Synthesis of Arenephosphonates by Copper(I) Iodide-Promoted Arylation of Phosphite Anions

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Considerable attention has been focused on arenephosphonates as precursors of phosphorus analogs of heterocyclic compounds such as phosphindoles[1a] and iodinanes[1b]. The Arbuzov reaction is one of the most versatile pathways for the formation of carbon-phosphorus bonds[2]. However, aryl halides are very unreactive under thermally-initiated conditions. Useful methods for the synthesis of arenephosphonates involve either (a) photochemical activation[3], (b) nickel(II) catalysis[4], (c) photostimulated $S_{RN}1$ conditions[5], (d) free radical phos-

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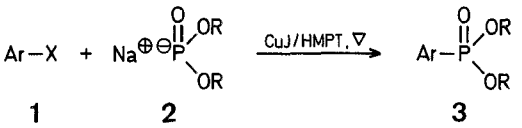
phonation conditions[6], or (e) strong base-induced rearrangement of aryl phosphate[7]. These methods have certain disadvantages such as the necessity to use a large excess of phosphite (a, c), the necessity to activate the substrate (a, c), inapplicability to substrates with steric hindrance (b) or with a free amino group (a, b, c, d, e), and low regioselectivity (d).

We report a convenient synthesis of arenephosphonates **3** via copper(I) iodide promoted arylation of phosphite anions **2** with aryl halides **1** in hexamethylphosphoric triamide (HMPT).



1 2 3

The reaction proceeds smoothly and affords satisfactory yields (Table). The arenephosphonates are appreciably soluble in water, which causes some losses of **3**.

In contrast to the nickel(II)-catalyzed Arbuzov reaction, this reaction is particularly useful for the preparation of hindered arenephosphonates **(3c, 3g, 3h,** and **3i).** The reaction is compatible with a free amino group, although functional group compatibility has not yet been studied thoroughly. The reaction with aryl chlorides requires a slightly higher temperature (170–180 °C) and results in poorer yields (20–30%).

The structures of all new products were established by analytical data and ^{1}H-N.M.R. and I.R. spectra. All melting points and boiling points are uncorrected.

Diphenyl 2,3,5,6-Tetramethylbenzenephosphonate (3c); Typical Procedure:

Sodium hydride (0.096 g, 4 mmol) is added to a stirred solution of diphenyl phosphite (**2a**; 0.94 g, 4 mmol) in HMPT (5 ml) at 70–80 °C under a nitrogen atmosphere. When the hydrogen evolution has ceased, copper(I) iodide (0.76 g, 4 mmol) is added. The solution gradually turns black and iododurene (0.52 g, 2 mmol) is added. The mixture is heated at 150–160 °C with stirring for 1 h. After cooling, the mixture is diluted with water (150 ml) and the product is extracted with ether (2 × 70 ml). The extract is washed with water (100 ml) and dried with sodium sulfate. The solvent is removed in vacuo and a residue is chromatographed on a short column of silica gel using ether/hexane (20/80) as eluent, giving **3c.** The product is recrystallized from hexane; yield: 549 mg (75%); m.p. 131.5–132.5 °C.

$C_{22}H_{23}O_3P$	calc.	C 72.12	H 6.33
(366.4)	found	72.07	6.31

I.R. (KBr): ν = 1595, 1485, 1270, 1200, 945, 930 cm^{-1}.

M.S.: m/e = 366 (M^+, 100).

Table. Arenephosphonates **3a–j** prepared

Product No.	R	Ar	X	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr[b]	Molecular formula[c] or Lit. data	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
3a	C_6H_5	C_6H_5	J	81	75–75.5°	$C_{18}H_{15}O_3P$ (310.3)	3070, 1760, 1600, 1500, 1270, 1220, 1195, 1145, 950, 940, 780, 755, 700	7.1 (m, 10H); 7.6–8.1 (m, 5H)
3b	C_6H_5	4-H_3C—C_6H_4	J	77	225–227°/2.5	$C_{19}H_{17}O_4P$ (340.3)	2920, 1590, 1490, 1270, 1215, 1190, 1130, 930, 760, 685	2.30 (s, 3H); 6.9–7.3 (m, 12H); 7.72 (dd, 2H, J = 8 Hz, 12 Hz)
3c	C_6H_5	2,3,5,6-tetra-H_3C—C_6H	J	75	131.5–132.5°	$C_{22}H_{23}O_3P$ (366.4)	2940, 1595, 1485, 1270, 1200, 945, 930, 775, 770, 695	2.30 (s, 6H); 2.70 (d, J = 1 Hz, 6H); 7.1 (m, 11H)
3d	C_6H_5	4-H_2N—C_6H_4	Br	66	130–132°	$C_{18}H_{16}NO_3P$ (325.3)	3420, 3350, 3160, 3070, 1590, 1490, 1190, 945, 685	7.1 (m, 14H)
3e	C_6H_5	4-H_3CO—C_6H_4	Br	70	233–235°/2.5	$C_{18}H_{17}O_4P$ (328.3)	3070, 2940, 1600, 1490, 1260, 1220, 1200, 1135, 1030, 940, 775, 690	3.55 (s, 3H); 7.1 (m, 10H); 6.78 (dd, 2H, J = 4 Hz, 8 Hz); 7.68 (dd, 2H, J = 8 Hz, 13 Hz)
3f	C_2H_5	4-H_3C—C_6H_4	J	62[d]	157–162°/20	118–119°/0.05[4a]	2980, 1610, 1450, 1395, 1250, 1170, 1135, 1060, 1030, 970, 800, 655	1.24 (t, 6H, J = 7 Hz); 2.36 (s, 3H); 4.0 (m, 4H); 7.09 (dd, 2H, J = 5 Hz, 8 Hz); 7.55 (dd, 2H, J = 5 Hz, 8 Hz)
3g	C_2H_5	2,4,6-tri-H_3C—C_6H_2	J	67[d]	156–161°/18	111–112°/0.05[4a]	2970, 1605, 1460, 1390, 1230, 1085, 1020, 960	1.24 (t, J = 7 Hz, 6H); 2.20 (s, 3H); 2.49 (d, 6H, J = 1 Hz); 6.72 (d, 2H, J = 5 Hz); 4.0 (m, 4H)
3h	C_2H_5	2,3,5,6-tetra-H_3C—C_6H	J	65[d]	181–186°/19	$C_{14}H_{23}O_3P$ (270.3)	2980, 2930, 1465, 1435, 1255, 1215, 1170, 1060, 1030, 965, 855, 800	1.24 (t, 6H, J = 7 Hz); 2.15 (s, 6H); 2.40 (d, 6H, J = 1 Hz); 4.0 (m, 4H); 6.91 (s, 1H)
3i	C_2H_5	2,3,4,5,6-penta-H_3C—C_6	J	73[d]	193–203°/17	$C_{15}H_{25}O_3P$ (284.3)	2970, 1555, 1455, 1390, 1245, 1220, 1160, 1095, 1020, 960, 770	1.24 (t, 6H, J = 7 Hz); 2.15 (s, 9H); 2.46 (d, 6H, J = 1 Hz); 4.0 (m, 4H)
3j	C_2H_5	4-H_3CO—C_6H_4	Br	54[d]	140–145°/18	168–169°/1.5[4a]	2970, 1595, 1570, 1505, 1445, 1390, 1370, 1295, 1240, 1160, 1130, 1115, 970, 810, 660	1.25 (s, 6H); 3.75 (s, 3H); 4.0 (m, 4H); 6.85 (dd, 2H, J = 4 Hz, 8 Hz); 7.55 (dd, 2H, J = 8 Hz, 13 Hz)

[a] Yield of isolated product.
[b] Kugelrohr distillation.
[c] Satisfactory microanalyses obtained: C ±0.26, H ±0.10, N ±0.09.
[d] Purity >98% by G.L.C.

Diphenyl 2-Aminobenzenephosphonate (3d):
A solution of sodium diphenyl phosphite (1.02 g, 4 mmol) in HMPT (5 ml) is reacted with *o*-bromoaniline (0.34 g, 2 mmol) in a similar manner as described for **3c.** The crude product is chromatographed over silica gel with dichloromethane and recrystallized from tetrachloromethane, yield 427 mg (66%); m.p. 130–132 °C.

$C_{18}H_{16}NO_3P$	calc.	C 66.46	H 4.96	N 4.31
(325.3)	found	66.34	4.86	4.22

I.R. (KBr): $\nu = 3420, 3350, 1590, 1490, 1190, 945, 685\ cm^{-1}$.

M.S.: $m/e = 325$ (M^+, 100), 231 (24), 214 (21), 168 (37), 94 (51).

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