

[CONTRIBUTION FROM GORGAS LABORATORY, ROHM & HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION, HUNTSVILLE, ALA.]

Oxidations with Oxygen Difluoride¹

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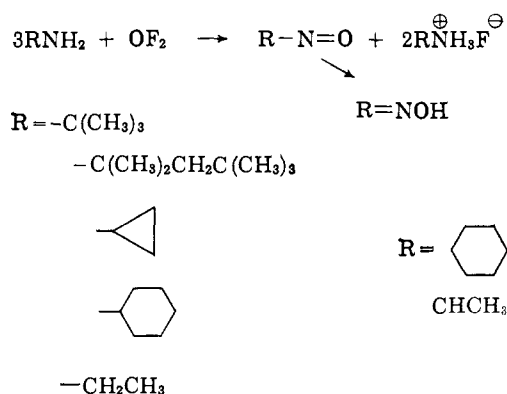
Oxygen difluoride has been shown to react rapidly and controllably with primary aliphatic amines to produce nitroso derivatives. Nitrosocyclopropane, unobtainable by other methods, was prepared by this method.

Oxygen difluoride (OF₂) was first isolated and identified by Lebeau and Damiens² in 1927. The product was found to accompany the fluorine produced from a medium-temperature cell with an electrolyte of KF·3-HF using a nickel or iron anode. An improved preparative procedure was shortly developed which consisted of the fluorination of a 2% aqueous caustic solution.³ With the increased availability of OF₂ came further exploratory work which was concentrated primarily on inorganic substrates.⁴ Organic systems reacted with explosive violence and hence were largely ignored (*e.g.*, methane and carbon monoxide detonated when mixed with OF₂). A complete summary of the known physical and chemical properties of OF₂ has been compiled by Mellor.⁵

The facile reaction between OF₂ and ammonia that had been previously reported⁴ suggested that with suitable precautions controlled oxidations of primary amines with oxygen difluoride could be achieved.

Results and Discussion

Primary aliphatic amines are oxidized smoothly at temperatures below -42° to the nitroso derivative or oxime, the latter being formed if a hydrogen atom was geminal to the amino group.



The oxidations may be conducted in solution at -78° using Freon 11 as the solvent. Such a procedure will result in short reaction time (<2 hr.) and high yields of nitroso monomer (>80%). However, it is very difficult to separate the monomers from the solvent by distillation (*e.g.*, 2-methyl-2-nitrosopropane will codistill with Freon 11, carbon tetrachloride, or diethyl ether). To eliminate this problem, the amine was dispersed on an inert diluent and oxidized at -42°. Diluents such as sodium fluoride or sodium chloride may be used but the

best results were obtained with 80/100 mesh Chromosorb P.⁶ The yields were lower than the solution oxidations but the monomers were obtained free of contaminants.

The gaseous OF₂ was slowly metered into the reaction flask at such a rate that the total pressure never exceeded 400 mm. Pressures of OF₂ above this cause the reaction to be too rapid resulting in extensive charring of the substrate. Flashes and occasional explosions occurred at OF₂ pressures greater than 1 atmosphere. Gas phase mixing or direct condensation of amine and OF₂ will result in detonations with surprising regularity.

t-Butylamine dispersed on Chromosorb was oxidized completely within 10 min. The OF₂ pressure was maintained at 45 mm. as this amine was the most reactive of those studied. The nitroso monomer was removed from the reaction under reduced pressure and allowed to stand at 0°. Dimerization of the monomer occurred slowly and a colorless solid, m.p. 129°, was obtained. During melting, the material turned blue and sublimed to produce another colorless solid, m.p. 82-84°. Repeated melting of the sublimed material caused no further change in the melting point. The infrared spectrum of the lower melting material was identical with a sample of *trans*-2-methyl-2-nitrosopropane dimer, m.p. 83-84°, prepared by the bromine oxidation of *N-t*-butylhydroxylamine according to the procedure of Emmons.⁷

Conversion of the higher melting material to the *trans* dimer could also be achieved by dissolving it in CCl₄ or other suitable solvents. Only the *trans* isomer could be recovered from solution, and the ultraviolet and proton n.m.r. spectra of the solution were identical with those obtained from a solution of the *trans* isomer. No time dependency of ultraviolet spectrum was observed indicating that the transformation occurring is relatively rapid.

Clearly the higher melting material is either a crystal modification or the first recorded example of the *cis* dimer.⁸ The infrared spectra of the two compounds when taken in a KBr pellet are very similar but differ in that the high melting dimer has absorption at 6.6 μ whereas the corresponding peak for the *trans* dimer appears at 6.9 μ. It is unlikely that crystal modification would cause such a significant change in the infrared spectrum. In the absence of X-ray analysis, definite characterization of the higher melting isomer as the *cis* isomer cannot be claimed.

Cyclopropylamine Oxidation.—The OF₂ oxidation of cyclopropylamine dispersed on Chromosorb P produced the blue nitroso monomer in 40% yield which could be

(1) Presented before the Division of Organic Chemistry at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963.

(2) P. Lebeau and A. Damiens, *Compt. rend.*, **185**, 652 (1927).

(3) P. Lebeau and A. Damiens, *ibid.*, **188**, 1253 (1929).

(4) O. Ruff and W. Menzel, *Z. anorg. allgem. Chem.*, **198**, 39 (1931).

(5) Mellor's "Comprehensive Treatise on Inorganic and Theoretical Chemistry," Supplement II, Part I, p. 186.

(6) Johns-Manville Corporation.

(7) W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 6522 (1957).

(8) B. G. Gowenlock and J. Trotman, *J. Chem. Soc.*, 4190 (1955), were unable to isomerize *trans*-2-methylnitrosopropane to the *cis* isomer with conditions successful with other *trans-cis* interconversions.

manipulated under high vacuum. The monomer is very sensitive to light and heat and transfer must be made rapidly. By passing the blue monomer slowly through a chilled (0°) U-tube the colorless crystalline dimer, m.p. $78-79^\circ$, was produced. This dimer also sublimed upon melting to yield a new material, m.p. $68-69^\circ$. The question of *cis-trans* isomerism is again suggested but product instability precluded further study.

The dimer is heat and light sensitive and must be stored in sealed opaque vials at low temperature. Solutions of the dimer are dark blue caused by dissociation to monomer. Examination of such solutions produced no evidence of cyclopropanone oxime formation. The oxime might be expected as nitroso functions geminal to a hydrogen atom easily rearrange to the oxime.

The proton n.m.r. spectrum of the dimer in CCl_4 solution shows the protons geminal to the nitrogen atom as a multiplet centered at 4.9δ . The two methylene protons of the cyclopropyl ring *cis* to the nitrogen atom are a multiplet centered at 1.0δ . The two *trans*-methylene protons are seen as a multiplet centered at 1.4δ . The three groups have area ratios of 1:2:2, respectively. After standing a short time, the solution becomes blue and additional peaks appear which are assigned to the monomeric form. Further work is in progress on the monomer-dimer equilibrium.

It was found that aromatic amines such as aniline and *p*-trifluoromethylaniline were slowly oxidized at room temperature producing highly colored polymeric products. In the case of aniline, only traces of nitrosobenzene and nitrobenzene could be detected. The $-\text{NH}_2$ group of aromatic and aliphatic amides is completely unreactive up to 80° when exposed to 3 atmospheres of OF_2 .

The exact nature of the OF_2 amine oxidation is unknown. The extensive study by Coppinger and Swalen⁹ and De la Mare¹⁰ of alkyl amine oxidations by *t*-butyl hydroperoxide, has established a free radical path for these reactions. It was pointed out that a primary amino function on a tertiary carbon reacted very sluggishly with *t*-butyl hydroperoxide to give low conversion to the nitro compound. However, primary amines bearing α -hydrogen react more rapidly to yield ketimine or aldimines as the principal product. All oxidations were carried out in excess amine. It was further shown that similar products were found when di-*t*-butyl peroxide was used as the oxidant. No indication of oxime or nitroso formation was given in any of the amines oxidized.

The behavior of OF_2 is quite opposite to the case stated above in that primary amines on tertiary carbon are the most reactive. The amines containing α -hydrogen produce oximes, indicative of nitrogen attack, and not imines. It therefore seems unlikely that prior dissociation of OF_2 into $\cdot\text{F}$ and $\cdot\text{OF}$ radicals followed by proton or electron abstraction¹¹ is occurring in this case.

Other oxidants which convert primary amines to nitroso derivatives are peracetic acid,¹² Caro acid,¹³ and potassium permanganate in aqueous formaldehyde.¹⁴

(9) G. M. Coppinger and J. D. Swalen, *J. Am. Chem. Soc.*, **83**, 4900 (1961).

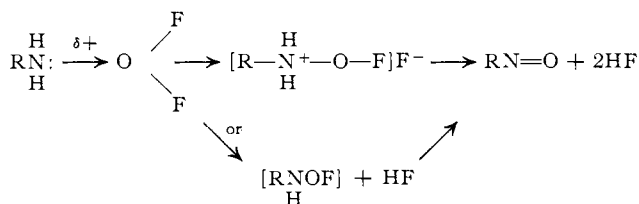
(10) H. E. De la Mare, *J. Org. Chem.*, **25**, 2114 (1960).

(11) J. Kenner, *Tetrahedron*, **3**, 78 (1958).

(12) W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 6522 (1957).

(13) E. Banberger and R. Seligman, *Ber.*, **36**, 685 (1903).

These reagents are all unique in that the major product is the result of oxygen transfer to the nitrogen. Oxygen difluoride belongs with this latter class. It is possible that the strongly electronegative fluorine results in an electropositive center on oxygen for nucleophilic attack. Loss of hydrogen fluoride from the postulated intermediate leads directly to nitroso products.



Further investigation on this system and others related to it is being pursued in an attempt to clarify the course of the reaction.

Experimental

Materials.—The amines used were distilled prior to use and their physical constants checked with established values. Melting points and boiling points are uncorrected.

The oxygen difluoride was prepared by passing gaseous fluorine through a 2% solution of sodium hydroxide in a suitable reactor.¹⁵ The OF_2 was trapped out of the fluorine stream at liquid oxygen temperatures and the oxygen and fluorine were then carefully distilled away. The purified material of purity $\sim 99\%$ (1% oxygen) was stored at room temperature in large volume glass bulbs.

The OF_2 was manipulated and stored in a Pyrex vacuum line in which all the stopcocks were lubricated with Kel-F No. 90 grease.¹⁶ The mercury manometers were protected with a layer of degassed Kel-F KF-10 oil.¹⁶ When the apparatus is clean and reasonably dry, stopcocks properly greased and manometers protected, the OF_2 can be stored indefinitely without decomposition.

General Procedure.—Prior to reaction, the amine solutions were thoroughly degassed and care was taken to avoid splashing the reactant high on the walls of the flask. The OF_2 was contained in a large volume bulb separated from the reaction flask by a single stopcock. When the substrate was at the proper temperature the stopcock between them was opened with a remote manipulator. Safety shields are required as unexplainable detonations occasionally occur. When the reaction was complete the volatile components were fractionated on the vacuum line and identified by standard methods. The nonvolatile products were separated according to their solubility in ether, the ammonium fluorides being easily removed by this procedure.

Oxidation of *t*-Butylamine on Chromosorb P.—*t*-Butylamine (1.1 g., 15 mmoles) was dispersed on 5 g. of dry 80/100 mesh Chromosorb P⁶ and thoroughly degassed. The dispersion was well stirred and cooled to -42° . The OF_2 (5 mmoles) was slowly admitted to the reactor and was totally consumed within 10 min. The blue nitroso monomer was pumped from the reactor (25°) and condensed at -80° . Upon warming to 0° , most of the blue liquid dimerized to give a colorless, light-unstable solid, m.p. 129° . This procedure produced 0.23 g. of solid and additional passes through the 0° trap yielded an additional 0.056 g. (66% total yield).

Solutions of the solid turn blue immediately upon mixing and give a λ_{max} (H_2O) $287 \text{ m}\mu$, ϵ_{max} 7300; lit.¹⁷ value for *trans*-1,1-dimethylnitrosoethane dimer is λ_{max} $287 \text{ m}\mu$.

The infrared spectrum showed bands characteristic of nitroso dimers at 1265, 1240, and 1170 cm^{-1} (KBr). Solution spectra cause dissociation and the $-\text{N}=\text{O}$ band at 1565 cm^{-1} (CCl_4) is then apparent.

Anal. Calcd. for $\text{C}_4\text{H}_9\text{NO}$: C, 55.14; H, 10.41; N, 16.08. Found: C, 54.62; H, 10.96; N, 15.34.

Oxidation of *t*-Butylamine in Freon 11.—*t*-Butylamine (0.65 g., 9 mmoles) was dissolved in 10 ml. of Freon 11 (CCl_2F) and the solution was degassed at -196° . The reaction mixture was

(14) I. Okamura, R. Sakurai, and T. Tanabe, *Chem. Abstr.*, **48**, 4225 (1954).

(15) H. S. Booth, *Inorg. Syntheses*, **1**, 109 (1939).

(16) Minnesota Mining and Manufacturing Co.

(17) B. G. Gowenlock and J. Trotman, *J. Chem. Soc.* 1670 (1956).

warmed to -78° and the vessel was charged with 3 mmoles of OF_2 . Stirring was initiated and the blue color of the nitroso monomer appeared immediately. Upon completion of the oxidation, the solvent and nitroso monomer were transferred out of the reaction flask, concentrated, and analyzed by vapor phase chromatography (silicon 710, 146°). Based on the OF_2 consumed (63%), v.p.c. analysis indicated essentially quantitative conversion to 2-methyl-2-nitrosopropane. The infrared spectrum was identical with that of an authentic sample. *t*-Butylammonium fluoride (0.302 g., 3.2 mmoles, 85% yield), identified by its infrared spectrum, remained as a nonvolatile residue.

Oxidation of Cyclopropylamine on Chromosorb P.—Cyclopropylamine (0.86 g., 15 mmoles) was dispersed on 5 g. of Chromosorb P and degassed. The mixture was cooled to -42° and 5 mmoles of OF_2 was admitted to the reactor. The OF_2 was completely consumed within 30 min. The volatile components were pumped out of the reactor and condensed at -80° giving a bright blue liquid which dimerized to 0.121 g. (34% yield) of a colorless solid, m.p. $78-79^{\circ}$. The solid melted to a blue solution which sublimed to another crystalline solid, m.p. $68-69^{\circ}$.

Both solids produce blue solutions in organic solvents showing characteristic absorption for both monomer ($-\text{N}=\text{O}$), 1515 cm^{-1} , and dimer, 1266 and 1177 cm^{-1} (CCl_4).

The n.m.r. spectrum of the dimer shows a single proton (multiplet) centered at $4.9\ \delta$ and two groups of two protons each as multiplets centered at 1.0 and $1.4\ \delta$.

Anal. Calcd. for $\text{C}_3\text{H}_7\text{NO}$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.63; H, 7.25; N, 19.36.

Oxidation of *t*-Octylamine.—A solution of *t*-octylamine (2.0 g., 15 mmoles) in 15 ml. of Freon 11 was treated with 4 mmoles of OF_2 at -78° . The work-up was similar to that described for *t*-butylamine and yielded 0.5 g. (88% yield) of nitroso-*t*-octane identified by its infrared and ultraviolet spectra. The nonvolatile

residue consisted of 1.01 g. (85%) of *t*-octylammonium fluoride, identified by infrared spectrum and neutralization to *t*-octylamine.

Oxidation of Cyclohexylamine.—A solution of freshly distilled cyclohexylamine (1.0 g., 10 mmoles) in 10 ml. of Freon 11 was repeatedly degassed and was treated with 3 mmoles of OF_2 . The reaction was essentially complete after 2 hr. at -78° . The solvent was removed and the residue extracted with 50 ml. of anhydrous ether. The ether-insoluble material was cyclohexylammonium fluoride, 0.54 g. (76% yield), m.p. 129° dec., identified by its infrared spectrum. The ether solution was evaporated to yield a colorless oil which upon crystallization from petroleum ether at -80° gave 0.224 g. (66% yield after purification) of cyclohexanone oxime as a colorless solid, m.p. $85-87^{\circ}$. The melting point and the infrared spectrum were identical with that of an authentic sample.

Oxidation of Ethylamine.—A solution of 12 mmoles of ethylamine in 10 ml. of Freon 11 was degassed and treated at -78° with 4 mmoles of OF_2 for 16 hr. The usual work-up yielded 0.103 g. (44% yield) of acetaldoxime identified by comparison of its infrared spectrum with that of an authentic sample. An ether-insoluble, water-soluble, hygroscopic, colorless solid was also isolated and presumed to be ethylammonium fluoride.

Warning.—Oxygen difluoride has proved to be somewhat treacherous and adequate precautions against explosions must be taken.

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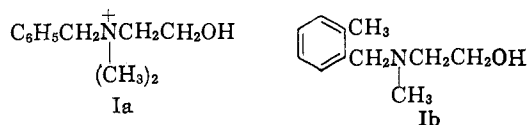
ortho-Substitution Rearrangement and Other Reactions of α -Substituted Benzyltrimethylammonium Ion-Alcohols with Potassium Amide in Liquid Ammonia^{1a}

BY WALTER H. PUTERBAUGH^{1b} AND CHARLES R. HAUSER

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A series of α -substituted benzyltrimethylammonium ions, which have hydroxyl and other substituents β to the quaternary nitrogen, underwent with excess potassium amide in liquid ammonia not only the *ortho*-substitution rearrangement, but also in most cases certain other types of reaction. The β,β -diphenyl quaternary ion IIa and the cyclopentyl quaternary ion IV exhibited almost exclusively the rearrangement to give aminocarbinols Va and VII, whereas the cyclohexyl quaternary ion III underwent mainly cyclization to form epoxide XI. These results are ascribed to steric factors. The β,β -dimethyl quaternary ion IIc underwent more cyclization and cleavage than rearrangement. The cyclization afforded epoxide IX, and the cleavage gave 2-methylbenzyltrimethylamine (X) and presumably acetone. Amine X resulted from rearrangement of intermediate benzyltrimethylammonium ion. The β -phenyl quaternary ion IIb underwent, besides rearrangement, a β -elimination type of reaction to form desoxybenzoin (VIII). Quaternary ion II'd apparently exhibited similar results. The monoanion of quaternary ion III underwent cyclization to form epoxide XI, whereas the monoanion of quaternary ion IIa failed to cyclize. Mechanisms for certain of these reactions are considered.

The benzyl type quaternary ammonium ion-alcohol Ia has recently been shown to undergo the *o*-substitution rearrangement with excess sodium amide in liquid ammonia to form Ib.² β -Elimination, which occurs to a considerable extent with the benzyl-*n*-propyltrimethylammonium ion,³ failed to occur appreciably with Ia apparently because of deactivation of the β -hydrogen by the negative charge on the intermediate alkoxide ion. Rather surprisingly, no intramolecular cyclization of the alkoxide ion of Ia to form ethylene oxide or benzyl β -dimethylaminoethyl ether was observed.



The α -substituted benzyltrimethylammonium ions IIa-d, III, and IV, which have hydroxyl and other substituents β to the quaternary nitrogen, have now been found to exhibit, with excess potassium amide in liquid ammonia, not only the *o*-substitution rearrangement but also, in most cases, certain other types of reaction.

The rearrangements of quaternary ion-alcohols IIa-d afforded aminocarbinols Va-d in yields of 88, 51, 17, and 37%, respectively. Presumably II'a-d and II''a-d would be intermediates (Scheme A).⁴

(1) (a) Supported in part by Army Research Office (Durham); (b) National Science Foundation Science Faculty Fellow, on leave from Thiel College.

(2) G. C. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 806 (1962).

(3) C. R. Hauser and A. J. Weinheimer, *J. Am. Chem. Soc.*, **76**, 1264 (1954).