tervals of more than 2 mμ, while in the neighborhood of maxima and minima the interval was decreased to 1 mμ. The absorption cells were of silica; the thickness of each was 1.000 ± 0.002 cm. The concentrations of the solutions varied from 0.00015 to 0.0002 molar. A reference solution with identical composition as that of the solvent was used as a blank in each measurement. The molecular extinction coefficients, ϵ, were calculated from the equation: $\epsilon = D/lC$, where D = optical density, l = thickness of the absorption cell, and C = the concentration of the sample in moles per liter.

Solvents. (a) **Alcohol.**—U.S.P. 190 proof ethyl alcohol, manufactured by U. S. Industrial Chemicals, Inc., was used. 10% ethanol was prepared volumetrically by diluting 12.80 cc. of 95% alcohol to 100 cc. with water.

(b) **Acid and Base.**—Approximately 0.02 *M* solutions of hydrochloric acid and sodium hydroxide were prepared from reagent grade chemicals and standardized. Calculated amounts of each solution were diluted to make exactly 0.01 *M* solutions.

Pyridine.—A C. P. J. T. Baker product was distilled over anhydrous calcium sulfate.

Quinoline.—A synthetic Eastman Kodak Co. product was distilled under reduced pressure.

All of the fluoropyridines and fluoroquinolines were prepared in this Laboratory[1] and were redistilled before use.

2- and 6-chloroquinolines were products of Eastman Kodak Co., and were distilled under reduced pressure before use.

Acknowledgment.—This work is part of a study of the preparation and properties of heterocyclic fluorine compounds being carried out at this Laboratory, and was supported in part by the Office of Naval Research. The authors' thanks are due Mr. S. H. Patten, who drew the absorption curves.

Summary

1. The ultraviolet absorption spectra of the isomeric fluoropyridines and fluoroquinolines as well as those of 2- and 6-chloroquinoline have been measured.

2. The fluorine atom produces a bathochromic shift of the pyridine maximum in either the 2- or 3-position in the pyridine series, but no such regularity is observed in the quinoline series.

3. The change from 10 to 95% alcohol as solvent produces a change in the spectrum of each compound.

4. Spectrophotometric evidence indicates that 2-fluoroquinoline forms a hydrochloride in 10% ethanol, but that 2-fluoropyridine does not.

CHAPEL HILL, N. C. RECEIVED AUGUST 10, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IMPERIAL COLLEGE, LONDON, AND HARVARD UNIVERSITY]

5,6-Dihydrostigmasterol[1]

BY D. H. R. BARTON[2] AND C. J. W. BROOKS

In 1941 Mazur[3] reported the isolation of 5,6-dihydrostigmasterol from the non-saponifiable matter of the fresh-water sponge *Spongilla lacustris*. Subsequently Bernstein, Wilson and Wallis[4] drew attention to the serious discrepancy between the optical rotations given by Mazur for his sterol and the proposed constitution. These criticisms were substantiated by Kind and W. Bergmann[5] who showed that clionasterol,[6] presumed by Mazur to be 5,6-dihydrostigmasterol, in fact possessed an ethylenic linkage at the 5,6-position. Now the preparation of a substance described as 5,6-dihydrostigmasterol, and evidently different from Mazur's sterol, had been recorded earlier.[7] The method of preparation was the reduction of stigmastadienone (I, R = $C_{10}H_{19}$) by sodium and amyl alcohol. Such a procedure would be expected to give both Δ^{22}-coprostigmasten-3α-ol (II, R = $C_{10}H_{19}$) and Δ^{22}-stigmasten-3β-ol (5,6-dihydrostigmasterol) (III, R = $C_{10}H_{19}$). Since Marker and Wittle[7] did not apply an adequate method for the separation of these two expected products, it seemed to us likely that their reputed 5,6-dihydrostigmasterol was not pure. In order to confirm this view we have prepared 5,6-dihydrostigmasterol together with some related compounds. As will be clear from the sequel, a study of stigmastane derivatives possessing an isolated ethylenic linkage at the 22(23)-position in the side chain was also of interest in another connection.

Hydrogenation of stigmastadienone,[8] until about 1.1 molecular proportions of hydrogen had been taken up, afforded a complex mixture of products, which was resolved by chromatography over alumina. The most easily eluted fraction was a mixture of hydrocarbons, which is further discussed below. The main products of the reaction were two isomeric ketones analyzing for $C_{29}H_{48}O$. The more easily eluted and lower melting ketone was shown to be Δ^{22}-coprostigmasten-3-one (IV, R = $C_{10}H_{19}$), for on reduction by sodium and *n*-propanol it furnished Δ^{22}-coprostigmasten-3α-ol

(1) This paper is Part XVI in our series on the "Application of the Method of Molecular Rotation Differences to Steroids." It was supported, in part, by a Research Grant from the Chemical Society, London. One of us (C. J. W. B.) is indebted to the D. S. I. R. for a maintenance grant.

(2) Visiting Lecturer, Harvard University, 1949–1950.

(3) Mazur, THIS JOURNAL, **63**, 2442 (1941).

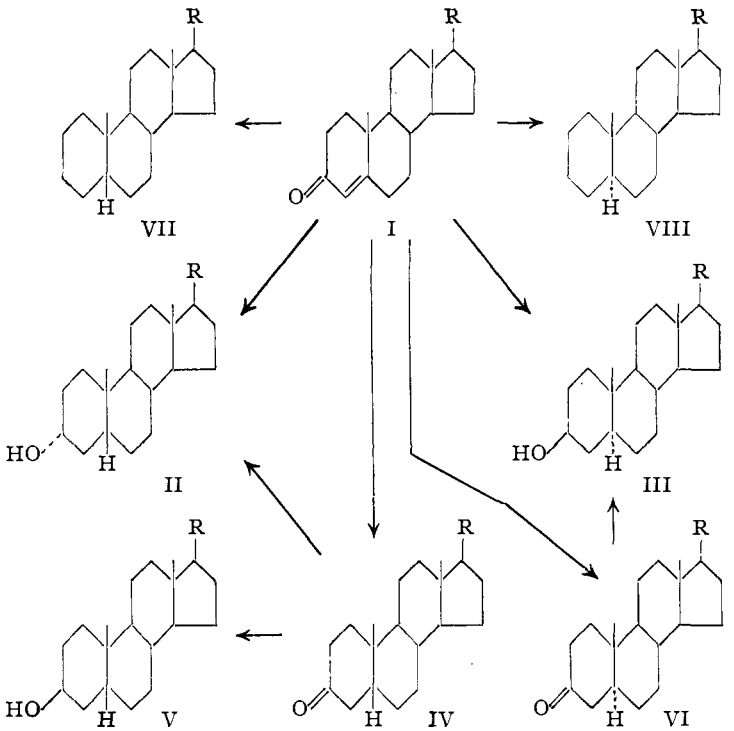
(4) Bernstein, Wilson and Wallis, *J. Org. Chem.*, **7**, 103 (1942).

(5) Kind and W. Bergmann, *ibid.*, **7**, 341 (1942).

(6) Valentine and W. Bergmann, *ibid.*, **6**, 452 (1941).

(7) Marker and Wittle, THIS JOURNAL, **59**, 2704 (1937).

(8) We are indebted to Dr. Wayne Cole of the Glidden Co. (Soya Products Division) for generously providing us with the stigmasterol used for the preparation of stigmastadienone. Also we thank Dr. Carl Djerassi (Ciba Pharmaceuticals, Inc., Summit, N. J.) for facilitating the transfer of this material.



(II, R = $C_{10}H_{19}$), the acetate of which gave coprostigmastan-3α-yl acetate (acetate of II, R = $C_{10}H_{21}$) on further hydrogenation in acid solution. A by-product of the reduction of Δ^{22}-coprostigmasten-3-one was Δ^{22}-coprostigmasten-3β-ol (V, R = $C_{10}H_{19}$). The more difficultly eluted and higher melting ketone was shown to be Δ^{22}-stigmasten-3-one (VI, R = $C_{10}H_{19}$), for on reduction by sodium and *n*-propanol it afforded Δ^{22}-stigmasten-3β-ol (5,6-dihydrostigmasterol) (III, R = $C_{10}H_{19}$), the acetate of which was hydrogenated in acid solution to stigmastan-3β-yl acetate (acetate of III, R = $C_{10}H_{21}$).

Hydrogenation of Δ^{22}-coprostigmasten-3-one in neutral solution and chromatography of the product gave coprostigmastan-3-one (IV, R = $C_{10}H_{21}$), coprostigmastan-3α-ol and, in minor amount, coprostigmastan-3β-ol. Similar hydrogenation of Δ^{22}-stigmasten-3-one afforded stigmastan-3β-ol.

Whereas Marker and Wittle[7] quoted m. p. 187° for their Δ^{22}-stigmasten-3β-ol and m. p. 122° for the acetate, we find m. p. 159° for our alcohol and m. p. 144–144.5° for the acetate.[9] As mentioned above, it seems likely that the 5,6-dihydrostigmasterol of Marker and Wittle[7] was a mixture of Δ^{22}-coprostigmasten-3α-ol and Δ^{22}-stigmasten-3β-ol. This would explain the high m. p. of the alcohol[14] and the low m. p. of the acetate. Support for this view was provided by the fact that crystallization of a mixture of equal amounts of our authentic Δ^{22}-coprostigmasten-3α-ol and Δ^{22}-stigmasten-3β-ol yielded a 1:1 complex, m. p. 188°, which was converted by acetylation to a mixture of acetates, m. p. 119°.

The mixture of hydrocarbons mentioned above was obtained only in small amount. It appeared to be a mixture of Δ^{22}-coprostigmastene (VII, R = $C_{10}H_{19}$), m. p. 67–68°, from which a characteristic dibromide was prepared, and Δ^{22}-stigmastene (VIII, R = $C_{10}H_{19}$), m. p. 125–126°. The difficultly eluted alcohol fraction from the chromatogram was shown to consist of Δ^{22}-coprostigmasten-3α-ol and Δ^{22}-stigmasten-3β-ol.

In Part X of this series[15] the preparation was reported of various derivatives of ergostane and coproergostane possessing an isolated ethylenic linkage in the side chain. It was shown that there is no "vicinal action"[13,16] between this structural feature and the 3-hydroxyl group for the conversion of the latter to the acetate, benzoate or ketone. It is of interest to compare the data now reported for stigmastane and coprostigmastane derivatives with the earlier work. The table confirms the absence of "optical anomalies"[13,16] on acylation or oxidation.

A further aspect of the molecular rotation data is the determination of the true Δ value for the reduction of the isolated ethylenic linkage at the 22(23)-position in the stigmastane series. Previously an analysis of the literature[17] had indicated a value of about +61 units. The revised value of +94 now found (see table) refers to compounds in which, from our previous studies,[13,16] "vicinal action" is very unlikely to be appreciable. It may be compared with a mean value of +103 units for corresponding compounds in the ergostane series.[15] One must conclude that "vicinal action" between two isolated ethylenic linkages, as in "α"-dihydroergosterol and stigmasterol, is more pronounced than had previously been thought.[18]

(9) It should be pointed out that the stigmastadienone used by Marker and Wittle in their experiments was said to have a m. p. 94°.[10] All later workers[11,12,13] have given m. p.s above 120° for this ketone.

(10) Compare Marker and Rohrmann, THIS JOURNAL, **60**, 1073 (1938).

(11) Fernholz and Stavely, *ibid.*, **61**, 2956 (1939).

(12) Jones, Wilkinson and Kerlogue, *J. Chem. Soc.*, 391 (1942).

(13) Barton and Cox, *ibid.*, 783 (1948).

(14) Pairs of 3β (*trans* A/B)- and 3α (*cis* A/B)-stanols form high-melting 1:1-complexes (compare Lettré, *Ann.*, **495**, 41 (1932); Dirscherl and Kraus, *Z. physiol. Chem.*, **253**, 64 (1938); Sobotka, "The Chemistry of the Sterids," Baillière, Tindall and Cox, London, 1938).

(15) Barton, Cox, and Holness, *J. Chem. Soc.*, 1771 (1949).

(16) Barton and Cox, *Nature*, **159**, 470 (1946).

(17) Barton, *J. Chem. Soc.*, 512 (1946).

(18) The reservation applied to such linkages in our prior classification (Barton and Cox, *ibid.*, 788 (1948)) is not, therefore, justified and the original table stands without qualification.

TABLE I

Substance	[M]D Alc.[a]	Ac.[b]	Benz.[c]	Ketone	Δ_1[d]	Δ_2	Δ_3
Δ^{22}-Ergosten-3β-ol[15]	− 40	− 75	− 40	+ 28	−35	± 0	+68
Δ^{22}-Stigmasten-3β-ol	+ 8	− 27	+ 5	+ 82	−35	− 3	+74
Stigmastan-3β-ol[e]	+100	+ 69	+104	+170	−31	+ 4	+70
Δ (Mean Δ = +94)	+ 92	+ 96	+ 99	+ 88			
Δ^{22}-Coproergosten-3α-ol[15]	− 16	+ 71	+ 45	− 4	+87	+61	+12
Δ^{22}-Coprostigmasten-3α-ol	+ 17	+100	+ 73	+ 54	+83	+56	+37
Coprostigmastan-3α-ol	+125	+211		+141	+86		+16
Δ	+108	+111		+ 87			

[a] Alcohol. [b] Acetate. [c] Benzoate. [d] [M]D Acetate − [M]D Alcohol, etc. [e] Data from Barton, *Angew. Chem.*, **61**, 57 (1949).

Experimental[19]

Partial Hydrogenation of Stigmastadienone.—Three grams of stigmastadienone, m. p. 123–124°, $[\alpha]_D$ + 62° (*c*, 1.51), prepared by Oppenauer oxidation of stigmasterol,[11,12,13] was dissolved in 100 ml. of ethyl acetate and shaken with 120 mg. of platinum oxide catalyst in an atmosphere of hydrogen until 1.13 molar proportions of hydrogen had been absorbed (about 35 minutes). The catalyst was removed by filtration and the solvent by evaporation at reduced pressure. The residue was dissolved in petroleum ether, b. p. 40–60° and chromatographed[20] over alumina. The following chromatogram is typical (each fraction was crystallized once from methanol or ethyl acetate).

TABLE II

Fraction		Eluent, ml.	M. p., °C.
1	500	Petroleum ether, b. p. 40–60°	*ca.* 85–90 (v. small amount)
2	650	Petroleum ether, b. p. 40–60°: benzene, benzene content increasing to 50%	Nothing eluted
3	50	Petroleum ether, b.p. 40–60°: benzene, benzene content 60%	100–104
4	50		104–107
5	30		102–106
6	30		102–106
7	30		136–140
8	30		*ca.* 136
9	30		144–146
10	30		144–146
11	30		144–147
12	30		160–165
13	30		156–162
14	30		160–164
15	30		162–166
16	150		164–166
17	450	Petroleum ether, b. p. 40–60°: benzene, benzene content increasing to 100%	Nothing eluted
18	450	Benzene: ether, ether content increasing from 5 to 10%	146–150
19	100	Benzene: ether, ether content 20%	Nothing eluted
20	200	Benzene: ether, ether content 50%	153–156

Δ^{22}-Coprostigmasten-3-one.—Fractions 3 to 6 inclusive from the above chromatogram were combined and recrystallized from ethyl acetate–methanol to give Δ^{22}-coprostigmasten-3-one, m. p. 107–108°, $[\alpha]_D$ + 13° (*c*, 2.06), + 13° (*c*, 3.34), $[M]_D$ + 54°.

Anal. Calcd. for $C_{29}H_{48}O$: C, 84.4; H, 11.7. Found: C, 84.1; H, 11.4.

The ketone gave a yellow 2,4-dinitrophenylhydrazone, purified by chromatography and recrystallization from chloroform–methanol, m. p. 213°.

Δ^{22}-Stigmasten-3-one.—Fractions 12 to 16 inclusive from the above chromatogram were combined and recrystallized from ethyl acetate–methanol to give Δ^{22}-stigmasten-3-one, m. p. 166–167°, $[\alpha]_D$ + 19° (*c*, 2.73), + 20° (*c*, 2.58), $[M]_D$ + 82°; no absorption in the ultraviolet in the range 220–260 mμ.

Anal. Calcd. for $C_{29}H_{48}O$: C, 84.4; H, 11.7. Found: C, 84.4; H, 11.3.

The yellow dinitrophenylhydrazone, purified as above, had m. p. 225°.

Fractions 9 to 13 inclusive were combined and recrystallized from ethyl acetate–methanol: m. p. 147–148°, $[\alpha]_D$ + 15° (*c*, 2.49), + 15° (*c*, 2.09). A mixture of 66% Δ^{22}-coprostigmasten-3-one and 34% Δ^{22}-stigmasten-3-one, recrystallized in the same way, had the same m. p. and rotation and gave no depression in m. p. on admixture. On prolonged recrystallization of the material from the chromatogram, the m. p. rose to 161–163°. Clearly these intermediate fractions consisted of a mixture of the two Δ^{22}-ketones.

Reduction of Δ^{22}-Coprostigmasten-3-one with Sodium and *n*-Propanol.—210 g. of Δ^{22}-coprostigmasten-3-one was reduced with sodium and *n*-propanol and the product worked up as described previously.[15] In this particular experiment the reduction period was somewhat prolonged (about two and one-half hours). The β-alcohol fraction amounted to about 20 mg. After acetylation, chromatography over alumina, and crystallization from ethyl acetate–methanol it gave Δ^{22}-coprostigmasten-3β-yl acetate, m. p. 123°, $[\alpha]_D$ + 2° (*c*, 0.50), + 4° (*c*, 0.64), $[M]_D$ + 14°, which, however, may not have been completely homogeneous.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.5; H, 11.5. Found: C, 81.3; H, 11.5.

The α-alcohol fraction was acetylated and purified as above to give Δ^{22}-coprostigmasten-3α-yl acetate, m. p. 150.5–151.5°, $[\alpha]_D$ + 22°, (*c*, 1.95), + 23° (*c*, 1.59), $[M]_D$ + 100°.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.5; H, 11.5. Found: C, 81.5; H, 11.4.

Hydrolysis of this acetate and recrystallization of the product from acetone gave Δ^{22}-coprostigmasten-3α-ol, m. p. 152–153°, $[\alpha]_D$ + 4° (*c*, 1.02), + 4° (*c*, 1.84), $[M]_D$ + 17°.

Anal. Calcd. for $C_{29}H_{50}O$: C, 84.0; H, 12.2. Found: C, 83.5; H, 12.0.

Benzoylation of the alcohol and recrystallization of the product from chloroform–methanol furnished Δ^{22}-coprostigmasten-3α-yl benzoate, m. p. 112–114°, $[\alpha]_D$ + 14° (*c*, 2.82), + 14° (*c*, 2.93), $[M]_D$ + 73°.

(19) M. p.'s are not corrected. All specimens were dried *in vacuo* at 20° below their m. p.'s, or at 120°, whichever was the lower temperature, before the rotations were measured. All rotations are for the NaD line and for chloroform solutions. The measurements were made at room temperature which varied from 15–25°. All values of $[\alpha]_D$ have been approximated to the nearest degree. Concentrations (c) are expressed in g. per 100 ml. of solution. Standard procedures (acetylation, benzoylation, alkaline hydrolysis) were carried out as in Part IV (Barton and Cox, *J. Chem. Soc.*, 783 (1948)). Micro-analyses are by Drs. Weiler and Strauss, Oxford.

(20) Barton and Jones, *ibid.*, 599 (1943).

Anal. Calcd. for $C_{36}H_{54}O_2$: C, 83.3; H, 10.5. Found: C, 83.1; H, 10.2.

Reduction of Δ^{22}-Stigmasten-3-one with Sodium and *n*-Propanol.—In this reduction the reaction time was limited to one hour and the product was almost entirely 3β-alcohol, with very little of the epimer. Acetylation of the 3β-alcohol fraction and purification by chromatography over alumina and recrystallization from ethyl acetate–methanol afforded Δ^{22}-stigmasten-3β-yl acetate, m. p. 144–144.5°, $[\alpha]_D$ −7° (*c*, 1.10), −6° (*c*, 3.14), $[M]_D$ − 27°.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.5; H, 11.5. Found: C, 81.4; H, 11.2.

Hydrolysis of the acetate and recrystallization of the product from methanol furnished Δ^{22}-stigmasten-3β-ol, m. p. 159°, $[\alpha]_D$ + 2° (*c*, 1.82), + 2° (*c*, 2.34), $[M]_D$ + 8°.

Anal. Calcd. for $C_{29}H_{50}O \cdot 0.5H_2O$: C, 82.1; H, 12.1. Found: C, 82.5; H, 11.9.

Benzoylation of the alcohol and recrystallization of the product from chloroform–methanol gave Δ^{22}-stigmasten-3β-yl benzoate, m. p. 153–154°, $[\alpha]_D$ + 1° (*c*, 1.13), + 1° (*c*, 1.06), $[M]_D$ + 5°.

Anal. Calcd. for $C_{36}H_{54}O_2$: C, 83.3; H, 10.5. Found: C, 83.4; H, 10.2.

Similar sodium–*n*-propanol reduction of the chromatogram fractions containing the mixed ketones (see above), again keeping the reaction time as short as possible, afforded Δ^{22}-stigmasten-3β-yl acetate and Δ^{22}-coprostigmasten-3α-yl acetate in comparable amounts.

Preparation of a Molecular Complex of Δ^{22}-Coprostigmasten-3α-ol and Δ^{22}-Stigmasten-3β-ol.—A mixture was prepared of 9 mg. of each of the above alcohols: one crystallization from chloroform–methanol yielded 14 mg. of material, m. p. 188°, which was more highly crystalline than either component, and which was converted on acetylation to a mixture of acetates, m. p. 119°, unchanged after three recrystallizations.

Hydrogenation of Δ^{22}-Coprostigmasten-3α-yl Acetate.—70 mg. of Δ^{22}-coprostigmasten-3α-yl acetate was dissolved in 50 ml. of 1:1 acetic acid–ethyl acetate and hydrogenated using a platinum catalyst for two and one-half hours. After working up in the usual way and recrystallization from ethyl acetate–methanol, coprostigmasten-3α-yl acetate, m. p. 95°, $[\alpha]_D$ + 46° (*c*, 1.28), + 45° (*c*, 1.28), $[M]_D$ + 211°, was obtained.

Anal. Calcd. for $C_{31}H_{54}O_2$: C, 81.2; H, 11.9. Found: C, 80.9; H, 11.9.

Hydrolysis of the acetate and recrystallization of the product from methanol afforded coprostigmastan-3α-ol, m. p. 134–136°, $[\alpha]_D$ + 30° (*c*, 2.96), + 30° (*c*, 0.97), $[M]_D$ + 125°. Dirscherl and Kraus[21] found m. p. 138–139°, $[\alpha]_D$ + 30° (in chloroform) for this alcohol.

Hydrogenation of Δ^{22}-Stigmasten-3β-yl Acetate.—25 mg. of Δ^{22}-stigmasten-3β-yl acetate was dissolved in 20 ml. of 1:1 acetic acid–ethyl acetate and hydrogenated as indicated above. After working up as usual, the product was recrystallized from ethyl acetate–methanol to give stigmastan-3β-yl acetate, m. p. 129°, not depressed in m. p. when mixed with an authentic specimen.[22] Hydrolysis and recrystallization of the product from methanol gave stigmastan-3β-ol, m. p. 134–135°, not depressed in m. p. on admixture with an authentic specimen.[22]

Neutral Hydrogenation of Δ^{22}-Coprostigmasten-3-one.—One gram of Δ^{22}-coprostigmasten-3-one was dissolved in 100 ml. of ethyl acetate and hydrogenated for four hours using a platinum catalyst in the usual way. After removal of catalyst and solvent, the product was chromatographed over alumina. The material eluted by 95:5-light petroleum (b. p. 40–60°):benzene was ketonic and gave a yellow 2,4-dinitrophenylhydrazone, purified as above, m. p. 204°. Recrystallization of the ketone from ethyl acetate–methanol afforded coprostigmastan-3-one, m. p. 113–114°, $[\alpha]_D$ + 34° (*c*, 1.87), $[M]_D$ + 141°. For this ketone Rosenheim and Webster[23] give m. p. 113–114°, and Marker and Wittle[7] m. p. 114°. The alcohol fractions, eluted from the column (as the main reduction product) by benzene–ether, were separated into α- and β-fractions in the usual way. From the former there was obtained coprostigmastan-3α-yl acetate identical with the specimen obtained as described above, while the latter afforded somewhat impure coprostigmastan-3β-yl acetate, m. p. 81–84°, $[\alpha]_D$ + 21° (*c*, 1.03), $[M]_D$ + 96°. On further hydrogenation the m. p. rose to 88–89° (Liebermann–Burchard reaction negative), the value previously recorded for this acetate.[7,23]

Neutral Hydrogenation of Δ^{22}-Stigmasten-3-one.—50 mg. of Δ^{22}-stigmasten-3-one was hydrogenated in ethyl acetate solution as for the copro-isomer (see above). Separation of the product by treatment with digitonin afforded as the main reaction product a β-alcohol fraction which on acetylation furnished an acetate mixture, m. p. 133–136°, $[\alpha]_D$ + 1°: this proved to be still unsaturated, but further hydrogenation in acetic acid solution, followed by hydrolysis, gave stigmastan-3β-ol (crystallized from methanol), m. p. 134–135°, not depressed by admixture with an authentic specimen.[22]

Examination of the Hydrocarbon Fraction.—The hydrocarbon fraction from the chromatogram (see above), combined with a similar small fraction from a second experiment, amounted to 50 mg., m. p. *ca.* 85–90°, $[\alpha]_D$ + 2° (*c*, 2.76). We regard this as a mixture of Δ^{22}-stigmastene and Δ^{22}-coprostigmastene: the calculated rotation[24] for such a mixture, assuming equal amounts and based on the rotations given above for Δ^{22}-stigmasten-3β-ol and Δ^{22}-coprostigmasten-3α-ol, is 0 ± 2° and excludes serious contamination by $\Delta^{4,22}$-stigmastadiene, stigmastane or coprostigmastane. Chromatography of the mixed hydrocarbons over alumina failed to achieve any significant separation but many recrystallizations from chloroform–methanol finally raised the m. p. to 125–126°. We regard the material of this m. p. as Δ^{22}-stigmastene: there was too little for accurate analysis. The mother-liquors from the crystallizations were combined and, after removal of solvent, treated with a slight excess of bromine in ether–acetic acid solution. After several hours the product was worked up, yielding a crystalline dibromide, recrystallized from chloroform–methanol, m. p. 167° (dec.), unchanged on further recrystallization.

Anal. Calcd. for $C_{29}H_{50}Br_2$: Br, 28.6. Found: Br, 27.4.

The low m. p. suggested that the dibromide was derived from Δ^{22}-coprostigmastene: this was confirmed by treatment with zinc dust in 1:1 chloroform–acetic acid on a boiling water-bath for one hour, which gave Δ^{22}-coprostigmastene, recrystallized from methanol, m. p. 67–68°.

Anal. Calcd. for $C_{29}H_{50}$: C, 87.4; H, 12.6. Found: C, 86.4; H, 12.4.

Marker and Wittle[7] obtained a hydrocarbon by-product (not analyzed), m. p. 72°, by reduction of stigmastadienone with sodium and amyl alcohol; this was probably substantially Δ^{22}-coprostigmastene.

Examination of the Alcohol Fraction.—Fractions 18 and 20 of the original chromatogram represent somewhat impure Δ^{22}-coprostigmasten-3α-ol and Δ^{22}-stigmasten-3β-ol, respectively. In a second experiment, the alcohols were eluted by ether as one fraction, m. p. 183–185°, which was evidently the 1:1 complex (see above). Resolution by the digitonin method and purification as the corresponding acetates afforded Δ^{22}-coprostigmasten-3α-yl acetate, m. p. 150–151°, undepressed in m. p. on admixture with authentic material (see above), and Δ^{22}-stigmasten-3β-yl acetate, m. p. 142.5–143.5°, the identity of which was similarly confirmed.

Summary

Stigmastadienone has been converted by partial

(21) Dirscherl and Kraus, *Z. physiol. Chem.*, **253**, 64 (1938).

(22) Barton and Cox, *J. Chem. Soc.*, 1354 (1948).

(23) Rosenheim and Webster, *Biochem. J.*, **35**, 928 (1941).

(24) Barton and Klyne, *Chem. and Ind.*, 755 (1948).

hydrogenation to Δ^{22}-stigmasten-3-one and Δ^{22}-coprostigmasten-3-one, as well as other products.

Reduction of the former ketone gave Δ^{22}-stigmasten-3β-ol (5,6-dihydrostigmasterol), and of the latter, Δ^{22}-coprostigmasten-3α-ol.

The changes in molecular rotation associated with the hydrogenation of the steroidal side chain 22(23)-ethylenic linkage have been discussed.

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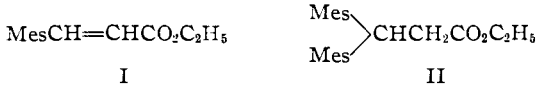
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Conjugate Addition of Mesitylmagnesium Bromide to Ethyl 2,4,6-Trimethylcinnamate and to Mesitalacetomesitylene

BY REYNOLD C. FUSON AND HAROLD L. JACKSON[1]

A mesityl radical in the *beta* position in an α,β-unsaturated carbonyl compound is known not to block the entry of hydrocarbon radicals into that position in reactions with Grignard reagents.[2] In particular it has been shown that the mesityl radical likewise can enter the *beta* position in such molecules.[3]

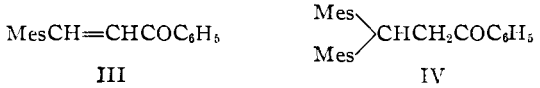
The present work was designed to determine whether mesitylmagnesium bromide would attack a *beta* carbon atom already holding a mesityl group in carbonyl compounds in which the carbonyl group is not blocked by hindering radicals, *i. e.*, is free to react in the normal manner. When ethyl 2,4,6-trimethylcinnamate (I) was treated with an excess of the Grignard reagent, ethyl β,β-dimesitylpropionate (II) was formed. Although the experiment was run on a small scale, it was possible to isolate the product in 47% yield. No other organic product could be detected.



I II

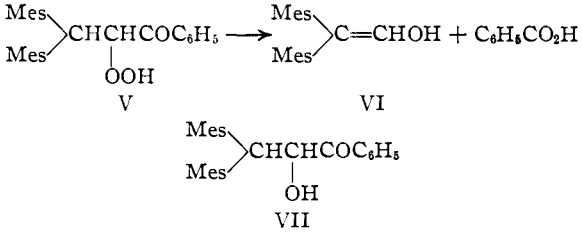
The structure of the dimesityl ester was established by hydrolysis; the β,β-dimesitylpropionic acid which formed was found to be identical with an authentic sample.[4]

Mesitalacetophenone (III) reacted with mesitylmagnesium bromide to give an 84% yield of the conjugate addition product, β,β-dimesitylpropiophenone (IV).



III IV

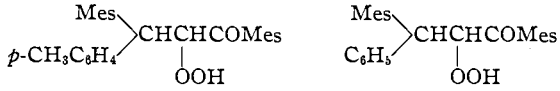
The structure of the new ketone was confirmed by the preparation of the oxime and reduction to the carbinol. By treatment of the solution of the enol with oxygen, it was possible also to prepare the hydroperoxide (V), which when heated above its melting point decomposed to dimesitylvinyl alcohol (VI) and benzoic acid.



V VI VII

Reduction of the hydroperoxide with either a mixture of potassium iodide and acetic acid or hydrogen over a platinum catalyst gave a product which melted at 137.0–139.5° and had the composition indicated by formula VII.

The formation of the hydroperoxide was surprising since no hindering radical is attached to the carbonyl carbon and since hydrogen, rather than a hydrocarbon residue, is attached to the *alpha* carbon atom.



VIII IX

The infrared absorption spectrum[5] of the hydroperoxide (V) shows a strong band at 1678 cm.$^{-1}$. Compounds VIII and IX[6] had absorption bands at 1685 and 1680 cm.$^{-1}$, respectively. Infrared absorption in this region is indicative of the presence of the singly conjugated carbonyl group. These results are in agreement with the recent findings of Rigaudy.[7] Because ultraviolet absorption spectra showed the presence of a carbonyl group, this author assigned the hydroperoxide structure rather than the cyclic peroxide structure suggested by Kohler[8] for such stable peroxides.

Experimental[9]

Ethyl β,β-Dimesitylpropionate (II).—A well-stirred, cold solution of mesitylmagnesium bromide, prepared from 32 g. of bromomesitylene, 3.9 g. of magnesium and 50 ml.

(1) Socony-Vacuum Oil Company Fellow 1948–1949. Present address: E. I. du Pont de Nemours and Company, Wilmington, Delaware.

(2) Kohler and Blanchard, THIS JOURNAL, **57**, 367 (1935).

(3) Fuson and Meek, *J. Org. Chem.*, **10**, 551 (1945).

(4) Fuson and Jackson, THIS JOURNAL, **72**, 351 (1950).

(5) The infrared absorption spectra were determined and interpreted by Miss Elizabeth M. Peterson.

(6) Fuson and Tan, THIS JOURNAL, **70**, 602 (1948).

(7) Rigaudy, *Compt. rend.*, **226**, 1993 (1948).

(8) Kohler, *Am. Chem. J.*, **36**, 185 (1906).

(9) The microanalyses were performed by Miss Emily Davis and Miss Rachel Kopel.