# The Aquo Ammono Phosphoric Acids. III. The N-Substituted Derivatives of Phosphoryl and Thiophosphoryl Triamide as Hydrogen Bonding Agents

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Introduction

The alkyl and aryl esters of phosphoric acid have found extensive application as solvents, and as plasticizers for various polymeric substances. They are most effective for those polymeric materials which contain active acceptor atoms, such as the polyamides, the phenol-formaldehyde resins, the urea-formaldehyde resins, and the vinyl polymers. Hydrogen bonding is considered to play a very important role in this particular application, for it is assumed that the oxygen atoms in the phosphoric acid esters serve as the donor atoms in bonding to active hydrogen atoms. Copley, Zellhoefer and Marvel[1,2] have shown that the extraordinary solubility of CH_2Cl_2 in a series of phosphoric acid esters, such as $(C_2H_5O)_3PO$, $(C_3H_7O)_3PO$, $(C_4H_9O)_3PO$, $(C_6H_5O)_3PO$, $(o\text{-}C_6H_4O\text{-}CH_3)_3PO$, and $(CH_3OCH_2CH_2O)_3PO$, may be explained on the basis of hydrogen bond theory. The high heat of mixing of triethyl phosphate with chloroform also indicates that loose compound formation through a hydrogen bond occurs.[3]

The present investigation was undertaken in order to determine if the nitrogen analogs of phosphoric acid might not also be capable of acting as potential hydrogen bonding agents. The N-alkyl and N-aryl substituted derivatives of phosphoryl triamide, $OP(NH_2)_3$, may be looked upon as the nitrogen analogs of the esters of phosphoric acid. Compounds in which one or two of the -OR groups are replaced by an amine radical may be regarded as the mixed aquo ammono phosphoric acid esters. With this concept in mind, the close relationship between the aquo phosphoric acid esters and the N-substituted phosphoryl triamides should be evident.

OP(OR)₃   OP<(OR/OR/NHR)   OP<(OR/NHR/NHR)

Aquo ester   Mixed aquo ammono esters

OP(NHR)₃ or OP(NR₂)₃
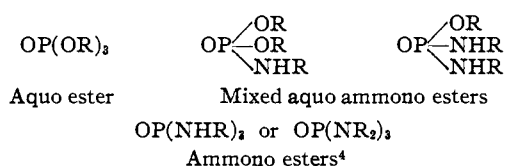
Ammono esters[4]

Theoretically, the ammono phosphoric acid esters should be capable of acting as hydrogen bonding agents because of the presence of both oxygen and nitrogen atoms which may be capable of acting as donor atoms. Donor molecules (hydrogen bonding agents) have been found to exhibit extraordinarily high solubility in such solvents as chloroform, which contains an acceptor hydrogen atom. On the other hand, solubility of these same materials in solvents such as carbon tetrachloride is considerably less, despite the fact that the structures of chloroform and carbon tetrachloride are quite similar. This difference has been ascribed to the absence of an active hydrogen atom in carbon tetrachloride. This does not mean that such donor compounds are abnormally soluble in all hydrogen containing solvents. The hydrogen atom must possess some lability. Petroleum ether, for instance, exhibits no tendency to act as an acceptor solvent since the hydrogen atoms are non-labile. However, these considerations should not be taken as absolute criteria since a substance, because of its structure, may still exhibit considerable solubility or insolubility in typical non-polar solvents. Consequently the relation of structure to potential hydrogen bonding ability is a factor which should not be overlooked. It has already been shown by the authors[5] that phenyl di-(morpholido)-phosphate is extraordinarily soluble in many solvents, including water, while the diphenyl morpholido-phosphate is insoluble in water, but nevertheless very soluble in organic solvents. In order to determine the effect of structure upon hydrogen bonding ability, a series of N-substituted phosphoryl triamides were prepared and these together with related compounds were investigated for their solubility in chloroform and in carbon tetrachloride. A number of N-substituted thiophosphoryl triamides, derivatives of the thio ammono phosphoric acid, $SP(NH_2)_3$, were also prepared to determine specifically the effect of replacing oxygen by sulfur.

In the course of this work standard methods for the preparation of N-substituted phosphoryl

(1) Copley, Zellhoefer and Marvel, THIS JOURNAL, 60, 2666 (1938).

(2) Copley, Zellhoefer and Marvel, ibid., 60, 2714 (1938).

(3) Marvel, Copley and Ginsberg, ibid., 62, 3109 (1940).

(4) Strictly speaking, the parent substance, PO(NH₂)₃, is still a mixed aquo ammono phosphoric acid from the Franklin point of view.

(5) Audrieth and Toy, THIS JOURNAL, 64, 1337 (1942).

TABLE I

THE N-SUBSTITUTED PHOSPHORYL TRIAMIDES

Compound	Amine	Grams	Moles	POCl₃ Grams	Moles	C₅H₅N Grams	Moles	Recrystallized from	G.	Yield, %	M. p., °C.	Ref.
PO(NHC₆H₅)₃	Aniline	111.7	1.2	30.78	0.2	47.4	0.6	75% EtOH	53	82	211–214; sl. dec. 250	8
PO(NHC₆H₁₁)₃	Cyclohexylamine	118.8	1.2	30.78	.2	47.4	.6	High b. pet. ether	49	72	245–246 dec.	a
PO(NHC₆H₄CH₃)₃	p-Toluidine	64.3	0.6	15.4	.1	23.7	.3	95% EtOH	32	87.5	198–199; sl. dec. 250	11
PO(NHC₆H₄CH₃)₃	o-Toluidine	64.3	.6	15.4	.1	23.7	.3	75% EtOH	20	55	229–230 dec.	11
PO(N₂H₂C₆H₅)₃	Phenylhydrazine	64.8	.6	15.4	.1	23.7	.3	Abs. EtOH	31	84.3	185–187 dec.	12
PO(NC₄H₈O)₃	Morpholine	104.4	1.2	30.78	.2	94.8	1.2	CCl₄	41	67.8	191–192; dec. 250	b
PO(NHC₆H₄OC₂H₅)₃	p-Phenetidine	82.2	0.6	15.4	.1	23.7	0.3	75% EtOH	25.3	55.6	172–173; dec. 250	6
PO(NHCH₂C₆H₅)₃	Benzylamine	64.2	.6	15.4	.1	23.7	.3	65% EtOH	15	42.2	98–99; dec. 250	10

^{a} Calcd. for PO(NHC₆H₁₁)₃: C, 63.35; H, 10.63; N, 12.6. Found: C, 63.71; H, 10.79; N, 12.42.

^{b} Calcd. for PO(NC₄H₈O)₃: C, 47.3; H, 7.87; N, 13.76. Found: C, 47.22; H, 7.95; N, 13.68.

triamides were investigated, but none found to be satisfactory. These compounds previously had been prepared from phosphoryl chloride and the corresponding amines, (a) in the presence of sodium hydroxide,[6] (b) by direct reaction in the cold and subsequent heating,[7,8] and (c) at higher temperatures under pressure in a closed tube,[9] or (d) in the presence of diluents.[10] The new and recommended procedure involves interaction of the phosphoryl chloride-pyridine complex with the amine in chloroform solution.

Experimental

A. Preparation of N-Substituted Phosphoryl Triamides.—To 15.4 g. (0.1 mole) of phosphoryl chloride dissolved in 200 cc. of chloroform in a 500-cc. 3-neck flask there was added slowly with stirring 23.7 g. (0.3 mole) of pyridine. The temperature of reaction was maintained at 0 ± 1° by means of an ice–salt-bath. The addition of the first few cc. of pyridine had to be slow since a great deal of heat was generated. After this initial reaction the rest of the pyridine could be added rapidly (ten minutes). This solution was then transferred to a dropping funnel and added slowly (thirty to forty minutes) to 0.6 mole of amine dissolved in 200 cc. of chloroform in a 1-liter 3-neck flask cooled to 0 ± 2° by an ice-salt-bath. The resulting product was heated on the steam-bath and refluxed for two hours to ensure complete reaction. If, upon cooling, a chloroform insoluble amine hydrochloride formed, it was removed by filtration and the residue was washed with chloroform. The combined filtrates were distilled over a steam-bath to remove most of the solvent, the last portions having been eliminated by heating over a very low free flame at a pressure of 3–4 mm. The residue was washed first with dilute hydrochloric acid and then with water until the washings gave no chloride test. The desired product was then recrystallized from a proper solvent.

Any amine hydrochloride residue was also washed with water, for in this way an additional quantity of the water insoluble product was often recovered. Specific preparative details are given in Table I.

In the recommended procedure a ratio of POCl₃:Amine: C₅H₅N = 1:6:3 was used. In similar reactions pyridine acts not only to moderate the reaction, but also serves to take up the hydrogen chloride which is formed. If the latter function is also served in the present case, then the use of six moles amine to one of phosphoryl chloride represents a needless hundred per cent. excess of amine. An experiment was therefore carried out using a POCl₃: Amine:C₅H₅N ratio of 1:3:3. The other conditions of the reaction were kept identical with those given above. Specifically, 15.4 g. (0.1 mole) of phosphoryl chloride, 23.7 g. (0.3 mole) pyridine, and 28 g. (0.3 mole) of aniline were used. The yield of phosphoryl trianilide was 10.5 g. (32.3%) as compared to a yield of 82% when a POCl₃: C₆H₅NH₂:C₅H₅N ratio of 1:6:3 was used. This seems to indicate that the presence of pyridine serves largely to moderate the reaction and not react to take up the hydrogen chloride to form pyridine hydrochloride. It should also be pointed out that phosphoryl chloride actually forms pyridinium complexes[13] of the type [POCl₄·Py]⁺Cl⁻, and that these complexes undergo solvolysis much more smoothly than the acid chloride by itself or in some inert solvent.

B. Preparation of the N-Substituted Thiophosphoryl Triamides.—The method first employed by Michaelis and Steinkopf[14] was used for the preparation of the N-substituted thiophosphoryl triamides. The general procedure involved the addition of one mole of thiophosphoryl chloride to six moles of amine at 5 ± 5°. The resultant mixture was heated on a steam-bath for twelve hours. It was then cooled and washed free of amine hydrochloride with water. The water insoluble portion was recrystallized from a proper solvent. In the case of the thiophosphoryl trimorpholide which is slightly soluble in water, the reaction product was extracted with chloroform to separate the desired compound from morpholine hydrochloride

(6) Autenrieth and Rudolph, *Ber.*, **33**, 2099 (1900).
(7) Schiff, *Ann.*, **101**, 299 (1857).
(8) Michaelis and Soden, *ibid.*, **229**, 334 (1885).
(9) Michaelis, *ibid.*, **326**, 256 (1903).
(10) Michaelis, *ibid.*, **326**, 177 (1903).
(11) Rudert, *Ber.*, **26**, 565 (1893).
(12) Michaelis and Oster, *Ann.*, **270**, 135 (1892).
(13) Boyd and Ladhams, *J. Chem. Soc.*, 215 (1928).
(14) Michaelis and Steinkopf. *Ann.*, **326**, 218 (1903).

TABLE II

THE N-SUBSTITUTED THIOPHOSPHORYL TRIAMIDES

Compound	Amine (0.6 mole)	Grams	PSCl₃ (0.1 mole) Grams	Re-cryst. from EtOH	Yield, Grams	%	M. p., °C.	Ref.	Carbon Calcd.	Found	Hydrogen Calcd.	Found	Nitrogen Calcd.	Found
PS(NC₅H₁₀)₃	Piperidine	51	16.9	95%	28.5	90.5	121–122	14ª						
PS(NC₄H₈O)₃	Morpholine	52.2	16.9	95%	28.5	89	145.5–146	ª	44.85	44.85	7.54	7.46	13.07	13.08
PS(NHC₆H₁₁)₃	Cyclohexylamine	59.4	16.9	Abs.	32	89.6	143.5–144.5	ᵇ	60.5	60.44	10.15	10.25	11.74	11.62

ª Stable at 200°, darkens at 250°, but m. p. does not change.   ᵇ Stable even at 250°.

TABLE III

SOLUBILITIES OF SOME MORPHOLINE DERIVATIVES AT 25°

Compound	Formula	G./100 g. H₂O	G./100 g. CHCl₃	G./100 g. CCl₄
Diphenyl morpholidophosphate	(C₆H₅O)₂PO(NC₄H₈O)	0.230	71.9	6.27
Phenyl di-(morpholido)-phosphate	C₆H₅OPO(NC₄H₈O)₂	336.0	138.0	20.80
Phosphoryl trimorpholide	PO(NC₄H₈O)₃	154.6	57.82	0.702
Thiophosphoryl trimorpholide	PS(NC₄H₈O)₃	0.322	47.20	1.341

TABLE IV

SOLUBILITIES OF SOME N-SUBSTITUTED PHOSPHORYL AND THIOPHOSPHORYL TRIAMIDES AT 25°

Compound	G./100 g. CHCl₃	G./100 g. CCl₄
PO(NHC₆H₅)₃	0.276	0.000
PO(p-NHC₆H₄CH₃)₃	1.10	.000
PO(o-NHC₆H₄CH₃)₃	1.87	.000
PO(N₂H₂C₉H₅)₃	0.064	.000
PO(p-NHC₆H₄OC₂H₅)₃	2.05	.000
PO(NHC₆H₁₁)₃	68.10	6.05
PO(NHCH₂C₆H₅)₃	56.50	0.236
PS(NHC₆H₁₁)₃	28.24	2.25
PS(NC₅H₁₀)₃	99.50	32.97

The chloroform extract was then evaporated and the residue washed with a small quantity of ice-water to remove the last traces of morpholine hydrochloride. The N-substituted thiophosphoryl triamides are listed in Table II.

C. **Solubility Determinations.**—The solubilities of all compounds in chloroform and carbon tetrachloride at 25° were determined. Only in the case of the morpholine derivatives were quantitative solubilities in water also determined. The solubility data are given in Tables III and IV.

Discussion

The marked differences in the solubility of the N-substituted phosphoryl triamides in chloroform and in carbon tetrachloride may be ascribed to hydrogen bonding. This difference is especially striking in the case of the morpholine derivatives where not only are there oxygen atoms in peripheral positions in the ring, but also nitrogen atoms devoid of hydrogen atoms. While the derivatives of aniline and of amines of similar structure also are much more soluble in chloroform than in carbon tetrachloride, the solubility in chloroform is low in every case. This low solubility may be due to the fact that the nitrogen is located next to a phenyl ring which permits the pair of free electrons on the nitrogen to resonate with the electrons in the double bonds of the phenyl ring. The availability of the nitrogen as

a donor atom is thus decreased. This hypothesis is substantiated by the observation that elimination of resonance (a) by reduction of the ring, as in the case of the cyclohexylamine derivatives, and (b) by separating the nitrogen from the phenyl group with a CH₂ group, as in the case of the benzylamine derivative, brings about a great increase in solubility in chloroform. The presence of an ether oxygen atom attached to the ring, as in the case of the p-phenetidine derivative, increases the solubility in chloroform presumably because the extra oxygen serves as another donor of electrons, that is, a point where hydrogen bonding may occur. However, this increase is not of the same order of magnitude as that observed in the case of the morpholine derivatives where the oxygen atom is in the ring. It may be that this difference is also due to the fact that the electrons in the oxygen next to the phenyl ring are in resonance with the electrons in the double bonds of the ring.

Our observations demonstrate clearly that the oxygen atom connected directly to the phosphorus atom also possesses some donor characteristics. The N-substituted thiophosphoryl triamides are in every case less soluble in chloroform than the corresponding phosphoryl compounds.

Summary

A number of phosphoryl and thiophosphoryl triamides have been prepared and their solubilities in chloroform, carbon tetrachloride, and water have been determined. The solubility data indicate that these substances are good hydrogen bonding agents and that the oxygen and the nitrogen atoms in these compounds are capable of acting as donor atoms in solvents such as chloroform which contains an active hydrogen atom.