Organic Syntheses

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). 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.

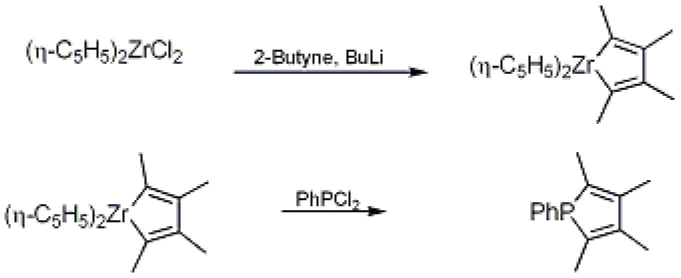
*September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

DOI:10.15227/orgsyn.070.0272

*Organic Syntheses, Coll. Vol. 9, p.653 (1998); Vol. 70, p.272 (1992).*

# 1-PHENYL-2,3,4,5-TETRAMETHYLPHOSPHOLE

## [1H-Phosphole, 2,3,4,5-tetramethyl-1-phenyl-]



Submitted by Paul J. Fagan and William A. Nugent[1].
Checked by Mark S. Jensen and James D. White.

## 1. Procedure

A 500-mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar, rubber septum-capped pressure-equalizing addition funnel on the center neck, rubber septum on one side neck, and a nitrogen inlet with stopcock on the other side neck is charged in a nitrogen-filled glove box (Note 1) with 27.0 g (92.5 mmol) of zirconocene dichloride [$(\eta\text{-}C_5H_5)_2ZrCl_2$] (Note 2), 150 mL of tetrahydrofuran (Note 3), and 16.0 mL (204 mmol) of 2-butyne (Note 4) added via syringe. The apparatus is removed from the glove box and attached via the nitrogen stopcock to a nitrogen bubbler. The flask is cooled to −78°C (dry ice-acetone bath) and 108 mL of 1.72 M butyllithium (186 mmol) in hexane (Note 5) is added via syringe to the addition funnel through the septum. The butyllithium solution is added dropwise to the stirred mixture in the flask. After the addition is complete, the reaction mixture is stirred at −78°C for 10 min (Note 6). The flask is allowed to warm by removing the dry ice-acetone bath, and the reaction mixture is stirred at room temperature for 2.5 hr at which point the mixture is dark orange-red (Note 7). The flask is again cooled to −78°C, and 17.5 mL (129 mmol) of dichlorophenylphosphine (Note 8) is added in a slow stream via syringe through the septum on the flask. The dry ice-acetone bath is removed and the flask is allowed to warm to room temperature. After 1 hr the orange-red color has dissipated and the septa are replaced with glass stoppers. The nitrogen inlet is connected to a vacuum line (0.1 mm) and the solvent is removed under reduced pressure. The stopcock is closed and the apparatus is placed in a nitrogen-filled glove box (Note 1). The reaction residue is extracted three times with 30-mL portions of hexane, each of which is filtered from the precipitate of $(\eta\text{-}C_5H_5)_2ZrCl_2$ and combined. The hexane is removed under reduced pressure (0.5 mm), and the oily liquid that remains is transferred into a 100-mL round-bottomed flask. The flask is attached to a vacuum distillation apparatus with a 10-cm Vigreux column. The distillation apparatus is removed from the glove box and attached to a vacuum line. Distillation at 0.35 mm yields a fraction which is collected between 40–92°C and discarded. A second fraction boiling between 92–104°C (Note 9) is collected; the clear oily liquid is 1-phenyl-2,3,4,5-tetramethylphosphole [14.9–15.5 g, 75–78% based on $(\eta\text{-}C_5H_5)_2ZrCl_2$)] (Note 10). The compound is air-sensitive and should be stored under nitrogen.

## 2. Notes

1. A nitrogen-filled glove bag may also be used.
2. Zirconocene dichloride was obtained from Aldrich Chemical Company, Inc. and used without further purification.
3. Tetrahydrofuran was distilled from sodium benzophenone ketyl before use.
4. 2-Butyne was obtained from Farchan Chemical Company and dried over 4 Å molecular sieves before use.
5. Butyllithium was obtained from Foote Mineral Co. The molarity was checked by titration of 2.00 mL of the butyllithium solution in 10 mL of diethyl ether with dry 2-butanol using 1,10-phenanthroline as

indicator.
6. The reaction mixture may become thick with a white solid at this point. The solid can be loosened by manually shaking the flask, or with the aid of an external permanent magnet using the magnetic stirring bar to break up the solid. The solid loosens some more upon warming, and stirring is not a problem.
7. If desired, the zirconium metallacycle can be isolated at this point: The flask is attached to a vacuum line via the nitrogen inlet, and solvents are removed from the flask under reduced pressure. With the aid of a 40°C water bath, the reaction residue is thoroughly dried. The flask is sealed and placed in a nitrogen-filled glove box (Note 1). The residue is extracted with small portions of toluene (total of 50 mL), each portion being filtered and combined. Toluene is removed from the filtrate under reduced pressure. Hexane (20 mL ) is added to the solid residue, and after trituration, the solid is collected by filtration, and washed once with 10 mL of hexane. It is dried under reduced pressure to yield 26.0 g (85%) of crystalline, orange-red $(\eta\text{-}C_5H_5)_2ZrC_4(CH_3)_4$ which is >95% pure by spectroscopic analysis. This compound is very stable thermally both in solution and in the solid state; however, it is air-sensitive and should be handled under nitrogen. It can be used as obtained as a reagent in the synthesis of other heterocycles. The NMR spectrum is as follows: $^1$H NMR (300 MHz, THF-$d_8$) δ: 1.54 (s, 6 H, $CH_3$), 1.57 (s, 6 H, $CH_3$), 6.15 (s, 10 H, $h\eta\text{-}C_5H_5$).
8. Dichlorophenylphosphine (Strem Chemicals, Inc.) was vacuum distilled and placed under a nitrogen atmosphere before use.
9. The boiling point has been reported previously as 105–110°C at 0.5 mm.[2]
10. The product has the following spectral properties: $^1$H NMR (300 MHz, THF-$d_8$) δ: 1.89 (d, 6 H, J = 10.6, $CH_3$), 1.93 (s, 6 H, $CH_3$), 7.24 (m, 5 H, phenyl); $^{13}$C NMR (75.5 MHz, THF-$d_8$) δ: 12.9 (dq, $J_{CH}$ = 126, $J_{PC}$ = 22, $CH_3$), 13.9 (q, $J_{CH}$ = 126, $CH_3$), 129.2 (dt, $J_{CH}$ = 160 and 6, $J_{PC}$ = 8, phenyl), 129.6 (dt, $J_{CH}$ = 162 and 6, phenyl), 134.3 (ddt, $J_{CH}$ = 161 and 5, $J_{PC}$ = 20, phenyl), 134.7 (d, $J_{PC}$ = 15), 136.4 (s, C=C), 143.4 (m, $J_{PC}$ = 11); $^{31}$P {$^1$H} NMR (121.7 MHz, THF-$d_8$) δ: 14 (s). Exact mass: Calcd. for $C_{14}H_{17}P$: m/e = 216.1068. Found: 216.1127.

## Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

## 3. Discussion

Phospholes and other related heterocycles are an important class of main group compounds. The chemistry of phospholes and their preparation has been reviewed extensively by Mathey.[3] We provide details here for a simple, one-pot procedure for the preparation of 1-phenyl-2,3,4,5-tetramethylphosphole applying zirconocene chemistry.[4] The procedure involves reduction of $(\eta\text{-}C_5H_5)_2ZrCl_2$ with butyllithium in the presence of 2-butyne which (as reported initially by Negishi, et al.[5]) forms a zirconium metallacycle. Addition of dichlorophenylphosphine to this reaction mixture produces the phosphole. One other procedure for the preparation of 1-phenyl-2,3,4,5-tetramethylphosphole has been reported by Nief, et al.[2] That procedure involved aluminum chloride-coupling of 2-butyne, followed by reaction with dichlorophenylphosphine to form a chlorophospholium tetrachloroaluminate which was then reduced with tributylphosphine to produce the phosphole in 68% yield.

Using a procedure similar to that described here, or using isolated zirconium metallacycles as reagents, we have been able to prepare not only phospholes, but also arsoles, stiboles, bismoles, siloles, germoles, stannoles, galloles, thiophenes, selenophenes, and borole Diels-Alder dimers.[4] Since a number of other titanium and zirconium metallacycles are readily available,[4] these reagents should be useful in the preparation of a variety of heterocycles.

---

## References and Notes

1. E. I. du Pont de Nemours and Co., Inc., Central Research and Development Department, Experimental Station, Box 80328, E328/364, Wilmington, DE 19880-0328. Contribution No. 5123. We thank Ronald J. Davis for technical assistance.
2. Nief, F.; Mathey, F.; Ricard, L.; Robert, F. *Organometallics* **1988**, *7*, 921.

3. Mathey, F. *Chem. Rev.* **1988**, *88*, 429; Mathey, F. *Phosphorus Sulfur* **1983**, *18*, 101; Mathey, F.; Fischer, J.; Nelson, J. H. *Struct. Bonding (Berlin)* **1983**, *55*, 153; Mathey, F. In "Topics in Phosphorus Chemistry"; Grayson, M.; Griffith, E. J., Eds.; Wiley: New York, 1980; Vol. 10, p. 1–128.
4. Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310; Fagan, P. J.; Burns, E. G.; Calabrese, J. C. *J. Am. Chem. Soc.* **1988**, 110, 2979; RajanBabu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, Paul, J. *J. Am. Chem. Soc.* **1988**, *110*, 7128; Buchwald, S. L.; Watson, B. T.; Lum, R. T.; Nugent, W. A. *J. Am. Chem. Soc.* **1987**, *109*, 7137.
5. Negishi, E.-i.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829.

---

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

sodium benzophenone ketyl

zirconocene dichloride

$\eta$-$C_5H_5)_2ZrCl_2$

$\eta$-$C_5H_5)_2ZrC_4(CH_3)_4$

diethyl ether (60-29-7)

nitrogen (7727-37-9)

toluene (108-88-3)

butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

hexane (110-54-3)

zirconium

2-butyne (503-17-3)

dichlorophenylphosphine (644-97-3)

2-Butanol (78-92-2)

tributylphosphine (998-40-3)

1,10-phenanthroline (66-71-7)

titanium (7440-32-6)

1-Phenyl-2,3,4,5-tetramethylphosphole,

1H-Phosphole, 2,3,4,5-tetramethyl-1-phenyl- (112549-07-2)

chlorophospholium tetrachloroaluminate