

The Use of *N,N*-Dimethylformamide-Sulfonyl Chloride Complex for the Preparation of Thiophenesulfonyl Chlorides

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Synopsis. A 1:1 *N,N*-dimethylformamide-SO₂Cl₂ complex was found to be a useful agent for the one-step preparation of thiophenesulfonyl chlorides.

Thiophenesulfonyl chlorides, key intermediates of the syntheses of sulfur derivatives of thiophene, have been mostly prepared by the chlorosulfonation of thiophenes with chlorosulfuric acid.¹⁾ In the reaction of acid-sensitive thiophenes, however, polymerization and the rearrangement and/or elimination of the substituent such as halogen on the thiophene ring disturb the formation of the desired sulfonyl chlorides. In addition, the thiophenesulfonic acids are formed as the main products in some cases, and further tedious procedures are needed for converting the sulfonic acids to the sulfonyl chlorides. It is also the case with an alternative method *via* sulfonation using SO₃-organic compound adducts.²⁾

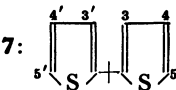
It has been briefly reported by Kojtcheff *et al.* that a 1:1 *N,N*-dimethylformamide (DMF)-SO₂Cl₂ complex serves as a chlorosulfonating agent depending on the substrate.³⁾ Despite the potential utility, little systematic study of the direct chlorosulfonation using DMF-SO₂Cl₂ complex seems to have been made. On searching for a simple and convenient procedure for the preparation of thiophenesulfonyl chlorides, we studied the reactions of some thiophene derivatives with the complex.

The reaction procedure simply consists of heating a mixture of the thiophene derivatives and the complex at an appropriate temperature for 1–3 h.

The results are summarized in Table 1.

By this procedure, all thiophene derivatives examined, except 2-methoxy- (**1d**), 2-(1-cyclohexenyl)- (**1j**), and 2-acetylthiophenes, gave the corresponding sulfonyl chlorides as the main products. It is noteworthy

TABLE 1. REACTION OF THIOPHENE DERIVATIVES WITH DMF-SO₂Cl₂ COMPLEX

Substituent R	Reaction Conditions ^{a)}	Product	Yield/ % ^{b)}	Bp, °C/mmHg or Mp, °C(lit.)
1a: H	A	2a: 2-SO ₂ Cl	79	bp 88–93/2.5(123–124/14 ^{1a)} , 82–84/2 ^{1b)} amide mp 141–142(146–147 ^{2a)} , 141–142 ^{1a)})
1b: 2-CH ₃	A	2b: 2-CH ₃ , 5-SO ₂ Cl	56	bp 105–110/4(96–98/3 ^{1d)}) amide mp 117–118(119–119.5 ^{1d)})
1c: 3-CH ₃	A	2c: 3-CH ₃ , 2-SO ₂ Cl } 2'c: 4-CH ₃ , 2-SO ₂ Cl } c)	78	bp 100–108/5(98–99/0.5 for 2c ^{1e)}) amide mp 120–143(146 for 2c ^{1e)})
1d: 2-CH ₃ O	B	3d: 2-CH ₃ O, 5-CHO	47	bp 97–99/4(79–81/0.9 ⁷⁾) acid mp 161.5–162.5(162–163 ⁷⁾)
1e: 2-Cl	A	2e: 2-Cl, 5-SO ₂ Cl	60	bp 101–102/3(mp 28 ^{1g)}) amide mp 113–114(116 ^{1e)})
1f: 2-Br	A	2f: 2-Br, 5-SO ₂ Cl	60	bp 105–110/4(mp 44–46 ^{1h)}) amide mp 138–139(144 ^{1g)} , 141 ^{2b)})
1g: 2-I	A	2g: 2-I, 5-SO ₂ Cl	43	mp 49–50(51–52 ^{1h)}) amide mp 162–163
1h: 2-C ₆ H ₅ CH ₂	C	2h: 2-C ₆ H ₅ CH ₂ , 5-SO ₂ Cl 3h: 2-C ₆ H ₅ CH ₂ , 5-CHO	54 10	(165 ^{1h)} , 163–164 ^{2a)}) oil; amide mp 98–99 mp 25–26(27.5–28 ⁸⁾) acid mp 128.5–129.5(129 ⁸⁾)
1i: 2-C ₆ H ₅	A	2i: 2-C ₆ H ₅ , 5-SO ₂ Cl 3i: 2-C ₆ H ₅ , 5-CHO	41 21	mp 86–86.5; amide mp 221–222 mp 93.5–94(93–93.5 ⁹⁾)
1j: 2-C ₆ H ₉ ^{d)}	B	3j: 2-C ₆ H ₉ , 5-CHO	7	mp 65.5–66
1k: 2-COOCH ₃	D	2k: 2-COOCH ₃ , 5-SO ₂ Cl } 2'k: 2-COOCH ₃ , 4-SO ₂ Cl } c)	9	oil; amide mp 149–151
1l: 2,5-(CH ₃) ₂	A	2l: 2,5-(CH ₃) ₂ , 3-SO ₂ Cl	66	bp 106–108/3(115–130/2.5 ^{1f)}) amide mp 138–139(138.5–140.5 ^{1f)})
7: 	E	8: 5-SO ₂ Cl 9: 5,5'-(SO ₂ Cl) ₂ 10: 5,5'-(CHO) ₂ 11: 5-CHO, 5'-SO ₂ Cl	23 30 4 12	mp 69–70; amide mp 61.5–62.5 mp 118–119; amide mp 164–165 mp 86.5–87.5 mp 52.5–53.5; anilide mp 125–126

a) Unless otherwise noted, substrate/DMF-SO₂Cl₂ = 1/1.3 (mole ratio). A: 95–98 °C, 1 h. B: 50–60 °C, 1 h. C: 80–85 °C, 1 h. D: 115–120 °C, 3 h. E: 65–70 °C, 1.5 h, substrate/DMF-SO₂Cl₂ = 1/2.6. b) Isolated yield based on the substrate used. c) 2c/2'c = 90/10 (NMR). Amide, Anal. (C₆H₇O₂NS₂) C, H. d) 1-cyclohexenyl. e) Amide, Anal. (C₆H₇NO₄S₂) C, H.

that methylthiophenes (**1b** and **1c**), which were expected to be much more reactive than anisole⁴) and to yield the aldehydes,³) afforded the sulfonyl chlorides. With 2-iodothiophene (**1g**), a replacement of the iodine atom by a chlorosulfonyl group was observed, but to a lesser extent than by the chlorosulfuric acid procedure.^{1b}) In some cases, the corresponding aldehydes were produced as the by-products in yields of up to *ca.* 20%, which could be easily separated from the sulfonyl chlorides by usual methods. The reaction of methyl 2-thiophenecarboxylate (**1k**) was attained only with difficulty, affording a mixture of the two isomeric sulfonyl chlorides (**2k** and **2'k**) in low yield.

Repeated attempts to chlorosulfonate **1d** and **1j** with the complex gave only tars, and when the reactions were carried out under mild conditions, only the aldehydes (**3d** and **3j**) were isolated from the reaction products. The results offer a sharp contrast with those of anisole³) and styrene,⁵) which were chlorosulfonated with the complex in the ring and in the side chain, respectively. 2-Acetylthiophene reacted easily with the complex to give unidentified materials. In this case DMF-SO₂Cl₂ complex probably functioned as a chloroformylating agent, and 2-acetylthiophene underwent the reaction in the side chain as in the Vilsmeier reaction.^{6,10}) Actually, the reaction of cyclohexanone with the complex was found to afford 2-chlorocyclohex-1-enecarbaldehyde in *ca.* 40% yield.

In conclusion, the DMF-SO₂Cl₂ procedure is particularly useful for the preparation of several thiophenesulfonyl chlorides. The yields are approximately equal or superior to the previously reported ones. The principal advantages of this procedure over the conventional ones are the operational simplicity, one-step procedure, and the use of easy-to-handle reagents.

Experimental

All melting and boiling points are uncorrected. The IR spectra were obtained on a Hitachi EPI-S2 spectrometer, and the NMR spectra on Hitachi R-22 spectrometer at 90 MHz using TMS as an internal reference.

Reaction of Thiophene (1a) with DMF-SO₂Cl₂ Complex (Typical Procedure). Freshly distilled SO₂Cl₂ (17.6 g, 0.13 mol) was added dropwise with shaking to ice-cooled DMF (9.5 g, 0.13 mol); the temperature was kept below 25 °C during the addition. The hygroscopic solid complex, thus formed within 10 min, was held at the same temperature for additional 30 min. Thiophene (**1a**; 8.4 g, 0.1 mol) was added to the complex and the mixture was heated on a water-bath at 95–98 °C for 1 h with occasional shaking. The viscous brown mixture was cooled, poured into ice-water, and then extracted with CHCl₃. The CHCl₃ solution was washed successively with water, 5% NaHCO₃ solution, and water and dried. Evaporation of the solvent left a liquid, which was distilled *in vacuo* to give 2-thiophenesulfonyl chloride (**2a**; 13.5 g, bp 88–93 °C/2.5 mmHg (1 mmHg ≈ 133.322 Pa)).

Reaction of 2-Phenylthiophene (1i) with DMF-SO₂Cl₂ Complex (Typical Procedure). 2-Phenylthiophene (**1i**; 3.2 g, 0.02 mol) was heated with 1.3 molar equivalent of DMF-SO₂Cl₂ complex at 95–98 °C on a water-bath for 1 h. Water was added to the cooled reaction mixture. The products were extracted with CHCl₃. The combined extracts were washed with water and dried. After evaporating the solvent, the residue was chromatographed (silica gel/

hexane-CHCl₃ (1:3)) to give 5-phenyl-2-thiophenesulfonyl chloride (**2i**; 2.1 g, mp 86–87 °C) and 5-phenyl-2-thiophenecarbaldehyde (**3i**; 0.3 g, mp 93–94 °C). The aqueous layers were concentrated under reduced pressure to *ca.* 10 ml and extracted with ether. Evaporation of the solvent from the extracts gave another crop of **3i** (0.5 g, mp 91–93 °C). **2i**: IR (CCl₄) 1175, 1385 cm⁻¹ (ν_{SO₂}). NMR (CCl₄) δ=7.23 and 7.75 (1H, d each, J_{3,4}=4.0 Hz, 3-H and 4-H), 7.3–7.7 (5H, m, phenyl). Anal. (C₁₀H₇ClO₂S₂) C, H. Sulfonamide: Anal. (C₁₀H₉NO₂S₂) C, H.

5-Benzyl-2-thiophenesulfonyl Chloride (2h): IR (CHCl₃) 1175, 1385 cm⁻¹ (ν_{SO₂}). NMR (CCl₄) δ=6.86 and 7.70 (1H, d each, J_{3,4}=3.9 Hz, 3-H and 4-H), 7.1–7.5 (5H, m, phenyl), 4.20 (2H, s, CH₂). Sulfonamide: Anal. (C₁₁H₁₁NO₂S₂) C, H.

5-(1-Cyclohexenyl)-2-thiophenecarbaldehyde (3j): IR (CCl₄) 1680 cm⁻¹ (ν_{CO}). NMR (CDCl₃) δ=9.75 (1H, s, CHO), 7.02 and 7.60 (1H, d each, J_{3,4}=4.1 Hz, 3-H and 4-H), 6.42 (1H, m, cyclohexenyl CH), 1.5–2.6 (8H, m, cyclohexenyl CH₂). Anal. (C₁₁H₁₂OS) C, H.

2-(5-Chlorosulfonyl-2-thienyl)-2-(2-thienyl)propane (8): IR (KBr) 1175, 1380 cm⁻¹ (ν_{SO₂}). NMR (CDCl₃) δ=7.76 (1H, d, J_{3,4}=4.0 Hz, 4-H), 7.92 (1H, ABXq, 5'-H), 6.9–7.1 (3H, m, 3-H, 3'-H and 4'-H), 1.88 (6H, s, C(CH₃)₂). Anal. (C₁₁H₁₁ClO₂S₃) C, H. Sulfonamide: Anal. (C₁₁H₁₃NO₂S₃) C, H.

2,2-Bis(5-chlorosulfonyl-2-thienyl)propane (9): IR (KBr) 1170, 1380 cm⁻¹ (ν_{SO₂}). NMR (CDCl₃) δ=7.76 and 7.00 (2H, d each, J_{3,4}=4.0 Hz, 4-H and 4'-H, and 3-H and 3'-H), 1.93 (6H, s, C(CH₃)₂). Anal. (C₁₁H₁₀Cl₂O₄S₄) C, H. Sulfonamide: Anal. (C₁₁H₁₄N₂O₄S₄) C, H.

2,2-Bis(5-formyl-2-thienyl)propane (10): IR (KBr) 1660 cm⁻¹ (ν_{CO}). NMR (CDCl₃) δ=9.86 (2H, s, CHO), 7.71 and 7.08 (2H, d each, J_{3,4}=4.2 Hz, 4-H and 4'-H, and 3-H and 3'-H), 1.89 (6H, s, C(CH₃)₂). Anal. (C₁₃H₁₂O₂S₂) C, H.

2-(5-Formyl-2-thienyl)-2-(5-chlorosulfonyl-2-thienyl)propane (11): IR (KBr) 1180, 1385 cm⁻¹ (ν_{SO₂}), 1670 cm⁻¹ (ν_{CO}). NMR (CDCl₃) δ=9.91 (1H, s, CHO), 7.82 and 7.74 (1H, d each, J_{3,4}=4.0 Hz, 4-H and 4'-H), 7.11 and 7.03 (1H, d, J_{3,4}=4.0 Hz, 3-H and 3'-H), 1.91 (6H, s, C(CH₃)₂). Anal. (C₁₂H₁₁ClO₃S₃) C, H. Sulfonanilide: Anal. (C₁₈H₁₇NO₃S₃) C, H.

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