NOTES

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Synthesis of Dialkylaminomethylenediphosphonic Acids

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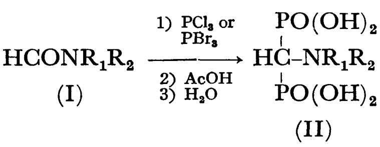
Synopsis. *N,N*-Dialkylformamides reacted with phosphorus trichloride or phosphorus tribromide to give the corresponding dialkylaminomethylenediphosphonic acids.

Although the reaction of amides with phosphoryl chloride has been studied as Vilsmeiyer reaction,[1] little is known concerning of the reaction of amides with phosphorus trichloride or phosphorus tribromide. In this paper, we wish to report the synthesis of dialkylaminomethylenediphosphonic acids by successive treatment of *N,N*-dialkylformamides with phosphorus trichloride and with acetic acid. In this experiment, the following amides were employed; *N,N*-dimethylformamide (Ia), *N,N*-diethylformamide (Ib), *N,N*-dipropylformamide (Ic), *N*-formylpyrrolidine (Id), *N*-formylpiperidine (Ie), and *N*-formylmorpholine (If). Phosphorus tribromide reacted also with the formamides to give the same products.



$$\underset{\text{(I)}}{HCONR_1R_2} \xrightarrow[\text{2) AcOH} \atop \text{3) } H_2O]{\text{1) } PCl_3 \text{ or} \atop PBr_3} \underset{\text{(II)}}{\overset{PO(OH)_2}{\underset{PO(OH)_2}{HC\text{-}NR_1R_2}}}$$

	R_1	R_2
Ia	Me	Me
Ib	Et	Et
Ic	Pr	Pr
Id	$-(CH_2)_4-$	
Ie	$-(CH_2)_5-$	
If	$-(CH_2)_2O(CH_2)_2-$	

These results are summarized in Table 1.

TABLE 1. PROPERTIES OF DIALKYLAMINOMETHYLENE-DIPHOSPHONIC ACIDS

Product	Yield (%)	Dp(°C)	pK_{a_1}	pK_{a_2}	pK_{a_3}
IIa	53.5	255	2.5	5.2	9.5
IIb	39.6	190—200	2.5	5.2	9.0
IIc	33.9	195—200	3.2	5.6	9.2
IId	44.0	220—225	2.7	5.3	9.5
IIe	28.9	250—255	3.0	5.5	9.4
IIf	15.7	250—260	3.0	5.2	9.0

The structure of IIa was confirmed to be dimethylaminomethylenediphosphonic acid by direct comparison with an authentic sample[2] by NMR and by dissociation constant (pK_a). The structures of the other products (IIb—IIf) were identified by elemental analysis and by alkalimetry.

Experimental

Preparation of Dimethylaminomethylenediphosphonic Acid (IIa). General Procedure: *N,N*-Dimethylformamide (7.3 g) was added dropwise to phosphorus trichloride (68.5 g) under cooling with ice-water. After stirring for an hour, the mixture was treated with 100 ml of glacial acetic acid. This was allowed to stand for several hours at room temperature with protection from moisture. After removal of the upper layer containing acetyl chloride by decantation, the lower layer was poured into 150 ml of ice-water, and this was concentrated to syrup under reduced pressure. After addition of absolute ethanol (300 ml), precipitate separated and it was filtered (17.5 g) and recrystallized from water. Mp 255 °C (dec.). NMR (D_2O): δ 3.12 (s, 6H, N-CH_3), 3.74 (t, 1H, P_2C-H, J_{PCH} 20 Hz). pK_{a1} 2.5, pK_{a2} 5.2, and pK_{a3} 9.5. Found: C, 15.22; H, 5.98; N, 5.87; P, 26.20%. Calcd for $C_3H_{11}NP_2O_6 \cdot H_2O$: C, 15.19; H, 5.49; N, 5.91; P, 26.16%.

In a similar manner, compounds IIb, IIc, IId, IIe, and IIf were obtained, as shown in Table 1.

References

1) H. H. Bosshard, R. Mory, M. Schmid, and H. Zollinger, *Helv. Chim. Acta*, **42**, 1653 (1959); H. H. Bosshard and H. Zollinger, *ibid.*, **42**, 1659 (1959); H. Bredereck, F. Effenberger, and G. Simchen, *Chem. Ber.*, **97**, 1403 (1964); M. Ochiai, *Kagaku no Ryoiki*, **19**, 900 (1965).

2) The synthetic sample was prepared by the procedure of Gross [H. Gross and B. Costisella, *Angew. Chem.*, **80**, 364 (1968).].