



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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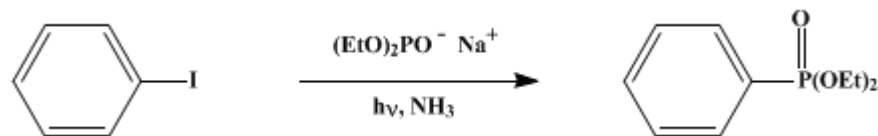
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## RADICAL ANION ARYLATION: DIETHYL PHENYLPHOSPHONATE

[Phosphonic acid, phenyl-, diethyl ester]



Submitted by Joseph F. Bunnett<sup>1</sup> and Robert H. Weiss.  
Checked by S. C. Busman and O. L. Chapman.

### 1. Procedure

*Caution! 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-l., three-necked, round-bottomed flask is fitted with an ammonia condenser (Note 1) with an outlet protected with a soda-lime drying tube, a dropping funnel, a nitrogen inlet, and a magnetic stirrer. As a slow stream of nitrogen is passed through the system, the condenser is charged with dry ice and 2-propanol, the funnel is briefly removed, about a liter of liquid ammonia is added straight from a commercial cylinder (Note 2), and the funnel is replaced. Bright, freshly-pared sodium metal (11.8 g., 0.513 g.-atom) is added, turning the mixture blue. Diethyl phosphonate (70.4 g., 0.510 mole) (Note 3) is cautiously added dropwise to the sodium in ammonia in the manner of a titration; the endpoint is the change from blue to colorless (Note 4). Iodobenzene (52.4 g., 0.257 mole) (Note 5) is slowly added, giving the solution a slight yellowish tint (Note 6). The dropping funnel is replaced by a stopper, the frost is wiped off the outside of the flask with a towel dampened with acetone, and the whole system is mounted in a photochemical reactor of adequate design (Note 7). *Caution! The lamps must be shielded to prevent exposure of the eyes or skin to ultraviolet radiation.* The flask is irradiated for 1 hour (Note 8), but every 20 minutes the lamps are shut off briefly while the exterior of the flask is freed of frost by spraying it, still mounted in the reactor, with 2-propanol from a wash bottle.

After irradiation, the flask is removed from the reactor, and about 50 g. (0.62 mole) of solid ammonium nitrate is added with stirring to acidify the mixture. About 200 ml. of diethyl ether is added, nitrogen flow is stopped, the condenser is removed, and the open flask is placed on a cork ring in an operating hood and allowed to stand overnight while the ammonia evaporates. The next day 300 ml. of water (Note 9) and 300 ml. of ether are added, the ether layer is separated, the water layer is extracted twice with ether, and the combined ether extracts are dried over anhydrous sodium sulfate. After evaporation of the ethyl ether, the residue is distilled under reduced pressure through a short Vigreux column. After a small forerun, 50.3–56.1 g. (90.4–92.5%) of diethyl phenylphosphonate (Note 10) is collected at 73–74° (0.020 mm.) (Note 11).

### 2. Notes

1. An ammonia condenser is an enlarged cold finger design. The interior of the "finger" is a reservoir for dry ice and 2-propanol.
2. When ammonia distilled from sodium metal is used, the yield is 3–5% greater, but use of ammonia straight from the tank is recommended because of the greater convenience.
3. Commercial diethyl phosphonate, formerly known as diethyl phosphite, was purchased from Aldrich Chemical Co., Inc. and used without further purification.
4. Some white foam forms as the diethyl phosphonate is added. Because water in the ammonia

consumes some of the sodium, not quite all the diethyl phosphonate is required to reach the endpoint. Excess diethyl phosphonate is deleterious.

5. Commercial iodobenzene was dried over molecular sieves. Use of ratios of potassium diethyl phosphite to iodobenzene smaller than 2:1 gives lower yields. Bromobenzene is much less reactive than iodobenzene and gives poor yields by this procedure.

6. When distilled ammonia is used, this yellow coloration vanishes as the reaction occurs.

7. The submitters used a Rayonet Model RPR-100 Photochemical Reactor, manufactured by the Southern New England Ultraviolet Company, Hamden, Connecticut 06514, equipped with 16 Cat. No. RPR-3500A fluorescent lamps (ca. 24 W. each), rated to emit maximally at 350 nm. Equally good results were obtained with lamps rated to emit maximally at 300nm. For reactions on a 0.05-mole scale excellent yields were obtained, without using the commercial photochemical reactor, by irradiating for 1 hour with two circular kitchen-type fluorescent lamps mounted on either side of the flask so as to partially encircle it.

8. The yield was not significantly improved by irradiating for 2 hours.

9. Diethyl phenylphosphonate is appreciably soluble in water. Therefore, excessive amounts of water should be avoided.

10. Spectral characterization is as follows: IR (neat)  $\text{cm}^{-1}$ : 1440 (P-C aryl), 1250 (P=O), 1020 ( $\text{POC}_2\text{H}_5$ ), and 3060 (H-C aryl);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ),  $\delta$  (multiplicity, coupling constant  $J$  in Hz., assignment): 1.3 (t,  $J = 7$ ,  $\text{CH}_3$ ), 4.13 (quintet,  $J = 7$ ,  $\text{CH}_2$ ), 7.33–8.06 (m,  $\text{C}_6\text{H}_5$ ).

11. The submitters obtained a yield of 46 g. (83%), b.p. 90–92° (0.1 mm.).

### 3. Discussion

The procedure reported here is based on a reaction discovered by Bunnett and Creary,<sup>2</sup> and was first employed for preparative purposes by Bunnett and Traber.<sup>3</sup> It is attractive because of the high yield, the ease of work-up, and the cleanliness of the reaction. The reaction is believed to occur by the  $\text{S}_{\text{RN}}1$  mechanism, which involves radical and radical anion intermediates.<sup>2,4</sup> The  $\text{S}_{\text{RN}}1$  arylation of other nucleophiles, especially ketone enolate ions,<sup>5</sup> ester enolate ions,<sup>6</sup> picolyl anions,<sup>7</sup> and arenethiolate ions,<sup>8</sup> has potential application in synthesis.

This procedure has been utilized successfully with a variety of aryl iodides, but aryl bromides are much less reactive. *m*- and *p*-Diiodobenzene, *m*- and *p*-bromiodobenzene, and *p*-chloriodobenzene give the corresponding phenylenediphosphonate esters.<sup>2,3</sup> *o*-Haliodobenzenes undergo a dark reaction leading to deiodination and other products, but the  $\text{S}_{\text{RN}}1$  reaction affording phosphate esters may be made to predominate if irradiation is started quickly.<sup>9</sup>

The esters of arylphosphonic acids are cleaved to the acids by hydrochloric, hydrobromic, or hydroiodic acid.<sup>10</sup> Arylphosphonic dichlorides ( $\text{ArPOCl}_2$ ) are easily converted to esters by reaction with the alcohol in pyridine solution.<sup>11</sup>

Other methods for synthesis of arylphosphonic acids or their derivatives fall into four main categories. First, many aromatic compounds react with phosphorus trichloride under aluminum trichloride catalysis, to form aryldichlorophosphines ( $\text{ArPCL}_2$ ).<sup>12,13</sup> These add chlorine to form aryltetrachlorophosphoranes ( $\text{ArPCL}_4$ ),<sup>14,13</sup> which may be hydrolyzed to arylphosphonic dichlorides or arylphosphonic acids. This sequence may be employed for preparations on a large scale, but is subject to the orienting effects of substituents when applied to substituted benzenes.

Second, arylphosphonic acids may be prepared by the copper-catalyzed reactions of arenediazonium tetrafluoroborates with phosphorus trichloride or tribromide. This method has found wide use.<sup>15</sup>

Third, arylphosphonic acid derivatives have been made by organometallic reactions, such as the reaction of phenylmagnesium bromide with diethyl chlorophosphate, or of phenyllithium with phosphorodipiperidic chloride.<sup>16,13</sup>

Fourth, the present procedure bears a resemblance to the photochemical reaction of aryl iodides with trialkyl phosphites, with which several dialkyl arylphosphonates have been prepared.<sup>17</sup> However, prolonged irradiation (>24 hours) in quartz vessels was employed.

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## References and Notes

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## Appendix

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

Diethyl phosphonate

m- and p-Diiodobenzene

m- and p-bromiodobenzene

hydrochloric, hydrobromic, or hydroiodic acid

phosphorus trichloride or tribromide

ammonia (7664-41-7)

Benzene (71-43-2)

ether,  
ethyl ether,  
diethyl ether (60-29-7)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

acetone (67-64-1)

aluminum trichloride (3495-54-3)

pyridine (110-86-1)

chlorine (7782-50-5)

sodium (13966-32-0)

2-propanol (67-63-0)

bromobenzene (108-86-1)

phosphorus trichloride (7719-12-2)

ammonium nitrate

Phenylmagnesium bromide (100-58-3)

Iodobenzene (591-50-4)

Phenyllithium (591-51-5)

diethyl phosphite (762-04-9)

diethyl chlorophosphate (814-49-3)

Diethyl phenylphosphonate,  
Phosphonic acid, phenyl-, diethyl ester (1754-49-0)

potassium diethyl phosphite

p-chloriodobenzene (637-87-6)

phosphorodipiperididic chloride