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N,N-DIHALOPHOSPHORAMIDES—I*

SYNTHESIS OF DIETHYL N,N-DICHLOROPHOSPHOROAMIDATE (DCPA) AND SOME OF ITS STRUCTURAL ANALOGUES

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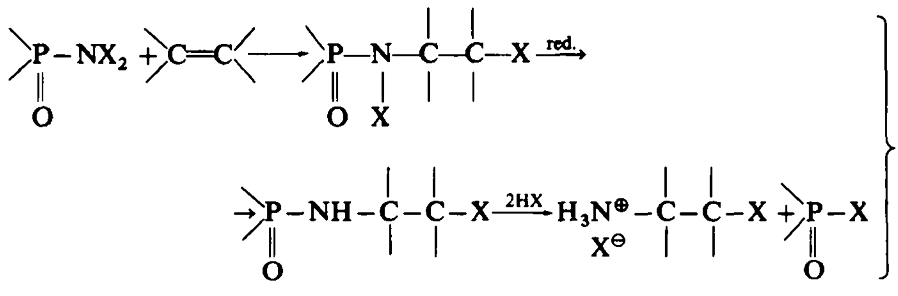
Abstract—Diethyl N,N-dichlorophosphoroamidate (DCPA), a stable, easily distillable, but very reactive pseudo-halogen containing phosphorus has been prepared in excellent yield by direct chlorination of diethyl phosphoroamidate in buffered aqueous acid solution. The reaction was found to be of general use for the preparation of some structural analogues of DCPA.

In recent years an increasingly active study of free-radical reactions of N-halo compounds[1] has shown that various synthetically important processes can be realized especially with N-halo and N,N-dihaloamides, Considerable attention is being given to the preparation of N,N-dichlorocarbamates as well as N,N-dichlorosulphonamides and their addition to a variety of unsaturated compounds.[2–10] These reactions offer a new approach to functionalization of olefins, i.e., to the syntheses of compounds containing halogen and C–N bond directly from unsaturated systems. Especially promising in this respect seem to be N,N-dihalophosphoramides, a novel class of organophosphorus pseudo-halogens, which are expected to add easily to unsaturated systems. N-(β-haloalkyl)-phosphoroamidates thus formed should be readily converted into the corresponding β-haloamines owing to the possibility of P—N bond fission by means of anhydrous acids:[11,12]


(1)

The purpose of our research program was to develop a new and convenient route to β-haloamines following the reaction sequence outlined above.

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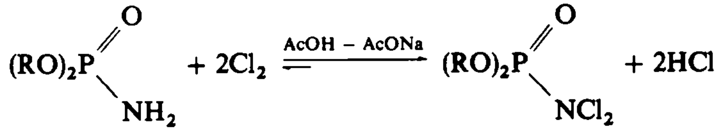
[*] Preliminary communication: A. Zwierzak and A. Koziara, *Angew. Chem.* **80**, 285 (1968). Paper CILVIII on organophosphorus compounds.

In this paper we report the preparation of the novel phosphorus containing pseudohalogen, diethyl N,N-dichlorophosphoroamidate (DCPA, I, R = Et) and some of its structural analogues.

N,N-dihalophosphoramides does not appear to be described except diphenyl N,N-dichlorophosphoroamidate which was obtained in an impure state by Petrov *et al.*[13] The Russian workers, however, apparently did not pursue the chemistry of this compound and did not try to prepare any structural analogues.

We have found that DCPA (I, R = Et) of analytical purity can be readily obtained in excellent yield (87%) by the reaction of a slight excess of chlorine with diethyl phosphoroamidate in buffered aqueous solution (pH = 6·3) containing acetic acid and sodium acetate (Eq. 2).



$$(RO)_2P(=O)NH_2 + 2Cl_2 \xrightleftharpoons{AcOH\ -\ AcONa} (RO)_2P(=O)NCl_2 + 2HCl \qquad (2)$$

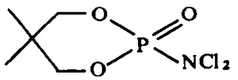
R = Et I

The temperature of the strongly exothermic reaction was maintained at 15–20°. Neutralization of the hydrochloric acid as it was formed shifted the equilibrium of the reaction (2) far to the right. DCPA, which is insoluble in the aqueous system, separated as a dense, greenish-yellow oil having a sharp, characteristic odour. The crude product could be easily purified by high-vacuum distillation affording analytically pure material. No symptoms of decomposition during distillation were encountered providing the bath temperature did not exceed 100–110°. Samples of distilled, analytically pure DCPA have been stored for 2 weeks in the dark at 0–5° without any appreciable loss of positive chlorine, as proved by iodometric titration. The crude material, when refrigerated for 2 weeks, lost about 10% of positive chlorine and should be redistilled just before use.

DCPA exhibited typical behaviour of positive chlorine containing reagents, like N,N-dichlorourethan[2] or N,N-dichlorosulphonamides.[3, 5–10] It reacted instantaneously with an aqueous solution of potassium iodide acidified with acetic acid, liberating a quantitative amount of free iodine. It was also found to be extremely reactive towards inorganic acid chlorides, e.g. thionyl chloride, sulphuryl chloride, sulphur dichloride, phosgene, thiophosgene, and phosphorus pentachloride as well as tervalent phosphorus esters and phosphines.[*]

Furthermore, DCPA was found to add easily, as expected, to the double bonds of various unsaturated compounds.[14] This combination of properties makes DCPA an attractive organophosphorus halogenoid reagent of important synthetic utility.

Structural analogues of DCPA, *viz* dimethyl N,N-dichlorophosphoramidate (I, R = Me), diisopropyl N,N-dichlorophosphoroamidate (I, R = i-Pr), and 2-(N,N-dichloroamino)-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinan (II) have been obtained by essentially the same preparative procedure starting from the corresponding phosphoroamidates.



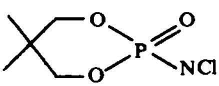
II

[*] Detailed studies on these and related reactions will be published elsewhere.

The first two compounds are relatively stable, distillable liquids resembling DCPA in their physical and chemical properties. Cyclic N,N-dichlorophosphoroamidate (II) is a pale-greenish crystalline solid (m.p. 118°), perfectly stable in the dark. It can be stored at low temperature for indefinite periods of time.

Physical constants, yields, and IR absorption bands of dialkyl N,N-dichlorophosphoroamidates (I) and of the cyclic compound (II) are summarized in the Table. Structural assignments are based upon elemental analysis, positive results of potassium iodide-starch tests, and spectral data. IR spectra are in all cases fully consistent with the structures proposed.

TABLE 1. N,N-DICHLOROPHOSPHORAMIDES

Compound	Yield %	B.p./mm[a] [m.p.], °C	n_D^{20}	IR spectral assignments[b]
$(MeO)_2P(O)NCl_2$	59	65–67/0·6 (115–120)	1·4690	2969m (C—H str.), 2864w (C—H str.), 1457m (C—CH_3 as. def.), 1294s (P=O str.), 1136m (C—O—(P) str.), 1108, 1051s [P—O—(C) str.], 895m, 855s, 778m, 762m
$(EtO)_2P(O)NCl_2$	87	56–57/0·01 (95–100)	1·4620	2991m (C—H str.), 2939w (C—H str.), 2920w (C—H str.), 2886w (C—H str.), 1482w (CH_2 sc.), 1450w (CH_3—C as. def.), 1400w (CH_3—C sym. def.), 1376w (CH_2 wag.), 1289s (P=O str.), 1169m [Et—O—(P)str.], 1102m, 1027s [P—O—(CH_2)str.], 989m [P—O—(CH_2)str.], 963m, 873m, 802m, 764w, 743w
$(i\text{-}PrO)_2P(O)NCl_2$	79	70/0·08 (110–120)	1·4530	2990m (C—H str.), 2947m (C—H str.), 2883w (C—H str.), 1474m, 1459w, 1393m (CH_3sym. def.), 1360m (—CH— def.), 1287s (P=O str.), 1184m, 1148m, 1110, 1017s [P—O—(CH)str.], 940w, 900m (CH_3 rock.?), 864m
	77	[118] from $CHCl_3$ —pet ether (1:1)	—	2968m (C—H str.), 2931m (C—H str.), 2907m (C—H str.), 2859m (C—H str.), 1638m, 1477m (CH_2 sc.), 1390m (CH_3 sym. def.), 1380m (CH_3 sym. def.), 1312s (P=O), 1303s (P=O), 1260s, 1061s, [P—O—(C) str.], 1012s [P—O—(CH_2) str.], 982s [P—O(CH_2)str.?], 951w, 928w, 918w, 890s, 860s, 788m[c]

[a] Bath temperatures given in parentheses; [b] Abbreviations: s, strong; m, medium; w, weak; str., stretching; as def., asymmetrical deformation; sym. def., symmetrical deformation: sc., scissoring; [c] IR spectrum was taken in KBr disc.

EXPERIMENTAL

Solvents and reagents were purified by conventional methods. Light petroleum refers to the fraction boiling at 60–80°. All extracts were dried over $MgSO_4$ and evaporated under reduced press. B.ps and m.ps (taken in capillaries) are uncorrected. IR spectra were recorded for liquid films, nujol mulls or KBr discs using an UR-10 spectrophotometer (C. Zeiss, Jena). Measurements were made on samples of analytical purity.

Diethyl phosphoramidate was obtained by the action of gaseous ammonia on diethyl phosphite in benzene-CCl_4 soln.[15] The crude amide was crystallized from cyclohexane-CCl_4 (1:1), yield 90%, m.p. 49–50°.

Diisopropyl phosphoroamidate was prepared as its diethyl analogue.[15] The crude amide was thoroughly washed with light petroleum and dried *in vacuo*, yield 83%, m.p. 56–58°.

Dimethyl phosphoroamidate. A stream of dry, gaseous ammonia was introduced into a mixture of freshly distilled dimethyl phosphite (165 g, 1·5 mole), CCl_4 (231 g, 1·5 mole), and benzene (400 ml) with stirring and efficient external cooling. The temp of the strongly exothermic reaction was kept below 10°. When the evolution of heat had abated, the introduction of ammonia was discontinued and the mixture stirred for additional 30 min at room temp: A white, voluminous ppt was filtered off and washed thoroughly with MeOH. The filtrate was evaporated, filtered once more, and distilled *in vacuo* to give 105 g (57%) of dimethyl phosphoroamidate, b.p. 98°/0·5 mm (bath temp 120°), n_D^{20} – 1·4347. The product crystallized on refrigeration. (Found: P, 24·9; N, 10·7; $C_2H_8O_3NP$ requires: P, 24·8; N, 11·2%). The IR spectrum (nujol mull) showed characteristic bands at: 3205s (NH), 1231s (P═O), 1180m [CH_3-O-(P)], 1031s [P-O-(CH_3)].

2-*Amino*-2-*oxo*-5,5-*dimethyl*-1,3,2-*dioxaphosphorinan.* A rapid stream of dry, gaseous ammonia was passed through a soln of 2-chloro-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinan (36·9 g, 0·2 mole) in benzene (200 ml) at 10–20° with stirring and efficient external cooling. After 2½ hr the white ppt of NH_4Cl and the amide was filtered off and washed with benzene (2 × 100 ml). The crystalline residue was extracted with hot EtOAc (2 × 200 ml) and the extract evaporated to dryness affording crude amide (28·0 g), m.p. 120–123°. On recrystallization from EtOAc (100 ml) colourless, lustrous plates (23·5 g, 63·5%) were obtained; m.p. 125–127°. (Found: C, 36·45; H, 7·8; P, 18·7; N, 8·5: $C_5H_{12}O_3PN$ requires: C, 36·4; H, 7·3; P, 18·8; N, 8·5%). The IR spectrum (nujol mull) showed characteristic bands at: 3301s (NH), 1241s (P═O), 1215s (P═O?), 1065s [P—O(C)], 1015s [P—O(C)].

Diethyl N,N-*dichlorophosphoroamidate* (DCPA, I, R = Et). Chlorine gas was introduced to a mixture of diethyl phosphoroamidate (15·3 g, 0·1 mole) and NaOAc (18·6 g, 0·227 mole), glacial AcOH (1·8 g, 0·031 mole), and water (40 ml) with stirring and external cooling. The temp of the strongly exothermic process was maintained at 15–20°. When the Cl_2 addition was complete, the reaction mixture acquired a permanent greenish-yellow colouration. The lower, oily layer was then separated and the aqueous layer extracted with $CHCl_3$ (2 × 25 ml). The combined oily layer and organic extracts were washed with water (2 × 25 ml), dried, evaporated, and distilled *in vacuo* affording 19·3 g (87%) of pure DCPA as greenish-yellow oil, b.p. 56–57°/0·01 mm (bath temp 95–100°), n_D^{20} – 1·4620. (Found: C, 22·2; H, 4·95; P, 13·75; N, 6·6; $C_4H_{10}O_3NPCl_2$ requires: C, 21·6; H, 4·5; P, 14·0; N, 6·3%). Iodometric analysis indicated a purity greater than 99·5%.

Dimethyl N,N-*dichlorophosphoroamidate* (I, R = Me). The reaction was carried out and the reaction mixture was worked-up as described in the previous experiment using the same molar proportions of all reagents. Pure I (R = Me) was obtained on distillation *in vacuo*, b.p. 65–67°/0·6 mm (bath temp 115–120°), n_D^{20} – 1·4690, yield 59%. (Found: C, 12·9; H, 3·1; $C_2H_6O_3PNCl_2$ requires: C, 12·4; H, 3·1%). Iodometric analysis indicated a purity not less than 98%.

Diisopropyl N,N-*dichlorophosphoroamidate* (I, R = i-Pr). The same preparative procedure as described immediately above was employed. Distillation *in vacuo* afforded pure I (R = i-Pr), b.p. 70°/0·08 mm (bath temp 110–120°), n_D^{20} – 1·4530, yield 79%. (Found: C, 28·8; H, 5·45; N, 6·2; $C_6H_{14}O_3PNCl_2$ requires: C, 28·8; H, 5·6; N, 5·6%).

2-(N,N-*Dichloroamino*)-2-*oxo*-5,5-*dimethyl*-1,3,2-*dioxaphosphorinan* (II). A soln of 2-amino-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinan (8·2 g, 0·05 mole) in $CHCl_3$ (20 ml), NaOAc (9·3 g, 0·114 mole), glacial AcOH (0·9 g, 0·016 mole), and water (20 ml) were placed in a 100 ml flask equipped with a stirrer, thermometer, and gas inlet tube. Cl_2 gas was introduced into the stirred soln over a period of 2 hr at 15–20°. The lower organic phase was then drawn off and water soln extracted with $CHCl_3$ (2 × 25 ml). The combined organic solns were washed with water (2 × 15 ml), dried, and evaporated to give 9·0 g (77%) of II as pale-greenish crystals, m.p. 95–100°. On recrystallization from $CHCl_3$-light petroleum (1:1) 8·5 g of analytically pure II was obtained, which melted at 118°. (Found: C, 26·0; H, 4·3; N, 6·2; P, 13·25; $C_5H_{10}O_3PNCl_2$ requires: C, 25·65; H, 4·3; N, 6·0; P, 13·2%). Iodometric analysis revealed the presence of almost theoretical amount of positive Cl_2. The product could be stored in the dark, tightly stoppered bottle for indefinite periods of time.

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