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.*
**THIATION WITH 2,4-BIS(4-METHOXYPHENYL)-1,3,2,4-DITHIADIPHOSPHETANE 2,4-DISULFIDE: N-METHYLTHIOPYRROLIDONE**

\[\text{[2-Pyrrolidinethione, 1-methyl-]}\]

Checked by Clayton H. Heathcock, Mark Sanner, and Terry Rosen.

### 1. Procedure

**Caution!** Preparation of 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide must be carried out in an efficient hood because hydrogen sulfide is evolved. Also, benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A. **2,4-Bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (1)**. A dry 1-L, three-necked, round-bottomed flask, fitted with a reflux condenser, mechanical stirrer, and ground-glass stopper, is charged with 111.0 g (0.25 mol) of phosphorus sulfide, P₄S₁₀ (Note 1) and 270 g (2.5 mol) of anisole (Note 1). Stirring is commenced and the mixture is heated at reflux temperature by use of a heating mantle. After 1 hr, the solution is homogeneous and after a second hour 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (1) begins to precipitate. The reaction mixture is allowed to cool to room temperature and the precipitate is filtered (Note 2) and washed with anhydrous ether (2 × 50 mL) and 50 mL of anhydrous chloroform (free of alcohols) to yield 160–165 g (79–82%) of pale-yellow crystals, mp 228°C (Note 3) and (Note 4).

B. **N-Methylthiopyrrolidone (2)**. A 200-mL, three-necked, round-bottomed flask is fitted with a rubber septum, thermometer, magnetic stirring bar, and reflux condenser equipped with a nitrogen bubbler. The flask is charged with 19.8 g (19.3 mL, 0.20 mol) of N-methylpyrrolidone (Note 5) and 40.4 g (0.10 mol) of 1, whereupon the temperature of the reaction mixture increases to 75–80°C. After 5 min, 35 mL of benzene (Note 6) is added by syringe and the mixture is stirred while being brought to reflux (Note 7). The mixture is heated at reflux for 2 hr (Note 8) and then cooled to room temperature, whereupon it again becomes heterogeneous. The benzene is removed with the aid of a rotary evaporator and the resulting yellow slurry is distilled under reduced pressure through a 5-cm Vigreux column to provide 23.0 g (100%) of N-methylthiopyrrolidone (2) as a yellow liquid, bp 94–97°C/0.03 mm (Note 9).

### 2. Notes

1. Commercial phosphorus sulfide, P₄S₁₀, is used without purification. Checkers used P₄S₁₀ from Matheson, Coleman and Bell and from Alfa Products, Morton Thiokol, Inc. Best results (yield, melting
point) were obtained with the Alfa sample, mp 291–295°C.
2. Excess anisole (137 g) can be recovered by distillation of the filtrate.
3. The product is somewhat hygroscopic and should be stored in an airtight container. It is also available as Lawesson's reagent from Aldrich, Fluka, and from Merck–Schuchard.
4. The checkers obtained 176 g (87%) of 1, mp 228–231°C.
5. Commercial material from the Aldrich Chemical Company was stored over Linde 4A molecular sieves.
6. Benzene was distilled from and stored over sodium wire.
7. During this operation most of the yellow solid gradually dissolves, affording a clear yellow solution with small amounts of suspended solid. When reflux begins, the internal temperature of the reaction mixture is 95°C.
8. The reaction time can be decreased to 3 min by the use of toluene as solvent.
9. The purified product freezes when stored in a refrigerator. The spectral properties are as follows: 1H NMR (CDCl3) δ: 2.07 (quintet, 2 H, J = 7), 3.03 (t, 2 H, J = 7), 3.29 (s, 3 H), 3.77 (t, 2 H, J = 7). IR (neat): 1520 cm⁻¹.

3. Discussion

A variety of thiating reagents are known: H₂S,² H₂S/HCl,³ H₂S₂/HCl,⁴ (Et₂Al)₂S,⁵ (EtAlS)₆,⁶ SiS₂,⁷ B₂S₃,⁷ PCl₅/Al₂S₃/Na₂SO₄,⁸ Na₂S/H₂SO₄,⁹ P₂S₅,¹⁰ P₂S₅/Pyridine,¹¹ P₂S₅/NEt₃,¹² P₂S₅/NaHCO₃,¹³ RPS (OR)²,¹⁴ PSClₓ(NMe₂)ₓ⁻ₓ (X = 0–3),¹⁵ and SCNCOOEt.¹⁶ The reagent described here, 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (1),¹⁷ offers a number of advantages as a thiating reagent. It is easily prepared in a simple one-step procedure employing commercially available starting materials. It has a satisfactory shelf life, provided it is protected from moisture. In contrast to commercial P₂S₅, compound 1 is a well-defined reagent that gives reproducible results, usually in high yield. Under defined conditions, certain selectivity has been observed.¹⁸,¹⁹,²⁰ Other methods for the preparation of analogs of 1 have been described.¹¹,²²,²³

The thiation procedure described here²⁴ is an example of a general synthetic method for the conversion of carbonyl to thiocarbonyl groups. Similar transformations have been carried out with ketones,²⁵ carboxamides,²⁶,²⁷,²⁸,²⁹,³⁰ esters,³¹,³² thioesters,³¹ lactones,¹⁸,³³ thiolactones,¹⁸ imides,²⁴ enaminones,³⁴ and protected peptides.³⁵

References and Notes

Appendix

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

Benzene (71-43-2)

ether (60-29-7)

chloroform (67-66-3)

hydrogen sulfide (7783-06-4)

Anisole (100-66-3)

toluene (108-88-3)

sodium wire (13966-32-0)

N-methylpyrrolidone (872-50-4)

2-Pyrrolidinethione, 1-methyl-,
N-Methylthiopyrrolidone (10441-57-3)

2,4-BIS(4-METHOXYPHENYL)-1,3,2,4- DITHIADIPHOSPHETANE 2,4-DISULFIDE,
2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (19172-47-5)

phosphorus sulfide

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