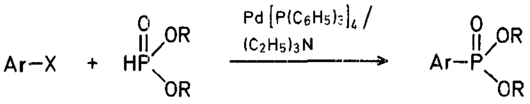
A Novel Synthesis of Dialkyl Arenephosphonates

Toshikazu Hirao*, Toshio Masunaga, Yoshiki Ohshiro, Toshio Agawa

Department of Petroleum Chemistry, Faculty of Engineering, Osaka University, Yamadakami, Suita, Osaka 565, Japan

The Michaelis-Arbuzov reaction is a well known method for the formation of carbon-phosphorus bonds, however, it is not applicable to the formation of aryl carbon-phosphorus bonds. For the synthesis of arenephosphonates, only few methods[1-6] have been reported. We have now found a new synthetic route to dialkyl arenephosphonates **3** using a palladium catalyst. Dialkyl arenephosphonates **3** were prepared in good yields by the reaction of an aryl bromide or iodide **1** with a dialkyl phosphite **2** in the presence of triethylamine and a catalytic amount of tetrakis[triphenylphosphine]palladium.



1 **2** **3**

The results are summarized in the Table. Although bromobenzene and iodobenzene readily underwent reaction with diethyl phosphite, chlorobenzene did not react under the same conditions. On treatment of *p*-bromochlorobenzene with diethyl phosphite, diethyl *p*-chlorobenzenephosphonate was obtained in 85% yield as the sole product. Diisopropyl phosphite and di-*n*-butyl phosphite were also allowed to react with bromobenzene in the presence of tetrakis[triphenylphosphine]palladium to give the corresponding diisopropyl and di-*n*-butyl benzenephosphonates, respectively. No significant effect of the substituents attached to the phenyl group was observed on the yields. It should be noted that *o*-dibromobenzene reacted with 2 equiv of diethyl phosphite to give diethyl *o*-bromobenzenephosphonate (34%) and

Table. Dialkyl Arenephosphonates 3

Product No.	Ar (X in **1**)	R	Reaction time [h][a]	Yield [%]	m.p. [°C] or b.p. [°C]/torr[b] observed	m.p. [°C] or b.p. [°C]/torr[b] reported	I.R. (neat) ν [cm^{-1}]
3a	C_6H_5 (Br)	C_2H_5	2.5	92	90°/0.2	96–98°/0.2[5]	1245, 1050–1020, 955
3a	C_6H_5 (J)	C_2H_5	2.5	96			
3b	C_6H_5 (Br)	i-C_3H_7	2.5	90	105°/0.25	96–97°/0.1[5]	1250, 1030–1010, 980
3c	C_6H_5 (Br)	n-C_4H_9	2.5	94	120°/0.25	166°/4[2]	1240, 1060–1010, 970
3d	4-H_3C—C_6H_4 (Br)	C_2H_5	17	94	125°/0.25	118–119°/0.05[5]	1240, 1050–1010, 950
3e	2-H_3C—C_6H_4 (Br)	C_2H_5	30	91	125°/0.2	117–118°/0.01[5]	1230, 1040–1010, 945
3f	4-Cl—C_6H_4 (Br)	C_2H_5	8[c]	85	125°/0.25	105–108°/0.15[5]	1250, 1050–1020, 970
3g	4-H_3CO—C_6H_4 (Br)	C_2H_5	17	95	140°/0.25	168–169°/1.5[5]	1240, 1060–1020, 960
3h	4-O_2N—C_6H_4 (Br)	C_2H_5	8[c]	73	170°/0.2	—[7]	1520, 1245, 1040–1010, 960
3i	4-H_3C—CO—C_6H_4 (Br)	C_2H_5	8[c]	90	175°/0.25	148–150°/0.06[5]	1685, 1250, 1050–1010, 960
3j	4-H_3C—CO—NH—C_6H_4 (Br)	C_2H_5	28[c]	64	143–145°	138–140°[6]	1695, 1220, 1045–1020, 965[d]
3k	4-NC—C_6H_4 (Br)	C_2H_5	2[c]	95	30–32°	31–35°[5]	2215, 1245, 1050–1010, 960[d]
3l[e]	4-Br—C_6H_4 (Br)	C_2H_5	8[c]	81	73–75°	71–72°[2]	1240, 1050–1010, 950[d]
3m[e]	2-Br—C_6H_4 (Br)	C_2H_5	64	34[f]	145°/0.1	—[g]	1245, 1050–1020, 965
3n	1-naphthyl (Br)	C_2H_5	24	96	170°/0.25	147–149°/0.05[2]	1245, 1050–1020, 965
3o	3-pyridyl (Br)	C_2H_5	3	77	105°/0.2	—[8]	1250, 1060–1010, 965

[a] Solvent was not used unless otherwise stated; reactions at 90 °C.

[b] Boiling temperature; oven temperature (Kugelrohr); melting points are uncorrected.

[c] Toluene added as solvent.

[d] Nujol mull.

[e] 2 equiv of diethyl phosphite used.

[f] 6% of **3a** also formed.

[g]

$C_{10}H_{14}BrO_3P$	calc.	C 40.98	H 4.81	Br 27.26	P 10.57
(293.1)	found	40.96	5.05	27.48	10.32

^{1}H-N.M.R.(CDCl$_3$): δ=1.37 (t, 6H, J=7.0 Hz); 4.20 (dq, 4H, J=7.0 Hz); 7.3–7.8 ppm (m, 4H_{arom}).

diethyl benzenephosphonate (6%), whereas with p-dibromobenzene replacement of both bromine atoms was observed.

This palladium-catalyzed phosphonation of aryl bromides provides a facile synthesis of dialkyl arenephosphonates.

Dialkyl Arenephosphonates 3; General Procedure:

To a stirred mixture of dialkyl phosphite **2** (4.4 mmol) and triethylamine (0.61 ml, 4.4 mmol) in the presence of a catalytic amount of tetrakis[triphenylphosphine]palladium (231 mg, 0.2 mmol), aryl bromide **1** (4.0 mmol) is added under a nitrogen atmosphere, and the resultant mixture is stirred at 90 °C for 2.5–64 h. When the aryl bromide **1** used is solid, toluene (1 ml) is added as a solvent. After the addition of ether (50 ml), triethylamine hydrobromide is removed by filtration. The residue obtained upon evaporation is purified by Kugelrohr distillation or column chromatography on silica gel eluting with chlorofrom.

G.L.C. analysis (conditions: 10% OV 17 column, 100 °C) of the product indicated a purity of $\geq$98%. The products **3** were identified by comparison of their I.R. and N.M.R. spectra with those of authentic samples.

Received: June 3, 1980
(Revised form: August 11, 1980)

---

[1] K. Sasse, in: Houben-Weyl, *Methoden der Organischen Chemie*, 4th Edn., E. Müller, Ed., Vol. XII/1, Georg Thieme Verlag, Stuttgart, 1963, p. 423.

[2] K. H. Worms, M. Schmidt-Dunker, in: *Organic Phosphorus Compounds*, G. M. Kosolapoff, L. Maier, Eds., Vol. 7, John Wiley & Sons, New York, 1976, p. 1.

[3] G. M. Kosolapoff, *Org. React.* **6**, 273 (1951).

L. D. Freedman, G. O. Doak, *Chem. Rev.* **57**, 479 (1957).

E. F. Jason, E. K. Fields, *J. Org. Chem.* **27**, 1402 (1962).

A. G. Varvoglis, *Tetrahedron Lett.* **1972**, 31.

J. F. Bunnett, X. Creary, *J. Org. Chem.* **39**, 3612 (1974).

J. B. Plumb, R. Obrycki, C. E. Griffin, *J. Org. Chem.* **31**, 2455 (1966).

R. Obrycki, C. E. Griffin, *J. Org. Chem.* **33**, 632 (1968).

P. Tavs, F. Korte, *Tetrahedron* **23**, 4677 (1967).

P. Tavs, *Chem. Ber.* **103**, 2428 (1970).

R. A. Naylor, A. Williams, *J. Chem. Soc. Perkin Trans. 2* **1976**, 1908.

A. S. Mukhtarov et al., *Zh. Strukt. Khim.* 17, 76 (1976).

D. J. Collins, J. W. Hetherington, J. M. Swan, *Aust. J. Chem.* **27**, 1355 (1974).