## 548. *The Application of the Method of Molecular-rotation Differences to Steroids. Part XIII. Some Bile Acid Derivatives.*

By D. H. R. Barton and C. J. W. Brooks.

The molecular rotations of various 12-keto-bile acids and their derivatives in dioxan, acetone, and chloroform are recorded. The solvent effects observed are correlated with other data in the steroid field. Several erroneous rotations in the literature, to which attention had previously been drawn (Part III, *J.*, 1946, 1116), are corrected. It is shown that there is no " vicinal action " between carboxy- or carbomethoxy-groups in the steroid side chain and hydroxy- or acetoxy-groups at position 3.

In spite of the growing importance of the molecular-rotation difference method in the correlation of optical activity and structure in steroidal compounds, very few reliable measurements have been reported on solvent effects. We have now remedied this omission so far as 12-keto-bile acids are concerned. As will be clear in the sequel the accurate measurement of the rotations of these substances was also of interest in another connection.

The four main solvents used in measuring the rotations of steroidal compounds are dioxan, acetone, chloroform, and alcohol. According to the theoretical treatment of Beckmann and Cohen (*J. Chem. Physics*, 1936, **4**, 784; 1938, **6**, 163) the optical rotations of non-polar molecules in alcohol and acetone should be substantially identical. Previous measurements that we made on cholestane derivatives (Part III, *loc. cit.*) were in agreement with this view, and Sarett (*J. Amer. Chem. Soc.*, 1949, **71**, 1177) has similarly found no significant differences for various 11-ketopregnane derivatives. Measurements were made therefore on a series of 12-keto-bile acids (many of which were very kindly supplied by Messrs. Ciba Pharmaceuticals Ltd., New Jersey,

U.S.A., through the courtesy of Dr. Carl Djerassi, to whom we extend our best thanks) in dioxan, acetone, and chloroform. Table I summarises the results. As before, $\Delta_1$ denotes the increment in molecular rotation on acetylation of a hydroxyl, in this case a 3α-hydroxyl, group. For a number of compounds in both the cholestane (Part III, *loc. cit.*) and cholane series the molecular rotations in chloroform were more negative by about 35 units than those in acetone. This confirms the results of Plattner and Heusser (*Helv. Chim. Acta*, 1944, **27**, 748) for various non-ketonic derivatives of cholic acid. Now it would seem reasonable to regard the shift in molecular rotation from solvent to solvent as made up of contributions from the various parts of the molecule (suitably the asymmetric centres) in the same way as the molecular rotation itself may be treated. For large molecules, then, minor structural changes should not alter greatly the " standard " solvent corrrections. The results discussed so far support this view. However, exceptions must be expected, for in the 12-keto-bile acid derivatives the molecular rotations were *more* positive in chloroform than in acetone by about 20 units (Table I). In the cholestane series molecular rotations were about 20 units less positive in dioxan than in acetone. In the 12-keto-bile acid series there was no significant difference between these two solvents. The results obtained emphasize the desirability, now admitted by most workers in the field, of determining the rotations of all steroidal compounds in one solvent, preferably chloroform.

TABLE I.

| Compound. | $[M]_D$. Dioxan. | Acetone. | Chloroform. | Alcohol. |
|---|---|---|---|---|
| Cholanic acid series : | | | | |
| 3(α)-Acetoxy- methyl ester | — | +207° | +186° | +203° |
| 3(α) : 12(α)-Dihydroxy- * | — | +155 | + 98 | +143 |
| 3(α) : 7(α) : 12(α)-Trihydroxy- * | — | +220 | +176 | +218 |
| Bisnorcholanic acid series : | | | | |
| 3(α)-Acetoxy- methyl ester | +123° | +131 | +119 | — |
| 12-Ketocholanic acid series : | | | | |
| 3(α)-Hydroxy- | +379 | +394 | +404 | — |
| 3(α)-Acetoxy- | +463 | +467 | +491 | — |
| $\Delta_1$ | **+ 84** | **+ 73** | **+ 87** | — |
| 3(α)-Hydroxy- methyl ester | +375 | +386 | +394 | — |
| 3(α)-Acetoxy- methyl ester | +462 | +460 | +491 | — |
| $\Delta_1$ | **+ 87** | **+ 74** | **+ 97** | — |
| 12-Ketonorcholanic acid series : | | | | |
| 3(α)-Hydroxy- | +386 | — | — | — |
| 3(α)-Acetoxy- methyl ester | +474 | +461 | +502 | — |
| $\Delta_1$ | **+ 88** | — | — | — |
| 12-Ketobisnorcholanic series : | | | | |
| 3(α)-Hydroxy- | +308 | — | — | — |
| 3(α)-Hydroxy- methyl ester | +330 | +333 | +347 | — |
| 3(α)-Acetoxy- methyl ester | +414 | +402 | +431 | — |
| $\Delta_1$ | **+ 84** | **+ 69** | **+ 84** | — |
| 12-Ketoætiocholanic acid series : | | | | |
| 3(α)-Hydroxy- | +454 | +463 | — | — |
| 3(α)-Acetoxy- | +563 | +567 | +595 | — |
| $\Delta_1$ | **+109** | **+104** | — | — |
| 3(α)-Hydroxy- methyl ester | +481 | +488 | +502 | — |
| 3(α)-Acetoxy- methyl ester | +580 | +567 | +599 | — |
| $\Delta_1$ | **+ 99** | **+ 79** | **+ 97** | — |

* Josephson, *Biochem. J.*, 1935, **29**, 1484.

TABLE II.

| | No. of examples. | A.M. Δ vals. | Mean error of A.M.* |
|---|---|---|---|
| Cholanic acid → nor-acid | 9 | + 5° | ± 6° |
| Cholanic acid → bisnor-acid | 23 | − 59 | ± 4 |
| Cholanic acid → ætio-acid | 12 | +113 | ±10 |

* Arithmetic mean. The limits of variation from the arithmetic mean are, of course, much larger.

Taking the rotations for 3α-hydroxy-12-ketocholanic acid and its derivatives in dioxan as a datum it is, of course, possible to calculate the molecular rotations of the various lower homologues

and their derivatives. Standard Δ values for this process are given in Table II and are based on a complete analysis of the literature up to the end of 1945, although in order to conserve space we do not give details here. The calculated molecular rotations are presented in Table III, and comparison of this table with the relevant data in Table I shows a close agreement in all cases except that of 3-α-hydroxy-12-ketoætiocholanic acid. As mentioned in the Experimental section this acid retains solvent tenaciously. Since large specific rotations are involved a small contamination by inert solvent exerts a relatively large effect on the molecular rotation. We doubt, therefore, whether this discrepancy is significant. The $\Delta_1$ values given in Table I for the various 12-keto-bile acids and their methyl esters are in good agreement with the standard value of +83° established by analysis of the literature (Part III, *J.*, 1946, 1116), except for the values for 3-α-hydroxy-12-ketoætiocholanic acid (see above).

TABLE III.

12-Ketocholanic acids (all rotations positive).

| Substance. | Standard $[M]_D$ (dioxan). | $[M]_D$ (dioxan), calc. by use of Table II. Nor-acid. | Bisnor-acid. | Ætio-acid. |
|---|---|---|---|---|
| 3α-Hydroxy- * ..... | 379° | 384° | 320° | 492° |
| 3α-Acetoxy- † ..... | 463 | 468 | 404 | 576 |
| 3α-Hydroxy- methyl ester ... | 375 | 380 | 316 | 488 |
| 3α-Acetoxy- methyl ester ... | 462 | 467 | 403 | 575 |

* Schwenk *et al.* (*loc. cit.*) found $[M]_D$ +339°, +263°, +308°, and +424°, respectively.
† Schwenk *et al.* (*loc. cit.*) found $[M]_D$ +418° and +267° for the nor-acid and bisnor-acid derivatives respectively.

Now in Part III of this series (*loc. cit.*) we pointed out that the rotations recorded by Schwenk, Riegel, Moffett, and Stahl (*J. Amer. Chem. Soc.*, 1943, **65**, 549) for 3α-hydroxy-12-keto-nor- and -bisnor-cholanic acid afforded anomalous $\Delta_1$ values. The present investigation has confirmed that the rotations given by the American workers for the nor-acid and for the bisnor-acid acetate are erroneous (Table III). It will be noted that all the rotations reported in the reference cited are *lower* than the expected values. In so far as there can be no serious doubt about the structures of the compounds, it seems probable that the discrepancy is explained by inadequate drying before weighing. Because of the high rotations these compounds are particularly liable to this sort of error. Dr. E. Schwenk has kindly informed us that he thinks that this is a not unreasonable explanation. The melting points in the two investigations are in good agreement.*

TABLE IV.

| Hydroxy-compound. | $[M]_D$ ($CHCl_3$). Alcohol. | Acetate. | $\Delta_1$. |
|---|---|---|---|
| *Cholestane series (standard values) :* * | | | |
| 3β-Hydroxy-Δ⁵- ..... | −154° | −188° | **−34°** |
| 3β-Hydroxy-5-*allo*- ..... | + 89 | + 60 | **−29** |
| Δ (Reduction) ..... | **+243** | **+248** | — |
| *Cholanic acid series :* | | | |
| 3β-Hydroxy-Δ⁵- methyl ester ..... | −175 | −198 | **−23** |
| 3β-Hydroxy-5-*allo*- methyl ester ..... | + 74 | + 48 | **−26** |
| Δ (Reduction) ..... | **+249** | **+246** | — |
| *Ætiocholanic acid series :* | | | |
| 3β-Hydroxy-Δ⁵- methyl ester ..... | − 70 | − 94 | **−24** |
| 3β-Hydroxy-5-*allo*- methyl ester ..... | +177 | +143 | **−34** |
| Δ (Reduction) ..... | **+247** | **+237** | — |

* Barton, *J.*, 1946, 1116.

During the course of work with a different object we prepared, and recorded the rotations of, pure specimens of 3β-hydroxy-*allo*- and -ætio*allo*-cholanic acid and their derivatives.† The molecular-rotation data are briefly summarised in Table IV. It will be seen that the Δ values

* A further anomaly to which attention was directed in Part III (*loc. cit.*) has now been corrected. Lieberman *et al.* (*J. Biol. Chem.*, 1948, **172**, 263) recently found $[\alpha]_D$ +97° (in alcohol), $[M]_D$ +309°, for *allo*pregnan-3α-ol-20-one. Coupling this with the $[M]_D$ of +342° (in alcohol) recorded earlier for the corresponding acetate (Fleischer, Whitman, and Schwenk, *J. Amer. Chem. Soc.*, 1938, **60**, 79) gives a revised $\Delta_1$ value of +33°, now in good agreement with the standard value of +24° found in Part III.

† We are much indebted to Messrs. Ciba, Basle, for generous gifts of chemicals, which served as starting materials in this work.

for these compounds agree closely with the corresponding derivatives of cholestane. There is, in fact, no " vicinal action " (Barton and Cox, *Nature*, 1946, **159**, 470; Part IV, *J.*, 1948, **783**) between the carboxy- or carbomethoxy-groups in the side chain and the 3-position. This is in agreement with our previous studies on the subject (Barton and Cox, *loc. cit.*).

## Experimental.

M. p.s are uncorrected. M. p.s above 200° were determined using an aluminium-block apparatus similar to that described by Fieser (" Experiments in Organic Chemistry," 1941, p. 329). All specimens were dried in a vacuum at 20° below their m. p.s or at 120°, whichever was the lower temperature. All rotations are for the $Na_D$ line and were determined at room temperature, which varied from 15° to 25°, with a 1-dm. micro-tube of about 1·5-ml. capacity. In the sequel concentrations are in g. per 100 ml. of solution. Tables of molecular rotations are given above.

Keto-acids were esterified with only a *slight* excess of ethereal diazomethane. Acids not containing keto-groups were esterified with an excess of this reagent in the usual way.

Standard chemical operations were carried out as described in detail in Part IV (*J.*, 1948, 783).

Light petroleum had b. p. 40—60°.

Most of the data determined during this investigation are summarised, together with the more important of the relevant literature, in Table V. Additional experimental data are summarised as follows.

3α-*Hydroxy*-12-*ketocholanic Acid.*—This acid was prepared from deoxycholic acid by the method of Bergstrom and Haslewood (*J.*, 1939, 540). It was best purified by crystallisation (needles) from ethyl acetate–light petroleum rather than from benzene. The corresponding acetate was similarly recrystallised. Methyl 3-α-hydroxy-12-ketocholanate was recrystallised from various solvents including aqueous acetone, aqueous methanol, and acetone–light petroleum. All specimens obtained had m. p.s in the range 116—120°, in disagreement with the values of 110—111·5° and 111—112° recorded in Table V and with the value of 143° given by Chakravarty and Wallis (*J. Amer. Chem. Soc.*, 1940, **62**, 318). As far as could be ascertained by fractionation from the above-mentioned solvents the specimen described here was homogeneous. The methyl ester was acetylated in the usual way, and the acetate purified by chromatography and then by crystallisation from methanol.

*Methyl* 3α-*Acetoxy*-12-*ketonorcholanate.*—The preparation supplied by Messrs. Ciba Pharmaceuticals Ltd. was recrystallised from methanol. Hydrolysis by N-methanolic potassium hydroxide at room temperature for 3 days furnished 3α-hydroxy-12-ketonorcholanic acid, which was recrystallised from ethyl acetate–light petroleum.

*Methyl* 3α-*Acetoxy*-12-*ketobisnorcholanate.*—The preparation supplied by Messrs. Ciba Pharmaceuticals Ltd. was recrystallised from methanol. 80 Mg. were treated with 20 ml. of N-methanolic potassium hydroxide and set aside at room temperature for 5 days. Working up in the usual way and recrystallisation from chloroform–light petroleum (needles) gave methyl 3α-hydroxy-12-ketobisnorcholanate. Hydrolysis of the acetate methyl ester according to the directions of Sorkin and Reichstein (*Helv. Chim. Acta*, 1944, **27**, 1631) furnished the corresponding hydroxy-acid, which was recrystallised from ether.

*Methyl* 3α-*Acetoxy*-12-*ketoætiocholanate.*—The preparation supplied by Messrs. Ciba Pharmaceuticals Ltd. was recrystallised from ether–light petroleum. 3α-Hydroxy-12-ketoætiocholanic acid was prepared from ætiodeoxycholic acid (supplied by Messrs. Ciba, Basle) by chromic acid oxidation of the 3-succinoyl derivative according to the directions of Schwenk, Riegel, Moffet, and Stahl (*loc. cit.*), the final hydrolysis of the succinate being effected by 30% methanolic potassium hydroxide at room temperature. The hydroxy-acid crystallised well from aqueous methanol and was identical in all respects with a specimen supplied by Messrs. Ciba Pharmaceuticals Ltd. The following rotations were observed: $[\alpha]_D$ +129° (*c*, 1·08) in dioxan, and +131·5° (*c*, 1·05), +133° (*c*, 1·02), +131·5° (*c*, 0·79) in acetone. A specimen recrystallised from aqueous acetone had $[\alpha]_D$ +122° (*c*, 1·22) in dioxan. In an attempt to determine whether the acid was solvated a sample was dried at room temperature and then further dried at 100°/1 mm. pressure until there was no further loss (total, 6%) in weight (about 4 hours) (Found: C, 70·24; H, 9·24. Calc. for $C_{20}H_{30}O_4,\frac{1}{2}CH_3{\cdot}OH$: C, 70·25; H, 9·20%). The rotation was then $[\alpha]_D$ +129·5° (*c*, 0·68) in dioxan. $[M]_D$ calculated for $C_{20}H_{30}O_4,\frac{1}{2}CH_3{\cdot}OH$ was +454° (dioxan), +463° (acetone). The hydroxy-acid was too sparingly soluble in chloroform for accurate measurement. On acetylation 3α-hydroxy-12-ketoætiocholanic acid afforded the corresponding acetate, which recrystallised (slowly) from aqueous methanol in long needles.

Methyl 3α-hydroxy-12-ketoætiocholanate was prepared by diazomethane and recrystallised from chloroform–ether.

*Lithocholic Acid.*—Lithocholic acid was prepared according to the directions of Heusser and Wuthier (*Helv. Chim. Acta*, 1947, **30**, 2165). Methyl 3α-succinoyloxy-7 : 12-diketocholanate, crystallised from benzene–light petroleum, had m. p. 181°, $[\alpha]_D$ +50° (*c*, 2·78), +49° (*c*, 1·49) in chloroform. The corresponding dimethyl ester, recrystallised from benzene–light petroleum, had m. p. 99—100°, $[\alpha]_D$ +46° (*c*, 3·63), +46° (*c*, 1·5) in chloroform. Lithocholic acid (3α-hydroxycholanic acid), recrystallised from methanol, had m. p. 185—186°, $[\alpha]_D$ +35° (*c*, 1·17), +35° (*c*, 1·15), $[M]_D$ +132° in ethanol. Lithocholic acid acetate, recrystallised from aqueous acetone, had m. p. 168—170°, $[\alpha]_D$ +49° (*c*, 1·05), +49° (*c*, 0·67), +49° (*c*, 0·65), $[M]_D$ +205° in ethanol, and $[\alpha]_D$ +45° (*c*, 3·40), $[M]_D$ +188° in chloroform; the corresponding methyl ester had m. p. 132—133°, $[\alpha]_D$ +48° (*c*, 2·66) in acetone, +47° (*c*, 2·27) in 9 : 1 ethanol : chloroform, and +43° (*c*, 2·86) in chloroform.

*Methyl* 3β-*Hydroxychol*-5-*enate.*—This ester was supplied by Messrs. Ciba, Basle. Recrystallised from ethyl acetate–methanol, it had m. p. 141—142°, $[\alpha]_D$ −45° (*c*, 1·71), −45° (*c*, 1·66) in chloroform. Acetylation gave the corresponding acetate, recrystallised from ethyl acetate, m. p. 155°, $[\alpha]_D$ −45° (*c*, 2·30), −47° (*c*, 1·26), −46° (*c*, 1·03) in chloroform. Hydrogenation of methyl 3β-hydroxychol-5-enate in ether–acetic acid solution with a platinum catalyst furnished methyl 3β-hydroxy*allo*cholanate, recrystallised from methanol in long needles, m. p. 149°, $[\alpha]_D$ +19° (*c*, 2·50), +19° (*c*, 2·00) in chloroform.

TABLE V.

| Compound. | M. p. | $[\alpha]_D$ (all positive) in dioxan. | acetone. | chloroform. |
|---|---|---|---|---|
| 12-Ketocholanic acid derivatives : | | | | |
| 3(α)-Hydroxy- * | 164—165° [1]<br>160—161 [7] | 87° [1] | 94° [7] | — |
| Found | **163—164** | **97**<br>(*c*, 1·28) | **101**<br>(*c*, 1·07, 0·87) | **103·5°**<br>[103 (*c*, 1·19)<br>103·5 (*c*, 2·07)<br>105 (*c*, 1·14)] |
| 3(α)-Hydroxy- methyl ester | 110—111·5 [4]<br>111—112 [7] | — | — | — |
| Found | see text | **92·5**<br>(*c*, 2·63) | **95·5**<br>[96 (*c*, 1·68),<br>94·5 (*c*, 1·67)<br>95·5 (*c*, 1·81)] | **97·5**<br>(*c*, 2·47, 2·58) |
| 3(α)-Acetoxy- | 197 [2] | — | — | — |
| Found | **197—198** | **107**<br>[107·5 (*c*, 1·85)<br>106·5 (*c*, 1·72)] | **108**<br>[108·5 (*c*, 1·91)<br>107·5 (*c*, 1·27)] | **113·5**<br>[113 (*c*, 2·10)<br>114 (*c*, 1·78)] |
| 3(α)-Acetoxy- methyl ester † | 153—154·5 [4]<br>150—151 [15] | — | 105,[4] 103 [5] | — |
| Found | **150—151** | **103·5**<br>[105 (*c*, 1·57)<br>103·5 (*c*, 1·99)<br>103·5 (*c*, 2·73)] | **103**<br>[103·5 (*c*, 1·24)<br>103 (*c*, 1·91)] | **110**<br>(*c*, 1·57) |
| 12-Ketonorcholanic acid derivatives : | | | | |
| 3(α)-Hydroxy- | 250—251° | 70 [1] | — | — |
| Found | **248—250** | **103**<br>[102·5 (*c*, 1·48)<br>103 (*c*, 0·75)] | — | — |
| 3(α)-Acetoxy- | 208—209·5 [1] | 100 [1] | — | — |
| 3(α)-Acetoxy- methyl ester | 184—186 [13] | — | — | — |
| Found | **183** | **109·5**<br>[110 (*c*, 0·93)<br>108·5 (*c*, 1·68)] | **106·5**<br>[107 (*c*, 1·32)<br>106·5 (*c*, 1·82)] | **116**<br>[116·5 (*c*, 1·23)<br>116 (*c*, 1·43)] |
| 12-Ketobisnorcholanic acid derivatives : | | | | |
| 3(α)-Hydroxy- | 295—297 [1]<br>298—299 [1] | 85 [1] | — | — |
| Found | **292** | **85**<br>(*c*, 1·13) | — | — |
| 3(α)-Hydroxy- methyl ester | 171—173 [14]<br>165—167 [16] | — | — | — |
| Found | **165—166** | **87·5**<br>[88 (*c*, 1·19)<br>87 (*c*, 1·57)] | **88**<br>(*c*, 1·19) | **92**<br>(*c*, 1·04) |
| 3(α)-Acetoxy- | 246—247 [1] | 66 [1] | — | — |
| 3(α)-Acetoxy- methyl ester | 168—170 [6]<br>166—166·5 [13] | — | 94 [6] | — |
| Found | **165** | **99**<br>(*c*, 1·92,<br>2·40) | **96**<br>[95·5 (*c*, 1·33)<br>97 (*c*, 1·91)] | **103**<br>[104 (*c*, 1·61)<br>102 (*c*, 2·72)] |
| 12-Ketoætiocholanic acid derivatives : | | | | |
| 3(α)-Hydroxy- | 213—215 [1]<br>213—216 [13] | 127 [1] | 130 [13] | — |
| Found | **211—212** | See text | See text | — |
| 3(α)-Hydroxy- methyl ester | 169—170 [3] | — | — | 144 [3] |
| Found | **166—167** | **139**<br>(*c*, 1·39) | **140**<br>(*c*, 0·94) | **144**<br>(*c*, 1·26) |
| 3(α)-Acetoxy- | 205—206 [1] | — | — | — |
| Found | **202—206** | **149·5**<br>(*c*, 1·02) | **150·5**<br>(*c*, 0·92) | **158**<br>(*c*, 1·18) |
| 3(α)-Acetoxy- methyl ester | 152—154 [3]<br>154—156 [13] | — | 150 [10] | 152 [3] |
| Found | **151—152** | **148·5**<br>(*c*, 1·41) | **145**<br>(*c*, 0·63) | **153·5**<br>[155 (*c*, 0·87)<br>152 (*c*, 1·34)] |

TABLE V (*continued*).

| Compound. | M. p. | $[\alpha]_D$ (all positive) in dioxan. | acetone. | chloroform. |
|---|---|---|---|---|
| Bisnorcholanic acid derivatives : | | | | |
| 3(α)-Acetoxy- methyl ester | 112—113 [13] | — | — | — |
| Found | **110—111** | **31** | **32·5** | **29·5** |
| | | [31 (*c*, 1·85) 30 (*c*, 2·01)] | (*c*, 1·54) | (*c*, 2·01, 0·99) |

* Recorded $[\alpha]_D$ in alcohol : 112°,[11] 110°.[12] † Recorded $[\alpha]_D$ in alcohol : 111°,[8] 108°.[9]

[1] Schwenk, Riegel, Moffett, and Stahl, *J. Amer. Chem. Soc.*, 1943, **65**, 549. [2] Chakravarty and Wallis, *ibid.*, 1940, **62**, 318. [3] Wenner and Reichstein, *Helv. Chim. Acta*, 1944, **27**, 965. [4] Reichstein and Sorkin, *ibid.*, 1942, **25**, 797. [5] Lardon and Reichstein, *ibid.*, 1943, **26**, 586. [6] *Idem*, *ibid.*, 1944, **27**, 713. [7] Seebeck and Reichstein, *ibid.*, 1943, **26**, 536. [8] Gallagher and Long, *J. Biol. Chem.*, 1946, **162**, 521. [9] Hicks, Berg, and Wallis, *ibid.*, 1946, **162**, 633. [10] Katz and Reichstein, *Pharm. Acta Helv.*, 1944, **19**, 231. [11] Wieland and Kishi, *Z. physiol. Chem.*, 1933, **214**, 47. [12] Kyogoku, *ibid.*, 1937, **246**, 99. [13] Values quoted by Messrs. Ciba Pharmaceuticals Ltd. for samples supplied. [14] Seebeck and Reichstein, *Helv. Chim. Acta*, 1944, **27**, 1631. [15] Gallagher and Long, *J. Biol. Chem.*, 1946, **162**, 495. [16] Riegel and Moffett, *ibid.*, 1946, **162**, 585.

Hydrogenation of the corresponding acetate methyl ester (see above) afforded methyl 3β-acetoxy*allo*-cholanate which, recrystallised from ethyl acetate, had m. p. 155°, $[\alpha]_D$ +11° (*c*, 5·32), +11° (*c*, 3·72) in chloroform.

*Methyl 3β-Hydroxyætiochol-5-enate.*—This ester was supplied by Messrs Ciba, Basle. Recrystallised from methanol (long needles) it had m. p. 179°, $[\alpha]_D$ −21° (*c*, 2·96), −21° (*c*, 1·29) in chloroform. Acetylation gave the corresponding acetate, recrystallised from methanol in prisms, m p. 150—151°, $[\alpha]_D$ −25° (*c*, 2·47) in chloroform. Hydrogenation of methyl 3β-hydroxyætiochol-5-enate in ether–acetic solution with a platinum catalyst gave methyl 3β-hydroxy*allo*ætiocholanate which, recrystallised from methanol, had m. p. 172°, $[\alpha]_D$ +54° (*c*, 1·83), +52° (*c*, 1·12) in chloroform. Acetylation furnished the corresponding acetate, recrystallised from methanol in plates, m. p. 149—150°, $[\alpha]_D$ +38° (*c*, 5·36), +38° (*c*, 5·13) in chloroform.

This work was carried out during the tenure of an I.C.I. Fellowship by one of us (D. H. R. B.). We are indebted to the Chemical Society for a grant and to the Department of Scientific and Industrial Research for financial assistance (C. J. W. B.).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
S. KENSINGTON, LONDON, S.W.7.

[*Received, May 30th*, 1949.]