Reactions of Trifluoroamine Oxide: A Route to Acyclic and Cyclic Fluoroamines and *N*-Nitrosoamines

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Received August 3, 1989

Abstract: Acyclic secondary fluoroamines and *N*-nitrosoamines R_2NF and R_2NNO (R = CH_3, C_2H_5, *n*-C_3H_7, *i*-C_3H_7, *n*-C_4H_9, *i*-C_4H_9, c-C_6H_{11}) and saturated nonaromatic heterocyclic fluoroamines and *N*-nitrosoamines R⁀NF and R⁀NNO [R = c-C_4H_8, c-C_5H_{10}, 2,6-$(CH_3)_2$-c-C_5H_8, 2,2,6,6-$(CH_3)_4$-c-C_5H_6] were prepared by reacting trifluoroamine oxide (NF_3O) with the respective amine at ≤0 °C in a 1:2 molar ratio. The amine hydrofluoride salts are also formed. Trifluoroamine oxide is a very effective fluorinating and nitrosating reagent and provides an excellent route to >NF- and >NNO-containing compounds. With PF_5, 2,2,6,6-$(CH_3)_4$-c-C_5H_6NF gave $[\overline{CH_2CH_2CH_2C(CH_3)_2N^+}{=}C(CH_3)_2]PF_6^-$.

The synthesis and reactivity of compounds that contain the nitrogen–fluorine bond have been studied extensively.[1-10] Many methods have been developed to prepare *N*-fluoroamines and *N*,*N*-difluoroamines by using either elemental fluorine or other fluorine-transfer reagents. While, in the vast majority of difluoroamino-containing compounds, the $-NF_2$ group is attached to a saturated carbon atom, a number of other compounds have been synthesized in which the NF_2 moiety is bonded to atoms such as S,[11,12] N,[13] or O.[14-17] In rather sharp contrast, the attempts to prepare compounds containing the >NF unit, especially when nonfluorinated alkyl or aryl groups are present, have not been as successful, as is demonstrated by the paucity of examples in the literature.[1,18]

Since the discovery of trifluoroamine oxide (NF_3O), a number of attempts have been made to prepare organic or fluoroorganic derivatives of this surprisingly stable compound.[19-21] Only recently has the synthesis of $-ONF_2$ derivatives from the BF_3-catalyzed addition of NF_3O to simple fluoroethenes been reported.[22] With AsF_5 as a catalyst, it is also possible to add trifluoroamine oxide, via the formation of NF_2O^+, directly to a variety of trifluoroethylene derivatives.[23,24] The thermal decomposition of trifluoroamine oxide has been examined[19] and was shown subsequently to be a potentially useful synthetic route for the preparation of nitroso compounds. An examination of the chemistry and the physical characteristics of trifluoroamine oxide confirms that its reactions have been limited largely to its Lewis base behavior and Lewis acid catalyzed addition reactions.

We have found that trifluoroamine oxide reacts readily with a variety of secondary amines to form the corresponding *N*-fluoro and *N*-nitroso derivatives. Many new *N*-fluoroamines and some previously difficult to obtain have been synthesized, e.g., R_2NF [R = CH_3 (**1**), C_2H_5 (**2**), *n*-C_3H_7 (**3**), *i*-C_3H_7 (**4**), *n*-C_4H_9 (**5**), *i*-C_4H_9 (**6**), c-C_6H_{11} (**7**)] and R⁀NF [R = C_4H_8 (**8**), C_5H_{10} (**9**), 2,6-$(CH_3)_2$-c-C_5H_8 (**10**), 2,2,6,6-$(CH_3)_4$-c-C_5H_6 (**11**)] as well as the respective nitrosoamines R_2NNO [R = CH_3 (**12**), C_2H_5 (**13**), *n*-C_3H_7 (**14**), *i*-C_3H_7 (**15**), *n*-C_4H_9 (**16**), *i*-C_4H_9 (**17**), c-C_6H_{11} (**18**)] and R⁀NNO [R = C_4H_8 (**19**), C_5H_{10} (**20**), 2,6-$(CH_3)_2$-c-C_5H_8 (**21**), 2,2,6,6-$(CH_3)_4$-c-C_5H_6 (**22**)]. These compounds have been isolated and characterized.

Results and Discussion

Trifluoroamine oxide was reacted smoothly with a rather large number of acyclic and cyclic amines under mild conditions (≤0 °C) to form *N*-fluoroamines (40–68% yields) as well as the corresponding *N*-nitrosoamines and the amine hydrofluorides

$$4R_2NH + NF_3O \xrightarrow{\leq 0\ ^\circ C} R_2NF + R_2NNO + 2R_2NH{\cdot}HF$$

where R = CH_3,[19] C_2H_5, *n*-C_3H_7, *i*-C_3H_7, *n*-C_4H_9, *i*-C_4H_9, and c-C_6H_{11} and

$$4R⁀NH + NF_3O \xrightarrow{\leq 0\ ^\circ C} R⁀NF + R⁀NNO + 2R⁀NH{\cdot}HF$$

where R = c-C_4H_8, c-C_5H_{10}, 2,6-$(CH_3)_2$-c-C_5H_8, and 2,2,6,6-$(CH_3)_4$-c-C_5H_6.

These *N*-fluoroamines are colorless liquids whose volatility decreases with increasing molecular weight. All are sufficiently volatile to be purified by fractional condensation techniques. In every case, ^1H NMR spectra confirm the absence of the N–H bond, and each ^{19}F NMR spectrum contains a broad resonance band that is assigned to fluorine bonded to nitrogen. There appears to be a direct correlation between the fluorine chemical shift with respect to elimination of HF and the thermal stability of the

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0002-7863/90/1512-2383$02.50/0

Table I. ^{19}F NMR Chemical Shifts and Relative Stability of the Fluoroamines

	^{19}F ϕ^a	stability at 25 °C
$(CH_3)_2NF$ (**1**)	−24.50	3–4 h → yellow oil
$(C_2H_5)_2NF$ (**2**)	−52.99	36 h → brown oil + HF
$(n\text{-}C_3H_7)_2NF$ (**3**)	−48.76	**3 > 1 ~ 2**; 2 days → yellow oil
$(i\text{-}C_3H_7)_2NF$ (**4**)	−87.97	stable, reacts with glass
$(n\text{-}C_4H_9)_2NF$ (**5**)	−48.01	**5 > 1 > 2 ~ 3 < 4**
$(i\text{-}C_4H_9)_2NF$ (**6**)	−45.34	**6 > 5 > 3 > 2 > 1 < 4**
$(c\text{-}C_6H_{11})_2NF$ (**7**)	−84.61	stable in solution
$c\text{-}C_4H_8NF$ (**8**)	−37.99	unstable
$c\text{-}C_5H_{10}NF$ (**9**)	−24.60	**9 > 8**; 1 h → decompn
$2,6\text{-}(CH_3)_2\text{-}c\text{-}C_5H_8NF$ (**10**)	−45.69	**10 > 9**
$2,2,6,6\text{-}(CH_3)_4\text{-}c\text{-}C_5H_6NF$ (**11**)	−96.19	**11 > 4 >>> 10 > 9**

[a] $CFCl_3$ reference.

N-fluoroamine compounds; i.e., the shifts for the three most stable compounds, **4**, **7**, and **11**, are found at ϕ −87.97, −84.61, and −96.19, respectively, compared to the least stable compounds, **1**, **2**, and **8**, at ϕ −24.50, −52.99, an −37.99. The instability of these compounds is a function of the proximity of hydrogen to the fluorine, which in turn governs the ease of loss of HF. For example, it is well-known that perfluoroalkylamines R_fNH_2 or bis(perfluoroalkyl)amines $(R_f)_2NH$ are typically unstable with respect to elimination of HF,[27] e.g.

$$CF_3CF_2NH_2 \xrightarrow{-HF} [CF_3CF{=}NH] \xrightarrow{-HF} CF_3C{\equiv}N$$

and it is most likely for the same reason that there are few if any stable RNF_2 and R_2NF compounds. We[8] and others have taken advantage of this lack of stability to prepare useful precursors to other compounds, e.g.

$$CF_2{=}CH_2 + N_2F_4 \rightarrow [NF_2CF_2CH_2NF_2] \xrightarrow{-2HF} NF_2CF_2C{\equiv}N$$

It should be noted, however, that bis(polyfluoroalkyl)amines and polyfluoroalkylamines are stable and are available commercially, e.g., $(CF_3CH_2)_2NH$.

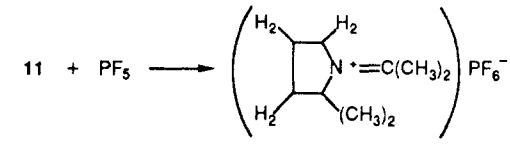
For the compounds described in this paper, two effects are observed. First, there is an increase of ^{19}F chemical shift (ϕ NF) with a decreasing number of protons on the α-carbon as the alkyl substituent changes from CH_3 (ϕ −24.50) to CH_3CH_2 (ϕ −52.99) to $(CH_3)_2CH$ (ϕ −87.97) and, more spectacularly, as the ligand progression is from $c\text{-}C_5H_{10}N$ (ϕ −24.60) to $2,2\text{-}(CH_3)_2\text{-}c\text{-}C_5H_8N$ (ϕ −45.69) to $2,2,6,6\text{-}(CH_3)_4\text{-}c\text{-}C_5H_6N$ (ϕ −96.19). This arises from the increased donation of electrons to the nitrogen as additional methyl groups are introduced and the concomitant enhancement of the shielding of the fluorine atom. Second, the stability of the fluoroamine increases as the opportunity for loss of HF decreases; i.e., as the number of available protons on the α-carbon(s) is decreased, stability increases **1 < 2 ≪ 4** and **9 < 10 ≪ 11** (Table I). Neither the length of the carbon chain nor branching in the chain remote from the α-carbon has any apparent influence on the stability of the fluoroamine; compare, for example, $(n\text{-}C_4H_9)_2NF$ (**5**) ~ $(i\text{-}C_4H_9)_2NF$ (**6**) ≪ $(i\text{-}C_3H_7)_2NF$ (**4**).

While it is possible to characterize the compounds with ^{19}F and ^1H NMR, infrared, and mass spectral measurements, the relatively low stability of many of these *N*-fluoroamines precludes elemental analyses. They can be preserved at −78 °C for indefinite periods. However, **1–3**, **5**, **6**, **8**, and **9** decompose at or below 25 °C after a relatively short time (Table I). For example, a solution of **1** in $CDCl_3$ was monitored by ^{19}F NMR. After 30 min, the septet assigned to >NF began to disappear concomitantly with the appearance of a peak upfield attributable to F^-. Ordering these compounds on the basis of increasing stability gives **1 ~ 8 < 2 < 9 < 3 ~ 5 < 6 < 10 < 7 < 4 < 11**. Fluoroamines **4**, **7**, and **11** are stable in solution for about 3 or 4 weeks in Pyrex glass at 25 °C, as determined by ^{19}F NMR spectral analysis. Additionally, **11** is stable as the neat liquid at 25 °C for several weeks. We believe these to be the first examples of stable R_2NF compounds, where R is a highly hydrogenated alkyl group. The decomposition products are yellow to brown involatile oils that are water soluble and, in some cases, oxidize acidic potassium iodide solution. These decomposition products have not been identified. To our knowledge, the reaction of trifluoroamine oxide with secondary amines provides the only known general method for the preparation of hydrocarbon *N*-fluoroamines.

In comparison to other synthetic routes to *N*-nitrosoamines, only small yields have been obtained as side products in the reactions mentioned above.[25] The suitability of trifluoroamine oxide as a useful source of nitrosyl fluoride in the syntheses of fluoroaliphatic nitroso derivatives was demonstrated earlier by the fact that the yields achieved with this method in the preparation of nitrosoperfluoroalkanes[23,24] were comparable to those obtained by traditional routes to nitroso-containing compounds.[26]

On the basis of the behavior of NF_3O with secondary amines (cyclic and acyclic), we attempted to prepare *N*-fluoroamines of partially or fully fluorinated secondary alkylamines. However, no reaction occurred when NF_3O was combined with $(CF_3CH_2)_2NH$ at 0, 25, 60, or 120 °C or with $(C_4F_9)_3N$ at 0, 80, 120, or 180 °C. This contrasts with the reaction of a nonfluorinated tertiary amine, $(CH_3)_3N$, that did react with NF_3O to give $(CH_3)_2NF$ and $(CH_3)_2NNO$ and an unidentified solid product.

The *N*-fluoroamines reported herein react readily with Lewis acids, such as PF_5 or BF_3. When $2,2,6,6\text{-}(CH_3)_4\text{-}c\text{-}C_5H_6NF$ (**11**) was reacted with PF_5, the corresponding stable iminium salt was obtained:



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Evidence for ring contraction and formation of the phosphorus hexafluoride anion was obtained from phosphorus, proton, and fluorine NMR spectra. A septet at −145.04 ppm in the ^{31}P NMR and a doublet at ϕ −72.82 in the ^{19}F spectrum ($J_{P\text{-}F}$ = 708 Hz) are readily detected. The ^1H NMR is consistent with the product formed. Mass spectral data obtained by using FAB negative and FAB positive show PF_6^- and $M^+ - PF_6$, respectively. While many of the *N*-fluoroamines are similarly reactive with PF_5, when α-protons are present in the reacting fluoroamine, the only product identified was HPF_6.

While several attempts were made to record the X-ray crystal structure of **23**, because of the small size of the crystals obtained, only partial refinement could be achieved. While the structure of the product was confirmed, i.e., that ring contraction had occurred and the iminium and PF_6^- moieties are present, the bond angles and lengths were not reliable. The crystal is orthorhombic, space group $Pna2_1$, with a = 8.623 (2) Å, b = 9.524 (5) Å, and c = 16.033 (2) Å. A Nicolet R3m/E diffractometer was used to collect the X-ray diffraction data, and the structure was solved and refined (16%) by using the SHELXTL package from Nicolet.

The behavior of trifluoroamine oxide toward secondary amines (cyclic/acyclic), a partially fluorinated secondary amine, and a perfluorinated tertiary amine has been explored. The mechanism by which the >NF and >NNO compounds are formed has not been ascertained and is the subject of further study. The work presented in this paper represents one of the few known modes of reaction for trifluoroamine oxide not involving Lewis acid/base chemistry.

Experimental Section

Materials. Trifluoroamine oxide (Allied) was passed through two traps cooled to −78 °C to remove NO_2. Dimethylamine, diethylamine, dipropylamine, diisopropylamine, dibutylamine, and diisobutylamine were obtained from Aldrich and used as received. Pyrrolidine, piperidine, 2,6-dimethylpiperidine, 2,2,6,6-tetramethylpiperidine, and dicyclohexylamine (Aldrich) were used after distillation.

General Procedures. A conventional Pyrex glass vacuum system equipped with a Heise Bourdon tube gauge was used to handle gases and volatile liquids. Most of the starting materials and products were measured quantitatively by using standard PVT techniques. The products

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were purified by fractional condensation (trap-to-trap distillation). Mass spectra were recorded with a VG-7070 HS mass spectrometer operating at 10 eV. ^{19}F NMR spectra were obtained on a JEOL FX-90Q FT NMR spectrometer with CCl_3F as internal reference. ^1H NMR spectra were recorded with TMS as internal reference with the same instrument. Infrared spectra were obtained on a Perkin-Elmer 1700 FTIR spectrometer with a 10-cm gas cell fitted with KBr windows. For involatile liquids, KBr disks were used. *N*-Nitrosoamines, isolated as the other major products in all reactions of NF_3O with secondary amines, were characterized by comparing mass, IR, and NMR spectra obtained in this laboratory with those reported in the literature.[24]

Caution. Trifluoroamine oxide is a strong oxidizer. Mixtures with both inorganic and organic materials are potentially explosive. Attempts to scale up the synthetic methods presented in this paper should be avoided. Appropriate safety precautions must be observed when these reactions are carried out. Certain of the nitrosoamines have been shown to be carcinogenic in test animals. Thus, all *N*-nitrosoamines produced must be considered hazardous, and precautions to avoid their release in the laboratory or the environment should be taken.

Reactions of NF_3O with Amines. Unless otherwise specified, the usual procedure was as follows: A dry 250-mL round-bottomed Pyrex flask equipped with a Teflon stopcock was evacuated, and the volatile amine was condensed into the flask at −196 °C. The flask was allowed to warm to ≤0 °C, and trifluoroamine oxide was titrated slowly into the vessel under vacuum. Involatile amines were weighed into a 250-mL round-bottomed Pyrex flask equipped with a 10/30 standard taper joint and a Teflon stopcock. The flask was cooled to −196 °C and evacuated, and NF_3O was added slowly as above.

(a) NF_3O + Dimethylamine To Form $(CH_3)_2NF$ (1) and $(CH_3)_2NNO$ (12). After 1 h at −22 °C, the products obtained from the reaction of trifluoroamine oxide (0.18 g, 2 mmol) and $(CH_3)_2NH$ (0.18 g, 4 mmol) were separated by trap-to-trap distillation [trap temperatures were −40 [ethanol (56%), water], −78 (ethanol, dry ice), −116 (ether, liquid N_2), and −196 °C (liquid N_2)] to give **1** (−116 °C, ~40% yield) and **12** (−40 °C, 30% yield).[24] The spectral data obtained for **1** are as follows: ^{19}F NMR ϕ −24.25 sept (J_{F-H} = 35.0 Hz); ^1H NMR δ 2.95 ppm d; MS (EI, 10 eV) [*m/e* (species) intensity] 63 (M^+) 62.5, 62 ($M^+ - 1$) 40.0, 43 ($M^+ - HF$) 52.6, 42 ($C_2H_4N^+$) 100, 41 ($C_2H_3N^+$) 18; IR (gas) 2995 vs, 2980 vs, 2920 s, 2840 vs, 1440 m, 1420 m, 1400 m, 1130 ms, 1115 m, 1100 w, and 750 s, br, cm^{-1}. Molecular weight determination for **1** gave 63.6 (calcd 63). Vapor pressure data have been published.[19]

(b) NF_3O + Diethylamine To Form $(C_2H_5)_2NF$ (2) and $(C_2H_5)_2NNO$ (13). Trap-to-trap distillation of the products (using baths at −40, −78, −136, and −196 °C) formed when NF_3O (0.18 g, 2 mmol) and $(C_2H_5)_2NH$ (0.36 g, 4 mmol) were allowed to react at −10 °C for 1.5 h gave **2** (−136 °C, ~45% yield) and **13** (−40 °C, ~30% yield).[24] Spectral data obtained for **2** are as follows: ^{19}F NMR ϕ −52.99 p (J_{F-H} = 39.06 Hz); ^1H NMR δ 1.10 t (CH_3, 6 H, J_{H-H} = 7.08 Hz), 3.10 dq (CH_2, 4 H, J_{H-F} = 40.5 Hz); MS (EI, 10 eV) [*m/e* (species) intensity] 91 (M^+) 2.60, 77 ($M^+ + 1 - CH_3$) 0.37, 76 ($M^+ - CH_3$) 5.6, 72 ($M^+ - F$) 15.33, 71 ($M^+ - HF$) 3.42, 58 ($C_3H_8N^+$) 100, 56 ($C_3H_6N^+$) 12; IR (gas) 2980 s, 2945 s, 2895 s, 1470 m, 1370 m, br, 1220 m, 1080 m, br, 800 m, br, 750 w, br, and 540 w, cm^{-1}. The vapor pressure of **2** at 25 °C is ~60 Torr.

(c) NF_3O + Di-*n*-propylamine To Form $(C_3H_7)_2NF$ (3) and $(C_3H_7)_2NNO$ (14). After 1.5 h at −15 °C, the reaction mixture of NF_3O (0.18 g, 2 mmol) and $(C_3H_7)_2NH$ (0.48 g, 4 mmol) was separated via trap-to-trap distillation (using baths at −40, −78, −136, and −196 °C) to give colorless **3** (−136 °C, ~40%) and yellow **14** (−40 °C, ~20%).[24] The spectral data obtained for **3** are as follows: ^{19}F NMR ϕ −48.76 p (J_{F-H} = 39.06 Hz); ^1H NMR δ 1.10 t (CH_3, 6 H), 1.72 m (CH_2, 4 H), 2.95 dt (NCH_2, 4 H, J_{H-F} = 40.1 Hz); MS (EI, 10 eV) [*m/e* (species) intensity] 119 (M^+) 0.2, 99 ($M^+ - HF$) 0.48, 85 ($C_5H_{11}N^+$) 1.05, 59 ($C_3H_9N^+$) 100, 57 ($C_3H_7N^+$) 3.54; IR (gas) 2980 vs, 2945 vs, 2900 vs, 1520 ms, 1320 ms, 1260 ms, 1155 ms, 910 vw, 795 ms, 750 vw, and 540 w, cm^{-1}.

(d) NF_3O + Diisopropylamine To Form $[(CH_3)_2CH]_2NF$ (4) and $[(CH_3)_2CH]_2NNO$ (15). When diisopropylamine (0.48 g, 4 mmol) and NF_3O (0.18 g, 2 mmol) were reacted at 0 °C for 2 h, trap-to-trap distillation (using baths at −40, −78, −136, and −196 °C) gave rise to colorless **4** (−136 °C, ~55% yield) and yellow **15** (−40 °C, ~30% yield).[24] The spectral data obtained for **4** are as follows: ^{19}F NMR ϕ −87.0 t (J_{F-H} = 39.06 Hz); ^1H NMR δ 1.15 d (CH_3, 6 H), 3.25 m, br (CH, 2 H); MS (EI, 10 eV) [*m/e* (species) intensity] 119 (M^+) 1.2, 104 ($M^+ - CH_3$) 3.5, 100 ($M^+ - F$) 3.29, 86 ($M^+ - CH_2F$) ($M^+ - C_2H_9$) 100, 70 ($C_4H_8N^+$) 89.0, 56 ($C_3H_6N^+$) 6.32; IR (liquid film) 2985 vs, 2940 s, 2900 m, 1440 s, 1400 s, 1370 s, 1230 s, 1215 s, 1140 s, 850 m, br, 740 m, and 655 m, cm^{-1}.

(e) NF_3O + Di-*n*-butylamine To Form $(C_4H_9)_2NF$ (5) and $(C_4H_9)_2NNO$ (16). Di-*n*-butylamine (0.58 g, 4 mmol) and NF_3O (0.18 g, 2 mmol) were reacted at 0 °C for 4–5 h. After trap-to-trap distillation (using baths at −40, −78, and −196 °C), colorless **5** was found at −78 °C (~45% yield). The residue in the flask was dissolved in acetone (15 mL), and the yellow solution was filtered. After the acetone was removed, a yellow liquid **16** (~30% yield) remained.[24] The spectral data obtained for **5** are as follows: ^{19}F NMR ϕ −48.01 p (J_{F-H} = 39.2 Hz); ^1H NMR δ 0.95 t (CH_3, 6 H), 1.7 m (CH_2, 8 H), 2.98 dt (NCH_2, 4 H, J_{H-F} = 40.1 Hz); MS (EI, 10 eV) [*m/e* (species) intensity] 147 (M^+) 2.41, 128 ($M^+ - F$) 0.57, 127 ($M^+ - HF$) 2.83, 104 ($M^+ - C_3H_7$) 29.09, 85 ($C_5H_{11}N^+$) 4.3, 84 ($C_5H_{10}N^+$) 68.07, 70 ($C_4H_8N^+$) 4.8, 57 ($C_4H_9^+$) 100; IR (liquid film) 2980 vs, 2890 vs, 2840 s, 1470 s, 1395 m, 1370 m, 1290 w, br, 1240 m, br, 1060 m, 950 w, br, 930 m, 770 m, and 500 w, cm^{-1}.

(f) NF_3O + Diisobutylamine To Form $[(CH_3)_2CHCH_2]_2NF$ (6) and $[(CH_3)_2CHCH_2]_2NNO$ (17). Diisobutylamine (0.58 g, 4 mmol) and NF_3O (0.18 g, 2 mmol) were reacted at 0 °C for 5 h. Trap-to-trap distillation (using baths at −40, −78, and −196 °C) resulted in a colorless liquid **6** (~50% yield) in a trap at −78 °C. The residue remaining in the flask was dissolved in acetone (15 mL), the solution was filtered, and the filtrate was evaporated to leave a yellow liquid **17** (~20% yield).[24] Spectral data obtained for **6** are as follows: ^{19}F NMR ϕ −45.34 p (J_{F-H} = 39.0 Hz); ^1H NMR δ 0.99 d (CH_3, 12 H), 2.1 m (CH, 2 H) 2.9 dd (NCH_2, 4 H, J_{H-F} = 41.0 Hz); MS (EI, 10 eV) [*m/e* (species) intensity] 147 (M^+) 0.2, 119 ($C_6H_{14}NF^+$) 1.4, 104 ($C_5H_{11}NF^+$) 3.2, 88 ($C_4H_7NF^+$) 9.97, 86 ($C_5H_{12}N^+$) 62.74, 84 ($C_5H_{10}N^+$) 100, 70 ($C_4H_8N^+$) 1.88, 57 ($C_4H_9^+$) 23.93; IR (liquid film) 2985 vs, 2895 vs, 2810 s, 1470 s, 1390 s, 1370 s, 1290 w, 1240 w, 1140 s, 1110 m, 930 w, 830 m, 750 s, br, and 500 w, cm^{-1}.

(g) NF_3O + Dicyclohexylamine To Form $(C_6H_{11})_2NF$ (7) and $(C_6H_{11})_2NNO$ (18). After 5 h at 5 °C, a mixture of dicyclohexylamine (0.72 g, 4 mmol) and NF_3O (0.18 g, 2 mmol) was separated by trap-to-trap distillation (using baths at −40, −78, and −196 °C) to give a colorless liquid **7** at −78 °C (~35% yield). Acetone (20 mL) was utilized to dissolve the yellow residue from the flask. After filtration, the solution was evaporated to leave a yellow liquid **18** (~20% yield).[24] The spectral data obtained for **7** are as follows: ^{19}F NMR ϕ −84.61 t (J_{F-H} = 34.18 Hz); ^1H NMR, complex pattern with broad multiplets centered at δ 2.65, 1.85, 1.25 (ratio 1:5:5); MS (EI, 10 eV) [*m/e* (species) intensity] 199 (M^+) 0.31, 180 ($M^+ - F$) 2.05, 179 ($M^+ - HF$) 3.14, 152 ($C_{10}H_{18}N^+$) 4.86, 138 ($C_9H_{16}N^+$) 100, 116 ($C_6H_{11}NF^+$) 0.54, 83 ($C_6H_{11}^+$) 12.44, 97 ($C_6H_{11}N^+$) 1.63, 56 ($C_3H_6N^+$) 65.23; IR (liquid film) 2940 s, 2860 s, 2800 w, 1450 s, 1370 m, 1260 m, 1130 s, br, 890 m, 710 m, br, 600 w, and 550 w, cm^{-1}.

(h) NF_3O + Pyrrolidine To Form c-C_4H_8NF (8) and c-C_4H_8NNO (19). After 1.5 h at −15 °C, a mixture of pyrrolidine (0.28 g, 4 mmol) and NF_3O (0.18 g, 2 mmol) was separated by trap-to-trap distillation (using baths at −40, −78, −136, and −196 °C) to give **8** (−136 °C, ~30% yield) and **19** (−40 °C, ~20% yield).[24] The spectral data obtained for **8** are as follows: ^{19}F NMR ϕ −37.99 t (J_{F-H} = 38.36 Hz); ^1H NMR δ 1.61 br s; MS (EI, 10 eV) [*m/e* (species) intensity] 89 (M^+) 53.5, 88 ($M^+ - H$) 31.59, 70 ($M^+ - F$) 10.14, 69 ($M^+ - HF$) 52.2, 42 ($C_3H_6^+$) 100; IR (gas) 2990 s, 2845 m, 1030 w, 913 m, br, 780 s, and 470 m, cm^{-1}.

(i) NF_3O + Piperidine To Form c-$C_5H_{10}NF$ (9) and c-$C_5H_{10}NNO$ (20). Freshly distilled piperidine (0.4 g, 4 mmol) and F_3NO (0.18 g, 2 mmol) were reacted at −15 °C for 2 h. Trap-to-trap distillation (using baths at −40, −78, −136, and −196 °C) gave colorless **9** (−78 °C, ~35% yield). The contents of the flask was dissolved in acetone (15 mL), the solution was filtered, and the resulting filtrate was concentrated to leave yellow **20** (~30% yield).[24] The spectral data for **9** are as follows: ^{19}F NMR ϕ −24.6 s, br; ^1H NMR δ 1.8, 3.0, 3.8 (ratio 3:1:1); MS (EI, 10 eV) [*m/e* (species) intensity] 103 (M^+) 11.43, 84 ($M^+ - F$) 100, 83 ($M^+ - HF$) 5.15, 70 ($C_5H_{10}^+$) 19.19, 56 ($C_4H_8^+$) 78.48; IR (liquid film) 2940 vs, 2860 s, 2800 m, 1450 m, br, 1360 m, 1280 m, 1260 m, 1220 m, 1180 m, 1090 m, br, 980 m, 780 m, 750 s, br, 550 m, br, and 450 w, cm^{-1}.

(j) NF_3O + 2,6-Dimethylpiperidine To Form 2,6-$(CH_3)_2$-c-C_5H_8NF (10) and 2,6-$(CH_3)_2$-c-C_5H_8NNO (21). 2,6-Dimethylpiperidine (0.52 g, 4 mmol) and NF_3O (0.18 g, 2 mmol) were allowed to react for 4 h at −10 °C. After trap-to-trap distillation (using baths at −40, −78, −136, and −196 °C), colorless **10** was obtained at −78 °C (~50% yield). Dry acetone (20 mL) was used to dissolve the residue in the flask. The solution was filtered, and the filtrate was concentrated to leave a yellow solid **21** (~20% yield).[24] The spectral data obtained for **10** are as follows: ^{19}F NMR ϕ −45.69 t (J_{F-H} = 21.92 Hz); ^1H NMR δ 2.5, 1.4, 0.89 (broad peaks); MS (EI, 10 eV) [*m/e* (species) intensity] 131 (M^+) 1.07, 112 ($M^+ - F$) 10.43, 111 ($M^+ - HF$) 1.86, 98 ($C_7H_{14}^+$) 100, 84 ($C_6H_{12}^+$) 9.23, 70 ($C_5H_{10}^+$) 50.21, 68 ($C_5H_8^+$) 5.85, 67 ($C_5H_7^+$) 2.35, 56 ($C_4H_8^+$) 26.82; IR (liquid film) 2950 s, 2865 m, 2820 m, 1460 m, br, 1380 m, 1310 m, 1195, w, br, 1105 w, 1040 w, 740 m, 555 w, and 495 m, cm^{-1}.

(k) NF_3O + 2,2,6,6-Tetramethylpiperidine To Form 2,2,6,6-$(CH_3)_4$-c-C_5H_6NF (11) and 2,2,6,6-$(CH_3)_4$-c-C_5H_6NNO (22). 2,2,6,6-Tetramethylpiperidine (0.63 g, 4 mmol) and F_3NO (0.18 g, 2 mmol) were reacted for 12 h at 0 °C. After trap-to-trap separation (using baths at

-40, -78, -136, and -196 °C), a yellow liquid **11** was found at -78 °C (~68% yield). The residue in the flask was dissolved in dry acetone (20 mL). The solution was filtered and the filtrate reduced to dryness, leaving a solid compound **22** (~22% yield).[24] The spectral data obtained for **11** are as follows: ^{19}F NMR ϕ -96.0; ^{1}H NMR, complex—no N-H resonance present; MS (EI, 10 eV) [*m/e* (species) intensity] 159 (M^+) 2.04, 144 ($M^+ - CH_3$) 100, 140 ($M^+ - F$) 94, 139 ($M^+ - HF$) 1.1, 109 ($C_7H_{11}N^+$) 31.57, 76 ($C_3H_7NF^+$) 20.12, 56 ($C_3H_6N^+$) 27.8; IR (liquid film) 2972 vs, 2942 vs, 2872 s, 1465 vs, 1449 vs, 1380 vs, 1368 s, 1125 s, 1033 m, 899 m, 735 w, 686 w, br, 669 w, and 540 w, cm^{-1}.

(l) 2,2,6,6-$(CH_3)_4$-c-C_5H_6NF (11) + PF_5 To Form [$\overline{CH_2CH_2CH_2}$-$\overline{C(CH_3)_2N^+}$=$C(CH_3)_2$]PF_6^- (23). Methylene chloride (10 mL) and 0.329 g (2 mmol) of 2,2,6,6-$(CH_3)_4$-c-C_5H_6NF (**11**) were combined in a dry 100-mL round-bottomed flask equipped with a Kontes Teflon stopcock and a Teflon-coated stirring bar. The vessel was evacuated at -196 °C, and 0.174 g (2 mmol) of phosphorus pentafluoride was condensed into the flask. The mixture was warmed to room temperature and stirred for 12 h. The solvent was evaporated under vacuum, and the resulting white solid **23** (~90% yield) was recrystallized from a mixture of acetonitrile/hexane/ether (2:1:1). The spectral data obtained for **23** are as follows: ^{19}F NMR ϕ -72.82 d (J_{P-F} = 708 Hz); ^{31}P NMR δ -145.04 sept; ^{1}H NMR δ 2.4 m (6 H), 1.5 m (6 H), 1.7 m (6 H); MS (FAB$^+$, glycerol) [*m/e* (species) intensity] 140 ($M^+ - PF_6$) 100; MS (FAB$^-$, glycerol) [*m/e* (species) intensity] 145 (PF_6^-) 100; IR (KBr pellet) 2940 vs, 2870 s, 1660 w, 1590 s, 1470 s, br, 1380 m, 1360 w, 1320 m, 1270 m, 1230 m, 1130 m, 930 m, 920 m, 720 w, 510 w, 470 m, cm^{-1}.

Acknowledgment is expressed to the National Science Foundation (Grant CHE-8703790) and to the Air Force Office of Scientific Research (Grant 87-0067) for support of this research. Dr. G. D. Knerr obtained the mass spectra.

Registry No. **1**, 14722-43-1; **2**, 125227-79-4; **3**, 125227-80-7; **4**, 125227-81-8; **5**, 125227-82-9; **6**, 125227-83-0; **7**, 125227-84-1; **8**, 125227-85-2; **9**, 17265-86-0; **10**, 24151-83-5; **11**, 24192-33-4; **12**, 62-75-9; **13**, 55-18-5; **14**, 621-64-7; **15**, 601-77-4; **16**, 924-16-3; **17**, 997-95-5; **18**, 947-92-2; **19**, 930-55-2; **20**, 100-75-4; **21**, 17721-95-8; **22**, 6130-93-4; **23**, 125227-87-4; NF_3O, 13847-65-9; Me_2NH, 124-40-3; Et_2NH, 109-89-7; Pr_2NH, 142-84-7; i-Pr_2NH, 108-18-9; Bu_2NH, 111-92-2; *i*-Bu_2NH, 110-96-3; (c-$C_6H_{11})_2NH$, 101-83-7; c-C_4H_8NH, 123-75-1; c-$C_5H_{10}NH$, 110-89-4; 2,6-$(CH_3)_2$-c-C_5H_8NH, 504-03-0; 2,2,6,6-$(CH_3)_4$-c-C_5H_6NH, 768-66-1; PF_5, 7647-19-0.

Gilvocarcin Photobiology.[1] Isolation and Characterization of the DNA Photoadduct

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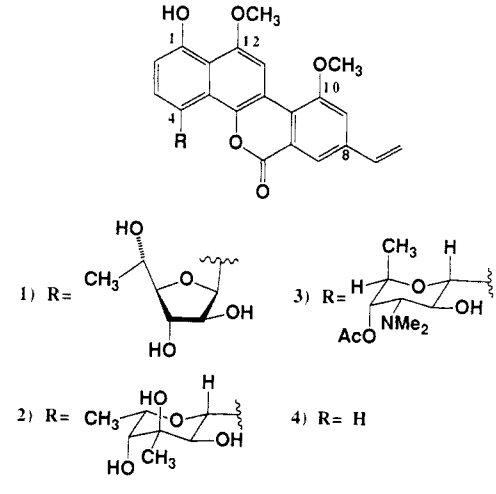
Abstract: Gilvocarcin V forms a covalent adduct with double-stranded DNA under the influence of light. The structure of this covalent modification is identified as a [2 + 2] cycloadduct between the vinyl group of gilvocarcin V and a thymine residue. The stereochemistry of this adduct is deduced from NMR.

Gilvocarcin V (**1**),[2,3] also known as toromycin[4] and anandimycin,[5] is representative of a new class of aromatic C-glycoside antibiotics possessing significant antitumor activity.[6] Other members of this family include chrysomycin A (**2**)[7] (albacarcin V,[8] virenomycin V[9]) and ravidomycin (**3**),[10] which incorporate the same aromatic aglycon attached to various glycosidic substituents. The aglycon of these antitumor antibiotics, defucogilvocarcin V[11] (**4**), has recently been isolated as a natural product. This aglycon has been the subject of a number of synthetic studies[12-16] including our own.[17] The related natural product, gilvocarcin M (**5**), possesses an aglycon in which the vinyl substituent at C8 is replaced by a methyl group.

Although gilvocarcin V is known to inhibit DNA synthesis,[18] little is known about the precise mechanism of action. The extreme potencies of some of the gilvocarcins in cell culture and in vitro tests, where DNA strand scission has been observed,[19] stand in sharp contrast to the apparent tolerance of whole animals for large doses. Elespuru and Gonda[20] identified light exposure of the gilvocarcins in the presence of DNA as a significant requirement for potency in cell culture and in vitro tests such as DNA strand nicking. Gilvocarcin V is 10^3-10^5 times more active than the photoactive psoralens, 8-methoxypsoralen (**6**) and trioxsalen (**7**), in the prophage-induction assay for DNA damage.[20] The wavelength dependence of the λ prophage induction assay with gilvocarcin V correlates strongly with the absorption spectra of the natural product.[21] Similar light-dependent activity has been



observed with the ravidomycin antibiotics.[22] Under visible light, gilvocarcin V is capable of generating both singlet oxygen and

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(1) Contribution No. 5162, Presented at the 3rd Chemical Conference of North America, Toronto, Canada, June 1988; Paper BIOL 48.

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