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Supplementary Material Available: X-ray data for 4 and 14 consisting of fractional atomic coordinates, temperature factors, and bond distances and bond angles, ^{13}C NMR spectra of 1, 4, 5, 9, 10, 14, and the reference compound *N*-octylurea (7 pages). Ordering information is given on any current masthead page.

Reactions of Primary and Secondary Amines with Fluoronitrene Generated from Isopropyl *N,N*-Difluorocarbamate[1]

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Isopropyl *N,N*-difluorocarbamate deaminates primary amines, RNH_2, affording RH, N_2, $RNHCO_2$-*i*-C_3H_7, and RNH_2·HF. With secondary amines, dibenzylamine gives bibenzyl, whereas pyrrolidine yields a ring-expansion product, 2,3,4,5-tetrahydropyridazine. The reactions are consistent with the generation of fluoronitrene and subsequent production of the intermediates RN=NH from RNH_2 and R_2N=N from R_2NH. The advantages of using isopropyl *N,N*-difluorocarbamate as a source of fluoronitrene are discussed.

Several studies have been done on reactions of primary and secondary amines with HNF_2[3-6] to yield deaminated and other products in which fluoronitrene has been implicated.[3] We report herein the use of isopropyl *N,N*-difluorocarbamate[7] as a convenient source of fluoronitrene,[8] the products obtained from the reaction of *i*-$C_3H_7OCONF_2$ with primary and secondary amines via NF as a postulated intermediate, and comparison with pertinent prior literature.

Fluoronitrene has previously been formed from a variety of sources, including FN_3,[9,10] NF_3,[11-13] N_2F_4,[14-17] HNF_2,[3-6,17-26] and F_2NCONH_2.[27] The first four of these precursors are gaseous, often explosive, and require vacuum-line techniques not suitable for preparative-scale work. *N,N*-Difluorourea is a sensitive explosive,[28] and one of its crystalline forms is hygroscopic.[28] In contrast, *i*-$C_3H_7OCONF_2$ is found to be a safe, convenient source of NF under a variety of conditions in quantities up to 0.3 mol.

Table I. Products from Primary Amines (RNH_2) and *i*-$C_3H_7OCONF_2$

	products, % yield			
R	RH	*i*-C_3H_7-OCONHR	N_2	$RNH_3^+F^-$
c-C_6H_{11}	14	87	63	88
n-C_8H_{17}	30	69	73	97
$C_6H_5CH_2$	42	71	75	91
o-$CH_3OC_6H_4$	60	74	69	
o-$CH_3C_6H_4$	37	66	54	81
C_6H_5	19[a]	80	60	88
C_6H_5	20[b]			
o-ClC_6H_4	3	62	50	

[a] Cf. ref 8. [b] With NHF_2, ref 3.

The feasibility of producing NF via reaction of *i*-

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$C_3H_7OCONF_2$ with nucleophiles was first demonstrated with potassium *tert*-butoxide[8] as shown in Scheme I. Quantitative formation of N_2F_2 provides good evidence for the intermediacy of fluoronitrene. Analogous behavior of *N,N*-dichlorourethane, *N,N*-dichloro amides, and *N,N*-dichloro carbamates toward alkoxide has recently been investigated.[29,30]

Scheme I

$$i\text{-}C_3H_7OCONF_2 + t\text{-}BuO^- \rightarrow i\text{-}C_3H_7OCO_2\text{-}t\text{-}Bu + NF_2^-$$

$$NF_2^- \xrightarrow{-F^-} NF \xrightarrow[\text{or } NF_2^-]{NF} FN{=}NF$$

Generation of NF from i-$C_3H_7OCONF_2$ and amines is thought to arise by nucleophilic attack of the amine on the carbonyl carbon followed by either production of NF_2^- and subsequent loss of F^- (eq 1 and 2)[31] or a concerted process (eq 3). Consistent with either mechanism is the isolation

$$RNHZ + i\text{-}C_3H_7OCONF_2 \xrightarrow[-H^+]{} \underset{\mathbf{1}}{i\text{-}C_3H_7OCONRZ} + NF_2^- \quad (1)$$

$$NF_2^- \xrightarrow{-F^-} NF \quad (2)$$

$$i\text{-}C_3H_7\overset{\delta-}{\underset{\|}{C}}(=O)\overset{\delta+}{\cdots}NF \longrightarrow HF + NF + \mathbf{1} \quad (3)$$

(RZNH---F)

Z = R or H

of isopropyl carbamates 1 in high yields, usually 70% or more. The possibility that the interaction of i-$C_3H_7OCONF_2$ with nucleophiles produces HNF_2[8] is deemed less likely.

The general equation for deamination of primary amines with i-$C_3H_7OCONF_2$ is illustrated in eq 4, and the results

$$4RNH_2 + i\text{-}C_3H_7OCONF_2 \rightarrow RH + i\text{-}C_3H_7OCONHR + N_2 + 2\overset{+}{R}NH_3F^- \quad (4)$$

for various aliphatic and aromatic amines are set forth in Table I. The mechanistic pathway is presumably the same as that postulated for the reaction of HNF_2 with primary amines,[3] differing only in the manner in which NF is formed. Scheme II outlines the probable steps in the reaction of NF with the amine: coordination, proton shift, loss of HF, and, finally, expulsion of N_2 to yield the alkane.

Scheme II

$$RNH_2 + NF \rightarrow \underset{\mathbf{2}}{RNH_2^+NF^-} \rightarrow RNHNHF \xrightarrow[-HF]{} RN{=}NH \xrightarrow[-N_2]{} RH$$

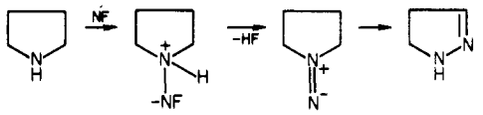
As seen in Table I, with aniline as the reference, the presence of electron-donating groups on aniline gave increased yields of the hydrocarbon, whereas electron-withdrawing substituents decreased the amount of deaminated product. These results can be attributed to influences affecting formation of intermediate **2**.

In the case of secondary amines, the nature of the product was determined by whether the substrate was heterocyclic or acyclic. Reaction of i-$C_3H_7OCONF_2$ with dibenzylamine gave a 55% yield of bibenzyl, which is essentially identical with that (53%) obtained with HNF_2.[3]

Scheme III

$$(C_6H_5CH_2)_2NH \xrightarrow{NF} (C_6H_5CH_2)_2NH^+NF^- \xrightarrow[-HF]{} (C_6H_5CH_2)_2N^+{=}N^- \rightarrow C_6H_5CH_2CH_2C_6H_5 + N_2$$

Scheme IV



The mechanistic sequence is thought to involve a diazene intermediate[32] (Scheme III).

The heterocyclic secondary amines aziridine and azetidine react with HNF_2[3] to give ethylene and cyclopropane, respectively. However, instead of generating cyclobutane by analogy, pyrrolidine combined with i-$C_3H_7OCONF_2$ to give the ring-expansion product 2,3,4,5-tetrahydropyridazine in 62% yield; this can be rationalized as shown in Scheme IV: attack of NF on pyrrolidine, loss of HF, diazene formation, and finally rearrangement to end product.

The only previously disclosed synthesis of 2,3,4,5-tetrahydropyridazine (68% yield) involved the reaction of pyrrolidine with Angeli's salt ($Na_2N_2O_3$).[33] In this case, nitroxyl (NHO) was postulated as a key intermediate, and a diazene was also invoked. Freeman reports that pyrrolidine did not undergo deamination with difluoramine, and ethylene, which has been identified as a product of the decomposition of the corresponding azamine obtained by an alternate route, was not detected.[34] Diallylamine and HNF_2 interacted with ring closure to give *N*-allylpyrazoline, presumably via a diazene intermediate.[4] The reaction pathway followed is quite sensitive to amine structure, both in the cyclic and acyclic series.[1]

In the previous work with HNF_2 and amines, NF was proposed as the deaminating agent.[3] The results of our studies on i-$C_3H_7OCONF_2$ with amines reinforce this postulate. The products from either i-$C_3H_7OCONF_2$ or HNF_2 with aniline and dibenzylamine under similar conditions are identical, both in structure and yield. As an indication of general similarity, the yields of deaminated product ranged from 3 to 60% (29% average) for seven primary amines in our system compared to 20–93% yield (51% average) for eight primary amines in the HNF_2 system.[3,4] Further evidence for involvement of fluoronitrene is provided by isolation of N_2F_2 in high yield from i-$C_3H_7OCONF_2$ and *tert*-butoxide.[8]

It should be mentioned that N_2F_2 generated from the analogous 2-ethylhexyl *N,N*-difluorocarbamate and *t*-BuOK has recently found use as a fluorinating agent for cyclic enamines, leading to cyclic α-fluoro ketones.[35]

Experimental Section

General Procedure. Reactions of i-$C_3H_7OCONF_2$ with amines were carried out in a three-necked flask equipped with a Herschberg stirrer, a constant-pressure addition funnel, and an ice bath or tap water as coolant, depending on the freezing point of the amine. The hydrocarbon products were isolated either by fractional distillation of the solution from pentane extraction or by direct distillation of the reaction mixture. The physical properties and spectra of the amine hydrofluorides isolated from the reaction mixtures were compared with those of authentic samples (some are hygroscopic) prepared from HF and the amines.

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The isopropyl *N*-alkyl- and *N,N*-dialkylcarbamates were identified by comparison of their physical properties and spectra with those of authentic samples prepared by reaction of the amines with isopropyl chloroformate. The amines were dried and then purified by distillation. Melting points and boiling points are uncorrected.

Primary Amines and i-$C_3H_7OCONF_2$. 1. Extraction Method. To chilled benzylamine (75 mL, 0.69 mol) was added i-$C_3H_7OCONF_2$ (13.5 g, 0.097 mol) during 1 h. The mixture was allowed to come to room temperature during a second hour with slow stirring during both hours. The solution turned yellow and a voluminous amount of the white HF salt was formed. After extraction with two 75-mL portions of pentane, filtration gave $C_6H_5CH_2NH_3^+F^-$, 22.43 g (91%) in essentially pure form, mp 152–153 °C, after recrystallization from 95% ethanol. Fractional distillation of the filtrate with a micro apparatus provided toluene, 3.72 g (42%), and i-$C_3H_7OCONHCH_2C_6H_5$, 13.3 g (71%), bp 107 °C (0.1 mm). In a separate experiment, when i-$C_3H_7OCONF_2$ (1.32 g, 0.0095 mol) was added to benzylamine (25 mL, 0.23 mol), evolution of N_2 (159 mL, 75%) was noted and measured.

2. Distillation Method. With *o*-anisidine as substrate after reaction was carried out as in the preceding section, the reaction flask was fitted with a short-path column; distillation of the mixture gave anisole, 6.48 g (60%). Isolation of the HF salt and carbamate was not attempted, since the distillation residue consisted of a water-soluble tar. The extraction method gave a 55% yield of anisole.

Secondary Amines and i-$C_3H_7OCONF_2$. 1. Dibenzylamine. With slow stirring, i-$C_3H_7OCONF_2$ (6.3 g, 0.045 mol) was added to chilled dibenzylamine (50 mL, 0.26 mol) during 1 h. The mixture was allowed to reach room temperature during another hour. After addition of HCl, extraction was carried out with petroleum ether (bp 30–60 °C). Removal of solvent from the extract afforded 15 mL of yellow, oily liquid which was chromatographed on a 3 × 30 cm neutral alumina column, with petroleum ether (bp 30–60 °C) as solvent. The first component eluted was bibenzyl, 3.61 g (55%), mp 51 °C (lit.[36] mp 52.2 °C). The second component was i-$C_3H_7OCON(CH_2C_6H_5)_2$, 7.64 g (60%), mp 68 °C. In a separate experiment designed for gas collection, addition of i-$C_3H_7OCONF_2$ (1.32 g, 0.0095 mol) to chilled dibenzylamine (20 mL, 0.01 mol) produced 197 mL (92%) of N_2.

2. Pyrrolidine. With slow stirring, i-$C_3H_7OCONF_2$ (5.13 g, 0.037 mol) was added to chilled pyrrolidine (40 mL, 0.48 mol) during 1 h. After the mixture was warmed to room temperature during another hour, distillation through a short-path column gave i-$C_3H_7OCONC_4H_8$, 4.31 g (74%), bp 124 °C (40 mm), and 2,3,4,5-tetrahydropyridazine: 2.3 g (62%); bp 84 °C (50 mm); IR (neat) 3333, 3039, 2967, 2849, 1692, 1634, 1464, 1428, 1335, 1321, 1264, 1218, 1100, and 1026 cm^{-1}; mass spectrum, *m/e* (relative intensity) 84 (100), 83 (34.06), 69 (18.02), 56 (39.70), 55 (41.09), 41 (30.40), 28 (85.15); NMR ($CDCl_3$) δ 2.09 (4, m), 3.08 (2, t), 5.33 (1, s), 6.73 (1, t). Physical and spectral properties were compared with those of an authentic sample,[37] benzoyl derivative, mp 117–120 °C.

Preparation of Authentic Materials. 1. Benzylamine Hydrofluoride. Hydrogen fluoride (48% aqueous, 20% molar excess) was poured into chilled benzylamine (4.9 g, 0.046 mol). The resulting milky white crystals were rinsed with benzene and then filtered. Recrystallization from ethanol afforded 5.2 g (90%) of the hydrofluoride salt: mp 152–153 °C; IR (KBr) 2900, 2600, 2350, 2250, 1650, 1575, 1460, 1390, 1075, 1020, 950, 725, and 690 cm^{-1}; NMR (D_2O) δ 4.22 (2, s), 7.53 (5, s).

Anal. Calcd for $C_7H_{10}NF$: C, 66.14; H, 7.88; N, 11.03. Found: C, 65.91; H, 7.71; N, 10.97.

2. Isopropyl *N*-Alkyl- and *N,N*-Dialkylcarbamates. a. From Benzylamine. To slowly stirred, chilled benzylamine (15 mL, 0.14 mol) was added isopropyl chloroformate (2.4 g, 0.019 mol) during 1 h. The mixture was allowed to come to room temperature during a second hour. A white solid formed as the reaction progressed. After the reaction mixture was washed with 75 mL of 3 N HCl, the solid dissolved and two layers formed. Addition of Skelly B followed by rotary evaporation of the organic layer yielded 1.7 g (41%) of isopropyl *N*-benzylcarbamate: mp 34–35 °C; IR (KBr) 3300, 2950, 1680, 1510, 1450, 1430, 1250, 1180, 1130, 1100, 1040, 950, 920, 780, 745, 695 cm^{-1}; NMR (CCl_4) δ 1.17 (6, d), 4.23 (2, d), 4.83 (1, m), 5.27 (1, br s), 7.20 (5, s); mass spectrum, *m/e* (relative intensity) 193 (31.9), 151 (40.6), 106 (76.8), 105 (23.2), 79 (37.7), 77 (29.0), 65 (24.6), 51 (26.1), 43 (100), 41 (39.1), 28 (85.5).

b. From Dibenzylamine. To slowly stirred, chilled dibenzylamine (50 mL, 0.26 mol) was added isopropyl chloroformate (5.5 g, 0.045 mol) during 1 h. The mixture was allowed to come to room temperature during a second hour. A white solid formed as the reaction progressed. After the reaction mixture was washed with 150 mL of 3 N HCl, the solid was filtered. Extraction of the solid with Skelly B followed by rotary evaporation of the extract gave approximately 5 mL of a yellow liquid which solidified upon cooling. Recrystallization from Skelly B gave 5.9 g (44%) of isopropyl *N,N*-dibenzylcarbamate as white crystalline needles: mp 65 °C; IR (KBr) 3000, 1700, 1500, 1450, 1420, 1350, 1310, 1240, 1110, 1030, 980, 955, 930, 865, 805, 770, 745, 735, 700 cm^{-1}; NMR ($CDCl_3$) δ 1.27 (6, d), 4.42 (4, s), 5.07 (1, m), 7.27 (10, s).

Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.36; H, 7.49; N, 4.84.

c. From Pyrrolidine. To slowly stirred, chilled pyrrolidine (40 mL, 0.48 mol) was added isopropyl chloroformate (4.5 g, 0.037 mol) during 1 h. The solution was allowed to come to room temperature during a second hour. Excess pyrrolidine was removed by atmospheric distillation. The residue was treated with 20 mL of 3 N HCl and then extracted with 10 mL of Skelly B. Rotary evaporation of the extract yielded a light yellow liquid which was vacuum distilled (6 mmHg) through a short-path column to give 1.9 g (33%) of colorless isopropyl pyrrolidinecarbamate: IR (neat) 3600, 2900, 1700, 1410, 1320, 1250, 1220, 1180, 1120, 1020, 965, 915, 858, 820, 770 cm^{-1}; NMR (neat) δ 1.20 (6, d), 1.80 (4, m), 3.25 (4, t), 4.78 (1, m); mass spectrum, *m/e* (relative intensity) 157 (11.8), 115 (25.8), 114 (34.9), 98 (32.3), 70 (41.9), 43 (100), 41 (31.7).

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Registry No. Cyclohexylamine, 108-91-8; octylamine, 111-86-4; benzylamine, 100-46-9; *o*-anisidine, 90-04-0; *o*-toluidine, 95-53-4; aniline, 62-53-3; *o*-chloroaniline, 95-51-2; cyclohexane, 110-82-7; octane, 111-65-9; toluene, 108-88-3; anisole, 100-66-3; benzene, 71-43-2; chlorobenzene, 108-90-7; isopropyl *N*-cyclohexylcarbamate, 3580-74-3; isopropyl *N*-octylcarbamate, 73069-86-0; isopropyl *N*-benzylcarbamate, 5338-49-8; isopropyl *N*-(*o*-methoxyphenyl)carbamate, 67648-18-4; isopropyl *N*-(*o*-tolyl)carbamate, 38365-93-4; isopropyl *N*-phenylcarbamate, 122-42-9; isopropyl *N*-(*o*-chlorophenyl)carbamate, 2150-22-3; N_2, 7727-37-9; cyclohexylamine hydrofluoride salt, 26593-77-1; octylamine hydrofluoride salt, 73069-87-1; benzylamine hydrofluoride salt, 55544-36-0; *o*-toluidine hydrofluoride salt, 73069-88-2; aniline hydrofluoride salt, 542-13-2; isopropyl *N,N*-difluorocarbamate, 24425-18-1; dibenzylamine, 103-49-1; bibenzyl, 103-29-7; isopropyl *N,N*-dibenzylcarbamate, 73069-89-3; pyrrolidine, 123-75-1; isopropyl 1-pyrrolidinecarboxylate, 5327-22-0; 2,3,4,5-tetrahydropyridazine, 694-06-4; isopropyl chloroformate, 108-23-6.

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