Reaction of the Bromohydrin with Silver Nitrate.—A mixture of 1.0 g (2.1 mmoles) of the bromohydrin and 80 ml of a 2% solution of silver nitrate in absolute ethanol was boiled under reflux for 30 min and then allowed to cool to room temperature. The liquid phase was decanted and the silver bromide residue was rinsed several times with small portions of ether, which were then added to the alcohol. More ether was then added to bring the total ether volume to 125 ml and then the organic layer was washed with 500 ml of water in portions. The combined water wash was washed with a small volume of ether, which was added to the organic layer. This was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. The residue was crystallized from 150 ml of absolute methanol to give 610 mg (63%) of white crystals, mp 49–50°. Tlc on Eastman Chromatogram sheets with 1:1 benzene–pentane gave two spots after development with a solution of 2,4-dinitrophenylhydrazine in ethanol containing hydrochloric acid. The major spot had R_f 0.65 and the minor spot R_f 0.15, possibly due to some nitrate ester as indicated by a small peak at 1645 cm^{-1} in the infrared spectrum. Four recrystallizations from methanol gave the analytical sample of the acetal **3**: mp 52.5–53.5°; R_f 0.65; $\nu_{max}^{CCl_4}$ 2950, 1480, 1385, 1128, 1062, and 1012 cm^{-1}; nmr, methyl peaks at 0.66, 0.69, 0.83, 0.92 and 1.15 ppm, a four-proton quartet at 3.51, and a one-proton doublet at 4.17 ppm. The mass spectrum exhibited a molecular ion peak at m/e 458 (only under high amplification), and major peaks at 103 (diethyl acetal side chain), 414 (steroid nucleus minus an ethoxy radical), and 29 (ethyl ion).

Anal. Calcd for $C_{31}H_{54}O_2$: C, 81.15; H, 12.08. Found: C, 80.89; C, 12.18.

A-Nor-5α-cholestane-2-carboxaldehyde (2).—A crude, noncrystallized sample of the acetal, obtained from the reaction as above of 1.0 g of bromohydrin was dissolved in a mixture of 80 ml of acetone and 15 ml of 10% hydrochloric acid and the solution was boiled under reflux for 1 hr, then cooled, and poured into 100 ml of water. The resulting mixture was extracted once with 100 ml and once with about 25 ml of ether and the combined extract was washed with three 100-ml portions of water, and then dried over anhydrous sodium sulfate. The ether was evaporated to yield a solid, nearly white product which could not be recrystallized. Chromatography on neutral alumina (Fluka AG Buchs SG) gave a new unidentified compound: mp 134.5–136°; $\nu_{max}^{CCl_4}$ 3620, 3525, 2930, 1720, 1470, 1380, 1173, and 1037 cm^{-1}; nmr (10% CCl_4), 3.28 (doublet), and 2.30 (singlet) ppm.

However, chromatography of 200 mg of the crude aldehyde on 8 g of silica gel (Baker Analyzed Reagent) and elution with 25-ml portions of 1:1 benzene–hexane gave 173.5 mg of A-norcholestan-2-carboxaldehyde from the second fraction: mp 70–71°; $\nu_{max}^{CCl_4}$ 2945, 2715, and 1735 cm^{-1}; nmr (10% CCl_4), 0.65 (singlet), 0.81 (singlet), 0.90 (singlet), and 9.60 (doublet, aldehyde proton) ppm; ORD (C 0.08, hexane 20°), $[\phi]_{400}$ −65°, $[\phi]_{326}$ −3,854°, $[\phi]_{317}$ −3,586°, $[\phi]_{272}$ +9,962°, $[\phi]_{245}$ 9,438°.

Anal. Calcd for $C_{27}H_{46}O$: C, 83.86; H, 11.99. Found: C, 82.08; H, 11.90.

The aldehyde appeared to decompose slowly on standing which accounts for the analytical results.

The 2,4-dinitrophenylhydrazine derivative was prepared by adding a solution of 542 mg of crude aldehyde to a solution of 400 mg of 2,4-dinitrophenylhydrazine in 2 ml of concentrated sulfuric acid, 3 ml of water, and 10 ml of ethanol. The reaction was allowed to proceed for 1 hr and was then cooled in ice for 1 hr. The resulting precipitate was recrystallized from a mixture of 25 ml of ethanol and 8 ml of ethyl acetate to yield 559 mg (75%) of product, mp 118.7–121° dec. Tlc on alumina with 1:1 benzene–pentane gave only one spot. Four more recrystallizations from the same solvent gave the analytical sample, mp 137–139°.

Anal. Calcd for $C_{33}H_{50}N_4O_4$: C, 69.93; H, 8.89; N, 9.89. Found: C, 70.10; H, 8.86; N, 10.01.

2β,3β-Oxidocholestane (6).—The compound was prepared from 2α-bromo-3β-hydroxy-5α-cholestane by the method of Alt and Barton[11] and had mp 86–88° (MeOH); infrared bands appeared at ν_{max}^{Nujol} 3650, 812, and 805 cm^{-1}. A mass spectrum showed the parent peak (strong) at m/e 386.

Reaction of the Oxide with Silver Nitrate.—A solution of 20 mg (0.05 mmole) of 2β,3β-oxidocholestane in 3 ml of a 2% solution of silver nitrate in ethyl alcohol was boiled under reflux on a steam bath for 20 min. No precipitate formed during the heating period. The solution was filtered into a separatory funnel, diluted with 12 ml of ether, and washed twice with distilled water. The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure to yield 20.1 mg of damp solid. The infrared spectrum of this crude material (dried) showed no carbonyl stretching. A mass spectrum of the sample was nearly identical with that of the starting material and showed no increase in intensity of the m/e 103 (diethyl acetal side chain) peak relative to the background.

Reaction of the Oxide with Silver Nitrate and Dilute Nitric Acid.—The procedure was essentially that of the previous reaction except that 1 ml of 0.05 *M* nitric acid in ethyl alcohol was added to the mixture containing 20 mg (0.05 mmole) of 2β,3β-oxidocholestane. No precipitate formed during the heating period. The same work-up yielded 19.5 mg of white crystalline solid. The infrared spectrum (CCl_4 solution) showed no carbonyl stretching, but exhibited peaks at 3650, 1645, 1270, 1090, and 1010 cm^{-1}. The mass spectrum showed strong peaks at m/e 449 (molecular weight of 2,3-cholestanediol-3-nitrate ester), 432 (nitrate ester minus a hydroxyl group), and 386 (oxide). No increase in the intensity of the m/e 103 peak (relative to background) was observed.

A-Nor-5α-cholestane-2-carboxylic Acid (4).—To a solution of 243 mg (0.60 mmole) of the crude aldehyde in 10 ml of acetone was added 7 drops of Jones oxidation[7] solution and the resulting mixture was allowed to stand at room temperature until the precipitation of green chromate salts ceased (about 10 min). The mixture was then filtered and the filtrate diluted with 80 ml of water and extracted twice with ether. The ether extract was washed three times with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure to give a white, solid residue. The infrared and mass spectra of this solid were nearly identical with those of an authentic sample of A-nor-5α-cholestane-2α-carboxylic acid. The nmr spectrum (5% solution in CCl_4) showed peaks at 0.66 (C-18 methyl), 0.71 (C-19 methyl), and 2.82 ppm (br).

Methyl A-Nor-5α-cholestane-2α-carboxylate (5).—A solution of 100 mg (0.20 mmole) of crude A-nor acid in 50 ml of 10% methanolic hydrogen chloride was allowed to stand at room temperature for 45 hr. At the end of this time the precipitate was collected to yield 26.6 mg of methyl A-nor-5α-cholestane-2α-carboxylate: mp 95–97° (lit.[12] mp 97.5–98°); $\nu_{max}^{CCl_4}$ 2940, 1735, 1165, and 1035 cm^{-1}; nmr (3% in CCl_4 0.67 (C-18); 0.70 (C-19), 2.84 (broad, proton on C-2), and 3.62 ppm (methyl protons of ester group, singlet).

The filtrate was allowed to stand at 0° for 24 hr and then the precipitate was collected to give 51.4 mg of crystalline material melting over a broad range up to 75°. The infrared spectrum was nearly identical with that of methyl A-nor-5α-cholestane-2α-carboxylate. However, the nmr spectrum, determined in 5% benzene solution showed two C-19 methyl resonances at τ 9.20 (2β ester) and 9.35 (2α ester) and the relative areas indicated that the mixture contained 54% of the 2α and 46% of the β ester. These assignments are based on the results of Cava, Weintraub, and Glamkowski,[9] who obtained the same two esters from a different source.

Registry No.—**1**, 3903-52-4; **2**, 14789-57-2; 2,4-dinitrophenylhydrazone of **2**, 14789-58-3; **3**, 14789-62-9; **4**, 2312-00-7; **5**, 2312-02-9; **6**, 2789-50-6.

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

(12) B. B. Smith and H. R. Nace, *J. Am. Chem. Soc.*, **76**, 6119 (1954).

The Reactions of α-Nitro Ketones with Mineral Acids

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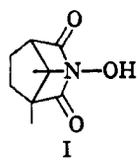
Though considerable work has been reported[1] on the preparation of hydroxamic and carboxylic acids

(1) (a) V. Meyer and C. Wurster, *Ber.*, **6**, 1168 (1873); (b) E. Bamberger and E. Rust, *ibid.*, **35**, 45 (1902); (c) S. B. Lippincott and H. B. Hass, *Ind. Eng. Chem.*, **31**, 118 (1939).

by the reaction of primary aliphatic nitro compounds with mineral acids,[2] little work has been reported on the reactions of α-nitro ketones with strong acids. Larson and Wat[3] found that in concentrated hydrochloric acid 3-nitrocamphor could be converted into N-hydroxycamphorimide (I) and, similarly, Hassner



I

and Larkin[4] found this same rearrangement of α-nitro ketone to N-hydroxyimide takes place in steroidal compounds. In this paper, we report on our investigations of the reactions of α-nitro ketones with mineral acids and demonstrate that they are converted in high yield into hydroxamic and carboxylic acids. The N-hydroxyimides found by other workers[3,4] are by inference reaction intermediates or subsequent reaction products of the carboxylic and hydroxamic acid fragments.

Results and Discussion

The results of the reactions of the various α-nitro ketones with mineral acids are shown in Table I. With sulfuric, phosphoric, or hydrochloric acid as reactant, a hydroxylamine salt was found to be the product accompanying the carboxylic acid. With nitric acid, the accompanying product was nitrogen dioxide.[5] As indicated in Table I, both primary and secondary α-nitro ketones can be cleaved in the acid media. In all cases, the yields were above 70%. The tertiary α-nitro ketone was unaffected by the acid reagents. The presence of hydroxamic acids were indicated by positive ferric ion tests on diluted sulfuric acid reaction solutions.

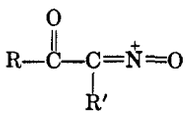
TABLE I
THE REACTION OF α-NITRO KETONES WITH MINERAL ACIDS

α-Nitro Ketone	Acid	Product
1-Nitro-2-pentanone	Phosphoric[a]	Butyric acid
1-Nitro-2-pentanone	Nitric[b]	Butyric acid
1-Nitro-2-dodecanone	Nitric	Undecanoic acid
1-Nitro-2-dodecanone	Sulfuric[c]	Undecanoic acid
1-Nitro-2-docosanone	Nitric	Uncosanoic acid
1-Nitro-2-docosanone	Sulfuric	Uncosanoic acid
α-Nitroacetophenone	Sulfuric	Benzoic acid
2-Nitro-3-pentanone	Nitric	Propionic acid
2-Nitro-3-pentanone	Sulfuric	Propionic and acetic acids
α-Nitrocyclohexanone	Hydrochloric[d]	Adipic acid
α-Nitrocyclohexanone	Sulfuric	Adipic acid
α-Nitropropiophenone	Sulfuric	Benzoic acid
3-Nitro-3-methyl-2-butanone	Sulfuric	No reaction

[a] 100% phosphoric acid at 75° for 30 min. [b] The nitric acid reactions were carried out in 3:1 v/v glacial acetic acid–37% nitric acid. [c] The sulfuric acid reactions were run in 96% acid. [d] 36% hydrochloric acid at reflux for 1 hr.

In comparison to the transformations of primary nitro alkanes to hydroxamic acids,[1] the conversion of α-nitro ketones into carboxylic and hydroxamic acids has been found to be exceedingly facile.[6] At conditions where 1-nitropropane is quantitatively recoverable (96% sulfuric acid at 60° for 30 min), α-nitro ketone conversions are complete.

In light of the ease of reaction of the α-nitro ketones in the anhydrous media, it is suggested that a species such as II, formed from dehydration of the α-nitro



II, R = alkyl or aryl;
R′ = alkyl or H

ketone is a reaction intermediate. Fragmentation of this species to an acylium ion[7] and a nitrile oxide followed by hydration of both fragments accounts for the observed products. The intermediacy of nitrile oxides has been proposed in the conversions of primary nitroalkanes into hydroxamic acids.[2]

Experimental Section

Preparation of the α-Nitro Ketones.—The several α-nitro ketones were prepared by previously described methods;[8] all gave satisfactory analysis.

Reactions of α-Nitro Ketones with Sulfuric, Hydrochloric, and Phosphoric Acids.—The several α-nitro ketones listed in Table I were all reacted in a similar manner with the three acids. Where solubility could not be effected at room temperature the systems were heated until solution was complete. The reaction of α-nitrocyclohexanone was typical. To 1.00 g of α-nitrocyclohexanone was added 25 ml of 96% sulfuric acid. The system warmed and turned light yellow. After standing for 15 min the acid solution was poured on ice and the resultant colorless aqueous solution was continuously extracted with ether for 24 hr. The resultant ether solution was dried over magnesium sulfate. Filtration and removal of the ether at reduced pressure at room temperature afforded 0.866 g of material (95.3% yield), mp 148°, whose infrared spectrum (Nujol null) showed it to be adipic acid (mp 151–153°).

Reaction of α-Nitro Ketones with Nitric Acid.—The several experiments conducted with nitric acid were all run in a similar manner. Because of the limited solubility of the α-nitro ketones in aqueous nitric acid, 3:1 v/v glacial acetic acid–37% nitric acid was used as the reaction medium. During reaction nitrogen dioxide was evolved. Work-up was as described above for α-nitrocyclohexanone.

Determination of Hydroxylamine in the Sulfuric Acid Reaction Systems.[9]—Using 177.5 g of 2-nitro-3-pentanone as reactant in 10 ml of concentrated sulfuric acid it was determined that after reaction 2.82 mequiv of hydroxylamine was formed. This is in excellent agreement with the predicted value, assuming 1 mole of hydroxylamine/mole of nitro ketone, of 2.71 mequiv.

Registry No.—1-Nitro-2-pentanone, 13245-76-6; 1-nitro-2-dodecanone, 14897-62-2; 1-nitro-2-docosanone, 14897-63-3; α-nitroacetophenone, 614-21-1; 2-nitro-3-pentanone, 13485-58-0; α-nitrocyclohexanone, 4883-67-4; α-nitropropiophenone, 14897-67-7; 3-nitro-3-methyl-2-butanone, 13292-96-1; phosphoric acid, 7664-38-2; nitric acid, 7697-37-2; sulfuric acid, 7664-93-9; hydrochloric acid, 7647-01-0.

(2) For a discussion of the mechanism of this and the related Nef reaction, see N. Kornblum and R. A. Brown, *J. Am. Chem. Soc.*, **87**, 1742 (1965).
(3) H. O. Larson and E. K. W. Wat, *ibid.*, **85**, 827 (1963).
(4) A. Hassner and J. Larkin, *ibid.*, **85**, 2181 (1963).
(5) The nitrogen dioxide is probably formed by reaction of hydroxylamine with the excess nitric acid.
(6) Nitroalkane conversions are effected by heating the compounds in concentrated acid at 130–160° for several hours; *cf.* ref 1c.
(7) N. C. Deno, C V. Pittman, Jr., and H. J. Wisotsky, *J. Am. Chem. Soc.*, **86**, 4370 (1964).
(8) T. Simmons, R. F. Love, and K. L. Kreuz, *J. Org. Chem.*, **18**, 2400 (1966).
(9) W. C. Bray, M. E. Simpson, and A. A. MacKenzie, *J. Am. Chem. Soc.*, **41**, 1363 (1919).