The Synthesis of α-Difluoraminocarbinols and Some Derivatives

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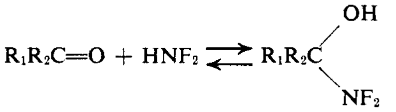
Abstract: α-Difluoraminocarbinols, a new class of compounds, are produced by reaction of difluoramine and aliphatic aldehydes or ketones. Some physical and chemical properties of these compounds are discussed, and several derivatives are described.

Difluoramine[1] reacts with aliphatic aldehydes and ketones to produce α-difluoraminocarbinols. These alcohols are isolable but of varying stability. Identifications were generally based upon infrared and ^{1}H and ^{19}F resonance spectra, but in certain cases derivatives have been prepared.

The preparation of the alcohols generally required only the mixing of carbonyl compound and difluoramine for short periods of time at room temperature or below. For example, difluoraminomethanol, the parent member of the series, was easily prepared by the reaction of solid paraformaldehyde with gaseous difluoramine in an evacuated glass bulb. Although this preparation could be carried out by heating the contents to 150°, equally good results were obtained by letting the contents stand at ambient temperatures. Purification of products was generally carried out under reduced pressure in order to avoid decomposition of the adduct. Decomposition involved the reversal of adduct formation to give carbonyl compound and difluoramine. Adduct formation followed the familiar trend of carbonyl additions: $CH_2O > RCHO \gg R_2C{=}O \sim ArCHO \gg ArCOR$. Aromatic aldehydes gave at best small yields of adducts and aromatic ketones no detectable adduct.

These facts point out the reversible nature of the reaction. Added catalysts were not necessary to establish the equilibrium rapidly. However, trace amounts of hydrogen fluoride produced by decomposition of difluoramine could have been present in all cases, and, of course, difluoramine can act as its own electrophilic catalyst. This reaction may be classified as another example of the alkylation reactions of difluoramine.[2]



$$R_1R_2C{=}O + HNF_2 \rightleftharpoons R_1R_2C(OH)NF_2$$

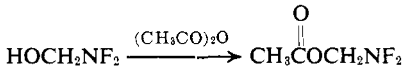
The addition of difluoramine to carbonyl compounds to yield stable adducts containing an intact difluoramino group contrasts with the reactivity of difluoramine with more basic organic reagents such as azomethines.[3] In these reactions it is believed that difluoramine reacts either by loss of hydrogen fluoride to produce fluoroazene, $\underset{\cdot\cdot}{\ddot{N}}$–F, which subsequently adds to the C=N double bond, or by direct addition of difluoramine followed by displacement of fluoride ion.

Stable adducts were prepared from formaldehyde, acetaldehyde, butyraldehyde, and in poorer yield and purity, benzaldehyde, acetone, cyclohexanone, diethyl ketomalonate, and 3-hydroxy-3-methyl-2-butanone.

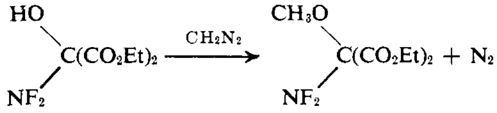
The infrared spectra of the carbinols were characterized by strong hydroxyl absorption at 3300–3500 cm^{-1}, a characteristic alcohol C–O deformation[4] at 1125–1175 cm^{-1}, and strong absorption in the 800–1000-cm^{-1} region characteristic of NF compounds.

The ^{19}F and ^{1}H resonance spectra were especially valuable as aids to structure determination. Adducts formed from aldehydes other than formaldehyde exhibited ^{19}F spectra of the ABX type. This type of spectrum, composed of two separate quartets, results when an NF_2 group is attached to an asymmetric carbon in which one of the substitutents is hydrogen.[5] The ^{19}F spectrum in $CDCl_3$ of difluoraminomethanol is a triplet centered at ϕ −29.9, J_{HF} = 23 cps; the ^{1}H spectrum is a triplet (CH_2), J_{HF} = 23 cps, at τ 5.24 and a singlet (OH) at τ 5.94. The latter peak shifted upon warming. See the Experimental Section for a description of individual fluorine and proton resonance spectra.

The reactions observed for these compounds were typical of those expected of alcohols of somewhat greater acidity than normal. Derivatives prepared included difluoraminomethyl acetate from the reaction of difluoraminomethanol and acetic anhydride at 85° and diethyl α-difluoramino-α-methoxymalonate from the reaction of diazomethane with diethyl α-difluoroamino-α-hydroxymalonate.



$$HOCH_2NF_2 \xrightarrow{(CH_3CO)_2O} CH_3\overset{O}{\overset{\|}{C}}OCH_2NF_2$$



$$(HO)(NF_2)C(CO_2Et)_2 \xrightarrow{CH_2N_2} (CH_3O)(NF_2)C(CO_2Et)_2 + N_2$$

Difluoraminomethanol yielded α,α-bis(difluoraminomethyl) ether upon treatment with concentrated sulfuric acid. This product apparently results from reaction of the oxonium ion or an intermediate difluoraminomethyl carbonium ion with another molecule of difluoraminomethanol. This carbonium ion is similar to monofluorimmonium ions reported recently.[6] It is of some interest that a difluoramino group may stabilize a carbonium ion and suggests the possible utility of these adducts as alkylating agents

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[1] W. H. Graham and C. O. Parker, *J. Org. Chem.*, **28**, 850 (1963), and references cited therein.

[2] W. H. Graham and J. P. Freeman, *J. Am. Chem. Soc.*, **89**, 716 (1967).

[3] W. H. Graham, *ibid.*, **88**, 4677 (1966).

[4] H. Zeiss and M. Tsutsui, *ibid.*, **75**, 897 (1953).

[5] F. A. Johnson, C. Haney, and T. E. Stevens, *J. Org. Chem.*, **32**, 466 (1967).

[6] K. Baum and H. M. Nelson, *J. Am. Chem. Soc.*, **88**, 4459 (1966).

$$NF_2CH_2OH \xrightarrow{H^+} [F_2NCH_2^+ \longleftrightarrow F_2\overset{+}{N}{=}CH_2] \xrightarrow{NF_2CH_2OH} O(CH_2NF_2)$$

under the influence of Lewis acids. (The most immediate analogy is to the formation and reactivity of α,α'-dichloromethyl ether.) α-Difluoramino ethers have been prepared previously by the reaction of orthoesters or unsaturated ethers with difluoramine.[2]

Experimental Section[7]

Caution: Exercise care when working with organic N–F compounds.

Reaction of Difluoroamine and Paraformaldehyde. Preparation of Difluoraminomethanol. Into a 300-cc evacuated bulb containing 0.12 g (0.003 mole) of paraformaldehyde was condensed 90 cc (0.004 mole) of HNF_2. The bulb was completely immersed in an oil bath which was warmed at 155–160° over the course of 30 min. After maintaining the temperature for 1.5 hr, bulb and contents were allowed to cool to room temperature. The bulb was transferred to a vacuum line, cooled to $-70°$, and degassed. The liquid was then transferred by bulb-to-bulb distillation into a $-80°$ trap. The liquid was redistilled and isolated, yield 0.3 g (90%).

Difluoraminomethanol was most conveniently prepared by combining equimolar (or excess HNF_2) quantities of solid paraformaldehyde and difluoramine in an evacuated bulb at room temperature. The reaction is complete in 3–6 hr, and the product may be isolated and purified as above. This compound fires at 4 kg/in. on the Picatinny drop-weight test (RDX = 10 kg/in.).

Anal. Calcd for CH_3ONF_2: C, 14.46; H, 3.63; N, 16.87; F, 45.77. Found: C, 15.35; H, 4.21; N, 17.09; F, 45.8.

Reactions of Acetic Anhydride and Difluoraminomethanol. Preparation of Difluoraminomethyl Acetate. Into a 75-cc evacuated U tube were condensed 0.85 g (0.01 mole) of difluoraminomethanol and 1 g (0.01 mole) of acetic anhydride. The contents were heated for 2.5 hr at 85°, cooled, removed under N_2, added to water, and shaken with CCl_4. The difluoraminomethyl acetate was isolated by vapor phase chromatography of the CCl_4 layer. The infrared spectrum had strong C=O absorption at 1775 cm^{-1} and C–O deformation at 1215 cm^{-1}. The proton resonance spectrum contained a singlet at τ 7.95 (methyl) and a triplet centered at τ 4.75, J_{HF} = 24 cps (methylene protons). The fluorine spectrum was a partially resolved triplet centered at ϕ -34.7 (J_{HF} = 24 cps).

Anal. Calcd for $C_3H_5NO_2F_2$: C, 28.8; H, 4.0; N, 11.2; F, 30.4. Found: C, 28.5; H, 4.53; N, 11.12; F, 31.0.

Reaction of Difluoramine and Acetyldehyde. Preparation of Difluoraminoethanol. A mixture of 525 cc (0.023 mole) of difluoramine and 500 cc (0.022 mole) of gaseous acetaldehyde was condensed into a glass bulb at $-128°$ and allowed to remain at that temperature for 30 min. The residual gases were then removed, and the liquid product was collected by bulb-to-bulb distillation. The ^{19}F spectrum was of the ABX type with large AB coupling ($J_{F_AF_B}$ = 570 cps), J_{HF_A} = 16 cps and J_{HF_B} = 24 cps. The large central peaks were centered near ϕ -27.0 (F_A) and -25.2 (F_B). The proton spectrum has the methyl doublet at τ 8.47 and singlet at τ 4.60 which is the region for OH protons. The multiplet near τ 5.00 is due to the complex splitting of the CH proton.

Anal. Calcd for $C_2H_5ONF_2$: C, 16.86; H, 3.54; N, 9.84; F, 26.68. Found: C, 16.35; H, 3.81; N, 9.40; F, 25.8.

Reaction of Difluoramine and Diethyl Ketomalonate. A 1-g sample of diethyl ketomalonate was stirred in an evacuated U tube on a vacuum line while excess difluoramine was expanded over the sample from an adjoining U tube. An immediate uptake of difluoramine was noted; a slow pressure decrease then occurred. After stirring overnight, the liquid phase was colorless. The reaction mixture was cooled to $-80°$ and degassed *in vacuo*. A solution of diazomethane in ether was then added to the residue at $-80°$ until a persistent yellow color remained. Excess diazomethane was then allowed to evaporate, and the diethyl α-difluoramino-α-methoxymalonate was distilled, bp 56° (0.1 mm).

Anal. Calcd for $C_8H_{13}O_5NF_2$: C, 39.84; H, 5.43; N, 5.81. Found: C, 41.43; H, 5.65; N, 5.10.

The infrared spectrum of the distilled product was identical with that of undistilled material. It featured a strong ester carbonyl band centered at 1770 cm^{-1} (*vs.* 1752 cm^{-1} in diethyl ketomalonate) and lacked the ketone band at 1839 cm^{-1}. The ^{19}F nmr spectrum showed a singlet at ϕ -24.3.

Reaction of Difluoramine and Acetone. Preparation of 2-Difluoraminopropanol-2. Acetone and difluoramine were condensed together in an evacuated U tube using a stoichiometric excess of HNF_2 over the quantity of acetone such that, when the mixture warmed to 0°, the pressure of the system was less than 1 atm. The mixture was allowed to stand at 0° for several hours, during which time a gradual pressure decrease was observed. The mixture was then cooled to $-80°$, and volatile material (excess HNF_2) passed into a second evacuated U tube cooled to $-128°$. Material retained in the $-80°$ receiver was a white, crystalline solid, which melted at approximately $+9°$ and showed a vapor pressure of 51 mm at its melting. On melting an abrupt pressure increase was observed, indicating dissociation into acetone and HNF_2. Prolonged cooling was required to restore the undissociated solid; ^{19}F resonance absorption: singlet at ϕ -19.6 (slow dissociation of HNF_2 gave weak pip at ϕ $+6.95$). ^1H resonance absorption showed an OH-type proton absorption band at τ 4.75 and methyl group bands at τ 7.92 (free acetone) and 8.62 due to the adduct.

The infrared spectrum of the adduct showed both –OH and carbonyl bands, indicating the presence of acetone as well as carbinol.

Reaction of Difluoraminomethanol with Sulfuric Acid. Preparation of α,α-Bis(difluoraminomethyl) Ether. Into an evacuated 120-ml U tube containing 10 ml of 100% H_2SO_4 was condensed 1.0 g (0.012 mole) of difluoraminomethanol. The mixture was allowed to warm to room temperature and was stirred for 1 hr by means of a small magnetic stirring bar.

The U tube was then opened to a train of two cold traps at -80 and $-130°$; the contents were pulled on under vacuum for 30 min. The $-80°$ trap held 0.9 g of clear liquid. The product was identified by its infrared ^1H and ^{19}F spectra.

The infrared spectrum was characterized by strong bands at 1165 cm^{-1} (ether C–O) and 920 and 835 cm^{-1} (N–F).

The ^{19}F spectrum was a triplet centered at ϕ -31.3 (J_{HF} = 21 cps) and the ^1H spectrum a triplet centered at τ 5.25 (J_{HF} = 21 cps).

Anal. Calcd for $C_2H_4N_2F_4O$: C, 16.20; H, 2.70; N, 18.94; F, 51.32. Found: C, 16.92; H, 3.21; N, 19.02; F, 49.0.

Acknowledgment. This work was carried out under the sponsorship of the U. S. Army Missile Command, Redstone Arsenal, Alabama, under Contract No. DA-01-021 ORD-5135.

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(7) All nmr spectra were run using a Varian 40-Mc spectrometer.