass Co. for supplying the β-sitosterol.

(5) C. W. Shoppee, *J. Chem. Soc.*, 1043 (1947).

(6) *Cf.* bis-cholestenyl sulfite, P. J. Daughenbaugh and J. B. Allison, THIS JOURNAL, **51**, 3665 (1929).

Stigmastane-3α-carboxylic Acid.—In a 500-ml. Parr hydrogenation flask were placed 145 mg. of platinum dioxide (according to Adams) and 2.25 g. of 5-sitostene-3α-carboxylic acid in a solution of 300 ml. of absolute ether and 30 ml. of glacial acetic acid. Hydrogenation with vigorous shaking at 3 atm. was carried out for 17 hours. After removal of the catalyst by filtration, the ether was evaporated and crystallization proceeded upon cooling of the acetic acid to give colorless crystals, m.p. 240–242°, $[\alpha]^{25}D$ +29.7°, *c* 2.78 in chloroform. A total of 2.08 g. of the acid was secured by further crystallization of water–acetic acid mixtures.

Anal. Calcd. for $C_{30}H_{52}O_2$: C, 81.02; H, 11.79. Found: C, 81.58; H, 11.45.

3α-Carbomethoxystigmastane.—Stigmastane-3α-carboxylic acid, 0.900 g. (2.03 mmoles), was suspended in 200 ml. of absolute methanol containing 20 drops of concentrated sulfuric acid. The mixture was heated at reflux temperature under anhydrous conditions for two hours and then poured onto *ca.* 400 g. of ice. The insoluble ester was filtered at the pump, washed well with many portions of cold, distilled water, and then taken into solution with 150 ml. of hot methanol. Fractional crystallization from this solution gives 0.905 g. (98%) of the carbomethoxystigmastane as colorless crystals, m.p. 99–100°, $[\alpha]^{24}D$ +28°, *c* 4.53 in chloroform.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.48. Found: C, 81.46; H, 11.71; C, 81.59; H, 11.62.

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2-Methyl-2-cyclohexenone

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In connection with another study we have had occasion to investigate the preparation of 2-methyl-2-cyclohexenone (I). This ketone has been obtained previously by a number of methods,[1] which suffer from either low over-all yields or lengthy procedures. Thus, the selenium dioxide[1a] or chromic acid[2] oxidation of 1-methylcyclohexene (II) led to difficultly separable mixtures of 2- and 3-methyl-2-cyclohexenone from which I has been obtained in low yield. The addition of nitrosyl chloride to II followed by dehydrochlorination and hydrolysis of the resulting oxime gave I in unspecified yield,[3,1b] whereas attempts to dehydrate 2-hydroxy-2-methylcyclohexanone by various procedures resulted in incomplete dehydration.[1a] The bromination of 2-methylcyclohexanone (III) with N-bromosuccinimide followed by dehydrobromination has given I in 17% yield.[1d] In the present work, a convenient synthesis of I from III in two operations (49% over-all yield) has been developed and is the subject of this note.

Since the reaction of sulfuryl chloride (IV) with methyl cyclohexyl ketone[4] and methyl isopropyl ketone[5] has been shown to effect chlorination exclusively at the methyne hydrogen, it was hoped that with 2-methylcyclohexanone (III) the product would be 2-chloro-2-methylcyclohexanone (V). This indeed proved to be the case, for on simply adding sulfuryl chloride to a solution of the ketone in carbon tetrachloride, V was produced in 84–86% yields. It is interesting to note that direct chlorination of III is apparently not selective.[6] The structure of V was shown by formation of I or its derivatives upon dehydrohalogenation. The action of 2,4-dinitrophenylhydrazine in methanol or ethanol at room temperature gave the 2,4-dinitrophenylhydrazone of the corresponding 2-alkoxy-2-methylcyclohexanone,[7] which on warming with dilute acid underwent elimination of alcohol to give the 2,4-dinitrophenylhydrazone of 2-methyl-2-cyclohexenone (I).[8]

For the preparation of I it was not necessary to isolate the chloro ketone which was simply obtained in a crude form and heated with collidine. An exothermic reaction occurred at 145–150°, and an almost quantitative yield of collidine hydrochloride separated. The filtrate yielded 49% of pure (redistilled) 2-methyl-2-cyclohexenone. The rest of the material was high boiling and has been shown[9] to consist mainly of the dimer of 2-methylenecyclohexanone, isolated in about 23% yield. The dehydrohalogenation thus occurred in both possible directions giving a mixture of isomers. When pyridine was used in place of collidine 2-methyl-2-cyclohexenone was produced in somewhat lower (36–38%) yields.

The purity and identity of 2-methyl-2-cyclohexenone (I) prepared as described above was confirmed by the constant boiling point and refractive index, by the high extinction (9,660) at 234 mμ, and by the fact that the known 2,4-dinitrophenylhydrazone was produced in 92% yield. Ozonization of I gave acetic and glutaric acids, isolated as the *p*-toluidides.

The unsaturated ketone I was also prepared by pyrolysis of 2-acetoxy-2-methylcyclohexanone (VI) which was produced by the action of potassium acetate on the chloro ketone. The yields, however, were not promising; so the study was not carried beyond the preliminary stages. It is interesting to note that the dimer of 2-methylenecyclohexanone was also produced in this reaction.[9]

Experimental[10]

2-Chloro-2-methylcyclohexanone (V).—To a solution of 224 g. (2.00 moles) of 2-methylcyclohexanone,[11] b.p. 162.5–

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[1] (a) For a list of references (except those listed here) to synthetic methods see L. W. Butz, B. L. Davis and A. M. Gaddis, *J. Org. Chem.*, **12**, 122 (1947); (b) W. N. Haworth, *J. Chem. Soc.*, **103**, 1242 (1913); (c) M. Mousseron, F. Winternitz and R. Jacquier, *Compt. rend.*, **224**, 1062, 1230 (1947); (d) W. W. Rinne, H. R. Deutsch, M. I. Bowman and I. B. Joffe, THIS JOURNAL, **72**, 5759 (1950); (e) A. J. Birch, *J. Chem. Soc.*, 593 (1946); (f) M. Godchot and P. Bedos, *Compt. rend.*, **181**, 919 (1925), report the preparation of I by the action of quinoline on 2-chloro-2-methylcyclohexanone, but the physical constants of their compound do not agree with those reported elsewhere.

(2) F. C. Whitmore and G. W. Pedlow, THIS JOURNAL, **63**, 758 (1941).

(3) O. Wallach, *Ann.*, **359**, 303 (1908).

(4) B. Tchoubar and O. Sackur, *Compt. rend.*, **208**, 1020 (1939).

(5) P. Delbaere, *Bull. soc. chim. Belg.*, **51**, 1 (1942).

(6) There are conflicting reports about the action of chlorine on III. A. Kötz and H. Steinhorst, *Ann.*, **379**, 1 (1911), report the formation of 2-chloro-6-methylcyclohexanone; M. Godchot and P. Bedos, ref. 1f, report the isolation of 2-chloro-2-methylcyclohexanone with physical properties which agree fairly well with those found in the present work; R. Cornubert and C. Borrel, *Bull. soc. chim.*, **43**, 804 (1928), report the formation of both the 2- and the 6-chloro isomers. *Cf.* ref. 1d for the action of bromine on III.

(7) *Cf.* the examples of analogous behavior: (a) K. von Auwers, *Ber.*, **50**, 1177 (1917); (b) V. R. Mattox and E. C. Kendall, THIS JOURNAL, **72**, 2290 (1950).

(8) *Cf.* ref. 7b; C. Djerassi, *ibid.*, **71**, 1003 (1949); F. Ramirez and A. F. Kirby, *ibid.*, **74**, 4331 (1952).

(9) E. W. Warnhoff and William S. Johnson *ibid.*, **75**, 496 (1953).

(10) All melting points are corrected for stem exposure.

(11) Prepared by chromic acid oxidation of 2-methylcyclohexanol.