



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at [http://www.nap.edu/catalog.php?record\\_id=12654](http://www.nap.edu/catalog.php?record_id=12654)). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

*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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## ***p*-CHLOROPHENOXYMETHYL CHLORIDE**

[Anisole, *p*-*a*-dichloro-]



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### 1. Procedure

*This preparation must be carried out in efficient hood.*

A 250-ml. round-bottomed flask with a side arm is equipped with a distillation head and condenser. The receiving flask is attached to the condenser with an adapter, and the exit from the flask goes to a bubble counter containing high-boiling petroleum ether. A thermometer is inserted in the side arm of the distillation flask, and it reaches to the bottom. With exclusion of moisture, 147 g. (0.704 mole) of phosphorus pentachloride and 100 g. (0.704 mole) of *p*-chloroanisole are added to the flask. The flask is heated in an oil bath; the reaction begins when the inside temperature reaches 120° and occurs rapidly at 140°. The temperature is raised to 160° over a period of 2 hours, thereby distilling the phosphorus trichloride (Note 1). After the gas evolution subsides, the reaction mixture is heated to 175° for a short time. About 73–75 g. of phosphorus trichloride is collected.

The residue is distilled through a 30-cm. column packed with glass beads giving 10 g. of a fraction, b.p. 85–105° (10 mm.), containing mainly *p*-chloroanisole, and 85–99 g. (68–80%) of *p*-chlorophenoxyethyl chloride, b.p. 105–108° (10 mm.),  $n_D^{25} = 1.5496$ , m.p. 28–29° (Note 2), (Note 3). The n.m.r. spectrum [ $\text{CCl}_4$ ,  $(\text{CH}_3)_4\text{Si}$  reference] had bands at  $\delta$  5.6 (*s*, 2H) and 6.6–7.3 p.p.m.

### 2. Notes

1. Some phosphorus pentachloride may solidify in the upper part of the condenser. This may be removed by rotating the condenser.
2. The literature values are b.p. 120–124 (18 mm.), m.p. 29–30°.<sup>2</sup>
3. Gas chromatography analysis using a silicone gum column indicated the product to be 97% pure.

### 3. Discussion

Aryloxymethyl chlorides may be prepared by the reaction of sodium aryloxymethanesulfonates with phosphorus pentachloride.<sup>2,3</sup> The chlorination of anisole does not, as previously reported,<sup>4</sup> give phenoxymethyl chloride, but rather a mixture of *p*- and *o*-chloroanisoles.<sup>5</sup> Similarly, anisole and other unsubstituted methyl aryl ethers undergo ring chlorination with phosphorus pentachloride and chlorine,<sup>6</sup> whereas ring-chlorinated anisoles, such as *p*-chloroanisole, undergo chlorination at the methyl group with chlorine at 190–195° in the presence of a catalytic amount of phosphorus pentachloride.<sup>6</sup> Ring-nitrated aryloxymethyl chlorides may be obtained by the aluminum chloride-catalyzed decarbonylation of the corresponding aryloxyacetyl chlorides.<sup>7,8</sup>

The present method is simple, proceeds easily and in good yield to give a single product. It is applicable to other cases, such as the preparation of 2,4-dichlorophenoxyethyl chloride (89–92%). The chlorination of *p*-chloroanisole with chlorine and phosphorus pentachloride gives considerable amounts of *p*-chlorophenoxydichloromethane which is difficult to separate from the desired compound by distillation.

The reaction of chloromethyl aryl ethers with nucleophilic reagents has been described by Barber *et al.*<sup>2</sup> Thus, by reaction with thiourea, potassium thiocyanate, or sodium cyanide, there are obtained aryloxyalkylisothiuronium salts, aryloxyalkyl thiocyanates, and aryloxyalkylacetonitriles, respectively.<sup>2</sup> With silver sulfonates the sulfonic acid esters of aryloxymethanols may be obtained.<sup>8</sup> The reaction of chloromethyl aryl ethers with butyllithium leads to an aryloxy carbene which on reaction with olefins gives aryloxy cyclopropanes.<sup>3</sup> The ethers react with triphenylphosphine and a base to give phenoxymethylene ylides which are useful in converting carbonyl compounds to aromatic enol ethers.<sup>9</sup> The reaction of the chloro ethers with trialkylphosphites gives aryloxymethanephosphonates.<sup>10</sup> Most of these reactions have been studied with phenoxymethyl chloride and the *p*-methyl derivative; they also proceed well and in good yield with the readily obtainable *p*-chlorophenoxymethyl chloride.<sup>10</sup>

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## References and Notes

1. Institute für Organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin, DDR-1199 Berlin-Adlershof.
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4. C. S. Davis and G. S. Loughheed, *Org. Syntheses*, **47**, 23 (1967).
5. M. Shamma, L. Novak, and M. G. Kelly, *J. Org. Chem.* **33**, 3335 (1968).
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10. H. Gross and W. Bürger, unpublished results.

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## Appendix

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

petroleum ether

phosphorus pentachloride (10026-13-8)

sodium cyanide (143-33-9)

Anisole (100-66-3)

chlorine (7782-50-5)

phosphorus trichloride (7719-12-2)

potassium thiocyanate (333-20-0)

thiourea (62-56-6)

butyllithium (109-72-8)

*p*-chloroanisole (623-12-1)

triphenylphosphine (603-35-0)

phenoxymethyl chloride

2,4-dichlorophenoxymethyl chloride

p-Chlorophenoxymethyl chloride,  
Anisole, p-a-dichloro- (21151-56-4)

p-chlorophenyldichloromethane