Diethyl N,N-Dibromophosphoroamidate (DBPA)[1]

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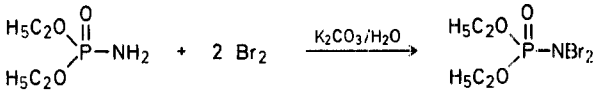
Synthetic applications of amide radicals which offer a new approach to functionalization of olefins have been reviewed recently[2]. Among the spectrum of various N,N-dihaloamides which can add to unsaturated hydrocarbons providing a host of chain-halogenated amine derivatives, N,N-dihalophosphoroamides seem to be very promising[1].

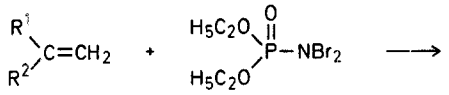
In the present paper we should like to report the first synthesis[3] of diethyl N,N-dibromophosphoroamidate (DBPA; **2**) which can be readily obtained by the action of bromine on diethyl phosphoroamidate (**1**):



1 **2**

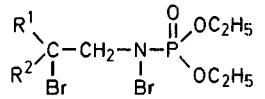
The bromination using elemental bromine was carried out in aqueous potassium carbonate solution at 0° to give analytically pure **2** in 92% yield. Crude diethyl N,N-dibromophosphoroamidate (DBPA, **2**) was an orange-red sirupy oil, sparingly soluble in water and easily soluble in typical organic solvents. It could not be distilled without decomposition, but was perfectly stable when stored in the dark at low temperature (0–5°). Bromination of **1**, carried out in the presence of sodium or lithium carbonate, afforded yellow solids (m.p. 118–120° and 108–112°), insoluble in water, to which the structures of molecular-type compounds 3 DBPA · NaBr (**3**) and 3 DBPA · LiBr (**4**) have been ascribed on the basis of elemental analysis and spectral data.

DBPA (**2**) was found to add readily and almost quantitatively to styrene (**5**) and isobutylene (**6**) in anti-Markovnikov fashion (which is evident from N.M.R. spectrometric examination) yielding the corresponding diethyl N-bromo-N-(2-bromoalkyl)-phosphoroamidates (**7**) which could be subsequently reduced by means of 20% aqueous sodium pyrosulfite at low temperature (10°) to diethyl N-(2-bromoalkyl)-phosphoroamidates (**8**, **9**):



5 $R^1 = C_6H_5$, $R^2 = H$
6 $R^1 = R^2 = CH_3$

2



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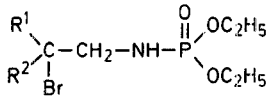
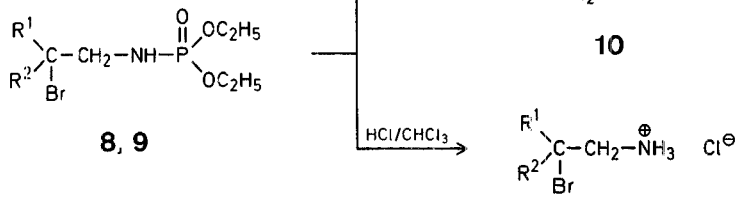


8 $R^1 = C_6H_5$, $R^2 = H$
9 $R^1 = R^2 = CH_3$

Both reactions, in which a radical or radical-like mechanism is probably involved, occured however spontaneously in boiling dichloromethane solution and did not require any initiation. In the case of isobutylene, no allylic bromination products were observed. It is noteworthy that DBPA (**2**) is not only much more reactive but, surprisingly, also much more selective than its N,N-dichloro analogue (DCPA) in this respect. The reaction of DCPA with isobutylene, occurring only at 80°, affords the corresponding adduct in moderate yield, considerable amounts of allylic chlorination products being produced[4].

The DBPA-olefin adducts (**8**, **9**) are well suited to their conversion with base into N-phosphorylated aziridines (**10**) or with gaseous hydrogen chloride to β-bromoamine hydrochlorides (**11**, **12**):



8, **9** **10**

11 $R^1 = C_6H_5$, $R^2 = H$
12 $R^1 = R^2 = CH_3$

The latter possibility, which has already been verified in our laboratory, offers a two-step, very convenient entry to functionalization of olefins.

Diethyl N,N-Dibromophosphoroamidate (DBPA, 2):
Bromine (32.0 g, 0.2 mol) was added dropwise with stirring and external cooling (ice-salt bath) to a solution of diethyl phosphoroamidate (15.3 g, 0.1 mol) and potassium carbonate (15.2 g, 0.11 mol) in water (120 ml) at 0°. The resulting mixture was stirred for 30 min. at 0° and finally for 1 hr at 20°. Dichloromethane (80 ml) was then added and the organic layer separated. The aqueous layer was extracted with dichloromethane (3 × 30 ml). The organic phase was washed with cold water (2 × 30 ml), dried, and concentrated to an oil from which the residual solvent was evaporated in high vacuum at room temperature; yield: 28.6 g (92%); n_D^{20}: 1.5244.

$C_4H_{10}Br_2NO_3P$	calc.	C 15.44	H 3.24	N 4.50	P 9.96
	found	15.55	3.12	4.85	9.80

I.R. (film): 1250 (P=O), 1161 (C_2H_5—O—P/), 1094, 1024, 970 (P—O—C/) cm^{-1}.

N.M.R. (CCl_4): δ 1.443, 1.457 (2t, 6H, J_{H-H} = 7.1 Hz, CH_3), 4.26 (2q, 4H, J_{H-H} = 7.1 Hz, J_{H-P} = 8.3 Hz, CH_2—CH_3).

Bromination of Diethyl Phosphoroamidate (1) in the Presence of Sodium Carbonate:
The reaction was carried out as described above starting from diethyl phosphoroamidate (**1**; 7.65 g, 0.05 mol), sodium carbonate (5.83 g, 0.055 mol), and bromine (16.0 g, 0.1 mol) in water (60 ml). After the addition of bromine was completed the mixture was stirred for 1 hr at 0°. The precipitated yellow solid was isolated by filtration, washed with water (2 × 15 ml), and dried in vacuo over sodium hydroxide; yield: 13.5 g (78%); m.p. 118–120° (Lit.[3]: m.p. 118–119°).

$(C_4H_{10}Br_2NO_3P)_3 \cdot NaBr$	calc.	C 13.93	H 2.91	N 4.06	P 8.99
	found	13.89	2.91	4.23	9.22

I.R. (KBr): 1260 (P=O), 1218, 1160 (C_2H_5—O—P/), 1029 (P—O—C/) cm^{-1}.

N.M.R. ($CDCl_3$): δ 1.412, 1.428 (2t, 6H, J_{H-H} = 7.5 Hz, CH_3), 4.31 (2q, 4H, J_{H-H} = 7.5 Hz, J_{H-P} = 8.3 Hz, CH_2—CH_3).

Bromination of Diethyl Phosphoroamidate (1) in the Presence of Lithium Carbonate:
The reaction was carried out as described above starting from diethyl phosphoroamidate (**1**, 7.65 g, 0.05 mol), lithium carbonate (4.1 g, 0.055 mol), and bromine (16.0 g, 0.1 mol) in water (80 ml); yield: 12.7 g (75%); m.p. 108–112°; yellow solid, insoluble in water.

$(C_4H_{10}Br_2NO_3P)_3 \cdot LiBr$	calc.	C 14.15	H 2.97	N 4.12	P 9.12
	found	14.22	2.97	4.09	9.18

I.R. (KBr): 1247 (P=O), 1198, 1157 (C_2H_5—O—/P/), 1031, 962 (P—O—/C/) cm^{-1}.

N.M.R. ($CD_3 \cdot CO \cdot CD_3$): δ 1.342, 1.358 (2t, 6H, $J_{H-H}=7.5$ Hz, CH_3), 4.23 (2q, 4H, $J_{H-H}=7.5$ Hz, $J_{H-P}=8.3$ Hz, CH_2—CH_3).

Diethyl N-(2-Bromo-2-phenylethyl)-phosphoroamidate (8):
A solution of freshly distilled styrene (2.08 g, 0.02 mol) in dichloromethane (15 ml) was added dropwise to a stirred solution of DBPA (**2**; 6.22 g, 0.02 mol) in dichloromethane (50 ml). The resulting mixture was refluxed for 1 hr, then cooled to 10°, and treated with a 20% aqueous solution of sodium pyrosulfite (20 ml). The organic layer was separated, washed with water (2 × 20 ml), dried, and evaporated under reduced pressure. The residue was heated at 40–45°/0.1 mm for 1 hr and afforded **8** as a pale yellow, sirupy oil; yield: 6.25 g (93%); n_D^{20}: 1.5264.

$C_{12}H_{19}BrNO_3P$	calc.	C 42.85	H 5.66	N 4.17
	found	42.29	5.51	4.21

I.R. (film): 3212 (NH), 1241 (P=O), 1170, 1130 (C_2H_5—O—/P/), 1060, 1036, 972 (P—O—/C/) cm^{-1}.

N.M.R. (CCl_4): δ 1.20, 1.28 (2t, 6H, $J_{H-H}=7.0$ Hz, CH_3), 3.15–4.00 (m, 2H, NH—CH_2), 3.91 (5 lines, 4H, $J_{H-H}=J_{P-H}=7.0$ Hz, CH_3—CH_2), 4.45–5.14 (broad singlet, 1H, disappearing on deuteration, NH), 4.95 (t, 1H, J = 7.5 Hz, —CH—Br), 7.10–7.60 (m, 5H, $H_{aromat.}$).

Diethyl N-(2-Bromo-2-methylpropyl)-phosphoroamidate (9):
A solution of DBPA (**2**; 12.44 g, 0.04 mol) in dichloromethane (15 ml) was added dropwise to a saturated solution of isobutylene in dichloromethane (70 ml) at room temperature at such a rate as to maintain a slightly yellow coloration of the reaction mixture (~4 hr). A slow stream of isobutylene was passed continuously through the solution. After the addition was completed the mixture was worked up as described in the previous experiment to give 11.2 g (97%) of crude **9** as pale yellow oil: n_D^{20}: 1.4742.

$C_8H_{19}BrNO_3P$	calc.	C 33.38	H 6.60	N 4.86
	found	33.25	6.59	4.46

I.R. (film): 3220 (NH), 1453 (as. CH_3), 1390, 1370 (sym. CH_3), 1240 (P=O), 1162 (C_2H_5—O—/P/), 1025, 965 (P—O—/C/), 510 (C—Br) cm^{-1}.

N.M.R. (CCl_4): δ 1.30 (t, 6H, J = 7.3 Hz, CH_3—CH_2), 1.75, 1.85 (2s, 6H, CH_3—C), 2.95–3.80 (m, 3H, CH_2—NH), 4.00 (5 lines, 4H, $J_{H-H}=J_{P-H}=7.3$ Hz, CH_3—CH_2).

Degradation of Diethyl N-(2-Bromo-2-phenylethyl)-phosphoroamidate (8) using Hydrogen Chloride; 2-Bromo-2-phenylethylamine Hydrochloride (11):
Dry hydrogen chloride was passed at room temperature for 3 hr through a solution of **8** (3.36 g, 0.01 mol) in chloroform (30 ml). The solution which was saturated with hydrogen chloride was allowed to stand at room temperature overnight; it was then degassed and partially evaporated. The crystalline precipitate was isolated by filtration and ether (30 ml) was added to the filtrate. A second crop of **11** was isolated after 48 hr; total yield: 1.82 g (77%); m.p. 158–159° (from acetone).

$C_8H_{11}BrClN$	calc.	C 40.60	H 4.65	N 5.92
	found	40.63	4.63	5.95

I.R. (KBr): 2025 ($NH_3^{\oplus}$), 1608, 1524 ($NH_3^{\oplus}$), 1463, 1230, 1152, 892, 765, 702 cm^{-1}.

N.M.R. (D_2O): ABX system δ_A 3.82, δ_B 3.95, δ_X 5.60 (12 lines, 3H, $J_{AX}=6.6$ Hz, $J_{BX}=8.7$ Hz, $J_{AB}=13.6$ Hz, CH_2—CH—Br), 5.00 (s, $NH_3^{\oplus}$), 7.47–7.80 (m, 5H, $H_{arom.}$).

Degradation of Diethyl N-(2-Bromo-2-methylpropyl)-phosphoroamidate (9) using Hydrogen Chloride; 2-Bromo-2-methylpropylamine Hydrochloride (12):
The experiment was carried out as described above starting from **9** (5.76 g, 0.02 mol) in chloroform (60 ml); yield: 1.73 g (45%); m.p. 140° (dec.).

$C_4H_{11}BrClN$	calc.	C 25.43	H 5.84	N 7.43
	found	25.23	5.99	7.30

I.R. (KBr): 1960, 1580, 1510 ($NH_3^{\oplus}$), 1450, 1399, 1378 (CH_3), 1150 cm^{-1}.

N.M.R. (D_2O): δ 1.82 (s, 6H, CH_3), 3.33 (s, 2H, CH_2), 4.71 (s, $NH_3^{\oplus}$).

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[1] N,N-Dihalophosphoramides. III. Part II: A. ZWIERZAK, A. KOZIARA, Tetrahedron **26**, 3527 (1970).

[2] R. S. NEALE, Synthesis **1971**, 1.

[3] A. M. PINCHUK L. N. MARKOVSKII, T. V. KOVALEVSKAYA, Zh. Obshch. Khim. **39**, 2142 (1969); Engl. Edit., p. 2094, report the preparation of $(DBPA)_3 \cdot NaBr$, but without giving any conclusive proof of its structure.

[4] A. ZWIERZAK, A. KOZIARA, to be published.