Synthesis of Aminophosphonium Salts by Arylation of Aminophosphines

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In an earlier study[1] of the arylation of compounds of the type $(C_6H_5)_2P—X$ we found that phenylation of diethylaminodiphenylphosphine (**1**, $R = C_2H_5$) with bromobenzene proceeds exclusively at the P-atom to give diethylaminotriphenylphosphonium bromide (**2**, $R = C_2H_5$).

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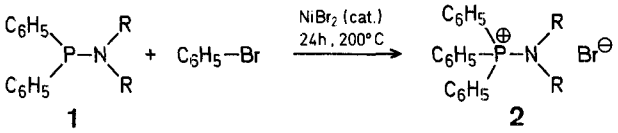
Table 1. Aminodiphenylphosphines (**1**) and Bis[diethylamino]-phenylphosphine (**3f**)

Product	R	R	Method	Yield [%]	m.p.[a] [°C]	b.p./torr [°C] found	b.p./torr [°C] reported	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$/TMS) $\delta_{N\text{-}CH}$ [ppm]	^{31}P-N.M.R. (CDCl$_3$)[b] δ [ppm]
1a	C_2H_5	C_2H_5	A	65	–	138°/0.25	126°/0.1[10]	1432 s; 1000 w; 745 vs; 700 vs	3.06 (dq, 4H, $^3J_{PH}$ = 10 Hz, $^3J_{HH}$ = 7 Hz)	+61.4
1b	n-C_4H_9	n-C_4H_9	A	75	–	165°/0.9	143°/0.2[11]	1435 s (d); 1000 w; 745 vs; 700 vs	3.05 (dt, 4H, $^3J_{PH}$ = 8 Hz, $^3J_{HH}$ = 8 Hz)	
1c	i-C_3H_7	i-C_3H_7	A	71	69°	150–155°/1.5	$C_{18}H_{24}NP$[c] (285.4)	1432 s; 1000 w; 745 vs; 702 vs	3.49 (dhp, 2H, $^3J_{PH}$ = 11 Hz, $^3J_{HH}$ = 7 Hz)	+37.6
1d	C_2H_5	C_6H_5	B	49	57.5° (ethanol)	–	161–164°/0.05[12]	1432 m; 1000 w; 745 vs; 700 vs	3.50 (dq, 2H, $^3J_{PH}$ = 2.5 Hz, $^3J_{HH}$ = 7 Hz)	+56.7
1e	—$(CH_2)_5$—		A	66	53°	156–160°/0.9	160–164°/0.5[9]	1430 m; 1028 m; 746 vs; 700 vs	2.90 (m, 4H, $\Delta\nu/2$ = 14 Hz)	+62.9
3f	C_2H_5 (n = 2)	C_2H_5	A	87	–	113–116°/2	91.5/0.1[10]	1435 m; 1000 w; 748 vs; 702 vs	3.10 (dq, 8H, $^3J_{PH}$ = 10 Hz, $^3J_{HH}$ = 7 Hz)	+97.2

[a] The melting points were determined using a Mettler FP 51 apparatus or a Leitz microscope hot-stage model 350.
[b] Positive values for low-field signals based on H_3PO_4 (85%) as external reference.
[c] calc. C 75.76 H 8.48 N 4.91 P 10.85
found 75.51 8.24 5.05 11.02



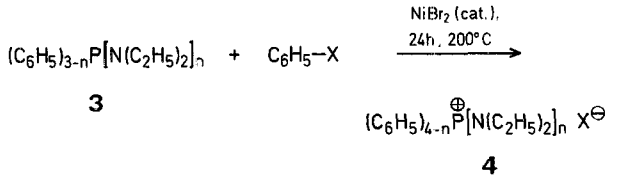
1 **2**

This reaction is of wider preparative interest since only few methods are available for the synthesis of aminophosphonium salts having two alkyl or aryl groups at nitrogen:

- alkylation of phosphinimines[2,3,4];
- reaction of *N*-bromoamines with tertiary phosphines[5];
- reaction of secondary amines with triphenylphosphine/tetrachloromethane[6,7] or with a dibromophosphorane[8].

These methods are often inconvenient because of limitations in the choice of reagents (as in the first two methods) or because purification of the product may be difficult (as in the third method).

We present here a two-step method for the synthesis of *N,N*-dialkylaminophosphonium salts (**2, 4**) from commercially available chlorophosphines. The first step consists of the reaction of chlorodiphenylphosphine or dichlorophenylphosphine, respectively, with excess secondary amines (Method A)[9-12] or (for **1d**) with lithium ethylphenylamide (Method B)[13] to give the aminophosphines (**1, 3**) in good yields. In the second step, the aminophosphine (**1, 3**) is converted into the aminophosphonium salt (**2, 4**) by reaction with bromobenzene in the presence of anhydrous nickel bromide at 200 °C.



3 **4**

In the second (arylation) step, the yields of aminophosphonium salts are generally good for unbranched *N*-alkyl groups. In the case of diisopropylaminodiphenylphosphine (**1**, R = i-C_3H_7), the reaction takes a different course to give tetraphenylphosphonium bromide, probably via arylation of triphenylphosphine which is formed by decomposition of the unstable aminophosphonium salt under the reaction conditions[14]. Another limitation of the present synthesis is found in the case of *N*-ethylanilinodiphenylphosphine (**1d**) which undergoes a phospha-semidine rearrangement prior to arylation to give finally a mixture of *ortho*- (25%) and *para*- (47%) *N*-ethylaminophenyltriphenylphosphonium bromide[15]. The reaction is also applicable to di- and triaminophosphines (**3**).

Aminodiphenylphosphines (1) and Diaminophenylphosphines (3f, n = 2):

Method A; *General Procedure:* The aminophosphines are prepared by a modification of the procedure described by Sisler and Smith[9]. A solution of diphenylchlorophosphine (9.2 ml, 50 mmol) in anhydrous benzene (20 ml) is added dropwise under nitrogen to a solution of amine (125 mmol) in anhydrous benzene (50 ml) with stirring and external cooling to maintain the temperature of the reacting mixture in the range of 5 to 10 °C. Stirring is then continued at room temperature for 12 h, the amine hydrochloride is filtered off with suction, and washed with anhydrous benzene (4 × 20 ml). The combined benzene layers are evaporated and the residual liquid distilled under reduced pressure.

Table 2. Aminophosphonium Salts (**2, 4**)

Product	R	R	$X^{\ominus}$	Yield [%]	m.p.[a] [°C] found	m.p.[a] [°C] reported, or Molecular formula[b]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ_{N-CH} [ppm]	^{31}P-N.M.R. ($CDCl_3$)[c] δ [ppm]
2a	C_2H_5	C_2H_5	$Br^{\ominus}$	81	161°[d]	136.5°[e,k]	1440 s; 1115 vs; 1000 w; 763 m; 695 m	3.42 (dq, 4H, $^3J_{PH}$ = 12 Hz, $^3J_{HH}$ = 7 Hz)	+46.4
2b	*n*-C_4H_9	*n*-C_4H_9	$Br^{\ominus}$	79	179°	$C_{26}H_{33}BrNP$ (470.4)	1440 s; 1110 vs; 998 s; 757 s; 698 s	3.30 (m, 4H)	+46.3
2e	—$(CH_2)_5$—		$Br^{\ominus}$	82	241.5°	226.5–229°[g]	1437 vs; 1113 vs; 995 m (d); 760 s; 690 vs	3.60–3.20 (m, 4H)	+44.4
4f	C_2H_5 (n = 2)	C_2H_5	$Br^{\ominus}$	81	163°	$C_{20}H_{30}BrN_2P$ (409.4)	1436 s; 1115 vs; 1000 s; 769 s; 705 s	3.42 (dq, 8H, $^3J_{PH}$ = 12 Hz, $^3J_{HH}$ = 7 Hz)	+52.9
4g	C_2H_5 (n = 3)	C_2H_5	$(C_6H_5)_4B^{\ominus}$	68	163°	$C_{42}H_{55}BN_3P$ (643.7)	1438 m; 1115 s; 1000 m; 755 s; 706 vs	2.88 (dq, 12H, $^3J_{PH}$ = 11 Hz, $^3J_{HH}$ = 7 Hz)	+50.3

[a] The melting points were determined using a Mettler FP 51 apparatus or a Leitz microscope hot stage model 350.
[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.21; H, ±0.16; Br, ±0.30; P, ±0.18.
[c] Positive values for low field signals based on H_3PO_4 (85%) as external reference.
[d] m.p. of monohydrate.
[e] m.p. of anhydrous compound.

Method B; N-*Ethyl*-N-*phenylaminodiphenylphosphine* (**1d**); *Typical Procedure*[13]: A suspension of lithium wire (0.4 g, 0.6 mol) in a mixture of *N*-ethylaniline (7.6 ml, 60 mmol), anhydrous hexamethylphosphoric triamide (1 g, 61 mmol) and anhydrous benzene (20 ml) is stirred at room temperature under nitrogen until the lithium disappears. Then, to the mixture is added dropwise a solution of chlorodiphenylphosphine (9.2 ml, 50 mmol) in anhydrous benzene (20 ml) with stirring and external cooling at such a rate as to maintain the temperature of the reacting mixture in the range of 5 to 10 °C. Then, the mixture is warmed for 1 h at 50 °C. After cooling at 10 °C, ice (50 g) is added slowly to the mixture. The layers are separated and the aqueous layer is extracted with benzene. The combined organic layers are dried with anhydrous sodium sulfate and evaporated under reduced pressure. The residue is triturated with ethanol and filtered to give the aminophosphine **1d**; yield: 7.4 g (49%); m.p. 57.5 °C (ethanol).

Dialkylaminotriphenylphosphonium Salts (2, 4); General Procedure:

Anhydrous nickel bromide is prepared by heating nickel(II) bromide trihydrate at 200 °C over phosphorus(V) oxide at 0.1 torr for 48 h.

A mixture of the aminophosphine (**1**; **3**; 10 mmol), bromobenzene (1.2 ml, 11 mmol), and anhydrous nickel bromide (22 mg, 0.1 mmol) is heated at 200 °C (bath temperature) for 24 h and is then hydrolyzed at 90 °C by the addition with stirring of 1 normal hydrobromic acid (15 ml). The mixture is extracted with chloroform (4 × 20 ml), the extract dried with sodium sulfate, and evaporated in vacuo to a volume of 40 ml. This residual liquid is added dropwise to ether (300 ml) with stirring. The precipitated product **2** or **4** is isolated by suction and recrystallized from chloroform/ethyl acetate.

The phenyl-tris[diethylamino]-phosphonium bromide obtained following the above procedure is converted into phenyl-tris[diethylamino]-phosphonium tetraphenylborate (**4g**) by dissolving the precipitated bromide in methanol (10 ml), adding this solution to a stirred solution of sodium tetraphenylborate (3.4 g, 10 mmol) in methanol (10 ml), isolation of the precipitated tetraphenylborate (**4g**), and washing the product with methanol (2 × 10 ml).

With diisopropylaminodiphenylphosphine (**1c**), the above procedure gives only tetraphenylphosphonium bromide; yield: 1.7 g (81%); m.p. 299–300 °C (Ref.[16], m.p. 288 °C).

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