Studies in Cyclophosphazenes. Part 6.[1,2] Configurations of the Non-geminal Tetrachlorobis(dialkylamino)cyclotri(λ^5-phosphazenes)

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A method for determining the *cis* and *trans* configurations of 2,4,6,6-tetrachloro-2,4-bis(dialkylamino)cyclotriphosphazenes has been developed, and its validity established for compounds of known configuration. The method employs the ^{19}F n.m.r. spectra of the *cis*- and *trans*-2,4-dichloro-2,4-bis(dialkylamino)-6,6-difluorocyclotriphosphazenes, which are prepared, with retention, from the corresponding isomers of the title compounds. These spectra enable unequivocal identification of the isomeric configurations of the precursors. By application of the method to the known pairs of compounds in the above class, the configurations previously assigned to the diethylamino- and piperidino-compounds have been confirmed. Prior conflicting assignments made for the morpholino- and pyrrolidin-1-yl isomers have been resolved. Some implications of these results are discussed.

SINCE the discovery of the first isomers of the cyclophosphazenes by Shaw and Stratton [3] in 1962, many isomeric cyclophosphazenes have been isolated and in many cases their configurations have been determined. Correct identification of these configurations is important in its own right and because it is a prerequisite for all attempts to rationalize the peculiar stereochemical reaction patterns that characterize so much of the substitution chemistry of the cyclophosphazenes.

A detailed and critical review of all methods used for isomer identification in cyclophosphazene chemistry has appeared.[4] From this it is apparent that there are only three general methods that are generally useful for assigning configurations to isomeric cyclophosphazenes. These are: (*i*) the isomer count method, (*ii*) the dipole-moment method, and (*iii*) the n.m.r. method in direct and indirect variations. All these methods, however, either suffer inherent difficulties or are limited in their application to certain classes of isomers.[4] In particular, the common non-geminal disubstituted chlorocyclotriphosphazenes,† $N_3P_3Cl_4A_2$ (A = substituent),[4] are especially difficult to identify. Direct n.m.r. spectroscopy, the preferred method, is *a priori* inapplicable to them.[4] The isomer-count method, besides being very tedious, is unreliable except when extreme care is taken and the dipole-moment method requires the isolation of not inconsiderable quantities of *both* isomers for meaningful measurements to be made. Thus the development of a convenient method for isomer identification for these compounds is most desirable, especially as they are represented, for example, by a large number of bis(amino)tetrachlorocyclotriphosphazenes, the configurations of many of which have not been established with certainty.

TABLE 1

Configurations of known [a] pairs of non-geminal tetrachlorobis(dialkylamino)cyclotriphosphazenes

Compound number	R	M.p. (θ_c/°C)	Literature assignments: Configuration	Methods used [b]	Ref.	Our assignment
(1)	NMe_2	86	*cis*	^1H, ^{19}F, μ [c]	5—7	*cis*
(2)		103	*trans*	^1H, ^{19}F, μ [c]	5—7	*trans*
(3)	NEt_2	Oil [d]	*cis*	g.c., i.c.	16	*cis*
(4)		21	*trans*	g.c., i.c.	16	*trans*
(5)	NC_5H_{10}	126	*cis*	^1H d.d.	15	*cis*
(6)		103	*trans*	^1H d.d.	15	*trans*
(7)	NC_4H_8O	200	*trans*	i.c.	17	*cis*
(8)		105	*cis*	i.c.	17	*trans*
(9)	NC_4H_8	92	*trans*	i.c.	18	*cis*
(10)		47	*cis*	i.c.	18	*trans*

[a] One more pair of compounds of this type is known: non-geminal 2,4,6,6-tetrachloro-2,4-bis(2,2,2-triphenylphosphazen-1-yl)-cyclotriphosphazenes.[24] These isomers were reported after completion of the work reported here. [b] ^1H = Direct ^1H n.m.r. spectroscopy, ^{19}F = ^{19}F n.m.r. spectroscopy, μ = dipole–moment measurements, g.c. = gas chromatographic relative retention times, i.c. = isomer-count method and ^1H d.d. = ^1H n.m.r. spectroscopy of dimethylamino-derivatives. [c] For additional evidence favouring these assignments, see Introduction. [d] A m.p. of 29 °C has been reported,[16] but see ref. 10*a*.

Table 1 lists the known pairs of non-geminal tetrachlorobis(dialkylamino)cyclotriphosphazenes and gives details of the configurations assigned to them. The configurations of one pair of these, *cis*- and *trans*-2,4,6,6-tetrachloro-2,4-bis(dimethylamino)cyclotriphosphazene, have been determined by several independent methods. Proton [5] and ^{19}F n.m.r.[6] spectroscopies and dipole-moment measurements [7] provide consistent assignments that are cited in Table 1. Also the inter-relationship between these isomers has been demonstrated by isomerization.[8] Additionally, their configurations can be unambiguously deduced by consideration of the configurations of the trisubstituted products resulting from their reactions with dimethylamine. The configurations of all three of these trisubstituted compounds, the trichlorotris(dimethylamino)cyclotriphosphazenes, have been

† These compounds are more correctly named as cyclotri(λ^5-phosphazenes), where the λ^5 indicates that the phosphorus atoms have a connecting number of five as opposed to the normal connecting number of three.

established by ^{1}H n.m.r. spectroscopy [5] and, rigorously, by *X*-ray diffraction.[9] The configurations of the precursors, thus positively identified, are consistent with those obtained by the other methods, and they were regarded by us as standards for testing the method to be described below.

The aim of this investigation was to develop a generally applicable, definitive, analytical method for determining the configurations of compounds belonging to the above class, and specifically for checking the configurations assigned to all compounds appearing in Table 1. The method calls for the preparation of 2,4-bis(amino)-2,4-dichloro-6,6-difluorocyclotriphosphazenes by difluorination of the 2,4,6,6-tetrachloro-compounds at the 6-phosphorus atom employing $K[SFO_2]$ according to Green and Sowerby.[6] The ^{19}F n.m.r. spectra of these products, where the *trans* isomers show one fluorine environment and the *cis* isomers two, give unequivocal information on the configurations of the amino-groups in the fluorinated compounds. The validity of the method for identifying the configurations of the precursors depends on there having been no isomerization whatever with respect to the amino-groups during fluorination. This seems most reasonable since fluorination does not take place at a phosphorus atom to which amino-groups are bonded. The results obtained by Green and Sowerby,[6] who difluorinated the dimethylamino-compounds, do not, however, permit any conclusions to be reached on the occurrence or absence of isomerization because they worked with a mixture of isomers and separated and identified the products after fluorination. As a first step we therefore had to rigorously confirm that no isomerization accompanies fluorination. We attempted this by repeating Green and Sowerby's work using the separated isomeric compounds.

EXPERIMENTAL

The syntheses have been described in detail elsewhere.[10] The ^{19}F n.m.r. spectra were recorded on a Varian HA 100 instrument equipped with a 94.1-MHz radiofrequency unit. The spectra were measured in the field-sweep mode, the lock signal being extended by a Hewlett–Packard model 200 ABR audio-oscillator. Trifluoroacetic acid was used as an external reference, but the values quoted have been converted into the $CFCl_3$ standard using a conversion factor of 78.45 p.p.m.[11] All compounds were examined at a concentration of 10% w/w in CCl_4, except the morpholino-derivatives which were measured as saturated solutions in tetrahydrofuran. The gas-chromatographic instrumentation and data have been described in detail elsewhere.[10]

RESULTS

As described in detail elsewhere, pure *cis*- [10a] and *trans*-2,4,6,6-tetrachloro-2,4-bis(dialkylamino)cyclotriphosphazenes [10b] $N_3P_3Cl_4(NR_2)_2$ (R = Me, Et, C_5H_{10}, C_4H_8O, or C_4H_8) were prepared and then fluorinated using $K[SFO_2]$.[10b] For each pair of tetrachlorobis(dialkylamino)-derivatives two pure difluorinated products having different retention times were isolated, one from each fluorination reaction. Gas-chromatographic examination of the crude products obtained from these reactions showed that each one contained exclusively one of these difluoro-compounds. This demonstrates clearly that fluorination proceeded without detectable isomerization.

The ^{19}F n.m.r. spectra of the products were recorded and are presented in Table 2. Two typical spectra are shown in the Figures 1 and 2. The ^{19}F n.m.r. spectra of the known compounds resemble those reported [6] but appear better resolved and several previously unobserved couplings are readily evident. The nature of the individual amine substituents have only a slight influence on the values of the chemical shifts and the coupling constants.

TABLE 2

Fluorine-19 n.m.r. spectral data for 2,4-dichloro-2,4-bis(dialkylamino)-6,6-difluorocyclotriphosphazenes

Compound number	Synthesized from	M.p. (θ_c/°C)	δ [a,b]/p.p.m.	^1J(PF) [a]/Hz	^3J(PF) [c]/Hz	^2J(FF) [a]/Hz	Configuration assigned
(11) [d]	(1)	60	−70.4, −66.2	898.5, 898	11.3 ± 3.5	82, 69, 82, 72	*cis*
(12) [e]	(2)	84	−68.3	907	13.8 ± 0.4		*trans*
(13)	(3)	42	−70.8, −66.4	888, 896	14.0 ± 2.3	81, 60, 80, 61	*cis*
(14)	(4)	30	−68.6	904	13.3 ± 0.8		*trans*
(15)	(5)	106	−70.5, −65.7	891, 888	13.6 ± 1.6	82, 62, 81, 61	*cis*
(16) [f]	(6)	73	−68.2	894	13.2 ± 1.2		*trans*
(17)	(7)	162	−71.9, −66.9	880, 891	12.0 ± 3.5	76, 62, 88, 64	*cis*
(18) [f]	(8)	113	−69.4	894	12.3 ± 0.9		*trans*
(19)	(9)	70	−70.4, −66.4	896, 897	13.1 ± 2.1	74, 60, 85, 64	*cis*
(20)	(10)	57	−68.4	907	12.5 ± 0.5		*trans*

[a] When several values are given the order is as read from the chart going from high field to low field. [b] Relative to $CFCl_3$. [c] Average of all values. [d] Ref. 6 reports −70.48, −66.12 p.p.m. These values (relative to $CFCl_3$) are obtained after correction by multiplying by 94.075 (D. B. Sowerby, personal communication). [e] Ref. 6 reports −68.35 p.p.m. (as in *d*). [f] The left-hand multiplet is not a triplet, as in the other cases, but appears as a quintuplet. See Figure 1.

Inspection of the n.m.r. spectral data shows two kinds of spectra, one for each isomer of every pair. For convenience these spectra are referred to as simple and complex. Both of these are only consistent with 6,6-difluorination, the two other difluorination patterns possible, *i.e.* 2,4- and 2,6-difluorination, being eliminated because they both require a signal in the range −57 to −66 p.p.m. for the $\equiv PF(NR_2)$ group.[12,13] In addition, a signal at *ca.* −30 p.p.m. is expected [12] for the $\equiv PCl(F)$ group in the 2,6-difluoro-product. Finally, the number of lines observed cannot be reconciled with the number predicted from a detailed consideration of these two possibilities.

Accepting that 6,6-difluorination has indeed occurred, the simple and complex spectra are assigned to the *trans* and *cis* isomers respectively in conformity with the earlier assignments made [6] and with data collected from measurements made with other fluorocyclophosphazenes. For both kinds of spectra, a first-order interpretation ascribes the

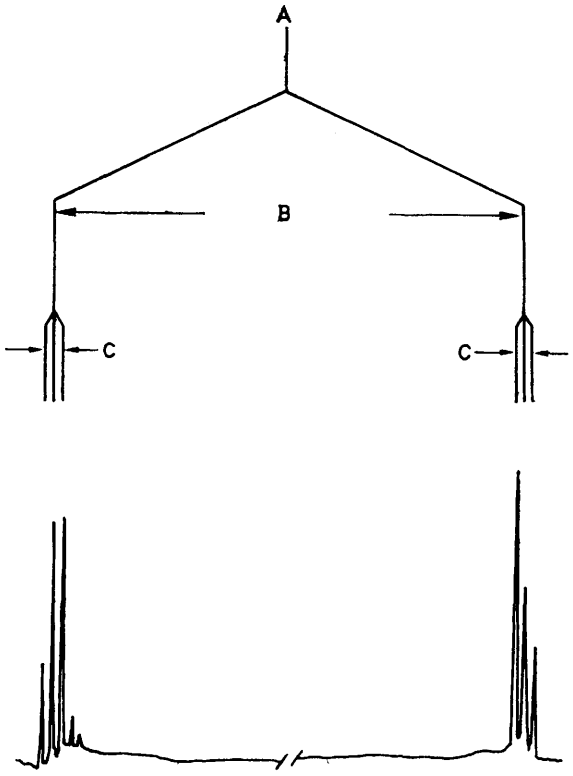


FIGURE 1 The ^{19}F n.m.r. spectrum of *trans*-2,4-dichloro-6,6-difluoro-2,4-dipiperidinocyclotriphosphazene: A, δ = −68.17 p.p.m.; B, J(PF) 894 Hz; C, J(PF) 13.3 Hz (average)

main splitting of *ca.* 900 Hz to ^1J(PF). The appearance of two sets of lines in the complex spectra is attributed to the existence of two fluorine environments in the *cis* compounds and the additional coupling observed is related to ^2J(FF). Our values of this splitting, which average 72 Hz, are in agreement with other measurements.[12,14] The fine structure triplets, with a splitting of *ca.* 13 Hz, that we observed in all these spectra are presumed to arise from ^3J(PF).[12]

DISCUSSION

Since, as shown above, fluorination proceeded with retention with respect to the amino-groups and the simple spectra arise from the *trans* isomers and the complex ones from the *cis* isomers, assignments can be made to all the bis(amino)tetrachloro-precursors, as listed in Table 1.

The assignments made for the *cis*- and *trans*-dipiperidino- and bis(diethylamino)-tetrachlorocyclotriphosphazenes conform to those made previously.[15,16] The earlier assignments to the dimorpholino-[17] and bis-(pyrrolidin-1-yl)-isomers[18] based on isomer count, which are those cited in Allcock's comprehensive and authoritative compilation,[19] are disproved, whilst later assignments based on dipole moments are sustained.[20]

From these results it can be surmized that, of the three preferred methods of isomer identification mentioned in the introduction, only one, the dipole-moment method, has given correct results whenever employed. The other two methods have on at least one occasion given incorrect assignments. We have shown here that the isomer-count method has led to erroneous conclusions. Additionally, the indirect n.m.r. method involving dimethylamination, exhaustive if possible, whilst mostly successful, has not permitted confident assignments to be made in specific cases.[15,21]

The corrected assignments made above lead to a clarification of some anomalies in the literature. As a rule, non-geminal diamination of hexachlorocyclotriphosphazene, in all solvents except acetonitrile, gives predominantly the *trans* isomers. The behaviour reported for the amines morpholine and pyrrolidine was exceptional,[17,18] the *cis* isomer apparently being pre-

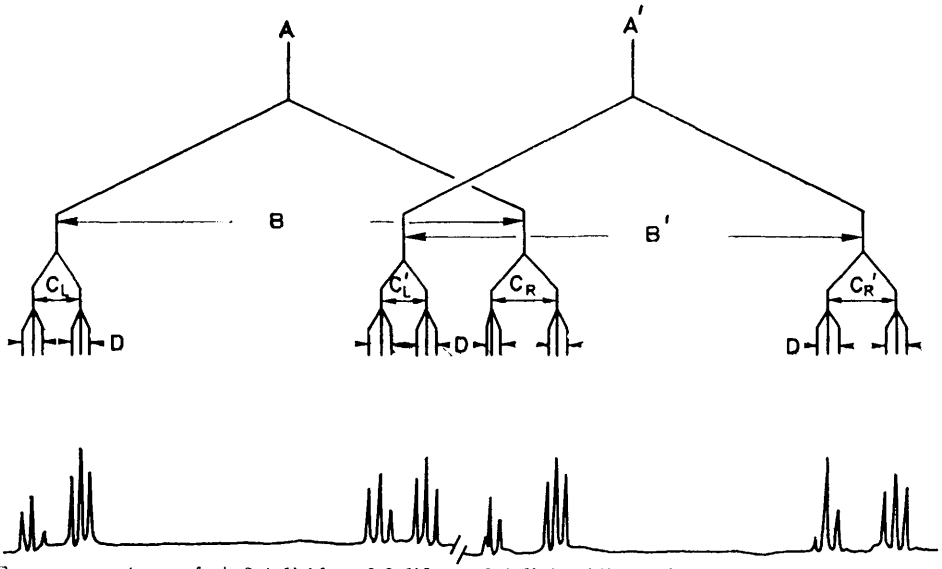
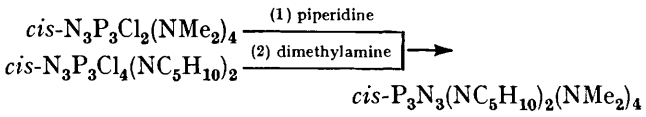


FIGURE 2 The ^{19}F n.m.r. spectrum of *cis*-2,4-dichloro-6,6-difluoro-2,4-dipiperidinocyclotriphosphazene: A, δ = −65.73 p.p.m.; A', δ = −70.51 p.p.m.; B, ^1J(PF) 888 Hz; B', ^1J(PF) 891 Hz; C_L, ^2J(FF) 61 Hz; C_R, ^2J(FF) 81 Hz; C_L', 62 Hz; C_R' ^2J(FF) 82 Hz; D, ^3J(PF) 13.6 Hz (average)

dominant. The reversed assignments now made remove the anomaly and reveal the general preference for *trans* isomers in these reactions.

Our confirmation of the configurations of the isomers of the dipiperidino-compounds verifies the assumption that no inversion occurred in the determination of their configurations.[15] This implies that the bulk of the single product obtained in *ca.* 70% yield from reactions (1) and (2) was indeed formed with net retention



of configuration, despite the fact that displacements occurred at two ' critical ' centres. In other cases,[21a,22] dimethylamination has been found to be accompanied by considerable isomerization. However, it is to be noted that primary amines are apparently involved in all those cases in which isomerization was detected.

Although we only applied our method to dialkylamino-derivatives, it is not inherently restricted to them, and can, in principle, be used with any other substituent which is electron-releasing with respect to the phosphazene ring (such as alkyl, alkoxy, *etc.*) and which directs fluorination to the 6-position. However, it should be noted that it cannot be used with alkylamino-substituents since fluorination of these compounds is accompanied by isomerization with reference to the amino-groups apparently by a mechanism involving deprotonation.[10b] Protection of the amino-groups before fluorination, which should overcome this complication and permit extension of the method to the determination of the configurations of the bis(alkylamino)-compounds, is being pursued.

Lastly, a significant advantage of our method is that it is also potentially applicable to those cases in which only one isomer has been isolated, such as with dicyclohexylamine,[23] di-isobutylamine,[23] and triphenylphosphine imide.[24] However, a condition is that no distortion of the phosphazene ring occurs, as might happen with very bulky substituents. This buckling of the ring might lead to more complex, possibly ambiguous, ^{19}F n.m.r. spectra. It should be noted that the only other reliable method of isomer identification, dipole-moment measurements, *requires* a comparison of the values measured for *both* isomers.

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