## THE SYNTHESES AND PROPERTIES OF TRICHLOROPHOSPHAZOCHLOROMETHANE AND TRIS(CHLOROMETHYL)AMINE

T. MOELLER and A. H. WESTLAKE Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois

## (Received 2 November 1966)

Abstract—The reaction between aminomethanesulphonic acid,  $H_2NCH_2SO_3H$ , and phosphorus (V) chloride has been shown to yield either dimeric trichlorophosphazochloromethane,  $(Cl_3P=NCH_2Cl)_2$ , or tris(chloromethyl)amine,  $N(CH_2Cl)_3$ , depending upon the mole ratio of the reactants. The latter compound is obtained in better yield as a product of the reaction of trisodium nitrilotrimethylene-sulphonate,  $N(CH_2SO_3Na)_3$ , with phosphorus (V) chloride. Certain of the physical and chemical properties of these new compounds are described.

AMINES and amides of the general formula  $\text{RNH}_2(\text{R} = \text{alkyl}, \text{aryl}, \text{acyl}, \text{sulphonylaryl})$  react with phosphorus (V) chloride to form trichlorophosphazo derivatives by elimination of hydrogen chloride (Kirsanov reaction),<sup>(1)</sup>

 $RNH_2 + PCl_5 \rightarrow RN = PCl_3 + 2HCl$ 

The reaction involving sulphamic acid yields trichlorophosphazosulphuryl chloride,  $Cl_3P$ —NSO<sub>2</sub>Cl,<sup>(2)</sup> which can be decomposed thermally to a mixture of the trimeric sulphanuric chlorides, (NSOCl)<sub>3</sub>.<sup>(3,4)</sup> It seemed reasonable that a parallel reaction sequence involving aminomethanesulphonic acid might yield polymeric products based upon nitrogen–carbon–sulphur heterocycles. However, sulphur dioxide elimination occurs in the first step, and, depending upon the mole ratio of reactants, the major isolable products are the new compounds dimeric trichlorophosphazochloromethane, ( $Cl_3P$ —NCH<sub>2</sub>Cl)<sub>2</sub>, and tris(chloromethyl)amine, N(CH<sub>2</sub>Cl)<sub>3</sub>. These results are in accord with an early observation that sulphonate groups bonded to carbon may be replaced by chlorine upon treatment with phosphorus (V) chloride.<sup>(5)</sup>

The chlorine atoms in these compounds are highly susceptible to nucleophilic substitution. Such reactions suggest use of the two substances as intermediates in synthesis.

## EXPERIMENTAL

*Materials and apparatus.* Aminomethanesulphonic acid was prepared by a standard procedure.<sup>(6,7)</sup> All other chemicals used were of analytical reagent quality. All solvents were dried carefully by standard techniques. Because of the hygroscopic natures of the products and certain reagents, materials were handled and studied under anhydrous conditions in closed systems and often under an atmosphere of dry nitrogen or argon.

- <sup>(3)</sup> A. V. KIRSANOV, J. gen. Chem. U.S.S.R. 22, 93 (1952).
- (4) A. VANDI, T. MOELLER and T. L. BROWN, Inorg. Chem. 2, 899 (1963).
- <sup>(5)</sup> L. CARIUS, Ann. 114, 140 (1860).
- <sup>(6)</sup> W. G. PALMER, Experimental Inorganic Chemistry, p. 359. University Press, Cambridge (1954).
- <sup>(7)</sup> G. SCHLESSINGER, Inorg. Synth. 8, 121 (1966).

<sup>&</sup>lt;sup>(1)</sup> R. A. SHAW, R. KEAT and C. HEWLETT, *Preparative Inorganic Chemistry* (Edited by W. L. JOLLY), Vol. 2, pp. 1–91. Interscience, New York (1965), also references cited therein.

<sup>&</sup>lt;sup>(2)</sup> A. V. KIRSANOV, J. gen. Chem. U.S.S.R. 22, 101 (1952).

Molecular weights were determined cryoscopically, using solutions in dry benzene and applying a technique previously described.<sup>(6)</sup> PMR spectra were measured with a Varian A-60 instrument, using carbon disulphide solutions with TMS as an internal standard. Phosphorus-31 NMR spectra were obtained with a Varian DP-60 instrument, using carbon disulphide solutions with 85% orthophosphoric acid as an external standard. I.R. spectra were obtained with a Beckman IR-5 instrument, using carbon disulphide and carbon tetrachloride solutions.

Reaction of  $H_2NCH_2SO_3H$  with  $PCl_5$ —Mole ratio 1:2. Twenty-five milliliters of phosphorus (V) oxytrichloride was added to a mixture of 9.3 g (0.084 mole) of aminomethanesulphonic acid and 34.8 g (0.167 mole) of phosphorus (V) chloride. This mixture was heated for 22 hr at an oil-bath temperature of 130°. A small quantity of unreacted aminomethanesulphonic acid was removed by filtration, and the filtrate was evaporated by heating *in vacuo*. The yellow viscous liquid that remained, when heated at ~140° and 0.2 mm, yielded a colourless sublimate contaminated with a small quantity of viscous liquid. The sublimate was dissolved in carbon tetrachloride. Evaporating the solution to ~5 ml and cooling yielded 0.6 g of a white crystalline product, subliming at 60° (0.2 mm) and melting at 90–92°. Anal. Calcd. for N(CH<sub>2</sub>Cl)<sub>8</sub>: C, 22·18; H, 3·72; N, 8·62; Cl, 65·49. Found: C, 21·60; H, 3·72; N, 8·62; Cl, 63·99.

Reaction of  $H_2NCH_2SO_3H$  with  $PCl_5$ —Mole ratio 1:3.5. To a mixture of 8.1 g (0.073 mole) of aminomethanesulphonic acid and 54.4 g (0.261 mole) of phosphorus (V) chloride, 25 ml of phosphorus (V) oxytrichloride was added as reaction medium. The mixture was heated for 20 hr at a bath temperature of 135°. The resulting cloudy, pale-yellow liquid was evaporated *in vacuo* to a volume of ~5 ml. The solid which had deposited was removed by filtration and extracted by heating with 150 ml of carbon tetrachloride. The liquid phase was separated from undissolved solid and evaporated to dryness. A second extraction with 100 ml of chloroform yielded a solution which deposited 7.5 g of pale yellow solid upon evaporation. Recrystallization from carbon tetrachloride gave a colourless crystalline product, m.p. 140–141°. Yield: 5.9 g (40%). Anal. Calcd. for Cl<sub>3</sub>PNCH<sub>2</sub>Cl: C, 5.98; H, 1.00; N, 6.98; Cl, 70.61; P, 15.43. Found: C, 6.00; H, 1.03; N, 7.00; Cl, 70.00; P, 14.72.

Reaction of  $N(CH_2SO_3Na)_3$  with PCl<sub>5</sub>. The hydrated salt,  $N(CH_2SO_3Na)_3'3H_2O$ , was prepared as previously described<sup>(9)</sup> and dehydrated by heating at 190° and 0·2 mm for 20 hr. To a mixture of 34 g (0·093 mole) of the anhydrous salt and 116 g (0·56 mole) of phosphorus (V) chloride, 150 ml of phosphorus (V) oxytrichloride was added. The mixture was heated for 21 hr at a bath temperature of 120°. Precipitated sodium chloride was removed from the cooled solution and the filtrate evaporated to dryness. Heating the residue at 60–90° and 0·2 mm gave a colourless sublimate contaminated with a small quantity of colourless, viscous liquid. The solid was recrystallized from carbon tetrachloride, resublimed, and recrystallized again. M.p. 92–93°. Yield 3·4 g (23%). Anal. Calcd. for N(CH<sub>2</sub>Cl)<sub>3</sub>: C, 22·18; H, 3·72; N, 8·62. Found: C, 21·92; H, 4·15; N, 8·83.

## **RESULTS AND DISCUSSION**

The PMR spectrum of trichlorophosphazochloromethane consists of a 1:2:1 triplet at a  $\tau$  value of 4.77 ppm ( $J_{P-H} = 300$  c/s). The protons are thus indicated to be coupled with two phosphorus atoms in identical environments. The observed molecular weight of the compound in benzene (399, 446 vs. 402 calculated for a dimer) indicates a dimeric composition. The <sup>31</sup>P NMR spectrum contains a single peak at 80 ppm relative to orthophosphoric acid, thus suggesting that both phosphorus atoms are equivalent. A four-membered ring structure,

is consistent with these observations. This cyclic structural unit has been proposed for

 <sup>&</sup>lt;sup>(8)</sup> T. L. BROWN, R. L. GERTEIS, D. A. BAFUS and J. A. LADD, J. Am. chem. Soc. 86, 2135 (1964).
<sup>(9)</sup> R. G. LACOSTE and A. E. MARTELL, J. Am. chem. Soc. 77, 5512 (1955).

a number of closely related compounds,<sup>(10–13)</sup> and its presence in the molecular structure of the species ( $Cl_3PNCH_3$ )<sub>2</sub> has been confirmed by X-ray diffraction studies.<sup>(14,15)</sup>

The i.r. spectrum of trichlorophosphazochloromethane (Table 1) showed no

Frequency (cm <sup>-1</sup> )	
(Cl <sub>3</sub> PNCH <sub>2</sub> Cl) <sub>2</sub>	N(CH <sub>2</sub> Cl) <sub>3</sub>
3030(vw) <sup>a</sup>	2980(vw)
2975(vw)	1450(w)
1442(m)	1370(m)
1307(w)	1310(vw)
1267(m)	1280(s)
1161(s)	1220(vw)
<b>998</b> (m)	1147(s)
821(s)	954(m)
710(m)	686(m,br)
681(m)	652(m,br)

TABLE 1.—I.R. DATA

<sup>a</sup> s = strong; m = medium; w = weak; vw = very weak; br = broad.

changes over the concentration range 0.3-15% with carbon tetrachloride and carbon disulphide as solvents. No changes were noted when the donor solvent tetrahydro-furan was used. The band at 821 cm<sup>-1</sup> may be assigned to the P–N vibration, since it is absent from the otherwise rather similar spectrum of tris(chloromethyl)amine (Table 1). This frequency is intermediate between that expected for a single phosphorus–nitrogen bond (680–750 cm<sup>-1</sup>)<sup>(16)</sup> and that expected for a double phosphorus–nitrogen bond (1325–1385 cm<sup>-1</sup>).<sup>(17)</sup> It is reasonable to conclude, therefore, that the P–N ring system achieves added stability through delocalization of the lone electron pairs on the nitrogen atoms. This conclusion is consistent with NMR data which show the protons in the compound to be better shielded than those in the amine N(CH<sub>2</sub>Cl)<sub>3</sub>. Evidence for electron delocalization in 4-membered P–N rings in related compounds has been obtained.<sup>(10.14.15.17)</sup>

The PMR spectrum of the compound  $N(CH_2Cl)_3$  consists of a single peak at a  $\tau$  value of 4.98 ppm. A monomeric composition is thus indicated. Support is provided by molecular weight data (observed 180, 181, 178 vs. 163 calculated for a monomer). The formulation given appears to be correct.

Both of these two new compounds are readily and rapidly decomposed by even traces of moisture. The amine,  $N(CH_2Cl)_3$ , is particularly prone to hydrolyse. Both reacted with methylamine, but readily identifiable products could not be isolated.

- (14) H. VON HESS and D. FORST, Z. anorg. allg. Chem. 342, 240 (1966).
- (15) L. G. HOARD and R. A. JACOBSON, J. chem. Soc. 1203 (1966).
- <sup>(16)</sup> L. BELLAMY, *The Infrared Spectra of Complex Molecules* (2nd Edn), p. 323. John Wiley, New York (1958).
- <sup>(17)</sup> I. N. ZHMUROVA, A. A. KISILENKO and A. V. KIRSANOV, J. gen. Chem. U.S.S.R. 32, 2544 (1962).

 <sup>(10)</sup> A. C. CHAPMAN, W. S. HOLMES, N. L. PADDOCK and H. T. SEARLE, J. chem. Soc. 1825 (1961).
(11) A. MICHAELIS, Ann. 326, 129 (1903).

<sup>(12)</sup> I. N. ZHMUROVA and B. S. DRACH, J. gen. Chem. U.S.S.R. 34, 3091 (1964).

<sup>(13)</sup> I. N. ZHMUROVA and A. V. KIRSANOV, J. gen. Chem. U.S.S.R. 30, 3018 (1960).

On the other hand, no reaction was detected between the compounds  $N(CH_2Cl)_3$ and  $(H_2N)_3PO$  in either the presence or absence of a proton acceptor. The effects of altering the basicity of the solvolysing nitrogen atom are thus apparent. Further studies of nucleophilic displacement processes are in progress. Neither the compound  $(Cl_3PNCH_2Cl)_2$  nor the compound  $N(CH_2Cl)_3$  is particularly soluble in inert solvents. Room-temperature solubility data are, roughly:  $CCl_4$ , both ~5%; CS<sub>2</sub>,  $(Cl_3PNCH_2Cl)_2 ~15\%$ ,  $N(CH_2Cl)_3, ~7\%$ .

It is of interest that under no reaction conditions was there evidence for the isolation of the expected compound  $Cl_3P=NCH_2SO_2Cl$ . Reaction in the 1:2 mole ratio expected to be optimum for the formation of this substance gave only the chlorinated amine,  $N(CH_2Cl)_3$ , and an oil which decomposed upon vacuum distillation to condensable products containing no sulphur. Although the desired sulphonyl chloride may logically have formed in the initial reaction between aminomethane-sulphonic acid and phosphorus (V) chloride, it is evidently unstable under conditions under which that reaction can proceed.

The formation of the tertiary amine  $N(CH_2Cl)_3$  as a reaction product is surprising, particularly since there are no obvious impurities in aminomethanesulphonic acid that bear any direct chemical relationship to this compound. A reaction route involving rearrangement must be involved. It is known that in hot water aminomethanesulphonic acid decomposes to a condensation product of methanolamine,  $H_2NCH_2OH$ , by elimination of sulphur dioxide. Under the reaction conditions used here, aminomethanesulphonic acid may yield ammonia and formaldehyde, by sulphur dioxide elimination, which could then condense to the hydroxyamine  $N(CH_2OH)_3$  as an intermediate to the formation of tris(chloromethyl)amine. Both sulphur dioxide and ammonia can react with phosphorus (V) chloride and thus reduce the yield.

Tris(chloromethyl)amine has been obtained also by the more obvious procedure summarized by the equation

$$N(CH_2SO_3Na)_3 + 6PCl_5 \rightarrow N(CH_2Cl)_3 + 6POCl_3 + 3NaCl + 3SOCl_2$$

Again, the yield is low, perhaps as a consequence of difficulty in freeing the sodium salt completely from water and other impurities. It is reasonable to assume that chlorinated amines would be products of reactions of phosphorus (V) chloride with other aminosulphonic acids or their salts. The acids  $N(CH_2SO_3H)_3$  and  $HN(CH_2SO_3H)_2$  could not be isolated as a consequence of the ease with which they form aminomethanesulphonic acid by loss of formaldehyde and sulphur dioxide.

In the light of observations that tumor growth appears to be enhanced in test animals when tris(chloromethyl)amine is administered,<sup>(18)</sup> it is suggested that anyone working with this compound do so only with adequate protection.

Acknowledgement—Support received for this investigation under Grant USP GM 11996 is gratefully acknowledged.

<sup>&</sup>lt;sup>(18)</sup> Preliminary reports from Cancer Chemotherapy National Service Center, National Cancer Institute, Bethesda, Maryland, U.S.A.