

Synthesis, structure and reactivity of a trifluoromethyl sulfide anionic salt stabilized with tetrakis(dimethylamino)ethylene dication (TDAE²⁺)

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A synthesis of the stable ionic trifluoromethanethiolate salts, TDAE²⁺2SCF₃⁻ (**1**) and TDAE²⁺SCF₃⁻Cl⁻ (**2**) was accomplished in quantitative yields via reduction of bis(trifluoromethyl) disulfide and trifluoromethanesulfenyl chloride using tetrakis(dimethylamino) ethylene (TDAE). The salts were found to be stable up to their melting points. The trifluoromethanethiolate salt [TDAE²⁺2SCF₃⁻ (**1**)] was for the first time characterized by X-ray structural analysis (orthorhombic, *Pbca*, *a* = 1434.0(1), *b* = 1178.1(1), *c* = 2203.2(1) pm) and cyclic voltammetry. Several reactions show the synthetic utility of this new reagent.

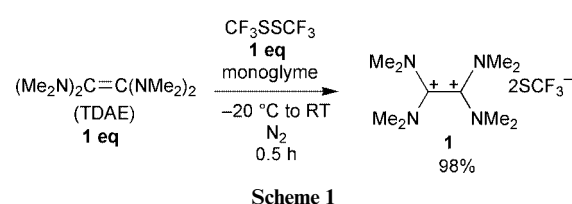
Introduction

Tetrakis(dimethylamino)ethylene (TDAE) has an ionization potential of 6.13 eV and a reducing power comparable to that of zinc.¹ There are a limited number of reports on the use of TDAE in organofluorine synthesis.² Médebielle *et al.*^{2,3} have recently found that TDAE is an effective reductant of bromodifluoromethylated heterocycles and chlorodifluoromethylated ketones; in such a way difluoromethyl heterocyclic and α,α -difluoroacetyl anions were generated and trapped *in situ* with several aldehydes and ketones. This methodology is useful for obtaining heterocyclic difluoromethylated alcohols as well as 2,2-difluoro-3-hydroxy ketone derivatives in reasonable yields. To the best of our knowledge there are no reports on the application of TDAE to reduction of fluorinated organo-element derivatives. Chambers *et al.* have shown that fluorinated cycloalkenes, such as perfluorobicyclopentylidene and perfluorobicyclobutylidene have low reduction potentials (close to -1.05 V vs. SCE)⁴ and therefore they have been efficiently reduced with TDAE to produce tertiary stable anions⁵ but the isolation and X-ray structure of these anions have not been reported. Similarly the TDAE salt of perfluoro-2-methylpentanoyl anion has been produced *in situ* and its NMR spectrum recorded but it was not isolated.⁶⁻⁸ Herein we report the utility of TDAE for the generation of stable perfluoroalkylated sulfur anions.

Results and discussion

Recently, stable covalent Hg(SCF₃)₂ and CuSCF₃ have been synthesized by reduction of (CF₃S)₂ with Hg(0) or Cu(0) respectively.⁹ The disulfide has been also reduced at low temperature by diamidoalkyl phosphites to form the corresponding alkyl

trifluoromethyl sulfides in high yield.¹⁰ The only example of a stable ionic trifluoromethanethiolate salt is TAS⁺SCF₃⁻, synthesized by Middleton *et al.* from thiocarbonyl fluoride and tris(dimethylamino)sulfonium difluorotrimethylsiliconate (TASF).¹¹ Meanwhile, it has been reported that potassium and tetramethylammonium trifluoromethanethiolates decompose even at 0 °C to form a range of SCF₃ containing by-products.¹² We have found that stable ionic trifluoromethanethiolates are produced in quantitative yield *via* reaction of (CF₃S)₂ or CF₃SCI with TDAE in different organic solvents (*e.g.* diethyl ether, monoglyme, THF, CH₃CN).¹³ In a typical experiment, to a -20 °C solution of one equivalent of (CF₃S)₂ in monoglyme, one equivalent of TDAE was added dropwise under nitrogen; immediately a copious precipitate was formed. After addition of TDAE was complete, the solution was stirred vigorously and warmed up to room temperature over 0.5 hours. The insoluble solid was filtered, washed with diethyl ether and the trifluoromethanethiolate **1** was isolated in high purity (Scheme 1).



Scheme 1

Compound **1** can be stored at ambient temperature under nitrogen without decomposition. It is unstable in both air and moisture. The resonance of the main fluorinated decomposition product (¹⁹F NMR δ -44.4; ¹³C NMR δ 128.9 (¹*J*_{CF} = 315.5 Hz) could be assigned to bis(trifluoromethyl) disulfide.¹⁴

(TDAE)²⁺[SCF₃]₂⁻ **1** and (TDAE)²⁺SCF₃⁻Cl⁻ **2** are thermally stable colorless solids with a considerable ionic character proven by the results of X-ray structural investigation for (TDAE)²⁺[SCF₃]₂⁻ (see Fig. 1). The F₃CS⁻ anion is well separated from the [TDAE]²⁺ cation (distance -CH₃...F₃CS⁻ 234.8 or 255.9 pm). The structural parameters of the dication are similar to those of the cation in the corresponding bromide,¹⁵ chloride¹⁵ or hexafluorophosphate.¹⁶ The trifluoromethylthio group with its not unusual C-S single bond lengths [C(3)-S(1) = 172.0(5) pm and C(4)-S(2) = 169.2(5) pm] is sufficiently chemically stabilized and can impart high lipophilicity and exert a strong electron withdrawing effect as a substituent.

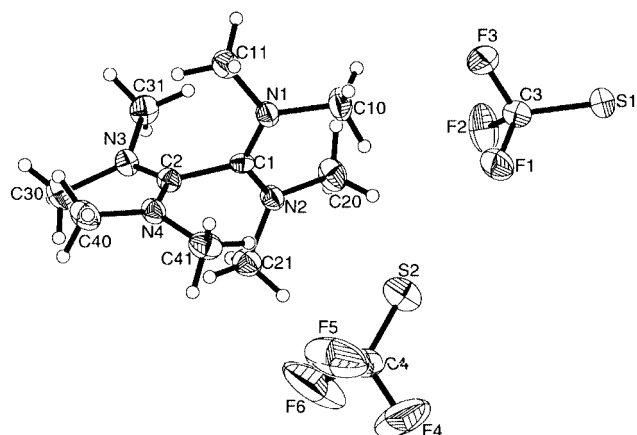
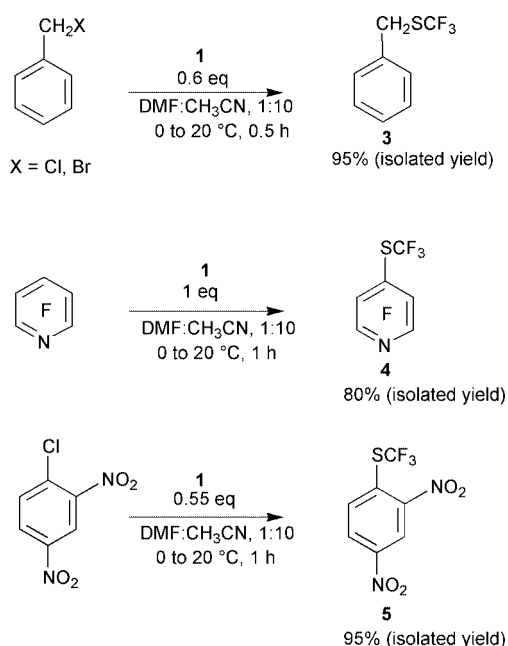


Fig. 1 Molecular structure of $(\text{TDAE})^{2+}[\text{SCF}_3]_2^{-}$ **1** (thermal ellipsoids with 50% probability). Selected bond distances (pm) and angles ($^\circ$) for the anion: S(1)–C(3) 172.0(5), S(1)–C(4) 189.7(3), C(3)–F(3) 135.1(5); F(3)–C(3)–S(1) 115.6(3), F(3)–C(3)–F(1) 102.5(4).

In CH_3CN , electrochemical reduction of $(\text{TDAE})^{2+}[\text{SCF}_3]_2^{-}$ occurs in two reversible one-electron reduction steps, to $(\text{TDAE})^{\cdot+}$ and TDAE at -0.602 V vs. SCE and -0.747 V vs. SCE [standard potential, $E^\circ = (E_{\text{pc}} + E_{\text{pa}})/2$]. In CH_3CN the irreversible oxidation (up to scan rate close to 1000 V s^{-1}) of $(\text{SCF}_3)^-$ occurs at $+0.61$ V vs. SCE (peak potential E_{p} at 0.2 V s^{-1}) leading to the formation of the dimer CF_3SSCF_3 . However, in DMF, a ‘two-electron reduction wave’ is observed at -0.645 V vs. SCE [standard potential, $E^\circ = (E_{\text{pc}} + E_{\text{pa}})/2$]. The superposition of the two one-electron steps points out that considerable conformational changes take place during reduction,² and this effect is enhanced in DMF. Similar observations have been observed for the oxidation of TDAE^{2+} and reduction of $(\text{TDAE})^{2+}\text{Br}_2^-$.

Dmowski and Haas¹⁷ generated trifluoromethanethiolate ion by reversible addition of fluoride ion to thiocarbonyl fluoride or its trimer in aprotic solvents and it may also be generated *in situ* by the reaction of thiophosgene and potassium fluoride in acetonitrile.^{12,18} The ionic character of salt **1** was proven by reactions with activated fluoroaromatics and benzyl halides, which lead to near quantitative formation of the corresponding trifluoromethylthio derivatives (Scheme 2). The main characteristics of **1** (mp 136 – 137 $^\circ\text{C}$) are its thermal stability, high solubility in polar organic solvents and high nucleophilicity, which is illustrated by the conversions in Scheme 2.



Scheme 2

The addition of DMF or *N*-methylpyrrolidine (NMP) as a cosolvent accelerated the nucleophilic substitution reactions. Compound **1** has a comparable reactivity to the only previously known stable anionic trifluoromethanethiolate salt $\text{TAS}^+\text{SCF}_3^-$ prepared from toxic difluorophosgene and expensive TASF .¹¹ Despite the toxicity of CF_3SSCF_3 (or CF_3SCI), our approach has the advantage of using the commercially available and cheap TDAE reagent.

Conclusion

We have demonstrated the utility of TDAE as an efficient reductant for organofluorine compounds; the stable ionic salt $(\text{TDAE})^{2+}[\text{SCF}_3]_2^{-}$ was obtained in nearly quantitative yield *via* reduction of CF_3SSCF_3 by two single-electron transfer steps, and was characterized by X-ray analysis and cyclic voltammetry. It was shown to be a stable and viable source of CF_3S^- for a series of transformations.

Experimental

NMR spectra were obtained on a Bruker AC 80 instrument operating at 75.39 MHz (^{19}F , internal standard CCl_3F) and a Bruker DPX-200 spectrometer operating at 200.13 MHz for ^1H and 188.31 MHz for ^{19}F . GCMS spectra were obtained on a Varian 3700 gas chromatograph connected to a Finnigan MAT 8200 instrument. All reactions and manipulations were conducted under an atmosphere of dry nitrogen. Cyclic voltammetry was performed using a ‘home-made’ potentiostat¹⁹ with a positive feedback ohmic drop compensation and a Tacussel GSTP4 signal generator. The working electrode was a glassy carbon (Tokai Corp.) disc (3 mm diameter) and the reference electrode a saturated calomel electrode (SCE). The supporting electrolyte was tetrabutylammonium hexafluorophosphate (NBu_4PF_6 ; Fluka *puriss.*). Bis(trifluoromethyl) disulfide²⁰ was kindly provided by Professor Alois Haas (Ruhr University, Bochum, Germany). All reactions with air-sensitive compounds were run under nitrogen atmosphere. The X-ray structural study was carried out on a Siemens P4 diffractometer using graphite monochromated $\text{MoK}\alpha$ radiation ($\lambda = 71.073$ pm).²¹

$[(\text{Me}_2\text{N})_2\text{CC}(\text{NMe}_2)]^{2+}[\text{SCF}_3]_2^{-}$ **1**

To a stirred solution of 2.02 g (10 mmol) of bis(trifluoromethyl) disulfide [**CAUTION** ($\text{CF}_3\text{S})_2$ is very toxic! It has to be handled with great care in a well ventilated fumehood!] in monoglyme (15 ml) was added portionwise at -20 $^\circ\text{C}$, under nitrogen, 2.00 g (10 mmol) of tetrakis(dimethylamino)ethylene within 10 min. The immediately formed colorless solid **1** was filtered and washed with 10 ml diethyl ether and dried *in vacuo* at 0.01 mbar. Yield 3.95 g (98.3%), mp 136 – 137 $^\circ\text{C}$ (decomp.); ^{19}F NMR (CD_3CN): $\delta = -7.8$ (s); ^1H NMR (CD_3CN): $\delta = 3.04$ (s), 3.33 (s).

$[(\text{Me}_2\text{N})_2\text{CC}(\text{NMe}_2)]^{2+}[\text{SCF}_3]_2^{-}$ and electrophiles: a typical procedure

To a cooled solution (0 $^\circ\text{C}$) of **1** (4.82 g, 12 mmol) in 15 ml of CH_3CN –DMF (10:1), was added 20 mmol of benzyl chloride (benzyl bromide) in one portion. The resulting stirred solution was left to reach ambient temperature within 0.5 h, hydrolyzed with water and extracted with Et_2O . The organic extracts were dried over MgSO_4 and final purification by distillation under reduced pressure gave pure benzyl trifluoromethyl sulfide **3**. Yield 3.65 g (19 mmol, 95%), bp 65 – 67 $^\circ\text{C}$ (17 mbar); ^1H NMR: $\delta = 4.20$ (2H, CH_2 , s), 7.31–7.62 (5H, H-arom, m); ^{19}F NMR: $\delta = -42.5$ (s).¹¹

The same protocol gave 4-(trifluoromethylthio)tetrafluoropyridine **4** [yield 80% (92% ^{19}F NMR yield), bp 75 – 76 $^\circ\text{C}$ (100 mbar), purity 99.5% (GC-MS, M^+ , 251); ^{19}F NMR: $\delta = -41.5$ (s, SCF_3), -91.7 (2F, m), -135.0 (2F, m)];¹⁷ 2,4-dinitrophenyl trifluoromethyl sulfide **5** [yield 95%, mp 46 – 47 $^\circ\text{C}$; ^1H NMR: $\delta = 9.11$ (1H, d, J 2.4, 3-H), 8.54 (1H, dd, J 2.4 and 8.8, 5-H), 8.04 (1H, d, J 8.8, 6-H)]; ^{19}F NMR: $\delta = -41.7$ (s, SCF_3); ^{13}C

NMR: δ = 121.8, 128.4, 128.7 (q, 3F, CF₃), 131.1, 135.1, 147.1, 147.3 (aromatic C)].^{9,18}

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- 21 Crystal data for **1**, colorless crystals, C₁₂H₂₄F₆N₄S₂, *M* = 402.47, orthorhombic, *Pbca*, *T* = 173(2) K, *a* = 1434.0(1), *b* = 1178.1(1), *c* = 2203.3(2) pm, *V* = 3721.42(2), μ = 0.345 mm⁻¹, $\alpha = \beta = \gamma = 90^\circ$, final *R* values [*I* > 2 σ (*I*)], *R*₁ = 0.0416, *wR*₂ = 0.0854; *R* value (all reflections) *R*₁ = 0.0592, *wR*₂ = 0.0933; 0.40 × 0.30 × 0.30 mm³ with *Z* = 8, reflections measured 12961, unique reflections 1730 (*R*_{int} = 0.0609). CCDC reference number 207/445. See <http://www.rsc.org/suppdata/p1/b0/b002252g/> for crystallographic files in .cif format.