by the bimolecular alkylation of VI by V (equation 4) are O,N-dibenzyl-N-ethylhydroxylamine (IX) and N,N-diethylhydroxylamine (VIII).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Selective Oxidation with N-Bromosuccinimide. I. Cholic Acid[1]

BY LOUIS F. FIESER AND SRINIVASA RAJAGOPALAN[2]

The first objective of this work was to find an improved method for the conversion of cholic acid, the preponderant acid of available biles, into desoxycholic acid, the starting material for the only known synthetic routes to Kendall's Compound E, for which an important therapeutic use requiring greatly expanded supplies has recently been announced.[3] Wieland and Dane[4] discovered that 7α,12α-dihydroxycholanic acid can be converted into the 7-keto derivative in good yield by partial oxidation with chromic acid and thereby established the first of several instances of disparity between susceptibility of steroid alcoholic groups to acylation and to oxidation (except in Oppenauer oxidation, in which the first step is analogous to an acylation[5]). Iwasaki[6] effected the selective chromic acid oxidation of both 3α,7α- and 3α,7β-dihydroxycholanic acid to 3α-hydroxy-7-ketocholanic acid, and Kaziro and Shimada[7] demonstrated the selective oxidation of desoxycholic acid to 3α-hydroxy-12-ketocholanic acid. These Japanese workers thus established the order of susceptibility as $C_7 > C_{12} > C_3$ and correctly inferred that cholic acid should be convertible by chromic acid oxidation into the 7-keto derivative[7]; the failure of their own attempts to demonstrate the conversion is possibly attributable partly to the unfavorable melting point behavior of the 3α-hydroxy-7,12-diketocholanic acid that they isolated, as suggested by Gallagher and Long,[8] and partly to the difficulty in isolation of 3α,12α-dihydroxy-7-ketocholanic acid with high recovery even as the ester (Experimental part).

Haslewood[9] was the first to report the partial oxidation of cholic acid at C_7; by addition of aqueous chromate to cholic acid in acetic acid buffered with sodium acetate and Wolff–Kishner reduction of the crude oxidation mixture he obtained desoxycholic acid in yield of about 40%. Oxidation with chromic acid in acetic acid was studied by Gallagher and Long,[8] who isolated the 7-keto derivative as the methyl ester diacetate in 40% yield by chromatography, and by Hoehn and co-workers,[10] who obtained the ethyl ester in 41% yield; the latter workers report a yield of 41% (as ethyl ester) by oxidation of cholic acid with bromine in alkali at −5°.

As a means of evaluating various processes of partial oxidation, we adopted a standard procedure of conducting Wolff–Kishner reduction of the total oxidation mixture by the Huang-Minlon procedure[11] and isolating desoxycholic acid as the ether complex, from which pure desoxycholic acid can be quantitatively recovered.[12] The oxidation procedure of Haslewood[9] seemed the most promising, but in our experience the over-all yield from cholic acid was only 29.6%. Improved yields were obtained on applying the chromate oxidation procedure to the following pure derivatives: methyl cholate (47.5%); methyl cholate 3-acetate (85% yield); methyl 3-carbethoxycholate (83%). These derivatives were obtained in yields of 85, 39 and 80%, respectively, and hence the best route is through the methyl ester and its carbethoxy derivative, but the over-all yield is only 54%.

We then investigated with promising results oxidation with N-bromoacetamide in an aqueous medium, a method briefly applied in other instances by Reich and Reichstein.[13] The over-all yield of desoxycholic acid etherate from cholic acid by use of N-bromoacetamide in aqueous acetone was 57%, and the yields from various 3-derivatives were not sufficiently higher to compensate for the losses attending their preparation.

We then turned to the more readily prepared and commercially available N-bromosuccinimide which as far as we are aware has not been employed for the oxidation of secondary alcohols,[14] and found that it is a superior reagent for selective oxidations of substantially different character from N-bromoacetamide. Initial oxidations of cholic acid in aqueous acetone afforded, after usual reduction, pure desoxycholic acid etherate

(1) This work was supported in part by a grant from Research Corporation.

(2) Fellow of the National Cancer Institute.

(3) Hench, Kendall, Slocumb and Polley, *Proc. Staff Meetings Mayo Clinic*, **24**, 181 (1949).

(4) Wieland and Dane, *Z. physiol. Chem.*, **210**, 268 (1932).

(5) Gallagher and Long, *J. Biol. Chem.*, **165**, 365 (1946).

(6) Iwasaki, *Z. physiol. Chem.*, **244**, 181 (1936).

(7) Kaziro and Shimada, *ibid.*, **249**, 220 (1937).

(8) Gallagher and Long, *J. Biol. Chem.*, **147**, 131 (1943).

(9) Haslewood, *Nature*, **150**, 211 (1942); *Biochem. J.*, **37**, 109 (1943).

(10) Schneider and Hoehn, THIS JOURNAL, **65**, 485 (1943); Hoehn and Linsk, *ibid.*, **67**, 312 (1945); Hoehn and Schneider, U. S. Patent 2,321,598 (1943).

(11) Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

(12) White, *Biochem. J.*, **23**, 1165 (1929).

(13) Reich and Reichstein, *Helv. Chim. Acta*, **26**, 562 (1943).

(14) Hebbelynck and R. H. Martin, *Experientia*, **5**, 69 (1949), have reported the oxidation of benzyl alcohol and benzhydrol to the carbonyl compounds with N-chloroacetamide in neutral solvents or pyridine under illumination.

in 70% yield. We then found that the process can be simplified by conducting the oxidation in aqueous sodium bicarbonate solution. The best yields (68%) were obtained with 1.25–1.5 moles of N-bromosuccinimide, but a still larger excess had little deleterious effect. We then submitted pure desoxycholic acid to treatment with 1.25 moles of reagent under the same conditions and recovered the starting material unchanged. The reagent thus does not merely attack cholic acid preferentially at C_7 but attacks this position and leaves C_3 and C_{12} untouched. Chromic acid effects preferential oxidation at C_7 but effects successive oxidations at C_{12} and then C_3, and the same is true of bromine in aqueous alkali,[15] and even of microbiological oxidation.[16] Lardon[17] found that methyl etiocholate can be oxidized selectively to the 7-keto derivative with N-bromoacetamide in aqueous acetone in "good yield," but Reich and Reichstein[13] cite experiments showing that the same reagent (in aqueous *t*-butanol) effects oxidation of the following alcoholic groups at room temperature: 3α-, 12α-, 12β-, 17β-; thus desoxycholic acid was oxidized to the diketo acid. Sarett[18] observed the smooth oxidation of a 3α-hydroxysteroid with N-bromoacetamide in pyridine–*t*-butanol. The lack of reactivity of N-bromosuccinimide for 3α- and 12α-hydroxyl groups under the conditions that we have employed suggests a fundamental difference between the seemingly similar reagents. Direct comparison of the specificities of the various oxidizing agents under comparable conditions is in progress.

The unique specificity of the new oxidation procedure suggested an expedient for further increasing the availability of desoxycholic acid from bile. Since the desoxycholic acid present in the total acids from a bile hydrolyzate is not attacked by N-bromosuccinimide, and since adequate purification is accomplished in the course of the oxidation–reduction–etherate process outlined, the separation and purification of the component bile acids can be dispensed with and the total crude bile acids oxidized with excess N-bromosuccinimide in aqueous soda solution and the oxidation mixture reduced and processed as before. Lithocholic acid and other contaminants are removed in the ether solution, and pure desoxycholic acid is obtained very easily in yield estimated to be 34% higher than obtainable by separating the components by the usual procedures and processing the cholic acid by the present method, or in over twice the yield realizable by previous methods.

We are indebted to Dr. Max Tishler and his group at the Merck Laboratories for supplies and for friendly coöoperation.

(15) Charonnet and Horeau, U. S. Patent 2,244,328 (1941).
(16) Hoehn, Schmidt and Hughes, *J. Biol. Chem.*, **152**, 59 (1944).
(17) Lardon, *Helv. Chim. Acta*, **30**, 597 (1947).
(18) Sarett, THIS JOURNAL, **71**, 1165 (1949).

Experimental[19]

Methyl Cholate.—The melting points recorded for this ester differ widely: 147°,[20,21] 141–142°,[22] 156–158°,[23] 160–162°.[24] We prepared the ester by a combination of previous procedures[22,24] as follows: 100 g. of technical grade cholic acid (m. p. 195–197°) was dissolved by warming in 400 cc. of methanol containing 1 g. of hydrogen chloride per 100 cc. and the mixture allowed to stand overnight and then cooled in ice. The crystalline product that separated was found to be solvated; it was collected, air-dried, and dissolved in 250 cc. of toluene, and 200 cc. of solvent was removed by distillation with a free flame. Enough benzene was added to bring the solid into solution at the boiling point, and the solution was filtered and diluted with ether to the point of distinct turbidity and let stand overnight. The methyl cholate that crystallized was washed freely with ether and amounted to 73 g., m. p. 155–156°. The methanol and ethereal solutions afforded a further 15 g. of ester, m. p. 155–156°; yield 85%. A sample recrystallized from toluene–ether formed colorless needles, m. p. 155–156°.

Anal. Calcd. for $C_{25}H_{42}O_5$: C, 71.06; H, 10.01. Found: C, 71.00; H, 10.00.

Methyl Cholate 3-Acetate.—Although Meystre and Miescher[24] report difficulties in preparing this derivative, we found the directions of Grand and Reichstein[22] satisfactory and obtained nearly the yield specified; thus 88 g. of methyl cholate afforded 37.5 g. (39%) of the pure acetate, m. p. 149–150°. Attempts to raise the yield by conducting the acetylation with limited amounts of acetic anhydride in pyridine were unsuccessful.

Methyl 3-Carbethoxycholate.—This derivative was found to melt considerably higher than reported by Borsche,[25] who records the m. p. 147°. A solution of 42 g. of methyl cholate in 100 cc. of pyridine was treated gradually with 50 g. of ethyl choloformate with occasional cooling under the tap. The mixture was allowed to stand overnight, diluted with water, and the precipitated solid collected and washed. The yield of crude product, m. p. 173–175°, was 46 g. Crystallization from methanol afforded 39 g. (80%) of product, m. p. 176–177°, with slight shrinking at 148°.

Anal. Calcd. for $C_{28}H_{46}O_7$: C, 67.98; H, 9.38. Found: C, 67.95; H, 9.25.

Oxidation with Chromate.—Oxidations were conducted by the procedure of Haslewood,[9] the crude oxidation mixture was reduced according to Huang-Minlon,[11] and the desoxycholic acid was isolated as the etherate as described below and this derivative was dried at 90–100° in vacuum for one-half hour. Although the etherate is described as a 1:1 complex,[12] recovery experiments such as that cited below indicate that material dried in this manner is more nearly a 1:6 complex and we have calculated yields on the basis of the empirically determined molecular weight 400; the yields from 5-g. samples were: cholic acid, 1.45 g. (29.6%); methyl cholate, 2.25 g. (47.5%); methyl cholate 3-acetate, 3.66 g. (85%); methyl 3-carbethoxycholate, 3.2 g. (83%). The free desoxycholic acid melted at 171–173°.

Oxidation of N-Bromoacetamide.—A solution of 5 g. of cholic acid in 150 cc. of pure acetone was diluted with 50 cc. of water and treated at 25° with 2 g. of N-bromoacetamide (m. p. 108°) and 10 cc. of acetic acid. The solution turned yellow and then brown and in about fifteen minutes became colorless. After about three hours 50 cc. of water was added, solvent was removed at reduced pressure to the point of distinct turbidity, and a large volume of water was added to precipitate the product as a gum. This crude

(19) Melting points are uncorrected.
(20) Schotten, *Z. physiol. Chem.*, **10**, 175 (1886).
(21) Utaki, *ibid.*, **207**, 16 (1932).
(22) Grand and Reichstein, *Helv. Chim. Acta*, **28**, 344 (1945).
(23) Barnet, Lardon and Reichstein, *ibid.*, **30**, 1542 (1947).
(24) Meystre and Miescher, *ibid.*, **29**, 33 (1946).
(25) Borsche, *Ber.*, **57**, 1620 (1924).

material was reduced and the desoxycholic acid isolated as the etherate (mol. wt. assumed, 400) as described in detail below; yield 2.8 g. (57%). Yields of etherate from 5-g. samples of pure derivatives were as follows: methyl cholate, 3.3 g. (69%); methyl cholate 3-acetate, 3.0 g. (70%); methyl 3-carbethoxycholate, 3.1 g. (77%).

Methyl 3α-Acetoxy-7-keto-12α-hydroxycholanate.—The oxidation product from methyl cholate 3-acetate was a granular solid that on crystallization from methanol afforded colorless platelets, m. p. 175–176°.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 69.93; H, 9.15. Found: C, 70.01; H, 9.25.

Methyl 3-carbethoxy-7-keto-12α-hydroxycholanate also separated as a solid on dilution; it crystallized from methanol as either plates or needles, m. p. 181–182°.

Anal. Calcd. for $C_{28}H_{44}O_7$: C, 68.26; H, 9.00. Found: C, 68.57; H, 9.24.

Oxidation with N-Bromosuccinimide[26]; Preferred Procedure.—Eighty grams of technical cholic acid (Armour Laboratories, m. p. 195–197°) was dissolved by warming in a solution of 50 g. of sodium bicarbonate in 1.6 l. of tap water and the solution was cooled to 25°, treated with 43.7 g. (1.25 equiv.) of N-bromosuccinimide, and shaken occasionally until the reagent had all dissolved (about one and one-half hours). The yellow solution was allowed to stand at 25° for about seventeen hours, heated on the steam-bath for one hour, cooled in ice and acidified with dilute hydrochloric acid (1:2), added slowly with vigorous stirring and scratching. The keto acid separated as a white, granular solid and after cooling in ice for one-half hour it was collected, washed well with water, dried superficially between filter papers, transferred to a 1-l. round-bottomed flask with a ground joint and dried by evaporation to dryness with methanol (500 cc.; this saves time in the next step).

The flask was then charged with 600 cc. of triethylene glycol, 90 cc. of 86% hydrazine solution (the amount can be reduced to about 2 equivs.) and 70 g. of potassium hydroxide pellets, and heated cautiously under reflux in an oil-bath to a temperature of about 130° (thermometer suspended through condenser), when a vigorous exothermic reaction sometimes sets in (*e. g.*, when the starting acid is very impure). The flask was removed from the bath a few times until the frothing had subsided and then the mixture was refluxed gently for one-half hour; the condenser was removed and distillation conducted until the temperature had risen to 190°, and refluxing was continued for two to three hours at 190–200°. The solution was cooled, diluted with tap water to about 2 l., and acidified with 1:2 hydrochloric acid. On standing overnight the crude desoxycholic acid became granular and could be filtered easily. It was washed well, dried between filter papers, and then dried by evaporation with 500 cc. of methanol nearly to dryness (toward the end with a current of air). The residue while still warm was dissolved in 500 cc. of warm absolute ethanol and the solution allowed to stand at room temperature for one-half hour for separation of a trace of impurity, and filtered by gravity (100 cc. of ethanol for washing). The clear yellowish filtrate was evaporated to dryness as before (air current) and the slightly brown residual sirup was treated with 400 cc. of dry ether and alternately shaken and briefly heated until the gum had dissolved and given rise to a precipitate of desoxycholic acid etherate (unreacted lumps can be broken up with a flattened rod). After three or four hours with occasional shaking, the white etherate was collected, washed with 150–200 cc. of dry ether, and dried at 90–100° in vacuum for one-half hour. The etherate melts unsharply above 145°; some samples partly melted, resolidified, and remelted to a clear liquid at 170–173°. The average yield in three concordant experiments was 53 g. (68%, calculated for mol. wt. 400).

For conversion to free desoxycholic acid the above complex was heated on the steam-bath with 2.5 l. of tap water with stirring for one and one-half hours, when the solid partly melted and then resolidified. The mixture was cooled and the acid collected, triturated with cold water in a mortar, collected, and dried in vacuum at 100–110° for two hours. The white solid melted at 170–172°; average yield 51.8 g. (68%).

Ethyl 3α,12α-Dihydroxy-7-ketocholanate.[27]—The crude oxidation mixture from 80 g. of cholic acid was dehydrated by evaporation with 400 cc. of methanol, refluxed with 400 cc. of absolute ethanol and 12 cc. of boron fluoride etherate for three hours, and the solution concentrated to half its volume and poured into water. The dark-brown gummy product that separated was washed and rubbed repeatedly with water and with bicarbonate solution and evaporated with 300 cc. of methanol. The resulting solid was dissolved in 300 cc. of methanol, and the solution slowly deposited a crop of small crystals of the keto ester of high purity, m. p. 158–159°; yield 34 g. (40%).

The dark mother liquor and washings were evaporated and the dark-red gummy residue reduced according to Huang-Minlon and the mixture processed for recovery of desoxycholic acid etherate by the usual procedure. The yield of pure complex was 27 g. (34.5%). The combined yield corresponds to that of the above oxidation–reduction process and the experiment shows that the 7-keto acid can be isolated easily in a pure form as the ethyl ester but only in yield slightly better than half the amount actually present.

Other Oxidation Conditions.—Oxidation of cholic acid (40 g.) in acetone (1 l.)–water (400 cc.) with N-bromosuccinimide (21.8 g.) and processing as usual afforded 27.4 g. (70%) of desoxycholic acid etherate. Oxidation of methyl cholate in the same way with 1.25, 1.5 and 2.0 equivalents of the bromoimide gave the etherate in yields of 68, 68 and 63%, respectively; with 1.0 equivalent of reagent the product was contaminated with traces of cholic acid. Oxidation of methyl cholate in aqueous acetone with 1.25 equivalents of N-bromophthalimide gave the etherate in 68% yield. Attempted oxidation with chloramine-T was unsuccessful. Oxidation of cholic acid (5 g.) in aqueous bicarbonate solution at 25° as above but with use of 1.2 equivalents of bromine resulted in a lower yield of etherate (2.4 g., 49%).

Resistance of Desoxycholic Acid to N-Bromosuccinimide.—Five grams of technical desoxycholic acid or of the etherate (dried as above) was treated in 150 cc. of acetone and 50 cc. of water with 2.5 g. of N-bromosuccinimide and 10 cc. of acetic acid. The solution was allowed to stand for sixteen hours (the usual color changes occurred) and processed exactly as above, including Wolff–Kishner reduction. Desoxycholic acid etherate of usual purity was the only product recovered; yields 5.0 g. and 4.7 g.

Desoxycholic Acid from Total Bile Acids.—One hundred grams of the total acid precipitate prepared by saponification of 198 g. of a 75% sheep bile concentrate with refluxing alkali for eighteen hours and acidification was dissolved in 1.5 l. of water containing 65 g. of sodium bicarbonate and treated with 56 g. of N-bromosuccinimide at 25°. The initially dark solution improved in color as the oxidation progressed. After twenty-four hours the light greenish-yellow solution was filtered by gravity from a fine gray solid and acidified, and the rubbery precipitate was kneaded with water and submitted to reduction with 110 cc. of 85% hydrazine, 700 cc. of triethylene glycol and 85 g. of potassium hydroxide. The rest of the processing was done in the usual way except that the desoxycholic acid etherate was ground in a mortar with ether before the final collection. The complex was nearly colorless and melted at 175–177°, after shrinking at 145–155°; yield 41.5 g. The reddish-brown ethereal mother liquor was not worked up further. The yield corresponds

(26) Commercial material was most conveniently purified by adding 300 g. to 3 l. of boiling water, filtering the hot solution quickly through a conical funnel fitted with a small plug of absorbent cotton, and cooling the filtrate; the colorless plates that separated melted at 178–179°; yield 210 g.

(27) Haslewood, *Biochem. J.*, **38**, 108 (1944).

to 21.7 g. of free desoxycholic acid per 100 g. of sheep bile concentrate. By the usual methods of separation, 100 g. of concentrate yields about 4.4 g. of desoxycholic acid and 16.8 g. of cholic acid, convertible into 10.9 g. of desoxycholic acid by our process to give a total of 15.3 g. of the acid.

Summary

An improved method for the conversion of cholic acid into desoxycholic acid has been found in oxidation of the free acid at C_7 with N-bromosuccinimide in aqueous bicarbonate solution, followed by Wolff–Kishner reduction according to Huang-Minlon; the over-all yield is 68%. The oxidizing agent is more selective than chromic acid, bromine or even N-bromoacetamide, for the alcoholic groups at C_3 and C_{12} remain unattacked in the presence of an excess. In consequence, desoxycholic acid can be prepared with greater efficiency and ease than heretofore by direct application of the procedure to the total crude acids of saponified bile.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Selective Oxidation with N-Bromosuccinimide. II. Cholestane-3β,5α,6β-triol[1]

BY LOUIS F. FIESER AND SRINIVASA RAJAGOPALAN[1]

On exploring further possible applications of a method of oxidation found particularly effective for the selective oxidation of the 7α-hydroxyl group of cholic acid, we found that cholesterol (I) on oxidation with N-bromosuccinimide in aqueous acetone is converted in moderate yield into cholestane-3β,5α-diol-6-one (III).[2] The reaction could conceivably proceed through an intermediate oxide, but cholesterol α-oxide (Va) under the same conditions was found to yield a mixture containing only a small amount of the diolone III together with cholesterol 5,6-dibromide, and a bromo α,β-unsaturated ketone of analysis and absorption spectrum consistent with formula VI. We then found that cholestane-3β,5α,6β-triol can be oxidized to the diolone III in extraordinarily high yield in aqueous dioxane, acetone, or even methanol–ether or methanol. The triol II is known to be attacked preferentially at C_6 on chromic acid oxidation,[3] but an oxidation conducted by adding the reagent gradually over a ten-hour period afforded the 6-ketone as 3-acetate in only 65% yield, for without careful control the 3,6-diketone is easily formed.[2] No control is required in the present procedure, for the same high yield was obtained with 2.1 as with 1.05 equivalents of N-bromosuccinimide.

The best previous methods for preparation of cholestane-3β,5α,6β-triol are by reaction of cholesterol on the 3-acetate with hydrogen peroxide in acetic acid over a period of four days and saponification of the resulting acetate mixture, or hydrolysis of cholesterol α,β-oxide mixture.[2,4,5] Cleavage of the oxides by acetolysis with organic acids and hydrolysis with dilute sulfuric acid are attended with extensive or partial ester formation. An interesting incidental observation is that both cholesterol α-oxide and cholesteryl α,β-oxide acetate can be cleaved in high yield to the triol II or its 3-acetate by the action of periodic acid in refluxing aqueous acetone. This acid apparently functions as a satisfactory catalyst but is incapable of forming esters; the *trans*-triol suffers no appreciable glycol cleavage under the mild conditions required for hydrolysis (one-half hour).

Of more practical importance is the development of a reliable procedure for hydroxylating the double bond of cholesterol with hydrogen peroxide and formic acid.[6] Brief heating of cholesterol with 88% formic acid produces the 3-formyl derivative, and on addition of hydrogen peroxide to the resulting suspension a clear solution soon results and precipitation with water gives a mixture of esters from which cholestane-3β,5α,6β-triol 3,6-diformate can be isolated by crystallization. Brief saponification of the total mixture affords the pure triol in 91% yield.

Since cholestane-3β,5α-diol-6-one (III) can thus be prepared very easily in quantity from cholesterol in 85.5% over-all yield, it may serve as a useful intermediate to steroids of importance. However, two possible routes from this substance to 7-dehydrocholesterol have been investigated with negative results. The 3,5-diacetate (IV), known as a by-product of the chromic acid oxidation of cholesteryl acetate,[7] can be prepared readily by treatment of the diolone III with acetic anhydride and boron fluoride at room temperature. Since the tertiary acetoxyl group at C_5 when once formed is very resistant to saponification,[7] it seems possible that the ready acylation at this position may be the consequence of enol acetate formation and migration of the acetyl

(1) For acknowledgments, see Paper I, notes 1 and 2; THIS JOURNAL, 71, 3935 (1949).

(2) Pickard and Yates, *J. Chem. Soc.*, 93, 1678 (1908).

(3) Ellis and Petrow, *ibid.*, 1078 (1939).

(4) Westphalen, *Ber.*, 48, 1064 (1915); Ruzicka and Bosshard, *Helv. Chim. Acta*, 20, 244 (1937).

(5) Petrow, *J. Chem. Soc.*, 1077 (1937).

(6) Swern, Billen and Findlay, THIS JOURNAL, 67, 1786 (1945); compare Roebuck and Adkins, *ibid.*, 70, 4041 (1948); "Organic Syntheses," 28, 35 (1948).

(7) Schenck, *Z. physiol. Chem.*, 243, 119 (1936); Ellis and Petrow[3] prepared the compound from the 3-acetate with use of potassium acid sulfate as catalyst.