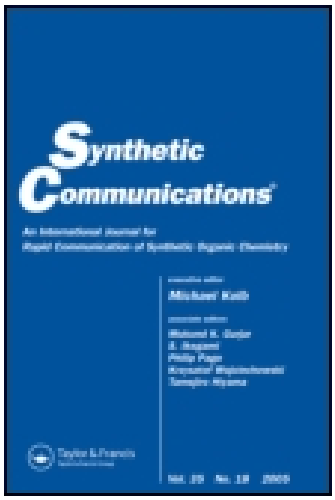


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A New Preparation of gem -bis(Difluoramino)- alkanes via Direct Fluorination of Geminal Bisacetamides

Robert D. Chapman [a] , Matthew C. Davis [a] & Richard Gilardi [b]

[a] Research Department (Code 4T4200D) , Naval Air Warfare Center Weapons Division , Naval Air Systems Command , China Lake, California, USA

[b] Laboratory for the Structure of Matter (Code 6030) , Naval Research Laboratory , Washington, DC, USA

Published online: 16 Aug 2006.

To cite this article: Robert D. Chapman , Matthew C. Davis & Richard Gilardi (2003) A New Preparation of gem -bis(Difluoramino)- alkanes via Direct Fluorination of Geminal Bisacetamides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:23, 4173-4184, DOI: 10.1081/SCC-120026361

To link to this article: http://dx.doi.org/10.1081/SCC-120026361

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 23, pp. 4173–4184, 2003

A New Preparation of *gem*-bis(Difluoramino)-alkanes via Direct Fluorination of Geminal Bisacetamides

Robert D. Chapman,[1,*] Matthew C. Davis,[1] and Richard Gilardi[2]

[1]Research Department (Code 4T4200D), Naval Air Warfare Center Weapons Division, Naval Air Systems Command, China Lake, California, USA
[2]Laboratory for the Structure of Matter (Code 6030), Naval Research Laboratory, Washington, DC, USA

ABSTRACT

A fundamentally new preparation of internal and terminal *gem*-bis-(difluoramino)alkanes has been demonstrated by the direct fluorination of corresponding *gem*-bisacetamides, specifically, 1,1-bisacetamidocyclohexane and 1,1-bisacetamidopropane, leading to 1,1-bis(difluoramino)cyclohexane and 1,1-bis(difluoramino)-propane, respectively.

*Correspondence: Robert D. Chapman, Research Department (Code 4T4200D), Naval Air Warfare Center Weapons Division, Naval Air Systems Command, China Lake, CA 93555, USA; Fax: (+1) 760-939-1617; E-mail: robert.chapman@navy.mil.

DOI: 10.1081/SCC-120026361 0039-7911 (Print); 1532-2432 (Online)

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

Key Words: Difluoramines; Geminal bisacetamides; Fluorination.

There has recently been a resurgence of interest in the class of (difluoramino)alkane derivatives due to the prospect of preparing *gem*-bis(difluoramino)-substituted analogs of conventional cyclic nitramines.[1] For example, this interest has prompted the development of a new route to alkyl fluoramines and difluoramines by electrophilic fluorination of nucleophilic primary and secondary amines with an N−F fluorinating agent (Selectfluor™).[2] Also, the utility of trityldifluoramine (Ph_3CNF_2)—a known source of difluoramine via acidic hydrolysis[3]—for effecting in situ difluoramination of ketones[4] has been recently rediscovered.[5] The latter system invokes the mechanism of difluoramine alkylation by carbenium ions generated in strong acids, as traditionally employed in conventional difluoraminations of ketones with added difluoramine.[6] Trityldifluoramine as an indirect difluoramine source suffers an economic disadvantage of a preparation requiring the radical reaction of trityl chloride with N_2F_4, itself prepared via oxidation of difluoramine.[7]

Conventional difluoramination of ketones has heretofore been the only practical preparation of *gem*-bis(difluoramino)alkane derivatives, but it has suffered some disadvantages with respect to the recent applications of interest. Although the historical hazards of handling difluoramine in such reactions[8] have been mitigated by improvements in experimental methodology,[9] the successful difluoramination of β,β′-diaminoketones—i.e., cyclic derivatives of 1,3-diaminoacetone—to β,β-bis-(difluoramino)-substituted nitrogenous heterocycles requires relatively exotic *N*-protection of heterocyclic nitrogens—e.g., by 4-nitrobenzenesulfonyl (nosyl)—in order to allow generation of the requisite β-carbenium ion in preference to simple *N*-protonation.[9] Suitable *N*-protecting groups for this transformation tend to result in particularly difficult nitrolytic deprotection to make corresponding nitramines.[10] A superior method leading to *gem*-bis(difluoramino)alkanes that obviates alkylation of difluoramine by heterocyclic carbenium ions is therefore needed.

Our premise for such an alternative method involves the direct fluorination of protected aminals, especially ketoaminals which would be the basis of internal *gem*-bis(difluoramino)alkanes. A model for this transformation was recognized in another electrophilic substitution of protected aminals: namely, the nitrolysis of variously *N*-protected hexahydro-1,3,5-triazines, reported by Gilbert et al.[11] In this system, simple acyl-protected hexahydrotriazines were efficiently nitrolyzed: triacetyl

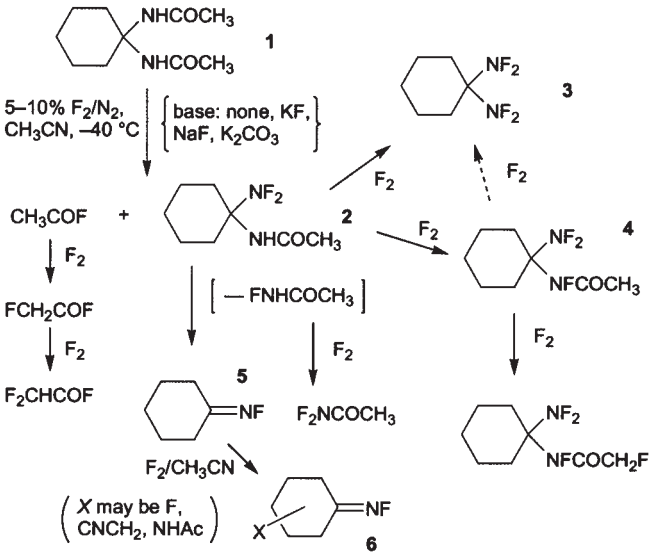
and tripropionyl derivatives in 80–95% yield by HNO_3–P_2O_5, 80–98% yield by HNO_3–$(CF_3CO)_2O$. In contrast, carbamate derivatives (trialkyl hexahydro-1,3,5-triazine-1,3,5-tricarboxylates), electronegatively substituted acyl derivatives—e.g., 1,3,5-tris(2-chloroacetyl)hexahydrotriazine—and derivatives with protecting groups subject to electrophilic attack themselves (1,3,5-triacryloylihexahydrotriazine) showed no conversion to the corresponding nitramine (RDX).

Our initial attempt to effect electrophilic deprotection of a geminal biscarbamate was consistent with the similar finding of Gilbert et al.[11] our direct fluorination (F_2/N_2) of diethyl cyclohexylidene biscarbamate resulted only in cleavage of the aminal linkage rather than fluorinolysis of the carbamate substituents.[12] Although geminal bisacylamides then appeared to offer the best prospect of a protected aminal amenable to electrophilic fluorinolysis to difluoramines, there was no *general* method to prepare that class of ketoaminal, so we developed potentially general methodology to produce such derivatives.[13] This method provided 1,1-bisacetamidocyclohexane (**1**) as a model compound expected to lead to a "typical" internal *gem*-bis(difluoramino)alkane, 1,1-bis(difluoramino)cyclohexane.

We have now confirmed that simple fluorination (5–20 vol% F_2/N_2) of **1** under a variety of mild conditions proceeds via 1-acetamido-1-(difluoramino)cyclohexane (**2**) to the desired 1,1-bis(difluoramino)cyclohexane (**3**), although the latter stages of fluorination are complicated by competing side reactions, as shown in Sch. 1.

The fluorination of **1** in acetonitrile solvent was generally conducted at low temperature ($\sim -40^\circ C$). The presence or absence of various Brønsted bases (NaF, KF, K_2CO_3) generally did not affect the course or product distribution of the reaction. The first stage of fluorinolysis of **1** showed concomitant generation of acetyl fluoride, as expected, as well as its subsequent fluorination to 2-fluoroacetyl fluoride and 2,2-difluoroacetyl fluoride, according to comparison to published ^1H and ^{19}F NMR data.[14] Intermediate **2** could be isolated by workup after monitoring aliquots of the mixture (^1H, ^{19}F NMR) for its formation, but isolation of **2** was not necessary to carry it on to **3**.

Crystals of **2** suitable for X-ray diffraction were obtained by crystallization from *n*-pentane–chloroform. The X-ray analysis results[15] completely corroborated the expected structure and provided another accurate determination of the geometry of the NF_2 group, which is consistently found to be extremely pyramidal in both aromatic[16] and aliphatic[10,17,18] situations. The bond angles in **2** (Fig. 1) are $C-N-F(1A) = 105.6(2)^\circ$, $C-N-F(1B) = 105.2(2)^\circ$, and $F-N-F = 99.8(1)^\circ$, all significantly less than "tetrahedral" (109.5°). The corresponding



Scheme 1.

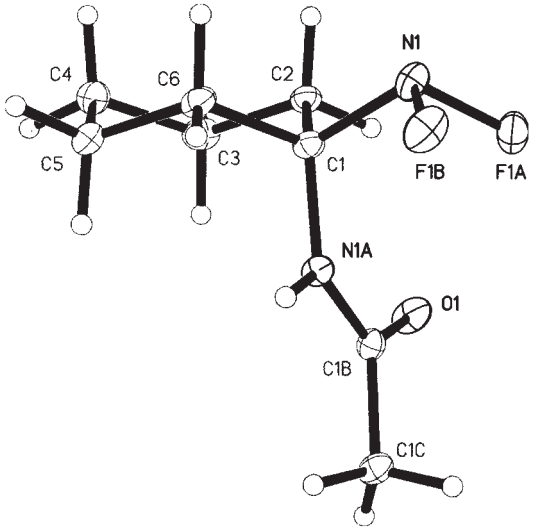


Figure 1. A drawing of 1-acetamido-l-(difluoramino)cyclohexane (**2**) as it occurs in the crystalline state. The difluoramino group is equatorial and the acetamido group is axial to the cyclohexane ring.

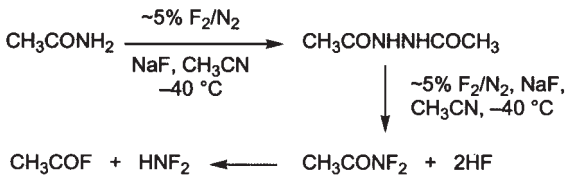
averages for all fifteen previously published NF_2 geometries[18] are $<C-N-F> = 105.2(7)^\circ$ and $<F-N-F> = 100.4(8)^\circ$.

Continued fluorination of **2** produced two major products based on the cyclohexane skeleton: **3** is formed, probably via 1-(difluoramino)-1-(*N*-fluoroacetamido)cyclohexane (**4**), a minor intermediate apparent by ^{19}F NMR during the course of the reaction; and, by elimination of *N*-fluoroacetamide from **2**, *N*-fluorocyclohexylimine (**5**) and, to a minor extent, similar, substituted derivatives (**6**) are formed, identified by comparison to literature ^{19}F NMR data.[19] The elimination of *N*-fluoroacetamide, via aminal cleavage of **2**, is apparent by the formation of *N*,*N*-difluoroacetamide.

We confirmed the identity of *N*,*N*-difluoroacetamide by simple direct fluorination of acetamide. Although other researchers[20] have reported difficulty in its preparation by this method,[21] we observed an interesting course of reaction by fluorinating acetamide in acetonitrile (5% F_2/N_2, $-40^\circ C$) in the presence of NaF (Sch. 2).

The initial product is unfluorinated *N*,*N*′-diacetylhydrazine—by comparison to literature data[22]—which undergoes fluorination to *N*,*N*-difluoroacetamide and HF by-product, a mixture that is observed subsequently to degrade to acetyl fluoride and difluoramine, as previously reported.[20] This behavior of coupling by the carbamoyl group of acetamide is analogous to that reported for urea by Glemser and Lüdemann,[23] forming hydrazodicarbonamide from fluorination (1:2 F_2/N_2) of urea in a temperature range of $-30^\circ C$ to r.t. This course of fluorination of a primary amide is distinctly different from that of secondary amides, which proceed simply to *N*-alkyl-*N*-fluoroamides and alkyldifluoramines.[24]

In Sch. 1, another minor side reaction that is apparent by ^{19}F NMR is the fluorination of the acetyl protecting group remaining in **4**. This reaction leaves the *N*-(2-fluoroacetyl) group unamenable to fluorinolysis under mild conditions, a result also consistent with the observations of Gilbert et al.[11] about the lack of reactivity of electronegatively substituted protecting groups (e.g., 2-chloroacetyl) toward nitrolytic deprotection.



Scheme 2.

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

The yield of 1,1-bis(difluoramino)cyclohexane (**3**) observed in our runs of the Sch. 1 reaction appears to maximize at ~10%, measured via an internal standard for quantitative integration of the NF region of ^{19}F NMR and confirmed by isolation of **3** by removal of solvent as the low-boiling *n*-pentane–acetonitrile azeotrope (~31°C) followed by purification by chromatography. It should be recognized, however, that conventional difluoramination of cyclohexanone also produces an atypically low yield of **3** (31%) compared to other ketones; thus, in contrast, conventional difluoramination of even 1,4-cyclohexanedione produces a yield of 1,1,4,4-tetrakis(difluoramino)cyclohexane of 75%.[6a] Another anomalous property of **3** is the chemical shift of NF_2 in its ^{19}F NMR spectrum: a reported δ 22.79[6a] and our measurement of δ 22.61 ($CFCl_3$ solvent) put it far upfield of all other "typical" internal *gem*-bis(difluoramino)alkane derivatives, which are predominantly in the range of δ 26–30.[25] This property as well as the low yield of **3** by conventional difluoramination may suggest unusual electronic or steric effects in **3** (and perhaps in **2**) that contribute to the susceptibility of cyclohexylidene aminals to the side reactions that occur, as in Sch. 1.

Although terminal *gem*-bis(difluoramino)alkanes are of less interest for practical applications, the fluorination of terminal *gem*-bisacetamides—aldoaminals readily prepared from aldehydes plus amides[26]—proceeds more efficiently than that of **1**. Thus, fluorination (5% F_2/N_2) of 1,1-bisacetamidopropane at ~−40°C in acetonitrile (no added base) proceeds, via 1-acetamido-1-(difluoramino)propane, to 1,1-bis(difluoramino)propane in ~45 min with ~40% yield according to ^{19}F NMR analysis—closer to a yield of 65% obtained by conventional difluoramination of propionaldehyde.[6a]

In conclusion, we have demonstrated the technical feasibility of the first fundamentally new preparation of *gem*-bis(difluoramino)alkanes since conventional difluoramination of ketones: namely, via direct fluorination of suitable *gem*-bisacylamides. The cyclohexylidene system may not be an ideal model for this transformation, in hindsight, due to unusual aspects of its spectral and chemical properties, summarized above. β,β-Bisacylamides of suitably *N*-protected heterocycles should be less susceptible to aminal cleavage than the simple cyclohexylidene system. Other technical modifications are apparent that should provide improved behavior of the protected aminal system. For example, *gem*-bispropionamides formed from corresponding ketones should still be amenable to fluorinolysis even following competitive terminal fluorination of the propionyl protecting group. This new methodology would eliminate a requirement for expensive *N*-protecting groups in order to prepare products based on 1,3-diaminoacetone derivatives,

since alkylation of difluoramine via heterocyclic carbenium ions is obviated. (The *N*-protecting groups in such systems need not be as exotic as nosyl, merely removable by nitrolysis and less readily displaced than simple *N*-acyl, e.g., methanesulfonyl.) Of course, a requirement for difluoramine generation (even in situ) is also avoided.

EXPERIMENTAL

Reagents were commercially available and used as received. Multinuclear NMR spectra were obtained on a Bruker AC-200 spectrometer (200 MHz ^{1}H) and referenced to solvent or tetramethylsilane. Microanalysis was performed by Galbraith Laboratories (Knoxville, TN).

Typical Experimental Procedure

1-Acetamido-1-(difluoramino)cyclohexane, 2. To a magnetically-stirred solution of 1.02 g (5.14 mmol) of **1**[13] in 100 mL CH_3CN–$CFC1_3$ (1:1) in a 2-neck round-bottom flask was added 2.16 g anhydrous NaF (51.4 mmol). The flask was cooled in a dry ice–CH_3CN bath (~−40°C) while a fluorine mixture (20 vol% F_2 in N_2) was very slowly bubbled through the reaction solution via "spaghetti" fluoropolymer tubing. After 4 h, no starting material remained, according to GC-MS analysis. Then N_2 was bubbled through the mixture briefly, and the reaction mixture was filtered through Celite 521. The filtrate was evaporated at r.t. to obtain a yellow oil that slowly solidified. This was dry-column chromatographed (silica; $CHCl_3$; $R_f = 0.4$) with fractions analyzed by ^{19}F NMR to obtain the title compound as a white solid; yield 0.25 g (25%). The solid recrystallized from *n*-pentane–chloroform as colorless needles. M.p.: 95–110°C (dec). ^{1}H NMR ($CDC1_3$) δ 1.22–1.55 (m, 3H), 1.62–1.85 (m, 5H), 2.08 (s, 3H), 2.35–2.55 (m, 2H), 5.43 (bs, 1H). ^{13}C NMR ($CDC1_3$) δ 21.79, 24.93, 25.07, 30.31 (t, $^3J_{CF} = 3.95$ Hz), 84.69 (t, $^2J_{CF} = 7.75$ Hz), 170.61. ^{19}F NMR (<5% $CDCl_3$ in $CFCl_3$) δ 21.53. ($CDCl_3$) δ 22.47. (CD_3CN) δ 23.54. (CD_3CN, 70°C) δ 23.49. IR (KBr): $\nu(NF_2)$ 841.5 cm^{-1}. Analysis calcd. for $C_8H_{14}N_2F_2O{\cdot}0.11H_2O$: C, 49.47; H, 7.38; N, 14.42. Found: C, 49.53; H, 7.44; N, 14.24. EIMS: m/z 140 ($M^+ - NF_2$), 98 (140 – C_2H_2O), 81 (140 – H_2NAc).

1,1-bis(Difluoramino)cyclohexane, 3. Fluorine in nitrogen (20 vol%) was diluted with a threefold excess flow of N_2 and slowly bubbled through a cooled (~−40°C), magnetically stirred solution of 0.10 g (0.50 mmol) of **1**

in 9 mL CD_3CN in a 25 mL 2-neck pear-shaped flask which contained 0.10 g dry KF. After 30 min, an aliquot was withdrawn, and ^{1}H NMR showed intermediate **2** still present. Apparent by ^{19}F NMR at this stage were minor amounts of intermediate 1-(difluoramino)-1-(*N*-fluoroacetamido)cyclohexane (**4**) and side product 1-(difluoramino)-1-(2,*N*-difluoroacetamido)cyclohexane. Fluorination of the reaction solution was continued for a total of 1 h, when ^{1}H NMR showed no residual **2**. The content of **3** was quantified by integration of the ^{19}F NMR signal of **3** vs. that of 3,3,7,7-tetrakis(difluoramino)octahydro-1,5-dinitro-1,5-diazocine (HNFX) in a solution made from measured quantities of HNFX stock solution and of reaction solution. Yields of **3** were typically 8–10% at the time of consumption of intermediate **2**. Product **3** could be isolated by adding excess *n*-pentane to distill off acetonitrile as a low-boiling azeotrope (~31°C). The pot residue was dissolved in a minimum volume of CCl_4 and chromatographed (silica gel/pentane); fractions were monitored by ^{19}F NMR. Excess pentane was easily distilled from higher-boiling **3**. ^{1}H NMR of **3** (CD_3CN) δ 1.5–1.9 (m), 2.08 (t). ^{13}C NMR (CD_3CN) δ 21.5, 25.0, 27.0, 96.8. ^{19}F NMR (1 : 10 $CDCl_3$–$CFCl_3$) δ 22.61; (CH_2Cl_2–$CDCl_3$) δ 23.22. (CD_3CN) δ 23.56. (CD_3CN, 70°C) δ 24.11.

1-(Difluoramino)-1-(*N*-fluoroacetamido)cyclohexane, 4, and 1-(difluoramino)-1-(2,*N*-difluoroacetamido)cyclohexane. Bisacetamide **1** was fluorinated similarly to the example above, but with NaF instead of KF. After 1 h, no residual intermediate **2** was apparent. Solid $NaHCO_3$ was added to the mixture, which was stirred at r.t. overnight. Volatiles, including some of product **3** and of *N*-fluorocyclohexylimine (**5**), were removed by rotary evaporation at reduced pressure. The residue was eluted through silica gel with chloroform, and the combined eluates were rechromatographed (silica gel–chloroform, eluted successively with *n*-pentane and dichloromethane). The final fraction, containing the title compounds, was concentrated to dryness by rotary evaporation. 1-(Difluoramino)-1-(*N*-fluoroacetamido)cyclohexane (**4**): ^{1}H NMR ($CDCl_3$) δ 1.52–1.94 (m), 2.29 (d, $^4J_{HF} = 9.8$ Hz), 2.69 (b), 2.75 (b). ^{19}F NMR ($CDCl_3$) δ 26.76 (d, $^4J_{FF} = 17.0$ Hz, NF_2), −71.1 (b, NF). $\{^1H\}^{19}$F NMR ($CDCl_3$) δ 26.76 (d, $^4J_{FF} = 17.0$ Hz, NF_2), −71.11 (t, $^4J_{FF} = 17.0$ Hz, NF). 1-(Difluoramino)-1-(2,*N*-difluoroacetamido)cyclohexane: ^{1}H NMR ($CDCl_3$) δ 1.52–1.94 (m), 2.69 (b), 2.75 (b), 5.16 (dd, $^2J_{HF} = 46.9$ Hz, $^4J_{HCCNF} = 3.5$ Hz). ^{19}F NMR ($CDCl_3$) δ 27.42 (d, $^4J_{FF} = 18.7$ Hz, NF_2), −92.7 (bt, NF), −234.66 (t of d, $^2J_{HF} = 46.9$ Hz, $^4J_{FCCNF} = 7.8$ Hz). $\{^1H\}^{19}$F NMR ($CDCl_3$) δ 27.42 (d, $^4J_{FF} = 18.7$ Hz, NF_2), −92.68 (t of d, $^4J_{FNCNF} = 18.7$ Hz, $^4J_{FCCNF} = 7.8$ Hz, NF), −234.66 (t of d, $^2J_{HF} = 46.9$ Hz, $^4J_{FCCNF} = 7.8$ Hz).

Typical Experimental Procedure

***N,N*-Difluoroacetamide.** Fluorine in nitrogen (20 vol%) was diluted with a threefold excess flow of N_2 and slowly bubbled through a cooled (~−40°C), magnetically stirred solution of 0.10 g of acetamide in 8 mL CD_3CN in a 25 mL 2-neck pear-shaped flask. After 10 min, NMR analysis showed that *N*,*N*′-diacetylhydrazine [^{1}H NMR (CD_3CN) δ 1.85 (s), 1.88 (s). Lit.[22] (DMSO-d_6) (*Z*,*Z*)—δ 1.83, (*E*,*E*)—δ 1.86] was the major solute besides starting material acetamide and HF by-product. After 40 min, *N*,*N*-difluoroacetamide was the major solute, and degradation products acetyl fluoride and difluoramine were significant. *N*,*N*-Difluoroacetamide: ^{1}H NMR (CD_3CN) δ 2.42 (t, $^4J_{HF} = 3.0$ Hz). ^{19}F NMR (CD_3CN) δ 26.2 (b).

1,1-bis(Difluoramino)propane. Fluorine in nitrogen (20 vol%) was diluted with a threefold excess flow of N_2 and slowly bubbled through a cooled (~−40°C), magnetically stirred solution of 0.1023 g of 1,1-bis-acetamidopropane[26] in 8 mL CD_3CN in a 25 mL 2-neck pear-shaped flask. After 15 min, 1-acetamido-1-(difluoramino)propane was the predominant fluorinated component, according to ^{19}F NMR, apparent as an AB quartet of doublets: δ 23.31, 26.39 ($^3J_{HF} = 28.0$ Hz); 35.09, 38.16 ($^3J_{HF} = 12.9$ Hz). After 45 min, starting material and this intermediate were gone, and 1,1-bis(difluoramino)propane was the most prevalent difluoramine derivative, according to ^{1}H and ^{19}F NMR. Yield ~40% by integration of the NF region of ^{19}F NMR [δ 35.3 (b). Lit[6a] δ 36.3].

ACKNOWLEDGMENTS

Financial support, managed by Dr. Judah Goldwasser, of the Office of Naval Research is gratefully acknowledged.

REFERENCES

1. Miller, R.S. Research on new energetic materials. Mater. Res. Soc. Symp. Proc. **1996**, *418*, 3–14.
2. Singh, R.P.; Shreeve, J.M. The first application of Selectfluor™ electrophilic fluorination of amines: a new route to $-NF_2$, $-NHF$, and $>NF$ compounds. Chem. Comm. **2001**, 1196–1197.
3. Graham, W.H.; Parker, C.O. The reaction of trityldifluoramine with sulfuric acid. A simple method of preparation of difluoramine. J. Org. Chem. **1963**, *28*, 850.

4. Fokin, A.V.; Kosyrev, Yu.M.; Shevchenko, V.I. Certain examples of difluoroamine alkylation reactions. Bull. Acad. Sci. USSR, Div. Chem. Sci. **1982**, 1626–1632.
5. Prakash, G.K.S.; Etzkorn, M.; Olah, G.A.; Christe, K.O.; Schneider, S.; Vij, A. Triphenylmethyldifluoramine: a stable reagent for the synthesis of *gem*-bis(difluoramines). Chem. Comm. **2002**, 1712–1713.
6. (a) Baum, K. Reactions of carbonyl compounds with difluoramine. J. Am. Chem. Soc. **1968**, *90*, 7083–7089; (b) Graham, W.H.; Freeman, J.P. The alkylation of difluoramine with carbonium ions. J. Org. Chem. **1969**, *34*, 2589–2595; (c) Fokin, A.V.; Kosyrev, Yu.M.; Makarov, V.A.; Novoselov, N.P. Synthesis of geminal bis(difluoroamino) derivatives (a new example of difluoroamine alkylation). Dokl. Chem. (Engl. Transl.) **1969**, *186*, 350–353.
7. Remanick, A.H.; Grakauskas, V. Process for Preparing Tetrafluorohydrazine. GB Patent 1,109,700, April 10, 1968.
8. (a) Lawton, E.A.; Weber, J.Q. The synthesis and reactions of difluoramine. J. Am. Chem. Soc. **1963**, *85*, 3595–3597; (b) Parker, C.O.; Freeman, J.P. 1,1-Difluorourea solutions and difluoroamine—extra-hazardous materials. Inorg. Synth. **1970**, *12*, 307–312.
9. Chapman, R.D.; Welker, M.F.; Kreutzberger, C.B. Difluoramination of heterocyclic ketones: control of microbasicity. J. Org. Chem. **1998**, *63*, 1566–1570.
10. Chapman, R.D.; Gilardi, R.D.; Welker, M.F.; Kreutzberger, C.B. Nitrolysis of a highly deactivated amide by protonitronium. Synthesis and structure of HNFX. J. Org. Chem. **1999**, *64*, 960–965.
11. Gilbert, E.E.; Leccacorvi, J.R.; Warman, M. The preparation of RDX from 1,3,5-triacylhexahydro-*s*-triazines. Am. Chem. Soc. Symp. Ser. **1976**, *22*, 327–340.
12. Davis, M.C.; Chapman, R.D.; Johnson, R. A New Preparation of *geminal* Bis(difluoramino)alkanes: Direct Fluorination of Geminal-Bisamides. 223rd National Meeting of the American Chemical Society, Orlando, FL, USA, 7–11 April 2002; FLUO 13, 2677–2684.
13. Davis, M.C.; Stasko, D.; Chapman, R.D. Conversion of a ketone to a geminal bisacetamide: synthesis of 1,1-bisacetamidocyclohexane. Synth. Commun. **2003**, *33*, 2677–2684.
14. (a) Schaumburg, K. Fluorination of organic compounds and long-range coupling constants in carbonyl fluorides. J. Magn. Reson. **1972**, *7*, 177–183; (b) Fokin, A.V.; Studnev, A.I.; Rapkin, Yu.N.; Sultanbekov, D.A.; Potarina, T.M. Reaction of 1,1,2-trifluoro-2-chloroethyldiethylamine with fluorocarboxylic acids. Bull. Acad. Sci. USSR, Div. Chem. Sci. **1984**, 372–375.

15. Crystal data for **2**: Orthorhombic space group Pbca, with $a = 10.325(3)$, $b = 9.722(3)$, $c = 19.175(6)$ Å (at data collection $T = -180^{\circ}C$), $V = 1924(1)$ Å^3, $Z = 8$. $R = 0.0422$ for 1010 observed [$I > 2\sigma(I)$ reflections, $R = 0.0669$ for all 1390 reflections. Additional crystal and molecular data have been deposited as supplementary publication CCDC 207557 with the Cambridge Crystallographic Data Centre; copies can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1 EZ, UK (or e-mail to deposit@ ccdc.cam.ac.uk).
16. (a) Batail, P.; Louër, M.; Grandjean, D.; Dudragne, F.; Michaud, C. Etude structurale de fluoramines aromatiques. III. Structure cristalline et moléculaire du (*N*,*N*-difluoroamino) dinitro-2,4 benzène, $C_6H_3O_4N_3F_2$. Acta Cryst. Sect. B **1976**, *32*, 2780–2786; (b) Batail, P.; Grandjean, D.; Dudragne, F.; Michaud, C. Etude structurale de fluoramines aromatiques. II. Structure cristalline et moléculaire du (*N*,*N*-difluoroamino) trinitro-2,4,6 benzène, $C_6H_2O_6N_4F_2$. Acta Cryst. Sect. B **1975**, *31*, 1367–1372; (c) Dalinger, I.L.; Vinogradov, V.M.; Shevelev, S.A.; Kuz′min, V.S. *N*-(Difluoroamino)azoles—a new class of *N*-substituted azoles. Mendeleev Commun. **1996**, 13–15.
17. Suries, J.R.; Bumgardner, C.L.; Bordner, J.J. Synthesis and crystal structure of para-bromophenyldiphenylcarbinyl difluoramine. J. Fluorine Chem. **1975**, *5*, 467–474.
18. Values cited are from Tables 6 and 7 in: Butcher, R.J.; Gilardi, R.; Baum, K.; Trivedi, N.J. The structural chemistry of energetic compounds containing gem-difluoramino groups. Thermochim. Acta **2002**, *384*, 219–227.
19. (a) Sharts, C.M. *N*,*N*-Difluoroalkylamines by direct fluorination of alkylamines. J. Org. Chem. **1968**, *33*, 1008–1011; (b) Smith, H.F.; Castellano, J.A. Fluorimino-cyclo-alkanes and Alkenes. US Patent 3,479,404, November 18, 1969.
20. Davydov, A.V.; Stolyarov, V.P. Fluorination of acetamide by elementary fluorine. Mendeleev Chem. J. **1977**, *22*, 21–22; and references therein.
21. *N*,*N*-Difluoroacetamide was first prepared by radical reaction of N_2F_4 with acetaldehyde. Petry, R.C.; Freeman, J.P. Tetrafluorohydrazine: a versatile intermediate for the synthesis of *N*-fluoro compounds. J. Am. Chem. Soc. **1961**, *83*, 3912.
22. Fritz, H.; Kristinsson, H.; Mollenkopf, M.; Winkler, T. ^{15}N and ^{13}C NMR study of acylated hydrazines. The instability of trifluoroacethydrazide in the solid state. Magn. Reson. Chem. **1990**, *28*, 331–336.

23. Glemser, O.; Lüdemann, H. Über die einwirkung von fluor auf harnstoff. Z. Anorg. Allg. Chem. **1956**, *286*, 168–173.
24. Grakauskas, V.; Baum, K. Direct fluorination of amides. J. Org. Chem. **1970**, *35*, 1545–1549.
25. (a) Jones, K.; Mooney, E.F. Fluorine-19 nuclear magnetic resonance spectroscopy. Annu. Rep. NMR Spectrosc. **1970**, *3*, 261–421; (b) Emsley, J.W.; Phillips, L. Fluorine chemical shifts. Prog. Nucl. Magn. Reson. Spectrosc. **1971**, *7*, 1–520.
26. Fernández, A.H.; Alvarez, R.M.; Abajo, T.M. Improved synthesis of symmetrical *N*,*N*′-alkylidene bisamides. Synthesis **1996**, 1299–1301.

Received in the USA June 2, 2003