Polychloroethyltrifluoromethylsulfonamides from *N*,*N*-dichlorotrifluoromethylsulfonamide and dichloroethenes

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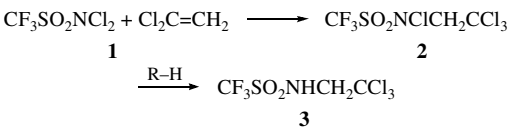
The interaction of trifluoromethylsulfonic acid *N*,*N*-dichloroamide with 1,1- and 1,2-dichloroethenes is a convenient way to *N*-(2,2,2-trichloroethyl)trifluoromethylsulfonamide, *N*-(2,2-dichloroethylidene)amide of trifluoromethylsulfonic acid and its derivatives.

The interaction of *N*,*N*-dichloroamides with 1,2-polychloroethenes offers convenient ways to polyfunctional polyhaloethylamides.[1] We studied the reactions of *N*,*N*-dichlorotrifluoromethylsulfonamide[2] **1** with 1,1- and 1,2-dichloroethenes to synthesise polychloroethyltrifluoromethylsulfonamides contaning pharmacophoric and synthetically attractive fragments.

We found that dichloroamide **1** reacts with 1,1-dichloroethene with a strong exothermic effect to form *N*-(2,2,2-trichloroethyl)amide of trifluoromethylsulfonic acid **3**; the reaction was accompanied by chloroethene polymerization.† At the first stage, *N*-chloro-*N*-(2,2,2-trichloroethyl)amide **2** was probably formed, and it was then reduced under the reaction conditions to give amide **3** (Scheme 1).



Scheme 1

A similar process was described for *N*,*N*-dichloroarylsulfonamides;[3] however, the corresponding *N*-chloro-*N*-(2,2,2-trichloroethyl)arylsulfonamides are more stable.

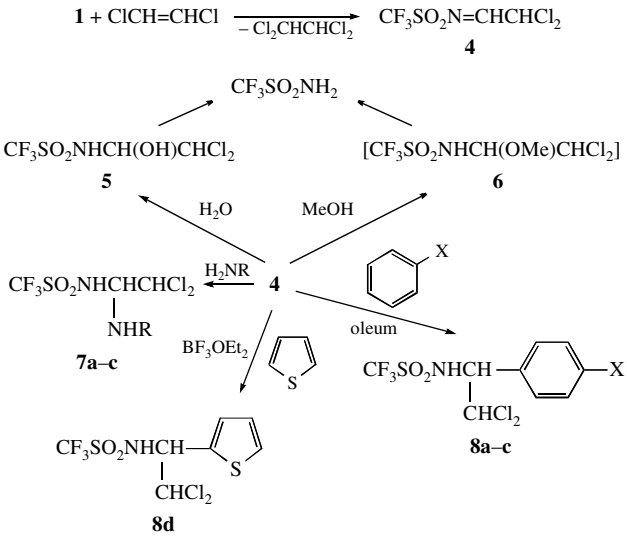
Recently,[4] we found that the interaction of compound **1** with 1,2-dichloroethylene follows only one direction and results in *N*-(2,2-dichloroethylidene)amide of trifluoromethylsulfonic acid **4** without trichloroethylamide and diamidopolychloroethane impurities in contrast to the reaction of *N*,*N*-dichloroarylsulfonamides with 1,2-dichloroethylene.[1,5]

We improved the synthesis of imine **4** and studied it in the reactions with O-, N-nucleophiles and aromatics.

Dichloroamide **1** reacts with *cis*-, *trans*- or a mixture of 1,2-dichloroethylene isomers to produce **4** under exposure to visible light. Other kinds of initiation are not necessary in the process in contrast to an analogous *N*,*N*-dichloroarylsulfonamide reaction.[1,5]

The isolation of pure compound **4** form is difficult because of its high activity. Therefore a solution of **4** was used for synthetic purposes (Scheme 2).‡

Compound **4** reacts with water even in contact with moist air. The addition of water or an alcohol to the solution of **4** causes a strong exothermic effect. The product of water addition, *N*-(1-hydroxy-2,2-dichloroethyl)trifluoromethylsulfonamide **5**, was identified by its spectrum. However, we failed to purify **5** and to determine methoxy derivative **6**. The reactions were accompanied by the formation of trifluoromethylsulfonamide and unidentified dichloroacetaldehyde oligomers.



Scheme 2

Amide addition products **7a–c** are stable. The reaction of **1** with phenylurea or phenylsulfonamide occurs exothermally to give expected 1,1-diamido-2,2-dichloroethane **7a**,**b**.

Thioamides are well-known S-nucleophiles in reactions with the acylimines of polyhaloaldehydes.[6] The addition of thioacetamide to **4** involves the NH_2 group to give *N*-(1-trifluoromethylsulfonamido-2,2-dichloroethyl)thioacetamide **7c**.

The C-amidoalkylation of benzene, toluene and chlorobenzene with imine **4** takes place in the presence of oleum as a catalyst to form *N*-(1-aryl-2,2-dichloroethyl)trifluoromethylsulfonamides **8a–c**. The reaction was unsuccessful with Lewis acids or sulfuric acid instead of oleum or without a catalyst. However, the C-amidoalkylation of thiophene occurs easily in the presence of BF_3 etherate with substitution at the α-position of a thienyl ring (compound **8d**).

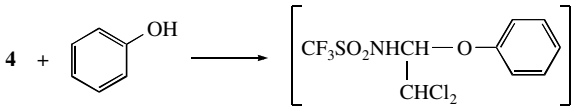
Imine **4** reacts with phenol in an unusual manner. Instead of expected O-addition product **9**, 1,1-bis(4-hydroxyphenyl)-2,2-dichloroethane **11** was isolated (Scheme 3). Intermediate structures **9** and **10** were not found.

In contrast to imine **4**, the arenesulfonylimines of polyhaloaldehydes interact with phenol to give *N*-(1-phenoxy-2-polychloroethyl)amides,[7] whereas *N*-[1-(4-hydroxyphenyl)ethyl]-amides are produced in the presence of oleum.[8] No diarylethanes like **11** were found.[7,8]

† NMR spectra were measured on a Bruker DPX-400 spectrometer. ^1H (400.13 MHz) and ^{13}C NMR (101.61 MHz) in [$^2H_6$]DMSO.

3: A solution of 1,1-dichloroethylene (0.81 ml, 10 mmol) in 2 ml of CCl_4 was added dropwise to a solution of *N*,*N*-dichlorotrifluoromethylsulfonamide **1**[4] (2.18 g, 10 mmol) in 2 ml of CCl_4 at –10 °C with stirring for 10 min. The mixture was heated to room temperature for 1 h and then evaporated in a vacuum (80–100 Torr). Yield 2.38 g (85 %), mp 112–113 °C (hexane, sublimated). ^1H NMR, δ: 4.23 (s, 2H, CH_2), 8.9 (br. s, 1H, NH). ^{13}C NMR, δ: 60.50 (CH_2), 97.18 (CCl_3), 119.51 (q, CF_3, $J_{C–F}$ 322.1 Hz). IR (KBr, ν/cm^{-1}): 3290 (NH), 1460, 1380, 1240, 1200 (CF_3SO_2). MS, *m*/*z* (%): 121 (5), 119 (23), 117 (43) $[CCl_3]^+$, 98 (12), 96 (63) $[M^+ – CF_3SO_2NH – Cl]$, 79 (30) $[M^+ – CF_3 – CH_2CCl_3]$, 69 (100) $[CF_3]^+$, 64 (40) $[SO_2]^+$. Found (%): C, 12.70; H, 1.07; Cl, 38.21; N, 5.02; S, 11.49. Calc. for $C_3H_3Cl_3F_3NO_2S$ (%): C, 12.85; H, 1.08; Cl, 37.92; N, 4.99; S, 11.43.

A comparison of the reactivity of N-sulfonylimines of polyhalogenated aldehydes[1] and compound **4** indicates that the latter is more active in the reaction with O-, N-nucleophiles and aromatics. Moreover, it is suggested that the trifluoromethylsulfonamide group is an easier leaving group than the arylsulfonamide group.



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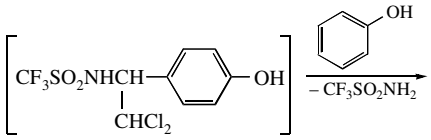

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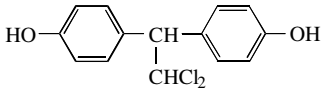

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Scheme 3

‡ **4**: A solution of *N*,*N*-dichloroamide **1**[4] (2.18 g, 10 mmol) in 7.7 ml (100 mmol) of 1,2-dichloroethene was allowed to stand for 12 h in sunlight under continuous bubbling of argon, avoiding spontaneous heating over 20 °C. The obtained mixture was used in the syntheses given below. ^{1}H NMR (in a mixture of *cis*- and *trans*-1,2-dichloroethenes), δ: 8.57 (d, 1H, HC=N, *J* 6.4 Hz), 6.24 (d, 1H, $CHCl_2$, *J* 6.4 Hz), 5.95 (s, 2H, $Cl_2HC–CHCl_2$). IR (microlayer, ν/cm^{-1}): 3095 (=CH), 1660 (C=N), 1150, 1200, 1240, 1360 (CF_3SO_2).

5: A solution of imine **4** was allowed to stand in air for 24 h to give a mixture (3.89 g) of amide **5** (unstable) and 1,1,2,2-tetrachloroethane. ^{1}H NMR, δ: 5.95 (s, 2H, 1,1,2,2-tetrachloroethane), 5.01 (d, 1H, CH–N, *J* 4.9 Hz), 6.05 (d, 1H, $CHCl_2$, *J* 4.9 Hz), 10.49 (br. s, 1H, NH). IR (KBr, ν/cm^{-1}): 3520 (OH), 3300 (NH), 1360, 1240, 1200, 1150 (CF_3SO_2).

General procedure for the preparation of **7a–c**. 10 mmol of an amide was added to the solution of imine **4**. The mixture was stirred for 1 h, avoiding spontaneous heating above 20 °C, and allowed to stand for 24 h; then, it was evaporated in a vacuum. The solid residue was recrystallised from hexane.

7a: yield 3.34 g (88%), mp 207 °C (decomp.). ^{1}H NMR (room temperature) δ: 5.77 (dd, 1H, CHN, $J_{CH–CHCl_2}$ 3.9 Hz, $J_{CH–NH}$ 9.6 Hz), 6.42 (d, 1H, $CHCl_2$, *J* 3.9 Hz), 6.94–7.45 (m, 6H, Ph + CNHC=O), 9.01 (s, 1H, NHPh), 10.60 (br. s, 1H, SO_2NH). ^{1}H NMR (at 60 °C) δ: 5.76 (dd, 1H, CHN, $J_{CH–CHCl_2}$ 3.9 Hz, $J_{CH–NH}$ 9.6 Hz), 6.42 (d, 1H, $CHCl_2$, *J* 3.9 Hz), 6.88 (d, 1H, CNHC=O, *J* 9.6 Hz), 6.95–7.45 (m, 5H, Ph), 8.55 (s, 1H, NHPh), 9.80 (br. s, 1H, SO_2NH). ^{13}C NMR, δ: 65.77 (NCH), 74.16 ($CHCl_2$), 119.43 (q, CF_3, $J_{C–F}$ 321.9 Hz), 118.16, 122.22, 128.96, 139.54 (Ph), 153.18 (C=O). IR (KBr, ν/cm^{-1}): 3335 (NH), 3280 (NH), 1650 (C=O), 1380, 1230, 1200, 1140 (CF_3SO_2). MS, *m*/*z* (%): 92 (85) $[PhNH]^+$, 85 (20), 83 (43) $[CHCl_2]^+$, 77 (14) $[Ph]^+$, 69 (100) $[CF_3]^+$, 64 (22) $[SO_2]^+$. Found (%): C, 31.40; H, 2.63; Cl, 18.56; N, 11.11; S, 8.47. Calc. for $C_{10}H_{10}Cl_2F_3N_3O_3S$ (%): C, 31.59; H, 2.65; Cl, 18.65; N, 11.05; S, 8.43.

7b: yield 2.52 g (63%), mp 175 °C. ^{1}H NMR, δ: 5.05 (dd, 1H, CHN, $J_{CH–CHCl_2}$ 4.2 Hz, $J_{CH–NH}$ 9.0 Hz), 5.97 (d, 1H, $CHCl_2$, *J* 4.2 Hz), 7.62 and 7.86 (m, 5H, ArH), 8.65 (d, 1H, $NHSO_2Ph$, $J_{CH–NH}$ 9.0 Hz), 10.2 (br. s, 1H, $NHSO_2CF_3$). IR (KBr, ν/cm^{-1}): 3250 (NH), 1380, 1350, 1225, 1200, 1170 (CF_3, SO_2). MS, *m*/*z* (%): 156 (11) $[PhSO_2NH]^+$, 85 (12), 83 (23) $[CHCl_2]^+$, 77 (7) $[Ph]^+$, 69 (100) $[CF_3]^+$, 64 (33) $[SO_2]^+$. Found (%): C, 26.54; H, 2.30; Cl, 17.21; N, 6.78; S, 15.79. Calc. for $C_9H_9Cl_2F_3N_2O_4S_2$ (%): C, 26.94; H, 2.26; Cl, 17.67; N, 6.98; S, 15.98.

7c: yield 2.65 g (83%), mp 97–98 °C. ^{1}H NMR, δ: 2.53 (s, 3H, Me), 6.36 (dd, 1H, CHN, $J_{CH–CHCl_2}$ 5.0 Hz, $J_{CH–NH}$ 7.3 Hz), 6.38 (d, 1H, $CHCl_2$, *J* 5.0 Hz), 10.95 [d, 1H, NHC(S), $J_{CH–NH}$ 7.34 Hz]. ^{13}C NMR, δ: 32.77 (Me), 69.70 (NCH), 70.86 ($CHCl_2$), 119.26 (q, CF_3, $J_{C–F}$ 321.7 Hz), 202.73 (C=S). IR (KBr, ν/cm^{-1}): 3350 (NH), 3250 (NH), 1380, 1225, 1200, 1130 (CF_3SO_2). Found (%): C, 18.54; H, 2.20; Cl, 22.10; N, 8.83; S, 20.19. Calc. for $C_5H_7Cl_2F_3N_2O_2S_2$ (%): C, 18.82; H, 2.21; Cl, 22.22; N, 8.78; S, 20.09.

General procedure for the preparation of N-*(1-aryl-2,2-dichloroethyl)trifluoromethylsulfonamides* **8a–c**. An arene (50 mmol) and 3–5 drops of oleum (5–22% SO_3) were added to the solution of imine **4**. The mixture was stirred for 3 h and evaporated in a vacuum (80–100 Torr). The residue was dissolved in an ammonia liquor (5% NH_3) and filtered; the rate was neutralised with hydrochloric acid (10%). The resulting precipitate was separated, dried and recrystallised from hexane.

8a: yield 1.51 g (47%), mp 102–103 °C. ^{1}H NMR, δ: 5.10 (d, 1H, CHN, *J* 5.0 Hz), 6.50 (d, 1H, $CHCl_2$, *J* 5.0 Hz), 7.34–7.57 (m, 5H, Ph), 10.77 (br. s, 1H, NH). ^{13}C NMR, δ: 65.55 (CHN), 74.92 ($CHCl_2$), 119.33 (q, $J_{C–F}$ 321.7 Hz), 127.69, 128.58, 128.85, 136.12 (Ph). IR (KBr, ν/cm^{-1}): 3290 (NH), 1380, 1230, 1200, 1140 (CF_3SO_2). MS, *m*/*z* (%): 238 (100) $[M^+ – CHCl_2]$, 173 (12) $[M^+ – CF_3SO_2NH]$, 104 (43) $[M^+ – CHCl_2 – – CF_3SO_2 – H]$, 83 (3) $[CHCl_2]^+$, 77 (30) $[Ph]^+$, 69 (32) $[CF_3]^+$, 51 (17) $[Ph^+ – C_2H_2]$. Found (%): C, 33.60; H, 2.48; Cl, 22.12; N, 4.37; S, 10.01. Calc. for $C_9H_8Cl_2F_3NO_2S$ (%): C, 33.56; H, 2.50; Cl, 22.01; N, 4.35; S, 9.95.

8b: yeild 1.41 g (42%), mp 93 °C. ^{1}H NMR, δ: 2.29 (s, 3H, Me), 5.01 (d, 1H, CHN, *J* 5.0 Hz), 6.44 (d, 1H, $CHCl_2$, *J* 5.0 Hz), 7.19–7.41 (AA′BB′ spin system, 4H, C_6H_4, *J* 8.0 Hz), 10.69 (br. s, 1H, NH). ^{13}C NMR, δ: 20.73 (Me), 65.22 (CHN), 74.99 ($CHCl_2$), 119.23 (q, $J_{C–F}$ 321.7 Hz, CF_3), 127.48, 129.07, 133.03, 138.21 (C_6H_4). IR (KBr, ν/cm^{-1}): 3290 (NH), 1385, 1230, 1200, 1145 (CF_3SO_2). Found (%): C, 35.61; H, 3.00; Cl, 20.93; N, 4.20; S, 9.58. Calc. for $C_{10}H_{10}Cl_2F_3NO_2S$ (%): C, 35.73; H, 3.00; Cl, 21.09; N, 4.17; S, 9.54.

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8c: yeild 1.42 g (40%), mp 105–107 °C. ^{1}H NMR, δ: 5.17 (d, 1H, CHN, *J* 5.38 Hz), 6.50 (d, 1H, $CHCl_2$, *J* 5.38 Hz), 7.49–7.61 (AA′BB′ spin system, C_6H_4, *J* 8.4 Hz), 10.98 (br. s, 1H, NH). ^{13}C NMR, δ: 64.73 (CHN), 74.68 ($CHCl_2$), 119.33 (q, CF_3, $J_{C–F}$ 321.7 Hz), 128.65, 129.67, 133.85, 135.14 (C_6H_4). IR (KBr, ν/cm^{-1}): 3300 (NH), 1380, 1230, 1200, 1140 (CF_3SO_2). MS, *m*/*z* (%): 272 (100) $[M^+ – CHCl_2]$, 139 (12) $[M^+ – – CHCl_2 – CF_3SO_2]$, 138 (19) $[M^+ – CHCl_2 – CF_3SO_2 – H]$, 83 (5) $[CHCl_2]^+$, 69 (26) $[CF_3]^+$. Found (%): C, 30.17; H, 1.96; Cl, 29.69; N, 3.95; S, 9.03. Calc. for $C_9H_7Cl_3F_3NO_2S$ (%): C, 30.32; H, 1.98; Cl, 29.83; N, 3.93; S, 8.99.

8d: Thiophene (2.38 ml, 30 mmol) and 3–5 drops of BF_3OEt_2 were added to the solution of imine **4**. The mixture was stirred for 30 h and evaporated in a vacuum. Yeild 1.48 g (45%), mp 82 °C (hexane). ^{1}H NMR, δ: 5.36 (d, 1H, CHN, *J* 4.5 Hz), 6.47 (d, 1H, $CHCl_2$, *J* 4.5 Hz), 7.05 (dd, 1H, $C^4H_{thienyl}$, *J* 3.5, *J* 5.0 Hz), 7.33 (d, 1H, $C^3H_{thienyl}$, *J* 3.5 Hz), 7.54 (d, 1H, $C^5H_{thienyl}$, *J* 5.0 Hz), 10.90 (br. s, 1H, NH). ^{13}C NMR, δ: 61.50 (CHN), 74.73 ($CHCl_2$), 119.41 (q, CF_3, $J_{C–F}$ 321.7 Hz), 127.06, 127.22, 128.00, 137.76 (thienyl). IR (KBr, ν/cm^{-1}): 3280 (NH), 1373, 1230, 1200, 1147 (CF_3SO_2). Found (%): C, 25.52; H, 1.83; Cl, 21.50; N, 4.30; S, 19.62. Calc. for $C_7H_6Cl_2F_3NO_2S_2$ (%): C, 25.62; H, 1.84; Cl, 21.61; N, 4.27; S, 19.54.

11: Phenol (0.94 g, 10 mmol) was added to the solution of imine **4**. The mixture was stirred for 100 h and evaporated in a vacuum. The residue was washed sequentially with $CHCl_3$ and water. Yield 0.43 g (23%), mp 173 °C. ^{1}H NMR, δ: 4.37 (d, 1H, C^1H, *J* 9.7 Hz), 6.65–7.22 (AA′BB′ spin system, 8H, $2C_6H_4$, *J* 7.6 Hz), 7.04 (d, 1H, $CHCl_2$, *J* 9.7 Hz), 9.28 (s, 2H, 2OH). ^{13}C NMR, δ: 61.17 (C^1), 76.42 ($CHCl_2$), 115.09, 128.9, 131.89, 156.15 (C_6H_4). Found (%): C, 59.33; H, 4.25; Cl, 24.91. Calc. for $C_{14}H_{12}Cl_2O_2$ (%): C, 59.39; H, 4.27; Cl, 25.04.