The Structure of the Solid By-product $C_{14}H_{20}N_2O_3$ Obtained from Nitromethane and Cyclohexanone[1]

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Appropriate degradation experiments (Chart I) have demonstrated that the compound described in the title has structure **1**.

A high-melting solid by-product **1**, $C_{14}H_{20}N_2O_3$, has been isolated by several workers[2–4] in the course of condensing cyclohexanone with nitromethane in the presence of a secondary amine catalyst. Although the chemistry of the by-product **1** was investigated rather extensively by Nightingale and co-workers,[4] no conclusion was reached as to the structure of this substance. A recent report[5] establishing, except for the location of the double bond and the stereochemistry of the oxime function, the structure **1** for this product, prompts us to report our independent investigations leading to the establishment of the same structure and also defining the nature of other degradation products whose constitution has not yet been reported.

Our experimental work is summarized in Chart I (the Roman numerals preceding the Arabic are the compound numbers previously used[4,5] to describe these substances). After obtaining samples of the hydrolysis product **2** and its ether **3**, examination of the infrared and ultraviolet spectra[6] of these products suggested the presence of five-membered cyclic ketone and γ-lactam functions in both products and a hydroxyl function in **2** but not **3**. The fact that compound **2**, but not **3**, gave a violet color with ferric chloride suggested the presence of an N—OH function in **2**. The n.m.r. spectra[6] of both **2** and **3** established the presence of a disubstituted carbon-carbon double bond in the environment $-CH_2-CH{=}CH-\overset{|}{\underset{|}{C}}-$. After considering the probable modes of reaction of the starting materials (see subsequent discussion and Chart II) and the aforementioned spectroscopic data, we reached the tentative conclusion that the hydrolysis product had structure **2** and, hence, the oxime should be formulated as **1**. Our subsequent work was, therefore, designed to establish these structures.

To avoid the problem of forming diastereoisomers, the carbon–carbon double bond of **2** was reduced to form **4** and remove the center of asymmetry in the molecule. Reduction of **4** with lithium aluminum hydride in ether produced the intermediate reduction products **5** and **6** whereas more vigorous hydride reduction in refluxing tetrahydrofuran produced the amino alcohol **7**.[7] The formation of the nitrone **5**, which was readily characterized by its characteristic spectroscopic properties[8] and its hydrogenation[9] to the amino alcohol **7**, provides unambiguous evidence for the presence of an N—O bond in compound **2**. Nightingale and co-workers had previously described the isolation of a $C_{14}H_{23}NO_2$ compound (designated as XIV), m.p. 190–191°, by the hydrogenation of a methanol solution of **3** over a copper chromite catalyst. However, this product XIV is not the nitrone **5**, but rather the isomeric hydroxy amide **8** which has subsequently been found to melt at 212–213° (see preceding paper) and at 216–218°.[5]

Acetylation and subsequent oxidation of the amino alcohol **7** produced the acetamido ketone **10** which is presumably the same as the compound previously designated[4b] XVIIIa, m.p. 170–171°, and has infrared absorption establishing the presence of a five-membered cyclic ketone. Furthermore, the n.m.r. absorption of compounds **5**, **9**, and **10** is only compatible with the presence of two quaternary carbon atoms within the five-membered ring. Cleavage of the amino alcohol with sodium metaperiodate established the 1,2-relationship of the amino and hydroxyl functions and, taken with the isolation of cyclohexanone 2,4-dinitrophenylhydrazone from this cleavage, requires part structure **4a** for compound **4**.

Nightingale and co-workers[4] had reported that the

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[1] This research has been supported by grant no. RG-8761 from the National Institutes of Health.

[2] A. Lambert and A. Lowe, *J. Chem. Soc.*, 1517 (1947).

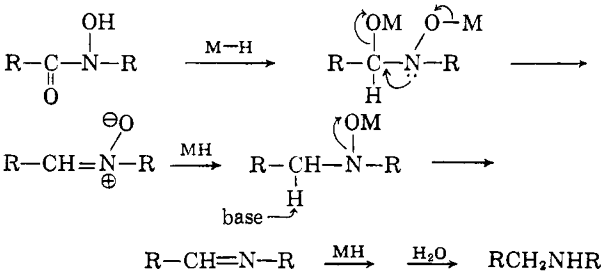
[3] Z. Eckstein, A. Sacha, and W. Sobotka, *Roczniki Chem.*, **34**, 1329 (1960); *Chem. Abstr.*, **55**, 18722 (1961).

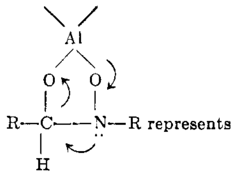
[4] (a) D. V. Nightingale, D. A. Reich, and F. B. Erickson, *J. Org. Chem.*, **23**, 236 (1958). (b) D. A. Reich, Ph.D. dissertation, University of Missouri, 1956.

[5] W. E. Noland and R. J. Sandberg, *Tetrahedron Letters*, No. **7**, 295 (1962).

[6] The peak positions are given in the experimental.

[7] Previous studies [F. Winternitz and C. Wlotzka, *Bull. soc. chim. France*, 509 (1960)] have indicated the complete reduction of hydroxamic acids to amines. In view of our findings and the reported [G. Zinner, *Angew. Chem.*, **71**, 311 (1959)] failure of lithium aluminum hydride to cleave readily N—O bonds, we suggest that this reduction follows the path indicated in the accompanying equations where M represents the metallic residue of the metal hydride.



The referee has pointed out that the formulation  represents a suitable alternative for the first intermediate drawn above.

[8] (a) J. Thesing and W. Sirrenberg, *Ber.*, **91**, 1978 (1959). (b) R. F. C. Brown, V. M. Clark, and A. Todd, *J. Chem. Soc.*, 2105 (1959). (c) K. Wiesner, M. Götz, D. L. Simmons, L. R. Fowler, F. W. Rachelor, R. F. C. Brown, and G. Büchi, *Tetrahedron Letters*, No. **2**, 15 (1959). (d) R. Bonnet, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. Todd, *J. Chem. Soc.*, 2094 (1959). (e) R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. Todd, *ibid.*, 2109 (1959).

[9] The reduction of an analogous nitrone to a pyrroline with zinc and acetic acid and to a pyrrolidine with tin and hydrochloric acid has been described (ref. 8d) and the complete hydrogenation of a nitrone to a saturated amine has been described (ref. 8b).

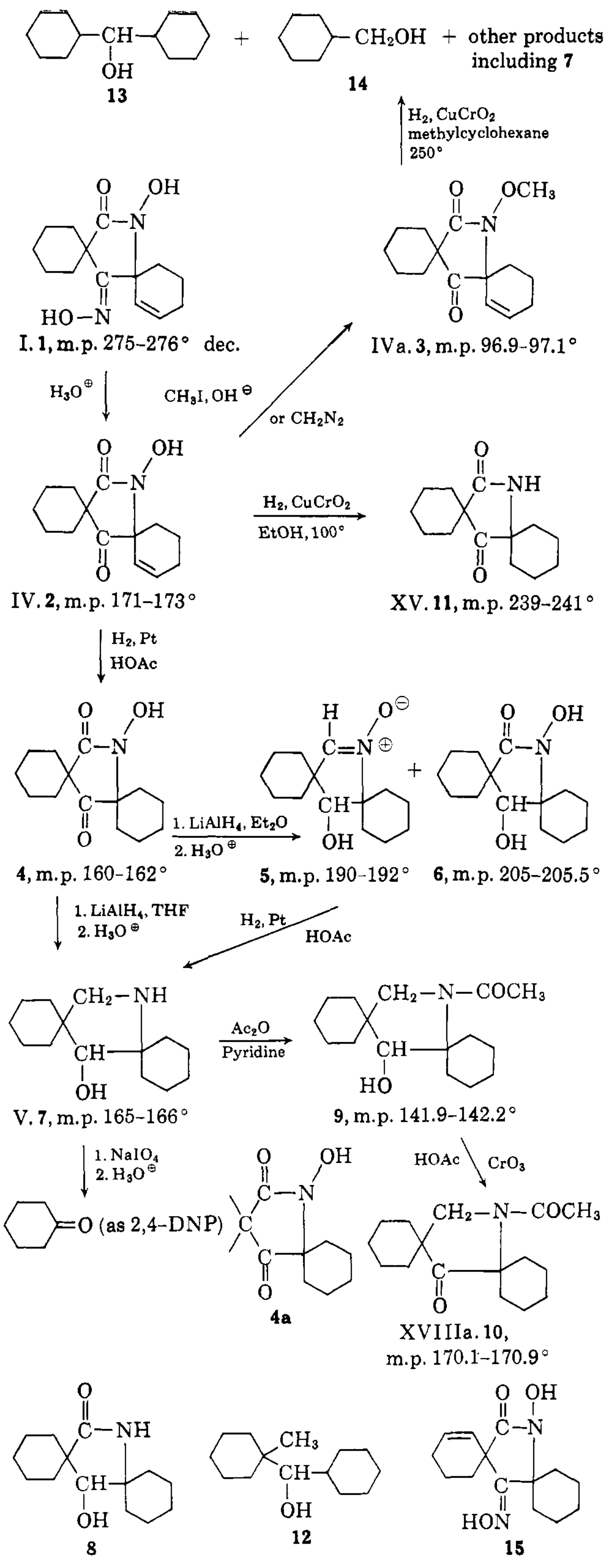


Chart I

hydrogenation of the keto amide **3** over copper chromite in methylcyclohexane at 250–280° yielded a $C_{14}H_{26}O$ alcohol (designated X), m.p. 56–57°, which formed a phenylurethane (designated Xa), m.p. 155–156°. Since a synthetic sample of the alcohol **12**, a logical possibility for this alcohol X, proved not to correspond in physical properties to the previously described material, we repeated the preparation of this alcohol. The product X was found not to have the composition $C_{14}H_{26}O$ but rather the composition $C_{13}H_{24}O$[10] and was readily identified as the previously known[11] dicyclohexylcarbinol (**13**). A second, neutral product of this hydrogenation was the cyclohexylcarbinol (**14**). This information taken with the part structure **4a** for the dihydro derivative **4** and the n.m.r. data for **3** limit the structural possibilities for the original condensation product to **1** and **15** (wherein the stereochemistry of the oxime function is uncertain.) The synthesis[5] of the keto amide **11** also leads to this conclusion.

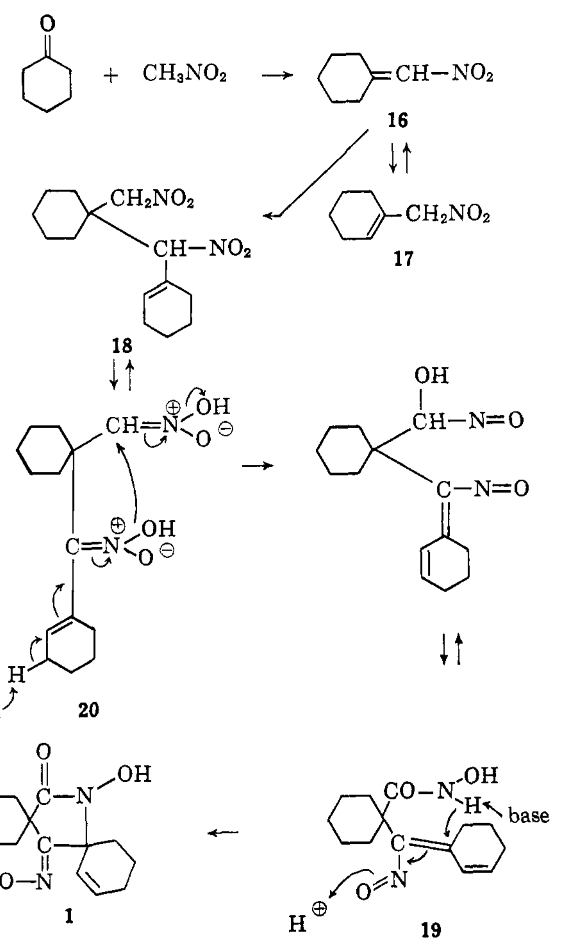


Chart II

Consideration of the probable mode of formation of the product (Chart II) leaves little doubt that the double bond should be located as indicated in structure **1**, since no rational sequence of steps is available to obtain structure **15** from the unsaturated nitro compounds **16** and **17**. The carbon skeleton of **1** can readily be obtained by a Michael condensation between **16** and **17** to form the adduct **18**. The sequence and timing of subsequent proton transfers and elimination of water is of course open to conjecture and only one of many possibilities is presented in Chart II. The sequence presented, if correct, implies that the conversion of a primary nitro compound—(*i.e.*, **18**)—to a hydroxamic acid—(*i.e.*, **19**)—may be effected without recourse to strongly acidic conditions,[12] when intra-

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[10] The previously reported (ref. 4) analytical data for both the alcohol and its phenylurethane fit either composition.

[11] (a) O. Neunhoeffer, *Ann.*, **509**, 115 (1934); (b) S. W. Chaikin and W. G. Brown, *J. Am. Chem. Soc.*, **71**, 122 (1949).

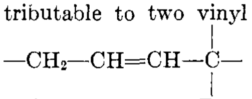
[12] W. E. Noland, *Chem. Rev.*, **55**, 137 (1955).

molecular transfer of a hydroxyl function is possible—(*e.g.*, **20**).

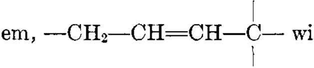
Experimental[13]

Preparation and Hydrolysis of the Condensation Product 1.—The crude condensation product, prepared as previously described,[4] separated from 2-ethoxyethanol as white needles, m.p. 275–276° dec. (lit.,[4] 270–271°), which give an immediate violet color with ferric chloride in aqueous ethanol and exhibit broad infrared absorption[14] in the 3500–3100-cm.$^{-1}$ region (assoc. O—H) and peaks in the 6-μ region at 1691, 1655 (shoulder), and 1641 cm.$^{-1}$ together attributable to the coupled stretching vibrations of an amide C=O and a C=N function. The material has only end absorption (ϵ 9500 at 210 mμ) in the ultraviolet.[15]

Anal. Calcd. for $C_{14}H_{20}N_2O_3$: C, 63.61; H, 7.63; N, 10.60. Found: C, 63.40; H, 7.49; N, 10.74.

After a mixture of 15.0 g. (0.057 mole) of the oxime **1**, 240 ml. of concentrated sulfuric acid, and 960 ml. of water had been refluxed, with stirring, for 58 hr., the resulting solid (12.5 g. or 88%, m.p. 170–171°) was collected and recrystallized from aqueous ethanol to separate the pure hydroxamic acid **2**, m.p. 171–173° (lit., 170–172°,[4] 176.5–177.5°[c5]). The product has infrared absorption[16] at 3120 (broad, assoc. OH), at 1757 cm.$^{-1}$ (cyclopentanone C=O) at 1680 cm.$^{-1}$ (5-membered lactam C=O) and at 1650 cm.$^{-1}$ (C=C) with end absorption (ϵ 10,100 at 210 mμ) in the ultraviolet[15] and a broad n.m.r. peak[17] at -0.42 τ (1H, O—H), a pair of triplets (J = 10 c.p.s. and 3 c.p.s.) centered at 3.74 τ as well as a doublet (J = 10 c.p.s.) centered at 4.79 τ together attributable to two vinyl hydrogen atoms in the environment  $—CH_2—CH=CH—\overset{|}{\underset{|}{C}}—$ and broad complex absorption in the region 6.5–8.5 τ. The acid **2** gave an immediate violet color with ferric chloride in aqueous ethanol.

Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.68; N, 5.62. Found: C, 67.57; H, 7.63; N, 5.57.

Reaction of 1.0 g. (4 mmoles) of the acid **2** with 1.53 g. (11 mmoles) of methyl iodide and 0.224 g. (4 mmoles) of potassium hydroxide in 50 ml. of refluxing methanol for 3 hr. followed by cooling and dilution with water precipitated 790 mg. (75%) of the crude methyl ether **3**. Recrystallization from aqueous methanol afforded 520 mg. (50%) of the pure ether **3** as white needles, m.p. 96.9–97.1° (lit., 94–95°,[4] 95–96°[c5]), with infrared absorption[18] at 1763 cm.$^{-1}$ (cyclopentanone C=O), 1710 cm.$^{-1}$ (5-membered lactam C=O), and at 1650 cm.$^{-1}$ (C=C) and an ultraviolet maximum[15] at 305 mμ (ϵ 73) and end absorption (ϵ 5,700 at 210 mμ). The product has n.m.r. absorption[17] centered at 3.75 τ (1H, pair of triplets with J = 10 c.p.s. and 3 c.p.s.) and at 4.62 τ (1H, doublet with J = 10 c.p.s.). together attributable to the vinyl protons in the system,  $—CH_2—CH=CH—\overset{|}{\underset{|}{C}}—$ with a singlet at 6.08 τ (3H, OCH_3) and broad absorption in the region 7.5–9.0 τ. In contrast to the previous report,[4] we found that the pure ether **3** gives no color with ferric chloride.

Anal. Calcd. for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.40; H, 7.80; N, 5.46.

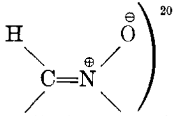
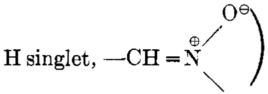
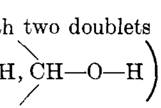
Reaction of a 2.49-g. sample of the acid **2** with excess ethereal diazomethane followed by the appropriate manipulations afforded 1.1 g. (42%) of the methyl ether **3**, m.p. 94.7–95.7°, identified with the aforementioned sample by mixed melting point and comparison of infrared spectra.

Hydrogenation of the Acid 2. A. Over Platinum.—A solution of 1.00 g. (4.0 mmoles) of the acid **2** in 15 ml. of acetic acid was hydrogenated at room temperature and atmospheric pressure over the catalyst from 100 mg. of platinum oxide. After the hydrogen absorption (86.0 ml. or 0.96 equiv.) ceased, the solution was diluted with water. Collection and recrystallization of the resulting solid from aqueous ethanol separated 700 mg. (70%) of the dihydro acid **4** as pale pink needles, m.p. 160–162°, with infrared absorption[16] at *ca.* 3100 cm.$^{-1}$ (broad, assoc. O—H), at 1748 cm.$^{-1}$ (cyclopentanone C=O), and at 1670 cm.$^{-1}$ (amide C=O) with end absorption (ϵ 8,100 at 210 mμ) in the ultraviolet[15] as well as a maximum at 301 mμ (ϵ 18). The product, which gives an immediate violet color with ferric chloride in aqueous ethanol, has a broad n.m.r. peak at -0.63 τ (1H, O—H) with broad absorption in the region 8.0–9.0 τ and no peaks attributable to vinyl protons.

Anal. Calcd. for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42; N, 5.57. Found: C, 67.04; H, 8.44; N, 5.79.

B. Over Copper Chromite.—A solution of 4.50 g. (0.0181 mole) of the acid **2** in 70 ml. of ethanol was hydrogenated over 6.0 g. of copper chromite catalyst at 100° and 1800 p.s.i. pressure until the hydrogen uptake ceased. After separation from the catalyst and concentration, recrystallization from acetone afforded 3.5288 g. (83%) of the keto amide **11** as white needles, m.p. 239–241° (lit., 233–234°,[4] 241–242°[c5]), with infrared absorption[14,19] at 3200 and 3080 cm.$^{-1}$ (assoc. N—H), at 1752 cm.$^{-1}$ (cyclopentanone C=O), and at 1688 cm.$^{-1}$ (5-membered lactam C=O) and end absorption (ϵ 1200 at 210 mμ) in the ultraviolet[15] as well as a maximum at 304 mμ (ϵ 18).

Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.45; H, 9.00; N, 5.95. Found: C, 71.51; H, 9.06; N, 6.15.

Reduction of the Dihydro Acid 4 with Lithium Aluminum Hydride. A. In Ether.—A 24.9891-g. (0.0996 mole) sample of the dihydro acid **4** was slowly added to a solution of 6.1952 g. (0.163 mole) of lithium aluminum hydride in 1700 ml. of refluxing ether using a Soxhlet extractor. After the mixture had been refluxed with stirring for 12 hr., the excess hydride was decomposed and the inorganic salts were precipitated by the successive additions of 6.2 ml. of water, 6.2 ml. of 15% aqueous sodium hydroxide, and 18.6 ml. of water. The aluminum salts were collected and extracted with ether. The combined ethereal solutions were extracted repeatedly with 1 *N* aqueous hydrochloric acid and the resulting aqueous extract was made alkaline and extracted with ether. Drying and concentration of this ethereal extract left 13.7164 g. (58%) of the crude nitrone **5**, m.p. 148–154°. Several recrystallizations from ethyl acetate afforded 4.7763 g. (20.2%) of the pure nitrone **5** as white needles, m.p. 190–192°, which gave no color with ferric chloride and was soluble in 5% aqueous hydrochloric acid but insoluble in 5% aqueous sodium hydroxide. The nitrone has infrared absorption[16] at 3600 cm.$^{-1}$ (unassoc. O—H) at 3220 cm.$^{-1}$ (assoc. O—H) and at 1590 cm.$^{-1}$  $\left(\overset{H}{\diagdown}C=\overset{\oplus}{N}\overset{O^{\ominus}}{\diagup}\right)^{20}$ with an ultraviolet maximum[15] at 239 mμ[20] (ϵ 11,000) and n.m.r. absorption[17] at 3.03 τ (1 H singlet,  $—CH=\overset{\oplus}{N}\overset{O^{\ominus}}{\diagup}$) with two doublets ($J$ = 6.5 c.p.s.) centered at 5.47 and 5.99 τ (2H,  $\diagdown CH—O—H$) and broad absorption in the region 7.7 to 9.0 τ. When a trace of acid was added to catalyze the exchange of the hydroxy proton, the two doublets collapsed to sharp singlets and the position of the peak attributable to the hydroxyl proton was shifted to 5.07 τ.

Anal. Calcd. for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found: C, 70.84; N, 9.86; N, 5.99.

The ethereal solution remaining after removal of the nitrone **5** was extracted with 1 *N* aqueous sodium hydroxide. After this aqueous extract had been acidified and extracted with ether, the

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[13] All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated, magnesium sulfate was employed as a drying agent. The infrared spectra were determined with either a Baird, Model B, or a Perkin-Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The n.m.r. spectra were determined at 60 Mc. with a Varian, Model A-60, n.m.r. spectrometer. The mass spectra were obtained with a CEC, Model 21-130, mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

[14] Determined as a suspension in a potassium bromide pellet.

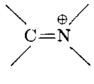
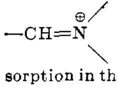
[15] Determined as a solution in 95% ethanol.

[16] Determined in chloroform solution.

[17] Determined in deuteriochloroform solution.

[18] Determined in carbon tetrachloride solution.

[19] Determined as a Nujol mull.

[20] Previous studies (ref. 8) have shown nitrones to have ultraviolet maxima in the region 229–235 mμ (ϵ 9000) with infrared absorption in the region 1600–1620 cm.$^{-1}$ for  $\diagdown C=\overset{\oplus}{N}\overset{O^{\ominus}}{\diagup}$ and 1570–1590 cm.$^{-1}$ for  $—CH=\overset{\oplus}{N}\overset{O^{\ominus}}{\diagup}$. The proton in the latter structure leads to n.m.r. absorption in the region of 4 τ.

ethereal extract was dried and concentrated to separate, after recrystallization from ethyl acetate, 138.7 mg. (0.5%) of the acid **6** as white needles, m.p. 205–205.5°.

The product gives a purple color with ferric chloride in aqueous ethanol and is soluble in 5% aqueous sodium hydroxide and insoluble in 5% aqueous hydrochloric acid. The product has infrared absorption[14,19] at 3500 and 3440 cm.$^{-1}$ (assoc. O—H) and at 1710 cm.$^{-1}$ (5-membered lactam C=O) with end absorption (ϵ 4,400 at 210 mμ) in the ultraviolet.[15]

Anal. Calcd. for $C_{14}H_{23}NO_3$: C, 66.37; H, 9.15; N, 5.53. Found: C, 66.47; H, 9.22; N, 5.60.

B. In Tetrahydrofuran.—To a solution of 7.34 g. (0.196 mole) of lithium aluminum hydride in 200 ml. of tetrahydrofuran was added, dropwise and with stirring over a 3-hr. period, a solution of 26.1877 g. (0.104 mole) of the dihydro acid **4** in 850 ml. of tetrahydrofuran. After the resulting mixture had been refluxed, with stirring for 45 hr., 14.1 ml. of water followed by 52.3 ml. of 3.75 *M* aqueous sodium hydroxide was added and the precipitated inorganic salts were collected and extracted with ether. The ethereal extract was added to the residue remaining after concentration of the tetrahydrofuran solution and the resulting ethereal solution was extracted with aqueous hydrochloric acid. The aqueous extract was made basic which precipitated the crude amino alcohol **7**, m.p. 160–165°, in quantitative yield (23.6172 g.). Recrystallization from ethyl acetate afforded the pure amino alcohol **7** as white needles, m.p. 165–166° (lit. 162–163°,[4] 166.5–167.5°[5]), with broad infrared absorption[14,19] in the 3-μ region (assoc. N—H and O—H) but no absorption attributable to a carbonyl function in the 6-μ region and weak end absorption (ϵ 220 at 210 mμ) in the ultraviolet.[15]

Anal. Calcd. for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27. Found: C, 75.08; H, 11.27; N, 6.22.

A solution of 164.6 mg. (0.695 mmole) of the nitrone **5** in 12 ml. of acetic acid was hydrogenated at room temperature and atmospheric pressure over the catalyst from 16.7 mg. of platinum oxide. After the hydrogen uptake (46.6 ml. or 1.36 equiv.) ceased, the catalyst was removed and the solution was made basic with aqueous sodium hydroxide and then extracted with ether. The ethereal extract was dried, concentrated, and crystallized from ethyl acetate to separate 39.6 mg. (26%) of the amino alcohol **7**, m.p. 163–164°, identified with the previously described sample by a mixed melting-point determination and comparison of infrared spectra.

Derivatives of the Amino Alcohol 7.—To a cold solution of 498 mg. (2.2 mmoles) of the amino alcohol **7** in 16 ml. of pyridine was added 4.57 g. (44.8 mmoles) of acetic anhydride. The resulting solution was allowed to warm to room temperature over an 80-min. period and acidified with aqueous hydrochloric acid and extracted with ether. After the ethereal solution had been washed with aqueous sodium bicarbonate, dried, and concentrated, the residual hydroxy amide **9**, (569.4 mg. or 96%, m.p. 142–144°) was recrystallized from an ethyl acetate-hexane mixture to separate 263.2 mg. (44%) of the pure amide **9** as white plates m.p. 141.9–142.2°. The product has infrared absorption[16] at 3620 cm.$^{-1}$ (unassoc. O—H), at 3360 cm.$^{-1}$ (assoc. O—H) and at 1625 cm.$^{-1}$ (amide C=O) with end absorption (ϵ 7600 at 210 mμ) in the ultraviolet[15] and n.m.r. absorption[17] (in the presence of a trace of hydrogen chloride) at 5.70 τ (1H, O—H), with singlet at 6.08 τ $\left(1\text{H}, >\text{CH—O}\right)$, a pair of doublets ($J$ = 10 c.p.s.) with a pattern typical of an AB system centered at 6.57 and 6.73 τ $\left(2\text{H}, -\overset{|}{\underset{|}{\text{C}}}-\text{CH}_2-\overset{|}{\text{N}}-\text{CO}\right)$, a singlet at 7.92 τ (3H, acetyl CH_3) and broad absorption in the region 8.2 to 8.9 τ. As noted for the n.m.r. spectrum of the nitrone, when no acid is added to the solution the singlet at 6.08 τ $\left(>\text{CH—O—}\right)$ becomes a doublet (J = 6 c.p.s.) indicating that exchange of the hydroxy proton is slow in neutral solution.

Anal. Calcd. for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26; N, 5.28. Found: C, 72.48; H, 10.29; N, 5.22.

To a solution of 500 mg. (1.9 mmoles) of the hydroxy amide **9** in 10 ml. of acetic acid was added, dropwise and with stirring, a solution of 280 mg. (0.95 mmole) of potassium dichromate and 279 mg. (2.85 mmoles) of sulfuric acid in 2.29 ml. of water. The resulting mixture was allowed to stir at room temperature overnight and then diluted with water and extracted with ether. After the ethereal extract had been washed with aqueous sodium bicarbonate, dried, and concentrated, the residual crude keto amide **10** (549.3 mg., m.p. 168.4–170.8°) was recrystallized from aqueous ethanol to separate 250 mg. (56%) of the pure ketone as white needles, m.p. 170.1–170.9° (lit.,[4b] 170–171°). The product has infrared absorption[16] at 1735 cm.$^{-1}$ (cyclopentanone C=O) and 1640 cm.$^{-1}$ (amide C=O) with an ultraviolet maximum[15] at 303 mμ (ϵ 25) as well as end absorption (ϵ 3200 at 210 mμ) and n.m.r. singlets[17] at 6.38 τ $\left(2\text{H}, -\overset{|}{\underset{|}{\text{C}}}-\text{CH}_2-\overset{|}{\text{N}}-\text{CO}-\right)$ and 7.87 τ (3H, acetyl CH_3) as well as broad absorption in the region 8.1–9.0 τ.

Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.91; H, 9.61; N, 5.29.

Reaction of Cyclohexylmagnesium Bromide with 1-Methylcyclohexanecarboxaldehyde.—To a solution of the Grignard reagent prepared from 3.88 g. (0.16 g.-atom) of magnesium, 22.4 g. (0.138 mole) of cyclohexyl bromide, and 100 ml. of ether was added, dropwise and with stirring under a nitrogen atmosphere, 7.8229 g. (0.062 mole) of the aldehyde.[21] After the addition was complete, the mixture was stirred overnight at room temperature and then treated with a saturated, aqueous solution of ammonium chloride (adjusted to *p*H 8 with aqueous ammonia). The ether layer was concentrated and the residue was distilled to separate 3.1936 g. (38%) of 1-methylcyclohexylcarbinol, b.p. 37–38° (0.13 mm.), n^{25}D 1.4684, and 4.3346 g. (32%) of the alcohol **12**, b.p. 87.5–90.5° (0.10 mm.), n^{25}D 1.4929. The known[22] 1-methylcyclohexylcarbinol, with infrared absorption[18] at 3625 cm.$^{-1}$ (unassoc. O—H) and 3340 cm.$^{-1}$ (assoc. O—H) and n.m.r. absorption[18] at 6.76 τ $\left(2\text{H broad}, -\overset{|}{\underset{|}{\text{C}}}-\text{CH}_2-\text{O},\right)$ at 7.19 τ (1H, broad, O—H) and at 9.12 τ (3H singlet, CH_3) as well as complex absorption in the region 8.0 to 9.0 τ, was identified by conversion[23] to its 3,5-dinitrobenzoate, m.p. 76–77° (lit.,[22] 76–77°), in 56% yield.

The alcohol **12** has infrared absorption[18] at 3620 cm.$^{-1}$ (unassoc. O—H) and at 3500 cm.$^{-1}$ (assoc. O—H) with no significant ultraviolet absorption[15] (ϵ 12 at 210 mμ) and n.m.r. absorption[18] at 7.03 τ $\left(1\text{H, no splitting discernible, } >\text{CH—O}\right)$ with broad, complex absorption in the region 8.0–9.0 τ and a singlet at 9.13 τ $\left(3\text{H}, -\overset{|}{\underset{|}{\text{C}}}-\text{CH}_3\right)$.

Anal. Calcd. for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 80.14; H, 12.39.

A solution of 500 mg. (2.4 mmoles) of the alcohol **12** and 410 mg. (3.4 mmoles) of phenyl isocyante in 5 ml. of hexane was refluxed for 5 min. and then filtered and cooled to separate 322.8 mg. (41%) of the **phenylurethane of 12** as white needles, m.p. 109–109.5°. Recrystallization raised the melting point of this derivative to 109.8–110.8°. The sample has infrared absorption[18] at 3440 and 3360 cm.$^{-1}$ (assoc. and unassoc. N—H) with a peak at 1735 cm.$^{-1}$ with shoulders at 1715 and 1700 cm.$^{-1}$ (C=O), an ultraviolet maximum[15] at 236 mμ (ϵ 19,000) with low intensity maxima (ϵ 720–820) in the region 260–280 mμ and n.m.r. absorption[18] in the region 2.5–3.3 τ (aryl C—H) with a peak (broad but splitting pattern not discernible) at 5.50 τ $\left(>\text{CH—O}\right)$, broad, complex absorption in the region 8.0–9.0 τ and a singlet at 9.07 τ $\left(-\overset{|}{\underset{|}{\text{C}}}-\text{CH}_3\right)$.

Anal. Calcd. for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.70; H, 9.48; N, 4.34.

Periodate Cleavage of Amino Alcohol 7.—A solution of 2.4902 g. (11.6 mmoles) of sodium metaperiodate and 1.2739 g. (5.70 mmoles) of the amino alcohol **7** in 200 ml. of 50% aqueous

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[21] 1-Methylcyclohexanecarboxaldehyde, b.p. 69–71° (23 mm.), n^{25}D 1.4468 [W. Parker and R. A. Raphael, *J. Chem. Soc.*, 1723 (1955) report b.p. 120° (546 mm.), n^{21}D 1.4490], was obtained by hydrogenation of the Diels–Alder adduct of butadiene and methacrolein.

[22] H. Pines, H. G. Rodenberg, and V. N. Ipatieff, [*J. Am. Chem. Soc.*, **76**, 771 (1954)] report b.p. 186–189°, n^{20}D 1.4672.

[23] J. H. Brewster and C. J. Cotti, Jr., *J. Am. Chem. Soc.*, **77**, 6214 (1955).

methanol was stirred for 95 hr. and then treated with 1.9 g. (7 mmoles) of barium acetate. The resulting mixture was filtered and the residue was washed with methanol. The combined filtrates were acidified with hydrochloric acid, saturated with sodium chloride, and repeatedly extracted with ether. After the ethereal extracts had been washed with aqueous sodium bicarbonate, dried, and concentrated under a 75-cm. Vigreux column, the concentrate was added to a boiling ethanolic solution of 1.41 g. (9.13 mmoles) of 2, 4-dinitrophenylhydrazine and 0.2 ml. of concentrated hydrochloric acid. The resulting solution was concentrated to dryness under reduced pressure and the residue was chromatographed on Silica-Gel. The 2, 4-dinitrophenylhydrazone of cyclohexanone, eluted with carbon tetrachloride-ether mixtures, was recrystallized from ethanol to separate 48.5 mg. (3.3%) of the pure derivative as orange plates, m.p. 159.5–160.3°, which was identified with an authentic sample by a mixed melting-point determination, comparison of infrared spectra and comparison of R_f values on thin-layer chromatography.[24]

Hydrogenation of the Methyl Ether 3.—A solution of 17.9 g. (0.0681 mole) of the methyl ether **3** in 325 ml. of methylcyclohexane was hydrogenated over 59.6 g. of a copper chromite catalyst employing an initial temperature of 27° and 1900 p.s.i. and a final temperature of 250° and 2790 p.s.i. After the resulting mixture had been filtered and the catalyst washed with ether, the combined organic solutions were washed successively with aqueous hydrochloric acid and aqueous sodium hydroxide. The basic fraction, isolated in the usual way, afforded 1.3228 g. (8.7%) of the amino alcohol **7**, m.p. 164.2–166°. The organic solution of the neutral products was dried and concentrated and the residue distilled in a short-path still to separate 190.1 mg. (2.7%) of a lower-boiling liquid, and 972.1 mg. of a higher-boiling solid fraction, m.p. 62–63°. The lower-boiling liquid, n^{24}_D 1.4638 (lit.,[25] n^{25}_D 1.4628), was identified with an authentic sample of cyclohexylcarbinol (**14**) by comparison of infrared and mass spectra.

The solid higher-boiling fraction, was chromatographed on Silica-Gel to separate, after elution with a pentane–ether mixture and sublimation (56° at 0.01 mm.), 754.8 mg. (5.65%), of dicyclohexylcarbinol (**13**) as white rosettes, m.p. 63.4–64.3°, and 35 mg. of the starting ether **3**, m.p. 94.5–96°. The dicyclohexylcarbinol (**13**) has infrared absorption[16] at 3605 and 3450 cm.$^{-}$ (unassoc. and assoc. O—H) with a broad n.m.r. peak[17] at 6.99 τ (1H, half band width *ca.* 9 c.p.s., $>$CH—OH) as well as broad, complex absorption (23H) in the region 8.0–9.1 τ.

Anal. Calcd. for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.29; H, 12.30.

An authentic sample of the carbinol **13**, as white cubes from ether m.p. 62.8–64° (lit.,[26,27] 63°), was prepared in 22% yield by reaction of ethereal cyclohexylmagnesium bromide with methyl formate following the previously described procedure.[27] The product was identified with the previously described sample by comparison of infrared spectra, R_f values on thin-layer chromatography,[24] and a mixed melting-point determination.

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[24] A silica gel coating was employed.

[25] W. J. Bailey, J. J. Hewitt, and C. King, *J. Am. Chem. Soc.*, **77**, 357 (1955).

[26] O. Neunhoeffer, *Ann.*, **509**, 115 (1934).

[27] P. Sabatier and A. Mailhe, *Bull. soc. chim. France*, [3] **33**, 74 (1905).

Organic Nitrogen Compounds. I. Peroxide Intermediates of Tertiary Alkylamine Oxidation by Hydrogen Peroxide

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The primary products of the reaction of tertiary alkylamines and hydrogen peroxide are trialkylammonium peroxides which decompose to yield trialkylamine oxides. The latter have a great tendency to form addition compounds with hydrogen peroxide. The course of the reaction can be best followed in the case of triethylenediamine which gives a well defined, crystalline diammonium diperoxide. On heating, this yields the corresponding diamine dioxide which can be converted to a dihydrogen peroxide adduct. Infrared spectra of the compounds support the proposed reaction route and indicate strong and characteristic hydrogen bondings in the trialkylamine– and trialkylamine oxide–hydrogen peroxide adducts.

The oxidation of tertiary aliphatic amines by aqueous hydrogen peroxide to yield amine oxides is a well known reaction. The first studies of the reaction were carried out at the end of the 19th century by Wolffenstein[1,2] in Germany and Dunstan[3] in England. The course of such oxidations was first discussed by Wieland.[4] He assumed that the hydrogen peroxide first adds to the amine to form an ammonium peroxide which on decomposition yields the amine oxide with the loss of water:

$$R_3N + H_2O_2 \longrightarrow R_3N\cdot H_2O_2 \longrightarrow R_3NO + H_2O$$

Another formulation of the reaction is also possible[5]:

$$R_3N + H_2O_2 \longrightarrow R_3{}^{+}NOH\ [{}^{-}OH] \longrightarrow R_3NO + H_2O$$

It was felt that the formation of alkylammonium peroxides from alkylamines and alkyl hydroperoxides in our earlier work[6,7] and the formation of ammonium peroxide from ammonia and hydrogen peroxide[8,9] supported the reaction route proposed by Wieland.

$$R_3N + R'O_2H \longrightarrow R_3N\cdot HO_2R'$$

$$NH_3 + H_2O_2 \longrightarrow NH_3\cdot H_2O_2$$

In the work reported here the reactions of trialkylamines with hydrogen peroxide to form amine oxides were studied. Using highly concentrated hydrogen peroxide reactant, ammonium peroxide intermediates of the reaction were isolated and converted to the corresponding amine oxides and their hydrogen peroxide adducts.

Trialkylamine–Hydrogen Peroxide Adducts.—Trialkylamine–hydrogen peroxide adducts (trialkylammonium peroxides) were formed on treating simple tertiary aliphatic amines with highly concentrated (90% +) hydrogen peroxide at low temperatures (about −50°). These trialkylammonium peroxides are unstable, color-

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[1] W. Wernick and R. Wolffenstein, *Ber.*, **31**, 1553 (1898).

[2] L. Mamlock and R. Wolffenstein, *ibid.*, **33**, 159 (1900).

[3] W. R. Dunstan and E. Goulding, *J. Chem. Soc.*, **75**, 1004 (1899).

[4] H. Wieland, *Ber.*, **54**, 2353 (1921).

[5] C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 595.

[6] A. A. Oswald, F. Noel, and A. J. Stephenson, *J. Org. Chem.*, **26**, 3969 (1961).

[7] A. A. Oswald, F. Noel, and G. Fisk, *ibid.*, **26**, 3974 (1961).

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[9] O. Maass and W. H. Hatcher, *J. Am. Chem. Soc.*, **44**, 2472 (1922).