Studies in Cyclophosphazenes. Part IV.[1] The Kinetics of the Reactions for the Formation of Methylaminodimethylaminotetrachlorocyclotriphosphazene in Tetrahydrofuran

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The rates of two reactions leading to the formation of *trans*-methylaminodimethylaminotetrachlorocyclotriphosphazene, *viz.* the reaction of methylaminopentachlorocyclotriphosphazene with dimethylamine and the reaction of dimethylaminopentachlorocyclotriphosphazene with methylamine have been measured in tetrahydrofuran at various temperatures. The rate of the first reaction is almost equal to that of the reaction of dimethylaminopentachlorocyclotriphosphazene with dimethylamine and the rate of the second reaction roughly equals that of the reaction of methylaminopentachlorocyclotriphosphazene with methylamine. The conclusion which is reached from these comparisons is that the rates of these amination reactions are strongly dependent on the nucleophile but virtually independent of the nature of the amino-substituent on the ring. The electronic and steric implications of these conclusions are examined. Apparently similar conclusions relating to the influence of the nucleophile and the substituents on the ring, observed in a preparative study are discussed in the light of the kinetic data.

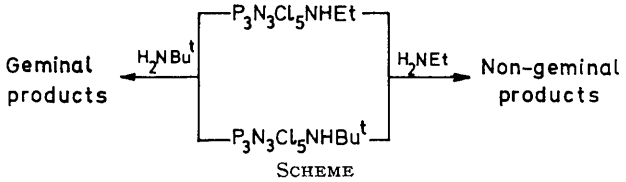
THE observation that substitution reactions of hexahalogenocyclotriphosphazenes yield characteristic ratios of *cis*-, *gem*-, and *trans*-isomers of tetrahalogenocyclotriphosphazenes ($P_3N_3X_4Y_2$; X = F, Cl, Br; Y = F, Cl, Br (but $\neq$ X), R, NR_2, OR, SR, *etc.*)—with one isomer often being preponderant—has generated frequent study aimed at understanding these phenomena. These reactions have generally been considered to proceed in two stages; the first produces a pentahalogenocyclotriphosphazene ($P_3N_3X_5Y$), although in some cases (*e.g.* $P_3N_3Cl_5NH_2$, $P_3N_3Cl_5C_6H_5$) this first product has eluded isolation by direct reaction. The subsequent substitution produces the mixture of di-substituted isomers. It is widely accepted that the first group introduced (Y) exerts a directing effect that determines the ratios of the isomers obtained in the second stage of substitution, and, in particular, which isomer is favoured. This presumption is in conformity with established theories governing the behaviour of substitution reactions in organic compounds, theories that are especially well illustrated by substituted benzenes whose aromaticity is formally analogous to that of the cyclophosphazenes. This analogy reinforces the concept of the operation of directive effects in the cyclophosphazenes.

The elucidation of these reaction patterns has been most often investigated for amination reactions, and several rationalizations of their behaviour have been proposed, but alkylation, arylation, fluorination, and several other reactions have also been studied though less intensively. For aminations, Becke-Goehring and co-workers [2] postulated that donation of the lone-electron pair from the amino-substituent to the ring results in higher electron density at the substituted phosphorus atom than at the other phosphorus atoms. This difference of electron density leads to preferred nucleophilic attack at an unsubstituted phosphorus atom in the subsequent substitution. This explanation rationalizes the non-geminal reaction pattern that was established from the reactions of several aliphatic amines. The contrasting behaviour of other amines (specifically ammonia [3] and t-butylamine [4]) that yield predominantly geminal isomers has been ascribed to a mechanism that produces a conjugate base in the first step of the second stage of amination. This de-protonated species then expels the geminal chloride ion, and finally the three-co-ordinate phosphorus centre reacts with a second molecule of amine to produce the geminal isomer in a fast reaction. In the non-geminal reactions it is the *trans*-isomer that is overwhelmingly obtained, and Keat and Shaw [5] proposed the '*cis*-effect' to explain this. They postulated that the lone-electron pair donation referred to above leads to preferential con-

[1] Part III, J. M. E. Goldschmidt and E. Licht, preceding paper.
[2] M. Becke-Goehring, K. John, and E. Fluck, *Z. anorg. Chem.*, 1959, **302**, 103.
[3] (*a*) W. Lehr, *Z. anorg. Chem.*, 1967, **350**, 18; (*b*) G. R. Feistel and T. Moeller, *J. Inorg. Nuclear Chem.*, 1967, **29**, 2731.
[4] S. K. Das, R. Keat, R. A. Shaw, and B. C. Smith, *J. Chem. Soc.*, 1965, 5032.
[5] R. Keat and R. A. Shaw, *J. Chem. Soc.* (*A*), 1966, 908.

centration of electron density on the same side of the phosphazene ring as the substituent. This increased electron density hinders attack on the substituent side of the ring, but following *relatively* ready attack on the opposite side, it assists chloride ion release from the substituent side. Allen and Moeller [6] modified the '*cis*-effect' to include additional π-bonding effects between the substituent and the ring. They could then rationalize what appeared to be anomalous behaviour observed in the arylation of hexafluorocyclotriphosphazene within the framework of the existing theory. As an alternative to the '*cis*-effect' we have recently proposed the substituent solvating effect [1] to explain the preference for the *trans*-isomer in non-geminal substitution. According to this hypothesis, substitution proceeds with inversion at the phosphorus centre with departure of the leaving group being rate-controlling because solvation of the ion being formed in this step contributes decisively to the large negative entropy of activation. An alkylamino-substituent assists in the solvation of the departing chloride ion through a *cis*-2,4-diaxial interaction, raising the entropy of activation for this process relative to non-assisted solvation by the solvent alone as occurs in the reaction that gives the *cis*-isomer. This effect enhances the rate of *trans*-substitution compared to *cis*-substitution, thus explaining the stereoselectivity of the reaction.

In contrast to the above, however, there is some evidence that it is not solely the substituent that governs the course of the reaction. Keat and Shaw [7] from a study of the configurations of the products of reactions that lead to di-substitution, as shown in the Scheme, demonstrated that, for specific cases, it is



SCHEME

the attacking amine that is decisive as to whether the product is geminal or non-geminal. No explanation for this observation was advanced. Furthermore, Green and Sowerby's results [8] showed that substitution by the same substituent, but employing different reagents (that presumably operate by different mechanisms), leads to different products. Therefore, more than simplistic consideration of the identity of the substituent as it effects the course of substitution is needed to permit full understanding of the stereochemical peculiarities of these reactions.

No rate studies explicitly aimed at evaluating in detail the kinetic effects associated with different substituent amino-groups have been reported, but Capon, Hills, and Shaw [9] established that the presence of an amino-substituent does retard the rate of further amination. Goldschmidt and Licht [1,10] showed that this retardation is due to a rise of enthalpy of activation: the amino-substituent also increases the entropy of activation although not in sufficient measure to offset the accompanying rise in the enthalpy of activation.

Special interest is attached to elucidation of the kinetic influence of the substituent since kinetic investigation should throw light on the two assumptions implicit in all the explanations suggested for the stereoselectivity observed. The first of these assumptions is that the reactions are kinetically rather than thermodynamically controlled and the second is that it is indeed the substituent that is ultimately responsible for the steric course of reaction. In addition to much supporting evidence for these assumptions, there is also some contradictory evidence. It has been shown [11] that, in certain cases at least, what appears to be thermodynamic control operates under readily attainable conditions, and Keat and Shaw's results on the importance of the nucleophile are apparently incompatible with the second assumption.

In this study we measured the rates of the following reactions in tetrahydrofuran:

$$P_3N_3Cl_5HNMe + 2HNMe_2 \longrightarrow P_3N_3Cl_4HNMeNMe_2 + H_2NMe_2^+Cl^- \quad (1)$$

$$P_3N_3Cl_5NMe_2 + 2H_2NMe \longrightarrow P_3N_3Cl_4HNMeNMe_2 + H_3NMe^+Cl^- \quad (2)$$

It has been shown [12] that both reactions yield the same product. This product is assumed to be the *trans*-isomer since both of the most abundant (*ca.* 80%) isomers, $P_3N_3Cl_4Y_2$ (Y = HNMe and NMe_2) formed under similar conditions are known to have this configuration.[13,14]

It was hoped that by comparing the rates for reactions (1) and (2) with those which have been measured previously [1,10] for reactions (3) and (4), that specific

$$P_3N_3Cl_5HNMe + 2H_2NMe \longrightarrow P_3N_3Cl_4(HNMe)_2 + H_3NMe^+Cl^- \quad (3)$$

$$P_3N_3Cl_5NMe_2 + 2HNMe_2 \longrightarrow P_3N_3Cl_4(NMe_2)_2 + H_2NMe_2^+Cl^- \quad (4)$$

inferences as to the influence of methylamine and dimethylamine as nucleophiles and as substituents could be deduced. A preliminary report of these results has appeared.[15]

[6] C. W. Allen and T. Moeller, *Inorg. Chem.*, 1968, **7**, 2177.
[7] R. Keat and R. A. Shaw, *Angew. Chem.*, 1968, **80**, 192.
[8] B. Green and D. B. Sowerby, *J. Chem. Soc.* (*A*), 1970, 987.
[9] B. Capon, K. Hills, and R. A. Shaw, *J. Chem. Soc.*, 1965, 4059.
[10] J. M. E. Goldschmidt and E. Licht, *J. Chem. Soc.* (*A*), 1971, 2429.
[11] J. M. E. Goldschmidt and M. Segev, unpublished results.
[12] J. M. E. Goldschmidt and J. Weiss, *Israel J. Chem.*, 1963, **1**, 306.
[13] W. Lehr, *Z. anorg. Chem.*, 1967, **352**, 27.
[14] H. Koopman, F. J. Spruit, F. Van Deursen, and J. Bakker, *Rec. Trav. Chim.*, 1965, **84**, 341.
[15] J. M. E. Goldschmidt and E. Licht, *Israel J. Chem.*, 1966, **4**, 2p.

EXPERIMENTAL

The reactants which were required for reactions (1) and (2), the solvents, *etc.*, were prepared as described previously.[1,10] The experimental technique employed in the kinetic measurements and the method for determining the rate of reaction by estimating the quantity of chloride ion liberated have been described in Part III of this series.[1]

RESULTS AND DISCUSSION

Tables 1 and 2, which refer to reactions (1) and (2) respectively, record details of the experiments performed

TABLE 1

Details of the kinetic runs for the reaction: $P_3N_3Cl_5HNMe + 2HNMe_2 \longrightarrow P_3N_3Cl_4HNMeNMe_2 + H_2NMe_2^+Cl^-$

Expt.	10^4 $[P_3N_3Cl_5HNMe]_i$*/ M	10^4 $[HNMe_2]_i$/ M	Reaction covered/ %	Temp. /°C	k_2 / l mol^{-1} s^{-1}
(1)	7·36	14·72	67	30	1·098 ± 0·022
(2)	8·52	8·52	80	30	1·070 ± 0·018
(3)	7·36	14·72	62	20	0·762 ± 0·022
(4)	8·52	8·52	79	20	0·733 ± 0·015
(5)	5·50	7·34	81	20	0·745 ± 0·003
(6)	7·36	14·72	65	10	0·508 ± 0·020
(7)	8·52	8·52	73	10	0·528 ± 0·012

* i = Initial concentration.

TABLE 2

Details of the kinetic runs for the reaction: $P_3N_3Cl_5NMe_2 + 2H_2NMe \longrightarrow P_3N_3Cl_4HNMeNMe_2 + H_3NMe^+Cl^-$

Expt.	10^4 $[P_3N_3Cl_5NMe_2]_i$*/ M	10^4 $[H_2NMe]_i$/ M	Reaction covered/ %	Temp. /°C	k_2 / l mol^{-1} s^{-1}
(8)	5·00	10·00	86	30	2·133 ± 0·033
(9)	7·52	7·52	80	30	2·150 ± 0·050
(10)	5·00	10·00	91	20	1·700 ± 0·050
(11)	7·52	7·52	82	20	1·717 ± 0·017
(12)	8·36	10·50	85	20	1·750 ± 0·033
(13)	5·00	10·00	89	10	1·383 ± 0·033
(14)	7·52	7·52	83	10	1·433 ± 0·050

* i = Initial concentration.

and the values of k_2 calculated on the basis of a second-order rate law. The applicability of this rate law was established by examination of the appropriate plots for each experiment. Table 3 contains the average values calculated from the data of the previous Tables together with the enthalpies and entropies of activation for reactions (1) and (2). In addition Table 3 contains the corresponding information for reactions (3) and (4). The second-order rate law and the magnitudes of the activation parameters indicate that reactions (1) and (2) proceed by the same mechanism as the reactions studied previously.[1,10]

Comparison of the activation parameters for reactions (1) and (2) with those for reactions (4) and (3), respectively, should give evidence of any effect, particularly a steric effect, that can be attributed to the amino-substituent on the phosphazene ring. However, this comparison shows that the methylamino- and the dimethylamino-groups hardly differ from one another as substituents, although they do, of course, differ from chlorine in this respect. The difference between the

TABLE 3

Summary of average results calculated for reactions (1)—(4)

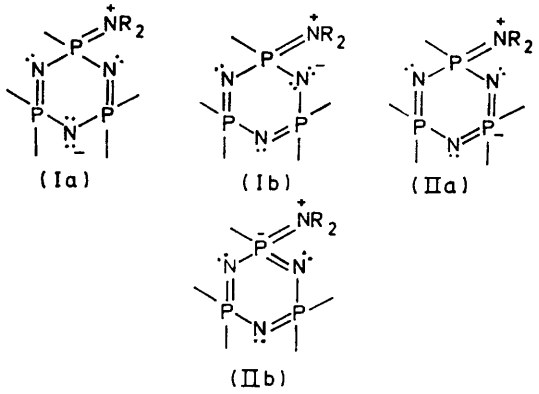
Data for reaction	k_2/l mol^{-1} s^{-1} at 30 °C	at 20 °C	at 10 °C	ΔH^* / kcal mol^{-1}	ΔS^* / e.u.
1	1·08 ± 0·025	0·75 ± 0·018	0·52 ± 0·018	5·7 ± 0·6	−39 ± 2
2	2·14 ± 0·043	1·72 ± 0·040	1·41 ± 0·050	3·0 ± 0·6	−46 ± 2
3 [a]	2·23 ± 0·070	1·80 ± 0·010	1·47 ± 0·050	3·0 ± 0·8	−46 ± 3
4 [b]	0·99 ± 0·013	0·71 ± 0·016	0·51 ± 0·018	5·1 ± 0·6	−38 ± 2

[a] From ref. 1. [b] From ref. 10.

two groups of reactions [(1) and (4) *vs.* (2) and (3)] demonstrates that the rates of these reactions are dependent primarily on the nature of the nucleophile, and as shown in Part III,[1] the differences for these particular amines arise from differences of their steric requirements.

In the approach developed in previously published Parts of this series, the enthalpy of activation was associated with the first step of reaction, *i.e.* with the attack of the nucleophile on the site of reaction. Furthermore, the rise of enthalpy in the second stage of reaction is caused by the donation of the lone-pair electrons from the exocyclic nitrogen to the ring. Therefore, the virtually equal enthalpies of activation found for reactions (1) and (4) and for reactions (2) and (3) imply that the electron density at the electrophilic centres in both substrates is almost the same, despite the differences of basicity of methylamine and dimethylamine.

Structures (Ia and Ib) and (IIa and IIb) typify the two main resonance forms of aminocyclotriphosphazenes involving lone-electron pair donation. The former



structures are substantially similar to those proposed by Becke-Goehring *et al.*,[2] with all phosphorus atoms being pentacovalent and the negative charge residing on the nitrogen atoms. Comparing these structures with a model, such as *NN*-dimethylaniline, indicates that the phosphazenic nitrogen atoms resemble the *ortho–para* carbon atoms both position- and charge-wise. In contrast, in the latter structures[18] the site of the negative charge is on the formally hexacovalent phosphorus atoms which electronically (though not geo-

metrically) are analogous to the *ortho–para* carbon atoms in the model: we refer to the phosphorus atoms as ' pseudo-*ortho–para* '. Similarly, the nitrogen atoms, bearing no charge, are ' pseudo-*meta* '.

The virtually equal reactivities of methylamino- and dimethylamino-pentachlorocyclotriphosphazenes, paralleling the equal values of σ_{para} for these two substituents (shown in Table 4) signify that the phosphorus

TABLE 4

σ-Coefficients and substituent constants for methylamino- and dimethylamino-groups

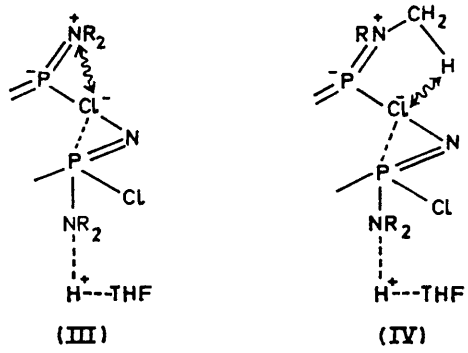
Amino group	σ_{para} [a]	σ_{meta} [a]	α_R [b]	γ_R [b]
Me	−0·592	−0·302	5·8	3·1
Me_2	−0·600	−0·211	5·6	2·8

[a] Values from H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191. [b] Values from D. Feakins, R. A. Shaw, P. Watson, and S. N. Nabi, *J. Chem. Soc.* (*A*), 1969, 2468.

centres are ' pseudo-*ortho–para* ' and that structures (IIa and IIb) best describe the electronic structures of these compounds.

Support for this hypothesis comes from the basicity measurements of cyclophosphazenes reported by Feakins and Shaw and their co-workers.[16] The values of the substituent constants calculated from the basicity data by these authors (and presented in Table 4) show that the methylamino-group is more electron donating than the dimethylamino-group. This unexpected inversion of electron donation parallels that measured by σ_{meta} for these same groups, and conforms to the description of the ring nitrogen atoms in the cyclotriphosphazenes as being ' pseudo-*meta* .' Thus, by criteria for estimating electron density at both the phosphorus and the nitrogen atoms, structures (IIa and IIb) apparently make the largest contributions to the resonance hybrid. In the absence of explicit information on the shape of the ring and the spatial orientation of the substituent, no acceptable description of the bonding in terms of simple *d*-orbital overlaps based solely on structures (IIa and IIb) can be proposed.

The rise of the entropy of activation on comparing the first stage of reaction with the second has been ascribed [1] primarily to the substituent solvating effect. The almost equal values of the entropy of activation found in reactions (1) and (4) and in reactions (2) and (3) show that, without regard to the identity of the nucleophile, the two substituents examined in this investigation appear to solvate substantially equally. This is contrary to predictable differences of solvating power of the groups that should reflect their different sizes. The lack of any detectable steric effect can best be understood in terms of a highly localized interaction with a particular atom (or group) of the substituent specifically participating in the solvation of the leaving group. This centre of solvation might be the exocyclic nitrogen atom which is relatively positive on account of the donation of its lone pair of electrons. A nitrogen–chlorine interaction would result in structure (III) with formation of a relatively strainless five-membered ring. The solvation is indicated by the wavy line. An



alternative possibility would be solvation by a hydrogen atom of a methyl group, as shown in (IV). A hydrogen–chlorine interaction would resemble a conventional hydrogen bond making it less unusual than the nitrogen–chlorine interaction. As opposed to this the hydrogen solvation of the chloride ion would require the formation of a seven-membered ring which is far less common than the five-membered ring which was proposed in the other alternative. In both cases the non-interacting parts of the substituent would not appreciably influence the solvation at the interacting centre.

The principal conclusion which is derived from the kinetic results is that the *rates* of these reactions are determined mainly by the nucleophile, rather than by the substituent on the ring. In their preparative study, Keat and Shaw [7] reached a superficially similar conclusion with the nucleophile and *not* the substituent determining the *configurations* of the products of the reactions.

A semi-quantitative correlation between Keat and Shaw's and our results can be established albeit indirectly. For this purpose certain basic premises need be examined. First, these reactions are stereoselective rather than stereospecific; [17] *i.e.* the geminal and non-geminal reactions take place concurrently and in competition, with one reaction mostly outpacing the others. Second, the geminal and non-geminal isomers are produced by different reaction mechanisms. The mechanism for the non-geminal reaction is associative, that is collision of the nucleophile and substrate molecules occurs before or as part of the rate-determining step. On the other hand, the geminal reaction involves a rate-determining ionization prior to attack by the nucleophile at the site of substitution as discussed in the introductory section.

The steric factor is considered third as it affects the nucleophile and the substituent on the ring for both reaction paths. There is ample experimental evidence from both kinetic [1,9] and non-kinetic [18] studies that, in the non-geminal reactions, increasing the size of the

[16] D. Feakins, R. A. Shaw, P. Watson, and S. N. Nabi, *J. Chem. Soc.* (*A*), 1969, 2468.

[17] R. A. Shaw, *Rec. Chem. Progr.*, 1967, **28**, 243.

[18] S. K. Ray and R. A. Shaw, *J. Chem. Soc.*, 1961, 872.

nucleophile retards the rates of these reactions. Quantitatively, it has been found [19] that on going from methylamine to t-butylamine the rates of amination decrease by over three orders of magnitude. With respect to the steric influence of the substituent, the results of the present study indicate the existence of no more than an undetectably small effect. Considering next the geminal reaction, the ionization mechanism which is believed to operate precludes any direct steric effect by the nucleophile. Moreover, the primary rapid deprotonation with the nucleophile acting as a base can be subject to no more than relatively moderate steric inhibition.[20] Similarly, the bulkiness of the substituent on the ring affects the rates of the geminal reactions to only a small degree as shown by v.p.c. studies [21] of the proportion of the geminal product in predominately non-geminal reactions in which various alkylaminopentachlorocyclotriphosphazenes reacted with a common nucleophile: only a very slight variation of the ratios of the isomers with the identity of the amino-substituent was observed: for methylamine (the most rapidly reacting amine studied), the geminal product always comprised roughly 5% of the total product. This percentage determines the rate of geminal reaction (irrespective of the nucleophile and the substituent) to be between one and two orders of magnitude slower than the non-geminal reactions with methylamine. In summary, the rate of the non-geminal reaction is, sterically, strongly influenced by the nucleophile, but is unaffected by the substituent: the rate of the geminal reaction is, to a first approximation constant, uninfluenced by either the nucleophile or the substituent.

The conclusion to be drawn from this analysis is that the ratio of the rates of the non-geminal and the geminal reactions depends only on the rates of the non-geminal reactions, which are a function of the size of the nucleophile. With a rapidly reacting amine, *e.g.* methylamine, the non-geminal reaction proceeds roughly at a rate one to two orders of magnitude faster than the geminal reaction. A sluggish amine, *e.g.* t-butylamine, will react in the geminal path at a rate roughly one order of magnitude more rapidly than the non-geminal reaction. The ratios of the isomers formed will thus be a function of the steric requirements of the nucleophile and be independent of the substituent, just as found by Keat and Shaw.

Finally it must be pointed out that this approach is in conformity with the results of other studies of substitution patterns carried out largely by Shaw and his co-workers and summarized in reference **17**. At one extreme, primary aliphatic amines (R = Me, Et, Pr^n, or Bu^n) follow non-geminal reaction patterns, whilst at the other extreme t-butylamine gives only geminal products. In the middle, isopropylamine reacts by mixed geminal and non-geminal pathways.

[1/1395 *Received*, 6*th*, *August* 1971]

[19] J. M. E. Goldschmidt and E. Licht, *Israel J. Chem.*, 1967, **5**, 9p, and unpublished results.

[20] F. Covitz and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1963, **85**, 1773.

[21] M. Davidor and J. M. E. Goldschmidt, unpublished results.