corresponding to **3** in 80% yield: mp 43–44 °C; NMR δ 0.85 (t, 3 H), 1.2–1.9 (m, 12 H), 3.42 (t, J = 6 Hz, 2 H), 7.73 (d, J = 2.7 Hz, 1 H), 8.06 (d, J = 2.7 Hz, 1 H); high-resolution MS calcd for $C_{14}H_{19}Cl_3O_2S$, 356.0171; found, 356.0179. Anal. Calcd for $C_{14}H_{19}Cl_3O_2S$: C, 47.01; H, 5.35; Cl, 29.73; S, 8.96. Found: C, 46.77; H, 5.36; Cl, 30.13; S, 9.39. Nine percent of a product, tentatively identified as octyl 2,4,6-trichlorophenyl sulfone by NMR, was also isolated.

Octyl 2-chlorophenyl sulfide: product was an oil; NMR δ 0.85 (t, 3 H), 1.2–1.9 (m, 12 H), 2.85 (t, J = 7.5 Hz, 2 H), 7.0–7.5 (m, 4 H). The product was oxidized to the sulfone (25% peracetic/acetic acid in CH_2Cl_2; 95% yield). Recrystallization from hexane gave mp 31–32 °C; NMR δ 0.92 (t, 3 H), 1.2–1.9 (m, 12 H), 3.13 (t, J = 8 Hz, 2 H), 7.45–8.0 (m, 4 H); high-resolution MS calcd for $C_{14}H_{21}ClO_2S$, 288.0951; found, 288.0963.

Octyl 3-chlorophenyl sulfide: product was an oil; NMR δ 0.9 (t, 3 H), 1.2–1.9 (m, 12 H), 2.91 (t, J = 7 Hz, 2 H), 7.1–7.35 (m, 4 H). Oxidation to the sulfone with peracetic acid afforded the sulfone in 87% yield: NMR δ 0.89 (t, 3 H), 1.2–1.9 (m, 12 H), 3.43 (t, J = 8 Hz, 2 H), 7.3–7.55 (m, 3 H), 8.1–8.25 (m, 1 H); high-resolution MS calcd for $C_{14}H_{21}ClO_2S$, 288.0951; found, 288.0972.

Acknowledgment. I thank Steven B. Dorn for providing high-resolution mass spectral data.

Registry No. **1a**, 89165-35-5; **1b**, 89165-36-6; **2**, 89165-37-7; **3**, 89165-38-8; **4**, 17733-23-2; **5**, 65662-89-7; **6**, 89165-39-9; **7**, 89165-40-2; 18-crown-6, 17455-13-9; PEG 300, 25322-68-3; Cy_3PC_{12}, 57441-08-4; 1,2,4,5-Cl_4Ph, 95-94-3; 1,2,4-Cl_3Ph, 120-82-1; 1,3,5-Cl_3Ph, 108-70-3; 1,2,3,5-Cl_4Ph, 634-90-2; m-Cl_2Ph, 541-73-1; n-$C_{12}H_{25}SH$, 112-55-0; n-$C_7H_{15}SH$, 1639-09-4; n-$C_8H_{17}SH$, 111-88-6; Bu_4PBr, 3115-68-2; m-bromophenyl octyl sulfide, 89165-41-3; 1,2,3-trichlorobenzene, 87-61-6; 2,4,5-trichlorobiphenyl, 15862-07-4; 2,3,4,5,6-pentachlorobiphenyl, 18259-05-7; m-dibromobenzene, 108-36-1; m-bromochlorobenzene, 108-37-2; heptyl 2,4,5-trichlorophenyl sulfide, 89165-42-4; octyl 2-chlorophenyl sulfide, 89165-43-5; octyl 3-chlorophenyl sulfide, 89165-44-6.

A Mild and Convenient Procedure for the N-Formylation of Secondary Amines Using Organosilicon Chemistry

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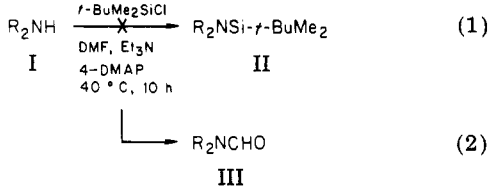
Received July 21, 1983

At the onset of our program to explore the utility of aminosilanes[1] as reactive aminating agents in heterocyclic synthesis, we attempted to prepare the requisite aminosilanes as shown in eq 1.[2]

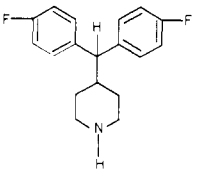
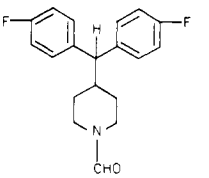
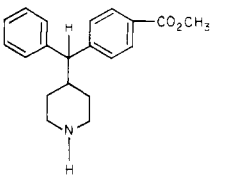
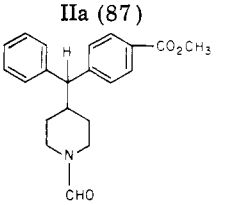
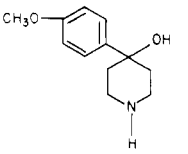
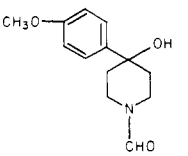
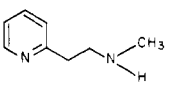
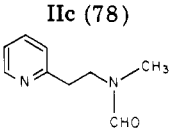
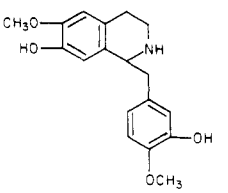
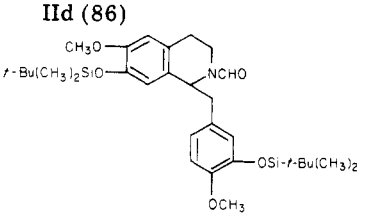
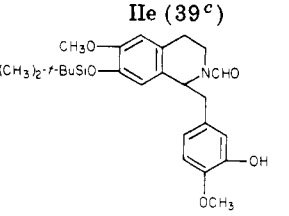
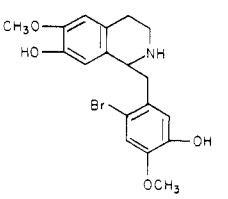
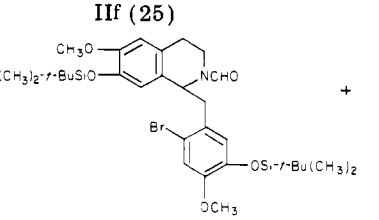
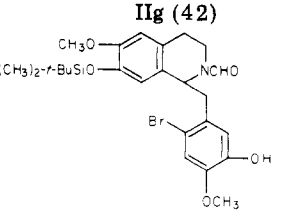


(1)

(2)

We were surprised to find that no aminosilane (II) could be isolated from the reaction mixture. However, the N-formyl derivative III could be isolated in good yield. This reaction proved to be general for a variety of secondary amines (Table I).

Table I

amine	temp, °C	product[b] (yield,[a] %)
 Ia	40	 IIa (87)
 Ib	45	 IIb (80)
 Ic	45	 IIc (78)
 Id	40	 IId (86)
 Ie	60	 IIe (39[c])
		 IIf (25)
 Ig	60	 IIg (42)
		 IIh (25)

[a] Yields are based on recovered starting material where appropriate. [b] All N-formyl derivatives gave satisfactory spectral data and, where possible, elemental analysis. [c] The N-formyl derivatives exist as discrete rotamers, as seen by ^{1}H NMR spectroscopy.[3]

(1) For a recent synthetic application of aminosilanes, see: Ando, W.; Tsumaki, H. *Chem. Lett.* **1981**, 693.

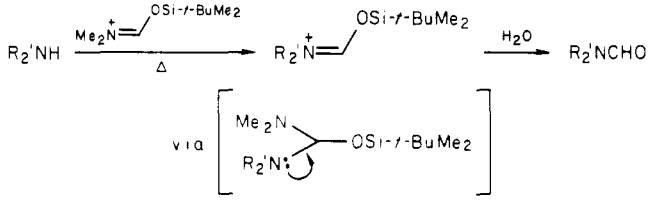
(2) Aminosilanes can be prepared by several procedures. See: Magnus, P. D.; Sarkar, T.; Djurić, S. "Comprehensive Organic Chemistry"; Pergamon Press: 1982; Chapter 48, p 586. See also: Mawhinney, T. P.; Madson, M. A. *J. Org. Chem.* **1982**, *44*, 3336.

0022-3263/84/1949-1311$01.50/0

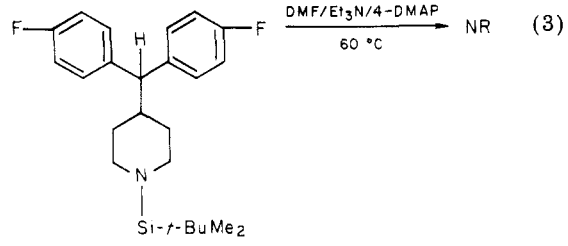
The formylation reaction could be considered to proceed through one of two mechanisms: (a) via a silylamine

$$R'_2NH \longrightarrow R_2NSi\text{-}t\text{-}BuMe_2 \xrightarrow{DMF} R_2NCHO$$

or (b) via a "Vilsmeier" type intermediate



In order to ascertain whether mechanism a was the operative one, 4, the requisite intermediate, was treated with an excess of DMF/Et_3N/4-DMAP at 65 °C for 10 h (eq 3).[4] No *N*-formyl derivative could be detected, however.



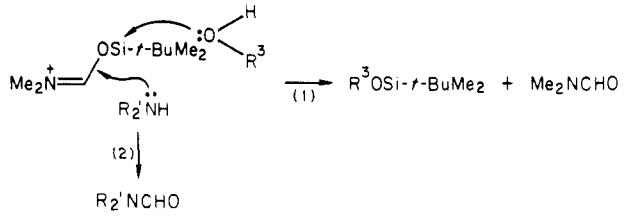
(3)

4

It would appear, therefore, that the formylation reaction proceeds through a "Vilsmeier" type intermediate. This assertion is supported by the subsequent observation that treatment of DMF with *tert*-butyldimethylsilyl triflate (1:1) at 45 °C, produced a colorless crystalline complex, which efficiently formylated any of the previously cited compounds. These results and their interpretation are in agreement with the literature report that DMF acetals can act as effective reagents for amine N-formylation.[5]

It is interesting to speculate as to whether, in certain cases, this complex represents a true reactive intermediate in silylation reactions run in DMF.[6]

This would give rise to the following rationale for silylation reactions:



In both cases, path 1 and 2 represent the thermodynamically favored processes.

Summarily, although several other procedures are available for the N-formylation of secondary amines,[7] the method presented herein is expected to find utility in organic synthesis due to its mildness and compatibility with a variety of molecular functionality.

We are currently investigating the synthetic application of this methodology and, in particular, the utility of the DMF/*t*-$BuMe_2Si$ triflate complex—an apparently unique reagent, whose reactivity is functional group dependent, i.e., it has the potential to act as a formylating reagent and/or a silylating reagent under a given set of conditions.

Experimental Section

Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian FT80 or XL100 spectrometer with chemical shifts reported in parts per million (δ) downfield from tetramethylsilane as an internal standard. Elemental analyses were performed by the microanalytical department at G. D. Searle & Co.

Typical Experimental Procedure: 4-[Bis(4-fluorophenyl)methyl]-1-piperidinecarboxaldehyde. Compound Ia (1.0 g, 3.5 mMol) was dissolved in dimethylformamide (3 mL) containing *tert*-butyldimethylsilyl chloride (0.58 g, 1.1 equiv), triethylamine (0.59 mL), and 4-(dimethylamino)pyridine (0.017 g, 0.04 equiv), and the mixture stirred at 35–40 °C, for 25 h under nitrogen. The mixture was then partitioned between ether and water, and the organic layer was separated, washed with brine, and dried (Na_2SO_4). Evaporation of the volatiles in vacuo afforded the *N*-formylpiperidine IIa as a colorless syrup (87%). The material could be crystallized from ether/hexane: mp 129–131 °C; ^1H NMR (80 MHz, δ, $CDCl_3$) 1.1–4.6 (10 H, m, piperidyl Hs and benzylic CH), 6.8–7.3 (8 H, m, Ar Hs) 7.9 (1 H, s, CHO); IR ($CHCl_3$) 1670, 1610, 1510, 850 cm^{-1}.

$C_{19}H_{19}NOF_2$ requires C, 72.4; H, 6.1; N, 4.5; F, 12.05. Found: C, 72.6; H, 6.1; N, 4.4; F, 11.54.

***N*-Methyl-*N*-[2-(2-pyridinyl)ethyl]formamide.** *tert*-Butyldimethylsilyl triflate (2.6 mL, 9 mMol) was added via a dry syringe to dimethyl formamide (0.7 mL, 9 mMol), and the mixture was warmed to 45 °C. At this point, the mixture became solid, and 2-(β-(methylamino)-ethyl)pyridine (10 g, 7 mMol) was added via syringe as a solution in dimethylformamide (2 mL). Triethylamine (2 equiv) was added and the mixture stirred for 1 h. The reaction mixture was poured into a 2 N sodium bicarbonate and extracted with methylene chloride. The organic layer was washed sequentially with water and brine and then dried (Na_2SO_4). Evaporation of the volatiles in vacuo afforded 1.5 of a yellow-brown oil, which was purified by flash chromatography (Merck 60, CH_2Cl_2/7% CH_3OH). Thus obtained was 0.9 g of *N*-formyl derivative: ^1H NMR (80 MHz, δ, $CDCl_3$) 2.75–3.1 (2 H, M, CH_2-py), 2.8 (3 H, s, N-CH_3), 3.7 (2 H, m, CH_2NCHO), 7.0–7.75 (3 H, m, py Hs), 7.8 (1 H, d, CHO), 8.5 (1 H, d, py 5 H); IR ($CHCl_3$) 1670 cm^{-1}; MS, *m/e* 164, 135, 106, 93, 44.

$C_9H_{12}N_2O$ requires C, 65.8; H, 7.4; N, 17.1. Found: C, 65.5; H, 7.4; N, 16.9.

Acknowledgment. I thank Dr. Kenner Rice for authentic samples of tetrahydroisoquinolines Ie and Ig and their corresponding *N*-formyl derivatives and his interest in the project. I also thank Drs. Chinn, Hansen (Searle), and Magnus (Bloomington, IN) for helpful comments.

Registry No. 4, 88780-66-9; Ia, 60285-00-9; Ib, 88780-57-8; Ic, 50329-87-8; Id, 5638-76-6; Ie, 13168-56-4; Ig, 14400-85-2; IIa, 88780-58-9; IIb, 88780-59-0; IIc, 88780-60-3; IId, 88780-61-4; IIe, 88780-62-5; IIf, 88780-63-6; IIg, 88780-64-7; IIh, 88780-65-8; dimethylformamide, 68-12-2; *tert*-butyldimethylsilyl chloride, 18162-48-6; 4-(dimethylamino)pyridine, 1122-58-3; *tert*-butyldimethylsilyl triflate, 69739-34-0; [[(*tert*-butyldimethylsilyl)oxy]-methylene]dimethylammonium triflate, 88780-68-1.

(3) Rice, K. C.; Brossi, A *J. Org. Chem.* **1980**, *45*, 592.
(4) Compound 4 was prepared by the reaction of the amine Ia with *t*-$BuMe_2SiCl$ in CH_2Cl_2/Et_3N.
(5) Abdulla, R. F.; Brinkmeyer, R. S. *Tetrahedron* **1979**, *35*, 1675.
(6) Corey, E. J.; Venkataswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(7) Blicke, E. G. F. F.; Lu, C.-J. *J. Am. Chem. Soc.* **1952**, *74*, 3933. Staab, H. A.; Polenski, B. *Liebigs Ann. Chem.* **1962**, *655*, 95. Sheehan, J. C.; Yang, D.-D. H. *J. Am. Chem. Soc.* **1958**, *80*, 1154.