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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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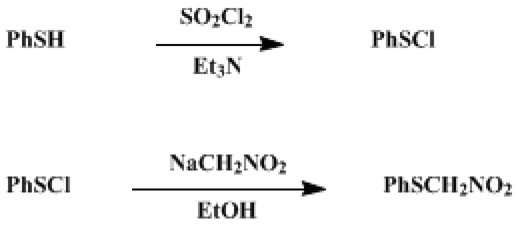
(PHENYLTHIO)NITROMETHANE

[Benzene, [(nitromethyl)thio]-]



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Checked by Zhou Zu-liang and Ekkehard Winterfeldt.

1. Procedure

Caution: Thiophenol (stench!!) and sulfuryl chloride are highly toxic. Steps A and B should be carried out in an efficient fume hood while wearing gloves and adequate eye protection. Sodium nitromethylate is explosive when dry and should be handled only as a slurry.

A. *Phenylsulfenyl chloride.* A 250-mL, three-necked, round-bottomed flask, fitted with a nitrogen inlet, a pressure-equalizing 125-mL dropping funnel, and a magnetic stirring bar, is charged with thiophenol (21 mL) (Note 1), dry triethylamine (0.25 mL), and dry pentane (100 mL) (Note 2) under a blanket of nitrogen. The remaining neck of the flask is stoppered and the nitrogen is allowed to sweep gently through the flask and out of the pressure-equalizing dropping funnel. The flask and its contents are cooled to 0°C with an ice bath and stirring is begun. The dropping funnel is charged with sulfuryl chloride (19 mL) (Note 1). The sulfuryl chloride is added dropwise over a 1-hr period to the chilled thiophenol solution with stirring. During this addition, a thick layer of white solid forms. It gradually dissolves as it is broken down. After the addition is complete, the ice bath is removed and the mixture is allowed to stir for 1 hr longer while slowly warming to room temperature. During the course of the addition and subsequent stirring, the clear, pale-yellow solution becomes dark orange-red. The dropping funnel is replaced with an outlet adapter connected to a vacuum pump and the nitrogen inlet is exchanged for a ground glass stopper. The pentane and excess sulfuryl chloride are removed under reduced pressure at room temperature. The outlet adapter is replaced by a short-path distillation apparatus adapted for use under reduced pressure. The oily red residue is distilled to give phenylsulfenyl chloride as a blood-red liquid (26 g, 87%), bp 41–42°C (1.5 mm) (Note 3). This compound is stored under nitrogen until used in Part B (Note 4).

B. *(Phenylthio)nitromethane.* Freshly cut sodium metal (4.8 g) is added to absolute ethanol (100 mL) in a 500-mL Erlenmeyer flask with a ground-glass joint and allowed to react until the metal is completely consumed (Note 5). To this mixture is added a solution of nitromethane (12 g) (Note 6) in absolute ethanol (100 mL) with swirling. The phenylsulfenyl chloride (prepared earlier) is quickly poured into a 1000-mL, three-necked, round-bottomed flask fitted with a mechanical stirrer, a nitrogen inlet/outlet adapter, and a calcium chloride drying tube, and is diluted with dry tetrahydrofuran (THF) (250 mL) (Note 7). Stirring is begun, the drying tube is removed, and the sodium nitromethane–ethanol slurry is added quickly in one portion to the THF solution (Note 8). The deep-red solution immediately turns yellow and stirring is continued for a further 10 min. The reaction mixture consists of solid and liquid. It is dissolved in 200 mL of a 1 *N* sodium hydroxide solution and poured into a 1000-mL separatory funnel. Dichloromethane (200 mL) is added (Note 9), the aqueous layer (lower layer) is separated, and the organic layer further extracted with 1 *N* sodium hydroxide (2 × 100 mL) (Note 10). The combined aqueous layers are washed with dichloromethane (500 mL) and acidified to pH 3 using 1 *N* hydrochloric acid. The brown organic layer that appears is separated, diluted with 50 mL of dichloromethane, dried over magnesium sulfate, filtered, and concentrated at water aspirator pressure to give 18–19 g (60–65%) of crude (phenylthio)nitromethane as an orange-red oil. This material is of sufficient purity for many purposes. Further purification may be effected by distilling at reduced pressure to give (phenylthio)nitromethane (14 g, 50%) as a pale-yellow oil, bp 85–95°C at 0.05 mm (Note 11),(Note 12),(Note 13),(Note 14).

2. Notes

1. Thiophenol (97%) and sulfuryl chloride (97%) were obtained from the Aldrich Chemical Company, Inc. and used without further purification.
2. Both pentane and triethylamine were obtained from the Aldrich Chemical Company, Inc. Before use they were dried over sodium wire and distilled from fresh sodium wire onto Linde 4A molecular sieves under an atmosphere of nitrogen.
3. The submitters report isolated yields of phenysulfenyl chloride of 82–92%.
4. Phenylsulfenyl chloride decomposes rapidly in moist air, and should be handled and stored under dry nitrogen.
5. The reaction is exothermic; cooling in an ice bath may be necessary to prevent the ethanol from refluxing.
6. Nitromethane was obtained from the Eastman Kodak Chemical Company and used without further purification.
7. Tetrahydrofuran was obtained from the Baker Chemical Company and distilled from sodium benzophenone ketyl before use.
8. The submitters preferred to transfer the phenylsulfenyl chloride via cannula. The sodium nitromethane–ethanol slurry is added by attaching the Erlenmeyer flask containing it to the reaction flask via an angle adapter and then simply inverting the Erlenmeyer flask. In either method additional absolute ethanol may be necessary to complete the latter addition.
9. Dichloromethane was purchased from the Baker Chemical Company and used without further purification.
10. The checkers used sodium hydroxide (3 × 100 mL) in one run, which improved the yield by about 5%.
11. Gases are evolved during the distillation.
12. A pump of sufficient capacity must be used to maintain reduced pressure of at least 0.10 mm or extensive decomposition results.
13. (Phenylthio)nitromethane has the following properties: ^{1}H NMR ($CDCl_3$, 90 MHz) δ: 5.45 (s, 2 H, CH_2), 7.25–7.5 (m, 5 H, aromatic); IR (film) cm^{-1}: 3060 m, 3025 m, 2960 m, 2905 m, 1960 w, 1885 w, 1810 w, 1550 s, (NO_2), 1485 s, 1475 s, 1440 s, 1390 s, 1355 s, (NO_2), 1260 s, 1185 s, 1070 m, 1025 m, 1005 w, 900 m, 805 m, 745 s, 690 s.
14. *Storage and handling of (phenylthio)nitromethane.* Although (phenylthio)-nitromethane will slowly decompose at room temperature, the submitters have found that the compound may be stored essentially unchanged in a freezer at −25°C. Since it has an unpleasant odor, it is best handled in a well-ventilated hood; any spillage may be cleaned up with commercial bleach.

3. Discussion

(Phenylthio)nitromethane is a convenient reagent for the synthesis of derivatives of 3-methylfuran,[2] for the preparation of α-substituted phenylthio esters via the homologation of aldehydes,[3] and for the preparation of bicyclic β-lactams from monocyclic precursors.[4] This method is an adaption of Seebach's procedure.[5] Alternatively, (phenylthio)nitromethane may be prepared from the nitration of the dianion derived from (phenylthio)acetic acid[2] or from ethyl nitroacetate and *N*-(phenylthio)morpholine.[6] Neither of these procedures are as convenient on a large scale.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 9, 82
- Org. Syn. Coll. Vol. 9, 207

References and Notes

1. Department of Chemistry, Northwestern University, Evanston, IL 60201. Present address: Department of Chemistry, Colorado State University, Ft. Collins, CO 80523.
2. Miyashita, M.; Kumazawa, T.; Yoshikoshi, A. *J. Org. Chem.* **1980**, *45*, 2945.
3. Barrett, A. G. M.; Graboski, G. G.; Russell, M. A. *J. Org. Chem.* **1986**, *51*, 1012.
4. Barrett, A. G. M.; Graboski, G. G.; Russell, M. A. *J. Org. Chem.* **1985**, *50*, 2603.
5. Seebach, D.; Lehr, F. *Helv. Chim. Acta* **1979**, *62*, 2239.
6. Bordwell, F. G.; Bartmess, J. E. *J. Org. Chem.* **1978**, *43*, 3101.

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sodium benzophenone ketyl

phenysulfenyl chloride

phenylthio esters

sodium nitromethane

ethanol (64-17-5)

calcium chloride (10043-52-4)

hydrochloric acid (7647-01-0)

sodium hydroxide (1310-73-2)

nitrogen (7727-37-9)

sulfuryl chloride (7791-25-5)

sodium (13966-32-0)

Pentane (109-66-0)

Nitromethane (75-52-5)

dichloromethane (75-09-2)

Thiophenol (108-98-5)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

triethylamine (121-44-8)

ethyl nitroacetate (626-35-7)

3-Methylfuran (930-27-8)

Phenylsulfenyl chloride (931-59-9)

(Phenylthio)nitromethane,
Benzene, [(nitromethyl)thio]-,
(phenylthio)-nitromethane (60595-16-6)

Sodium nitromethylate

(phenylthio)acetic acid (103-04-8)

N-(phenylthio)morpholine