Reaction of Trifluoronitrosomethane with Arenesulfonohydrazides. Synthesis of *N*-Trifluoromethyl-*N*-hydroxyarenesulfonamides

Akira SEKIYA and Teruo UMEMOTO*

Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229

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The reaction of trifluoronitrosomethane **1** with arenesulfonohydrazides resulted in the formation of *N*-trifluoromethyl-*N*-hydroxyarenesulfonamides **3** which were characterized by spectral and elemental analyses. It showed a sharp contrast to the reaction of **1** with acyl- or carbamoylhydrazines, which afforded the corresponding trifluoromethylazo compounds. As an alternative route, **3** could be synthesized by the reaction of **1** with arenesulfinic acids or their salts. The sulfonamides **3** were converted to the corresponding methyl ethers or tosylates.

Trifluoronitrosomethane[1] **1** is an interesting blue gas, which is expected to have high reactivity because of a combination of a reactive nitroso group and a highly electronegative trifluoromethyl group. It has been known that **1** condensed with amino compounds such as aromatic amines,[2] alkylamines,[3] amino acids,[4] and other amines[5] to give the corresponding trifluoromethylazo compounds. Recently, we reported that electron-deficient amino compounds, arenesulfonamides, condensed with **1** only in the presence of a base to give trifluoromethylazosulfonylarenes in high yields.[6] This paper described that the reaction of arenesulfonohydrazides **2** with **1** led to unexpected compounds, *N*-trifluoromethyl-*N*-hydroxyarenesulfonamides **3**.

Results and Discussion

Benzenesulfonohydrazide **2a** in *N*,*N*-dimethylformamide (DMF) reacted with two molar equivalent amount of **1** at room temperature. After the solvent was removed under vacuum, the residue was column-chromatographed on silica gel using ether as an eluent to give a stable colorless compound. The ^{19}F NMR spectrum showed a singlet at 65.00 ppm which could be assigned to trifluoromethyl group bonding to a nitrogen atom. The ^{1}H NMR showed a AB_2X_2 pattern in the region of aromatic protons, characteristic of benzenesulfonyl group, and a broad peak at 7.88 ppm which was assigned to a hydroxyl group by deuterium oxide exchange experiment. The infrared spectrum showed strong absorption bands at 3410 and 1370 cm^{-1} due to OH and SO_2 stretching vibration, respectively. It was found that the compound contains a nitrogen atom in the molecule from the elemental analysis. From the above results, the structure of the product was assigned to be entirely unexpected *N*-trifluoromethyl-*N*-hydroxybenzenesulfonamide **3a**.

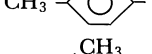
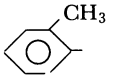
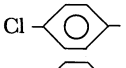
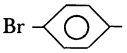
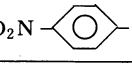
$$2\,CF_3NO + ArSO_2NHNH_2 \longrightarrow CF_3-\overset{OH}{\overset{|}{N}}-SO_2Ar$$
1 **2a—f** **3a—f**

The reaction proceeded smoothly in several kinds of solvents (Table 1). As a result, methanol was the best solvent because of its low boiling point and shorter reaction time. Several *N*-trifluoromethyl-*N*-hydroxyarenesulfonamides **3a—f** were synthesized under the conditions in high yields (Table 1).

p-Toluenesulfonohydrazide **2b** was allowed to react with **1** in DMF, and the same post-treatment gave 61% yield of **3b** and 28% yield of a 2:1 complex of **3b** with DMF. The complex was characterized by IR, NMR, and elemental analyses.

From the fact that two molar equivalent amount of **1**

TABLE 1. SYNTHESIS OF **3a—f** FROM **1** AND **2a—f**

Run	Ar		Solv.	Time / min	Yield of **3a—f**[a]/%
1	Ph-	**3a**	DMF	50	96
2	Ph-	**3a**	CH_3CN	540	92
3	Ph-	**3a**	THF	90	99
4	Ph-	**3a**	CH_3COOH	90	94
5	Ph-	**3a**	CH_3OH	15	96
6		**3b**	CH_3OH	40	97
7		**3c**	CH_3OH	35	88
8		**3d**	CH_3OH	35	87
9		**3e**	CH_3OH	35	74
10		**3f**	CH_3OH	35	91

a) Based on the amount of **2a—f**.

to **2** was consumed in the reaction, it is clear that the reaction consists of at least two steps. In order to isolate the intermediate, the reaction of **1** with an equimolar amount of **2** was carried out. The reaction solution contained no intermediate but a 1:1 mixture of **3** and **2**, which indicated that the second reaction with **1** should be faster than the first one.

Interestingly, these results showed a sharp contrast to the reaction of **1** with acyl- or carbamoylhydrazines.

$$\underset{\mathbf{4}}{PhCONHNH_2} \xrightarrow{1} \underset{\mathbf{5}}{CF_3N{=}NNHCOPh} \quad 97\%$$

$$\underset{\mathbf{6}}{CH_3CONHNH_2} \xrightarrow{1} \underset{\mathbf{7}}{CF_3N{=}NNHCOCH_3}{}^{5a)} \quad 50\%$$

$$\underset{\mathbf{8}}{PhNHCONHNH_2} \xrightarrow{1} \underset{\mathbf{9}}{CF_3N{=}NNHCONHPh} \quad 98\%$$

Hydrazines **4**, **6**, and **8** were treated with two molar equivalent of **1** in methanol at room temperature for 3 d to produce normal condensation products **5**, **7**, and **9** with recovery of one molar equivalent of **1**.

From a different point of view, **3** can be regarded as the combination of **1** and arenesulfinic acid. As an alternative route, we tried the reaction of **1** with arenesulfinic acid. Benzene- and toluenesulfinic acids

$$\mathbf{1} + ArSO_2H \longrightarrow \underset{\mathbf{3a}\ (95\%)\\ \mathbf{3b}\ (91\%)}{CF_3\text{-}\overset{\overset{OH}{|}}{N}\text{-}SO_2Ar}$$

absorbed smoothly an equivalent amount of **1** at room temperature to produce **3a** and **3b** in high yields. This experimental result afforded another proof of the structural assignment of **3** and suggested the following reaction mechanism for the formation of **3** in the reaction of **1** with hydrazides **2**. Probably, the intermediate resulting from the first step decomposes so as to produce arenesulfinic acid, which reacts with **1** to afford **3**. Unfortunately, an attempt to isolate the other part of decomposition products from the intermediate was failed. This result demonstrates the quite difference in the reactions between **2** and other hydrazines **4**, **6**, and **8**. This may be because acyl or carbamoyl groups cannot act as leaving groups, while arenesulfonyl groups are relatively strong leaving groups.[7]

On the other hand, sodium benzenesulfinate gave **3a** in a low yield in its reaction with **1** in methanol. The salt absorbed **1** very smoothly, but several undetermined by-products were produced in addition to **3a**. It indicates that high nucleophilicity of the salt compared to the sulfinic acid causes side reactions.

$$\mathbf{1} + PhSO_2Na \longrightarrow \mathbf{3a} \quad 40\%$$

Since **3** have free hydroxyl groups, it is possible to derive some ethers or esters as follows. Treatment of **3** with methyl iodide afforded the methyl ethers **10a—c** in 33—85% yields. Tosyl chloride gave the esters **11a** and **11b** in 20 and 55% yields, respectively.

$$\mathbf{3} \xrightarrow{CH_3I} \underset{33\text{—}85\%}{CF_3\text{-}\overset{\overset{OCH_3}{|}}{N}\text{-}SO_2Ar} \quad \begin{matrix}\mathbf{10a}\ (Ar{=}Ph)\\ \mathbf{10b}\ (Ar{=}p\text{-Tolyl})\\ \mathbf{10c}\ (Ar{=}o\text{-Tolyl})\end{matrix}$$

$$\mathbf{3} \xrightarrow{TsCl} \underset{20\text{—}55\%}{CF_3\text{-}\overset{\overset{OTs}{|}}{N}\text{-}SO_2Ar} \quad \begin{matrix}\mathbf{11a}\ (Ar{=}Ph)\\ \mathbf{11b}\ (Ar{=}p\text{-Tolyl})\end{matrix}$$

Experimental

General. Melting and boiling points were uncorrected. ^1H NMR spectra were determined with a Varian HA-100 NMR spectrometer or a Varian EM 390 NMR spectrometer. ^{19}F NMR spectra were determined with a Varian XL-100A NMR spectrometer or a Hitachi R-20B NMR spectrometer. ^{19}F chemical shifts are given in ppm upfield from trichlorofluoromethane as an internal standard. IR spectra were measured on a Jasco A-202 diffraction grating infrared spectrophotometer.

Materials. Trifluoronitrosomethane **1** was prepared as previously.[8] Arenesulfonohydrazides, *p*-toluenesulfinic acid, and sodium benzenesulfinate used were commercial products and used without further purification.

N-Trifluoromethyl-N-hydroxyarenesulfonamides 3a—f. The reactions were carried out in 200 ml glass vessels fitted with valves. Arenesulfonohydrazide **2** (5.5 mmol) was dissolved in a solvent (10 ml) in the reactor and the vessel was cooled to −196 °C and then evacuated. The amount of **1** (11.1 mmol) was determined by PVT measurements assuming ideal gas behavior and it was condensed into the reactor. The vessel was warmed to room temperature with a water bath and the solution was stirred by magnetic stirrer. After the blue color of **1** disappeared, the solvent was removed under vacuum. The residue was column-chromatographed on silica gel eluted with ether to give **3**. The results are summarized in Table 1.

3a: Bp 146—148 °C/800 Pa, mp 42—43 °C; IR (KBr, cm^{-1}) 3410 (OH), 1370 (SO_2); ^{19}F NMR ($CDCl_3$) 65.00 (s); ^1H NMR ($CDCl_2$); δ=7.4—7.8 (3H, m, ArH), 7.88 (1H, bs, OH), 7.98 (2H, m, ArH). Found: C, 34.78; H, 2.46; N, 5.83%. Calcd for $C_7H_6F_3NO_3S$: C, 34.86; H, 2.51; N, 5.81%.

3b: Mp 65—71 °C; IR (KBr, cm^{-1}) 3370 (OH), 1370 (SO_2); ^{19}F NMR ($CDCl_3$) 65.74 (s); ^1H NMR ($CDCl_3$); δ=2.44 (3H, s, CH_3), 7.35 (2H, d, J=8.0 Hz, ArH), 7.68 (1H, bs, OH), 7.86 (2H, d, J=8.0 Hz, ArH). Found: C, 37.71; H, 3.18; N, 5.48%. Calcd for $C_8H_8F_3NO_3S$: C, 37.65; H, 3.17; N, 5.49%.

3c: Mp 79.5—80 °C; IR (KBr, cm^{-1}) 3320 (OH), 1355 (SO_2); ^{19}F NMR (CD_3CN) 63.25 (s); ^1H NMR (CD_3CN); δ=2.70 (3H, s, CH_3), 7.2—8.1 (4H, m, ArH), 8.56 (1H, s, OH). Found: C, 37.48; H, 3.21; N, 5.46%. Calcd for $C_8H_8F_3NO_3S$: C, 37.65; H, 3.16; N, 5.49%.

3d: Mp 114—114.5 °C; IR (KBr, cm^{-1}) 3320 (OH), 1375 (SO_2); ^{19}F NMR (CD_3CN) 64.33 (s); ^1H NMR (CD_3CN); δ=7.68 (2H, d, J=9.0 Hz, ArH), 7.95 (2H, d, J=9.0 Hz, ArH), 9.27 (1H, bs, OH). Found: C, 30.56; H, 1.95; N, 5.11%. Calcd for $C_7H_5ClF_3NO_3S$: C, 30.50; H, 1.83; N, 5.08%.

3e: Mp 134—134.5 °C; IR (KBr, cm^{-1}) 3360 (OH), 1370 (SO_2); ^{19}F NMR (CD_3CN) 64.15 (s); ^1H NMR (CD_3CN); δ=7.85 (4H, s, ArH), 9.26 (1H, bs, OH). Found: C, 26.40; H, 1.69; N, 4.34%. Calcd for $C_7H_5BrF_3NO_3S$: C, 26.27; H, 1.57; N, 4.38%.

3f: Mp 116—116.5 °C; IR (KBr, cm^{-1}) 3370 (OH), 1530 (NO_2), 1385 (SO_2), 1345 (NO_2); ^{19}F NMR (CD_3CN) 66.33 (s); ^1H NMR (CD_3CN); δ=8.38 (4H, m, ArH), 9.48 (1H, bs, OH). Found: C, 29.45; H, 1.81; N, 9.50%. Calcd for $C_7H_5F_3N_2O_5S$: C, 29.38; H, 1.76; N, 9.79%.

DMF Complex of 3b. *p*-Toluenesulfonohydrazide **2b**

in DMF was treated with **1** in a similar manner as described above. After removing the solvent under vacuum, the residue was washed with water, extracted with benzene, and the benzene solution was dried with magnesium sulfate. The compound **3b** and the complex **3b**·1/2DMF were isolated by column chromatography on silica gel eluted with benzene in 61 and 28% yields, respectively. **3b**·1/2DMF: Mp 55—56 °C (hexane); IR (KBr, cm^{-1}) 3390 (OH, sh), 3160 (OH), 2890 (CH), 1645 (C=O), 1380 (SO_2); ^{19}F NMR ($CDCl_3$) 64.75 (s); ^1H NMR ($CDCl_3$); δ=2.45 (3H, s, CH_3), 2.90 (1.5H, s, 1/2CH_3), 3.00 (1.5H, s, 1/2CH_3), 7.35 (2H, d, J=9.0 Hz, ArH), 7.85 (2H, d, J=9.0 Hz, ArH), 8.02 (0.5H, s, 1/2CHO), 9.65 (1H, bs, OH). Found: C, 39.01; H, 3.87; N, 7.23%. Calcd for $C_{9.5}H_{11.5}F_3N_{1.5}O_{3.5}S$: C, 39.11; H, 3.97; N, 7.20%.

Trifluoromethylazo Compounds **5**, **7**, *and* **9**. The reaction between 5.5 mmol of hydrazides **4**, **6**, or **8** and 11.1 mmol of **1** in 11 ml of methanol was carried out in a similar way as described above. The blue color of **1** didn't disappear even after stirring for 3 days at room temperature and 4 mmol of **1** was recovered by trap to trap separation. After removing methanol under vacuum, the residue was column-chromatographed on silica gel eluted with ether to give the normal condensation products **5**, **7**, and **9** in the yields of 97, 50, and 98%, respectively.

5: Mp 110—111 °C; IR (KBr cm^{-1}) 3150 (NH), 1680 (C=O); ^{19}F NMR (CCl_4) 67.5 (s); ^1H NMR (CCl_4); δ=7.4—8.1 (5H, m, ArH), 11.1 (1H, bs, NH). Found: C, 44.18; H, 2.83; N, 19.60%. Calcd for $C_8H_6F_3N_3O$: C, 44.25; H, 2.79; N, 19.35%

7: Mp 42—43 °C (lit,[5a] 51 °C); IR (KBr, cm^{-1}) 3110 (NH), 1715 (C=O); ^{19}F NMR (CCl_4) 67.5 (s); ^1H NMR (CCl_4) δ=2.40 (3H, s, CH_3), 11.30 (1H, bs, NH). Found: C, 23.48; H, 2.73; N, 26.80%. Calcd for $C_3H_4F_3N_3O$: C, 23.24; H, 2.60; N, 27.10%.

9: Mp 136—136.5 °C; IR (KBr, cm^{-1}) 3310 (NH), 3165 (NH), 1680 (C=O); ^{19}F NMR (CCl_4) 67.5 (s); ^1H NMR (CCl_4) δ=7.1—7.6 (5H, m, ArH), 7.8 (1H, bs, NH), 11.5 (1H, bs, NH). Found: C, 41.68; H, 3.13; N, 24.43%. Calcd for $C_8H_7F_3N_4O$: C, 41.39; H, 3.04; N, 24.13%.

The Reaction of **1** *with* p-*Toluenesulfinic Acid.* Into a flask containing a solution of 0.50 g (3.2 mmol) of *p*-toluenesulfinic acid in 6 ml of methanol, **1** was gradually introduced at room temperature till the absorption of **1** stopped. The methane **1** (0.3 g, 3 mmol) was absorbed and 20 min was needed as the reaction time. After evaporation of the solvent, the residue was column-chromatographed on silica gel using a mixture of ethyl acetate and pentane (15:85) as an eluent, giving 0.74 g (91%) of **3b**.

The Reaction of **1** *with Benzenesulfinic Acid.* Benzenesulfinic acid derived from sodium benzenesulfinate (2 hydrates) by treatment with hydrochloric acid was treated with **1** in a similar manner as described above, except that THF was used as a solvent instead of methanol. The yield of **3a** was 95%.

The Reaction of **1** *with Sodium Benzenesulfinate.* Sodium benzenesulfinate (2 hydrates) (11.1 mmol) in 10 ml of methanol was treated with **1** (11.1 mmol) in a similar manner as the case of the reaction of **1** with arenesulfonohydrazides **2**. After 3 min at room temperature, the absorption of **1** was completed. The solvent was then evaporated under vacuum. The residue was extracted with ether, washed with water, and dried with magnesium sulfate. Evaporation of ether gave an oily product, of which TLC analysis indicated that it contained at least six components. Distillation gave 1.07 g (40%) of pure **3a**. Bp 141—142 °C/1600 Pa.

N-*Trifluoromethyl*-N-*methoxyarenesulfonamides* ***10a—c.*** Into a solution of **3** (4 mmol) in methyl iodide (1 ml) and DMF (7 ml), sodium carbonate (10 mmol) was added, and the mixture was stirred for 5 days at room temperature. The reaction mixture was poured into water and extracted with ether. The ether layer was dried over magnesium sulfate. Methyl ethers **10** were obtained by column chromatography on silica gel eluted with benzene. **10a**: Ar=phenyl 52%; **10c**: Ar=*o*-tolyl 33%; **10b**: Ar=*p*-tolyl 85% yield (in this case, 4.5 mmol of calcium oxide was employed instead of sodium carbonate).

10a: Liquid; IR (neat, cm^{-1}) 1392 (SO_2); ^{19}F NMR (CCl_4) 65.00 (s); ^1H NMR (CCl_4); δ=3.98 (3H, s, CH_3), 7.60 (3H, m, ArH), 7.93 (2H, d, J=8.0 Hz, ArH). Found: C, 37.62; H, 3.04; N, 5.41%. Calcd for $C_8H_8F_3NO_3S$: C, 37.65; H, 3.16; N, 5.49%.

10b: Mp 30—30.5 °C; IR (KBr, cm^{-1}) 1392 (SO_2); ^{19}F NMR (CCl_4) 65.25 (s); ^1H NMR (CCl_4); δ=2.45 (3H, s, CH_3), 3.98 (3H, s, OCH_3), 7.27 (2H, d, J=9.0 Hz, ArH), 7.75 (2H, d, J=9.0 Hz, ArH). Found: C, 39.90; H, 3.62; N, 5.12%. Calcd for $C_9H_{10}F_3NO_3S$: C, 40.15; H, 3.74; N, 5.20%.

10c: Liquid; IR (neat, cm^{-1}) 1380 (SO_2); ^{19}F NMR (CCl_4) 64.88 (s); ^1H NMR (CCl_4); δ=2.69 (3H, s, CH_3), 3.87 (3H, s, OCH_3), 7.2—7.65 (3H, m, ArH), 8.0 (1H, m, ArH). Found: C, 40.00; H, 3.61; N, 5.01%. Calcd for $C_9H_{10}F_3NO_3S$: C, 40.15; H, 3.74; N, 5.20%.

N-*Trifluoromethyl*-N-*(p-tolylsulfonyloxy)arenesulfonamides* ***11a—b.*** The reaction of **3** (5 mmol) with *p*-toluenesulfonyl chloride (5 mmol) in pyridine (15 ml) were carried out for 23 h at 5 °C. The reaction mixture was treated in a similar manner as described in the preparation of **10**. Tosylates **11a** and **11b** were obtained from **3a** and **3b** in 20 and 55% yields, respectively.

11a: Mp 60—62 °C; IR (KBr, cm^{-1}) 1400 (SO_2); ^{19}F NMR ($CDCl_3$) 62.63 (s); ^1H NMR ($CDCl_3$); δ=2.47 (3H, s, CH_3), 7.3—8.0 (9H, m, ArH). Found: C, 42.14; H, 3.06; N, 3.41%. Calcd for $C_{14}H_{12}F_3NO_5S_2$: C, 42.53; H, 3.06; N, 3.54%.

11b: Mp 110—111 °C; IR (KBr, cm^{-1}) 1400 (SO_2); ^{19}F NMR ($CDCl_3$) 62.50 (s); ^1H NMR ($CDCl_3$); δ=2.45 (6H, s, 2×CH_3), 7.2—8.0 (8H, m, ArH). Found: C, 44.16; H, 3.54, N, 3.42%. Calcd for $C_{15}H_{14}F_3NO_5S_2$: C, 44.01; H, 3.45; N, 3.42%.

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