COMMUNICATIONS

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Diethyl *N*-Bromo-*N*-alkylphosphoramidates and Their Potential Preparative Utility[1]

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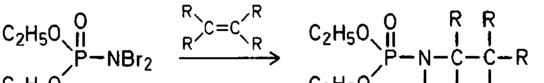
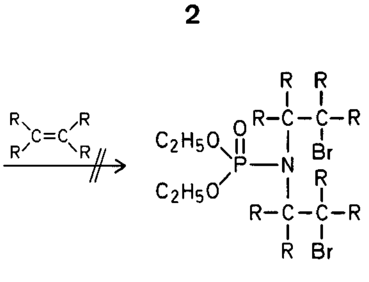
Diethyl *N*,*N*-dibromophosphoramidate (**1**) is of significant value for the facile two-step aminobromination of unsaturated compounds[2]. The preliminary addition step of **1** to an olefinic double bond is the formation of the corresponding diethyl *N*-bromo-*N*-(2-bromoalkyl)-phosphoramidate **2** which can be subsequently reduced *in situ* by 20% aqueous sodium hydrogen sulfite to diethyl *N*-(2-bromoalkyl)-phosphoramidate (1:1 adduct). Addition of **2** to another molecule of olefin to form the 2:1 adduct **3** was never observed.



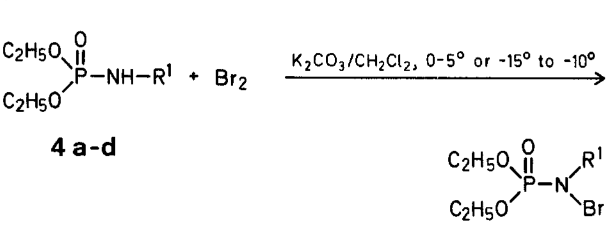
1 **2**



3 (2:1 adduct)

This unusual behaviour of adducts **2**, which undoubtedly still have distinct pseudohalogen character, can be reasonably explained in terms of their markedly decreased reactivity (in comparison to **1**) towards olefins. This assumption can be rationalized by the effectively diminished positive character of bromine and also the considerable steric hindrance around the nitrogen atom in **2**.

We have now studied the addition of diethyl *N*-bromo-*N*-alkylphosphoramidates **5** to olefinic double bonds. We have found that diethyl *N*-bromo-*N*-alkylphosphoramidates **5** of analytical purity can be readily obtained in excellent yields by direct bromination of diethyl *N*-alkylphosphoramidates **4**.



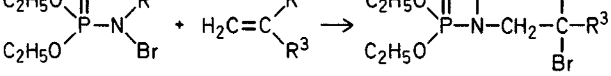
4 a-d **5**

	a	b	c	d
R^1	CH_3	C_2H_5	n-C_4H_9	s-C_4H_9

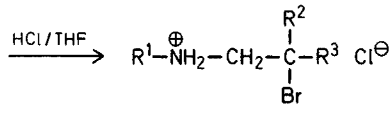
The reaction with bromine was carried out in dichloromethane solution containing a small excess (~10 mol%) of finely powdered potassium carbonate suspension to neutralize the hydrogen bromide as it was formed; this rendered the reaction practically irreversible and almost quantitative. Bromination of **4** in an aqueous potassium carbonate solution at low temperature was less satisfactory.

Diethyl *N*-bromo-*N*-alkylphosphoramidates **5** are yellow or orange-yellow oils, practically insoluble in water, but readily soluble in typical organic solvents. They are thermally unstable and cannot be distilled without decomposition. Pure samples of **5** decompose, sometimes violently, after few hours of storage at room temperature with liberation of bromine and formation of unidentified tarry materials. Solutions of **5** in organic solvents are more stable and can be safely used without any special precautions. When exposed to dispersed day-light they decompose slowly at room temperature and should be prepared just before use. The thermal and photochemical stability of **5** sharply decreases with increasing the length of the alkyl chain. Yields, physical constants, and spectroscopic data for diethyl *N*-bromo-*N*-alkylphosphoramidates **5** are compiled in Table 1.

Compounds **5a** ($R^1 = CH_3$) and **5b** ($R^1 = C_2H_5$) were found to add easily and regiospecifically to styrene (**6a**) and 2-methyl-1-butene (**6b**) in an anti-Markovnikov fashion (as deduced from ¹H-N.M.R. spectra examination) yielding the corresponding diethyl *N*-alkyl-*N*-(2-bromoalkyl)-phosphoramidates **7** which could be subsequently degraded (in crude form) by means of gaseous hydrogen chloride in tetrahydrofuran at room temperature to *N*-alkyl-*N*-(2-bromoalkyl)-amine hydrochlorides **8**.



5 a, b **6 a** $R^2 = C_6H_5$, $R^3 = H$; **b** $R^2 = CH_3$, $R^3 = C_2H_5$ **7**



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Additions of **5a** and **5b** to styrene, in which a radical or radical-like mechanism is probably involved, occurred spontaneously in boiling dichloromethane solution. Compound **5b** reacted considerably slower and required 5 h to complete the addition, which was practically finished after 3 h in the case of **5a**. Such prolonged heating resulted in partial decomposition of **5b** and contamination of the respective adduct **7**. Attempted additions of **5c** and **5d** to styrene failed, probably due to markedly decreased reaction rates and low thermal stability of *N*-bromoamides **5** containing relatively long *N*-alkyl residues. The reactions with 2-methyl-1-butene (**6b**) were also limited to **5a** and **5b**. To secure rea-

Table 1. Preparation of Diethyl *N*-Bromo-*N*-alkylphosphoramidates **5**

Product No.	R^1	Yield [%]	n_D^{20}	Molecular formula[a]	I.R. (film)[b] ν_{max} [cm^{-1}]	^{31}P-N.M.R. (CH_2Cl_2)[c] δ [ppm]	^{1}H-N.M.R. (CCl_4)[d] δ [ppm], J [Hz]
5a	CH_3	96	1.4722	$C_5H_{13}BrNO_3P$ (246.1)	1255; 1160; 1020; 970	−9.25	1.31 (t, 6H, $J_{HH}=7.25$); 3.13 (d, 3H, $^3J_{PH}=11.0$); 4.10 (dq, 4H, $J_{HH}=7.25$, $^3J_{PH}=8.0$)
5b	C_2H_5	91	1.4650	$C_6H_{15}BrNO_3P$ (260.1)	1255; 1160; 1120; 1030; 960	−7.80	1.18 (t, 3H, $J_{HH}=6.95$); 1.29 (t, 6H, $J_{HH}=7.1$); 3.31 (dq, 2H, $J_{HH}=6.95$, $^3J_{PH}=8.5$); 4.10 (dq, 4H, $J_{HH}=7.1$, $^3J_{PH}=8.0$)
5c	*n*-C_4H_9	97	1.4652	$C_8H_{19}BrNO_3P$ (288.1)	1250; 1160; 1030; 970	−8.25	0.96 (dist t, 3H, $J_{HH}=7.0$); 1.33 (t, 6H, $J_{HH}=7.2$); 1.20–1.82 (m, 4H); 3.24 (q, 2H, $J_{HH}\approx{}^3J_{PH}\approx6.8$); 4.08 (dd, 4H, $J_{HH}=7.2$, $^3J_{PH}=8.2$)
5d	*s*-C_4H_9	96	1.4728	$C_8H_{19}BrNO_3P$ (288.1)	1230; 1165; 1040; 965	−6.75	0.91 (t, 3H, $J_{HH}=7.2$); 1.14 (d, 3H, $J_{HH}=6.5$); 1.28 (t, 6H, $J_{HH}=7.0$); 1.15–1.88 (m, 2H); 3.03 (m, 1H); 4.05 (qt, 4H, $J_{HH}\approx{}^3J_{PH}\approx7.25$)

[a] All crude products gave satisfactory microanalyses (C ±0.2%; H ±0.1%; N ±0.2%; P ±0.4%).

[b] The I.R. spectra were recorded on a Specord 71 IR (C. Zeiss) spectrophotometer.

[c] The ^{31}P-N.M.R. spectra were measured at 24.3 MHz with a Jeol JNM-C-60 HL spectrometer using 85% H_3PO_4 as external reference. A Heteronuclear Spin Decoupler, JNM-SD-HC, was used for precise ^{31}P chemical shift determinations.

[d] The ^{1}H-N.M.R. spectra were measured at 80 MHz with a Tesla BS 487C spectrometer using TMS as internal standard.

Table 2. *N*-Alkyl-*N*-(2-bromoalkyl)-amine Hydrochlorides **8**

Product	R^1	R^2	R^3	Yield [%][a]	m.p.	Molecular formula[b]	I.R. [KBr][c] ν_{max} [cm^{-1}]	^{1}H-N.M.R. (D_2O)[d] δ [ppm][d], J [Hz]
8a	CH_3	C_6H_5	H	68	143–145°	$C_9H_{13}BrClN$ (250.6)	2940; 2730; 2435; 1585; 1460; 1380; 758; 695	3.18 (s, 3H, CH_3); dist ABX system: $\delta=3.80$–4.33 (AB part, m, 2H), $\delta=5.75$, 5.79, 5.81, 5.84. (X part, 4 lines, 1H); 7.87 (s, 5H, H_{arom})
8b	C_2H_5	C_6H_5	H	29	153–156°	$C_{10}H_{15}BrClN$ (262.6)	2940; 2730; 2460; 1590; 1460; 760; 695	1.75 (t, 3H, $J_{HH}=7.0$, $C\underline{H}_3$ CH_2); 3.65 (q, 2H, $J_{HH}=7.0$, CH_3 $C\underline{H}_2$); dist ABX system: $\delta=4.00$–4.44 (AB part, m, 2H), $\delta=5.75$, 5.79, 5.81, 5.84 (X part, 4 lines, 1H); 7.97 (s, 5H, H_{arom})
8c	CH_3	CH_3	C_2H_5	29	129–130°	$C_6H_{15}BrClN$ (216.6)	2960; 2750; 2450; 1595; 1463; 1160	.55 (t, 3H, $J_{HH}=7.5$, $C\underline{H}_3$ CH_2); 2.27 (s, 3H, $C\underline{H}_3$ C); 2.20–2.65 (m, 2H, CH_3 $C\underline{H}_2$); 3.34 (s, 3H, $C\underline{H}_3$ N); 3.98 (s, 2H, $C\underline{H}_2$ N)
8d	C_2H_5	CH_3	C_2H_5	10	131–133°	$C_7H_{17}BrClN$ (230.6)	2960; 2800; 2460; 1590; 1460; 805	1.54 (t, 3H, $J_{HH}=7.3$, $C\underline{H}_3$ CH_2 C); 1.83 (t, 3H, $J_{HH}=7.5$, $C\underline{H}_3$ CH_2 N); 2.27 (s, 3H, $C\underline{H}_3$ C); 2.16–2.65 (m, 2H, CH_3 $C\underline{H}_2$ C); 3.75 (q, 2H, $J_{HH}=7.5$, CH_3 $C\underline{H}_2$ N); 3.96 (s, 2H, C $C\underline{H}_2$ N)

[a] Calculated for the corresponding diethyl *N*-alkylphosphoroamidate (**4a** or **4b**).

[b] The microanalyses of all compounds were in good agreement with the calculated values: C, ±0.3; H, ±0.2; N, ±0.2%.

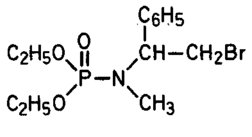
[c] The I.R. spectra were recorded on a Spectromom 2000 (MOM, Budapest) spectrophotometer. The strongest and most typical absorptions are only given.

[d] The ^{1}H-N.M.R. spectra were measured at 80 MHz with a Tesla BS 487C spectrometer using TMS as external standard.

sonable reaction rates and to avoid undesirable decomposition of the substrates upon prolonged heating, both reactions had to be initiated and/or accelerated by U.V. irradiation. They were thus completed within 0.5–1 h (negative KJ test for positive bromine) but overall yields of the adducts were rather low due to extensive (20–60%) decomposition of **5a** and **5b** upon irradiation. No attempts to optimize the procedure have been made. The removal of diethyl *N*-methyl- (**4a**) or *N*-ethylphosphoramidate (**4b**) (formed by decomposition of **5a** or **5b**) from the adducts **7** could be done simply by washing them with water. Subsequent degradation of crude **7** with hydrogen chloride in tetrahydrofuran at room temperature afforded pure *N*-alkyl-*N*-(2-bromoalkyl)-amine hydrochlorides **8** in moderate overall yields and analytical purity (Table 2).

The reaction sequence: **6a** or **b**→**8**, albeit limited only to the addition of **5a** and **5b** to terminal olefins, offers a reasonable entry to *N*-methyl- and *N*-ethylaziridines which are available in one step from their β-bromoamine precursors.

Attempted ionic-type additions of **5a–c** to styrene and cyclohexene in the presence of boron trifluoride etherate[3] were generally unsuccessful. Bromine addition and/or allylic bromination occured extensively and the formation of an impure adduct **9** was observed only in the case of styrene. As deduced from the mass spectrum of this adduct and ^{1}H-N.M.R. spectrum of its degradation product **10** they were both regioisomers of the respective compounds obtained by free-radical addition of **5a** to styrene.



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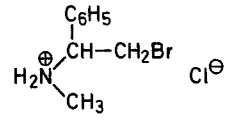

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Diethyl N-Bromo-N-alkylphosphoramidates 5; General Procedure:
Bromine (3.2 g, 0.02 mol) is added dropwise with stirring and external cooling (ice/salt or ice/calcium chloride bath) to a solution of diethyl *N*-alkylphosphoramidate[4] (4; 0.02 mol) in dichloromethane (20 ml) containing finely powdered potassium carbonate (3.0 g, 0.022 mol). After the addition of bromine is completed the mixture is stirred for ~2 h at 0-5° (for **4a** and **4b**) or −15 to −10° (for **4c** and **4d**). The end of bromination is recognized by a paling of the dark-brown bromine color. The solution is then filtered and the precipitate washed with small amount of dichloromethane. The organic phase is concentrated to an orange-yellow oil from which the residual solvent is evaporated under high vacuum at room temperature. Crude *diethyl* N-*bromo*-N-*alkylphosphoramidates* **5**, thus obtained, are analytically pure; yields, physical constants, and relevant spectral assignments are summarized in Table 1. The filtered solutions of **5** in dichloromethane are used directly for addition to olefins.

Diethyl N-Methyl-N-(2-bromo-2-phenylethyl)-phosphoramidate (7; $R^1 = C_6H_5$, $R^2 = H$, $R^3 = CH_3$):
Styrene (**6a**; 2.1 g, 0.02 mol) is added to the freshly prepared [by bromination of diethyl *N*-methylphosphoramidate (3.34 g, 0.02 mol) in dichloromethane (20 ml)] solution of diethyl *N*-bromo-*N*-methylphosphoramidate (**5a**) and the mixture is heated gently under reflux for 3 h until it becames pale yellow and gives a negative test for positive bromine. The resultant solution is washed with water (2 × 20 ml), dried with anhydrous magnesium sulfate, and evaporated in vacuo to give **7** as a pale yellow, syrupy oil; yield: 5.3 g (76% with respect to **4a**).

$C_{13}H_{21}BrNO_3P$	calc.	C 44.58	H 6.04	N 4.00	P 8.84
(350.2)	found	44.7	5.8	4.1	9.1

^{1}H-N.M.R. (CCl_4): $\delta = 1.16$, 1.23 (2t, 6H, $J_{HH} = 7.0$ Hz, $C\underline{H}_3$ CH_2 O); 2.50 (d, 3H, $^3J_{PH} = 9.25$ Hz, N $C\underline{H}_3$); 3.48-4.17 (m, 6H, CH_3 $C\underline{H}_2$ O, $C\underline{H}_2$ N); 5.15 (t, 1H, $J_{HH} = 8.0$ Hz, $C\underline{H}$ Br); 7.15-7.60 ppm (m, 5H, H_{arom}).

^{31}P-N.M.R. (CH_2Cl_2): $\delta = -9.25$ ppm (from H_3PO_4).

Diethyl N-Ethyl-N-(2-bromo-2-phenylethyl)-phosphoramidate (7; $R^1 = C_6H_5$, $R^2 = H$, $R^3 = C_2H_5$):
The experiment is carried out as described above starting from styrene (0.2 mol) and an equimolar amount of **5b** (freshly prepared solution in dichloromethane). The addition is completed after 5 h; yield: 2.9 g (40%) of slightly impure adduct which could not be satisfactorily analyzed but gave correct ^{1}H-N.M.R. spectrum.

^{1}H-N.M.R. (CCl_4): $\delta = 0.98$ (t, 3H, $J_{HH} = 7.0$ Hz, $C\underline{H}_3$ CH_2 N); 1.17, 1.20 (2t, 6H, $J_{HH} = 7.5$ Hz, $C\underline{H}_3$ CH_2 O); 2.57-3.17 (m, 2H, CH_3 $C\underline{H}_2$ N); 3.62 (dd, 2H, $J_{HH} = 7.5$ Hz, $^3J_{PH} = 12.0$ Hz, CH $C\underline{H}_2$ N); 3.80, 3.87 (2 qt, 4H, $J_{HH} \approx {}^3J_{PH} \approx 7.5$ Hz, CH_3 $C\underline{H}_2$ O); 5.18 (t, 1H, $J_{HH} = 8.0$ Hz, $C\underline{H}$ Br); 7.10-7.60 ppm (m, 5H, H_{arom}).

^{31}P-N.M.R. (CH_2Cl_2): $\delta = -9.75$ ppm (from H_3PO_4).

Addition of 5a or 5b to 2-Methyl-1-butene (6b):
2-Methyl-1-butene (**6b**; 2.8 g, 0.04 mol) is added to an equimolar amount of freshly prepared **5a** or **5b** in dichloromethane (40 ml). The mixture is heated under reflux and continuously irradiated by a U.V. lamp until disappearance of the yellow coloration and until it gives a negative test for positive bromine (~30 min for **5a** and 1 h for **5b**). Dichloromethane is then evaporated, the residue dissolved in benzene (50 ml), and washed with water (3 × 50 ml) to remove diethyl *N*-alkylphosphoramidate **4** formed by photolytic decomposition of **5**. After removal of solvent the residue (impure adduct **7**) is not characterized but subjected to degradation in the crude state.

Degradation of the Adducts 7; Preparation of N-Alkyl-N-(2-bromoalkyl)-amine Hydrochlorides 8:
Dry hydrogen chloride is passed at 0-5° for 1 h through a solution of crude adduct **7** [prepared by bromination of **4** (0.02 mol) and its subsequent addition to the olefin] in tetrahydrofuran (20 ml). The solution is allowed to stand at room temperature for 24 h; it is then evaporated and ether (40 ml) is added to the residue. The crystalline precipitate of **8** is filtered off, washed with ether, and crystallized from ethanol/ether (1:1) (Table 2).

Ionic Addition of 5a to Styrene; Preparation of N-Methyl-N-(2-bromo-1-phenylethyl)-amine Hydrochloride (10):
Boron trifluoride etherate (1.4 g, 0.01 mol) is added to a solution of freshly prepared **5a** [by bromination of **4a** (0.01 mol) in tetrachloromethane (20 ml)]. The mixture is cooled to −20° and styrene (1.04 g, 0.01 mol) is added dropwise with stirring at this temperature. Stirring is continued for 1 h at −20° and the mixture is then warmed to room temperature. It is washed with 10% aqueous sodium hydrogen sulfite and water, dried with anhydrous magnesium sulfate, and evaporated to give crude **9** as a yellow, sirupy oil.

^{31}P-N.M.R. (CCl_4): $\delta = -9.0$ ppm (from H_3PO_4);

M.S. (70 eV): $m/e = 350$ (M + 1, 0.34%); 256 ($M - CH_2Br$, 100%).

Crude adduct **9** is degraded with gaseous hydrogen chloride as described above to give the pure β-bromoamine hydrochloride **10**; yield: 1.05 g (42%); m.p. 141-143° (from ethanol/ether, 1:1).

$C_9H_{13}BrClN$	calc.	C 43.12	H 5.23	N 5.59
(250.7)	found	43.1	5.1	5.6

^{1}H-N.M.R. (D_2O): $\delta = 2.97$ (s, 3H, $C\underline{H}_3$); 4.38 (d, 2H, $J_{HH} = 6.0$ Hz, $C\underline{H}_2Br$); 5.07 (t, 1H, $J_{HH} = 6.0$ Hz, $C\underline{H}$); 7.65 ppm (s, 5H, H_{arom}).

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