Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 6101–6104
Tetrahedron Letters

S-Trifluoromethyl esters of thiocarboxylic acids, $RC(O)SCF_3$

Mikhail M. Kremlev,[a] Wieland Tyrra,[b,*] Dieter Naumann[b] and Yurii L. Yagupolskii[a]

[a]*Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Murmanskaya St. 5, UA-02094 Kiev, Ukraine*
[b]*Institut für Anorganische Chemie, Universität zu Köln, Greinstr. 6, D-50939 Köln, Germany*

Received 9 June 2004; revised 16 June 2004; accepted 16 June 2004
Available online 2 July 2004

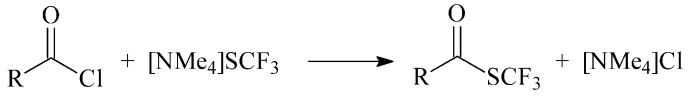
Abstract—*S*-Trifluoromethyl esters of different types of thiocarboxylic acids have been prepared in moderate to excellent yields from halide substitution reactions of the corresponding acid chlorides and tetramethylammonium trifluoromethylthiolate. $C_6F_5C(O)SCF_3$ undergoes a surprising rearrangement on attempted isolation to give $4\text{-}CF_3SC_6F_4C(O)F$, which was converted into the corresponding acid.

The number of *S*-trifluoromethyl esters of thiocarboxylic acids is limited so far to very few examples.[1] To our knowledge only one publication describes the synthesis of $EtC(O)SCF_3$ and $CF_3C(O)SCF_3$ via halide substitution of the corresponding acid chlorides with $Hg(SCF_3)_2$.[2] On the other hand, *S*-trifluoromethyl and other *S*-perfluoroorgano esters of dialkyldithiocarbamic acids can be easily prepared from the reactions of perfluoroorgano silver or cadmium compounds or the system Me_3SiR_f/F^- and the corresponding dithiuram-disulfides,[3] while the synthesis of *S*-trifluoromethyl xanthates starting from sodium *O*-phenethyl xanthate and trifluoroacetic acid anhydride followed by a decarbonylation reaction appears to be far from trivial.[4] Herein we describe a convenient synthesis of different examples of this class starting from the corresponding acid chlorides and the newly accessible source of SCF_3 nucleophiles, $[NMe_4]SCF_3$.[5]

Reactions[6] of carboxylic acid chlorides **1** and $[NMe_4]SCF_3$ proceed nearly selectively in MeCN to give the corresponding *S*-trifluoromethyl ester **2** in good yields (Scheme 1). The low solubility of $[NMe_4]Cl$ in acetonitrile must be assumed to be the driving force for these reactions since it begins to precipitate after combining both reactants. Formation of the corresponding acid fluoride as a by-product is negligibly small in all cases. To demonstrate the general utility of $[NMe_4]SCF_3$, we have chosen chlorides of different kinds of carboxylic acids as reagents.

Di-substitution has been achieved using the acid chloride of 2,6-pyridine dicarboxylic acid (**3**) (Scheme 2).[14]

The reaction of pentafluorobenzoic acid chloride (**1g**) and $[NMe_4]SCF_3$ proceeds in a similar manner to give

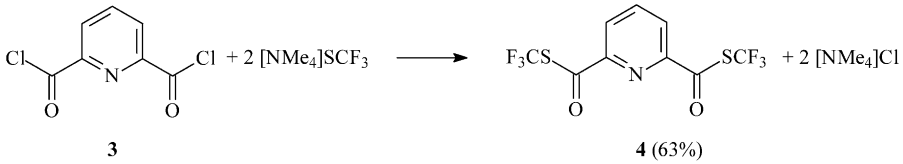


1 **2**

Scheme 1. R = 4-$NO_2C_6H_4$ (**a**, 82%),[7] 2-furan (**b**, 79%),[8] 2-thiophene (**c**, 69%),[9] *trans*-cinnamic (**d**, 82%),[10] Et_2N (**e**, 75%),[11] $CH_2{=}CH(CH_2)_8$ (**f**, 82%),[12] C_6F_5 (**g**).[13]

Keywords: *S*-Trifluoromethyl esters; Acid chlorides; Halide substitution.
* Corresponding author. Tel./fax: +49-221-4703276; e-mail: tyrra@uni-koeln.de

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.06.073

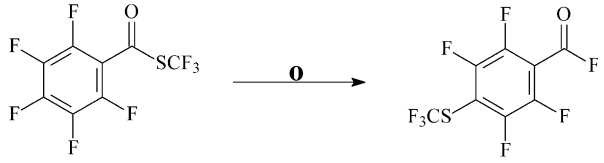


3 4 (63%)

Scheme 2.

primarily the expected *S*-trifluoromethyl ester (**2g**) (cf. Scheme 1), which could be unambiguously identified by its characteristic ^{19}F NMR spectrum.[13]

After prolonged stirring at ambient temperature or upon working up, **2g** undergoes a rearrangement with formation of the acid fluoride of 4-trifluoromethylthio-2,3,5,6-tetrafluorobenzoic acid (**5**) (Scheme 3).[15]



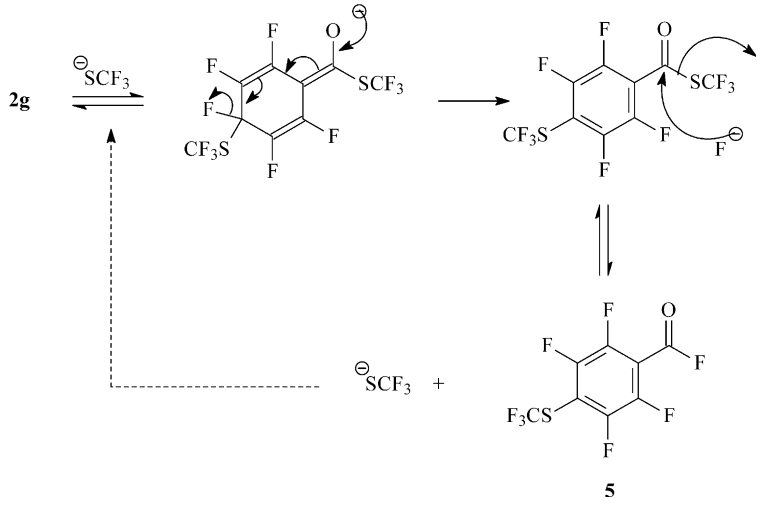
2g 5

Scheme 3.

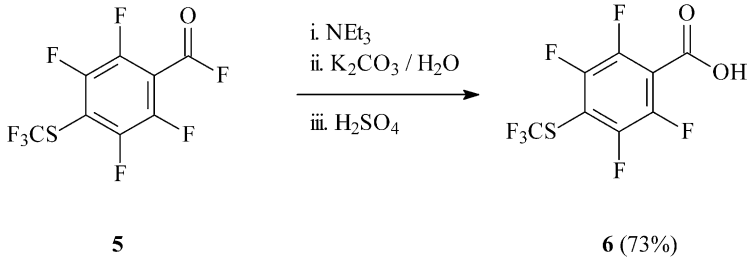
This formal HSAB directed rearrangement proceeds selectively with exclusive formation of the *para*-isomer. Not even ^{19}F NMR spectroscopic evidence is found for the *ortho*-isomer. The formation of **5** can be understood most probably as an intermolecular rearrangement. On the basis of the HSAB concept it seems to be logical that the *soft* SCF_3 moiety tends to attack the *soft* C-4 atom of the aromatic ring, replacing the *hard* fluoride ion, which again combines with the *hard* carbonyl carbon atom. The reaction presumably proceeds by an ionic chain mechanism as shown in Scheme 4. Further experiments are necessary for a deeper insight into the mechanism.

Compound **5** is easily converted into the corresponding acid **6** (Scheme 5) by common procedures.[16]

The method described offers a convenient access to the poorly investigated class of *S*-trifluoromethyl esters of carboxylic acids.



Scheme 4.



5 6 (73%)

Scheme 5.

Acknowledgements

This work was generously supported by the Deutsche Forschungsgemeinschaft (436 UKR 113). We thank our technicians Sigrid Buslei and Silke Quadt for the preparation of $[NMe_4]SCF_3$.

References and notes

1. For example, (a) Haas, A.; Radau, G. *J. Fluorine Chem.* **1998**, *89*, 9–18; (b) Munavalli, S.; Rossman, D. I.; Rohrbaugh, D. K.; Ferguson, C. P.; Durst, H. D. *J. Fluorine Chem.* **1996**, *76*, 7–13; (c) Munavalli, S.; Rossman, D. I.; Rohrbaugh, D. K.; Ferguson, C. P.; Szafraniec, L. J. *J. Fluorine Chem.* **1992**, *59*, 91–99; (d) Haas, A.; Lieb, M. *Chem. Ber.* **1978**, *111*, 2891–2894.
2. Man, E. H.; Coffman, D. D.; Muetterties, E. L. *J. Am. Chem. Soc.* **1959**, *81*, 3575–3577.
3. (a) Wessel, W.; Tyrra, W.; Naumann, D. Z. *Anorg. Allg. Chem.* **2001**, *627*, 1264–1268; (b) Tyrra, W.; Buslei, S.; Quadt, S. Unpublished results.
4. Bertrand, F.; Pevere, V.; Quiclet-Sire, B.; Zard, S. Z. *Org. Lett.* **2001**, *3*, 1069–1071.
5. Tyrra, W.; Naumann, D.; Hoge, B.; Yagupolskii, Yu. L. *J. Fluorine Chem.* **2003**, *119*, 101–107.
6. General procedure. To a solution of the corresponding acid chloride (2 mmol) in 5 mL acetonitrile at −30 °C, a solution of tetramethylammonium trifluoromethanethiolate (2 mmol) in 10 mL acetonitrile was added drop-wise over a period of 10 min. The reaction mixture was warmed slowly to ambient temperature under stirring within 1 h, filtered from tetramethylammonium chloride and all volatile materials were evaporated at reduced pressure. The residue was extracted with diethyl ether and filtered again. Diethyl ether was evaporated and the crude material was purified by recrystallisation or distillation. ^{19}F and ^{13}C NMR ($CDCl_3$, 21 °C) and EI mass spectrometric data as well as results of elemental analyses of the products are incorporated in the corresponding references. ^1H NMR data do not significantly deviate from those reported for the corresponding *O*-alkyl esters.
7. 4-Nitrothiobenzoic acid *S*-trifluoromethyl ester **2a**: 0.31 g (82%), mp 84–86 °C (*n*-hexane). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −40.0 (s, SCF_3); ^1H NMR (200.1 MHz, $CDCl_3$): δ 8.36 (m, 2H), 8.00 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$; 50.4 MHz): δ 173.8 (s, C(O)S), 151.2 (s, C-4), 132.5 (q, C-1, $^4J_{FC} \approx 3.5$ Hz), 130.5 (q, SCF_3, $^1J_{FC} = 308.7$ Hz), 128.6 (s, C-3,5), 124.3 (s, C-2,6). Anal. Calcd for $C_8H_4F_3NO_3S$: C, 38.25; H, 1.61; N, 5.57; S, 12.77. Found: C, 38.18; H, 1.62; N, 5.82; S, 12.16.
8. Furan 2-thiocarboxylic acid *S*-trifluoromethyl ester **2b**: 0.31 g (79%), bp 32–34 °C (0.14 mbar). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −39.4 (s, SCF_3). ^1H NMR (200.1 MHz, $CDCl_3$): δ 7.64 (s, H-5, 1H), 7.29 (m, H-3, 1H), 6.62 ('d', H-4, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$; 50.4 MHz): δ 171.2 (s, C(O)S), 148.5 (q, C-2, $^4J_{FC} \approx 3.0$ Hz), 147.8 (s, C-5), 127.8 (q, SCF_3, $^1J_{FC} = 309.7$ Hz), 118.3 (s, C-3), 113.2 (s, C-4). EI-MS, (20 eV): 196 (M^+), 95 (M^+-SCF_3). Anal. Calcd for $C_6H_3F_3O_2S$: C, 36.74; H, 1.54; S, 16.35. Found: C, 36.59; H, 1.32; S, 16.17.
9. Thiophene 2-thiocarboxylic acid *S*-trifluoromethyl ester **2c**: 0.29 g (69%), mp 44–46 °C (*n*-hexane). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −39.4 (s, SCF_3). ^1H NMR (200.1 MHz, $CDCl_3$): δ 7.78 (d, H-5, 1H), 7.74 (d, H-3, 1H), 7.17 ('t', H-4, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$; 50.4 MHz): δ 174.6 (s, C(O)S), 139.4 (q, C-2, $^4J_{FC} \approx 3.0$ Hz), 135.7 (s, C-5), 133.1 (s, C-4), 128.5 (s, C-3), 127.8 (q, SCF_3, $^1J_{CF} = 309.7$ Hz). EI-MS, (20 eV): 212 (M^+), 111 (M^+-SCF_3). Anal. Calcd for $C_6H_3F_3OS_2$: C, 33.96; H, 1.42; S, 30.22. Found: C, 34.47; H, 1.22; S, 30.75.
10. *trans*-Thiocinnamic acid *S*-trifluoromethyl ester **2d**: 0.32 g (82%), mp 33–35 °C (*n*-hexane). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −39.9 (s, SCF_3). ^1H NMR (200.1 MHz, $CDCl_3$): δ 7.66 (d, CH=, 1H, $^3J_{HH} = 15.6$ Hz), 7.45 (overlapping m, phenyl H, 5H), 6.60 (d, CH=, 1H, $^3J_{HH} = 15.6$ Hz); $^{13}C\{^1H\}$ NMR (50.4 MHz, $CDCl_3$): δ 180.7 (s, C(O)S), 145.0 (s, CH=),132.8 (s, C-1 or C-4#), 131.7 (s, C-1 or C-4#), 129.1 (s, C-2,6 or C-3,5#), 128.8 (s, C-2,6 or C-3,5#), 127.9 (q, SCF_3, $^1J_{CF} = 309.4$ Hz), 122.5 (q, =CHC(O)S, $^4J_{FC} \approx 2.4$ Hz). Marked values (#) may be interchangeable. EI-MS, (20 eV): 232 (M^+), 131 (M^+-SCF_3), 103 ($C_6H_5CH{=}CH^+$). Anal. Calcd for $C_{10}H_7F_3OS$: C, 51.72; H, 3.03; S, 13.81. Found: C, 51.94; H, 2.92; S, 12.99.
11. *N*,*N*-Diethylthiocarbamic acid *S*-trifluoromethyl ester **2e**: 0.30 g (75%), bp 34–36 °C (0.09 mbar). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −40.2 (s, SCF_3). ^1H NMR (200.1 MHz, $CDCl_3$): 3.38/3.18 (broad m, CH_2, 4H), 1.20/1.16 (broad m, CH_3, 6H). $^{13}C\{^1H\}$ NMR (50.4 MHz; $CDCl_3$): δ 158.0 (s, C(O)S), 128.0 (q, SCF_3, $^1J_{FC} = 307.3$ Hz), 42.7/42.2 (s, CH_2), 13.6/12.8 (s, CH_3). EI-MS, (20 eV): 100 (M^+-SCF_3). Anal. Calcd for $C_6H_{10}F_3NOS$: C, 35.82; H, 5.00; N, 6.96; S, 15.94. Found: C, 35.47; H, 4.78; N, 6.63; S, 15.61.
12. Undec-10-enoic acid *S*-trifluoromethyl ester **2f**: 0.44 g (82%), bp 65–67 °C (0.10 mbar). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −40.7 (s, SCF_3). ^1H NMR (200.1 MHz, $CDCl_3$): δ 5.78 (m, CH=, 1H), 4.95 ('d', CH_2=, 2H), 2.60 (t, CH_2, 2H), 2.02 (m, CH_2, 2H), 1.67 (CH_2, 2H), 1.28 (overlapping signals, CH_2, 10H); $^{13}C\{^1H\}$ NMR ($CDCl_3$; 50.4 MHz): δ 190.2 (s, C(O)S), 140.0 (s, CH=), 127.7 (q, SCF_3, $^1J_{FC} = 309.9$ Hz), 114.1 (s, CH_2=), 44.5 (q, $CH_2C(O)S$, $^4J_{FC} \approx 2.4$ Hz), 33.7 (s), 29.1 (s), 29.0 (s), 28.9 (s), 28.8 (6), 28.6 (s), 24.6 (s). EI-MS, (20 eV): 268 (M^+), 199 (M^+-CF_3), 167 (M^+-SCF_3), 149 (M^+-SCF_3, $-H_2O$). Anal. Calcd for $C_{12}H_{19}F_3OS$: C, 53.71; H, 7.14; S, 11.95. Found: C, 53.31; H, 7.97; S, 10.76.
13. Pentafluorothiobenzoic acid *S*-trifluoromethyl ester **2g**: ^{19}F NMR (188.3 MHz, MeCN/external $(CD_3)_2CO$): δ −40.5 (t, SCF_3, 3F, $^1J_{FC} = 310.3$ Hz, $J_{FF} \approx 1.6$ Hz), −139.5 (m, F-2,6, 2F), −146.2 (tt, F-4, 1F), −160.3 (m, F-3,5, 2F).
14. Pyridine 2,6-di(thiocarboxylic acid) bis(*S*-trifluoromethyl ester) **4**: 0.21 g (63%), mp 119–122 °C (*n*-hexane). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −41.4 (s, SCF_3). ^1H NMR (200.1 MHz, $CDCl_3$): δ 8.24 (overlapping m, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$; 50.4 MHz): δ 184.7 (s, C(O)S), 149.0 (q, C-2,6, $^4J_{FC} \approx 2.4$ Hz), 140.3 (s, C-4), 128.1 (q, SCF_3, $^1J_{FC} = 310.6$ Hz), 125.8 (s, C-3,5). EI-MS, (20 eV): 234 (M^+-SCF_3), 206 ($M^+-COSCF_3$), 150 ($C_7H_3NOS^+$), 105 ($C_6H_3NO^+$). Anal. Calcd for $C_9H_3F_6NO_2S_2$: C, 32.24; H, 0.90; N, 4.18; S, 19.13. Found: C, 32.80; H, 0.78; N, 4.35; S, 18.87.
15. 4-Trifluoromethylthio-2,3,5,6-tetrafluorobenzoic acid fluoride **5**: ^{19}F NMR (188.3 MHz, MeCN/external $(CD_3)_2CO$): δ +47.8 (t, C(O)F, 1F, $J_{FF} = 42.6$ Hz), −40.6 (t, SCF_3, 3F, $J_{FF} = 4.5$ Hz), −127.5 (m, F-3,5, 2F), −133.6 (m, F-2,6, 2F).
16. 4-Trifluoromethylthio-2,3,5,6-tetrafluorobenzoic acid **6**: To a mixture of 2 mmol pentafluorobenzoyl chloride and 5 mL acetonitrile at −30 °C, a solution of 2 mmol tetramethylammonium trifluoromethanethiolate in 10 mL acetonitrile was added dropwise. The reaction mixture was slowly warmed to ambient temperature (3 h) and 0.2 mL of triethylamine were added. The mixture was stirred for

further 30 min; then 10 mL of an aqueous KOH solution (3%) were added and stirring was continued for another 30 min. The aqueous solution was washed with diethyl ether, filtered and acidified with 2% aqueous sulfuric acid to pH 4–5. The mixture was extracted with diethyl ether, dried over $MgSO_4$, filtered again and all volatile components were evaporated. **6** was obtained as a solid crystallising from chloroform in colourless needles. Yield 0.43 g (73%), mp 136–138 °C (chloroform). ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −41.0 (t, SCF_3, 3F, $J_{FF} = 5.1$ Hz), −128.0 (m, F-3,5, 2F), −136.0 (m, F-2,6, 2F). ^1H NMR (200.1 MHz, $CDCl_3$): δ 9.4 (broad, $\Delta_{1/2} \approx 25$ Hz). ^{13}C NMR ($CDCl_3$; 50.4 MHz): δ 162.8 (s, C(O)OH), 147.9 (dm, C-2,6, $^1J_{FC} = 253$ Hz), 144.7 (dm, C-3,5, $^1J_{FC} = 258$ Hz), 127.8 (q, SCF_3, $^1J_{FC} = 312$ Hz), 115.3 (t, C-4, $^2J_{FC} \approx 15$ Hz), 108.0 (t, C-1, $^2J_{FC} \approx 20$ Hz). EI-MS, (20 eV): 294 (M^+), 277 (M^+−OH), 212 (M^+-CF_2S), 195 (M^+-CF_2S, –OH). Anal. Calcd for $C_8HF_7O_2S$: C, 32.67; H, 0.34; S, 10.90. Found: C, 32.77; H, 0.15; S, 11.16.