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PRELIMINARY NOTE

Synthesis of N-Trifluoromethyl-N-nitrosamine Derivatives

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SUMMARY

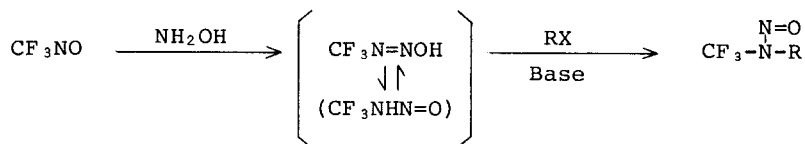
N-Trifluoromethyl-N-nitroso-sulfonamide, -amide, -carbamate, and -urea derivatives were synthesized by the reaction of trifluoronitrosomethane with hydroxylamine at low temperature, followed by treatment with a base in the presence of arene- or alkane-sulfonyl halides, acid halides, acid anhydrides, haloformates, or carbamoyl halides.

INTRODUCTION

Since the displacement of hydrogen atoms with fluorine atoms in compounds brings about remarkable changes in chemical and physical properties, much attention is being devoted to fluorinated compounds [1]. It is of interest to synthesize fluorine-analogues of alkylnitrosamines which are important compounds in nitrogen chemistry [2]. We now wish to report the synthesis and characterization of N-trifluoromethyl-N-nitrosamine derivatives starting from trifluoronitrosomethane [3].

The synthetic methods for the alkylnitrosamines are not applicable to the fluorinated compounds because of the special properties [4]. Makarov et al. reported that trifluoronitrosomethane reacted with hydroxylamine in methanol at -75°C and, when warmed to -55°C, nitrogen and trifluoromethyl methyl ether were evolved [5]. They suggested the formation of trifluoromethyldiazohydroxide as a thermally labile intermediate. We

succeeded in isolating N-trifluoromethyl-N-nitrosoarenesulfonamides by the treatment of the solution, prepared from trifluoronitrosomethane and hydroxylamine in DMF/THF/ether (9/10/1), with arenesulfonyl halides and potassium t-butoxide at  $-78^{\circ}\text{C}$ .










When the halides were added to the solution after the addition of the base, the sulfonamides were not obtained, indicating that the intermediate, trifluoromethyldiazoxyhydroxide or trifluoromethylnitrosamine, is also labile to bases. Accordingly it is necessary to treat the intermediate with the base in the presence of the sulfonyl halides. The method could be applied to the synthesis of several kinds of N-trifluoromethyl-N-nitrosamine derivatives by using acid halides, acid anhydrides, haloformates, and carbamoyl halides. Table 1 summarizes the results and physical properties of the nitrosamines.

#### EXPERIMENTAL

A typical experimental procedure is as follows; At  $-78^{\circ}\text{C}$ , trifluoronitrosomethane (blue gas, bp  $-84^{\circ}\text{C}$ ) was blown into a solution of hydroxylamine which was prepared by the treatment of hydroxylamine hydrochloride (0.48 g, 6.9 mmol) with potassium t-butoxide (0.77 g, 6.9 mmol) in 7.7 ml of DMF/THF/ether (9/10/1). The introduction of the nitrosomethane was stopped when the reaction mixture remained blue. An excess of the nitrosomethane was removed by flowing argon. After the addition of a solution of *o*-nitrobenzenesulfonyl chloride (1.53 g, 6.9 mmol) in 9 ml of THF/ether (1/2), potassium t-butoxide (0.82 g, 7.3 mmol) was added in several portions. The reaction mixture was warmed to  $-50^{\circ}\text{C}$  for 2 h. The usual post-treatment gave N-trifluoromethyl-N-nitroso-*o*-nitrobenzenesulfonamide as a crystalline solid in a 58% yield.

TABLE 1

## Synthesis of N-trifluoromethyl-N-nitrosamine compounds

Run	CF <sub>3</sub> N(NO)R	RX	Yield <sup>a)</sup> (%)	Mp (°C)	<sup>19</sup> F-NMR <sup>b)</sup> (ppm)	IR <sup>c)</sup> (cm <sup>-1</sup> )
1	R=SO <sub>2</sub> Ph	X=Cl	56	57-8	70.5 (bs)	1360 (SO <sub>2</sub> ) 1510 (NO)
2	SO <sub>2</sub> -  -CH <sub>3</sub>	Cl	35	48-9	70.7 (bs)	1375 (SO <sub>2</sub> ) 1510 (NO)
3	SO <sub>2</sub> -  -OCH <sub>3</sub>	Cl	59	46-7	70.7 (bs)	1373 (SO <sub>2</sub> ) 1520 (NO)
4	SO <sub>2</sub> -  -F	Cl	51	61-61.5	70.3 (bs)	1380 (SO <sub>2</sub> ) 1530 (NO)
5	SO <sub>2</sub> -  -Cl	Cl	44	52.5-53	70.4 (bs)	1370 (SO <sub>2</sub> ) 1520 (NO)
6	SO <sub>2</sub> -  -NO <sub>2</sub>	Cl	41	91-2	70.2 (bs)	1380 (SO <sub>2</sub> ) 1520 (NO)
7	SO <sub>2</sub> -  -NO <sub>2</sub>	Cl	58	52-3	70.3 (bs)	1375 (SO <sub>2</sub> ) 1520 (NO)
8 <sup>d)</sup>	SO <sub>2</sub> CH <sub>3</sub>	Cl	21	oil	70.6 (bs)	1360 (SO <sub>2</sub> ) 1520 (NO)
9	COPh	Cl	39	85/14 <sup>e)</sup>	70.7 (bs)	1520 (NO) 1730 (CO)
10	"	OCOPh	29	"	" (")	" "
11	COOPh	Cl	33	78-9/16 <sup>e)</sup>	70.5 (bs)	1535 (NO) 1790 (CO)
12	CONPh <sub>2</sub>	Cl	18	44-5	71.8 (bs)	1535 (NO) 1725 (CO)
13	CO-  -Ph	Cl	19	36-7	71.5 (bs)	1510 (NO) 1710 (CO)

a) Isolated yields.

b) Upfield from internal CCl<sub>3</sub>F in CDCl<sub>3</sub>.

c) Method; Nujol (Run 1, 2, 4, 5, 6, 7, and 13), Neat (Run 3, 8, 9, 11, and 12).

d) Sodium hydride (50% in oil) was used as a base.

e) Boiling points (°C/mmHg).

## RESULTS AND DISCUSSION

The structures of the products were determined by the analysis of the spectral data. The  $^{19}\text{F}$ -NMR spectra show only the signals of trifluoromethyl groups. In the IR spectra, strong absorption bands appear at about  $1520\text{ cm}^{-1}$ , which are characteristic of nitroso functional groups. The data of the elementary analyses are in good agreement with the calculated ones. In the mass spectra of the sulfonamides, the peaks (m/e) of the molecular ions were not observed except for the products of Runs 3 and 4. The molecular weight measurement (Found 262) of the product of Run 1 is inconsistent with the calculated one (254).

The N-trifluoromethyl-N-nitrosamine compounds prepared above have distinct properties compared with the corresponding N-methyl analogues. The trifluoromethyl compounds are much more stable than the methyl compounds. Whereas the methyl compounds are useful sources for diazomethane, the trifluoromethyl-nitrosoarenesulfonamides have been found to be good trifluoromethylating agents photochemically. We will report on the trifluoromethylation elsewhere.

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