



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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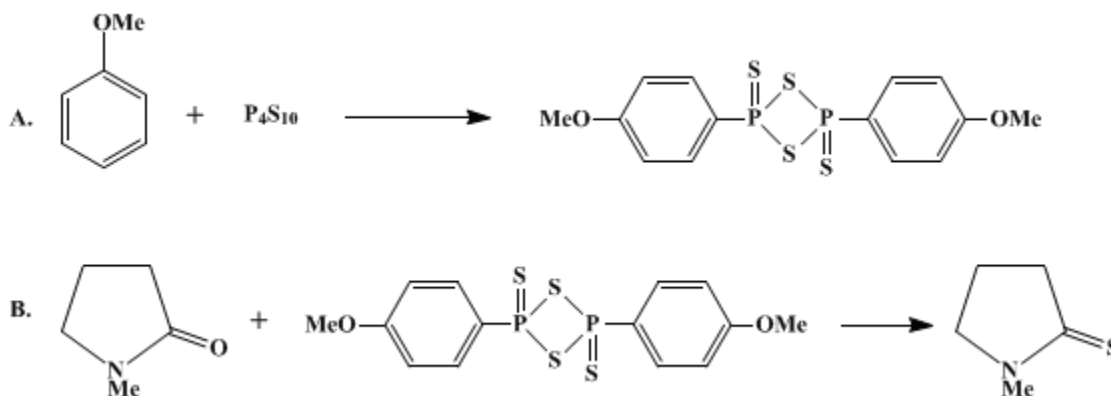
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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

[2-Pyrrolidinethione, 1-methyl-]



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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.
- Excess anisole (137 g) can be recovered by distillation of the filtrate.
 - 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.
 - The checkers obtained 176 g (87%) of **1**, mp 228–231°C.
 - Commercial material from the Aldrich Chemical Company was stored over Linde 4A molecular sieves.
 - Benzene was distilled from and stored over sodium wire.
 - 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.
 - The reaction time can be decreased to 3 min by the use of toluene as solvent.
 - 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)_{*n*},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)¹,¹⁴ PSCl_{*x*} (NMe₂)_{3-*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 P₄S₁₀, 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.^{21,22,23}

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 enamines,³⁴ and protected peptides.³⁵

References and Notes

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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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