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Fluoride-assisted trifluoromethylation of aromatic thiones with (trifluoromethyl)trimethylsilane

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Abstract

In the presence of a stoichiometric amount of $Bu_4NF\cdot 3H_2O$, (trifluoromethyl)trimethylsilane reacts with aromatic thiones in both thiophilic and carbophilic ways to deliver, in medium yield, a mixture of (trifluoromethylthio)diarylmethane and 1,1-diaryl-2,2,2-trifluoroethanethiol, the former product being the major one.

Keywords: Trifluoromethylation; (Trifluoromethyl)trimethylsilane; Trifluoromethyl sulfides; α-(Trifluoromethyl)thiols

1. Introduction

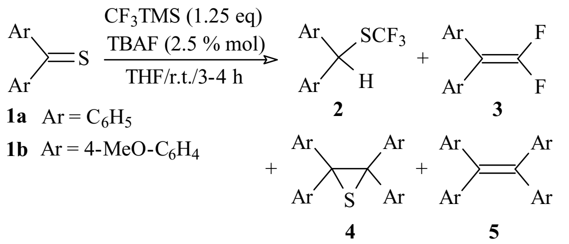
(Trifluoromethyl)trimethylsilane constitutes an ubiquitous and powerful tool for the introduction of a trifluoromethyl moiety on organic substrates [1]. Nevertheless, though this reagent has been extensively added to carbonyl functions, little work has been focused on its reaction with sulfur-containing compounds, despite the economic interest of trifluoromethyl sulfides, especially in the agrochemical field [2]. From the few papers that exist, it appears that, under fluoride catalysis, the Ruppert–Prakash reagent allows the preparation of trifluoromethyl sulfides from disulfides [3] or thiocyanates [4]. Recently, Mloston et al. [5] described the reaction, under moisture free conditions, of (trifluoromethyl)trimethylsilane with thiones, especially diaryl thiones, in the presence of a catalytic amount of thoroughly dried tetrabutylammonium fluoride (TBAF) (Scheme 1).

As proposed by the authors, product **2** arose from a thiophilic attack of a formal trifluoromethyl anion upon the thione but, surprisingly, the α-(trifluoromethyl)thiol resulting from a carbophilic attack was not observed, since it was probably consumed to deliver product **3**. As far as products **4** and **5** were concerned, they were proposed to issue from reactions consecutive to the thiophilic process.

These interesting results, which were previously presented in a symposium in 1998 [6], prompt us to report briefly on similar work we simultaneously and independently carried out and that we mentioned in a poster session during the same meeting.

2. Results and discussion

For our part, we also trifluoromethylated thiones **1a** and **1b** with CF_3TMS but under different conditions than



	2 a)	**3** a)	**4** a)	**5** a)
from **1a**	30 % (22 %)	8 % (6 %)	(45 %)	(3 %)
from **1b**	29 % (21 %)	7 % (5 %)	b)	b)

a) Crude yield. In parentheses : isolated yield.
b) Not determined

Scheme 1. Fluoride-catalyzed reaction of CF_3SiMe_3 on aromatic thiones.

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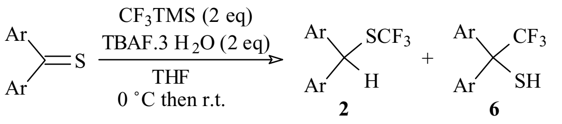


1a	Ar = C_6H_5	37 % (30 %) a)	14 % (10 %) a)
1b	Ar = 4-MeO-C_6H_4	35 % (35 %) a)	13 % a)

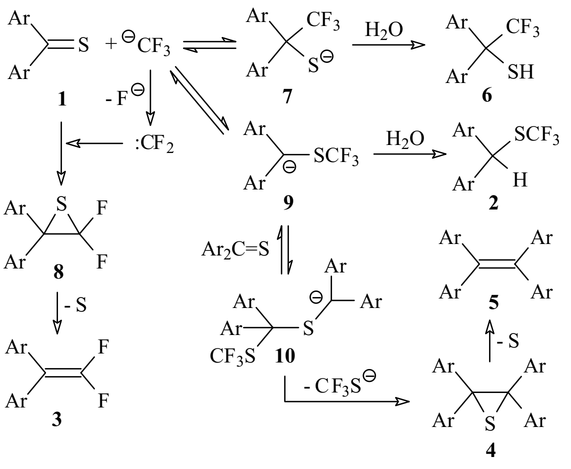
a) Crude yield. In parentheses : isolated yield.

Scheme 2. Reaction of CF_3TMS upon thiones with stoichiometric TBAF·3 H_2O.

Mloston et al., since we applied the conditions we used for the trifluoromethylation of disulfides [3b], that is, 1 eq. of thione, 2 eq. of CF_3TMS and 2 eq. of $Bu_4NF{\cdot}3H_2O$ (1 M in THF), introduced at 0 °C by means of a syringe-pump, before warming up to room temperature. Consequently, our results were different from those of Mloston, since, along with the major trifluoromethyl sulfide **2**, the trifluoromethylated thiol **6** was formed and isolated (Scheme 2). Product **3**, also claimed to result from a carbophilic attack, was not detected by ^{19}F NMR. Moreover, the reaction was faster and the global yield of fluorinated species was higher than under Mloston's conditions. By-products such as **4** and **5** may have been formed but we did not succeed in isolating them after chromatography.

Such a difference in the results can be easily rationalized from the reaction mechanisms proposed by Mloston et al. (Scheme 3) and was due mainly to the fact that we used commercial TBAF·$3H_2O$ in excess; that means that an abundant source of protons was present to quench rapidly the intermediate anions **7** and **9** before they reversibly collapse (for **7**) or enter further reactions (for **9**).

Moreover, Mloston et al. demonstrated in the same paper that fluoride anions, thoroughly dried over molecular sieves, are able to catalyze the transformation of diphenylthione into benzhydryl disulfide. If such a reaction might occur in our experiments, the disulfide formed should be readily transformed into the trifluoromethyl sulfide **2**, since the conditions we used are those we reported to be efficient for the trifluoromethylation of disulfides [3b].



Scheme 3. Reaction mechanisms (according to [5]).

3. Conclusion

In conclusion, our work complements that of Mloston et al. These two studies demonstrate that tetrabutylammonium fluorotrimethyl(trifluoromethyl)silicate, which is probably the real trifluoromethylating agent generated from CF_3TMS, is a nucleophile which stands at the border between soft and hard. However, since thiophilic attack of thiones was more important than carbophilic, its soft character predominates.

4. Experimental

Prior to use, THF was distilled over sodium-benzophenone then stored over 3 Å molecular sieves under N_2. Diphenylthione **1a** was prepared according to [7]. bis-(4-Methoxyphenyl)thione was obtained from Prof. Alois Fürstner. Other reagents were used as received. TLC analyses were carried out on silica gel (Kieselgel 60F 254) deposited on aluminum plates, detection being by UV (254 nm). Flash-chromatographies were performed on silica gel Geduran SI 60. Unless stated otherwise, NMR spectra were recorded in $CDCl_3$. ^1H NMR were recorded at 200 MHz or 300 MHz and ^{13}C NMR spectra at 50 MHz or 75 MHz. The substitution pattern of the different carbons were determined by a "DEPT 135" sequence. ^{19}F NMR spectra were recorded at 188 MHz. Chemical shifts (δ) are given in ppm versus TMS (^1H, ^{13}C) or $CFCl_3$ (^{19}F) used as internal references. Coupling constants are given in hertz. Crude yields were determined by ^{19}F NMR versus $PhOCF_3$ ($\delta_F = -58.3$ ppm) used as standard. GC was carried out on an apparatus fitted with a semi-capillary column (length: 15 m, diameter: 0.53 mm, film thickness (DB1): 1 μm) and a catharometric detector. Mass spectrometry, coupled with gas chromatography, was carried out under electron impact at 70 eV.

4.1. Trifluoromethylation of thiones with (trifluoromethyl)trimethylsilane

4.1.1. General procedure

(Trifluoromethyl)trimethylsilane (300 μl, 2 mmol) was added at 0 °C, under nitrogen, to a solution of thione (1 mmol) in THF (1 ml). At the same temperature, $Bu_4NF{\cdot}3H_2O$ (2 ml of a 1 M solution in THF, 2 mmol) was slowly dropped with a syringe pump (1 ml min^{-1}). Then the reaction mixture was warmed up to room temperature and stirred for 2 h. After evaporation of the solvent, the crude residue was deposited at the top of a chromatographic column and eluted.

4.1.1.1. (Trifluoromethylthio)diphenylmethane ***2a***. Elution with pure petroleum ether (PE): 77 mg (30%) of a colorless oil. ^{1}H, ^{13}C and ^{19}F NMR spectra, as well as mass spectrum, are in accordance with the literature [5].

4.1.1.2. 1,1-Diphenyl-2,2,2-trifluoroethanethiol ***6a***. Elution with pure petroleum ether: 27 mg (10%) of a colorless oil. ^{1}H NMR and IR spectra were in accordance with [8], in which **6a** was prepared through an independent way from 1,1-diphenyl-2,2,2-trifluoroethanol. ^{19}F NMR (188 MHz): δ −73.92 (s).

4.1.1.3. (Trifluoromethylthio)-bis-(4-methoxyphenyl)-methane ***2b***. Elution with petroleum ether/acetone (7:1): 77 mg (30%) of a colorless oil (according to [5], **2b** is a low-melting solid mp = 36−38 °C). ^{13}C NMR spectrum is in accordance with the literature [5]. ^{1}H NMR (300 MHz): δ 3.78 (s, 6H), 5.65 (s, 1H), 6.86 (d, $J = 8.0$, 4H), 7.31 (d, $J = 8.0$, 4H). ^{13}C NMR (75 MHz): δ 52.60 (q, $J = 1.9$), 55.26, 114.09, 129.33, 130.03 (q, $J = 308$), 131.47, 159.17. ^{19}F NMR (188 MHz): δ −41.34 (s). MS: *m/z* 227 (100, $M^{\bullet +}$–SCF_3), 212, 196, 113.

4.1.1.4. 1,1-bis-(4-Methoxyphenyl)-2,2,2-trifluoroethanethiol ***6b***. ^{1}H NMR (200 MHz): δ 2.95 (broad s, 1H), 3.72 (s, 6H), 7.00–7.80 (M, 10H). ^{19}F NMR (188 MHz): δ −73.90 (s).

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