Studies in Cyclophosphazenes. Part 9.[1] Influence of the Steric Requirements of the Amino-substituents on the Rates of Amination of 2-Amino-2,4,4,6,6-pentachlorocyclotri(λ^5-phosphazenes)

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Measurements of the rates of amination of a number of aminopentachlorocyclotriphosphazenes, $N_3P_3Cl_5(NRR')$ (R = Bu^n, R' = H; R = R' = Bu^n; R = Pr^i, R' = H; RR' = C_5H_{10}), with dimethylamine to give non-geminal disubstituted products have been made at two temperatures in tetrahydrofuran with the aim of elucidating the steric effects of the amino-substituents in these reactions. The values of the rate constants and of the activation parameters determined showed that steric effects are only very small. To resolve the conflict between these findings and others in the literature in which appreciable steric influences were observed, the division of these amination reactions into three classes, each of which is affected by steric factors in its own way, is proposed. This enables much of the kinetic and preparative data on steric effects in these reactions to be rationalised in the framework of one general hypothesis.

THE distinction between steric effects that are due to the substituting amines and those that are due to the amino-substituents in the amination reactions of amino-chlorocyclotriphosphazenes has been elaborated upon in Part 5 [2] of this series in which a detailed kinetic investigation of the former effects was reported. This paper is concerned with a parallel study of the latter effects. The consequences of both effects as manifested in preparative studies have recently been reviewed.[3,4] In the only reported kinetic study of the steric effects of the substituents in these reactions, the reactivities of methylamino- and dimethylamino-pentachlorocyclotriphosphazenes with methylamine and with dimethylamine were compared.[5] With both amines the steric effects of the two substituents were found to be almost equal, but the relatively small difference between the two groups restricts the generality of the finding. In order to elucidate these influences more fully we have now extended the study of these steric effects to a wider selection of amino-groups, measuring the rates of several appropriate amination reactions at two temperatures to evaluate rate constants and activation parameters. The results confirm that the steric influence of the amino-groups is quite small. At first glance this finding contradicts the results of preparative studies,[3,4] but detailed consideration of all the data available leads to recognition of several types of amination reactions, clarifies the operation of the steric factors in these reactions, and permits the conflicts to be resolved. The present results have been the subject of a previous brief communication.[6]

EXPERIMENTAL

Materials.—The hexachlorocyclotriphosphazene, an Albright and Wilson product, was purified as described previously.[7] The isopropyl-, n-butyl-, and di-n-butylamines were B.D.H. reagent-grade materials. The *puriss* grade piperidine was from Fluka. Before use these amines were all refluxed over K[OH] and then distilled. Solutions of dimethylamine were prepared by a published procedure.[7] The monoaminopentachlorocyclotriphosphazenes were synthesised according to literature methods.[8] All were shown to be gas chromatographically (g.c.) pure. All solvents were dried and then redistilled by standard procedures.

Chromatography.—Starting materials and reaction products were analysed by t.l.c. and g.c. In the former method glass plates coated with Kieselguhr G (Merck) were activated at 110 °C for 1 h before use. The eluants were appropriate benzene–light petroleum (b.p. 60—80 °C) mixtures. Development was with alcoholic methyl red.[9] An F & M 720 gas chromatographic instrument fitted with a thermal conductivity detector and attached to an Infotronics CSR-100 integrator was used for the g.c. analyses. The glass columns (length 4 m, diameter 5 mm) were filled with Chromasorb W loaded with 2.7% SE-52. The oven temperature was 168 °C and the helium gas flow rate was in the range 45—60 $cm^3\ min^{-1}$. The signals of the isomeric, mixed, diamino-reaction products were identified assuming the known general order of elution, *gem* > *trans* > *cis*.[9]

Kinetic Experiments.—Details of the method used in the kinetic runs and in the analysis of the samples have been described.[2]

RESULTS AND DISCUSSION

The kinetics of the general reactions (1) [R = Bu^n, R' = H; R = R' = Bu^n; R = Pr^i, R' = H; and RR' = C_5H_{10} (piperidyl)] as carried out in tetrahydrofuran (thf) were measured at 18 and 30 °C. Table 1 gives details of the experiments performed and values of k_2. All the reactions obeyed second-order rate laws, being first order in the concentrations of the phosphazenic substrates and dimethylamine. Average values of k_2 at each temperature and calculated values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are presented in Table 2 together with the corresponding values for the same reactions with R = Me, R' = H and R = R' = Me, based on earlier results.[5,7]

$$N_3P_3Cl_5(NRR') + 2NMe_2H \longrightarrow N_3P_3Cl_4(NRR')(NMe_2) + [NMe_2H_2]Cl \quad (1)$$

T.l.c. and g.c. analysis of the reaction products showed them to consist of *ca.* 3 : 7 mixtures of *cis* : *trans* isomers of the phosphazenic products shown in equation (1).

Approximately 1% of the *gem* isomers was detected too. The amounts of *trans* isomer ranged from 68 to 72% of the total, the lowest amount being found in the reaction of the di-n-butylamino-derivative, which was also the least reactive. Despite the considerable variation of the amino-groups, no clear trends were discerned in the isomer ratios. The significance of the virtual constancy of the ratio between the two non-geminal isomers has been discussed elsewhere.[10]

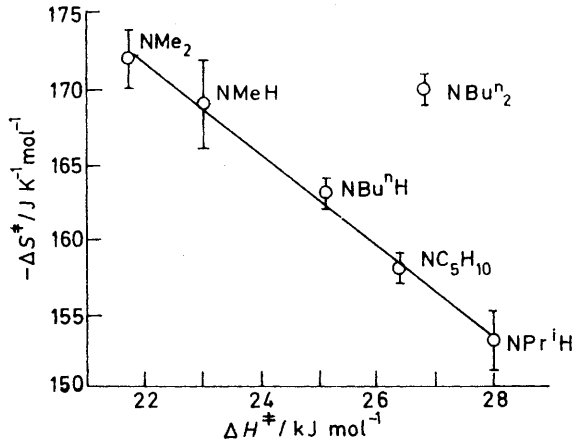
Table 2 shows that, with the exception of the value for reaction (iv), they are all almost equal. However, the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ do vary, although in quite narrow ranges. The Figure shows that in these reactions a good linear relationship (with a correlation coefficient of 0.995) exists between $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. With increasing bulk of the amino-substituent the value of $\Delta H^{\ddagger}$ tends to increase in a general way. However, with the *trans* isomers predominating and attack presumed to proceed with

TABLE 1

Details of the kinetic runs for the reaction $N_3P_3Cl_5(NRR') + 2NMe_2H \longrightarrow N_3P_3Cl_4(NRR')(NMe_2) + [NMe_2H_2]Cl$

Expt. no.	$N_3P_3Cl_5(NRR')$ R	R'	θ_c/°C	$10^4[N_3P_3Cl_5(NRR')]$ / mol dm^{-3}	$10^4[NMe_2H]$ / mol dm^{-3}	k_2 / dm^3 mol^{-1} s^{-1}
1	Bu^n	H	18	4.82	9.64	0.612 ± 0.001
2				9.64	9.64	0.623 ± 0.001
3				5.36	10.72	0.614 ± 0.002
4			30	4.82	9.64	0.969 ± 0.007
5				9.64	9.64	0.963 ± 0.023
6				5.36	10.72	0.953 ± 0.004
7	Bu^n	Bu^n	18	5.42	10.84	0.1308 ± 0.0001
8				5.20	10.40	0.1285 ± 0.0001
9				10.40	10.40	0.1295 ± 0.0003
10			30	5.42	10.84	0.2089 ± 0.0003
11				5.20	10.40	0.2079 ± 0.0003
12				10.40	10.40	0.2129 ± 0.0008
13	Pr^i	H	18	5.00	10.00	0.574 ± 0.001
14				5.00	5.00	0.563 ± 0.012
15			30	5.00	10.00	0.933 ± 0.002
16				5.00	5.00	0.942 ± 0.005
17	C_5H_{10}		18	5.00	10.00	0.592 ± 0.001
18				5.00	5.00	0.592 ± 0.002
19			30	5.00	10.00	0.951 ± 0.002
20				5.00	5.00	0.947 ± 0.007

Inspection of Table 2 shows that the kinetic behaviour observed in all these reactions conforms to that found to be typical in our earlier studies of related reactions: $\Delta S^{\ddagger}$ was always found to be rate-controlling. Therefore,



Plot of $\Delta H^{\ddagger}$ against $\Delta S^{\ddagger}$; line is least-squares fit excluding point for $N_3P_3Cl_5(NBu^n_2)$

the previously proposed multi-step mechanism with the final step, chloride-ion departure, being rate-determining is thought to operate in these reactions too.

Examination of the k_2 values at 30 °C assembled in inversion, it is not immediately clear why this is so, nor why $\Delta S^{\ddagger}$ also increases in the same way. Any simple rationalisation of the relationship found between the activation parameters in these reactions is of dubious validity, because in spite of the predominance of *trans*-isomer formation, the data do refer to the two combined reactions that lead to the *trans* and the *cis* isomeric products whose kinetics were not studied separately as done in another case.[10]

The value of k_2 for the di-n-butylamino-substituted compound, although anomalous, is really only very slightly smaller than the others, it being reduced by a factor of less than five compared to the rest. This contrasts with a 200-fold reduction in the nucleophilic reactivity of di-n-butylamine, relative to dimethylamine, in their reactions with hexachlorocyclotriphosphazene.[2]

However, considering the entire picture, the anomalous value of k_2 for the di-n-butylamino-derivative can be clarified. Although at first sight its low value appears due to a combination of a high value of $\Delta H^{\ddagger}$ and a low value of $\Delta S^{\ddagger}$, actually the main factor responsible is the deviant value of $\Delta S^{\ddagger}$, since the value of $\Delta H^{\ddagger}$ is close to the range expected for a bulky amine. Then with the *trans* reaction leading, the low value of $\Delta S^{\ddagger}$ can be ascribed, in part, to reduction of the substituent-

solvating effect (s.s.e.) that is postulated to raise the value of $\Delta S^{\ddagger}$ of the *trans* reactions only, through an interaction between the amino-substituent and the departing group *via* a type of hydrogen bond in the transition state.[10] This requires that these groups be in proximity and consequently, as has been pointed out,[10] it calls for some puckering of the $(PN)_3$ ring. The partial inhibition of s.s.e. can then be traced to too large a separation of the two groups as would result from difficulty in puckering the ring because, in the expected chair-like conformation, placing the very bulky substituent in the pseudo-axial position is exceptionally unfavourable. This explanation is consistent with the somewhat larger and sterically unexpected amount of *cis* isomer found in this reaction, *ca.* 10% higher than in the other cases. This, too, of course, would tend to reduce $\Delta S^{\ddagger}$ for the combined reactions.[10] The exceptional behaviour of the di-n-butylamino-group is in line with its unique steric bulk compared to the other groups studied: it is the only secondary amine with two long-chain alkyl groups.

The overall relatively small steric effects of the substituent amines observed in the present study contrasts with the large ones found in our study of these amines acting as nucleophiles [2] and with the observations made in preparative reactions.[3,4] For instance, in the latter, the reaction of hexachlorocyclotriphosphazene with dibenzylamine did not progress beyond disubstitution [11] and its reaction with t-butylamine stopped at tetrasubstitution except when extreme forcing conditions were employed.[12] The second of these reactions, furthermore, proceeded by the less common geminal pathway. Moreover, both of the products of the above reactions, 2,4,6,6-tetrachloro-2,4-bis(dibenzylamino)-cyclotriphosphazene (I) and 2,2-dichloro-4,4,6,6-tetrakis(t-butylamino)cyclotriphosphazene (II) did react relatively readily with dimethylamine, a ' small ' amine: (I) only gave the 2,4-dichloro-2,4-bis(dibenzylamino)-6,6-bis(dimethylamino)-derivative (III), whilst (II) proceeded to complete amination giving 2,2-bis(dimethylamino)-4,4,6,6-tetrakis(t-butylamino)cyclotriphosphazene (IV).

This basically typical pattern of reactivity, as illustrated by the preparative reactions cited, can easily be ascribed to the steric effects of the substituents, but, mostly, other rationalisations can also be proposed. However, the case of the reaction that produced (III), and the fact that it could not be made to proceed any further, almost certainly must be the result of the steric influence of the dibenzylamino-substituents. Thus, at least in this last case, it is clear that the substituents do indeed cause steric inhibition, whilst our present results indicate the lack of importance of such effects in other cases. These apparently contradictory facts and much other data can be accommodated if the following distinction between three types of amination reaction is recognized.

The first type of amination is non-geminal substitution relative to a given amino-substituent at an ' unsubstituted ' phosphorus atom, *i.e.* at a $\equiv PCl_2$ centre. It is this kind of reaction which we have studied in this paper, and it shows only minor steric retardation chiefly because the substituent is too remote from the site of the reaction to have much influence. Our results establish the absence of appreciable steric influences in these reactions for cases in which monosubstituted derivatives react to produce non-geminal disubstituted ones. We presume that similar quite limited steric effects operate in this type of reaction involving more highly substituted compounds as analogous spatial relations apply, but this has not yet been verified. The intervention of mesomeric effects, the fact that for any kind of systematic kinetic study of these reactions the necessary compounds are in large part unknown, and lastly the inconveniently low reactivities expected make these reactions unamenable, at present, to kinetic study using the techniques we have available.

The second type of amination is geminal substitution involving a primary amino-substituent under such conditions that a conjugate base (c.b.) mechanism operates.[5,12,13] These reactions also only show slight steric effects,[5] for as has been pointed out they go through three-co-ordinate intermediates. Another quasi-kinetic demonstration of the lack of steric effects in this type of reaction comes from consideration of the 2,2,4-trisubstituted intermediate that must be involved in the synthesis of (II). This intermediate (like similar ones) has never been isolated, probably because the rate at which it reacts by a c.b. mechanism to produce (II) exceeds that of the reaction in which it is produced from its geminally disubstituted precursor by a type 1

TABLE 2

Summary of average rate constants and activation parameters for reactions of Table 1

	$N_3P_3Cl_5(NRR')$		k_2/dm^3 mol^{-1} s^{-1} at				$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
Reaction	R	R'	30 °C	20 °C	18 °C	10 °C	kJ mol^{-1}	J K^{-1} mol^{-1}
(i) [a]	Me	H	1.043 ± 0.017	0.743 ± 0.003		0.513 ± 0.005	23.0 ± 2.1	−169 ± 3
(ii) [b]	Me	Me	0.986 ± 0.005	0.715 ± 0.001		0.497 ± 0.004	21.7 ± 0.4	−172 ± 2
(iii)	Bu^n	H	0.959 ± 0.004		0.612 ± 0.001		25.1 ± 0.4	−163 ± 1
(iv)	Bu^n	Bu^n	0.208 ± 0.001		0.129 ± 0.001		26.8 ± 0.4	−170 ± 1
(v)	Pr^i	H	0.937 ± 0.003		0.569 ± 0.006		28.0 ± 0.8	−153 ± 2
(vi)	C_5H_{10}		0.949 ± 0.003		0.592 ± 0.001		26.4 ± 0.4	−158 ± 1

[a] Values recalculated from data of ref. 5 using corrected computer programs. [b] Values from ref. 7 as per footnote *a*.

mechanism. This latter reaction is relatively slow because of the bulkiness of the nucleophile involved.[2] The next stage of the reaction is faster than the previous one, notwithstanding the bulkiness of the amine, because it proceeds by a c.b. mechanism in which steric factors are of little importance. Mesomeric effects need not be considered in this qualitative analysis since they affect both reactions roughly equally.

The third type of amination is replacement geminal to an amino-substituent by direct nucleophilic attack. This type of reaction can only be meaningfully discussed for secondary amines, as with primary ones type 2 behaviour probably intervenes. This type of reaction is characterised by strong steric inhibition as illustrated by the lack of reactivity of (III) even with a 'small' amine such as dimethylamine, and by the fact that 2-chloro-2-dibenzylamino-4,4,6,6-tetrakis(dimethylamino)cyclotriphosphazene is a stable compound that resists replacement of the last chlorine atom except when forcing conditions are applied.[11] Incidentally, it should be emphasised that the considerable steric hindrance observed in this type of reaction lends support to the assumption that these reactions involve attack on the phosphorus atom from the same side of the ring as the amino-substituent and proceed with inversion.[2]

The above analysis has been confined to steric influences but the well established [7,14] mesomeric effects resulting from back donation to the phosphazene ring of electron pairs on the nitrogen atoms of the substituents cannot be completely ignored. No less than a combination of mesomeric deactivation and steric retardation, which can cause effective total inhibition of replacement reactions, can explain the reticence of certain reactions, such as those that lead to (I) and (II), to proceed to complete substitution. The fact that these reactions do go further with dimethylamine than with the bulkier amines, though not necessarily to completion, serves to emphasise the delicate interplay of the mesomeric and of the various steric factors.

Although only selected and rather extreme examples of steric effects have been analyzed here in detail, the differentiation between the steric effects of the substituting amines and of the substituents, and between the three types of amination reactions, does enable much of the data available in the literature to be rationalised consistently. Taken together with proposals concerning geminal, non-geminal, and *cis,trans* preferences and mesomeric effects they comprise a general hypothesis that permits many of the peculiar reaction patterns of this class of compounds in these reactions to be understood and even to be predicted with a reasonable degree of confidence. Only the little studied but important solvent effects remain very perplexing.

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