Direct Conversion of Thiols to Sulfinyl Chlorides by Sulfuryl Chloride

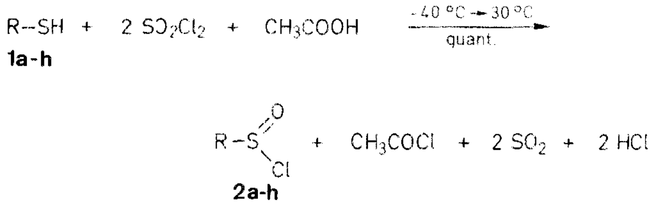
Joo-Hack Youn, Rudolf Herrmann*

Organisch-Chemisches Institut der Technischen Universität München,
Lichtenbergstraße 4, D-8046 Garching, West Germany

Sulfinyl chlorides are prepared in quantitative yield by the reaction of thiols with sulfuryl chloride/acetic acid at low temperature.

The current interest in chiral sulfoxides for the synthesis of natural products[1,2,3] had led to their efficient preparation via the chiral menthyl sulfinates.[4,5] However, the sulfinyl chlorides used for the synthesis of the menthyl sulfinates are generally quite sensitive and unstable, and have to be prepared from the sulfinic acids with thionyl chloride or from the disulfides or thiol esters with chlorine/acetic acid.[6] As only few sulfinic acids are commercially available, we looked for a simple and efficient procedure to convert thiols directly to sulfinyl chlorides. The methods available up to now for this conversion are limited to special cases (mercaptocarboxylic acids)[7] or use chlorine which is difficult to handle and may lead to overoxidation forming sulfonyl chlorides.[8]

The observation that thiols can be oxidized to disulfides by sulfuryl chloride[9] suggested to use the oxidizing and chlorinating properties of this reagent for the preparation of sulfinyl chlorides. We found that, under carefully controlled reaction conditions, the clean and quantitative conversion of thiols (**1**) to sulfinyl chlorides (**2**) takes place according to the following Scheme.



$$\underset{\mathbf{1a\text{-}h}}{R{-}SH} + 2\,SO_2Cl_2 + CH_3COOH \xrightarrow[\text{quant.}]{-40\,°C \to 30\,°C} \underset{\mathbf{2a\text{-}h}}{R{-}S(=O){-}Cl} + CH_3COCl + 2\,SO_2 + 2\,HCl$$

As only volatile and low-boiling by-products are formed, the sulfinyl chlorides (**2**) are obtained in virtually pure state. Due to their high reactivity, they are too sensitive for microanalysis. We therefore converted the new sulfinyl chlorides to the ethyl sulfinates (ethanol/pyridine) which gave satisfactory analytical data.

The reaction proceeds well in the presence of ester groups, but no sulfinyl chloride is obtained from 2-mercaptoethanol. Secondary and primary amides (e.g. $C_6H_5CH_2{-}NH{-}CO{-}CH_2{-}SH$) give mixtures of unidentified products. This indicates that acid-sensitive groups or groups that may react with sulfuryl chloride should be protected during the conversion of the thiol to the sulfinyl chloride.

Thiols, sulfuryl chloride and acetic acid are commercial products and were used without further purification. ^{1}H-NMR spectra were measured with a Jeol PMX 60 instrument.

Sulfinyl Chlorides 2; General Procedure:

A well stirred mixture of the thiol (**1**; 0.50 mol) and acetic acid (30.0 g, 0.50 mol) is cooled to −40 °C. Sulfuryl chloride (141.8 g 1.05 mol) is added dropwise over a period of 30 min. Gas evolution is observed during the addition of the first quarter of the sulfuryl chloride, and the color changes to yellow. Stirring is continued for 30 min at −40 °C, and the mixture then allowed to come to room temperature over a period of 2 h. Gas evolution commences again and the color changes to red. The mixture is warmed at 30 °C until gas evolution ceases (~ 4 h), while the pale yellow color of the sulfinyl chloride appears. Acetyl chloride is distilled off in vacuum to leave the crude sulfinyl chloride in quantitative yield. Alkanesulfinyl chlorides can be distilled in vacuum, while other sulfinyl chlorides, due to danger of explosion,[6] are better transformed to alkyl sulfinates by standard procedures for characterization.

Table. Sulfinyl Chlorides **2** from Thiols **1** and Sulfuryl Chloride

2	R	Yield[a] (%)	b.p. (°C)/torr	Molecular Formula or b.p. (°C)/torr reported	^{1}H-NMR (60 MHz, CDCl$_3$) δ(ppm)
a	C_2H_5	95	67/26	66–67.5/27[11]	1.49 (t, 3H); 3.36 (q, 2H, J = 7.0 Hz)
b	i-C_3H_7	95	49/12	64/17[8]	1.29 (d, 6H); 3.30 (sept, 1H); J = 6.5 Hz)
c	sec-C_4H_9	93	65/15	–[10,e]	1.12 (t, 3H, J = 7.0 Hz); 1.50 (d, 3H, J = 7.0 Hz); 1.83 (m, 2H); 3.13 (m, 1H)
d	$C_6H_5CH_2$	–	[d]	–[11,e]	4.58 (s, 2H); 7.29 (m, 5H)
e	C_6H_5	–	[d]	65/0.012[12]	7.55 (m)
f	4-CH_3C_6H	–	[d]	79/0.012[12]	2.45 (s, 3H); 7.35 (dd, 4H)
g	$CH_3O_2C{-}CH_2$	–	[b,d]	$C_3H_5ClO_3S$ (156.5)	3.97 (s, 3H); 4.58 (s, 2H)
h	$C_2H_5O_2C{-}CH_2$	–	[c,d]	$C_4H_7ClO_3S$ (170.6)	1.37 (t, 3H); 4.33 (q, 2H, J = 7.0 Hz); 4.47 (s 2H)

[a] Yield of distilled product.

[b] For characterization, product **2g** was converted into methyl ethoxysulfinylacetate by reaction with ethanol/pyridine at 20 °C (15 h); yield: 72% b.p. 70 °C/0.4 torr.

$C_5H_{10}O_4S$	calc.	C 36.14	H 6.06
(166.2)	found	36.36	5.91

^{1}H-NMR (CDCl$_3$): δ = 1.37 (t, 3H); 3.78 (s, 5H); 4.13 ppm (q, 2H, J = 7.0 Hz).

[c] For characterization, product **2h** was converted into ethyl ethoxysulfinylacetate by reaction with ethanol/pyridine at 20 °C (15 h); yield: 75% b.p. 70 °C/0.1 torr.

$C_6H_{12}O_4S$	calc.	C 39.99	H 6.71
(180.2)	found	40.27	6.67

^{1}H-NMR (CDCl$_3$): δ = 1.32 (t, 3H); 1.38 (t, 3H); 3.75 (s, 2H); 4.17 (q, 2H); 4.27 ppm (q, 2H).

[d] Not distilled due to danger of explosion.

[e] B.p. not reported.

The authors thank Prof. Dr. Ivar Ugi, TU München, for supporting this work.

Received: 31 January 1986
(Revised form: 15 April 1986)

(1) Solladié, G. *Synthesis* **1981**, 185.
(2) Colonna, S., Annunziata, R., Cinquini, M. *Phosphorus Sulphur* **1981**, *10*, 197.
(3) Solladié, G. *Chimia* **1984**, *38*, 233.
(4) Andersen, K.K. *Tetrahedron Lett.* **1962**, 93.
(5) Drabowicz, J., Bujnicki, B., Mikołajczik, M. *J. Org. Chem.* **1982**, *47*, 3325.
(6) Kee, M.L., Douglass, I.B. *Org. Prep. Proced.* **1970**, *2*, 235.
(7) Vasileva, T.P., Linkova, M.G., Kildisheva, O.V., Knunyants, I.L. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1981**, 159.
(8) Douglass, I.B., Farah, B.S., Thomas, E.G. *J. Org. Chem.* **1961**, *26*, 1996.
(9) Courant, E., v. Richter, V. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 3178.
(10) Venier, C.G., Barager, H.J. *J. Chem. Soc. Chem. Commun.* **1973**, 319.
(11) Hilditch, T.P., Smiles, S. *Ber. Dtsch. Chem. Ges.* **1908**, *41*, 4113.
Douglass, I.B., Norton, R.V. *J. Org. Chem.* **1968**, *33*, 2104.
(12) Herbrandson, H.F., Dickerson, R.T., Weinstein, J. *J. Am. Chem. Soc.* **1956**, *78*, 2576.