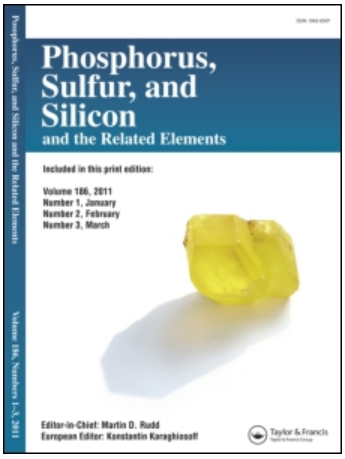


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

NEW STRATEGY FOR THE SYNTHESIS OF THIOLS[1]

Rafail A. Bekker[a]; Vera Ya. Popkova[a]
[a] A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Moscow, Russia

To cite this Article Bekker, Rafail A. and Popkova, Vera Ya.(1996) 'NEW STRATEGY FOR THE SYNTHESIS OF THIOLS[1]', Phosphorus, Sulfur, and Silicon and the Related Elements, 119: 1, 161 — 168
To link to this Article: DOI: 10.1080/10426509608043474
URL: http://dx.doi.org/10.1080/10426509608043474

Phosphorus, Sulfur, and Silicon, 1996, Vol. 1, pp. 161–168
Reprints available directly from the publisher
Photocopying permitted by license only

NEW STRATEGY FOR THE SYNTHESIS OF THIOLS[1]

RAFAIL A. BEKKER and VERA YA. POPKOVA*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Vavilov str. 28, Moscow, 117813 (Russia)

(Received 18 September 1996)

A new, general, one-step method for the synthesis of fluorine-containing thiols is reported. It consists of the reduction of the corresponding sulfenyl chlorides by an excess of hydrogen sulfide in an autoclave at room temperature. The method is notable for the simplicity of execution, the easiness of isolation of the final products in individual state, the absence of by-products, and the high yields.

Keywords: Fluorine-containing thiols; fluorine-containing sulfenyl chlorides; hydrogen sulfide

INTRODUCTION

The role of the thiols as synthons in organic chemistry can scarcely be exaggerated. A large number of reviews, patents, monographs devoted to the synthesis, properties and application of this class of compounds is the best evidence for this.[2] There are presently many approaches to the synthesis of these compounds, however it is safe to say, that of the simple inorganic sulfur derivatives utilized as the reagent in common or direct methods of preparation of thiols, the most widely used is hydrogen sulfide. The methods of synthesis of thiols on the base of hydrogen sulfide can be subdivided into three groups:[2d]

1. The substitution reactions of halogens, hydroxyl, arenesulfonyl or other good leaving groups by a mercapto-group.
2. The addition reactions of hydrogen sulfide to unsaturated bonds.
3. The opening reactions of three-membered heterocyclic compounds (thiiranes, oxiranes, aziridines) by the action of hydrogen sulfide.

*Corresponding author.

In organic chemistry of fluorine the second method is most widely used. In particular, the free radical addition of hydrogen sulfide to fluoroolefins under the influence of X-rays or ultraviolet light appears to be a general method for the preparation of highly fluorinated thiols.[2e] However, it has a number of considerable shortcomings, such as the formation of a mixture of regioisomers in case of addition to unsymmetrical fluoroolefins, the presence of by-products including high-boiling telomers, and some times the dangerously explosive character of the reaction.[3]

We have found one more effective general method of the synthesis of thiols, which employs hydrogen sulfide as a reducing agent. This new method involves the redox transformation of fluorine-containing sulfenyl chlorides into the corresponding thiols.

To our knowledge, earlier there was no method of synthesis of thiols from sulfenyl chlorides.[2,4] On the contrary, thiols were frequently used as starting materials for the synthesis of unfluorinated sulfenyl chlorides.[2c,4] It is probably due to the fact that the direct synthesis of thiols make them in general more easily available than sulfenyl chlorides. Nevertheless, in some particular cases the sulfenyl chloride → thiol transformation may be necessary. Fluorinated sulfenyl chlorides are known to be easily available and are considerably more stable than their fluorine-free analogues.[4b] Therefore, the strategy of the synthesis of thiols *via* sulfenyl chloride → thiol transformation becomes important.

At the beginning we succeeded in finding only one example of the above-mentioned transformation. It was shown that the free-radical reactions of several fluoroalkane- and chlorofluoroalkanesulfenyl chlorides with hydrocarbons (toluene, cyclohexane and butane) lead to a mixture of products in which the thiols were found.[5] It is only in those reactions where the sulfenyl chloride component was represented by perfluoro-tert-butanesulfenyl chloride (**1a**) that the only major products detected were thiol **2a** and a chlorinated hydrocarbon (Scheme 1).

$$(CF_3)_3C-SCl \quad + \quad RH \quad \xrightarrow{h\nu} \quad (CF_3)_3C-SH \quad + \quad RCl$$

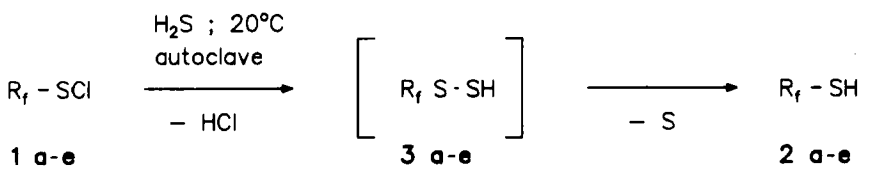
1 a **2 a**

SCHEME 1

In this case, the complete separation of products of the reaction may be achieved by preparative GC. Therefore, the above-mentioned reaction represents a special case and has no practical significance.

RESULTS AND DISCUSSION

In the course of our systematic investigation of the ways of synthesis and reactivity of sulfur-containing fluoroorganic compounds we have discovered that fluorine-containing thiols **2a–e** can be successfully obtained from the corresponding sulfenyl chlorides **1a–e** by the reduction of the latter with excess hydrogen sulfide in an autoclave at room temperature (Scheme 2).



R_f= $(CF_3)_3C-$ (**a**) ;  (**b**) ; $CFClHCF_2-$ (**c**) ;

CF_2ClCH_2- (**d**) ; $CF_3\cdot\underset{|}{C}HCH_2Cl$ (**e**)

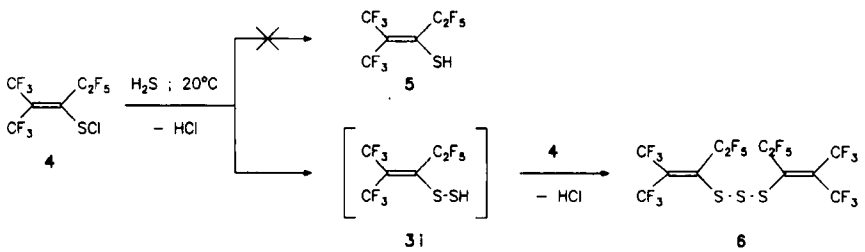
SCHEME 2

The reaction proceeds through the intermediate formation of the less stable hydrodisulfides **3**, which in some cases can be successfully isolated in individual form. However, already on mild heating (20–100 °C) they lose sulfur with the formation of thiols. Thus, compound **3e** can be isolated and subjected to the distillation in vacuum. More strong heating of **3e** (distillation at atmospheric pressure) leads to the corresponding thiol **2e**. Compounds **3a–d** lose sulfur already in the course of the reaction at room temperature.

Thus, we propose a new method of a one-step synthesis of fluorine-containing thiols, which permits to obtain the target products in individual form from the available sulfenyl chlorides. The method is notable for its simplicity and good yields (46–74%). The earlier known methods of preparation of compounds **2a–d**[6–9] are technologically inconvenient and in many cases are of limited applicability. The method proposed by us doesn't rule out the known methods of preparation of fluorine-containing thiols, but will rather serve as an important supplement to them.

When perfluoro-2-methyl-2-penten-3-yl sulfenyl chloride (**4**) was introduced in the above-mentioned reaction the expected enethiol **5** could not be obtained. As a result of the reaction a mixture of products was isolated in which it was possible to identify sulfur and the thermodynamically more stable isomer of

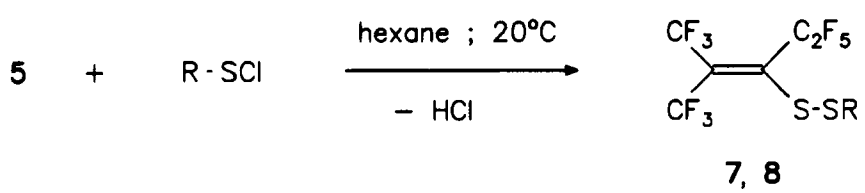
enethiol **5**, 2-trifluoromethyl-2*H*-perfluoropentanethione-3, identical (GLC, NMR) to the known specimen.[6b] If the reaction of sulfenyl chloride **4** with H_2S is carried out by bubbling gaseous H_2S into the reaction mixture rather than in an autoclave, trisulfide **6**, the product of the interaction of the initially formed hydrodisulfide **3i** with the starting sulfenyl chloride **4** is obtained (Scheme 3).



SCHEME 3

This result indicates that the homogeneous interaction of **3i** with sulfenyl chloride **4** (**3i** → **6**) is much faster than the heterogeneous reaction involving gaseous H_2S (**4** → **3i**).

The easiness of interaction of the enethiol **5**, desulfurinated analogue of **3i**, with sulfenyl chlorides was demonstrated in the reactions of **5** with trichloromethanesulfenyl chloride[10] and phenylsulfenyl chloride, which lead to disulfides **7** and **8** respectively (Scheme 4).



SCHEME 4

EXPERIMENTAL

General Methods

^1H and ^{19}F NMR spectra were obtained with a Bruker AC-200 (200.0 and 188.3 MHz) and Perkin-Elmer R-32 (90.0 and 84.6 MHz). TMS was used as a reference standard for ^1H NMR and CF_3COOH as external standard for ^{19}F NMR. IR spectra were recorded on a Zeiss UR-20 spectrophotometer. The purity of the

compounds was monitored by GLC methods on a LKhM-8 MD (model 3) chromatograph using a column (3 m × 4 mm) packed with 20 % QF on Chromaton.

Perfluoro-tert-butanethiol (**2a**)

A mixture of 4.0 g (13.96 mmol) of perfluoro-tert-butanesulfenyl chloride (**1a**)[9] and 11 ml of liquid dry H_2S was shaken in a steel autoclave for 10 h at ~20 °C. The excess of H_2S was removed, and the product was evaporated at 20 °C under reduced pressure (0.5 mmHg), and collected in a trap (−78 °C). Obtained: 2.0 g (60 %) **2a**, m.p. 63–64 °C. ^1H and ^{19}F NMR spectra were in good agreement with those published in ref. 5 and 9.

2-Chloroperfluoro-1-cyclohexene-1-thiol (**2b**)

A mixture of 1.83 g (5.60 mmol) of 2-chloroperfluoro-1-cyclohexen-1-yl sulfenyl chloride (**1b**)[6] and 4.5 ml of liquid dry H_2S was shaken in a steel autoclave for 10 h at ~20 °C. The gaseous products were removed, and the residue was distilled to give 1.08 g (66.3 %) **2b**, b.p. 134–137 °C. ^1H and ^{19}F NMR spectra were in good agreement with those published in ref. 6.

1,1,2-Trifluoro-2-chloroethane-1-thiol (**2c**)

Analogously to the preceding procedure from 4.23 g (22.86 mmol) of 1,1,2-trifluoro-2-chloroeth-1-yl sulfenyl chloride (**1c**)[7] and 10 ml of liquid dry H_2S. After distillation 1.64 g (47.7 %) of **2c** was obtained, b.p. 70–76 °C (compare with that published in ref. 7). ^1H NMR (neat) δ: 3.52 (t, 1H, S*H*, $^3J_{HF}$ = 15.1), 6.30 (dt, 1H, CFCl*H*, $^2J_{HF}$ = 49.0, $^3J_{HF}$ = 5.6). ^{19}F NMR (neat) δ: −0.06 (F_A), −0.34 (F_B) [2F, C*F*^{2}—AB system with additional coupling of each component, $^2J(F_A\text{-}F_B)$ = 235.0, $^3J(F_A\text{-SH})$ = $^3J(F_B\text{-SH})$ = $^3J(F_A\text{-F})$ = $^3J(F_B\text{-F})$ = 15.1, $^3J(F_A\text{-H})$ = $^3J(F_B\text{-H})$ = 5.6], −68.4 (dt, 1F, C*F*ClH, $^2J_{FH}$ = 49.0, $^3J_{FF}$ = 15.1).

2,2-Difluoro-2-chloroethanethiol (**2d**)

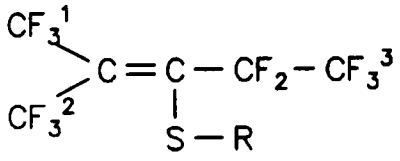
Analogously to the preceding procedure from 12.0 g (90.52 mmol) of 2,2-difluoro-2-chloroethanesulfenyl chloride (**1d**)[8] and 30 ml of liquid dry H_2S. After two distillations 4.4 g (46.3 %) of **2d** was obtained, b.p. 75–77 °C (compare with that published in ref. 8). ^1H NMR (neat) δ: 1.65 (t, 1H, S*H*, $^3J_{HH}$ = 9.0), 2.95 (td, 2H, C*H*$_2$, $^3J_{HF}$ = 11.5, $^3J_{HH}$ = 9.0). ^{19}F NMR (neat) δ: 22.4 (t, C*F*$_2$, $^3J_{FH}$ = 11.5).

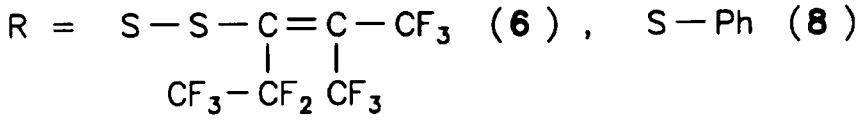
1,1,1-Trifluoro-3-chloropropane-2-thiol (2e)[11]

Analogously to the preceding procedure from 6.45 g (32.41 mmol) of 1,1,1-trifluoro-3-chloroprop-2-yl sulfenyl chloride (**1e**)[11] and 13 ml of liquid dry H_2S. After distillation 5.5 g (86.3 %) of 1-(trifluoromethyl)-2-chloroethyl hydrogen disulfide (**3e**) was obtained, b.p. 38–40 °C (4 mmHg). Analysis: Calc. for $C_3H_4F_3ClS_2$ (196.651): C, 18.32; H, 2.05; F, 28.99; S, 32.61 %. Found: C, 18.22; H, 1.99; F, 28.84; S, 32.73 %. ^{1}H NMR (neat) δ: 3.7 (s, 1H, S*H*), 3.9 (m, 1H, C*H*), 4.4 (m, 2H, CH_2Cl). ^{19}F NMR (neat) δ: 10.2 (d, CF_3, $^3J_{FH}$ = 7.5). At atmospheric pressure, 2.6 g (13.22 mmol) of **3e** were distilled, and the fraction with b.p., up to 115 °C, which was distilled repeatedly, was collected. Obtained: 1.6 g (73.2 %) of **2e**, b.p. 111–113 °C. Analysis: Calc. for $C_3H_4F_3ClS$ (164.584): C, 21.88; H, 2.45; F, 34.63 %. Found: C, 21.69; H, 2.48; F, 34.51 %. IR (ν, cm^{-1}): 2585 (SH), 2975 (CH). ^{1}H NMR (neat) δ: 2.7 (d, 1H, S*H*, $^3J_{HH}$ = 10.0), 4.0 (m, 1H, C*H*), 4.2 (m, 2H, CH_2Cl). ^{19}F NMR (neat) δ: 7.2 (d, CF_3, $^3J_{FH}$ = 7.5).

Bis(perfluoro-2-methyl-2-pentenyl)trisulfide (6)

Dry H_2S gas was passed through 3.0 g (8.61 mmol) of perfluoro-2-methyl-2-penten-3-yl sulfenyl chloride (**4**)[10] until the yellow colour of the reaction mixture appeared. Distillation of the reaction mixture gave 1.5 g (53.0 %) **6**, b.p. 91–92 °C (2 mmHg). Analysis: Calc. for $C_{12}F_{22}S_3$ (658.318): C, 21.89; F, 63.53 %. Found: C, 21.87; F, 63.53 %. ^{19}F NMR (neat) δ: 19.8 (q, 3F, C$F_3{}^2$, $^4J_{FF}$ = 11.6), 18.9 (tqq, 3F, C$F_3{}^1$, $^5J_{FF}$ = 18.8, $^4J_{FF}$ = $^6J_{FF}$ = 11.6), 0.0 (q, 3F, C$F_3{}^3$, $^6J_{FF}$ = 11.6), −23.6 (q, 2F, CF_2, $^5J_{FF}$ = 18.8).





FORMULA 1

Phenyl(perfluoro-2-methyl-2-pentenyl)disulfide (8)

3.11 g (9.90 mmol) of perfluoro-2-methyl-2-pentene-3-thiol (**5**)[6] and 1.4 g (9.61 mmol) of phenylsulfenyl chloride in 15 ml of abs. hexane were stirred at room temperature until the end of the evolution of HCl. Distillation of the reaction mixture gave 2.8 g (69.0 %) **8**, b.p. 74–77 °C (2 mmHg). Analysis: Calc. for $C_{12}H_5F_{11}S_2$ (422.292): C, 34.128; H, 1.19; F, 49.49; S, 15.19 %. Found: C, 34.18; H, 1.06; F, 49.47; S, 15.23 %. ^{1}H NMR (neat) δ: 7.0 (m, Ph). ^{19}F NMR (neat) δ: 20.2 (tqq, 3F, CF_3^1, $^5J_{FF}$ = 18.8, $^4J_{FF}$ = 9.4, $^6J_{FF}$ = 8.5), 19.6 (q, 3F, CF_3^2, $^4J_{FF}$ = 9.4), 0.4 (q, 3F, CF_3^3, $^6J_{FF}$ = 8.5), −23.6 (q, 2F, CF_2, $^5J_{FF}$ = 18.8).

Acknowledgements

Prof. R.A. Bekker 46 years old deceased August 18th 1983. He realized the pioneering synthesis and investigations of properties of perfluoropropen-2-ol—CF_2=C(OH)-CF_3—enol, which is remarkably stable with respect to tautomerization

References and Notes

[1] For previous communication, see: R. A. Bekker, V. Ya. Popkova, G. Ya. Bekker and I. L. Knunyants, *USSR Inventor's Certificate N 1,108,730*, (1984), *Pat. RF N 1,108,730*, *Byull. Izobret.*, (1997).

[2] a) *The Chemistry of the Thiol Group* (Wiley, London-New York-Sydney-Toronto, An Interscience Publication, 1974), Part 1, and 2, ed. S. Patai; b) *Organic Chemistry of Sulfur* (Plenum Press, New York-London, 1977), ed. S. Oae; c) *Sulfur Compounds*, ed. D. Neville Jones, *in Comprehensive Organic Chemistry*, *The Synthesis and Reactions of Organic Compounds* (Pergamon Press, Oxford-New York-Toronto-Sydney-Paris-Frankfurt, 1979), Series ed. D. Barton and W. D. Ollis, v. 3; d) I. V. Koval', *Usp. Khim.*, **62**, 813, (1993) (Russ. ed.); *Russ. Chem. Rev.*, **62**, 769, (1993) (Engl. Transl.) and literature cited therein; e) W. J. Middleton, *Organic Sulfur-Fluorine Compounds*, *in Organic Chemistry of Bivalent Sulfur* (Chemical Publishing Company, INC., New York), ed. E. Emmet Reid, p. 331, (1966).

[3] A. V. Fokin and Yu. N. Studnev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1867, (Russ. ed.), (1982).

[4] a) E. Kühle, *The Chemistry of Sulphenic Acids* (Georg Thieme Publishers, Stuttgart, 1973); b)A. Haas and U. Nieman, *Preparation and Reactions of Perfluorohalogenoorganosulfenyl Halides*, *in Advances in Inorganic Chemistry and Radiochemistry* (Academic Press, INC., New York-San Francisco-London), v. 18, p. 143, (1976); c) *The Chemistry of Sulphenic Acids and Their Derivatives* (Wiley, Chichester, 1990), ed. S. Patai.

[5] J. F. Harris, Jr., *J. Org. Chem.*, **44**, 563, (1979).

[6] a) R. A. Bekker, V. Ya. Popkova and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2175, (Russ. ed.)(1980); *Chem. Abstr.* **94**: 30232k (1981)—incorrect information, see correction in CA File on STN International in 1993; b) R. A. Bekker, V. Ya. Popkova and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2347, (1982)(Russ. ed.); *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **32**, 2066, (1982) (Engl. Transl.).

[7] A. V. Fokin, A. A. Skladnev and I. L. Knunyants, *Doklady Akad. Nauk SSSR*, **138**, 1132, (Russ. ed.)(1961); *Chem. Abstr.*, **55**, 24549e, (1961).

[8] I. L. Knunyants and E. G. Bykhovskaya, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk*, **852**, (Russ.ed.), (1995); *Chem. Abstr.* **5** 9322h, (1956).

[9] B. L. Dyatkin, S. R. Sterlin, L. G. Zhuravkova, B. I. Martynov, E. I. Mysov and I. L. Knunyants, *Tetrahedron*, **29**, 2759, (1973).
[10] V. Ya. Popkova, M. V. Galakhov and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (Russ.ed.), **116**, (1989); *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, (Engl. Transl.), **38**, 104, (1989).
[11] R. A. Bekker, V. Ya. Popkova, L. A. Rozov and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2558 (1984) (Russ. ed.); *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **33**, 2342, (1984) (Engl. Transl.).