was maintained at 60–65 °C for 4 h. Ethanol was removed under reduced pressure to yield an oil blue residue. Ether (200 mL) was added; the mixture was stirred at room temperature for 1 h and filtered. This afforded 2.9 g of a bright blue precipitate that could not be characterized. From the ether filtrate a precipitate formed after 1 h and was filtered. Crystallization from hexanes/ethanol gave the monosubstituted compound as purple fluffy needles: 0.2 g (6%); mp 191–192 °C; IR (KBr) ν_{OH} 3420, ν_{CO} 1615 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.92 (d, 1, $J_{2,4}$ = 2.33 Hz, H_2), 8.43 (d, 1, $J_{4,2}$ = 2.33 Hz, H_4), 7.29 (s, 2, H_6 and H_7), 3.53 (q, 2, J = 6.26 Hz, NCH_2), 2.68 (t, 2, J = 6.26 Hz, CH_2CH_3), 2.56 (s, 3, CH_3), 2.35 [s, 6, $N(CH_3)_2$]; MS (CI), m/z [M + 1] 326 (100). Anal. Calcd for $C_{18}H_{19}N_3O_3$: C, 66.44; H, 5.89; N, 12.92. Found: C, 66.38; H, 5.90; N, 12.90.

Notes

Nonacidic Nitration of Secondary Amines

Jeffrey C. Bottaro,* Robert J. Schmitt, and Clifford D. Bedford*†

Energetic Materials Program, Chemistry Laboratory, Physical Sciences Division, SRI International, Menlo Park, California 94025

Received September 30, 1986

The N-nitration of secondary amines under neutral conditions poses a unique problem of N-nitrosation as a competing side reaction. When nitrogen dioxide,[1] nitryl chloride,[2] nitrogen pentoxide, nitryl fluoride, nitronium fluoroborate,[3] and tetranitromethane[4] are used in the N-nitration of amines, they all result in substantial yields (≥30%) of nitrosamine side products, which are extremely toxic and difficult to separate from the target nitramines. Nitramines are potentially useful as explosives, biocides, and pharmaceuticals, necessitating a high-yielding synthesis devoid of carcinogenic nitrosamine byproducts.

To overcome the problems associated with N-nitrosation, we studied a series of novel covalent nitrating agents and examined the effect of amine blocking groups on the outcome of the nitration reaction. The use of amine protecting groups on the nitro/nitrosamine product distribution proved futile. When the *N*-trimethylsilyl, *N*-trimethoxysilyl, *N*-trichlorosilyl, and *N*-difluoroboryl derivatives of piperidine (our model amine substrate) were treated with the conventional nitrating agents mentioned above, they all produced products contaminated with nitrosamine byproducts. Nitrations with nitryl fluoride were complicated by unavoidable contamination of NO_2F with NO_2, which occurred as a result of contact of NO_2F with glass, air, and organic solvents. This approach was abandoned in favor of developing novel nonacidic nitrating agents.

The production of nitrosamines is a result of the redox reaction between secondary amines and nitrating agent. We sought to attenuate the oxidizing power of the nitrating agent by varying the electronegativity of the leaving group. For example, when nitryl fluoride was reacted with secondary amines, it gave unacceptable yields of nitrosamines (≃50%). In our hands similar results were obtained with tetranitromethane, *N*-nitrocollidinium fluoroborate,[10] and nitryl chloride. In response to this problem, we chose to examine nitrating agents with leaving groups that were less electronegative than fluorine. Since ordinary nitrate esters failed to nitrate secondary amines at all, we concluded that the viable range of electronegativities for the nitro transfer reaction lay somewhere between alkoxide (the leaving group on a nitrate ester) and fluoride (the leaving group on nitryl fluoride). Thus, we examined a series of electron-deficient nitrate esters as our target category of neutral nitrating agents for secondary amines.

Scheme I. Amine-Induced Elimination of Nitrous Acid

$$CX_3CH_2ONO_2 + HNR_2 \rightarrow \begin{cases} CX_3CHO \xrightarrow{R_2NH} CX_3CH(OH)NR_2 \\ + \\ R_2NH_2^+NO_2^- \xrightarrow[\Delta]{} R_2NNO + H_2O \end{cases}$$

This approach was attempted by Emmonds and Freeman,[5] who studied some electron-deficient nitrate esters and found that acetone cyanohydrin nitrate[6,7] does indeed produce the nitration of amines at elevated temperatures. Unfortunately, this reagent releases acetone and hydrogen cyanide, which react with amines to give amino nitriles, rendering this method low yielding with respect to the amine substrate. The use of trichloroethyl nitrate[6] also did not solve this problem; the nitrate ester suffered an elimination of nitrous acid to give a mixture of dialkylammonium nitrite and trichloroacetaldehyde, which itself reacted with 1 equiv of the amine to form the hemiaminal side product (Scheme I).

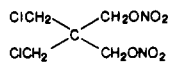
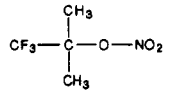
We sought to design nitrating agents that could achieve the desired acyl transfer (here, acyl = nitro) without any undesirable side reactions. Our initial efforts focused on the use of polyfluoroalkyl nitrates. Hexafluoroisopropyl nitrate and trifluoroethyl nitrate were synthesized by direct nitration of the corresponding alcohols in fuming nitric/sulfuric acid. Treating these materials with piperidine, our preliminary test amine, yielded predominantly elimination products as depicted in Scheme I. In the case of trifluoroethyl nitrate, a small amount of nitramine was formed in competition with the elimination products. Only elimination products were detected in the case of hexa-

†Present address: Naval Surface Weapons Center, Code R-11, White Oak Laboratory, Silver Spring, MD 20910.

(1) (a) Challis, B. C.; Kyrtopoulos, S. A. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1296. (b) Williams, D. L. H. *Adv. Phys. Org. Chem.* **1983**, *19*, 381.
(2) Shineman, R. S. Thesis Ohio State University, 1957; University Microfilms, Ann Arbour, MI, Card No. M.C. 58-2104.
(3) Ilyushin, M. A.; Golod, E. L.; Gidaspov, B. V. *Zh. Org. Khim.* **1977**, *13*, 8.
(4) (a) Riordan, J. F.; Vallee, B. L. *Methods Enzymol.* **1972**, 25 (part B), 515. (b) Castonguay, A.; VanVunakis, H. *Toxicol. Lett.* **1979**, *4*, 475. (c) Lagercrantz, C. *Acta, Chem. Scand.* **1964**, *18*, 382. (d) Bruice, T. C.; Gregory, M. J.; Walters, S. L. *J. Am. Chem. Soc.* **1968**, *90*, 1612. (e) Bruice, T. C.; Walters, S. L. *J. Am. Chem. Soc.* **1971**, *93*, 2269.
(5) Emmonds, W. D.; Freeman, J. *J. Am. Chem. Soc.* **1965**, *77*, 4387.
(6) Emmonds, W. D.; McCallum, K. S.; Freeman, J. P. *J. Org. Chem.* **1952**, *19*, 1472.
(7) Freeman, J.; Shepherd, I. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 839.

0022-3263/87/1952-2292$01.50/0

Table I. Candidate Nitrate-Transfer Reagents

compd	structure	yield, %	properties
1		5	mp 62 °C; dec >150 °C
2		60	bp 98 °C; slight dec at bp; stable for weeks at room temp
3		80[a]	mp 93 °C

[a] Reference 9.

Table II. Nitration of Amines with 2-(Trifluoromethyl)-2-propyl Nitrate

amine	yield, % nitramine	nitrosamine
piperidine	75	0[a]
morpholine	72	0
N-benzylmethamine	75	0
pyrrolidine	100	0
diethylamine	58	0

[a] As detected by TLC which is consistently sensitive to ≤1% yields of nitrosamines and/or nitramines.

fluoroisopropyl nitrate. Also detected were small amounts of nitrosation products resulting from the thermal decomposition of the nitrite salts.

The trend established by hexafluoroisopropyl nitrate (no nitration) and trifluoroethyl nitrate (low yield of nitration) prompted us to design alkyl nitrates that were less electron poor and, if possible, endowed with structural attributes that precluded the elimination reaction shown in Scheme I, which ultimately leads to nitrosamines by self-condensation of the resulting nitrite salts.

Candidates for this new generation of nitrate-transfer reagents are shown in Table I. All these structures preclude the elimination side reaction shown in Scheme I. The pentaerythritol dinitrate derivative **1** has a degree of steric hindrance to base attack on the protons α to the nitrate esters, and fluorinated *tert*-butyl nitrate (**2**) is devoid of such protons entirely. *N*-Nitropyrazole (**3**) also enjoys an immunity to elimination reactions.

Compounds **1–3** were synthesized by direct nitration of the corresponding protic compound. Perfluoro-*tert*-butyl nitrate and hexafluoro-*tert*-butyl nitrate could not be prepared and were abandoned as potential targets. Compound **2** [2-(trifluoromethyl)-2-propyl nitrate] was synthesized by nitration of 2-(trifluoromethyl)-2-propanol in nitric acid/trifluoroacetic anhydride. Compound **1** [2,2-bis(chloromethyl)propane-1,3-diol dinitrate][8] was prepared by hydrolysis and nitration of 3,3-bis(chloromethyl)oxetane in nitric acid/oleum.

Both compounds **1** and **2** nitrate secondary amines under mild conditions (room temperature to 55 °C) without nitrosation, except in isolated cases. In general, **2** is a more convenient, cleaner, and efficient nitrating agent, which allows for a facile workup. The results obtained with selected amines for both reagents are shown in Tables II and III. *N*-Nitropyrazole (**3**) failed to transfer its nitro group to diethylamine even when refluxed in a solution with diethylamine as solvent. This compound was abandoned as a nitrating agent.

Table III. Nitration of Amines with 2,2-Bis(chloromethyl)propane-1,3-diol Dinitrate

amine	yields, % nitramine	nitrosamine
piperidine	65	0
morpholine[b]	40	tr
N-benzylmethanamine	42	6
pyrrolidine	86	0
diethylamine[a]	17	4
dimethylamine	55	0

[a] Probable loss in isolation due to high volatility. [b] As detected by TLC.

Attempts to nitrate primary amines and ethylenediamine derivatives met with difficulty. For example, attempted dinitration of piperazine with **2** resulted in a low yield of *N*-nitroso-*N'*-nitropiperazine. The same result was obtained with *N,N'*-dimethylethylenediamine, giving mixed nitro and nitroso compounds in poor yields. Furthermore, the nitration of 3-methyl-3-[(*N*-ethylamino)-methyl]oxetane, a highly hindered amine, gave only a poor yield of nitramine, with no nitrosation. Finally, nitrations of benzylamine and phenethylamine gave low yields of corresponding primary nitramines, which could not be purified to analytical specifications. Evidently, amines of diminished nucleophilicity due to inductive or steric encroachments yield nitrosation products through the slow decomposition of the nitrating agent. The poor performance of compound **2** in N-nitration of primary amines is probably due to decomposition of the product under the prolonged heating necessary to drive the nitro-transfer reaction.

In conclusion, we have developed two effective reagents, 2-(trifluoromethyl)-2-propyl nitrate and 2,2-bis(chloromethyl)propane–1,3-diol dinitrate, for the neutral nitration of secondary amines. These materials have complementary properties, the first being useful for volatile substrates and the second for nonvolatile substrates. The 2-(trifluoromethyl)-2-propyl nitrate will enjoy a broader application in synthesis because it reacts in a cleaner manner and in higher yield than 2,2-bis(chloromethyl)propane–1,3-diol dinitrate for the nonacidic nitration of basic amines.

Experimental Section

General Methods. ^{1}H NMR spectra were determined on a Varian T-60 NMR spectrometer as solutions in $CDCl_3$ or CCl_4. IR spectra were determined on a Perkin-Elmer 1420 IR spectrophotometer.

Synthesis of Hexafluoroisopropyl Nitrate. Oleum (100 g of 30% SO_3) was cooled to 0 °C under argon and treated with 25 mL of 90% nitric acid (*Caution! Exotherm!*) followed by addition of hexafluoroisopropyl alcohol (35 g, 210 mmol). The reaction was stirred under argon for 1 h, warming to room temperature over that time. The crude product was distilled out of the biphasic reaction mixture at ~30 Torr, trapping the product in a dry ice/acetone bath. The crude product was stirred over 4 g of Na_2CO_3, treated with 2 mL of H_2O, and decanted. It contained some free alcohol and was stored at 0 °C. Even at 0 °C, it slowly decomposed, giving off NO_2 gas: ^{1}H NMR (CCl_4) δ 5.8 (septet, J = 6 Hz).

Synthesis of Trifluoroethyl Nitrate. Oleum (360 g of 30% SO_3) was cooled to 0 °C under argon and was carefully treated with 80 mL of 90% nitric acid. After this mixture had cooled, trifluoroethanol (77 g, 0.77 mol) (Aldrich) was added, and the reaction mixture was allowed to warm to room temperature over 1 h. The resulting biphasic reaction mixture was then distilled, under an aspirator vacuum, into a dry ice cooled receiver, neutralized by stirring over 2 g of Na_2CO_3/4 mL of H_2O, followed

(8) German Patents 638432 and 638433, Westfälisch-Anhaltische Sprengstoff A.G. Nov 14, 1936 (Cl.78c.18).
(9) Huttel, R.; Büchele, F. *Chem. Ber.* **1955**, *88*, 1586.
(10) Ho, T.-L.; Olah, G. A. *J. Org. Chem.* **1977**, *42*, 3097.

by addition of 5 g of Na_2CO_3 to remove H_2O. The supernatant liquid was decanted and found to be sufficiently pure for synthesis. The yield of clear colorless liquid was 101 g (85%): ^1H NMR (CCl_4) δ 4.9 (quart., J = 8 Hz); IR (neat) 1400, 1430, 1680 cm^{-1}.

Synthesis of 2-(Trifluoromethyl)-2-propyl Nitrate. Trifluoroacetic anhydride (16 g, 75 mmol) was cooled to 0 °C with stirring under argon, in a 50-mL round-bottomed flask. Nitric acid (4.5 g, 75 mmol) was carefully added over 5 min to avoid excessive heating. After the addition was complete, the mixture was stirred for 20 min at 0 °C, 2-(trifluoromethyl)-2-propanol (6.5 g, 50 mmol) was added, and the reaction mixture was stirred for an additional 30 min. The reaction mixture was diluted with 25 mL of dichloromethane, extracted with 100 mL of ice–water, dried over Na_2CO_3, and distilled at ~400 Torr. The yield of clear, colorless liquid was 5.3 g (62%): bp 60 °C (400 torr); ^1H NMR (CCl_4, 60 MH_z) δ 1.7 (s); IR (neat) 1660 cm^{-1}. The neat compound gave off traces of NO_2 gas after 1 month of storage at room temperature, but its NMR spectrum was unchanged. At low temperatures (0 °C) no decomposition has been observed, even after 1 year.

Reaction of 1,1,1-Trifluoroethyl Nitrate with Piperidine. Piperidine (4.3 g, 50 mmol) was dissolved in 50 mL of diethyl ether and the resultant mixture treated with trifluoroethyl nitrate (9 g, 60 mmol). An exotherm ensued, causing the solvent to reflux. After 1 h, the exotherm had subsided, and a solid had precipitated from the reaction mixture. The solid was isolated by filtration, and the filtrate was freed of acidic and basic compounds by extraction with aqueous base and acid, respectively. The ether layer was found to contain approximately 600 mg (~10% yield) of *N*-nitropiperidine, as determined by IR, NMR, and TLC in comparison with those of an authentic sample. The solid (2.3 g) was unstable, degrading to *N*-nitrosopiperidine on standing. The solid had an NMR spectum identical with that of piperidine·HNO_3, but its IR spectrum was different from that of an authentic sample. On this basis, and due to its tendency to degrade to *N*-nitrosopiperidine, the solid was assumed to be piperidine·HNO_2.

Reaction of 2-(Trifluoroethyl)-2-propyl Nitrate with Secondary Amines. The secondary amine (1 mmol) was mixed neat with 2-(trifluoromethyl)-2-propyl nitrate (250 mg, 1.5 mmol) and kept at 50 °C for 7 days. Volatiles including 2-(trifluoromethyl)-2-propanol were evaporated in vacuo, and the crude product was filtered through a short plug of silica gel to give pure *N*-nitramines. The products were identical with known materials in their spectroscopic and physical properties. The yields were not further optimized (see Table II).

Synthesis of 2,2-Bis(chloromethyl)propane-1,3-diol Dinitrate. Fuming nitric acid (90%) (100 mL) was saturated with $NaNO_3$ at room temperature. Next, 3,3-bis(chloromethyl)oxetane (20 g, 130 mmol) was added. A mild exotherm was observed, and ice cooling was applied. The mixture was stirred at 0–15 °C for 5 h, with gradual warming from 0 to 15 °C over that interval. The reaction mixture was cooled to 0 °C and was carefully treated with 40 mL of 30% fuming H_2SO_4, stirring and adding the acid in 2-mL aliquots. The resulting mixture was warmed to room temperature over 15 min and poured over ice, giving a white solid. The solid was collected by filtration, dissolved in 150 mL of warm carbon tetrachloride, and crystallized to give 25 g (73%) of large, colorless prisms: mp 63 °C; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.7 (s), 4.6 (s); IR (CCl_4 smear) V_{max} 1670, 1300 cm^{-1}. Anal. Calcd for $C_5H_8Cl_2N_2O_6$: C, 22.83; H, 3.07; N, 10.65; Cl, 26.95. Found: C, 22.90; H, 2.98; N, 10.60; Cl, 26.78.

Reaction of 2,2-Bis(chloromethyl)propane-1,3-diol Dinitrate with Secondary Amines. The amine (10 mmol) was mixed with 2,2-bis(chloromethyl)propane-1,3-diol dinitrate (1.3 g, 5 mmol) and the resultant mixture heated in a sealed vial at 55 °C for 3 days. Unreacted nitrate ester was destroyed by adding 5 mL of ethyl alcohol and 2 mL of hydrazine and heating at 80 °C for 1 h. The reaction mixture was partitioned between 100 mL of ether and 100 mL of water. The ether layer was concentrated and chromatographed, eluting chloroform over silica gel, yielding the pure nitramines, which were visualized by UV. The products were chromatographically and spectroscopically identical with known samples of the target compounds (see Table III).

Acknowledgment. We thank Dr. Anthony Matuszko of the Air Force Office of Scientific Research (Contract No. F49620-83-K-0023) for his encouragement and support of this work.

Registry No. $(F_3C)_2CHOH$, 920-66-1; $(F_3C)_2CHONO_2$, 107149-24-6; F_3CCH_2OH, 75-89-8; $F_3CCH_2ONO_2$, 461-38-1; $F_3CC(CH_3)_2OH$, 507-52-8; $F_3CC(CH_3)_2ONO_2$, 107149-25-7; $C_6H_5CH_2NHCH_3$, 103-67-3; $NH(CH_3)_2$, 124-40-3; $H_3CN(NO_2)CH_2C_6H_5$, 36239-05-1; $O_2NN(CH_2CH_3)_2$, 7119-92-8; $O_2NN(CH_3)_2$, 4164-28-7; $C_6H_5CH_2N(NO)CH_3$, 937-40-6; $O_2NOCH_2C(CH_2Cl)_2CH_2ONO_2$, 107149-26-8; piperidine, 110-89-4; morpholine, 110-91-8; pyrrolidine, 123-75-1; *N*-nitropiperidine, 7119-94-0; *N*-nitromorpholine, 4164-32-3; *N*-nitropyrrolidine, 3760-55-2; 3,3-bis(chloromethyl)oxetane, 78-71-7.

Nitroacetylenes: Synthesis of 1-Nitro-2-(trialkylsilyl)acetylenes via Nitrodesilylation of Bis(trialkylsilyl)acetylenes

Robert J. Schmitt,* Jeffery C. Bottaro, Ripudaman Malhotra, and Clifford D. Bedford*†

Energetic Materials Program, Chemistry Laboratory, SRI International, Menlo Park, California 94025

Received September 30, 1986

As part of a study to develop a new synthetic route to nitroacetylenes, this report describes a general synthesis of 1-nitro-2-(trialkylsilyl)acetylenes 1. The method in-

$$R_3SiC{\equiv}CNO_2$$
1

volves direct reaction between a nitronium ion source [i.e., nitronium tetrafluoroborate (NTFB), nitronium hexafluorophosphate (NHFP), or nitryl fluoride], bis(trialkylsilyl)acetylene, and a fluoride ion source. Only five nitroacetylenes have been reported previously,[1-6] and all are reported to be thermally unstable. The synthesis routes to known nitroacetylenes are shown in eq 1 and 2.

$$RC{\equiv}CSnMe_3 + N_2O_5 \xrightarrow{\text{inert solvent}} RC{\equiv}CNO_2 \quad (1)$$

R = Ph, Me_3Si, *n*-Pr, *i*-Pr

$$RC{\equiv}CH + NO_2I \rightarrow R(I)C{=}C(H)NO_2 \xrightarrow{\text{base/heat}} RC{\equiv}CNO_2 \quad (2)$$

R = *t*-Bu

We report here a general synthesis method for preparing 1-nitro-2-(trialkylsilyl)acetylenes. This unique one-step procedure allows for the preparation of numerous nitroacetylenes not accessible through the known synthesis methods.

Recently, we reported[7] an improved, one-step synthesis of 1-nitro-2-(trimethylsilyl)acetylene by treating bis(trimethylsilyl)acetylene with NTFB in methylene chloride (eq 3). When freshly triturated NTFB is used, a 70%

$$Me_3SiC{\equiv}CSiMe_3 + NO_2BF_4 \xrightarrow{CH_2Cl_2} Me_3SiC{\equiv}CNO_2 \quad (3)$$

yield of the nitroacetylene is obtained. The effects of alkyl substituents on both the acetylene and silyl substrate, the nitronium ion source, and reaction solvents have been studied. A special feature of this one-step nitrodesilylation reaction is the regioselectivity observed with bis(trialkylsilyl)acetylene substrates, allowing for the preparation of numerous 1-nitro-2-(trialkylsilyl)acetylenes, not easily

† Present address: Naval Surface Weapons Center, Code R-11, White Oak Laboratory, Silver Spring, MD 20910.

0022-3263/87/1952-2294$01.50/0