Bile Acids

XIII. FURTHER CONTRIBUTIONS TO THE CONSTITUTION OF MURICHOLIC ACIDS


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Our recent studies on the metabolism of bile acids led to the isolation of four new acids (1–3). Chemical studies and partial syntheses have established that three of these new acids are 3β, 6,7-trihydroxycholanic acids, isomeric with hyocholic acid (3α, 6α, 7α-trihydroxycholanic acid) which was isolated and named by Haslewood (4); it was also isolated and studied by Ziegler (5). Two of these new acids, Acid I (3α, 6β, 7β-trihydroxycholanic acid) (6) and Acid II (3α, 6β, 7α-trihydroxycholanic acid) (7), are normal constituents of rat bile (1); recently they have been found as metabolites of chenodeoxycholic-24-C14 acid in the bile of mice (8) and in the urine of surgically jaundiced mice. The fourth epimeric 6,7-glycol, Acid IV (3α, 6β, 7α-trihydroxycholanic acid) (9), was isolated as a metabolite of hyodeoxycholic acid (3α, 6β, 7α-trihydroxycholanic acid) (10). For the fourth and last epimeric 6,7-glycol, Acid IV (3α, 6β, 7α-trihydroxycholanic acid) (9), was isolated as a metabolite of hyodeoxycholic acid in the rat (2). In order to designate these new acids by trivial names more appropriate to their origin we have chosen the name “muricholic acids” from the Latin mus, meaning rat or mouse. We propose to use the prefixes “α” and “β” to signify the orientation of the hydroxyl group at C-7; thus the 6β,7α-glycol (Acid II) is α-muricholic acid, and the 6β,7β-glycol (Acid I) is β-muricholic acid. The 6α,7α-glycol which we isolated from hog bile and referred to as Hog Acid was later shown to be identical with Haslewood’s hyodeoxycholic acid (4, 5, 10). For the fourth and last epimeric 6,7-glycol, Acid IV (6α, 7α) we propose the name, α-muricholic acid.

This paper presents the results of additional chemical studies relevant to the structures of these acids and a comparison of some of their physical and chemical properties.

EXPERIMENTAL PROCEDURE

A. Hydrogenolysis of Thioketals Related to α-Muricholic Acid

Previous communications have reported that hyocholic and α-muricholic as well as synthetic 3α, 6α-dihydroxy 7-ketochohlanic acid were converted to hyodeoxycholic (3α, 6α-dihydroxy-

1 Unpublished observations in our laboratories.

2 These names have been discussed with Professors G. A. D. Haslewood and S. Bergström.

3 All melting point determinations were taken on the Fisher-Johns apparatus and are reported as read. Specific rotations were taken in a 1-dm tube. Infrared spectra were determined in Nujol with a Perkin-Elmer spectrometer, model 21, with rock salt optics. The method of partition chromatography was the same as described previously (1). We have abbreviated the designation of fractions from this column according to the per cent of benzene in Skellysolve B. Each solvent mixture was collected in four portions. For example, 60-3 represents the third fraction of the eluate containing 60% benzene in Skellysolve B.

Cholanic) acid through an ethylenethioketal derivative at C-7 by hydrogenolysis with Raney nickel, thus establishing the 6α-hydroxyl group in the original compounds (10–12). In these instances the ketol contained the more stable equatorial 6α-hydroxyl group. It is of interest to ascertain if the axial 6β-hydroxyl group adjacent to a ketone could be treated similarly and retain its orientation. For this purpose, the diaxial glycol α-muricholic acid and its derivatives were subjected to the same sequence of reactions.

Partial Oxidation of α-Muricholic Acid (I, Scheme I) with Chronic Anhydride—A solution of 278 mg of α-muricholic acid in 30 ml of acetic acid and 3 ml of water was cooled in an ice bath and treated by the dropwise addition of a solution of 46.8 mg (1.0 equivalent) of chronic anhydride in 5 ml of acetic acid. The temperature of the mixture was kept below 5° for 24 hours. Water was then added and the product extracted with ether and purified by partition chromatography.2 The major portion (II) amounting to 196 mg was eluted in 60-2 and 60-3, fractions in which 3α, 6α-dihydroxy-7-ketochohlanic acid had been found in earlier work (10). Reduction of 20 mg of this oil with sodium borohydride gave a product which on chromatography was eluted in Fractions 80-3 and 80-4, and was identified as α-muricholic acid by melting point, mixed melting point, and infrared spectroscopy (Scheme I).

Desulfuration with Raney Nickel—The remainder of the oil (176 mg) was converted to the ethylenethioketal derivative (III) as described previously (10); it yielded 169 mg of material which also resisted crystallization. This oil was refluxed with 1 g of Raney nickel in 10 ml of acetone and 2 ml of water for 21 hours. The products were separated by partition chromatography; 36 mg of lithocholic acid (IV) were obtained from Fractions 0-1 and 0-2, and 15 mg of another acid from Fractions 40-1 and 40-2. The latter acid was identified as 6-ketolithocholic acid (V), m.p. 158–160°. Mixed melting point of these acids with authentic samples gave no depression. The infrared absorption spectra were also comparable with those of authentic lithocholic acid and 6-ketolithocholic acid, respectively.

The isolation of 6-ketolithocholic acid (V) in this experiment was unexpected. An explanation was difficult partly because it was not clear which hydroxyl group of α-muricholic acid was oxidized by treatment with chronic anhydride. In order to clarify this ambiguity, the 6β-acetoxyl-7-ketone (X) was prepared and studied.

3α, 6β-Diacetate of α-Muricholic Acid (IX) (Scheme II)—Methyl 3α-acetoxy-6α, 7α-epoxychohlanic (VI) (7) (1.5 g) was
SCHEME I

\[
\begin{align*}
\text{COOH} & \quad \text{NaBH}_4 \quad \text{HO} \\
\text{OH} & \quad \text{S} \\
\text{OH} & \quad \text{OH} \\
\text{H} & \quad \text{H}
\end{align*}
\]

(1.2 g), m.p. 228°, needles from aqueous methanol.

\[
\text{C}_{24}\text{H}_{30}\text{O}_4
\]

Calculated: C 73.80, H 9.81

Found: C 73.65, H 9.76

Acetylation of this acid (VIII) with a mixture of acetic anhydride and pyridine yielded 3α-acetoxy-6α,7α-epoxycholanic acid (VIII) (1.1 g), m.p. 211-213°.

\[
\text{C}_{26}\text{H}_{40}\text{O}_8
\]

Calculated: C 72.18, H 9.32

Found: C 72.55, H 9.26

Acetolysis of 700 mg of the epoxide (VIII) was effected by refluxing in 30 ml of glacial acetic acid for 3.5 hours. To hydrolyze any anhydride which might have been formed during the reaction, 10 ml of water were added to the reaction mixture and the refluxing continued for another half hour. The products were then extracted and separated by partition chromatography. The major product (IX) appearing in Fractions 20-1, 20-2, and 20-3, weighed 694 mg, and could not be crystallized.

Oxidation of 3α,6β-Diacetate of α-Muricholic Acid (IX) and Desulfuration of Thioketal Derivative (XI)—Of the oil (IX) obtained from above, 534 mg were dissolved in 5 ml of acetic acid and oxidized with 87 mg (1.2 equivalent) of chromic anhydride. The product of oxidation was purified by partition chromatography; 488 mg of an oil (X) were obtained in Fractions 0-3, 0-4, and 20-1. The shift in the chromatographic pattern is strongly indicative of oxidation of a secondary alcohol to a ketone.

Previously we have described the formation of a 6β-bromo-7α-hydroxy derivative from the α-epoxide (VI) by treatment with HBr (7); by analogy, Compound (X) should be the 6α-acetoxy-7-ketone. Its ultraviolet absorption maximum at 294 mp can therefore be compared with that of 8-acetoxy-7-ketocholanic acid (288 mp) (10). The shift of 6 mp to a longer wave length as compared to the absorption of the parent ketone indicates the presence of an axial 6α-acetoxyl group according to the studies of Cookson and Dandegaonker (13). Introduction of an equatorial acetoxyl group causes a shift in absorption to a shorter wave length.

The thiolketic derivative (XI) was prepared from 386 mg of this product (X) with ethylenedithiol and boron fluoride as described in the previous experiment to yield 319 mg of an oil. Desulfuration was carried out in 40 ml of ethanol and 5 ml of water with 1.6 g of W-2 Raney nickel by stirring at room temperature for 16 hours and then refluxing for 6 hours. The catalyst was removed by filtration, the filtrate made alkaline with NaOH, heated for 1 hour on a water bath, and then left at room temperature overnight. After chromatography the main product was identified as lithocholic acid (IV) (57 mg). A small amount (23 mg) of 6-ketoallolithocholic acid (XII) was found in Fractions 20-1 and 20-2.

In another experiment, 500 mg of the thiolketic derivative (XI) were desulfurized with 2.4 g of W-2 Raney nickel by refluxing for 21 hours in an acidic medium containing 25 ml of ethanol, 8 ml of water, and 8 ml of acetic acid. The products (390 mg) were treated with methanolic KOH. After separation by partition chromatography, lithocholic acid (IV) (56 mg), and 3α-hydroxy-6β,7β-epoxycholanic acid (XIII) (6) (28 mg, m.p. 174-176°; Fractions 20-1 and 20-2) were identified by melting point, mixed melting point and infrared spectra. The structure of the epoxide (XIII) was established by converting it to 6β-hyodeoxycholic acid (XV) as described in the subsequent paragraph.

6β-Hyodeoxycholic Acid (XV) from 6α-Hydroxy-6β,7β-epoxycholanic Acid (XIII)—One milliliter of 48% aqueous HBr was added to a solution of 100 mg of (XIII) in 15 ml of acetone. The mixture was chilled in an ice bath for 1 hour, diluted with water, and extracted with ether. The product (XIV) was crystallized from a mixture of benzene and acetone, (110 mg), m.p. 145-148°. This material was highly solvated, and evolved gas upon melting. After dehalogenation with Raney nickel as described previously (6), chromatographic separation yielded 34 mg of 6β-hyodeoxycholic acid (XV), m.p. 208-210°. The identity was established by mixed melting point and infrared absorption spectrum.

B. Replacement of 6β-Bromide

Both α and β muricholic acids were obtained previously from methyl 3α,6β-diaceotoxy-7α-bromocholane (6, 11) by treatment with silver acetate in acetic acid. Debromination of the same bromocholane with Raney nickel followed by hydrolysis
with methanolic KOH yielded 3α,6β-dihydroxycholanic acid.
This provides strong evidence for the configuration of the 6β-hydroxyl in both α- and β-muricholic acids. To obtain additional information on the structures of the glycols and the stereochemistry at C-6 and C-7, similar experiments were carried out with the isomeric methyl 3α,7α-diacetoxy-6β-bromocholanate (XVII, Scheme III).

Hyocholic Acid (XX) from Methyl 3α,7α-Diacetoxy-6β-bromocholanate (XVII) (Scheme III)—The bromohydrin acetate (XVII) was prepared by acetylation of methyl 3α-acetoxy-6β-bromo-7α-hydroxycholanate (XVI) (7) with pyridine and acetic anhydride at room temperature. It has a melting point of 123-125°; \( \nu_{\max} = 1742, 1232, \) and 737 cm\(^{-1}\).

\[
\text{C}_9\text{H}_{14}\text{O}_4\text{Br}
\]

Calculated: C 61.15, H 7.97, Br 14.05
Found: C 61.82, H 7.89, Br 14.19

Compound (XVII), 100 mg, was refluxed in 10 ml of acetic acid and 1 ml of water with 40 mg of silver acetate for 8 hours. After cooling, the mixture was filtered, and gave 26 mg of silver bromide which corresponds to about 80% of the theoretical amount. The filtrate was diluted with water and extracted with ether. The oily residue from the ether extract (108 mg) was chromatographed on 10 g of silica gel. From the fractions eluted with 40 and 60% ether in Skellysolve B, 86 mg of colorless oil were obtained. After hydrolysis with methanolic KOH, and separation by partition chromatography, 50 mg (62% of theoretical) of hyocholic acid (XX) were obtained; m.p. 186-187°; the identity was established by mixed melting point and the infrared absorption spectrum.

In another experiment, the bromide (XVII) was treated with silver acetate under anhydrous conditions in acetic acid containing acetic anhydride (11): 48 mg of silver acetate were refluxed in 15 ml of glacial acetic acid and 5 ml of acetic anhydride for 30 minutes and then 150 mg of (XVII) were added and the mixture heated at 100-110° for 9.5 hours. After cooling, the mixture was filtered and yielded 35 mg (70% of theoretical) of silver bromide. The filtrate was diluted with water and extracted with ether. The residue after evaporation was hydrolyzed with 10% methanolic KOH by refluxing for 3 hours. The acidic products were subjected to partition chromatography and yielded 52 mg of hyocholic acid. No α-muricholic acid was found.

Chenodeoxycholic Acid (XIX) from (XVII)—Compound (XVII), 109 mg, was refluxed in 25 ml of ethanol, 10 ml of water, and 1 ml of acetic acid with 1.2 g of Raney nickel for 20 hours and yielded 92 mg of crystals, m.p. 123-127°. This material was identified as the methyl ester diacetate of chenodeoxycholic acid (XVIII) by comparing its infrared spectrum with that of an authentic sample. After hydrolysis with 15% methanolic KOH by refluxing for 5 hours, the product was purified by partition chromatography, yielding 38 mg (77% theoretical) of chenodeoxycholic acid (XIX), m.p. 140-142°; mixed m.p. with an authentic sample of chenodeoxycholic acid gave no depression. The infrared spectrum was comparable with that of chenodeoxycholic acid.

C. Oxidation of 3α,6,7-Trihydroxycholanic Acids by Periodic Acid

Previous studies have shown differences in the rate of oxidation of the four isomeric trihydroxy acids by periodic acid (7, 8, 9).

The experiment was repeated with more dilute solutions so that the rates of oxidation were slower and the course of the reaction could be better followed. A stock solution of each acid in methanol (1.0 mg per ml) was prepared. Aliquots of 1 ml were taken and each was diluted with 2 ml of methanol before the addition of 0.2 ml of periodic acid solution (1.24 g of \( \text{H}_2\text{O}_2 \) dissolved in 200 ml of water) (10). After a predetermined interval of time, the reaction was arrested by the addition of 2 ml of \( 0.01 \text{N} \) sodium arsenite followed by four drops of saturated \( \text{Na}_2\text{CO}_3 \) solution and four drops of \( 20\% \text{KI} \) solution. After 10 minutes, the excess of arsenite was titrated with \( 0.01 \text{N} \) iodine solution. A blank (3 ml of methanol) was treated similarly. The difference in the volume of iodine solution consumed by the sample and that by the blank represents the periodic acid consumed by the glycol. Theoretically, 0.50 ml of \( 0.010 \text{N} \) iodine solution corresponds to 100% oxidation. The experiment was conducted at 26° ± 0.2°. The results are presented in Fig. 1.
or-Muricholic acid IV 3α,6α,7β-226-228 +61.5° +234 +257

Hyocholic acid 3α,6α,7β-189-191

ω-Muricholic acid 3α,6α,7β-152 +36+2 +127 +147

D. Molecular Rotations

The molecular rotations of the four isomeric trihydroxy bile acids are given in Table I. The calculated values are derived by addition of the molecular rotatory contribution of the individual hydroxyl groups (14) to the molecular rotation of lithocholic acid (M = +132°, [α]s = +35°).

DISCUSSION

The course of desulfuration in the present study deviates remarkably from that of our previous experiments (10, 11). After desulfuration of the ethylennethioketal obtained from α-muricholic acid, no 3α,6β-dihydroxycholanolic acid was obtained; in stead, lithocholic acid was the major product accompanied by either a ketone (V or XII) or an epoxide (XIII). The ketone was obtained from a reaction medium of alcohol or acetone and the epoxide from acetic acid.

The isolation of 6-ketones and the 6β,7β-epoxide was unexpected. The mechanism of desulfuration is not understood, but the present results may be explained by postulating the formation of monothioethers as intermediates. Support for this view is found in a recent report by Clarke and Martini (15), who observed that a thioketal was partially desulfurated to yield a thioether. In our experiment, the medium may determine the conformation of the monothioether; complete desulfuration may then lead to the formation of the ketone or the epoxide in a manner analogous to the action of alkali on cis or trans halohydrins to yield ketones or epoxides, respectively (16, 17). Acceptance of this explanation must, however, await further investigation.

On the other hand, the ketone may be formed by dehydrogenation in the presence of Raney nickel (18). In unpublished experiments, however, it has been found that 3α,6α- or 3α,6β-dihydroxycholanolic acid is recovered unchanged after refluxing with Raney nickel. The possible influence of α-thiosubstituents is not known. The 6-ketoallithocholic acid (XII) apparently was a product of isomerization from 6-ketolithocholic acid (V) during alkaline hydrolysis (19, 20).

Retention of orientation of the remaining hydroxyl group after partial oxidation of α-muricholic acid (Scheme I) was shown by the reduction of (II) to α-muricholic acid (I) with sodium borohydride; however, it was not clear whether the main product (II) was a 6- or a 7-ketone. In the subsequent experiment (Scheme II) the 6β-acetoxy-7-ketone (X) was prepared for comparison. Since a 6-ketone was found in both instances after desulfuration with Raney nickel, it appears that (II) is also a 7-ketone. Thus, of the two axial hydroxyl groups, 6β and 7α, the latter appears to be more easily oxidized by chromic anhydride. Since substances at C-7 are more hindered than at C-6, this result contributes to the current view that the release of "compression energy" accelerates oxidation by chromic anhydride (17).

In these experiments desulfuration did not follow the course of the reaction reported for the 6α derivative, in that it did not produce any dihydroxy acid which would support our views of the structure of the original glycol (7). The results, nevertheless, support the structural evidence provided in our earlier experiments on the 6α-ketol; the axial 6β-hydroxyl group did not undergo inversion to yield the equatorial 6α-isomer. Thus, the hyodeoxycholic acid obtained previously from hyocholic and α-muricholic acids by desulfuration of the 7-thioketal (11) was not a result of inversion at C-6, but indeed constitutes a part of the structure of the original glycols.

The experiments outlined in Scheme III support the presence of a 7α-hydroxyl group in hyocholic acid, which is in agreement with the structure already proposed (4, 5, 10, 11). Acetylation of the bromohydrin acetate with silver acetate (XVII), either under anhydrous conditions or in the presence of water yielded hyocholic acid and not α-muricholic acid. This is in contrast with our previous experiment on the acetylation of methyl 3α,6β-diacetoxy-7α-bromocholanate (11), in which α-muricholic acid was obtained in 56% yield under anhydrous conditions. It was also noted that the rate of debronnization was different in the two instances; debromination of the 6b-bromide (XVII) proceeded at a much slower rate. The mechanism of acetylation of trans-bromohydrin acetates as proposed by Weinstein and Buckles (21) involves the formation of a cyclic orthoacetate intermediate which gives rise to the cis-glycol in the presence of water and trans-glycol under anhydrous conditions. This is evidently the case with acetylation of methyl 3α,6β-diacetoxy-7α-bromocholanate (6, 11). However, acetylation of (XVII) in the present study seems to have followed a different course. The conforma tion of Rings A and B of the bile acid nucleus is such that the 4a-hydrogen is in close proximity of the α-side of C-6 and C-7 and apparently can prohibit participation of the 7α-acetoxyl group in the formation of the cyclic orthoacetate. Replacement of the 6b-bromide may have been accomplished by a direct attack of an acetoxyl group from the opposite α-side. The result is a 6α configuration with Walden inversion. Hindrance to the α-side of Ring B is also noted in the hydroxylation of methyl 3α-acetoxy-D4-cholenate with osmium tetroxide (6, 22); the product was the 6β,7β-glycol and not the 6α,7α-glycol. In this case, a cyclic intermediate must be formed between osmium tetroxide and the steroid nucleus. Apparently the α-side of C-6 and C-7 is sterically unfavorable for the formation of such a

4 In an unpublished experiment, a mixture of 50 mg of cheno deoxycholic acid and 50 mg of 6β-hydroxydeoxycholic acid was oxidized with 8.5 mg of chromic anhydride in 90% aqueous acetic acid at 2-3°. The products were subjected to partition chromatography. The two main bile acids were identified as 7ketolithocholic acid (35 mg) and 6β-hydroxydihydroxycholanic acid (34 mg).

5 Debromination of methyl 3α,6β-diacetoxy-7α-bromochol anate by silver acetate in wet acetic acid was essentially complete in 1.0 hour (7), whereas under comparable conditions, only 35% of the 6b-bromide (XVII) was debrominated in 1 hour, 88% in 3 hours, and 98% in 8 hours.

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### Table I

<table>
<thead>
<tr>
<th>Trivial name</th>
<th>Previous rotation</th>
<th>OH groups</th>
<th>m.p.</th>
<th>[α]d°</th>
<th>M&lt;sub&gt;D&lt;/sub&gt;</th>
<th>Calcd</th>
<th>Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Muricholic</td>
<td>Acid II</td>
<td>3α,6α,7α</td>
<td>200</td>
<td>+38±2</td>
<td>+60</td>
<td>+155</td>
<td></td>
</tr>
<tr>
<td>β-Muricholic</td>
<td>Acid I</td>
<td>3α,6α,7β</td>
<td>228-229</td>
<td>+61.5±2</td>
<td>+254</td>
<td>+257</td>
<td></td>
</tr>
<tr>
<td>Hyocholic</td>
<td>Acid II</td>
<td>3α,6α,7β</td>
<td>185-186</td>
<td>+8±2</td>
<td>-47</td>
<td>+3</td>
<td></td>
</tr>
<tr>
<td>ω-Muricholic</td>
<td>Acid IV</td>
<td>3α,6α,7β</td>
<td>215</td>
<td>+36+2</td>
<td>+127</td>
<td>+147</td>
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</tr>
</tbody>
</table>

Retention of orientation of the remaining hydroxyl group after partial oxidation of α-muricholic acid (Scheme I) was shown by the reduction of (II) to α-muricholic acid (I) with sodium borohydride; however, it was not clear whether the main product (II) was a 6- or a 7-ketone. In the subsequent experiment (Scheme II) the 6β-acetoxy-7-ketone (X) was prepared for comparison.
complex, and the reaction takes place overwhelmingly on the β-side of Ring B.

The rate of oxidation of the four acids with periodic acid is also related to the stereochemistry of the bile acid nucleus. Arranged in the order of decreasing rate of oxidation, the four acids are: α-muricholic (diequatorial, trans), > β-muricholic (axial, equatorial, cis), > hyocholic (equatorial, axial, cis), > α-muricholic (diarxial, trans). The last mentioned, α-muricholic, is practically resistant to oxidation. These results are compatible with the concept of the formation of a cyclic intermediate between the glycol and periodic acid during oxidation (23, 24). The projected angle of 150° between the dialxial trans 6β- and 7α-hydroxyl groups in α-muricholic acid appears to be too great for the formation of a cyclic intermediate with periodic acid and hence oxidation does not proceed. Similar results were reported for dialxial hexose derivatives (25) and cholestane-3β,6α,7α-triol (26). On the other hand, the projected angle of 60° in the other three isomeric glycols permits rapid oxidation by periodic acid. The difference in rate among these three acids may be again explained by considering the stereochemistry concerning C-6 and C-7. If the α-side of the bile acid nucleus is sterically hindered for the formation of an omate or an orthoacetate, it must also hinder the formation of the periode complex. Hyocholic acid (the cis 6α,7α-glycol) is in fact oxidized at a rate appreciably less than that of β-muricholic acid. The diequatorial trans α-muricholic acid was oxidized at a faster rate than the cis β-muricholic acid. Similar results have been reported for the oxidation of cholesterol-3β,6α,7α-triol (26). These are apparent exceptions to the general rule that cis glycols are oxidized more rapidly than trans glycols (27). The oxidation of the cis β-glycol may be impeded by the proximity of the C-19 methyl group (1,3-diaxial interference (17)); this interference by the methyl group is not possible in the case of the diequatorial glycol and the cyclic periode intermediate may be formed more easily.

In comparing the molecular rotation values of the four glycols, a general agreement is found between the calculated and the observed values, although quantitative agreement is lacking. The discrepancy is due perhaps to "vicinal effects" of the glycols. All calculated values are lower than the observed value. It will be noted that the difference between the observed and the calculated M₉ values for the 7β derivatives is about the same (+17° and +23°) and that the difference for the 7α derivatives is of the same order (+86° and +95°). Similar correlation is not found in the 3α,11,12-trihydroxycholanic acids (28) or the cholestane-2,3-diols (29). Kagan (22) and Ziegler (5) have used the values of molecular rotation to support the structures proposed for β-muricholic acid and hyocholic acid, respectively.

SUMMARY

1. The trivial names "α-, β-, and ω-muricholic acids" are proposed for the new bile acids previously referred to as Acids II, I, and IV, respectively.

2. Hydrogenolysis of the 7-ethylthiethioketal derivative from ω-muricholic acid did not produce 6β-hydroxycholesterol; instead, lithocholic acid, 6-ketolithocholic acid, 6-ketoallithocholic acid, and 3α-hydroxy-6β,7β-epoxycholanic acid were among the products identified.

3. Acetolysis of methyl 3α,7α-diacetoxo-6β-bromocholaminate yielded hyocholic acid but not α-muricholic acid. The steric significance was discussed.

4. The rate of oxidation of each of the four acids with periodic acid was determined and found to be in the following order: α-muricholic > β-muricholic > hyocholic > ω-muricholic. Less than 3% of α-muricholic acid was oxidized during a period of 2 hours.

5. The calculated and observed values of molecular rotation of the four acids were compared and found to be in general agreement.

REFERENCES


Bile Acids: XIII. FURTHER CONTRIBUTIONS TO THE CONSTITUTION OF MURICHOLIC ACIDS


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