

NOTES

BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 48 (3), 1030 (1975)

Synthesis of Dialkylaminomethylenediphosphonic Acids

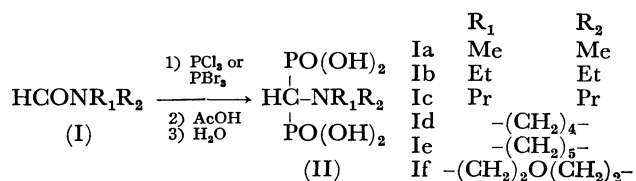
Masahiro FUKUDA, Yoshiki OKAMOTO, and Hiroshi SAKURAI

The Institute of Scientific and Industrial Research, Osaka University, Yamada-kami, Suita shi, Osaka 565

(Received May 10, 1974)

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 Vilsmeier reaction,¹⁾ little is known concerning 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*-diisopropylformamide (Ic), *N*-formylpyrrolidine (Id), *N*-formylpiperidine (Ie), and *N*-formylmorpholine (If). Phosphorus tribromide reacted also with the formamides to give the same products.



These results are summarized in Table 1.

TABLE 1. PROPERTIES OF DIALKYLAMINOMETHYLENE-DIPHOSPHONIC ACIDS

Product	Yield (%)	Dp(°C)	pK _{a1}	pK _{a2}	pK _{a3}
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
IIIf	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 sample²⁾ by NMR and by dissociation constant (pK_a). The structures of the other products (IIb—IIIf) 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 (D₂O): δ 3.12 (s, 6H, N-CH₃), 3.74 (t, 1H, P₂C-H, J_{POCH} 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 C₃H₁₁NP₂O₆·H₂O: C, 15.19; H, 5.49; N, 5.91; P, 26.16%.

In a similar manner, compounds IIb, IIC, IId, IIe, and IIIf 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)].