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Studies of Organophosphorochloridates. Part III.[1] Synthesis of *N*-Substituted Pyrophosphoramides

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The synthesis of a series of novel *N*-symmetrical and unsymmetrical pyrophosphoramides is described, and their i.r., n.m.r., and mass spectra are discussed. The hydrolysis of the pyrophosphoramides and their reactions with other nucleophilic reagents have been investigated.

Published on 01 January 1971 on http://pubs.rsc.org | doi:10.1039/J39710002028
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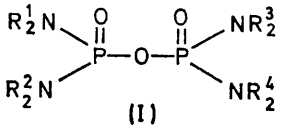
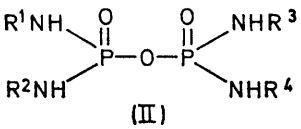
ALTHOUGH several *N*-substituted pyrophosphoramides (I) derived from secondary amines are effective insecticides,[2-5] comparatively little work has been reported on pyrophosphoramides derived from primary amines: Zeile and Kruckenberg[6] prepared *NN'N''N'''*-tetra-



(I)

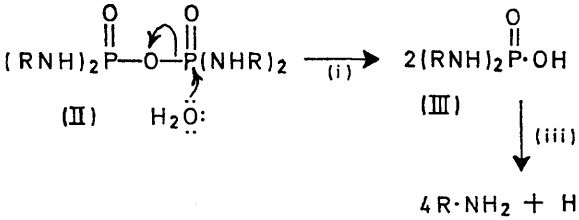


(II)

phenylpyrophosphoramide (II; $R^1 = R^2 = R^3 = R^4 =$ Ph) by selective hydrolysis of *NN'*-diphenylphosphorodiamidic chloride, and by condensation of the chloride with the corresponding phosphorodiamidic acid. Boger and Friedman[7] obtained *s-OO'*-dibenzyl-*NN'*-diphenylpyrophosphorodiamide by the action of dicyclohexylcarbodi-imide on *O*-benzyl-*N*-phenylphosphoramidic acid. By application of these general methods, we have synthesised a range of novel substituted pyrophosphoramides (Tables 1a and b); the optimum yields were obtained at room temperature (*cf.* refs. 2—4), probably because the intermediate *NN'*-disubstituted phosphorodiamidic chlorides are more sensitive to alkaline hydrolysis than the corresponding tetrasubstituted compounds. Dicyclohexylcarbodi-imide, although a well-established reagent for the synthesis of pyrophosphates,[8] has not previously been used for the preparation of *N*-tetrasubstituted pyrophosphoramides. In the formation of the unsymmetrical pyrophosphoramides (II) by condensation of the *NN'*-disubstituted phosphorodiamidic chloride with the appropriate *NN'*-disubstituted phosphorodiamidic acid, it was observed that improved yields resulted when the less basic amine was attached to the phosphorus atom of the acid.

The tetrasubstituted pyrophosphoramides were relatively stable towards nucleophilic attack, both because of the reduction in the electrophilic character of the phosphorus atoms resulting from the electron-releasing power of the four nitrogen atoms and the steric shielding of the phosphorus atoms by the attached groups. Thus, tetraphenyl pyrophosphoramide was substantially unchanged when boiled with water, ethanol, aqueous tetrahydrofuran, or aqueous pyridine for 24 hr.

The hydrolysis of a number of the pyrophosphoramides by hot aqueous dioxan was studied by potentiometric titration of the liberated acid with tetra-n-butylammonium hydroxide. The rates of hydrolysis appeared to be slow, and in addition, the hydrolysis was subject to an autocatalytic effect similar to that previously reported by Dudek and Westheimer[9] for the propanolysis of tetrabenzyl pyrophosphate. In an attempt to eliminate autocatalysis, the hydrolysis was repeated in the presence of varying amounts of a strong sterically hindered base (tribenzylamine) (*cf.* ref. 9). With large proportions of base, the overall rate of hydrolysis increased but the autocatalytic effect remained, as it did in other experiments in the presence of a large excess of lithium perchlorate.[10] These results suggest that the autocatalysis does not arise from acid formation or the increase in the ionic strength of the solution, though possibly it may be due to phosphate ion as has been claimed[11] for the hydrolysis of tetraethyl pyrophosphate. We found[12] that, compared with pyrophosphoramides, *NN'*-disubstituted phosphorodiamidic acids (III) are very rapidly hydrolysed in aqueous dioxan to the amine and phosphoric acid [isolated as $Ba_3(PO_4)_2$]; accordingly, these were the only isolable products from pyrophosphoramide hydrolysis. Two possible mechanisms of



(i) P—O fission (slow) (ii) P—N fission (rapid)

hydrolysis are as follows: (*a*) attack by a water molecule at the electrophilic phosphorus atom, followed by P–O bond fission to give the *NN'*-phosphorodiamidic acid which then undergoes P–N fission to give the final

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[1] Part II, R. J. W. Cremlyn and N. A. Olsson, preceding paper.
[2] B.P. 631,549/1949.
[3] U.S.P. 2,717,249/1955.
[4] U.S.P. 2,671,109/1954.
[5] U.S.P. 2,502,966/1950.
[6] K. Zeile and W. Kruckenburg, *Ber.*, 1942, **75***B*, 1127.
[7] E. Boger and O. M. Friedman, *J. Amer. Chem. Soc.*, 1958, **80**, 2583.
[8] H. G. Khorana and A. R. Todd, *J. Chem. Soc.*, 1953, 2257.
[9] G. O. Dudek and F. A. Westheimer, *J. Amer. Chem. Soc.*, 1959, **81**, 2641.
[10] Personal communication from Dr. D. M. Brown of the University of Cambridge.
[11] D. Samuel and B. Silver, *J. Chem. Soc.*, 1961, 4321.
[12] R. J. W. Cremlyn, B. B. Dewhurst, and D. H. Wakeford, *J. Chem. Soc.* (*C*), 1971, 300.

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products and (*b*) similar attack at phosphorus, followed by P–N and subsequent P–O bond fission.

Evidence in favour of mechanism (*a*) comes from alkaline hydrolysis (sodium hydroxide) of pyrophosphoramides where the intermediate phosphorodiamidic acid can be isolated, since the anion is relatively stabilised to nucleophilic attack.

In the presence of a large amount of tribenzylamine, the attacking species will be the hydroxide anion rather than a water molecule; and since there is a gradual increase in the raction rate with increasing proportions of base, it seems probable that attack by a water molecule also proceeds by route (*a*). In further support of this argument Heath and Casapieri [13] found that in the hydrolysis of octamethylpyrophosphoramide (Schradan) (I; $R^1 = R^2 = R^3 = R^4 = Me$) by water, the P–N bond was not broken and only P–O fission occurred. The initial rate constants for the hydrolysis of the various pyrophosphoramides are given in Table 2. Important factors in this reaction include: electronic effects, the degree of steric shielding of the phosphorus atoms, and the relative effectiveness of the substituted phosphoramidic acid anion to function as a leaving group. In the symmetrical pyrophosphoramides, the leaving group effect and the susceptibility of phosphorus to nucleophilic attack will be enhanced by increased electron-withdrawing properties of the attached radicals. Thus *P*(1)-dibenzyl *P*(2)-diphenyl pyrophosphoramide (13) hydrolysed faster than either the tetrabenzyl (5) or the tetraphenyl (1) derivatives due to the favourable electron-withdrawing effect of the anilino-groups facilitating attack by water at the relatively unhindered *P*(1)-phosphorus atom with subsequent expulsion of the better leaving group. The *s*-dimethoxy-di-*p*-toluene derivative (19) hydrolysed faster than the other pyrophosphoramides [except (13)], owing to the presence of only two nitrogen atoms and the relatively small steric shielding of the phosphorus atoms in this compound. The relative rates of hydrolysis of most of the other pyrophosphoramides are governed by similar considerations. The *P*(1)-diphenyl *P*(2)-dipiperidino (20) and *P*(1)-diphenyl-*P*(2)-dimorpholino-(21) derivatives are comparatively stable to hydrolysis, presumably due to the substantial steric shielding of the phosphorus atom by the piperidino- and morpholino-groups respectively. The base-catalysed reaction for (4) is slightly slower than the neutral reaction; this may be due to *NN'*-dicyclohexylphosphorodiamidic acid being a weaker acid than the *NN'*-diarylphosphorodiamidic acids, so that hydrolysis of (4) is relatively little influenced by base.

[13] D. F. Heath and P. Casapieri, *Trans. Faraday Soc.*, **1951**, **47**, 1093.

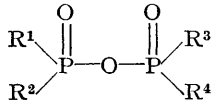
TABLE 1(a)

Tetrasubstituted pyrophosphoramides (II)

No. of compd.	R^1	R^2	R^3	R^4	M.p.	Yield (%)	Solvent	Formula	Analyses: Found (%) C	H	N	P	Required (%) C	H	N	P
(1)	Ph	Ph	Ph	Ph	212—214° lit.[1] 222°	65 *a* 60 *b* 78 *c*	EtOH	$C_{24}H_{24}N_4O_3P_2$	60·0	5·1	11·7	13·3	60·2	5·1	11·7	12·9
(2)	*p*-MeO·C_6H_4	*p*-MeO·C_6H_4	*p*-MeO·C_6H_4	*p*-MeO·C_6H_4	164—168	53 *a*	C_6H_6	$C_{28}H_{32}N_4O_7P_2$	56·6	5·6	9·6	10·0	56·2	5·4	9·4	10·4
(3)	*n*-$C_{10}H_{21}$	*n*-$C_{10}H_{21}$	*n*-$C_{10}H_{21}$	*n*-$C_{10}H_{21}$	80·5	80 *a*	EtOH	$C_{40}H_{68}N_4O_3P_2$	65·4	12·0	7·7	8·8	65·4	12·1	7·6	8·4
(4)	C_6H_{11}	C_6H_{11}	C_6H_{11}	C_6H_{11}	210—213	55 *a* 40 *c*	CH_3CN	$C_{24}H_{48}N_4O_3P_2$	57·5	9·7	11·1	12·1	57·3	9·6	11·1	12·3
(5)	Ph·CH_2	Ph·CH_2	Ph·CH_2	Ph·CH_2	93—94	35 *a*	C_6H_5Cl	$C_{28}H_{32}N_4O_3P_2$	62·8	6·1	10·4	11·8	62·9	6·0	10·5	11·6
(6)	*m*-CH_3·C_6H_4	*m*-CH_3·C_6H_4	*m*-CH_3·C_6H_4	*m*-CH_3·C_6H_4	212	48 *a*	EtOH	$C_{28}H_{32}N_4O_3P_2$	63·2	6·1	10·7	11·5	62·9	6·0	10·5	11·6
(7)	*p*-CH_3·C_6H_4	*p*-CH_3·C_6H_4	*p*-CH_3·C_6H_4	*p*-CH_3·C_6H_4	201—205	65 *a* 52 *c*	CH_3CN	$C_{28}H_{32}N_4O_3P_2$	63·0	6·0	10·6	11·8	62·9	6·0	10·5	11·6
(8)	Ph	*n*-$C_{10}H_{21}$	Ph	*n*-$C_{10}H_{21}$	148—150	40 *a*	EtOH	$C_{32}H_{56}N_4O_3P_2$	63·6	9·4	9·3	10·0	63·3	9·3	9·2	10·2
(9)	Ph	*n*-C_4H_9	Ph	*n*-C_4H_9	170—172	11 *a*	EtOH	$C_{20}H_{32}N_4O_3P_2$	54·9	7·4	12·9	13·7	54·8	7·4	12·8	14·1
(10)	Ph	Ph·CH_2	Ph	Ph·CH_2	190—193	71 *a*	EtOH	$C_{26}H_{28}N_4O_3P_2$	61·6	5·5	11·1	12·5	61·7	5·6	11·1	12·2
(11)	Ph	Ph	C_6H_{11}	C_6H_{11}	178—179	71 *b* 10 †	$CH_3·C_6H_5$	$C_{24}H_{36}N_4O_3P_2$	58·8	7·5	11·2	13·0	58·8	7·4	11·4	12·6
(12)	Ph	Ph	*p*-CH_3·C_6H_4	*p*-CH_3·C_6H	187—190	20 *b* 45 †	CH_3CN	$C_{26}H_{28}N_4O_3P_2$	62·1	6·0	10·9	12·4	61·7	5·6	11·1	12·2
(13)	Ph	Ph	Ph·CH_2	Ph·CH_2	146—147	58 *b*	C_6H_6	$C_{26}H_{28}N_4O_3P_2$	62·1	5·8	11·1	12·3	61·7	5·6	11·1	12·2
(14)	Ph	Ph	Ph	Ph·CH_2	168—170	60 *b* 42 †	CH_3CN	$C_{25}H_{26}N_4O_3P_2$	60·6	5·3	11·5	12·7	61·0	5·3	11·4	12·6
(15)	Ph	Ph·CH_2	Ph·CH_2	Ph·CH_2	135—137	55 *b*	C_6H_6	$C_{27}H_{30}N_4O_3P_2$	62·2	5·7	10·5	12·3	62·3	5·8	10·8	11·9
(16)	Ph	Ph·CH_2	C_6H_{11}	C_6H_{11}	185—186	30 *b* 80 †	CH_3CN	$C_{25}H_{36}N_4O_3P_2$	59·0	7·4	11·2	12·8	59·5	7·5	11·1	12·3
(17)	C_6H_{11}	C_6H_{11}	Ph·CH_2	Ph·CH_2	120—123	23 *c*	C_6H_6	$C_{26}H_{40}N_4O_3P_2$	60·2	7·8	10·6	11·9	60·2	7·8	10·8	11·9

TABLE 1(b)

Unsymmetrical pyrophosphoramides



No. of compd.	R^1	R^2	R^3	R^4	M.p.	Yield (%)	Solvent	Formula	Analyses: Found (%) C	H	N	P	Required (%) C	H	N	P
(18)	PhNH	OMe	PhNH	OMe	160—165°	22 *a*	MeCN	$C_{14}H_{18}N_2O_5P_2$	47·2	5·0	7·5	17·3	47·2	5·1	7·9	17·4
(19)	*p*-$CH_3C_6H_4NH$	OMe	*p*-$CH_3C_6H_4NH$	OMe	190—192	57 *a*	Dioxan	$C_{16}H_{22}N_2O_5P_2$	50·3	5·8	7·3	16·2	50·0	5·8	7·3	16·1
(20)	Ph·NH	Ph·NH	$C_5H_{10}N$	$C_5H_{10}N$	212—216	45 *b*	EtOH	$C_{22}H_{32}N_4O_3P_2$	57·5	7·0	12·0	13·4	57·1	7·0	12·1	13·4
(21)	Ph·NH	Ph·NH	C_4H_8NO	C_4H_8NO	241	60 *b*	EtOH	$C_{20}H_{28}N_4O_5P_2$	51·7	6·3	12·1	13·0	51·5	6·1	12·0	13·3
(22)	Ph·NH	Ph·NH	$C_{27}H_{45}O$	$C_{27}H_{45}O$	175	40 *b*	Dioxan	$C_{66}H_{102}N_3O_5P_2$	74·5	9·7	2·6	5·5	74·5	9·6	2·6	5·8
(23)	*p*-ClC_6H_4NH	MeO	*p*-ClC_6H_4NH	MeO	155—158	55 *a*	MeCN	$C_{14}H_{16}Cl_2N_2O_5P_2$	39·0	3·7	6·7	14·3	39·5	3·8	6·6	14·6
(24)	Ph·NH	C_4H_8NO	PhNH	C_4H_8NO	226—227	60 *	MeCN	$C_{20}H_{28}N_4O_5P_2$	51·7	6·1	12·0	13·1	51·5	6·1	12·0	13·3

a Method 1. *b* Method 2. *c* Method 3. † Method 2, except that the phosphorochloridate of R^1R^2 is condensed with the phosphorodiamidic acid of R^3R^4.

* Method 1, except that it was carried out in tetrahydrofuran with triethylamine and the product was isolated by evaporation, after removal of the precipitated hydrochloride.

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The reactions of some of the pyrophosphoramides with cyclohexylamine have been investigated. With *NN'N''N'''*-tetraphenylpyrophosphoramide P–O bond fission occurred to give the cyclohexylammonium salt of *NN'*-diphenylphosphorodiamidic acid. Tetrasubstituted pyrophosphates are quantitatively split by treatment with cyclohexylamine at room temperature,[14] but with tetraphenylpyrophosphoramide the analogous reaction required prolonged boiling to obtain the optimum yield of the cyclohexylammonium salt. This compound was also obtained by the action of cyclohexylamine on dimorpholino-derivative (21) the signals for the protons of the CH_2–O–CH_2 and CH_2–N–CH_2 groups are at τ 6·5 and 6·95 respectively;[16] in the dipiperidino-compound (20) the latter protons signal at τ 7·0.

^{31}P-*N.m.r.*—Whilst electron withdrawal from the phosphorus atom by an attached arylamino-group caused the ^{31}P chemical shift to move upfield to values of 7·5—9·5 p.p.m. relative to 85% phosphoric acid, electron donation by an alkylamino-group resulted in a downfield movement of the ^{31}P chemical shift to −3·5 to −7·1 p.p.m. This effect, the opposite to that anticipated from electronegativity considerations, has been previously reported[17] in other pentavalent organophosphorus compounds.

TABLE 2

Spectral data and rate constants (hydrolysis) of pyrophosphoramides

Compd. no.	I.r. bands (cm.$^{-1}$) NH	P=O	P–O–P		N.m.r. bands (τ) NH	ArH	Me	^{31}P (p.p.m.) [a]	Rate constant (k) × 10^{-6} k_a	k_b
(1)	1380	1250	960		1·75(4) B	2·8—3·3(20)		+9·5 C	1·5	6·3 (½ life 18 hr.)
(2)	3360, 3290, 3140	1250—1220	935	710	2·1—2·6(4) B	2·85—3·4(16)	6·35(12)			
(3)	3200	1230	965	—	7·05(4) A	Alip. H 8·4—9·3(84)				4·0 (½ life 41½ hr.)
(4)	3400, 3270, 3200	1210	950	710	6·87(4) A	Alip. H 7·85—9·05(44)		−5·5 E	0·74	0·62
(5)	3410, 3260	1200	960	710	6·84(4) A	2·65—3·0(20)	Ar-CH_2 6·05(8)	−7·1 C	2·3	
(6)	3220	1230	955	—	1·85(4) B	2·9—3·35(16)	7·83(12)			
(7)	3360, 3220, 3140	1240	920	710	1·98(4) B	3·0(16)	7·8(12)	+7·5 D	1·0	6·6 (½ life 21½ hr.)
		1220 [b]	910	—						
(8)	3390, 3200	1220—1210	930	—						
(9)	3230	1230—1210	930	—						
(10)	3380, 3160	1220	910	710	4·4(2) 2·1(2) B	2·6—3·25(20)	Ar-CH_2 5·8—6·1(4)	−1·0 D		6·1 (½ life 16½ hr.)
(11)	3380, 3260, 3160	1250 1220	940	720	6·9(2) 2·9(2) A	2·7—3·15(10) Alip. H 8·0—9·1(22)		−6·5 +9·5 C	3·2	
(12)	3370, 3150	1240—1220	915	705	1·9(4) B	2·7—3·3(18)	7·83(6)			
(13)	3380, 3310, 3120, 3400 [b]	1230 1210	910	710	6·2(2) 2·9(2) A	2·7—3·2(20)	Ar-CH_2 ≏6·1		7·85	25 (½ life 3½ hr.)
		1245 1230	925	—						
(14)	3370, 3180	1240 1210	925	—				+0·7 +8·7 C	2·2	16 (½ life 8½ hr.)
(15)	3390, 3270, 3200 3140	1235 1215	915	—				−8·5 +0·5 D		
(16)	3420, 3200	1245 1220	945	—						
(17)	3360, 3200	1240 1215	925	680?						
(18)	3120, 3080	1260 or 1240	950	710				+6·5 D		30 [c] (½ life 6½ hr.)
(19)	3160	1255 or 1240	950	710	1·75(2) A	2·7—3·2(8) MeO 6·41(6)	7·78(6)	+7·5 D	7·2	
		1270 [b] or 1235	945	—						
(20)	3140, 3080	1240 1225	935	—	1·85(2) B	2·7—3·1(10) Alip. H 8·55(12)	CH_2–N–CH_2 7·0(8)		0·41	
(21)	3130, 3080, 3430 [b]	1250 1230	970?	910	1·75(2) B	2·7—3·2(10)		−3·5 +9·5 D	0·58	
		1260 1240	910	—						
(22)	3150	1260 1230	935	—						

A = $CDCl_3$, B = $(CD_3)_2SO$, C = tetrahydrofuran, D = $(CH_3)_2SO$, E = $CHCl_3$. [a] ^{31}P N.m.r. chemical shifts relative to 85% H_3PO_4. [b] Solution spectra in D.

k_a = Initial rate constant for hydrolysis in 25% aq. dioxan at 80·8°. k_b = Initial rate constant for hydrolysis in boiling 20% aq. dioxan with tribenzylamine (10 mole) [c] No tribenzylamine added.

The *P*(1)-dicyclohexyl-*P*(2)-diphenyl- (11) and *P*(1)-dibenzyl-*P*(2)-diphenyl- (13) pyrophosphoramides showing that in both cases the anion of the stronger acid is preferentially eliminated. However with the *P*(1)-diphenyl-*P*(2)-dimorpholino-derivative (21) none of this compound was isolated, indicating that attack by cyclohexylamine has now occurred at the *P*(1)-phosphorus atom due to strong steric shielding of the *P*(2)-phosphorus by the attached morpholino groups.

N.m.r. Spectra.—The spectra of the pyrophosphoramides are given in Table 2; the signal for the NH proton was at τ 1·75—2·9 or at 6·2—7·05 when it was attached to aromatic or aliphatic radicals respectively. The aromatic protons appeared in the range τ 2·6—3·4. In the dimethoxy-di-*p*-toluene compound (19) the P–O–CH_3 signal is split into a doublet[15] (J 2Hz). In the diphenyl

I.r. Spectra.—The N–H stretching bands occurred in the region 3410—3080 cm.$^{-1}$,[18a] and these bands were often broad. In accord with previous observations[18b] the P=O stretching bands mainly occurred in the 1250—1210 cm.$^{-1}$ region. The antisymmetrical stretching vibration due to the P–O–P linkage was in the 965—910 cm.$^{-1}$ region, with sometimes an additional weak band at 710 cm.$^{-1}$ assigned to the symmetrical stretching vibrations.[18c] In agreement with Thomas and Chittenden,[19] we found no correlation between the position of

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[16] J. Riess, *Bull. Soc. chim. France*, 1965, 3552.
[17] J. A. Pople, W. G. Schneider, and H. J. Bernstein, 'High Resolution Nuclear Magnetic Resonance,' McGraw-Hill, New York, 1959, p. 349.
[18] D. E. C. Corbridge, 'The Infrared Spectra of Phosphorus Compounds,' Topics in Phosphorus Chemistry, John Wiley, New York, 1969, vol. 6, (*a*) p. 289, (*b*) p. 258, and (*c*) p. 282.
[19] L. C. Thomas and R. A. Chittenden, *Spectrochim. Acta*, 1964, **20**, 489.

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the P–O–P stretching bands and the nature of the attached groups.

Mass Spectra.—The spectra of 13 *N*-substituted pyrophosphoramides were determined at ion-chamber temperatures of 180—220°. Compounds (19), (20), (21) and (24) gave the molecular ion (*M*) without loss of water. Compounds (4), (7), and (16) also showed the molecular ion, and in addition the *M* — 18 ion was apparent. The remaining pyrophosphoramides did not show the molecular ion, though all these compounds gave a strong *M* — 18 ion corresponding to loss of water. Fragment ions due to loss of the various alkyl or arylamino-radicals were also observed, and the base peaks in the spectra corresponded to the amine ion of lowest molecular weight.

Since comparatively little work has been published on the mass spectra of organophosphorus compounds, it is difficult to formulate the precise breakdown pattern of these pyrophosphoramides. However the mass spectra of these and similar compounds are under further investigation.

Several of the *N*-substituted pyrophosphoramides (II) have been screened for insecticidal properties, but they appear to be inactive.

EXPERIMENTAL

I.r. spectra were measured as Nujol mulls with an Infracord 257 spectrometer. N.m.r. spectra were determined with a Varian A60A spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained with an A.E.I. MS902 spectrometer operating at 70 eV.

Potentiometric titrations were carried out by the method of Haslam *et al.*[20] M.p.s were determined with a Kofler hot-stage apparatus.

Preparation of Pyrophosphoramides.—These were obtained by the following general methods.

Method 1: *by selective hydrolysis of the corresponding* N *substituted phosphoramidic chloride.* The phosphoramidic chloride (0·01 mole) was dissolved in pyridine * (10—15 ml.) and 1N-aqueous pyridine (5 ml.) was added with stirring. After 1 hr. at room temperature, the solution was poured onto ice–water (1 l.); the solid product was collected, washed with water, dried *in vacuo*, and recrystallised from a suitable solvent (See Tables 1(a) and (b)).

Method 2: *by condensation of an* N*-substituted phosphoramidic chloride with an* N*-substituted phosphoramidic acid.* The phosphoramidic acid (0·01 mole) was dissolved in anhydrous pyridine (30—50 ml.) and the phosphoramidic chloride (0·01 mole) was added with stirring at room temperature. After ½ hr., the solution was poured into ice–water (1·5 l.) and the product was collected.

Method 3: *by the use of dicyclohexylcarbodi-imide.* The appropriate *N*-substituted phosphoramidic acid (0·01 mole) and dicyclohexylcarbodi-imide (0·005 mole) was dissolved in tetrahydrofuran (100 ml.) and the solution left overnight at room temperature. The solution was cooled at −5°, and the precipitated dicyclohexylurea filtered off. The filtrate was evaporated under reduced pressure and the product crystallised from a suitable solvent.

Hydrolysis of the Pyrophosphoramides.—(a) *With aqueous dioxan.* The pyrophosphoramide [0·02 molar solution in aqueous dioxan † (25% v/v)] was kept at 80·8° in a constant-temperature bath in a septum-sealed vessel. Samples (5 ml.) were withdrawn periodically, and diluted with ethanol (60 ml.); these were then titrated with an automatic potentiometric titrimeter against 0·1N-tetra-n-butylammonium hydroxide (standardised against sulphamic acid). Other hydrolytic experiments were carried out in boiling 20% aqueous dioxan under reflux.

(b) *With sodium hydroxide.* Tetraphenylpyrophosphoramide (1 g.) was boiled with 4N-aqueous sodium hydroxide (50 ml., 2·5 mole) under reflux for 4 hr. The major portion of the solid dissolved; the suspension was filtered and the filtrate was acidified (dilute hydrochloric acid) to give *NN'*-diphenylphosphorodiamidic acid (650 mg.), m.p. 176—180° (m.p. and i.r. spectrum identical to that of a previously prepared sample [12]).

Reaction of Cyclohexylamine.—(a) *With tetraphenylpyrophosphoramide.*—Tetraphenylpyrophosphoramide (500 mg.) in acetone (25 ml.) and cyclohexylamine (0·4 g., 4 mole) was boiled under reflux for 24 hr. The solution, on cooling, gave the cyclohexylammonium salt of *NN'*-diphenylphosphorodiamidic acid (300 mg.), m.p. 176—179° (lit.,[12] 175—178°). The filtrate, on evaporation, gave an uncrystallisable brown oil.

(b) *With* P(1)-*dicyclohexyl*-P(2)-*diphenylpyrophosphoramide* (11). The pyrophosphoramide (0·7 g.) and cyclohexylamine (0·3 g.) in dioxan (25 ml.) were boiled under reflux for 4 hr. to give the cyclohexylammonium salt of *NN'*-diphenylphosphorodiamidic acid (0·4 g.), m.p. 179—180° (lit.,[12] 175—178°).

(c) *With* P(1)-*dibenzyl*-P(2)-*diphenylpyrophosphoramide* (13). The pyrophosphoramide (0·75 g.) and cyclohexylamine (0·3 g.) were boiled for 2 hr. to give the cyclohexylammonium salt of *NN'*-diphenylphosphorodiamidic acid (0·4 g.), m.p. 179—180°.

(d) *With the* P(1)-*diphenyl*-P(2)-*dimorpholino-derivative* (21).—The pyrophosphoramide (0·93 g.) and cyclohexylamine (0·4 g.) were boiled under reflux in dioxan (25 ml.) for 24 hr. to give the cyclohexylammonium salt of dimorpholino-phosphoric acid (500 mg.), m.p. 250—252°. N.m.r. (D_2O) showed no aromatic protons.

We thank the Hertfordshire County Council for the award of a Research Assistantship (to D. H. W.), the Chemical Society for a research grant (to R. J. W. C.); I.C.I. Ltd. (Pharmaceuticals Division for some microanalyses), and Professor V. M. Clark of The University of Warwick for his interest in this work, and for arranging the mass spectral and ^{31}P n.m.r. determinations.

[0/1994 *Received, November 23rd,* 1970]

* In certain cases it was advantageous to dissolve the phosphoramidic chloride in tetrahydrofuran.

† Dioxan was dried with sodium wire and subsequently chromatographed on an aluminium oxide column.

[20] J. Haslam, D. C. M. Squirrell, and K. R. Clarke, *J. Appl. Chem.*, 1960, **10**, 93.

Published on 01 January 1971 on http://pubs.rsc.org | doi:10.1039/J39710002028
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