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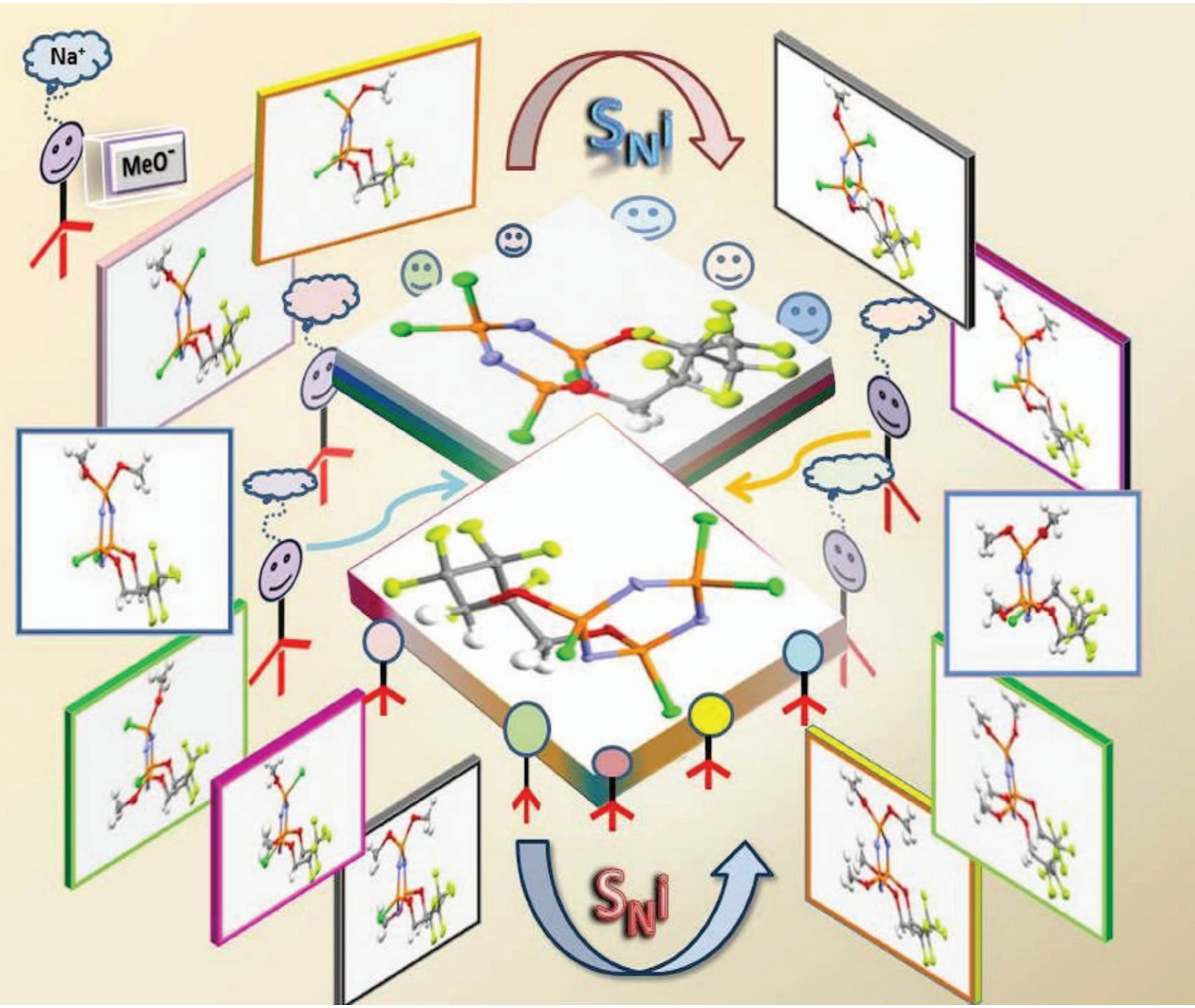

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Nucleophilic substitution reactions of 10- and 11-membered fluorodioxy ansa cyclotriphosphazene derivatives†

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The reactions of cyclophosphazenes with 10-membered ansa-{$N_3P_3Cl_4[OCH_2(CF_2)_3CH_2O]$ (**1a**)} and 11-membered ansa-{$N_3P_3Cl_4[OCH_2(CF_2)_4CH_2O]$ (**1b**)} rings with the sodium salts of methanol in a THF solution at different molar ratios were used to investigate the reaction pathways and mechanism of nucleophilic substitution at the PCl_2 and PCl(OR) phosphorus atoms. The reactions afforded eleven products, whose structures have been characterized by elemental analysis, mass spectrometry, ^1H, ^{19}F and ^{31}P NMR spectroscopy and X-ray crystallography; mono-methoxy derivatives (**2a**, **3a**, **3b**), di-methoxy derivatives (**5a–7a**, **5b**), tri-methoxy derivatives (**8a**, **8b**) and the tetra-methoxy derivatives (**9a**, **9b**). The X-ray crystallographic studies of four compounds (**6a–8a** and **8b**) demonstrated unambiguously that nucleophilic substitution reactions at the ansa-ring PCl(OR) phosphorus atoms of the cyclotriphosphazene compounds $N_3P_3Cl_4[OCH_2(CF_2)_nCH_2O]$ n = 3 (**1a**) and 4 (**1b**) occurred with a retention of configuration for both the 10- and 11-membered fluorodioxy ansa rings, respectively. The results confirmed that the reactions with **1a** containing the 10-membered ansa-ring occurred competitively at both the PCl_2 and P(OR)Cl moieties with an approximate 8 : 1 preference at the PCl_2 group, whereas reactions with **1b** containing the 11-membered ansa-ring occurred exclusively at the PCl_2 group before the P(OR)Cl moiety. The results were mainly rationalized in terms of the P–Cl bond lengths of the reactants and the cation-assisted mechanism of reaction.

Introduction

There are a wide range of nucleophilic substitution reactions in phosphazene chemistry and the formation of regio- and stereo-chemical isomers continues to attract attention.[1–38] Therefore, investigating the mechanism of the nucleophilic substitution reaction at phosphorus(v) atoms is important for the prediction of the regio- and stereo-chemical isomer distribution. S_N1 (racemization) and S_N2 (inversion) mechanisms[39–42] are seen predominantly whereas the S_Ni (retention of configuration) mechanism is only rarely observed at the reaction centre.[43,44] However, the effects of the substituent already present on the phosphazene ring must not be forgotten. For example an inversion of configuration occurred in the nucleophilic substitution reactions on the two phosphorus atoms adjacent to the *cis*-ansa groups consisting of a macrocyclic ring with sixteen atoms,[42] whilst the nucleophilic substitution of cyclophosphazene derivatives with nine-membered *cis*-ansa rings led to the retention of configuration.[43]

Hence, in order to investigate in more detail the size of the ansa ring on the reaction mechanism and determine the reaction pathway for ansa fluorodiol derivatives, we selected the fluorodioxy *cis*-ansa derivatives of cyclotriphosphazene; the hexafluoropentanedioxy derivative, $N_3P_3Cl_4[OCH_2(CF_2)_3CH_2O]$ (**1a**),[45] which has a *cis*-ansa ring with ten atoms and the octafluorohexanedioxy derivative, $N_3P_3Cl_4[OCH_2(CF_2)_4CH_2O]$ (**1b**),[46] which has an eleven membered *cis*-ansa ring.

Compounds **1a** and **1b** were reacted with a strong nucleophile, the sodium salt of methanol, in different molar ratios in THF at room temperature. The results may be summarized as follows: (i) the reactions of compound **1a** with the sodium derivative of methanol resulted in eight new products whereas the reactions of compound **1b** with same alkoxide resulted in only four products, (ii) all the nucleophilic substitution reactions of the strong anionic nucleophile, NaOMe, with compounds **1a** and **1b** took place with a retention of configuration of the *cis*-ansa moiety, (iii) in general the two P–Cl bonds of the PCl_2 group are more reactive than those of the P(OR)Cl moiety but the differences between the reactivity of compounds **1a** and **1b** are rationalized in terms of the P–Cl bond lengths and the cation-assisted mechanism of the reaction.

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Results

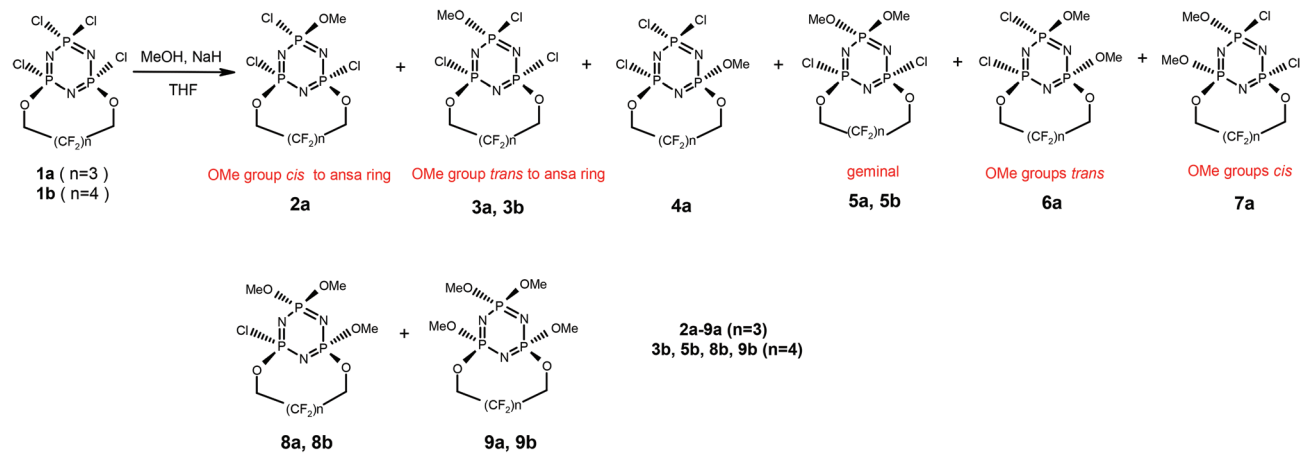
(i) The synthesis and characterization of reaction products by ^{1}H, ^{19}F and ^{31}P NMR spectroscopy

The mono-ansa fluorodioxy derivatives of cyclotriphosphazene, compounds **1a** and **1b**, were reacted with the sodium salt of methanol at different molar ratios in a THF solution and the remaining four PCl bonds were replaced with one, two, three, and then four methoxy groups as shown in Scheme 1. The nucleophilic substitution reactions of compound **1a** led to eight products; three mono-methoxy substituted compounds (one with the methoxy group *cis* to the ansa ring, **2a**; one with it *trans* to the ansa ring, **3a**; and one with methoxy group attached to an ansa ring P atom, **4a**), three di-methoxy substituted compounds (geminal, **5a**; non-geminal *trans*, **6a**; non-geminal *cis*, **7a**), the tri-methoxy substituted compound (geminal, **8a**) and the tetra-methoxy substituted compound (**9a**). On the other hand, the same reaction with compound **1b** gave only four products: the mono-methoxy substituted compound, in which the methoxy group is *trans* to the ansa ring (**3b**), the di-methoxy substituted geminal compound (**5b**), the tri-methoxy substituted geminal compound (**8b**) and the tetra-methoxy substituted compound (**9b**).

Compound **4a** was only observed in the ^{31}P NMR spectrum of a reaction mixture but all other products were isolated and characterized by elemental analysis, mass spectrometry, ^{1}H, ^{19}F and ^{31}P NMR spectroscopies and by X-ray crystallography. The results of the mass and elemental analyses and ^{1}H and ^{19}F NMR spectroscopy for each new compound are provided as part of the analytical data in the synthesis section. The ^{31}P NMR results are summarized in Table 1.

The ^{31}P NMR investigations of the reaction mixtures gave valuable information on the relative amounts of each isomer. The proton decoupled ^{31}P NMR spectra of the reaction mixture of compound **1a** in a 1 : 1 molar ratio with the sodium salt of methanol shows the formation of about equal amounts of the two mono-substituted derivatives (**2a** and **3a**) observed as pairs of A_2B spin systems with similar chemical shifts and coupling constants (Fig. 1). It is expected that the mono-substituted derivatives (**2a** and **3a**) of compound **1a** correspond to isomers in which the methoxy group can be *cis* or *trans* to the ansa ring. There is also a small amount of a compound with an AMX spin system, which was not isolated but has the NMR characteristics of a mono-substituted derivative at the P(OR)Cl moiety, compound **4a** (Scheme 1). On the other hand, the ^{31}P NMR spectrum of the reaction mixture of **1b** with the sodium salt of methanol in a 1 : 1 molar ratio only exhibited an AB_2 spin system that belongs to compound **3b**. The [PCl(O-ansa)] centers of the mono-substituted derivatives are stereogenic and as they are equivalent, one might expect that *meso* and racemic forms can exist, but due to the ansa ring being constrained to the *cis* configuration only *meso* isomers (*SR* or *RS*) can form. There is still the possibility of two *meso* forms in which the OMe group can be *cis* or *trans* to the ansa group and so the configurations of **2a**, **3a** and **3b** need to be characterized by X-ray crystallography.

When compound **1a** is reacted with the sodium salt of methanol in a 1 : 2.5 molar ratio, the proton decoupled ^{31}P NMR spectrum of the reaction mixture in Fig. 2 shows the formation of four products; the major product (*ca.* 39%, **5a**) has an A_2B spin system, two other products (**6a**, *ca.* 8% and **7a**, *ca.* 30%) have similar ABX spin systems due to the different environments for the three phosphorus nuclei of the cyclotriphosphazene ring, and the remaining product (**8a**, *ca.* 22%) has an ABC spin system. Theoretically there are four isomers for di-substituted derivatives of the *cis*-mono ansa compounds **1a** and **1b**. One in which the two methoxy groups replace both Cl atoms of the PCl_2 group (geminal, **5a**) and one in which they replace both Cl atoms of the PCl(OR) groups (non-geminal); the ^{31}P NMR spectra of both isomers should give AX_2 (AB_2) spin systems. However, there are two other isomers where one of the methoxy groups replaces one of the Cl atoms of the PCl_2 group and the other replaces the Cl atom of either PCl(OR) group; the methoxy groups may be *trans* (**6a**) or *cis* to each other (**7a**) and both should give rise to ^{31}P NMR ABX spin systems. Later studies show that the non-geminal product does



Scheme 1 The products of the reaction of compounds **1a** and **1b** with the sodium salt of methanol.

Table 1 ^{31}P NMR parameters of compounds[a]

	^{31}P chemical shift (ppm)					$^{2}J_{PNP}$[b] (Hz)						
Cpd	PCl_2 (1)	PCl(OR) (2)	PCl(OMe) (3)	P(OR)(OMe) (4)	$P(OMe)_2$ (5)	1,2	1,4	2,3	2,4	2,5	3,4	4,5
(a) 2,2,3,3,4,4-Hexafluoro-1,5-pentanedioxy ansa derivatives												
1a[c]	25.30	20.10				67.9						
2a		22.83	22.31					77.9				
3a		22.34	21.89					74.9				
4a[d]	26.83	24.10		9.21		75.6	70.6		66.2			
5a		24.82			12.62					79.2		
6a		27.60	26.24	13.19				82.8	68.8		79.4	
7a		27.15	25.25	12.60				80.9	68.9		78.0	
8a		29.72		16.13[e]	16.43[e]				70.4[e]	83.6[e]		80.8
9a				21.24	20.17							84.2
(b) 2,2,3,3,4,4,6,6-Octafluoro-1,6-hexanedioxy ansa derivatives												
1b[f]	26.70	19.64				69.2						
3b		22.78	21.67					75.9				
5b		23.86			13.84					81.1		
8b		27.70		16.7[g]	15.5[g]				[h]	[h]		[h]
9b				20.28	19.73							80.8

[a] 202.38 MHz ^{31}P NMR chemical shifts (ppm) in $CDCl_3$ with respect to external 85% H_3PO_4. [b] $^{2}J_{PNP}$ values checked by spin simulation. [c] Values taken from ref. 45. [d] Values calculated from ^{31}P NMR spectrum of reaction mixture. [e] Assignments are not unequivocal and may be interchanged. [f] Values taken from ref. 46. [g] Assignments were made on the breadth of the proton-coupled spectra so are not unequivocal and may be interchanged. [h] $^{2}J_{PNP}$ values could not be calculated accurately due to broad peaks.

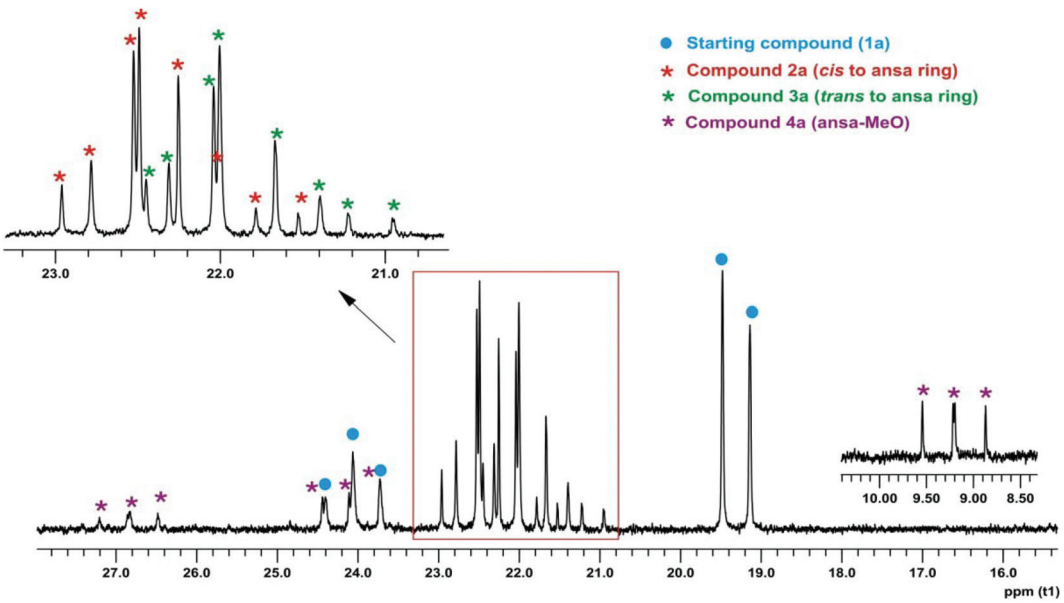


Fig. 1 The proton-decoupled ^{31}P NMR spectrum of the reaction mixture of compound **1a** with the sodium salt of methanol in a 1 : 1 ratio in THF solution; the reaction mixture was filtered and the solvent was removed prior to dissolving in a $CDCl_3$ solution.

not form and that the fourth component in the ^{31}P NMR spectrum in Fig. 2 is the geminal tri-methoxy derivative **8a**. The analogous reaction of compound **1b** with the sodium salt of methanol leads to the formation of the di-substituted geminal (**5b**) and tri-substituted geminal (**8b**) derivatives (Scheme 1).

The di-substituted geminal products (**5a** and **5b**) have two equivalent stereogenic centres at the PCl(OR) groups and for the *cis*-ansa ring derivatives they are of opposite configuration (*RS*) and so the compounds are *meso*. The non-geminal di-substituted *trans* and *cis* derivatives (**6a** and **7a**, respectively) have three different stereogenic centres. The configurational properties may be represented as *R*/*S* for the PCl(OMe) group, as *R*′/*S*′ for the PCl(O-ansa) group and as *R*″/*S*″ for the P(OMe)-(O-ansa) group. Assuming that each centre of chirality can exist in both configurations (*e.g.* *R* and *S*), there should be eight stereoisomers observed for different racemic forms. However, if only the *cis*-ansa cyclophosphazene derivatives are formed, then two racemic forms (*SS*′*S*″/*R*″*R*′*R* and *SR*′*R*″/*S*″*S*′*R* configuration) do not form because the ansa ring is constrained to the *cis* configuration. Hence, these compounds are expected to exist as other racemic forms (diastereoisomers), in which the methoxy groups are *trans* (*SR*′*S*″/*R*″*S*′*R* configuration)

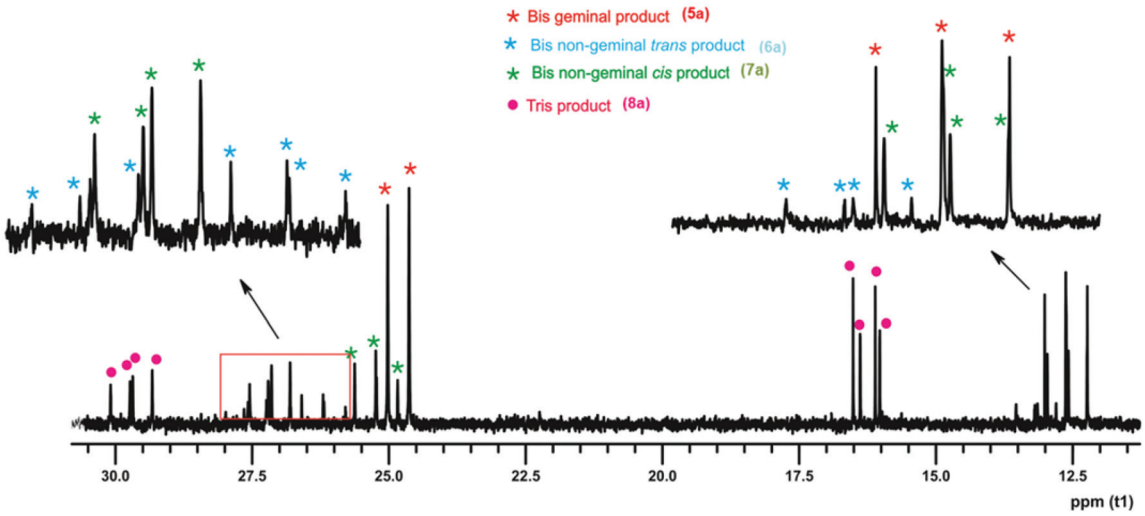


Fig. 2 The proton-decoupled ^{31}P NMR spectrum of the reaction mixture of compound **1a** with the sodium salt of methanol in a 1 : 2.5 ratio in a THF solution; the reaction mixture was filtered and the solvent was removed prior to dissolving in a $CDCl_3$ solution.

(**6a**) or *cis* (*SS′R″*/*S″R′R* configuration) (**7a**) to each other. Again X-ray crystallography is needed to characterize the isomers.

The geminal tri-methoxy substituted compounds **8a** and **8b** have two different stereogenic centres, which may be designated as *R*/*S* for the PCl(O-ansa) group and as *R′*/*S′* for the P(OMe)(O-ansa) group, theoretically giving rise to two different racemic forms (*RR′*/*S′S* and *RS′*/*R′S*). However, due to the constraints of only forming *cis*-ansa ring derivatives, only one racemate form is expected (*RR′*/*S′S* for both **8a** and **8b**).

When an excess of the sodium salt of methanol is reacted with either starting compounds **1a** or **1b**, the fully substituted tetra-methoxy derivatives (**9a** and **9b**, respectively) are formed and their proton decoupled ^{31}P NMR spectra are observed as A_2B spin systems, whose NMR parameters (Table 1) have been determined by spectral simulation. Each P(OMe)(O-ansa) group in compounds **9a** and **9b** is a stereogenic center but as the two centers are equivalent and only derivatives with a *cis*-ansa ring are formed and they are *meso* (*RS* configuration).

(ii) The characterisation of compounds by X-ray crystallography

The crystal structures of eleven cyclotriphosphazene (N_3P_3) derivatives, **2a**, **3a**, **5a–9a** and **3b**, **5b**, **8b** and **9b**, are presented in Fig. 3–7 and the data collection and refinement parameters are reported in Table 2 (**a** series) and Table 3 (**b** series). The compounds contain either the 2,2,3,3,4,4-hexafluoro-1,5-pentanedioxy- (**2a**, **3a**, **5a–9a**) or 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanedioxy- (**3b**, **5b**, **8b** and **9b**) chain attached to two adjacent phosphorus atoms of the phosphazene ring, in which these 10- or 11-membered ansa-rings have the same *cis* configuration as in their corresponding starting compounds **1a** and **1b**, respectively.[45,46] It is convenient to discuss the X-ray structures for compounds having the same number of methoxy-units.

The mono-methoxy compounds **2a**, **3a** and **3b** (Fig. 3) are all obtained by the substitution of one of the Cl atoms of the PCl_2 groups of the starting compounds, **1a** and **1b**. The P1 and P2 phosphorus atoms of all three molecules are equivalent stereogenic centers with opposite configurations, *RS*, so that each structure shown in Fig. 3 is *meso*. The methoxy-substituent can take up two different configurations that are either *cis* or *trans* with respect to the ansa ring. Compounds **2a** and **3a** are geometrical isomers, in which the methoxy-unit is in a *cis*-configuration with respect to the ansa ring in compound **2a** and in a *trans*-configuration in compound **3a**. Only one of the geometrical isomers has been characterized for the octafluoro *cis*-ansa derivative **3b** and the X-ray structure in Fig. 3 shows that it is the isomer with the methoxy-unit in a *trans*-configuration to the ansa ring.

X-ray crystallographic analysis confirms the structures of the di-methoxy-substituted derivatives (**5a**, **5b**, **6a** and **7a**). Both Cl atoms of the PCl_2 group are substituted with methoxy moieties to form the geminal compounds **5a** and **5b** (Fig. 4). The PCl(OR) groups of these *cis*-ansa ring derivatives are stereogenic and, as the two centres are equivalent and of opposite configuration (*RS*), so compounds **5a** and **5b** are both *meso*. The X-ray crystallographic structures of the non-geminal di-methoxy-substituted isomers, compounds **6a** and **7a**, are shown in Fig. 5. The two methoxy-groups are in a *trans* configuration in compound **6a** and in a *cis* configuration in compound **7a**, hence compounds **6a** and **7a** are configurational isomers (Fig. 5). It can be seen that the substitution patterns at the three phosphorus atoms of compounds **6a** and **7a** are different [P1(Cl)(OMe), P2′(Cl)OR, and P3″(OMe)OR] giving rise to three different stereogenic centers, so that both compounds **6a** and **7a** are racemic and diastereoisomers. Although compounds **6a** and **7a** have centro-symmetric space groups ($P\bar{1}$ and *Pbca*, respectively), in the crystal there are equal

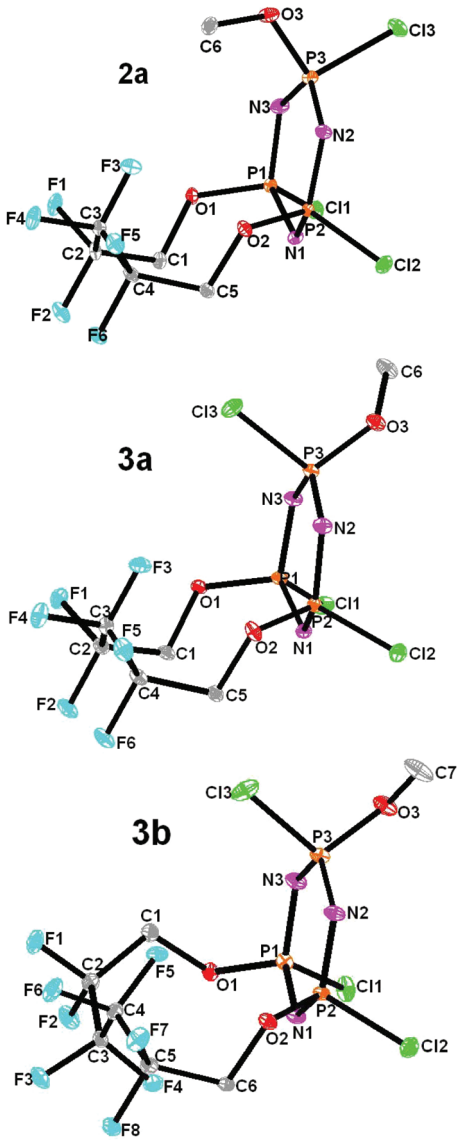


Fig. 3 A view of the molecular structures for **2a**, **3a** and **3b** with the atom-numbering scheme. The displacement ellipsoids are drawn at the 30% probability level and the hydrogen atoms have been omitted for clarity. All three structures are *meso* having two equivalent stereogenic centers on the P1 and P2 phosphorus atoms with opposite configurations, *RS*.

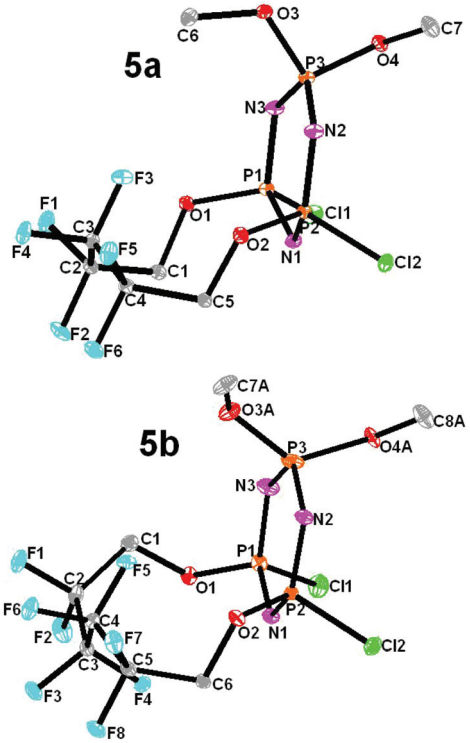


Fig. 4 A view of the molecular structures for **5a** and **5b** with the atom-numbering scheme. The displacement ellipsoids are drawn at the 30% probability level. The hydrogen atoms have been omitted, and only one orientation of the disordered two methoxy-units which are substituted on P phosphorus atom of **5b** has been presented for clarity. Both structures are *meso* having two equivalent stereogenic centers on the P1 and P2 phosphorus atoms with opposite configurations, *RS*.

numbers of molecules in the crystal with the opposite chirality and the enantiomers shown in Fig. 5 are *SR′S″* for **6a** and *SS′R″* for **7a**.

Compounds **8a** and **8b** are the tri-methoxy-substituted derivatives, consisting of the geminal [$P(OMe)_2$] groups with the third methoxy-group attached to one of the ansa-substituted [P(Cl)OR] groups (Fig. 6). The phosphorus atoms that are part of the *cis*-ansa ring [P(OR)Cl and P(OR))Me] are both stereogenic and, as they are different centers of chirality, compounds **8a** and **8b** are both racemic and the *RR′* enantiomers for both compounds are shown in Fig. 6. Although compounds **8a** and **8b** have centro-symmetric space groups ($P21/n$ and $P\bar{1}$, respectively), there are equal numbers of molecules in the crystals with the opposite chirality. The tetra-methoxy compounds, **9a** and **9b** (Fig. 7), are obtained by the methoxy-substitution of all four chlorine atoms of the starting compounds, **1a** and **1b**. The phosphorus atoms that are part of the *cis*-ansa ring [P(OR)Me] are both stereogenic and, as they are equivalent centers of chirality but of opposite configuration (*RS*), both compounds **9a** and **9b** are *meso*.

Some bond and conformational parameters of compounds **2a**, **3a**, **5a–9a** (10-membered) and **3b**, **5b**, **8b**, and **9b** (11-membered ansa-dioxy rings) are summarized (ESI table†) and are found to be similar to those observed for the starting compounds **1a**[45] and **1b**[46] and in the normal range found for ansa substituted cyclotriphosphazene derivatives.[42,43,45–47] In particular, the size of the ansa ring has an effect on the P2–N2–P3 bond angle encompassing the nitrogen atom belonging to both the phosphazene and the ansa rings, *i.e.* it is slightly smaller (117.6–120.9°) in compounds **2a**, **3a**, **5a–9a** containing the 10-membered ansa-ring compared to those observed (121.2–122.5°) in compounds containing the 11-membered ansa-ring (**3b**, **5b**, **8b**, and **9b**). These observations are similar to those observed for the starting compounds, in which the average P–N–P bond angle is 119.8 ± 0.8 in compound **1a** and 121.4 ± 0.8 in compound **1b**, although the P–N–P bond angle of the nitrogen atom belonging to the ansa

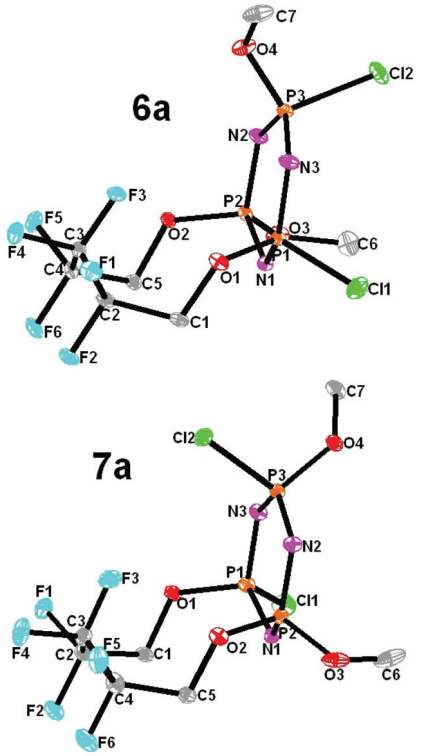


Fig. 5 A view of the molecular structures for compounds **6a** and **7a** with the atom-numbering scheme. The displacement ellipsoids are drawn at the 30% probability level and the hydrogen atoms have been omitted for clarity. Both molecules are racemates having different stereogenic centers [P1(Cl)OR, P2′(OMe)OR, and P3′′(Cl)(OMe), where R = $-CH_2(CF_2)_3CH_2O-$ for both structures], for the three phosphorus atoms of the P_3N_3 rings. Although they have centro-symmetric space groups ($P\bar{1}$ and *Pbca*, respectively), there are an equal number of molecules in the crystal with the opposite chirality than shown here for the *RS*′S′′ enantiomer of **6a** and the *SR*′S′′ enantiomer of **7a**.

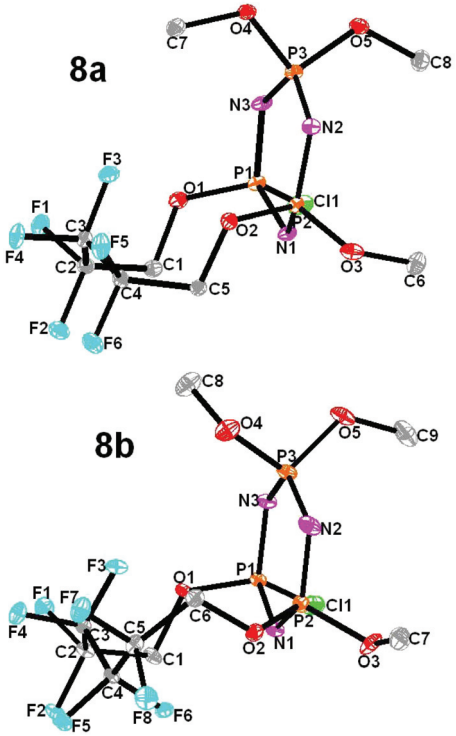


Fig. 6 A view of the molecular structures for compounds **8a** and **8b** with the atom-numbering scheme. The displacement ellipsoids are drawn at the 30% probability level and the hydrogen atoms have been omitted for clarity. Both molecules are racemates having two different stereogenic centers on P1 and P2 phosphorus atoms. Although they have centro-symmetric space groups ($P2_1/n$ and $P\bar{1}$, respectively), there are an equal number of molecules in the crystal with the opposite chirality to the *RR*′ enantiomers for both compounds shown here.

ring is not smaller than the other P–N–P bond angles in compound **1a**.[45,46] The other slight variations in the bond parameters of the N_3P_3 rings are caused by the progressive replacement of the electron-withdrawing chlorine atom with the electron donating methoxy-group. A convenient way to represent the conformation of a ring is by the puckering amplitude, Q[48] and the values of Q for all of the compounds are summarized in the ESI tables;† the conformations of the 10- and 11-membered ansa-rings in compounds **2a**, **3a**, **5a–9a** (average Q is 1.452 ± 0.004) and **3b**, **5b**, **8b**, and **9b** (average 1.439 ± 0.016), respectively, are similar to those of the parent compounds (**1a**, 1.475;[45] **1b**, 1.390[46]) and there is no systematic variation with the number and location of the methyl groups.

Previous studies on cyclotriphosphazene derivatives containing fluorinated alkanedioxy ansa-rings clearly showed that the size of the ansa-ring affects the conformational parameters of the cyclotriphosphazene rings. The cyclotriphosphazene ring in $N_3P_3Cl_6$ is nearly planar,[49,50] whereas it is slightly twisted out-of-the-plane by *ca.* 0.1 Å by strain in the 9-membered ring of the tetrafluorobutanedioxy derivative[47] and the 10-membered ring of the hexafluoropentanedioxy starting compound **1a**,[45] although where there is less strain in the 11-membered ansa ring of the octafluorohexanedioxy derivative **1b**, the maximum deviation from the plane of the cyclophosphazene ring is only *ca.* 0.024 Å.[46] For compounds **2a**, **3a**, **5a–9a**, the 10-membered hexafluoropentanedioxy-ansa ring causes some strain resulting in the deformation of the planarity of the phosphazene ring to a half-chair (**2a** and **3a**), flattened boat (**5a** and **6a**), flattened chair (**7a**) or slightly twisted (**8a** and **9a**) conformation. The maximum deviation from the plane of the N_3P_3 ring is found for the cyclophosphazene ring nitrogen atom N2, which is also part of the exocyclic ansa ring [*viz.* 0.1342 (17) Å for **2a**; 0.1125(17) Å for **3a**; 0.1517(15) for **5a**; 0.1143(18) for **6a**; 0.144(2) for **7a**; 0.1698(19) for **8a**; and 0.1869 (14) for **9a**]. On the other hand, there is less strain in the cyclotriphosphazene rings of compounds containing 11-membered ansa-rings and the N_3P_3 rings of the majority of the compounds (**3b**, **5b** and **8b**) are nearly planar, except for **9b** where it has a slightly twisted form; the maximum deviation from the plane of the cyclophosphazene ring is 0.0218(8) Å (P3) for **3b**; 0.0167(15) (N1) for **5b**; 0.0635(14) (P1) for **8b**. Only for **9b** is the N2 atom, which is involved in both the ansa and cyclophosphazene rings, the one that is furthest from the plane, 0.096 (3), as found for all the hexafluoropentanedioxy derivatives **2a**, **3a**, **5a–9a**.

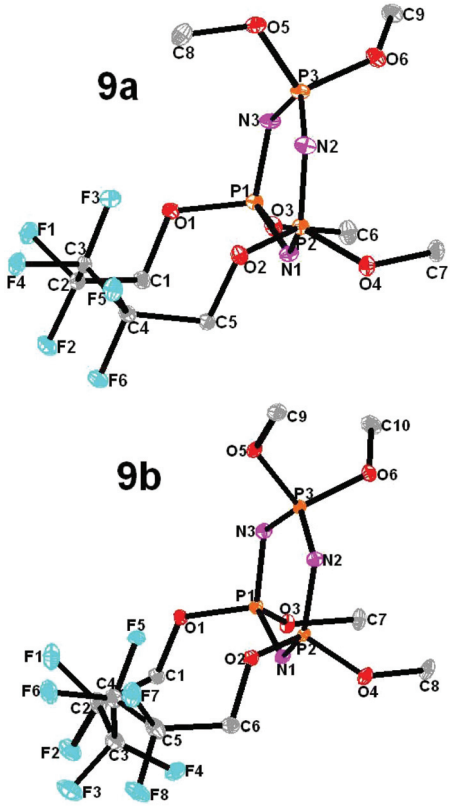


Fig. 7 A view of the molecular structures for **9a** and **9b** with the atom-numbering schemes. Displacement ellipsoids are drawn at the 30% probability level. The hydrogen atoms have been omitted for clarity. Both structures are *meso* having two equivalent stereogenic centers on the P1 and P2 phosphorus atoms with opposite configurations, *RS*.

It is noted that there are variations in the maximum deviations from the cyclophosphazene plane that mainly correspond to the disposition of the methoxy substituents (ESI table†). Comparing the isomers **2a** and **3a**, it is found that the deviation from the plane for compound **3a**, where the methoxy group is *trans* to the ansa ring, is similar to the starting compound **1a**, but when the methoxy group is *cis* to the ansa ring as in **2a** there is some interaction between them that causes strain in the molecule, which is partly relieved by a greater deviation of N2 from the plane of the cyclophosphazene. For all of the gem di-methoxy derivatives (**5a**, **8a**, **9a**), where the methoxy groups are both *cis* and *trans* to the ansa ring, there is an increase in the strain in the molecule causing an increase in the maximum deviation from the plane and the increase is greater for increasing numbers of methoxy groups in the molecules. A similar trend is observed for the gem di-methoxy derivatives (**5b**, **8b**, **9b**), although the magnitudes of the maximum deviations are somewhat smaller in molecules containing the 11-membered ansa rings (**5b**, **8b**, **9b**) compared to 10-membered ansa ring analogues (**5a**, **8a**, **9a**). Exceptions to this behavior are the non-gem dimethoxy isomers (**6a**, **7a**), where the maximum deviation from the plane of the isomer with the PCl(OMe) methoxy group *trans* to the ansa ring (**7a**) is significantly greater than that for that methoxy group being *cis*

Table 2 The X-ray crystallographic data and refinement parameters for compounds **2a**, **3a**, **5a**, **6a**, **7a**, **8a** and **9a**

Compound	**2a**	**3a**	**5a**	**6a**	**7a**	**8a**	**9a**
Empirical formula	$C_6H_7Cl_3F_6N_3O_3P_3$	$C_6H_7Cl_3F_6N_3O_3P_3$	$C_7H_{10}Cl_2F_6N_3O_4P_3$	$C_7H_{10}Cl_2F_6N_3O_4P_3$	$C_7H_{10}Cl_2F_6N_3O_4P_3$	$C_8H_{13}ClF_6N_3O_5P_3$	$C_9H_{16}F_6N_3O_6P_3$
Formula weight	482.41	482.41	477.99	477.99	477.99	473.57	469.16
Temperature (K)	120(2)	120(2)	130(2)	120(2)	130(2) K	120(2)	130(2)
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic	Orthorhombic	Monoclinic	Monoclinic
Space group	*P*1211	*C*1*c*1	*P*1211	$P\bar{1}$	*Pbca*	*P*121/*n*1	*P*1211
a (Å)	7.76460(10)	8.6100(4)	7.8562(11)	6.5257(8)	14.6768(14)	7.9206(7)	8.1912(8)
b (Å)	12.8687(2)	14.0284(4)	12.7286(18)	8.4635(10)	13.2608(14)	12.5912(12)	12.8636(12)
c (Å)	8.54690(10)	13.3930(7)	8.6574(12)	15.8000(19)	17.1259(18)	17.2780(16)	9.3727(9)
α (°)	90	90	90	76.146(6)	90	90	90
β (°)	116.2410(10)	94.079	111.409	78.797(5)	90	92.146(5)	114.478(4)
γ (°)	90	90	90	89.580(5)	90	90	90
Volume (Å^3)	765.997(18)	1613.57(12)	806.0(2)	830.40(17)	3333.1(6)	1721.9(3)	898.82(15)
Z	2	4	2	2	8	4	2
Density (calc., Mg m^{-3})	2.092	1.986	1.970	1.912	1.905	1.827	1.734
Absorption coefficient (mm^{-1})	0.993	0.943	0.787	0.764	0.761	0.590	0.424
F(000)	476	952	476	476	1904	952	476
Crystal size (mm^3)	0.04 × 0.05 × 0.27	0.07 × 0.08 × 0.16	0.12 × 0.17 × 0.20	0.16 × 0.17 × 0.50	0.14 × 0.22 × 0.36	0.05 × 0.11 × 0.19	0.28 × 0.34 × 0.43
θ_{max} (°)	28.290	28.270	28.360	28.340	28.390	28.260	28.390
Reflections collected	13 812	15 864	14 404	30 234	44 234	29 500	15 740
Independent reflections	3819	3980	4018	4125	4159	4258	4477
R_{int} (merging *R* value)	0.0313	0.0252	0.0322	0.0390	0.0728	0.0345	0.0330
Parameter	218	218	228	228	228	238	248
R ($F^2 > 2\sigma F^2$)	0.0214	0.0221	0.0203	0.0350	0.0484	0.0382	0.0221
wR (all data)	0.0547	0.0565	0.0539	0.0918	0.1383	0.1013	0.0603
Goodness-of-fit on F^2	1.045	1.067	1.030	1.050	1.046	1.039	1.071
$\Delta\rho_{max}$/min (e Å^{-3})	0.351/−0.227	0.398/−0.235	0.341/−0.295	1.547/−0.665	0.890/−1.273	1.302/−0.635	0.365/−0.249

Table 3 X-ray crystallographic data and refinement parameters for compounds **3b**, **5b**, **8b** and **9b**

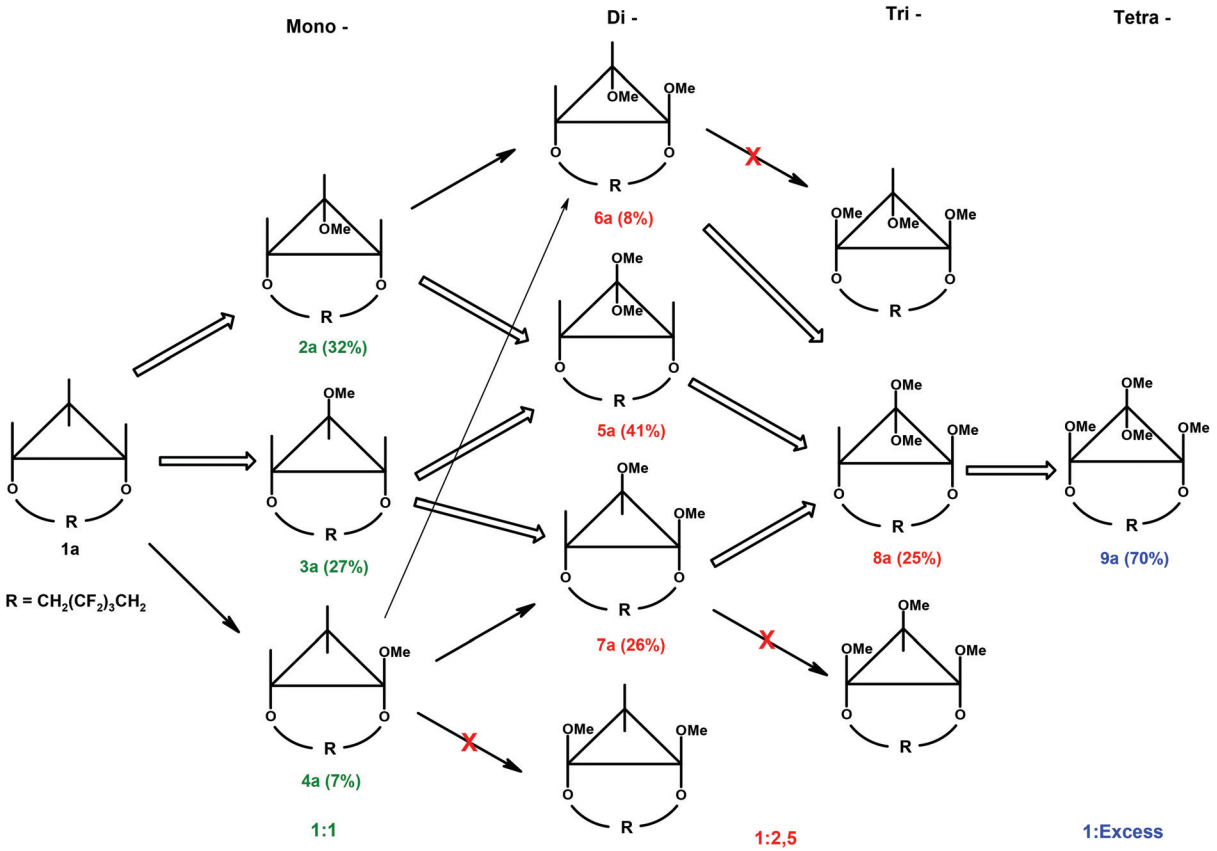
Compound	**3b**	**5b**	**8b**	**9b**
Empirical formula	$C_7H_7Cl_3F_8N_3O_3P_3$	$C_8H_{10}Cl_2F_8N_3O_4P_3$	$C_9H_{13}ClF_8N_3O_5P_3$	$C_{10}H_{16}F_8N_3O_6P_3$
Formula weight	532.42	528.00	523.58	519.17
Temperature (K)	120(2)	120(2)	120(2)	130(2)
Crystal system	Monoclinic	Triclinic	Triclinic	Monoclinic
Space group	$P121/n1$	$P\bar{1}$	$P\bar{1}$	$P121/n1$
a (Å)	8.9174(8)	9.354(2)	9.2665(16)	14.8998(7)
b (Å)	8.0071(7)	10.499(2)	10.899(2)	6.4328(3)
c (Å)	25.359(2)	10.863(3)	10.973(2)	20.6068(10)
α (°)	90	103.714(9)	103.989(9)	90
β (°)	96.467(4)	109.372(8)	108.557(9)	107.967(2)
γ (°)	90	105.644(9)	107.445(9)	90
Volume (Å^3)	1799.2(3)	904.4(4)	930.0(3)	1878.79(15)
Z	4	2	2	4
Density (calc., Mg m^{-3})	1.966	1.939	1.870	1.835
Absorption coefficient (mm^{-1})	0.871	0.726	0.570	0.430
$F(000)$	1048	524	524	1048
Crystal size (mm^3)	0.12 × 0.12 × 0.25	0.19 × 0.20 × 0.20	0.07 × 0.09 × 0.16	0.14 × 0.16 × 0.19
θ_{max} (°)	28.350	28.360	25.020	27.100
Reflections collected	31 095	31 131	13 327	16 140
Independent reflections	4477	4511	3268	4140
R_{int} (merging R value)	0.0322	0.0382	0.0353	0.0315
Parameter	245	295	265	275
R ($F^2 > 2\sigma F^2$)	0.0344	0.0272	0.0466	0.0582
wR (all data)	0.0883	0.0721	0.1130	0.1557
Goodness-of-fit on F^2	1.100	1.088	1.068	1.041
$\Delta\rho_{max}$/min (e Å^{-3})	0.953/−0.327	0.449/−0.540	0.877/−0.884	2.018/−0.691

to the ansa ring (**6a**), in the opposite direction to that found for the mono-substituted isomers (**2a**, **3a**). An explanation of this behavior is given by a detailed analysis of the crystal structure, where it is observed that the PCl_2-substituted methoxy-group that has a *cis* configuration with respect to the ansa-ring is bent towards the 10-membered ansa-rings of **2a**, **5a**, **8a**, and **9a** whereas, this methoxy unit in **6a** is oriented upward with a different P–O–C bond angle. The upward orientation of the *cis* methoxy-group in **6a** minimizes any intramolecular interaction between the methoxy-protons and the central fluorine atoms of the ansa ring that occurs in compounds **2a**, **5a**, **8a**, and **9a** contributing to strain in the phosphazene rings; *viz.* the closest methyl H···F3 distance in **2a**, **5a**, **8a**, and **9a** is in the range of 2.55–2.82 Å, whereas it is 4.43 Å in **6a**.

Discussion

The configuration mechanism (inversion or retention) in the *cis*-ansa derivatives of cyclotriphosphazene was investigated using X-ray crystallographic evidence previously.[42,43] The inversion of configuration occurs in the nucleophilic substitution reactions on the two phosphorus atoms adjacent to the *cis*-ansa groups consist of macrocyclic ring with sixteen atoms,[42] whereas nucleophilic substitution of cyclophosphazene derivatives with nine-membered *cis*-ansa rings leads to retention of configuration.[43] In order to investigate how general the retention/inversion of configuration mechanism might be, we selected as starting compounds the fluorodioxy-ansa derivatives $N_3P_3Cl_4[OCH_2(CF_2)_nCH_2O]$ n = 3 (**1a**) and n = 4 (**1b**), which have ten and eleven membered mono-*cis*-ansa rings. The mono-*cis*-ansa fluorodioxy derivatives of cyclotriphosphazene, **1a** and **1b**, are obtained in a good yield and the fluorodioxy derivatives are very stable and suitable for single crystal analysis due to easily crystallization.[45,46] Stepwise substitution reactions of compounds **1a** and **1b** were investigated at different molar ratios (1 : 1, 1 : 2.5 and 1 : excess) with the sterically small, but strong, anionic nucleophile NaOMe. The nucleophilic substitution of **1a** and **1b** replaces the four remaining P–Cl bonds with 1, 2, 3 then 4 methoxy groups as shown in Scheme 2. The single crystal X-ray results of the non-geminal di-substituted products (**6a**, **7a**) and the tri-substituted products (**8a**, **8b**) prove that a retention of configuration occurs for all the nucleophilic substitution reactions of the cyclophosphazene derivatives with ten and eleven membered ansa rings, as found previously for the nine-membered *cis*-ansa analogue.[43]

The tetrachlorocyclophosphazene derivatives (**1a**, **1b**) used in this work contain one PCl_2 group and two non-geminal chlorine atoms adjacent to the *cis*-ansa fluoroalkoxy substituent, thus providing the possibility for both geminal and non-geminal substitution.[45,46] Important details have been obtained about the pathways of the reactions of the cyclophosphazene derivatives (**1a**, **1b**) with the sodium salt of methanol at different molar ratios (1 : 1, 1 : 2.5 and 1 : excess). Although it is possible to compare the yields of the products isolated from different reactions, it is more informative to measure the ^{31}P NMR spectra of the reaction mixtures, because minimum work up is required and because one might observe intermediates that have not been isolated. In the present work the ^{31}P NMR spectrum of the reaction mixture of compound **1a** with sodium methoxide at a 1 : 1 molar ratio in Fig. 1 shows the

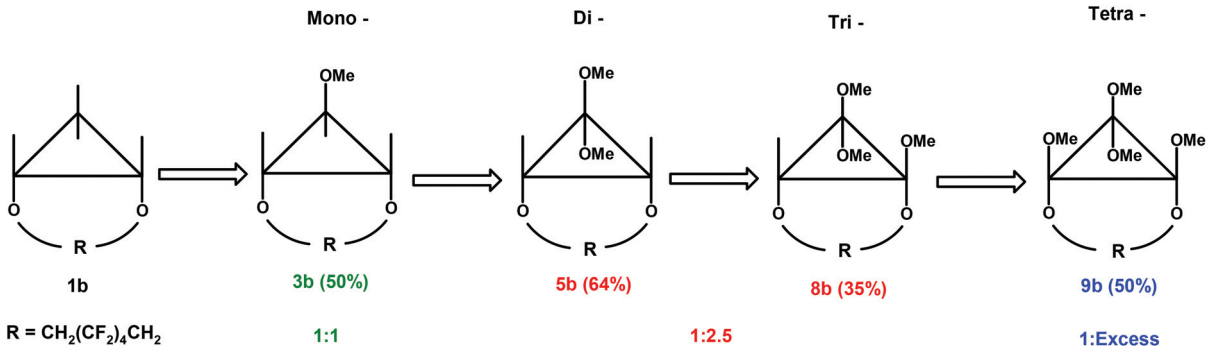


Scheme 2 The pathways of the reaction of compound **1a** with different molar ratios of the sodium salt of methanol (a) 1 : 1, (b) 1 : 2.5, (c) 1: excess. The relative proportions of the products were determined by the proton-decoupled ^{31}P NMR of the reaction mixtures.

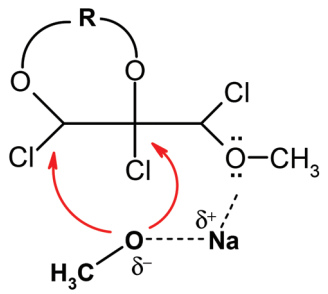
relative amounts of formation of the mono-methoxy derivatives **2a–4a**. There is a strong preference for the nucleophilic reaction to occur at the PCl_2 group to form derivatives with the OMe group *cis* (**2a**, 32%) and *trans* (**3a**, 27%) to the ansa ring and only a small amount of compound **4a** (7%) with substitution at the P(OR)Cl moiety; in fact one could say that reaction at the PCl_2 group is about eight times more likely than at the two P(OR)Cl moieties. There is only a small preference for formation of **2a** compared to **3a** and the essential equal isomer distribution shows an unusual *cis* preference (presumably from the cation-assisted mechanism). Although the predicted stereochemistry for a di-substituted rings system in general is *trans* due to steric effects, in here the steric effect of the small methoxy group will be relatively low. On the other hand, the ^{31}P NMR spectrum of the reaction mixture of compound **1a** with sodium methoxide at a 1 : 2.5 molar ratio (Fig. 2) shows the relative amounts of formation of the di-methoxy derivatives **5a–7a**, in which the major product is the gem compound **5a** (41%) and smaller amounts of the non-gem derivatives in which the OMe groups are *trans* (**6a**, 8%) or *cis* (**7a**, 26%) to each other; in this case there is a significant difference in the relative amounts of compounds **6a** and **7a**, which indicates that the formation of the derivative in which the OMe groups are *cis* to each other is enhanced by the cation-assisted mechanism. Assuming that the molecules in the reaction mixture are at equilibrium when measured by ^{31}P NMR, one might estimate the free energy of the cation-assisted effect at ambient temperature as ΔG [$= -RT \ln K = -RT \ln(26/8)$], *i.e.* – *ca.* 2900 J. As expected, the reaction of compound **1a** with sodium methoxide in excess leads to the formation of the fully-substituted derivative **9a**. The reactions are summarized in Scheme 2, which shows the major reaction routes in broad lines, the minor reaction routes in narrower lines and even more minor routes where possible derivatives were not observed by ^{31}P NMR of the reaction mixtures (shown by the red cross on the line).

By comparison compound **1b** reacts with sodium methoxide exclusively at the PCl_2 group to give the mono- (**3b**) and di-substituted (**5b**) derivatives prior to the reaction at the P(OR)Cl moiety to give the tri- (**8b**) and tetra-substituted (**9b**) derivatives (Scheme 3). These observations may be contrasted with those for previous work on macrocyclic phosphazene derivatives[51–55] and may be mainly rationalized in terms of a consideration of the P–Cl bond lengths and the occurrence of the cation-assisted mechanism (Scheme 4).

The nucleophilic substitution reactions of cyclophosphazenes having a *cis*-ansa macrocyclic polyether substituent instead of an ansa fluoroalkoxy group were thoroughly investigated by Brandt and co-workers[51–55] for reactions with alcohols,[51] diamines[52,53] and diols.[54,55] In almost all that work, the



Scheme 3 The pathways of the reaction of compound **1b** with different molar ratios of the sodium salt of methanol (a) 1 : 1, (b) 1 : 2.5, (c) 1 : excess. The relative proportions of the products were determined by proton-decoupled ^{31}P NMR of the reaction mixtures.



Scheme 4 The *cis*-directing effect of the sodium cation of the incoming nucleophile coordinating to the oxygen lone pairs of the methoxy group of compound **3a** to form **7a**.

incoming nucleophile reacts first with the non-geminal chlorine atoms adjacent to the macrocyclic polyether and this situation was explained by the crown-related cation assistance mechanism for ansa substitution at the macrocycle bearing P-atoms.[51–55] On the other hand, in the present work with the fluorodioxy *cis*-ansa compounds **1a** and **1b**, nucleophilic substitution occurs predominantly at the PCl_2 group to give mono- and di-substituted products for reactions with **1a** (compounds **2a**, **3a**, **5a**) prior to reaction of the P(OR)Cl moieties, and for the reactions of **1b** giving derivatives **3b** then **5b**.

It is known that nucleophilic substitution with aliphatic ROH and aromatic ArOH alcohols follows the non-geminal pathway almost exclusively,[3–6,49,50] which is explained in terms of the O-atom of the P(OR)Cl group giving some electron density to the P-atom to make the P(OR)Cl group more stable than the PCl_2 group.[2,6,56] In our previous work we investigated using the crystallographic results a possible relationship between the P–Cl bond lengths and the formation of spiro or ansa products with diols (not containing fluorine atoms).[56] In each case the P–Cl bond in the P(OR)Cl group is longer than that in the PCl_2 group so that spiro compounds might be formed more readily than ansa compounds. In this work we have compared the P–Cl bond lengths in the PCl_2 and P(OR)Cl groups for fluorodioxy-ansa derivatives and for macrocyclic ansa using their crystal structures. The P–Cl bond lengths (average is 2.023 Å) adjacent to the macrocyclic group are longer than the P–Cl bonds (average is 1.995 Å) of the PCl_2 group[57] and they can leave from the cyclophosphazene ring more easily during a nucleophilic substitution reaction so that the formation of the non-geminal products is no surprise. The opposite situation is found for the *cis*-ansa fluorodiols **1a** and **1b**. As result of the electrophilic fluorine atoms in the ansa ring withdrawing electrons pairs from the O atoms of the P(OR)Cl moiety, the P–O bonds of compound **1a**[45] lengthens compared to the analogous bonds in the pentanediol,[56] and the P–Cl bonds (average is 1.977 Å for **1a** and average is 1.989 Å for **1b**) adjacent to the ansa group shorten compared to the P–Cl bonds of the PCl_2 groups (average for **1a** is 1.997 Å and average for **1b** is 1.994 Å). Hence it is not surprising that nucleophilic substitution occurs preferentially at the PCl_2 groups rather than at the P(OR)Cl moieties. Moreover, after the first substitution at the PCl_2 groups the remaining P–Cl bond gets longer (2.010 Å for **2a** and **3b**; 2.018 for **3a**) and the geminal product is readily formed.

In addition there is a difference in the distributions of mono- and di-substituted products for the reaction of sodium methoxide with compounds **1a** and **1b**. Firstly, reactions with **1b** only occur at the PCl_2 group to form the mono- (**3b**) and geminal di-substituted (**5b**) derivatives, whereas with **1a** there are three mono- (**2a–4a**) and three di-substituted (**5a–7a**). Secondly, with **1b** only the mono-substituted derivative with the methoxy group *trans* to the ansa ring, whereas with **1a** there is a significant amount of both *cis* (**2a**) and *trans* (**3a**) monomethoxy derivatives as well as a small amount of the derivative (**4a**) resulting from reaction at the P(OR)Cl group. Except for the preferential formation of compound **3b** with the methoxy group *trans* to the ansa ring (rather than *cis*), these results may be explained if the reactivity of the P–Cl bond of the P(OR)Cl moiety in **1b** is much lower than that for the PCl_2 group, which is likely because of the effect of more fluorine atoms in compound **1b** compared to **1a**. Some evidence for the very low activity of the P(OR)Cl group in **1b** compared to **1a** is that, in order to obtain the tetrakis-methoxy derivatives, stronger reaction conditions such as prior preparation of the sodium methoxide and using a greater excess of reagent (about 6-fold for **1a** and 30-fold for **1b**) were required to even give a lower yield for reaction with **1b** (50%) compared to **1a** (70%).

Experimental

Materials and physical measurements

Hexachlorocyclotriphosphazene (Aldrich) was purified by fractional crystallization from hexane. 2,2,3,3,4,4-hexafluoro-1,5-pentanediol (Aldrich) and 2,2,3,3,4,4,5,5-octafluoro-1,6-hexanediol (Aldrich) were used as received. Methanol (Merck) was dried over 4 Å molecular sieve. THF (Merck) was distilled over a sodium/potassium alloy under an atmosphere of dry argon. Sodium hydride, 60% dispersion in mineral oil (Merck); prior to use the oil was removed by washing with dry hexane (Merck) followed by decantation. All reactions were performed under a dry argon atmosphere. $CDCl_3$ for NMR spectroscopy was obtained from Merck. Analytical thin layer chromatography (TLC) was performed on Merck silica gel plates (Merck, Kieselgel 60, 0.25 mm thickness) with F_{254} indicator. Column chromatography was performed on a silica gel (Merck, Kieselgel 60, 70–230 mesh; for 3 g crude mixture, 100 g silica gel was used). Elemental analyses were obtained using a Thermo Finnigan Flash 1112 Instrument. Mass analyses were recorded on a Bruker MicrOTOF LC/MS spectrometer using the electro spray ionization (ESI) method; ^{35}Cl values were used for calculated masses. ^{1}H and ^{31}P NMR spectra were recorded for all compounds in $CDCl_3$ on a Varian INOVA 500 MHz spectrometer using TMS as an internal reference for ^{1}H and 85% H_3PO_4 as an external reference for ^{31}P NMR measurements. ^{19}F NMR spectra were recorded for all compounds in $CDCl_3$ on a Bruker Biospin 300 MHz spectrometer using $CFCl_3$ as an internal reference.

X-ray crystallography

The intensity data were recorded on a Bruker APEX II QUAZAR diffractometer using mono-chromatized Mo Kα X-radiation (λ = 0.71073 Å). Absorption correction was performed by the multi-scan method implemented in SADABS[58] and space groups were determined using XPREP implemented in APEX2.[59] Structures were determined using the direct methods procedure in SHELXS-97 and refined by full-matrix least squares on F^2 using SHELXL-97.[60] All non-hydrogen atoms were refined with anisotropic displacement factors and C–H hydrogen atoms were placed in calculated positions and allowed to ride on the parent atom. The final geometrical calculations were carried out with the PLATON[61] and MERCURY[62] programs and the molecular drawings were done with the DIAMOND[63] program. Structure determinations have been deposited with the Cambridge Crystallographic Data Centre with CCDC numbers 926250–926260 for eleven structures, **2a**, **3a**, **5a**, **6a**, **7a**, **8a**, **9a**, **3b**, **5b**, **8b** and **9b**, respectively.

Synthesis

Compounds **1a**[45] and **1b**[46] were prepared as in the literature.

The synthesis of compounds 2a and 3a

Ansa-$[N_3P_3Cl_4(OCH_2(CF_2)_3CH_2O)]$ (**1a**) (0.365 g, 0.75 mmol) and methanol (0.024 g, 0.75 mmol) were dissolved in 15 mL of dry THF in a 50 mL three-necked round-bottomed flask. The reaction mixture was cooled in an ice-bath and NaH (60% oil suspension, 0.03 g, 0.75 mmol) in 5 mL of dry THF was quickly added to the stirred solution under an argon atmosphere. The reaction was stirred for a further 24 h at room temperature and followed by TLC on silica gel plates using hexane–dichloromethane (1 : 1) as the mobile phase. Two products were observed. The reaction mixture was filtered to remove the sodium chloride and any other insoluble material. The solvent was removed under reduced pressure and the crude product was subjected to column chromatography using hexane–dichloromethane (1 : 1) as the eluent. The unreacted starting compound **1a** was eluted first from the column. The first product was the mono-methoxy compound **2a** and the second product was an isomer, compound **3a**, which were crystallized from hexane–dichloromethane (3 : 1) and obtained as white crystals. Anal. calc. for **2a** and **3a**; $C_6H_7Cl_3F_6N_3O_3P_3$: C, 14.94; H, 1.46; N, 8.71%, M, 482.4.

2a: (0.09 g, 25%, mp 174 °C). Found: C, 14.92; H, 1.45; N, 8.60%, $[M - CH_3]^+$, 467.4. ^{1}H NMR, $CDCl_3$, 298 K; δ (4.80, m, 2H; 4.40 m, 2H; –C*H*$_2$–), 3.81 (d, 3H, –OC*H*$_3$, $^{3}J_{P-H}$ = 13.5 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −112.22, −114.32 (m, 4F, –CH$_2$–C*F*$_2$–, $^{2}J_{F-F}$ = 295.2. Hz), −119.53, −122.24 (m, 2F, –CH$_2$–CF$_2$–C*F*$_2$, $^{2}J_{F-F}$ = 295.8 Hz).

3a: (0.07 g, 19%, mp 178 °C). Found: C, 14.94; H, 1.46; N, 8.60%, M^+, 481.9, ^{1}H NMR, $CDCl_3$, 298 K; δ (4.83, m, 2H; 4.41 m, 2H; –C*H*$_2$–), 3.82 (d, 3H, –OC*H*$_3$, $^{3}J_{P-H}$ = 14.0 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −112.12, −114.22 (m, 4F, –CH$_2$–C*F*$_2$–, $^{2}J_{F-F}$ = 297.9 Hz), −119.22, −122.30 (m, 2F, –CH$_2$–CF$_2$–C*F*$_2$, $^{2}J_{F-F}$ = 296.6 Hz).

The synthesis of compounds 5a, 6a, 7a and 8a

Ansa-$[N_3P_3Cl_4(OCH_2(CF_2)_3CH_2O)]$ (**1a**) (0.487 g, 1 mmol) and methanol (0.080 g, 2.5 mmol) were dissolved in 20 mL of dry THF in a 100 mL three-necked round-bottomed flask. The reaction mixture was cooled in an ice-bath and NaH (60% oil suspension, 0.1 g, 2.5 mmol) in 10 mL of dry THF was quickly added to the stirred solution under an argon atmosphere. The reaction was stirred for a further 24 h at room temperature and followed by TLC on silica gel plates using hexane–THF (5 : 1) as the mobile phase. Four products were observed. The reaction mixture was filtered to remove the sodium chloride and any other insoluble material. The solvent was removed under reduced pressure and the crude product was subjected to column chromatography using hexane–THF (5 : 1) as the eluent. The products were eluted from the column in the order of the bis-geminal methoxy compound (**5a**), bis-nongeminal *trans*-methoxy compound (**6a**), bis-nongeminal *cis*-methoxy compound (**7a**) and tris-geminal methoxy compound (**8a**). The compounds were crystallized from *n*-hexane–dichloromethane (3 : 1) and obtained as white crystals. Anal. calc. for **5a**, **6a** and **7a**; $C_7H_{10}Cl_2F_6N_3O_4P_3$: C, 17.59; H, 2.11; N, 8.79%, M, 478.0 and anal. calc. for **8a**; $C_8H_{13}ClF_6N_3O_5P_3$: C, 20.29; H, 2.77; N, 8.87%, M, 473.6.

5a: (0.14 g, 30%, mp 129 °C). Found: C, 17.57; H, 2.10; N, 8.69%, M^+, 478.0. ^{1}H NMR, $CDCl_3$, 298 K; δ (4.94 m, 2H; 4.43 m, 2H; –C*H*$_2$–), 3.74, (d, 3H, –OC*H*$_3$, $^{3}J_{P-H}$ = 13.2 Hz), 3.72

(d, 3H, –OCH_3, $^3J_{P–H}$ = 12.9 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −113.04, −114.63 (m, 4F, –CH_2–CF_2–, $^2J_{F–F}$ = 297.9 Hz), −119.89, −122.92 (m, 2F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 297.3 Hz).

6a: (0.03 g, 6%, mp 95 °C). Found: C, 17.57; H, 2.11; N, 8.70%, M^+, 478.4. ^{1}H NMR, $CDCl_3$, 298 K; δ (4.83 m, 1H; 4.59 m, 1H; 4.32 m, 2H; –CH_2), 3.80 [d, 3H, PCl(OCH_3) $^3J_{P–H}$ = 15.1 Hz], 3.73 [d, 3H, P(OR)(OCH_3) $^3J_{P–H}$ = 13.3 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −114.01 (m, 2F, –CH_2–CF_2–), −112.63, −114.88 (m, 2F, –CH_2–CF_2, $^2J_{F–F}$ = 296.3 Hz), −120.57, −122.57 (m, 2F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 298.7 Hz).

7a: (0.11 g, 22%, mp 141 °C). Found: C, 17.58; H, 2.10; N, 8.70%, M^+, 478.4. ^{1}H NMR, $CDCl_3$, 298 K; δ (4.87 m, 1H; 4.62 m, 1H; 4.34 m, 2H; –CH_2), 3.80 (d, 3H, PCl(OCH_3) $^3J_{P–H}$ = 15.4 Hz), 3.71 (d, 3H, P(OR)(OCH_3), $^3J_{P–H}$ = 13.1 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −113.99 (m, 2F, –CH_2–CF_2–), −112.04, −114.89 (m, 2F, –CH_2–CF_2, $^2J_{F–F}$ = 290.9 Hz), −119.94, −122.63 (m, 2F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 295.1 Hz).

8a: (0.08 g, 17%, mp 102 °C). Found: C, 20.26; H, 2.76; N, 8.85%, M^+, 474.36. ^{1}H NMR, $CDCl_3$, 298 K; δ (4.90 m, 1H; 4.64 m, 1H; 4.29 m, 2H; –CH_2), 3.71 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.1 Hz), 3.64 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.1 Hz), 3.63 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.4 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −114.58 (m, 2F, –CH_2–CF_2–), −113.38, −115.26 (m, 2F, –CH_2–CF_2, $^2J_{F–F}$ = 298.7 Hz), −120.62, −123.33 (m, 2F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 295.5 Hz).

The synthesis of compound 9a

Ansa-[$N_3P_3Cl_4$($OCH_2(CF_2)_3CH_2O$)], (**1a**) (0.122 g, 0.25 mmol) and methanol (0.05 g, 1.6 mmol) were dissolved in 15 mL of dry THF in a 50 mL three-necked round-bottomed flask. The reaction mixture was cooled in an ice-bath and NaH (60% oil suspension, 0.06 g, 1.6 mmol) in 5 mL of dry THF was quickly added to the stirred solution under an argon atmosphere. The reaction was stirred for a further 24 h at room temperature and followed by TLC on silica gel plates using hexane–dichloromethane (1 : 3) as the mobile phase. The reaction mixture was filtered to remove the sodium chloride and any other insoluble material. The solvent was removed under reduced pressure and the crude product was subjected to column chromatography using hexane–dichloromethane (1 : 3) as the eluent. Compound **9a** was isolated and crystallized from hexane–dichloromethane (3 : 1). Anal. calc. for **9a**; $C_9H_{16}F_6N_3O_6P_3$: C, 23.04; H, 3.44; N, 8.96%, M, 469.16.

9a: (0.08 g, 70%, mp 124 °C). Found: C, 22.97; H, 3.43; N, 8.93%, M^+, 470.58. ^{1}H NMR, $CDCl_3$, 298 K; δ 4.65, 4.23 (m, 4*H*, –CH_2–), 3.69 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.1 Hz), 3.68 (d, 3H, –OCH_3–, $^3J_{P–H}$ = 13.1 Hz), 3.624 (d, 3H, –OCH_3–, $^3J_{P–H}$ = 12.0 Hz), 3.618 (d, 3H, –OCH_3–, $^3J_{P–H}$ = 12.0 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −115.26 (m, 4F, –CH_2–CF_2–), −121.33, −123.67 (m, 2F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 294.6 Hz).

The synthesis of compound 3b

Ansa-[$N_3P_3Cl_4$($OCH_2(CF_2)_4CH_2O$)], (**1b**) (0.403 g, 0.75 mmol) and methanol (0.024 g, 0.75 mmol) were dissolved in 15 mL of dry THF in a 100 mL three-necked round-bottomed flask. The reaction mixture was cooled in an ice-bath and NaH (60% oil suspension, 0.03 g, 0.75 mmol) in 5 mL of dry THF was quickly added to the stirred solution under an argon atmosphere. The reaction was stirred for a further 24 h at room temperature and followed by TLC on silica gel plates using hexane–dichloromethane (1 : 1) as the mobile phase. Only one product was observed. The reaction mixture was filtered to remove the sodium chloride and any other insoluble material. The solvent was removed under reduced pressure and the crude product was subjected to column chromatography using hexane–dichloromethane (1 : 1) as the eluent. The starting compound **1b** was eluted first from the column and then product **3b**, which was isolated and crystallized from hexane–dichloromethane (3 : 1). Anal. calc. for **3b**; $C_7H_7Cl_3F_8N_3O_3P_3$: C, 15.79; H, 1.33; N, 7.89%, M, 532.4.

3b: (0.18 g, 45%, mp 105 °C). Found: C, 16.88; H, 1.42; N, 8.44%, $[M - Cl]^+$, 498. ^{1}H NMR, $CDCl_3$, 298 K; δ 4.44 (broad signal, 4H, –CH_2–), 3.83 (d, 3H, –OCH_3, $^3J_{P–H}$ = 15.1). ^{19}F NMR, $CDCl_3$, 298 K; δ −114.73, −117.87 (broad signals, 4F, –CH_2–CF_2–), −118.85, −120.21 (m, 4F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 300.8 Hz).

The synthesis of compounds 5b and 8b

Ansa-[$N_3P_3Cl_4$($OCH_2(CF_2)_4CH_2O$)], (**1b**) (0.215 g, 0.4 mmol) and methanol (0.032 g, 1.0 mmol), were dissolved in 15 mL of dry THF in a 100 mL three-necked round-bottomed flask. The reaction mixture was cooled in an ice-bath and NaH (60% oil suspension, 0.040 g, 1.0 mmol) in 5 mL of dry THF was quickly added to the stirred solution under an argon atmosphere. The reaction was stirred for a further 24 h at room temperature and followed by TLC on silica gel plates using hexane–dichloromethane (1 : 1) as the mobile phase. Three products were observed. The reaction mixture was filtered to remove the sodium chloride and any other insoluble material. The solvent removed under reduced pressure and the crude product was subjected to column chromatography using hexane–dichloromethane (1 : 1) as the eluent. The first product was a trace of compound **3b**; the second product was the bis-geminal compound (**5b**) and the third product was the tris-geminal compound (**8b**). Compounds **5b** and **8b** were crystallized from hexane–dichloromethane (3 : 1) and obtained as white crystals. Anal. calc. for **5b**; $C_8H_{10}Cl_2F_8N_3O_4P_3$: C, 18.20; H, 1.91; N, 7.96%, M, 528.0 and anal. calc. for **8b**; $C_9H_{13}ClF_8N_3O_5P_3$: C, 20.65; H, 2.50; N, 8.03%, M, 523.6.

5b: (0.14 g, 68%, mp 119 °C). Found: C, 18.14; H, 1.90; N, 7.93%, M^+, 529.8. ^{1}H NMR, $CDCl_3$, 298 K; δ 4.33 (broad signal, 4H, –CH_2–), 3.67 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.2 Hz), 3.64 (d, 3H, –OCH_3, $^3J_{P–H}$ = 12.9 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −113.96, −117.99 (broad signals, 4F, –CH_2–CF_2–), −118.47, −120.29 (broad signals, 4F, –CH_2–CF_2–CF_2).

8b: (0.05 g, 24%, mp 79 °C). Found: C, 20.61; H, 2.50; N, 8.01%, M^+, 524.5. ^{1}H NMR, $CDCl_3$, 298 K; δ 4.30 (broad signal, 4H, –CH_2–), 3.66 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.1 Hz), 3.65 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.0 Hz), 3.63 (d, 3H, –OCH_3, $^3J_{P–H}$ = 12.8 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −115.49, −118.05 (broad signals, 4F, –CH_2–CF_2–), −118.88, −120.20 (broad signals, 4F, –CH_2–CF_2–CF_2).

The synthesis of compound 9b

NaH (60% oil suspension, 0.49 g, 12.30 mmol) in 5 mL of dry THF was added in a 50 mL three-necked round-bottomed flask under an argon atmosphere. Methanol (0.5 mL; 12.30 mmol) was added to the reaction flask to form the sodium salt of the alcohol. The reaction mixture was cooled in an ice-bath and compound **1b** (0.22 g, 0.41 mmol) dissolved in 2 mL of THF was added dropwise under an argon atmosphere. The reaction was stirred for a further 24 h at room temperature and followed by TLC on silica gel plates using hexane–dichloromethane (1 : 3) as the mobile phase. The reaction mixture was filtered to remove the sodium chloride and any other insoluble material. The solvent was removed under reduced pressure and the crude product was subjected to column chromatography using hexane–dichloromethane (1 : 3) as the eluent. The tetramethoxy compound (**9b**) was isolated and crystallized from hexane–dichloromethane (3 : 1). Anal. calc. for **9b**; $C_{10}H_{16}F_8N_3O_6P_3$: C, 23.14; H, 3.11; N, 8.09%, M, 519.2.

9b: (0.10 g, 47%, mp 84 °C). Found: C, 23.10; H, 3.10; N, 8.08%, M^+, 520.0. ^{1}H NMR, $CDCl_3$, 298 K; δ 4.30 (m, 4H, –CH_2–), 3.64 (d, 3H, –OCH_3, $^3J_{P–H}$ = 13.2 Hz), 3.63 (d, 3H, –OCH_3, $^3J_{P–H}$ = 12.5 Hz), 3.62 (d, 6H, –OCH_3, $^3J_{P–H}$ = 12.8 Hz). ^{19}F NMR, $CDCl_3$, 298 K; δ −115.57 (broad, 4F, –CH_2–CF_2–), −119.03, −120.37 (m, 4F, –CH_2–CF_2–CF_2, $^2J_{F–F}$ = 298.9 Hz).

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