containing 1.5 ml. of 70% perchloric acid and 900 mg. of platinum oxide catalyst, and hydrogenated at atmospheric pressure. At the end of 3 days uptake was essentially complete and the reaction mixture was poured into 1000 ml. of water containing sodium bisulfite, and extracted repeatedly with ether. The combined ether extract was washed with saturated sodium carbonate solution and finally with saturated sodium chloride solution to neutrality, and then dried over magnesium sulfate. Drying reagent was filtered off and solvent removed leaving 19.5 g. of ester as a yellow oil.

α,α-Dimethyl-β-ferrocenylpropionic Acid (XXI).—Five grams of the above ester were dissolved in 200 ml. of methanol containing 10 g. of potassium hydroxide. The solution was heated at reflux in a nitrogen atmosphere for 4 hours, cooled and poured into water. Workup gave 2.94 g. of the acid, m.p. 143–147°. An analytical sample was obtained by recrystallization of the product from ether–petroleum ether.

Anal. Calcd. for $C_{15}H_{18}O_2Fe$: C, 62.93; H, 6.29. Found: C, 62.80; H, 6.35.

Cyclization of α,α-Dimethyl-β-ferrocenylpropionic Acid.—The acid (3.0 g., 0.01 mole), dissolved in 40 ml. of dry methylene chloride, was added, in a nitrogen atmosphere, to a refluxing solution of 5.5 g. of trifluoroacetic anhydride (0.03 mole) in 30 ml. of the same solvent. At the end of 24 hours, the solution was cooled and poured into 100 ml. of a 1% aqueous sodium hydroxide solution. After workup, the product was chromatographed on 600 g. of Merck alumina, eluting with petroleum ether–ether mixtures. Two bands developed; the first, light orange in color, gave 1.2 g. of crystalline ketone XXII which after one recrystallization from ether–petroleum ether had m.p. 134–135°.

Anal. Calcd. for $C_{15}H_{16}OFe$: C, 67.16; H, 5.97. Found: C, 67.00; H, 6.37.

The deeper orange band which followed this afforded 1.1 g. of the isomeric ketone as an orange oil.

Reduction of α-Keto-β,β-dimethyl-1,1′-trimethyleneferrocene. —The bridged ketone (1.8 g.) was taken up in 200 ml. of glacial acetic acid containing 2 ml. of 70% perchloric acid and hydrogenated in the presence of 200 mg. of platinum oxide catalyst at a pressure of 27 lb. After 24 hours, uptake was essentially complete and the reaction mixture was worked up in the normal manner. The crude product was taken up in a small volume of ether–petroleum ether (b.p. 30–60) and chromatographed on 200 g. of Merck alumina (2% water added) employing petroleum ether as eluent. In this manner 1.4 g. of product was obtained, m.p. 98–101°. Recrystallization from petroleum ether gave an analytical sample, m.p. 101–103°.

Anal. Calcd. for $C_{15}H_{18}Fe$: C, 70.86; H, 7.08. Found: C, 70.59; H, 7.22.

Deuterium Exchange Reactions.—β-Keto-1,1′-tetramethyleneferrocene (50.8 mg.), dissolved in 25 ml. of tetrahydrofuran freshly distilled from lithium aluminum hydride, was treated with 5 ml. of deuterium oxide and 54 mg. of sodium methoxide. After stirring the reaction mixture in a nitrogen atmosphere at room temperature for 16 hours, workup gave 44 mg. of ketone, m.p. 113–114°, whose infrared spectrum exhibited two new bonds at 4.5 and 4.54 μ as well as deep seated alteration in peak positions between 7 and 12 μ.

Similar treatment of α-keto-1,1′-trimethyleneferrocene for a period of 22 hr. gave a product whose infrared spectrum was identical with that of the starting material.

Optical Rotatory Dispersion Studies. LXXIX.[1] The Location of the n–π* Absorption Band of α-Iodo Ketones and its Relation to Circular Dichroism and Optical Rotatory Dispersion[2]

BY CARL DJERASSI, H. WOLF AND E. BUNNENBERG

The ultraviolet absorption, circular dichroism and optical rotatory dispersion curves have been measured of six optically active α-iodo ketones, in which the iodine atom either possessed the axial or equatorial orientation. or was attached to a methyl ketone grouping. In all but one instance, the ultraviolet absorption spectrum was nearly or totally useless in locating the n–π* absorption band in the 300 mμ region. It could, however, be recognized very readily by means of circular dichroism or optical rotatory dispersion measurements. The location of this band, as well as that of the iodine absorption in the 260 mμ region. can be related to the orientation (axial vs. equatorial) of the iodine atom in the same manner as has been done earlier with α-bromo· and α-chloro-ketones. Attention is called to the observation that, in the two steroidal α-iodo methyl ketones available for study. both optical rotatory dispersion and circular dichroism indicated the presence or even preponderance of that rotamer in which the I—C—C=O geometry approaches that of an axial α-iodocyclohexanone. For comparison purposes, ultraviolet absorption. circular dichroism and optical rotatory dispersion curves are also recorded for the analogous α-bromo ketones, where the n–π* absorption can be readily recognized by all three methods.

The ultraviolet absorption spectra of α-bromo- and α-chlorocyclohexanones (notably in the steroid series) have been studied in detail by Cookson,[3] who has noted characteristic shifts of the n–π* absorption band depending upon the axial or equatorial orientation of the halogen atom. The identical shifts were noted[4,5] in the optical rotatory dispersion curves and this physical tool is at times preferable for configurational assignments—especially among equatorially substituted α-halo ketones—where the ultraviolet absorption maxima are often ill defined.

In contrast to the wealth of published information on the close correlation of ultraviolet absorption and optical rotatory dispersion among α-bromo- and α-chlorocyclohexanones, very little is known about the corresponding situation among α-iodo ketones. The

two measurements which have been recorded[6] indicate that while a hypsochromic shift is noted in the ultraviolet absorption maximum—when compared with that of the halogen-free parent ketone—the rotatory dispersion extrema suffer a bathochromic shift. The following explanation was offered[7] for this apparent major discrepancy: "*The absorption band at 258 mμ is due to the iodine atom and apparently is not optically active, whereas the Cotton effect is associated with a second ultraviolet absorption maximum in the 290 mμ region—of sufficiently low intensity as to be masked by the iodine absorption and not detectable under the experimental condition employed—which is optically active and which corresponds to the carbonyl group. Circular dichroism studies would be very instructive with such α-iodo ketones, since they would settle this point unambiguously.*" The present paper is concerned with such measurements, which confirm completely the correctness of our earlier views.[7] Furthermore, we wish to call attention to some observations on the relative preference of axial vs. equatorial orientation in α-iodo ketones.

Just as in our earlier[1] communication on the relation of ultraviolet absorption, circular dichroism and optical

(1) Paper LXXVIII, C. Djerassi, H. Wolf and E. Bunnenberg, *J. Am. Chem. Soc.*, **84**, 4552 (1962).

(2) Supported by the National Science Foundation (grant No. G 19905) and the National Cancer Institute (grant No. CRTY-5061) of the National Institutes of Health, U. S. Public Health Service.

(3) R. C. Cookson, *J. Chem. Soc.*, 282 (1954); R. C. Cookson and S. H. Dandegaonker, *ibid.*, 352 (1955).

(4) C. Djerassi, J. Osiecki, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, **80**, 1216 (1958).

(5) C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 9.

(6) C. Djerassi, I. Fornaguera and O. Mancera, *J. Am. Chem. Soc.*, **81**, 2383 (1959).
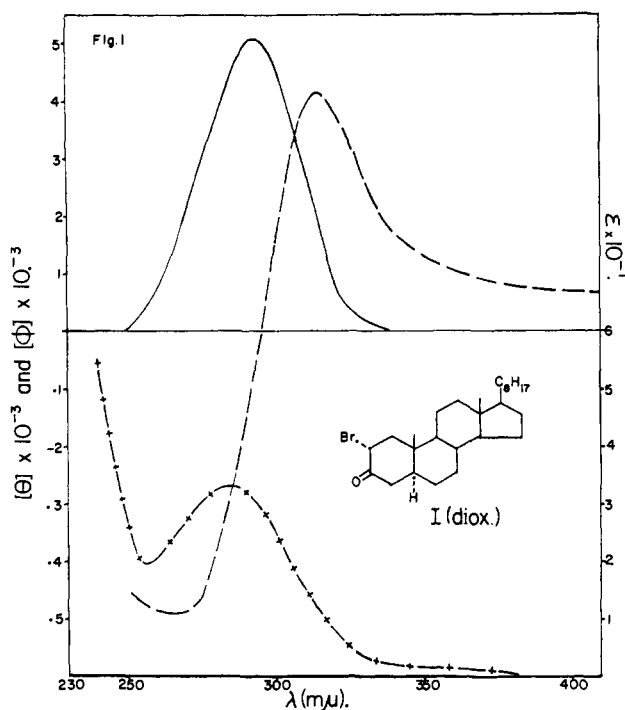
(7) Reference 5, p. 118.

Fig. 1.—Circular dichroism (————), optical rotatory dispersion (– – – –) and ultraviolet absorption (– + – +) curves of 2α-bromocholestan-3-one (1) in dioxane solution.
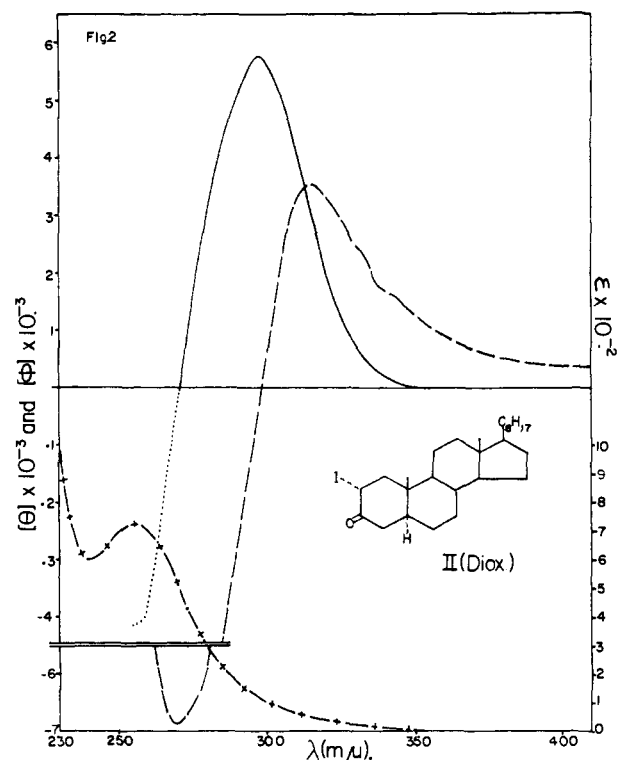

Fig. 2.—Circular dichroism (————), optical rotatory dispersion (– – – –) and ultraviolet absorption (– + – +) curves of 2α-iodocholestan-3-one (II) in dioxane solution.

Fig. 3.—Circular dichroism (————), optical rotatory dispersion (– – – –) and ultraviolet absorption (– + – +) curves of 3α-bromocholestan-2-one (III) in dioxane solution.

Fig. 4.—Circular dichroism (————), optical rotatory dispersion (– – – –) and ultraviolet absorption (– + – +) curves of 3α-iodocholestan-2-one (IV) in methanol solution.

rotatory dispersion among substances containing the C=S chromophore, all three parameters are recorded for each substance in Fig. 1–11.

For reference purposes, there are reproduced in Fig. 1 the ultraviolet absorption, circular dichroism and optical rotatory dispersion curves of a typical equatorial α-bromo ketone, 2α-bromocholestan-3-one (I). The appropriate maxima occur at the same wave lengths as
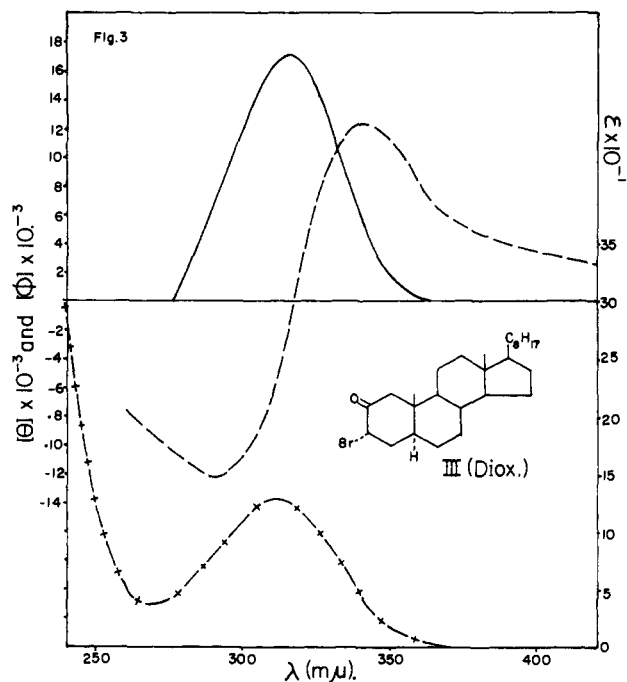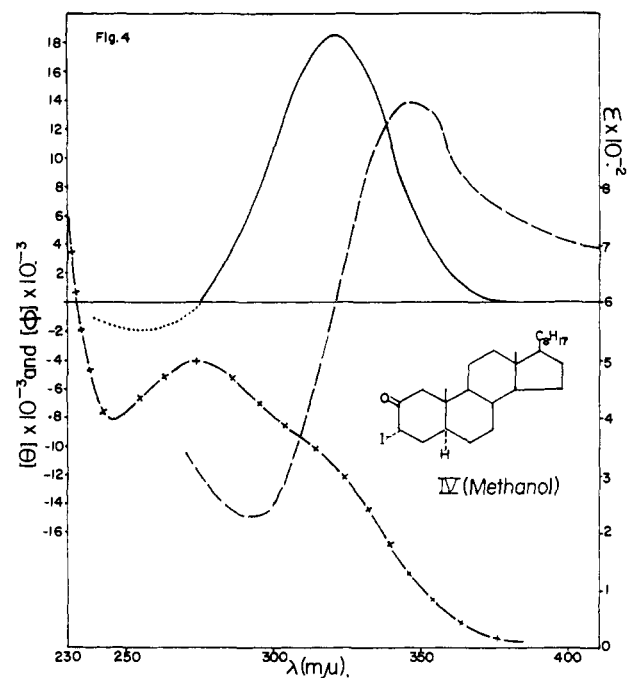
were observed earlier[1,8] for the parent ketone cholestan-3-one, since introduction of equatorial bromine is known[3,4] not to produce important wave length shifts. The midpoint between the two extrema of the positive O.R.D. Cotton effect coincides closely with the position (293 mμ) of the circular dichroism (C.D.) maximum, while the ultraviolet absorption maximum occurs at 286 mμ. This small, but typical, red shift in the C.D. and O.R.D. curves of ketones has been noted by Kuhn and by Lowry among members of the camphor series and has already been discussed by these and other
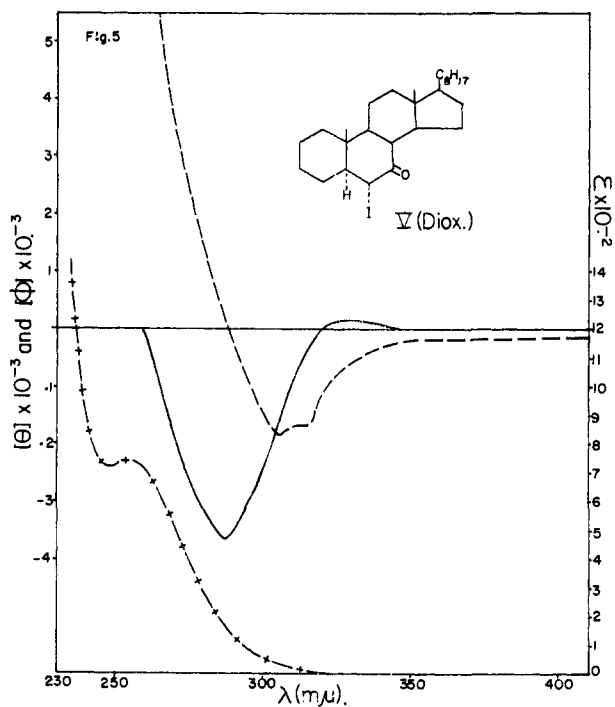
(8) L. Velluz and M. Legrand, Angew. Chem., 73, 603 (1961).

Fig. 5.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (—+—+) curves of 6α-iodocholestan-7-one (V) in dioxane solution.

Fig. 7.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (—+—+) curves of 6α-bromocholestan-7-one (VII) in dioxane solution.

Fig. 6.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (—+—+) curves of 6β-iodocholestan-7-one (VI) in dioxane solution.
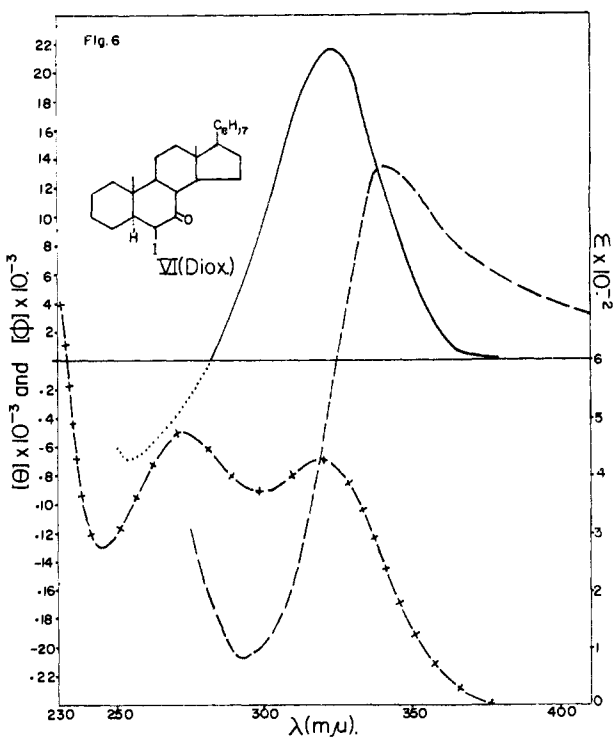

Fig. 8.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (—+—+) curves of 6β-bromocholestan-7-one (VIII) in dioxane solution.

authors.[9] In summary, Fig. 1 represents a typical example where optical rotatory dispersion and circular dichroism measurements confirm independently that the 286 mμ n–π* absorption of 2α-bromocholestan-3-one (I) is optically active.

In striking contrast is the situation existing with 2α-iodocholestan-3-one, (II)[10] where the O.R.D.[6] and C.D.[11]

curves point toward the existence of an ultraviolet absorption band near 290 mμ which, however, cannot be observed in its spectrum. Our earlier assumption[6,7] that the n–π* absorption of this iodo ketone is simply

(9) For summary see T. M. Lowry, "Optical Rotatory Power," Longmans, Green and Co., London, 1953, pp. 405–408. For an alternate explanation, see W. Moffitt and A. Moscowitz, J. Chem. Phys., 30, 648 (1959).
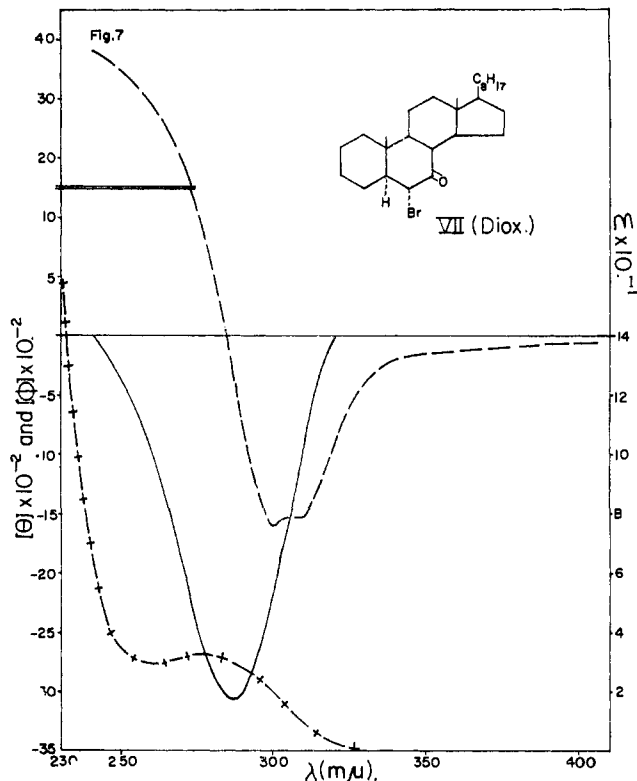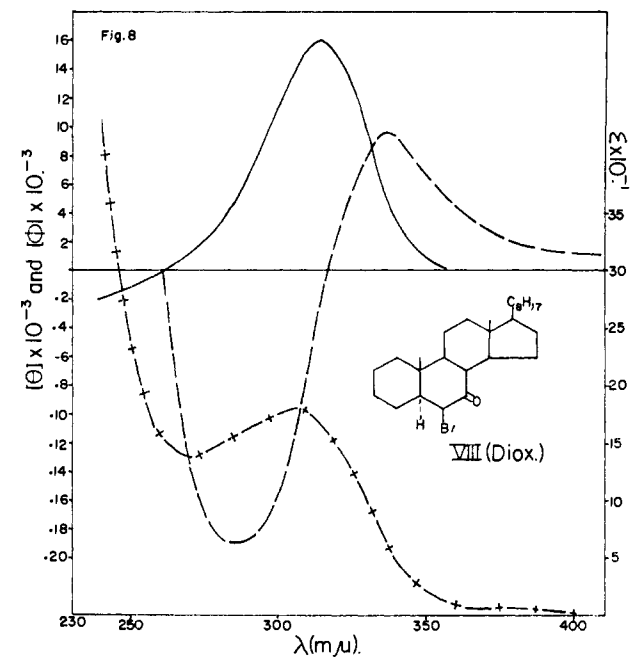
(10) G. Rosenkranz, O. Mancera, J. Gatica and C. Djerassi, J. Am. Chem. Soc., 72, 4077 (1950).

(11) Since completion of our work, there appeared a note (A. K. Bose, M. S. Manhas, R. C. Cambie and L. N. Mander, ibid., 84, 3201 (1962)) mentioning that 2α-iodocholestan-3-one (II) possesses a C.D. maximum at 295 mμ (molecular ellipticity not indicated).
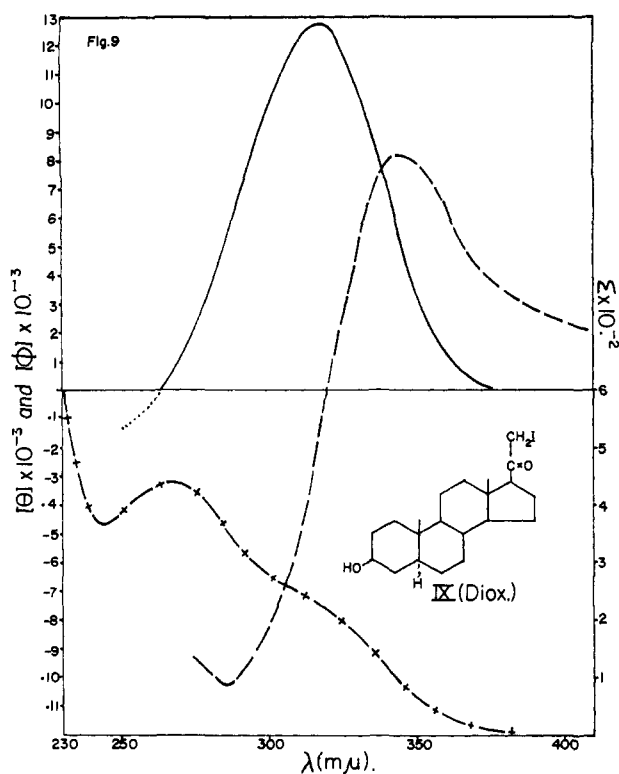
Fig. 9.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (— + — +) curves of 21-iodo-5α-pregnan-3β-ol-20-one (IX) in dioxane solution.

too weak to be detectable is thus fully confirmed and Fig. 2 represents still another example[1] of the utility of C.D. and O.R.D. measurements for uncovering hidden or overlapping absorption bands. Attention should be called to the dotted portion of the C.D. curve (Fig. 2) below 270 mμ. Although of doubtful quantitative significance,[1] it demonstrates quite clearly the beginning of a C.D. minimum in the 250 mμ region, thus suggesting that the iodine absorption band (255 mμ) in 2α-iodocholestan-3-one may also be optically active.

In Fig. 3 are collected the ultraviolet absorption, C.D. and O.R.D. curves of a typical axial α-bromo ketone, 3α-bromocholestan-2-one (III),[12,13] where the characteristic bathochromic shifts associated with an axial bromine atom are clearly defined. This figure serves as background for the corresponding iodo analog, 3α-iodocholestan-2-one (IV), the C.D. and O.R.D. extrema (Fig. 4) of which suffered the expected red shift when compared,[14] for instance, with the equatorially oriented 2α-iodocholestan-3-one (II, Fig. 2). Here, again, the ultraviolet absorption spectrum shows only a faint inflection in the 320 mμ region, where the C.D. and O.R.D. curves demonstrate the existence of the n—π* absorption band. It is instructive to note that the clearly-defined second absorption maximum, due to iodine, has now moved from the usual 255 mμ position to 274 mμ and it appears (see also V, Fig. 5, vs. VI, Fig. 6) that this red shift can be used as a spectral criterion for assigning an axial orientation to an α-iodocyclohexanone. The quantitatively dubious region[1] (dotted portion) in the C.D. curve (Fig. 4) below 275 mμ points toward the existence of an optically

(12) G. H. Alt and D. H. R. Barton, J. Chem. Soc., 4284 (1954).

(13) C. Djerassi and T. Nakano, Chem. Ind. (London), 1385 (1960); T. Nakano, M. Hasegawa and C. Djerassi, Chem. Pharm. Bull. (Tokyo), in press.

(14) In contrast to the other figures, which refer to measurements in dioxane solution, the data in this figure involve methanol because of clearer definition of the low wave length regions. The corresponding dioxane data are listed in the Experimental section.
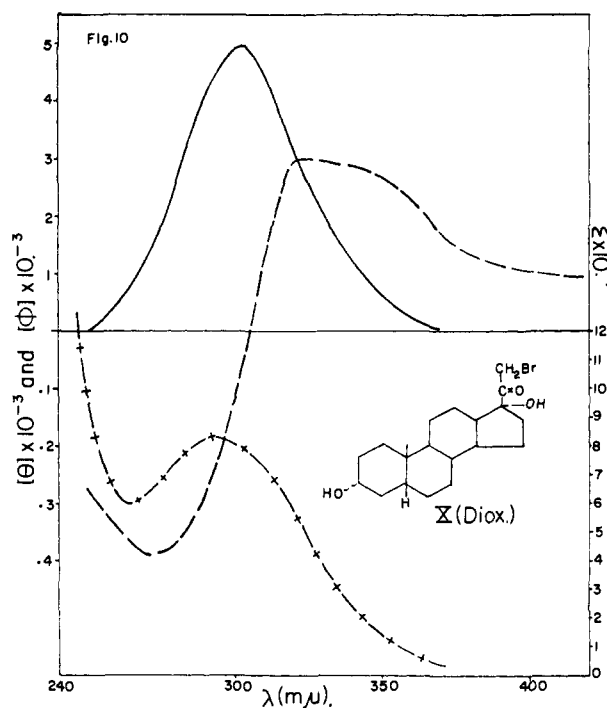

Fig. 10.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (— + — +) curves of 21-bromopregnane-3α,17α-diol-20-one (X) in dioxane solution
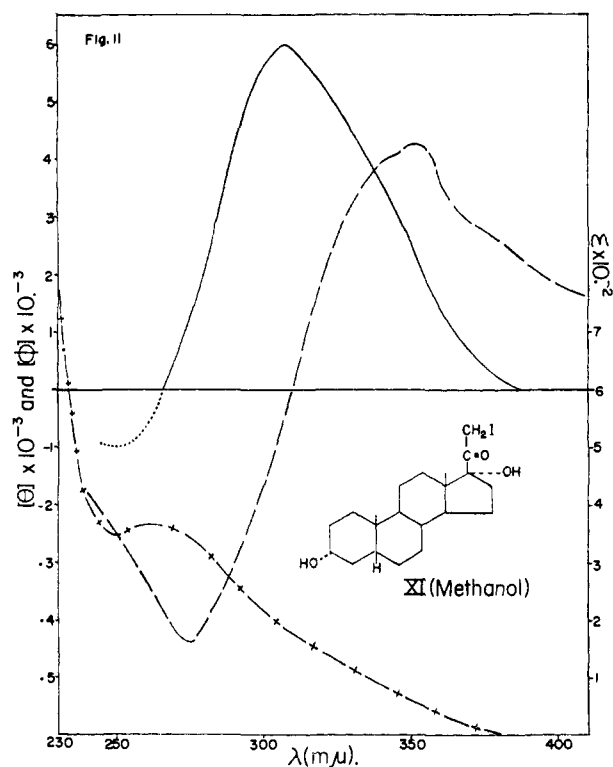
Fig. 11.—Circular dichroism (————), optical rotatory dispersion (— — — —) and ultraviolet absorption (— + — +) curves of 21-iodopregnane-3α,17α-diol-20-one (XI) in methanol solution.

active absorption near 255 mμ (see also Fig. 2). This absorption, however, is not reflected in the ultraviolet spectrum.

At this point, it is profitable to discuss the mode of formation of 3α-iodocholestan-2-one (IV).[15] This sub-

(15) As noted in a paper by E. G. Cummins and J. E. Page (J. Chem. Soc., 3847 (1957)) dealing with infrared absorption spectra, this substance has been prepared earlier by an unpublished procedure by C. W. Bird and R. C. Cookson.

stance was obtained by treatment of 3α-bromocholestan-2-one (III) with sodium iodide in acetone solution, precisely the conditions employed earlier[10] in the preparation of 2α-iodocholestan-3-one (II) from 2α-bromocholestan-3-one (I). While the initial product of such an S$_N$2 reaction would be the hitherto undescribed axial 2β-iodocholestan-3-one, one would expect—by analogy to the instability[16] of 2β-bromocholestan-3-one vis-a-vis its 2α-epimer I—epimerization during the reaction conditions, the driving force being the iodine–methyl diaxial interaction. In the case of 3α-bromocholestan-2-one (III), the product should be the unknown 3β-iodocholestan-2-one, yet what was isolated after several recrystallizations was the axial 3α-iodide IV in 30% yield. In order to check whether epimerization had occurred during the recrystallization or during the original reflux period in acetone solution, the total water-precipitated product was subjected to C.D. and O.R.D. measurement (see Experimental). In terms of wave length, both curves of the crude reaction product (shown by elementary analysis not to contain any starting bromo ketone III) were typical of an axial α-iodo ketone, but the amplitudes were lower. The exact composition of axial and equatorial isomer could not be calculated since the C.D. or O.R.D. properties of the 3β-iodocholestan-2-one are not known. In any event, the driving force for this epimerization to the axial isomer must be the electrostatic repulsion between the equatorial halogen and the carbonyl dipole,[17] which in this instance is not counterbalanced (see II) by an unfavorable interaction with an axial methyl group. The same factor is responsible for the observed[13] equilibrium between 3α- and 3β-bromocholestan-2-one. The availability of the 3β-bromo ketone in pure form[13] prompted us to investigate the stereochemical course of the iodide–acetone reaction with this isomer. As shown in the Experimental section, O.R.D., C.D. and ultraviolet spectral measurements of the total crude reaction product indicate the anticipated presence of a larger amount of the 3α-iodo ketone IV as compared to the above-described iodide exchange reaction with the 3α-bromo analog.

Recently there has become available[18] another pair of α-iodocyclohexanones, 6α- (V) and 6β- (VI) iodocholestan-7-one. In accordance with the axial haloketone rule,[4,5,19] the equatorial isomer V exhibited (Fig. 5) a negative O.R.D. Cotton effect and a negative C.D. curve—as had already been observed earlier for the parent ketone cholestan-7-one[1,20]—while positive curves were encountered (Fig. 6) for the axial 6β-isomer VI. The n–π* absorption near 285 mμ in the equatorial 6α-iodocholestan-7-one (V) was again not noticeable in the ultraviolet absorption spectrum (Fig. 5) but was, of course, revealed by the O.R.D. and C.D. curves. It is interesting that the axial 6β-iodocholestan-7-one (VI) represents the only α-iodoketone which we have encountered where the n–π* absorption is clearly recognizable as a distinct maximum in the ultraviolet absorption spectrum (Fig. 6). Its location at 319 mμ is typical of an axial α-halocyclohexanone[3] and corresponds very well with the location of the C.D. maximum or the midpoint of its O.R.D. Cotton effect. Just as with the other axial iodoketone, 3α-iodocholestan-2-one (III, Fig. 3), the iodide absorption band is red-

shifted to 272 mμ, while the C.D. curve in that region (dotted portion in Fig. 6) points toward the existence of an absorption maximum near 255 mμ. For comparison purposes with the two iodo ketones V and VI, there are collected in Fig. 6 and 7 the ultraviolet absorption, C.D. and O.R.D. curves of the corresponding bromo ketones, 6α-bromo- (VII)[18] and 6β-bromo- (VIII)[18] cholestan-7-one, the amplitudes and wave length shifts being as expected.[3-5]

The discussion was hitherto limited to α-iodocyclohexanones. In our earlier contribution,[6] we called attention to the fact that the same wave length discrepancy between ultraviolet absorption maxima and optical rotatory dispersion extrema existed also in 21-iodo-5α-pregnan-3β-ol-20-one (IX), a substance where the α-iodo ketone moiety resides in the aliphatic portion of the molecule and hence is subject to free-rotational isomerism. The C.D. and O.R.D. curves of this prototype of an aliphatic α-iodo ketone are shown in Fig. 9, both of them corresponding to an optically active absorption band at 318 mμ, a spectral region typical of axial rather than equatorial halo ketones. Indeed, the ultraviolet absorption spectrum (Fig. 9) actually shows an inflection between 310 and 330 mμ, while the iodine absorption band is again red-shifted to 266 mμ, similar to the observation made above with the cyclic axial α-iodo ketones IV (Fig. 4) and VI (Fig. 6).

In order to have available a second α-iodo ketone, where free rotation is theoretically possible, 21-bromo-pregnane-3α,17α-diol-20-one (X)[21] was transformed into the 21-iodo derivative XI. Its C.D. and O.R.D. curves (Fig. 11)[14] are centered in a spectral region suggestive of a substantial amount of axial halo ketone, but the ultraviolet absorption spectrum (Fig. 11) is again devoid of any characteristic features in the 300 mμ range. For comparison purposes, in Fig. 10 there are shown the three parameters of the bromo precursor, 21-bromopregnane-3α,17α-diol-20-one (X). The very broad peak of the O.R.D. Cotton effect, also noted to a lesser extent in Fig. 11 with the 21-iodide XI, suggests a mixture of rotomers.

In summary, the data collected in Fig. 2, 4, 5, 6, 9 and 11 show that the n–π* absorption of α-iodo ketones is usually so weak as to be generally non-detectable by standard ultraviolet spectral techniques. This absorption is, however, strongly optically active (i.e., substantial magnetic dipole[22]) and hence is easily recognized by optical rotatory dispersion or circular dichroism techniques. The location, in terms of wave length, of this band shows the same dependence upon the angle between the C=O and the carbon—iodine bonds as has been noted earlier[3] for α-bromo and α-chloro ketones. Those iodo ketones in which this angle approaches that existing in axial α-halocyclohexanone exhibit a red shift (in the ultraviolet absorption maximum, the circular dichroism maximum or the midpoint of the O.R.D. Cotton effect extrema) of over 20 mμ (as compared to the equatorial epimer or the halogen-free parent ketone) and this criterion can be employed to estimate the preponderance of a given rotomer composition in aliphatic α-iodo ketones. The 21-iodo-20-ketones IX and XI represent a case in point.

Experimental[23]

2α-Bromocholestan-3-one (I), (Fig. 1) C.D. in dioxane: c 0.536 (350–260 mμ), c 0.268 (260–250 mμ), $[\theta]_{293}$ +5050; O.R.D.

(16) C. Djerassi, N. Finch, R. C. Cookson and C. W. Bird, J. Am. Chem. Soc., 82, 5488 (1960).

(17) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, ibid., 74, 2828 (1952); E. J. Corey, ibid., 75, 2301 (1953).

(18) We are greatly indebted to Prof. Alex Nickon of Johns Hopkins University for providing us with these substances, the synthesis of which will be reported in a forthcoming paper from his laboratory.

(19) C. Djerassi and W. Klyne, J. Am. Chem. Soc., 79, 1506 (1957).

(20) C. Djerassi and W. Klyne, J. Chem. Soc., in press (1963).

(21) B. A. Koechlin, T. H. Kritchevsky and T. F. Gallagher, J. Am. Chem. Soc., 73, 189 (1951).

(22) See chapter 12 (in ref. 5) by A. Moscowitz and especially pp. 167–170.

(23) All circular dichroism and optical rotatory dispersion data are reported in the manner outlined in footnote 28 of ref. 1. The following instru-

in dioxane: c 0.130 (410–250 mμ), $[\phi]_{314}$ +4150°, $[\phi]_{266}$ –4930°; ultraviolet in dioxane: ϵ_{286}^{max} 33.

2α-Iodocholestan-3-one (II), (Fig. 2) C.D. in dioxane: c 0.940 (350–285 mμ), c 0.188 (285–265 mμ), c 0.047 (265–255 mμ), $[\theta]_{293}$ +5740; O.R.D. in dioxane: c 0.144 (410–260 mμ), $[\phi]_{315}$ +3520°, $[\phi]_{270}$ –6850°; ultraviolet in dioxane: ϵ_{255}^{max} 725.

3α-Bromocholestan-2-one (III), (Fig. 3) C.D. in dioxane: c 0.547 (365–290 mμ), c 0.105 (290–280 mμ), c 0.021 (280–275 mμ), $[\theta]_{316}$ +17200; O.R.D. in dioxane: c 0.121 (420–260 mμ), $[\phi]_{340}$ +12500°, $[\phi]_{290}$ –12200°; ultraviolet in dioxane: ϵ_{312}^{max} 128.

3α-Iodocholestan-2-one (IV).—A solution of 70 mg. of 3α-bromocholestan-2-one (III)[13] in 5 cc. of acetone and 84 mg. of sodium iodide was heated under reflux for 5.5 hr. After cooling and discharging the iodine color by the addition of sodium thiosulfate solution, the product was precipitated by the addition of water, filtered, washed well with water and dried for 48 hr. at 25° (0.01 mm.); yield 58 mg., m.p. 95–98°, $\lambda_{max}^{CS_2}$ 5.88 μ (inflection at 5.84 μ); C.D. in dioxane: c 0.830 (400–305 mμ), c 0.166 (305–250 mμ), $[\theta]_{325}$ +9830. O.R.D. in dioxane: c 0.083 (410–310 mμ); $[\phi]_{350}$ +7160°; ultraviolet in dioxane: ϵ_{265}^{max} 563.

Anal. Calcd. for $C_{27}H_{45}IO$: C, 63.27; H, 8.85; I, 24.76. Found: C, 64.95; H, 9.02; I, 21.27; Br, 0.0.

Several recrystallizations from methanol provided the analytical specimen (30% over-all yield) of 3α-iodocholestan-2-one (IV), m.p. 118–119°, $\lambda_{max}^{CS_2}$ 5.90 μ (same location in CCl_4); (Fig. 4) C.D. in methanol: c 0.770 (390–295 mμ), c 0.385 (295–240 mμ), $[\theta]_{321}$ +18400, $[\theta]_{255}$ –1970. O.R.D. in methanol: c 0.026 (410–270 mμ), $[\phi]_{346}$ +13800°, $[\phi]_{294}$ –15000°; ultraviolet in methanol: $\epsilon_{330-310}^{shoulder}$ 253–359, ϵ_{274}^{max} 494; C.D. in dioxane: c 0.896 (390–320 mμ), c 0.448 (320–280 mμ), c 0.0896 (280–250 mμ), $[\theta]_{324}$ +16600; O.R.D. in dioxane: c 0.026 (410–270 mμ), $[\phi]_{346}$ +13200°, $[\phi]_{290}$ –10400°; ultraviolet in dioxane: $\epsilon_{330-310}^{shoulder}$ 248–316, ϵ_{274}^{max} 495.

Anal. Found: C, 63.54; H, 8.83; I, 24.79.

Sodium Iodide–Acetone Treatment of 3β-Bromocholestan-2-one.—The exchange reaction of 218 mg. of 3β-bromocholestan-2-one[13] was performed exactly as described above for the 3α-isomer and the total crude product (185 mg.) exhibited the properties: m.p. 97–101°, $\lambda_{max}^{CS_2}$ 5.91 μ (inflection 5.83 μ); C.D. in dioxane: c 1.13 (400–320 mμ), c 0.226 (320–207 mμ), c 0.113 (270–250 mμ), $[\theta]_{323}$ +13000; O.R.D. in dioxane: c 0.113 (420–350 mμ); c 0.0226 (320–285 mμ), c 0.0113 (285–275 mμ), $[\phi]_{347}$ +10450°, $[\phi]_{290}$ –9970°; ultraviolet in dioxane: $\epsilon_{335-313}^{shoulder}$ 140–235, ϵ_{267}^{max} 633.

Anal. Calcd. for $C_{27}H_{45}IO$: C, 63.27; H, 8.85; I, 24.76. Found: C, 65.01; H, 9.02; I, 22.54.

ments were employed in this study: Cary Applied Physics Model 14 Spectrophotometer (ultraviolet absorption); Baird-Atomic/Jouan Dichrographe (circular dichroism); Japan Spectroscopic Manufacturing Company automatically recording spectropolarimeter (optical rotatory dispersion).

6α-Iodocholestan-7-one (V), (Fig. 5) C.D.[24] in dioxane: c 1.595 (350–295 mμ), c 0.399 (295–275 mμ), c 0.100 (275–260 mμ), $[\theta]_{327}$ +120, $[\theta]_{287}$ –3670; O.R.D. in dioxane: c 0.122 (410–295 mμ), c 0.0244 (295–265 mμ), $[\phi]_{315}$ –1680°, $[\phi]_{305}$ –1840°; ultraviolet in dioxane: ϵ_{255}^{max} 740.

6β-Iodocholestan-7-one (VI), (Fig. 6) C.D. in dioxane: c 0.298 (390–280 mμ), c 0.0745 (280–250 mμ), $[\theta]_{323}$ +21700, $[\theta]_{255}$ –6800; O.R.D. in dioxane: c 0.120 (410–275 mμ), $[\phi]_{342}$ +13500°. $[\phi]_{292}$ –20700°; ultraviolet in dioxane: ϵ_{319}^{max} 427, ϵ_{272}^{max} 747.

6α-Bromocholestan-7-one (VII), (Fig. 7) C.D. in dioxane: c 2.45 (325–240 mμ), $[\theta]_{287}$ –3060; O.R.D. in dioxane: c 0.244 (410–260 mμ), c 0.0488 (260–240 mμ), $[\phi]_{310}$ –1530°, $[\phi]_{300}$ –1600°; ultraviolet in dioxane: ϵ_{280}^{max} 32.

6β-Bromocholestan-7-one (VIII), (Fig. 8) C.D. in dioxane: c 0.980 (370–255 mμ), c 0.109 (255–240 mμ), $[\theta]_{313}$ +15850; O.R.D. in dioxane: c 0.098 (410–320 mμ), c 0.012 (320–260 mμ), $[\phi]_{335}$ +9600°, $[\phi]_{285}$ –19000°; ultraviolet in dioxane: ϵ_{303}^{max} 178.

21-Iodo-5α-pregnan-3β-ol-20-one (IX).—A freshly prepared[6] specimen was recrystallized from methanol (m.p. 138–139°) and analyzed prior to the optical and spectral measurements; (Fig. 9) C.D. in dioxane: c 1.080 (380–295 mμ), c 0.216 (295–250 mμ), $[\theta]_{318}$ +12750; O.R.D. in dioxane: c 0.100 (410–275 mμ), $[\phi]_{345}$ +8180°, $[\phi]_{285}$ –10240°; ultraviolet in dioxane: $\epsilon_{330-310}^{shoulder}$ 176–247, ϵ_{266}^{max} 438.

Anal. Calcd. for $C_{21}H_{33}IO_2$: C, 56.76; H, 7.48; I, 28.56. Found: C, 56.15; H, 7.55; I, 28.29.

21-Bromopregnane-3α,17α-diol-20-one (X), (Fig. 10) C.D. in dioxane: c 0.816 (370–265 mμ), c 0.163 (265–250 mμ), $[\theta]_{303}$ + 4940; O.R.D. in dioxane: c 0.102 (420–250 mμ), $[\phi]_{322}$ +3000°, $[\phi]_{270}$ –3890°; ultraviolet in dioxane: ϵ_{295}^{max} 83.

21-Iodopregnane-3α,17α-diol-20-one (XI).—A solution of 413 mg. of the above 21-bromide X^{21} in 25 cc. of acetone and 300 mg. of sodium iodide was heated under reflux for 30 minutes. After cooling in ice, the product was precipitated by the addition of water and the filtered and washed solid was recrystallized three times from aqueous methanol. The colorless needles (133 mg.) proved to be homogeneous on thin-layer chromatography (benzene–methanol 9:1 on silica gel) and exhibited m.p. 143–146°; (Fig. 11) C.D. in methanol: c 0.705 (390–285 mμ), c 0.282 (285–245 mμ), $[\theta]_{307}$ +6000, $[\theta]_{250}$ –1000; O.R.D. in methanol: c 0.0892 (410–325 mμ), c 0.0446 (325–290 mμ), c 0.0178 (290–240 mμ), $[\phi]_{352}$ +4260°, $[\phi]_{274}$ –4380°; ultraviolet in methanol: ϵ_{262}^{max} 368; C.D. in dioxane: c 1.315 (400–300 mμ), c 0.526 (300–270 mμ) c 0.263 (270–250 mμ), $[\theta]_{315}$ +4780; O.R.D. in dioxane: c 0.1184 (410–320 mμ), c 0.0592 (320–260 mμ), c 0.0237 (260–240 mμ), $[\phi]_{360}$ +3110°, $[\phi]_{280}$ –2930°; ultraviolet in dioxane: $\epsilon_{330-310}^{shoulder}$ 128–183, ϵ_{263}^{max} 403.

Anal. Calcd. for $C_{21}H_{33}IO_3$: C, 54.78; H, 7.22; I, 27.57. Found: C, 55.02; H, 7.42; I, 27.44.

(24) The small maximum at 327 mμ probably indicates the presence of a trace amount of 6β-iodo contaminant.

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Kinetic Studies of Hydrogen Exchange in Dialkylanilines.   Part I

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A kinetic study of hydrogen exchange in a series of substituted dialkylanilines indicates that the reaction is a typical electrophilic substitution and that the data conform to the Hammett substituent relationship. Thermodynamic parameters have been obtained which have been considered in relation to the steric inhibition of resonance in the dialkylaniline system.

Introduction

During the past 25 years a number of aromatic hydrogen exchange reactions have been examined in order to determine whether or not the mechanism of exchange conforms to normal aromatic substitution. The early work was carried out with deuterium in which the extent of hydrogen exchange was measured by change in density or infrared spectra.

The acid-catalyzed hydrogen exchange reaction of dimethylaniline with deuterium in aqueous solution was first reported by Ingold, *et al.*,[2] who suggested that

exchange occurred by electrophilic substitution of the aromatic hydrogen by the deuterium ion. Kharasch, *et al.*,[3,4] extended the investigation to a study of the exchange in deuterated alcohol. They considered three possible mechanisms but preferred the one based

(1) Part of this material was taken from a thesis of B. B. P. Tice submitted in partial fulfillment of the degree of Ph.D., University of London, at Sir John Cass College.

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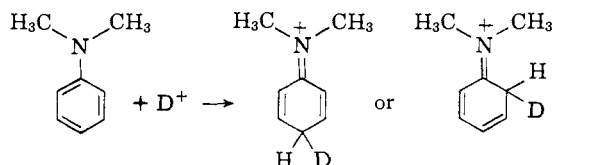
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