[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

The Ultraviolet Absorption Spectra of the Monofluoropyridines and the Monofluoroquinolines

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The preparation of the monofluoropyridines and the monofluoroquinolines in this Laboratory[1] has made possible a study of the absorption spectra of these compounds. The investigation was carried out to determine the effect which the introduction of fluorine into pyridine and quinoline has on the absorption spectra of these compounds. The effect on the absorption spectra of varying the *p*H and the concentrations of ethanol and water as the solvent was also studied.

The absorption spectra of all of the fluoropyridines and -quinolines, with the exception of the unstable 4-isomers,[1] were measured. For comparison, the absorption spectra of pyridine and quinoline, as well as those of the 2- and 6-chloroquinolines, were determined. The spectra of all the fluoro compounds were measured in 95% ethanol, 10% ethanol by weight in water, 10% ethanol which was 0.01 *M* with sodium hydroxide, and 10% ethanol which was 0.01 *M* with hydrochloric acid. The spectra of pyridine and quinoline were measured in the same solutions, while that of 3-fluoroquinoline was also determined in 40% ethanol. 2- and 6-Chloroquinoline were studied only in 95% ethanol. The maxima obtained are reported in Table I. The absorption spectra of other halopyridines and haloquinolines will be studied when they become available at this Laboratory.

Hartley[2] reported absorption spectra of both pyridine and quinoline in alcohol. Purvis[3] confirmed the results of Hartley and concluded that in general the weighting of the nucleus by the introduction of another atom or radical to an aromatic structure resulted in a shift of the absorption band to a longer wave length and an increase in its intensity. Baker and Baly[4] found that the introduction of a methyl group into the pyridine nucleus exhibited both a bathochromic and a hyperchromic effect. Spiers and Wibaut[5] measured the absorption of pyridine, some of the halopyridines, a number of the dihalopyridines and the aminopyridines, using heptane as a solvent. It was concluded that the halogen atom tends to shift the absorption toward longer wave lengths, and that this tendency increased from the chloro through the iodo derivatives; the displacement appears greater when the halogen is closer to the nitrogen atom. A second halogen tends to shift still more toward the red end of the spectrum, while the amino group has a far greater bathochromic effect than any of the halogens. Anderson and Seeger[6] and Steck and Ewing[7] have studied the absorption spectra of the aminopyridines, and the latter authors, in addition, measured those of the amino derivatives of quinoline and isoquinoline. Ewing and Steck[8] also studied the absorption of pyridinols and quinolinols. These investigations were made for the purpose of assigning structure, but the results verified the strong bathochromic effect of the amino and hydroxyl groups.

If the fluoropyridines were to fit into the pattern proposed by Spiers and Wibaut[5] for the halopyridines, we should expect them to absorb at longer wave lengths than pyridine, but at shorter wave lengths than the chloro derivatives. That they absorb farther toward the red than pyridine is shown in Fig. 1, and the maxima of both fluoro

TABLE I

SPECTRAL DATA OF SOME HALOPYRIDINES AND QUINOLINES[a]

Compound	Maxima: λ in mμ, ε × 10⁻³ (given in parentheses) In 95% ethanol	In 10% ethanol	In 0.01 *M* hydrochloric acid[b]
Pyridine	251 (2.37), 257 (2.61)	251 (2.56), 257 (2.85)	255–256 (5.32)
2-Fluoropyridine	358 (3.26)	358 (3.20)	[c]
3-Fluoropyridine	263 (3.11)	262 (3.22)	262–263 (5.22)
Quinoline	300 (3.13), 276–277 (3.59), 313 (3.41)	277 (3.47), 300 (3.26), 313 (3.45)	313 (6.92)
2-Fluoroquinoline	269–270 (3.81), 299 (2.55), 312 (2.88)	271–272 (3.77), 299 (2.70), 312 (2.64)	271–272 (6.18), 424 (6.20)
3-Fluoroquinoline	280–287 (3.18), 306 (3.27), 319 (3.52)	286–288 (3.19), 306 (3.33), 318 (3.33)	317 (5.26)
5-Fluoroquinoline	281–289 (3.18), 300–301 (2.62), 314 (1.85)	288–289 (3.21), 300 (2.80), 313 (2.03)	312–313 (4.59)
6-Fluoroquinoline	269–272 (3.82), 302 (3.01), 316 (3.74)	271–273 (3.71), 302 (3.04), 315 (3.53)	311–312 (6.85)
7-Fluoroquinoline	270 (3.15), 303 (3.18), 316 (3.80)	271–272 (3.18), 303 (3.31), 315 (3.65)	311–315 (6.18)
8-Fluoroquinoline	280–288 (3.30), 300 (2.59), 313 (1.67)	288 (3.30), 299–300 (2.78), 313 (1.92)	312 (4.61)
2-Chloroquinoline	276–280 (3.57), 304 (2.75), 318 (4.69)		
6-Chloroquinoline	273 (3.97), 306 (2.96), 320 (3.85)		

[a] The spectra in 10% ethanol which is 0.01 *M* with sodium hydroxide is almost identical with that in 10% ethanol [b] The hydrochloric acid solution contains 10% ethanol by weight. [c] Identical with that in 10% ethanol.

(1) Roe and Hawkins, THIS JOURNAL, **69**, 2443 (1947); **71**, 1785 (1949).
(2) Hartley, *J. Chem. Soc.*, **47**, 685 (1885).
(3) Purvis, *ibid.*, **95**, 294 (1909); **97**, 1035 (1910).
(4) Baker and Baly, *ibid.*, **91**, 1122 (1907).
(5) Spiers and Wibaut, *Rec. trav. chim.*, **56**, 573 (1937).
(6) Anderson and Seeger, THIS JOURNAL, **71**, 340 (1949).
(7) Steck and Ewing, *ibid.*, **70**, 3397 (1948).
(8) Ewing and Steck, *ibid.*, **68**, 2181 (1946).

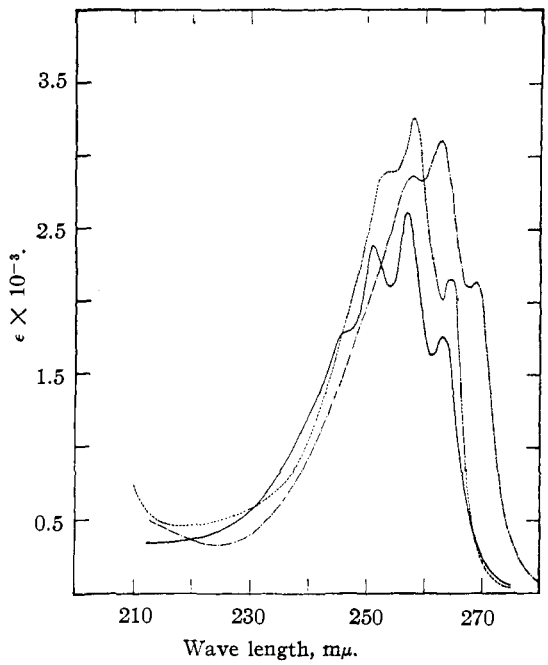

Fig. 1.—Ultraviolet absorption of the fluoropyridines in 95% ethanol: —, pyridine; ..., 2-fluoropyridine; ·—, 3-fluoropyridine.

derivatives occur at shorter wave lengths than those reported by Spiers and Wibaut for the chloropyridines. However, the fluoropyridines form an exception to the generalization, in that the spectrum of the 3-isomer is displaced more toward the red than that of the 2-isomer. The molecular extinction coefficient of the 2-fluoropyridine at the maximum is greater than that of the 3-isomer as would be predicted, although the difference is not great. It is interesting to note that the introduction of the fluorine atom has very little effect on the general shape of the pyridine curve, producing only a bathochromic and hyperchromic shift.

The ultraviolet spectrum of quinoline in the region beyond λ230 exhibits three maxima (Fig. 2) at λ276–277, λ300 and λ313, with wave lengths expressed in mμ. The molecular extinction coefficients at these wave lengths are, respectively, 3.59×10^3, 3.13×10^3 and 3.41×10^3. This differs from the results of some of the earlier investigators,[2,3] but compares very well with Ewing and Steck,[8] although a close comparison is impossible because of the scale which the latter authors used.

Although the absorption spectra of the haloquinolines have not been reported in the literature, we might predict that the introduction of a halogen would produce a bathochromic shift as well as an increase in extinction since the general tendency has been in this direction when an aromatic nucleus is weighted by the addition of another atom or radical. Of the six monofluoroquinolines only three, the 3-, 5- and 8-isomers (Figs. 2 and 3), produce the expected bathochromic shift of the first or principal (276–277 mμ) band of quinoline, while the 2-, 6- and 7-isomers produce an unexplained hypsochromic shift of the first maximum. All three isomers which exhibit the expected bathochromic shift, as well as 7-fluoroquinoline, show an unexpected decrease in extinction at that maximum. The extinction coefficients of the 2- and 6-fluoroquinolines are increased over that of quinoline at the main absorption band. No shifts of the 2nd and 3rd maxima are apparent for the 2-, 5- and 8-isomers, but bathochromic shifts are exhibited by the other three compounds. The 3-, 6- and 7-isomers show a marked increase in extinction at the third maximum, while the second and third absorption bands almost disappear in the 5- and 8-isomers.

It is readily seen from Fig. 2 that the 5- and 8-fluoroquinolines have almost identical absorption curves in 95% ethanol. (This similarity of absorption is just as apparent in other solutions, including that containing hydrochloric acid.) It is interesting to note in this connection that these two isomers both bear formal analogy to α-fluoronaphthalene, and both have the fluorine in the benzenoid ring. No such similarity is noticed in the 6- and 7-isomers, which are analogous to β-fluoronaphthalene.

Figure 4 shows the absorption spectra of quinoline, 2-chloroquinoline and the 2-fluoro derivative; Fig. 5 shows the spectra of quinoline and the corresponding 6-halo derivatives. There are bathochromic shifts of the first maxima in passing from the fluoroquinolines to the chloroquinolines, but the principal band of 6-chloroquinoline is still displaced toward shorter wave lengths than that of quinoline. The extinction coefficient at the maximum of 6-chloroquinoline is decreased over that of the corresponding fluoro derivative, while the order is reversed for the 2-haloquinolines. The second and third maxima are both shifted toward the red in the chloroquinolines with the extinction coefficients decreasing at the second maximum and increasing at the third in both cases. Since the exceptions are about as numerous as the generalizations based on the work of previous investigators, it is believed that a complete series of the haloquinolines will have to be examined before a definite pattern of absorption can be designated.

Of prime interest in connection with the absorption spectra of the fluoropyridines and fluoroquinolines is the effect produced by varying the solvent. Fischer and Steiner[9] measured the absorption of pyridine in hexane, ether, carbon tetrachloride, alcohol and water. They found five small bands in the spectra determined in the nonpolar solvents which were not detected in alcohol and water. In addition, the latter two solvents shifted the position of maximum absorption slightly to the far ultraviolet. Two explanations for the differences are forthcoming. First, the

(9) Fischer and Steiner, *Compt. rend.*, **175**, 882 (1922).

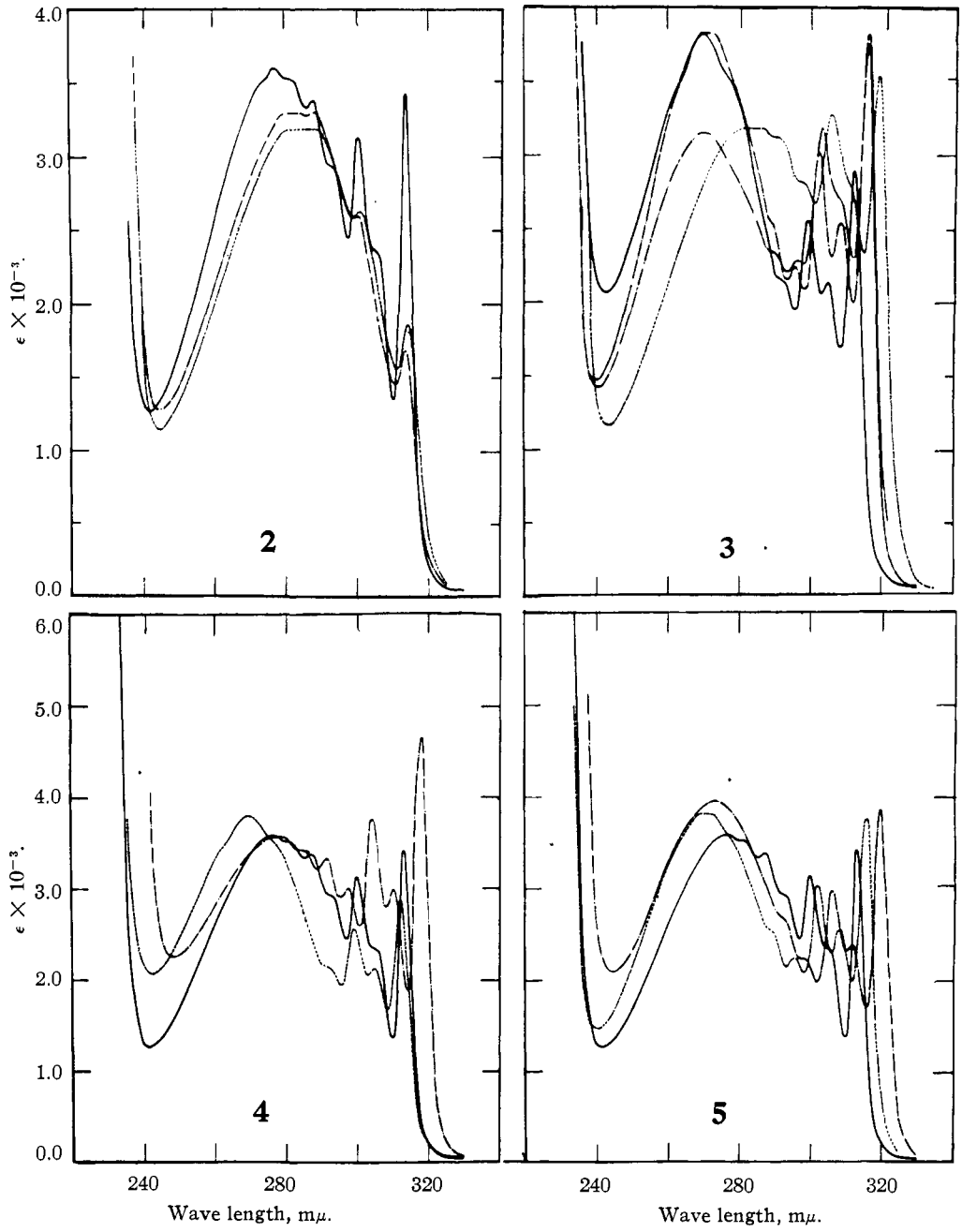

Fig. 2.—Ultraviolet absorption in 95% ethanol of: —, quinoline; . . ., 5-fluoroquinoline; ·—·, 8-fluoroquinoline.
Fig. 3.—Ultraviolet absorption in 95% ethanol of: —, 2-fluoroquinoline; . . ., 3-fluoroquinoline; ·—·, 6-fluoroquinoline; – – –, 7-fluoroquinoline.
Fig. 4.—Ultraviolet absorption in 95% ethanol of: —, quinoline; . . ., 2-fluoroquinoline; ·—·, 2-chloroquinoline.
Fig. 5.—Ultraviolet absorption in 95% ethanol of: —, quinoline; . . ., 6-fluoroquinoline; ·—·, 6-chloroquinoline.

molecules of the polar solvent would be expected to have a greater effect on the vibrations of the pyridine ring than the non-polar molecules, and consequently the absorption would be different. Secondly, the solvent molecules probably react with pyridine to form solvates, which would tend to change the absorption. Various hydrates of pyridine have been reported[10,11] and the solubility of pyridine in water is attributed to this compound formation. Although the fluoropyridines, quinoline and the fluoroquinolines are not soluble in water, the tendency to form hydrates and possibly

(10) Kornfield, *Monatsh.*, **36**, 865 (1915).
(11) Pariselle, *Compt. rend.*, **172**, 673 (1921).

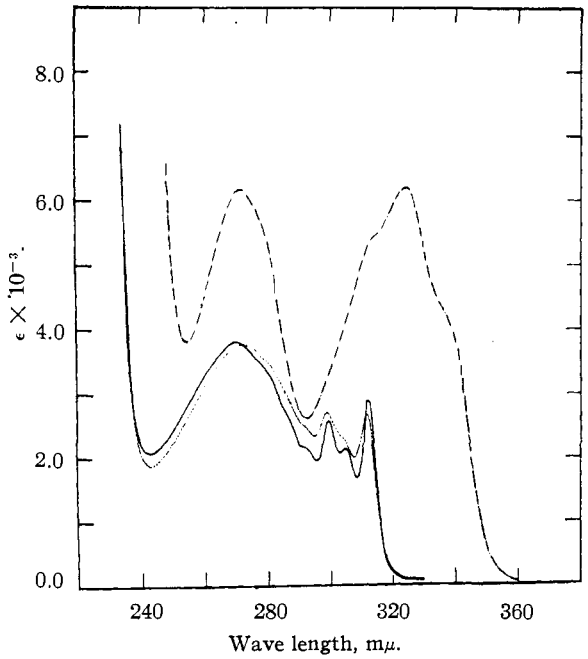

Fig. 6.—Ultraviolet absorption of 2-fluoroquinoline in: —, 95% ethanol; . . ., 10% ethanol; ·—·, 10% ethanol 0.01 *M* in hydrochloric acid.

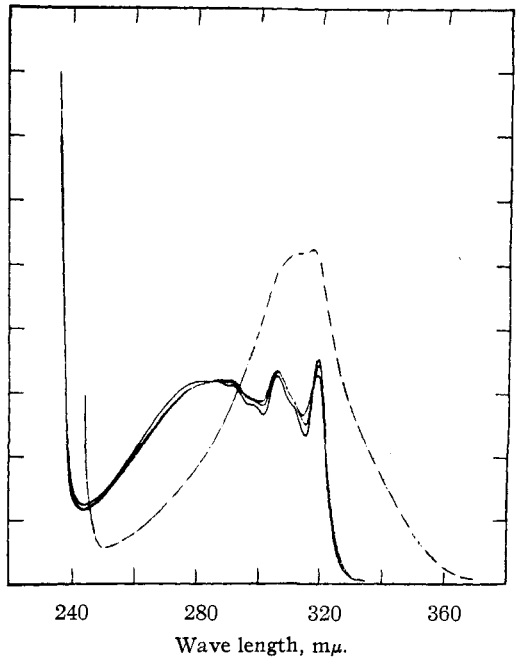

Fig. 7.—Ultraviolet absorption of 3-fluoroquinoline in: —, 95% ethanol; . . ., 40% ethanol; ·—·, 10% ethanol; – –, 10% ethanol 0.01 *M* in hydrochloric acid.

alcoholates is probably appreciable. As evidence, the formation of solid hydrates of 3- and 6-fluoroquinoline has been reported.[1] The extent of solvation, if it does occur, would be expected to depend on the concentration of the reacting solvent, and it is possible that solvation may be responsible for the differences in the spectra of the compounds in 95% ethanol and in 10% ethanol as seen in Figs. 6 and 7. If there is no solvation, then the variation must be due to the differences in polarity between alcohol and water and their relative effects on the nuclear vibration of the aromatic structures. The dilution of the ethanol has a similar effect on the spectra of all of the compounds which were studied.

One of the most interesting aspects of the study of the spectra of quinoline and pyridine compounds is the marked bathochromic shift which is produced by the addition of acid to the solvent. Baker and Baly[4] explain this shift in pyridine derivatives on the assumption that the benzenoid resonance is restrained by the unsaturated nature of the nitrogen atom, but that the restraint is removed by the addition of the hydrogen atom to the nitrogen in acid solution. Since the resonance energies of benzene and pyridine are now known to be very nearly the same, this explanation does not sound feasible. A more plausible explanation is given by Ewing and Steck,[8] who postulate additional resonance forms of quinoline in acid solution due to the positive charge migrating to different positions on the nucleus.

Quinoline and all of the fluoroquinolines exhibit the bathochromic shift of their spectra in 0.01 *M* hydrochloric acid solution as shown in Figs. 6 and 7. In acid solution, the three maxima which appear in alcohol solution for quinoline and the fluoroquinolines are replaced by a single maximum of longer wave length and increased extinction. The 2-fluoroquinoline is an exception to this (Fig. 6) since it shows two maxima in acid solution. As a matter of fact, it is surprising that the spectrum of 2-fluoroquinoline in acid solution exhibits a shift since it is reported[1] that the 2-fluoro derivatives of both quinoline and pyridine are insoluble in dilute hydrochloric acid, indicating that they do not form hydrochlorides. A possible explanation is that the difference in dielectric constants of water and 10% ethanol in water is sufficient to increase the basicity of 2-fluoroquinoline enough to form the hydrochloride in the 10% ethanol solution. The spectrum of 2-fluoropyridine in both acid and base are identical proving the inability of that compound to form a hydrochloride even in 10% ethanol. The spectra of pyridine and 3-fluoropyridine in acid solution showed a marked increase in extinction over that in neutral 10% alcohol, but the position of maximum absorption was not shifted. The addition of base was found not to have any appreciable effect on the spectra of any of the compounds.

Experimental

Absorption Spectra.—All spectra were determined with a Beckman quartz spectrophotometer, model DU, serial no. 958. Density measurements were never made at in-

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.