One More Stable Enol: 2,2-Bis[(trifluoromethyl)thio]ethenol. Synthesis and Reactivity[1]

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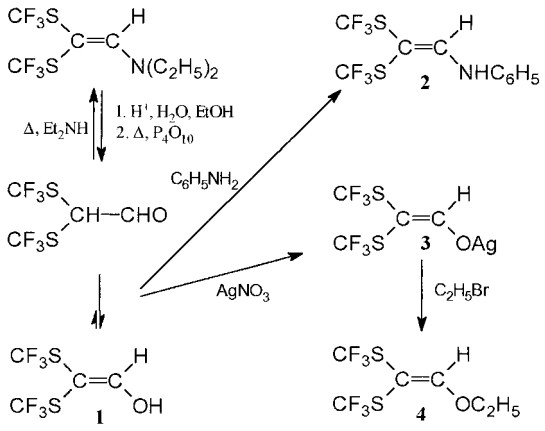
The efficient synthesis of 2,2-bis[(trifluoromethyl)thio]acetaldehyde by acidic hydrolysis of 1-(*N*,*N*-diethylamino)-2,2-bis[(trifluoromethyl)thio]ethene is presented. The tautomeric equilibrium for the compound obtained is strongly shifted to enol form, so with silver nitrate in water solution a corresponding silver salt is formed that reacts with ethyl bromide to ethyl 2,2-[(trifluoromethyl)thio]-vinyl ether. The enol reacts with amines to form respective enamines. IR, MS, ^{1}H, ^{13}C, and ^{19}F NMR data for compounds synthesized are given to support their structure elucidation.

Mono[(trifluoromethyl)thio]-substituted carbonyl compounds bearing this pseudohalogen substituent at the α-carbon are readily obtained from corresponding aldehydes or ketones and trifluoromethylsulfanyl chloride, and they show interesting chemical and biological properties.[2−4] Our attempts, however, to carry out the reaction of CF_3SCl with acetaldehyde under similar or more severe conditions (e.g. either without a catalyst in *n*-pentane or with ethanol as the catalyst, or with pyridine as HCl trapping agent, or in a two-phase system with solid Na_2CO_3 in dichloromethane) were unsuccessful. In contrast to well-known bis- and tris[(trifluoromethyl)thio] derivatives of acetic acid,[5−8] very little is known about bis(CF_3S)-substituted aldehydes or ketones. The only example has been hitherto the synthesis of 1,1-bis[(trifluoromethyl)thio]-2-propanone.[3] The simplest representative of this class of compounds i.e., bis[(trifluoromethyl)thio]acetaldehyde has not been described in the literature yet. The improved synthesis of 1-(*N*,*N*-diethylamino)-2,2-bis[(trifluoromethyl)thio]ethene[9] has now opened the way to this compound. This starting material, however, is unexpectedly unreactive. All our attempts to carry out reactions typical for enamines such as alkylation, oxidation, reduction, addition of CH acids, or trifluoromethylsulfanyl chloride, failed. This enamine is also resistant to strong acids e.g. 20% hydrochloric acid on heating. It is probably due to its strong hydrophobicity. In this paper we present an efficient acidic hydrolysis of 1-(*N*,*N*-diethylamino)-2,2-bis[(trifluoromethyl)thio]ethene.

Results and Discussion

The hydrolysis could be carried out successfully under the condition that an excess of hydrochloric acid in diluted ethanol as a solvent was used, and the crude product was distilled over P_4O_{10}. Such a procedure leads to bis[(trifluoromethyl)thio]acetaldehyde **1** that can be also treated as bis[(trifluoromethyl)thio]acetal of glyoxal. This could be assumed, however, only formally because in contrast to RS groups, the CF_3S substituent is a very poor leaving group.



Compound **1** shows unexpected spectral and chemical properties. According to the ^{1}H and ^{19}F NMR spectra, it shows at equilibrium more than 80% of enol form, which could be also confirmed by its chemical behavior, e.g. when treated with iron trichloride water solution it forms red-brown complexes. With amines, compound **1** gives respective enamines as nucleophilic substitution products. So with diethylamine 1-(*N*,*N*-diethylamino)-2,2-[(trifluoromethyl)thio]ethene was formed, and with aniline, 1-(*N*-phenylamino)-2,2-[(trifluoromethyl)thio]ethene **2** was obtained. Only weak bases such as pentafluoroaniline do not react with compound **1** under similar conditions. The reactions typical for aldehydes, as aldol condensation, dioxolane, or semicarbazone formation, do not occur in this case. With hydrazine derivatives or the $SOCl_2$/

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(2) Bayreuther, H.; Haas, A. *Chem. Ber.* **1973**, *106*, 1418.
(3) Trockmorton, J. R. U.S. Cl 260/593, Apr 25, 1974.
(4) Kolasa, A. *J. Fluorine Chem.* **1987**, *36*, 29.
(5) Mendelson, W. L.; Liu, J.-H.; Killmer, L. B., Jr.; Levinson, S. H. *J. Org. Chem.* **1983**, *48*, 298.
(6) DeMarinis, R. M.; Bryan, W. M. *J. Org. Chem.* **1977**, *42*, 2024.
(7) Umemoto, T.; Miyano, O. *Tetrahedron Lett.* **1982**, *23*, 3929.
(8) Boese, R.; Haas, A.; Lieb, M.; Roeske, U. *Chem. Ber.* **1994**, *127*, 449.
(9) Kolasa, A.; Lieb, M. *J. Fluorine Chem.* **1995**, *70*, 45.

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pyridine system, decomposition of compound **1** takes place. When treated with silver nitrate water solution, **1** gives immediately silver salt **3**. Silver precipitation, typical for aldehydes, occurs at first on heating **3** in an organic solvent. An analogous attempt to prepare the potassium enolate by reacting **1** with potassium carbonate water solution resulted in a complete decomposition of the starting material. Silver enolate **3** was used for the preparation of ethyl 2,2-bis[(trifluoromethyl)thio]-vinyl ether **4**. The latter is easily accessible by the reaction of **3** with ethyl bromide, proceeding smoothly and with a high yield.

The unusual stability of 2,2-bis[(trifluoromethyl)thio]-acetaldehyde enol could be explained by the captodative effect of substituents present in its molecule. The OH group as the electron donor and two CF_3S groups as electron acceptors cause resonance stabilization of this *push*−*pull* olefin, which is confirmed by ^{13}C NMR data. The OH group is at the same time very acidic (determined pK_a value for this enol in acetonitrile equals 2.6 which is comparable, meaning only a crude empirical relation, with the pK_a of phosphoric or fluoroacetic acid in a water solution) but it shows a relatively strong upfield shift of enolic proton in ^1H NMR spectrum (∼7 ppm). This is probably due to the lack of possibility of internal hydrogen bond formation.

The described 2,2-bis[(trifluoromethyl)thio]ethenol, as a surprisingly stable enol, could not be formally put on the list of simple enols,[10−13] because of pseudohalogen[14] substituents. The recognition of its properties, however, can contribute to the general knowledge of this widely discussed class of compounds.

Experimental Section

General. Melting and boiling points are uncorrected. For ^{19}F NMR spectra negative values are given in ppms upfield from $CFCl_3$.

2,2-Bis[(trifluoromethyl)thio]ethenol [Bis[(trifluoromethyl)thio]acetaldehyde] (1). A mixture of 6.0 g (0.02 mol) of 2,2-bis[(trifluoromethyl)thio]-1-(*N*,*N*-diethylamino)-ethene, 3 mL of 36% hydrochloric acid (0.03 mol), 3 mL of water, and 12 mL of ethanol was refluxed for 3 h and then poured into iced water. The oily product was extracted thoroughly with dichloromethane or chloroform. The combined organic extracts were washed with water (caution: washing with a neutralizing agent, e.g. sodium carbonate solution, should be avoided because it removes the product from the organic layer completely!) and dried over P_4O_{10}. The residue after the removal of the solvent was distilled over the new portion of P_4O_{10} through a Vigreux column that gave 3.8 g (77.6%) of compound **1**. Colorless liquid of unpleasant smell. Bp 106 °C. Anal. Calcd for $C_4H_2F_6OS_2$: C, 19.67; H, 0.83; S, 26.26. Found: C, 19.97; H, 0.55; S, 26.36. IR (film) cm^{-1}: 3440w, 1740w, 1630w, 1590s, 1295w, 1210−1070vs, b, 950w, 930w, 760m, 630w, 615w. MS *m*/*z* (%): 244 (36.3) M^+, 224 (21.3) $M^+ - HF$, 215 (24.0) $(CF_3S)_2CH^+$, 175 (9.1) $M^+ - CF_3$, 143 (15.0) $M^+ - CF_3S$, 115 (16.4), 95 (8.9), 88 (67.5), 83 (10.1), 74 (25.2), 73 (63.7), 69 (62.4) CF_3^+, 58 (53.2), 57 (15.6), 45 (100.0) CHS^+, 43 (20.3). ^1H NMR (100 MHz, $CDCl_3$) δ for enol form (83%): 6.96 (s, 1H), 7.60 (s, 1H); for aldehyde form (17%): 5.15 (d, J = 1.8 Hz, 1H), 9.50 (broad s, 1H). ^{19}F NMR (100 MHz, $CDCl_3$) δ for enol form (81%): −43.19 (s, 3F), −46.47 (s, 3F); for aldehyde form (19%): −39.84 (s, 6F). ^{13}C NMR (fully coupled, 250 MHz, $CDCl_3$) δ for enol form: 86.55 (d, $^2J_{CH}$ = 11.4 Hz), 128.76 (q, $^1J_{CF}$ = 312.2 Hz), 129.34 (q, $^1J_{CF}$ = 310.3 Hz), 167.54 (d, $^1J_{CH}$ = 192.6 Hz); for aldehyde form: 53.56 (dd, $^1J_{CH}$ = 154.5 Hz, $^2J_{CH}$ = 36.2 Hz), 129.14 (q, $^1J_{CF}$ = 309.0 Hz), 187.04 (dd, $^1J_{CH}$ = 196.4 Hz, $^2J_{CH}$ = 5.7 Hz). Aldehyde−enol contents (±2%) were determined, after equilibrium was established, from the integrated areas of ^1H or ^{19}F signals.

Determination of pK_a value of compound **1** (for enol−aldehyde tautomeric mixture) was performed by potentiometric titration (Metrohm 691 pH-meter, Ingold 405−87 glass electrode) of 0.01 M solution of $(CF_3S)_2C{=}CHOH$ in acetonitrile with 1 M NaOH water solution. The acidity constant obtained as pH at half-neutralization equals 2.6.

General Procedure for the Reaction of 2,2-Bis[(trifluoromethyl)thio]ethenol (1) with Amines. To the solution of 2,2-bis[(trifluoromethyl)thio]ethenol in benzene were added, the excess of the respective amine and traces of *p*-toluenesulfonic acid, and the mixture was refluxed under Dean−Stark water separator for 3 h. After filtration and the evaporation of benzene, the product was distilled under reduced pressure. The amounts of starting materials and the yields of products are given below.

2,2-Bis[(trifluoromethyl)thio]-1-(*N*-phenylamino)ethene (2). From 2.85 g (0.012 mol) of compound **1** and 1.3 g (0.013 mol) of aniline in 50 mL benzene was obtained 1.0 g of compound **2** (61.7% yield). Colorless liquid, bp 110 °C/2_{Torr}, colorless crystals, mp 38 °C. Anal. Calcd for $C_{10}H_7F_6NS_2$: C, 37.62; H, 2.21; N, 4.39; S, 20.08. Found: C, 37.64; H, 2.16; N, 4.62; S, 19.60. IR (film) cm^{-1}: 3380m, 3050w, 1630s, 1600s, 1595s, 1500m, 1475m, 1400m, 1190−1055s, 950m, 750s, 690s, 675m, 630m, 575w, 540w, 510m. MS *m*/*z* (%): 319 (59.5) M^+, 250 (46.4) $M^+ - CF_3$, 206 (15.2), 149 (45.1), 148 (35.4), 121 (10.1), 117 (28.3), 104 (100.0) $C_6H_5NCH^+$, 93 (20.7), 89 (3.8), 77 (53.6), 69 (11.0) CF_3^+, 65 (8.4), 63 (4.2), 51 (24.9), 45 (38.0). ^1H NMR (100 MHz, $CDCl_3$) δ 6.84−7.51 (m, >5H), 7.76 (s, 1H), 7.94 (s, <1H). ^{19}F NMR (100 MHz, $CDCl_3$) δ for enamine form (97%): −43.70 (s, 3F), −47.69 (s, 3F); for aldimine form (3%): −46.97 (s, 6F). ^{13}C NMR (250 MHz, $CDCl_3$) δ 74.09 (s), 116.54 (s), 124.52 (s), 129.51 (q, $^1J_{CF}$ = 314.7 Hz), 129.72 (q, $^1J_{CF}$ = 310.9 Hz), 129.95 (s), 138.59 (s), 154.72 (s).

2,2-Bis[(trifluoromethyl)thio]-1-(*N*,*N*-diethylamino)ethene was obtained by the same procedure from 1.9 g of compound **1** and a great molar excess of diethylamine (because of its bp, lower than that of the solvent) in benzene in 30.4% yield.

Silver 2,2-Bis[(trifluoromethyl)thio]ethenolate (3). Into the stirred solution of 1.3 g (0.0076 mol) of silver nitrate in 10 mL water was dropped 1.8 g (0.0074 mol) of compound **1**. The white precipitate of silver salt, that was formed immediately, was filtered off after 10 min of stirring, washed thoroughly with water, and dried. A 1.8 g amount (96.7% yield) of silver salt **3** was obtained. No crystallization was possible because exposure to heat as well as to light caused decomposition with deposition of metallic silver, so compound **3** was purified by solving it in diethyl ether and precipitating it with *n*-hexane at room temperature. Colorless powder, mp 116−117 °C with decomposition. Anal. Calcd for $C_4HAgF_6OS_2$: C, 13.69; H, 0.29; S, 18.27. Found: C, 14.55; H, 0.36; S, 17.92. IR (KBr) cm^{-1}: 3665w, 3620−2500m, broad, 1620m, 1595m, 1540s, broad, 1380m, 1355m, 1250m, 1205−1030vs, broad, 940m, 760w, 750w, 570w, 500m. MS *m*/*z* (%): 243 (100.0) $M^+ - Ag$, 227 (13.2) $M^+ - OAg$, 224 (23.2) $M^+ - AgF$, 215 (46.7), 158 (25.3), 154 (11.8), 145 (16.5), 126 (13.1), 89 (17.3), 77 (10.3), 74 (15.2), 73 (46.7), 69 (83.1) CF_3^+, 57 (62.0), 45 (74.8), 41 (32.9), 36 (53.2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (broad s, 1H). ^{19}F NMR (100 MHz, $CDCl_3$) δ −46.30 (s, 3F), −49.51 (s, 3F).

1-Ethoxy-2,2-bis[(trifluoromethyl)thio]ethene (4). To the stirred solution of 0.4 g (0.0011 mol) of compound **3** in 20 mL of diethyl ether was added 0.5 mL (0.73 g, 0.0067 mol) of ethyl bromide. After ca. 2 min the precipitation of AgBr started. The reaction was completed after 15 min. After filtration, the crude product was separated from the rest of AgBr by condensation into the cooled trap at the vacuum system. Preparative GC (12.5 cm column SE 54) was used

(10) Hart, H.; Sasaoka, M. *J. Chem. Educ.* **1980**, *57*, 685.
(11) Kresge, A. J. *CHEMTECH* **1986**, 250.
(12) Capon, B.; Guo, B.-Z.; Kwok, F. C.; Siddhanta, A. K.; Zucco, C. *Acc. Chem. Res.* **1988**, *21*, 135.
(13) Rappaport, Z.; Biali, S. E. *Acc. Chem. Res.* **1988**, *21*, 442.
(14) Haas, A. *Pure Appl. Chem.* **1991**, *63*, 1577.

for further purification in order to separate small amounts of compound **1** formed parallel as a result of hydrolysis. Compound **4** was obtained with nearly quantitative yield. Colorless liquid, bp 130−131 °C. Anal. Calcd for $C_6H_6F_6OS_2$: C, 26.47; H, 2.22. Found: C, 26.47; H, 2.16. IR (film) cm^{-1}: 2995m, 2905w, 1590s, 1475w, 1450w, 1395m, 1370w, 1320m, 1300m, 1225s, 1180−1105vs, 1030s, 955m, 850m, 755m, 670w, 585m, 515m. MS *m*/*z* (%): 272 (90.2) M^+, 244 (25.8) $M^+ - C_2H_4$, 224 (29.1) $M^+ - C_2H_4 - HF$, 205 (6.2), 203 (5.5) $M^+ - CF_3$, 175 (41.0) $M^+ - C_2H_4 - CF_3$,158 (7.6), 155 (12.0), 145 (7.6), 127 (11.6), 89 (20.4), 73 (100.0), 69 (57.5) CF_3^+, 57 (6.2), 45 (58.2), 29 (89.1).^{1}H NMR (100 MHz, $CDCl_3$) δ 1.40 (t, $^3J_{HH} = 7.5$ Hz, 3H), 4.25 (q, $^3J_{HH} = 7.5$ Hz, 2H), 7.47 (s, 1H). ^{19}F NMR (100 MHz, $CDCl_3$) δ −43.36 (s, 3F), −46.62 (s, 3F). ^{13}C NMR (250 MHz, $CDCl_3$) δ 15.16 (s), 72.01 (s), 86.04 (s), 117.49 (q, $^1J_{CF} = 336.2$ Hz), 129.54 (q, $^1J_{CF} = 310.5$ Hz), 170.51 (s).

Caution: The described compounds should be handled with care as they have not been checked for their toxicity, and there are many examples of very toxic CF_3S derivatives. An efficient hood is absolutely needed for experiments!

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