the reaction of the amino compounds with benzoyl chloride in pyridine solutions in the conventional manner.

Phenacyl esters and ethers. The sulfonic acids or substituted amino acids, amino phenols and amino thiols were placed in solution with equimolar quantities of the substituted α-diazo acetophenone in commercial dioxane. No appreciable reaction occurred until a trace (5 mg.) of anhydrous cupric chloride was added. The reaction mixture was then heated to 60–70° for 15 to 20 min. The reaction product was separated and purified by one of the following four methods:

Method A. The reaction mixture is poured slowly into 500 ml. of ice cold water containing 5–10 ml. of 10% K_2CO_3 solution. The ester precipitates and may be collected and recrystallized from alcohol.

Method B. The reaction mixture is heated to boiling and water is slowly added until the solution becomes permanently turbid. The solution is then cooled and the ester or ether crystallizes and may be recrystallized from alcohol.

Method C. Water is added as in method B and the mixture is shaken with an equal volume of chloroform. The chloroform layer is then washed first with 2% K_2CO_3 solution and then with distilled water, and then is dried over anhydrous calcium chloride. The chloroform solution is then concentrated and slowly cooled to −50° by the use of an acetone–dry ice bath. The ester crystallizes, may be rapidly filtered and then may be recrystallized from alcohol.

Method D. The anhydrous chloroform solution of the ester as obtained in method C is evaporated to dryness at low temperature under reduced pressure. The resulting material is recrystallized from alcohol with decolorizing charcoal added.

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Preparation and Degradation of 3α-Hydroxycholanic Acid[1]

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For another research program, a convenient method was desired for the preparation of 3α-hydroxynorcholanic acid on large scale and in high yield. Since the Barbier-Wieland degradation of 3α-hydroxycholanic acid has been described by several authors,[3,4] this degradation was undertaken.

The first step was the conversion of cholic acid into 3α-hydroxycholanic acid. This conversion was accomplished in 95% over-all yield by the modified Wolf-Kishner reduction[5] of the intermediate, methyl 3α - succinoxy - 7,12 - diketocholanate. The yield reported here could be obtained only when the modified procedure for alkali-sensitive carbonyls was adopted. Otherwise, the yields did not exceed 40%, and the purification of the reduction product was rather tedious. It appears that, unlike the monoketocholanic acids which are smoothly reduced by the ordinary Huang-Minlon modification,[5,6] the above mentioned diketocholanic acid derivative is sensitive to alkali.

The next step was the conversion of methyl 3-hydroxycholanate (I) into 3α-acetoxy-24,24-diphenylchol-23-ene (II). This conversion was accomplished in 90% yield by the known procedures.[3,4] The oxidation step of II with chromic acid in glacial acetic acid was found to be largely dependent upon reaction temperature. The highest yield (65%) of 3α-acetoxynorcholanic acid (III) was attained only when this oxidation was performed at 40–45°. Above and below this narrow temperature range, it was observed that the yield of III tended to decrease rather markedly.

The success of the ruthenium oxide–catalyzed oxidation of olefinic bonds with periodate[7] prompted the investigation of this new method for the oxidation of II into III. The present note describes the results of the use of ruthenium oxide as catalyst for the oxidation step involved in the Barbier-Wieland degradation of I.

The new method has proved to be successful with II. This involved the use of aqueous acetone (80–85%), 5 mole % of ruthenium tetroxide, and 140 mole % of solid sodium metaperiodate at 15–25°. II was readily oxidized to III and benzophenone in 78–83% yield. The over-all yield of 3α-hydroxynorcholanic acid from cholic acid was more than 70%. Osmium tetroxide,[8] used in place of ruthenium tetroxide, was found to be completely ineffective.

EXPERIMENTAL[9]

Preparation of 3α-hydroxycholanic acid. Methyl cholate (106 g.) was first converted into methyl 3α-succinoxy-7,12-diketocholanate (not isolated) by the procedure previously described,[10] and then it was mixed with 85% hydrazine hydrate (500 ml.) and ethylene glycol (1000 ml.) and the mixture was heated for 1 hr. at 100°. The resulting clear solution was cooled and then potassium hydroxide pellets (200 g.) were added portionwise through the condenser during 30 min. at room temperature. The condenser was then removed and the reaction mixture was slowly heated allowing the temperature to rise to about 200°. After re-

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fluxing at this temperature for about 2 hr. the reaction mixture was cooled, diluted with water (3 l.), and the separated potassium salt of 3α-hydroxycholanic acid was centrifuged. The free acid (92 g.), obtained after adding concentrated hydrochloric acid to a solution of the potassium salt in hot water, was practically pure. Recrystallization from methanol yielded 90 g. of crystals melting at 184° α_D^{16} +36.5° ± 0.5° (0.68% in EtOH) (reported[10] m.p. 187–188° α_D^{11} +32.1°). The yield based upon methyl cholate used is 95%.

When the ordinary Huang-Minlon procedure was adopted for the reduction of methyl 3α-succinoxy-7,12-diketocholanate, as described previously,[11] the yield of 3α-hydroxycholanic acid was less than 40% and at the same time the free acid was obtained in an impure state requiring many recrystallizations for its purification.

Methyl 3α-hydroxycholanate (I). The esterification of 3α-hydroxycholanic acid (80 g.) was effected in quantitative yield on treatment with boiling methanolic hydrochloric acid (2.5%) (1500 ml.) for 2 hr. Recrystallization from petroleum-ether (40–60°), after chromatography over alumina, yielded the labile form of m.p. 90–92°,[12] transforming into the stable form, m.p. 125–126° (reported[12] m.p. 126–127°), after two days standing in a vacuum desiccator.

3α-Acetoxy-24,24-diphenylchol-23-ene (II). For the preparation of this compound, the usual Barbier-Wieland procedure was employed. I (0.2 mole) was treated with an excess of phenyl magnesium bromide (3.0 mole) in boiling benzene for 24 hr. The resulting carbinol (not isolated) was acetylated by means of acetic anhydride (60 ml.) and dry pyridine (100 ml.). After removal of solvents by vacuum distillation it was then dehydrated by boiling with glacial acetic acid (200 ml.) for 20 hr. The acetylated diphenylethylene (II), which crystallized out on cooling, was practically pure. Recrystallization from acetone afforded white needles melting at 160° (reported[4] m.p. 160–167°); α_D^{20} +67° (1% in $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 255–257 mμ, (log ε 4.18).

Anal. Calcd. for $C_{38}H_{50}O_2$: C, 84.7; H, 9.35. Found: C, 84.7; H, 9.39.

The infrared spectrum (KBr) showed bands (cm.$^{-1}$) at 3077, 2963, 2899 (CH), 1733 (acetate CO), 1650, 1595, 1495 (double bonds), 1246 [acetate (C—O)], 757–760, 696–700 (CH aromatic).

24,24-Diphenyl-chol-23-en-3α-ol. II was readily deacetylated by means of ethanolic potassium hydroxide. Recrystallization from ethanol gave crystals melting at 140–141° (reported[4] m.p. 110–140°); $\lambda_{max}^{CHCl_3}$ 255–258 mμ (log ε 4.23); α_D^{17} +52° ± 2° (0.2% in $CHCl_3$).

Anal. Calcd. for $C_{36}H_{48}O$: C, 87.0; H, 9.74. Found: C, 86.5; H, 9.70.

The infrared spectrum shows bands (cm.$^{-1}$) at 3460, 3413 (OH), 2950, 2878 (CH), 1653, 1600, 1493 (double bonds), 1499, 1445, 1418, 1375 (CH deformation), 757–760, 695 (phenyl).

3α-Acetoxynorcholanic acid (III). (a) *Ruthenium oxide-catalyzed periodate oxidation of* II. When the solutions of II (2 g.) in acetone (200 ml.) and ruthenium tetroxide[7] (120 mg.) in aqueous sodium periodate (5%) (10 ml.) were mixed at room temperature, an immediate black precipitate of ruthenium oxide was obtained. While the temperature of the stirred mixture was maintained at 20–25°, a total of 4.5 g. of finely powdered sodium metaperiodate was added in portions over a period of 4 hr. To the mixture (now dark brown) a few ml. of isopropanol was added to reduce the catalyst (now black), which was then removed by filtration. After removal of solvent, water was added and the mixture was extracted with ether. The extract proved to contain a mixture of benzophenone and III. They were easily separated on treatment of the ethereal extract with aqueous sodium carbonate (10%). The benzophenone, left in the ether extract, was identified by its 2,4-dinitrophenylhydrazone derivative. III was first chromatographed over silica gel (7.5 g.) using benzene as eluting solvent, and then recrystallized from aqueous acetone, giving 1.20–1.25 g. (80–83%) of pure 3α-acetoxynorcholanic acid (III) of m.p. 177–178° (reported[7] m.p. 175–176°), α_D^{20} +51° (1% in $CHCl_3$).

(b) *Chromium trioxide oxidation of* II. A suspension of II (3 g.) in glacial acetic acid (10 ml.) was mixed with a solution of chromium trioxide (3 g.) in glacial acid (80 ml.) and then left to stand in a thermostat at 40–45° for 12 hr. Excess of reagent was destroyed by the addition of dry methanol, followed by removal of solvent in vacuum and then ether extraction. The desired acid was isolated and purified in a fashion here reported, giving 1.5 g. (65%) of crystalline product of m.p. 177–178°. II was oxidized only partially at 35–36°, whereas at 100°, even after a short time, the required acid could not be obtained. This apparently led to the formation of a complex mixture of oxidation products.

3α-Hydroxynorcholanic acid. Deacetylation of III in a manner here reported, afforded in almost quantitative yield the pure 3α-hydroxynorcholanic acid after recrystallization from methanol, m.p. 185–186° (reported[12] m.p. 181–182°), α_D^{20} +32° ± 3° (0.4% in EtOH).

Anal. Calcd. for $C_{23}H_{38}O_3$: C, 76.55; H, 10.71. Found: C, 76.59; H, 10.82.

The infrared spectrum of this hydroxyacid shows bands (cm.$^{-1}$) at 3410–3390, 3096 (OH), 2920, 2857 (CH), 1716, 1688 (CO), 1468, 1455–1449, 1414, 1377 (CH deformation).

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Studies in Purine Chemistry. IV. Hypoxanthine-1-*N*-oxide[1]

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Purine-*N*-oxides are receiving current attention,[2–9] not only because of their potential as possible purine antimetabolites, but also because of the possibility that they may function as intermediates in biological interconversions of purines.

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