Synthesis and inclusion behavior of cyclotriphosphazene molecules with asymmetric spiro rings†

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Two novel cyclic phosphazenes with asymmetric spiro rings were synthesized *via* reactions of hexachlorocyclotriphosphazene with chiral amino alcohol residues. The reactions showed preferential formation of the *cis* isomer possibly due to the delocalization of the lone pair electrons of the spirocylic nitrogen, which reduces its ability to solvate protons. Crystals of these phosphazenes were analyzed by X-ray crystallography which confirmed the formation of *cis* isomers and showed their ability to include guest molecules within the crystal lattices. The selective inclusion of epoxides by one of the phosphazenes was an effective method for the separation of thermally sensitive guest molecules.

Introduction

Inclusion complexes are host-guest aggregates that form when the interactions between the host molecule and the guest molecule are thermodynamically stabilizing. Hydrogen bonding forces and van der Waals forces coordinate the guest molecule inside the lattice structure of the host molecule to form the complex. Inclusion complexes are significant because the host can show selective inclusion of the guest within the complex. Therefore, they can be used as storage materials or in molecular separation applications.

The cyclotriphosphazene skeleton is a convenient building block for host molecules because of the ease of preparation of various molecules with trigonal symmetry. Cyclic phosphazenes that bear spirocyclic side groups have been used as host molecules in clathrate adducts since 1964.[1] The first of these species was tris(*o*-phenylenedioxy)cyclotriphosphazene (**1**) which was formed by allowing a difunctional nucleophile, 1,2-dihydroxybenzene, to react with hexachlorocyclotriphosphazene to form a spirocyclic molecule with a paddle-wheel structure (Fig. 1). Since then, various other phosphazene molecules bearing spirocyclic side groups have been synthesized and found to undergo clathration behavior.[2,3] The clathration properties of these molecules have been utilized in various applications, such as selective inclusion of organic compounds,[2,4] stereocontrolled polymerization of unsaturated monomers,[5] and the construction of 1D supramolecular-wires.[6–8] They have also been proposed as components in organic superconductors.[9]

Up to this time, the phosphazene molecules that show clathration behavior are spirocyclic phosphazenes with symmetric spiro rings. To extend the design and utility of phosphazene clathrates, we have attempted to synthesize spirocyclic phosphazenes with asymmetric spiro side groups. Phosphazenes **2** and **3** were synthesized with residues of chiral amino alcohols and they undergo selective formation of the *cis* isomer in which all the amino groups are on the same side of the phosphazene ring. The isomerically selective synthesis of these cyclotriphosphazenes with asymmetric spiro rings broadens the design choice for future host molecules with trigonal symmetry. In this paper, we report the synthesis, characterization, and the inclusion behavior of two novel cyclotriphosphazenes with asymmetric spiro rings, and propose a possible mechanism for the preferential formation of the *cis* isomer.

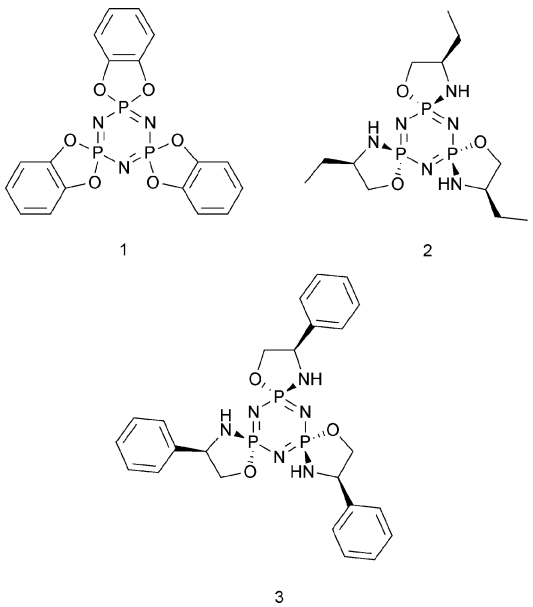

Fig. 1 Cyclic phosphazenes with symmetric spiro rings and novel cyclic phosphazenes with asymmetric spiro rings.

Experimental methods

Reagents and solvents

Hexachlorocyclotriphosphazene (Fushimi Pharmaceutical Co., Ltd., Japan) was purified by recrystallization from hexanes followed by sublimation. Tetrahydrofuran, triethylamine, and benzene (99.99%, EMD) were dried using Glass Contour solvent

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purification columns.[10] (R)-(−)-2-amino-1-butanol (98%, Aldrich), (R)-(−)-2-phenylglycinol (98%, Alfa Aesar), 1,2-epoxybutane (96%, Aldrich), 1,2-epoxy-2-methylbutane (97%, Aldrich), *trans*-2,3-epoxybutane (97%, Alfa Aesar), *cis*-2,3-epoxybutane (98%, Alfa Aesar), 1,2-epoxyhexane (97%, Alfa Aesar), diethyl ether, hexanes, ethanol, ethyl acetate and dichloromethane (EMD) were used as received. Propylene sulfide (96%, Aldrich) was stored in a refrigerated glove box and propylene oxide (99%, Aldrich) was stored under argon. All reactions were carried out under argon using standard Schlenk-line techniques.

Equipment

^{31}P and ^{1}H NMR spectra were obtained using a Bruker AMX 360 WM instrument at 145 MHz and 360 MHz respectively. Single crystal X-ray diffraction data were collected on a Bruker AXS diffractometer, a molybdenum sealed-tube X-ray source equipped with a capillary collimator (MonoCap), SMART APEX 4K CCD detector and a Rigaku-MSC X-stream 2000 low temperature device. Mass spectrometric analysis data were collected using turbospray ionization technique on an Applied Biosystems API 150EX LC/MS mass spectrometer.

Synthesis of phosphazene 2

Hexachlorocyclotriphosphazene (0.014 mol, 4.87 g) in THF (150 mL) was introduced into a 500 mL three-neck round-bottom flask. Three equivalents of (R)-(−)-2-amino-1-butanol (0.042 mol, 3.74 g) and 6 equivalents triethylamine (0.084 mol, 8.50 g) were dissolved in THF (240 mL) and placed in an addition funnel. Each equivalent of the (R)-(−)-2-amino-1-butanol was allowed to react with the phosphazene in the following manner. An 80 mL aliquot of the (R)-2-amino-1-butanol (1 equivalent) and triethylamine (2 equivalents) solution was added dropwise to the chlorophosphazene solution and allowed to react for 24 h. The same procedure was repeated for the next two 80 mL aliquots of the (R)-2-amino-1-butanol and triethylamine solution. The progress of the reaction was monitored by ^{31}P NMR spectroscopy. Excess (R)-(−)-2-amino-1-butanol (0.011 mol, 0.98 g) was added directly to the reaction solution both as a reactant and proton acceptor to complete the formation of the trispiro phosphazene. The reaction solution was filtered after 6 days of stirring at room temperature (25 °C). The filtrate was concentrated by rotary evaporation to produce a yellow adhesive solid. The product was purified through a silica gel column with a mobile phase of ethyl acetate:hexanes:methanol (45 : 45 : 10). The product was then recrystallized from a mixture of hexanes and benzene to give white crystals. The yield based on hexachlorocyclotriphosphazene was 36% (2.012 g). δ_P (*d*-THF): 33.2 (3P, s). δ_H (*d*-THF): 4.69 (3H, br s, OC*H*H), 4.19 (3H, m, NC*H*), 3.75 (3H, m, POCH*H*), 3.47 (3H, br s, N*H*), 1.41 (6H, m,CH_2CH$_3$); 0.85 (9H, t, CH_3).

Synthesis of monospiro phosphazene 3a

Hexachlorocyclotriphosphazene (0.0144 mol, 5.00 g) was dissolved in THF (150 mL) in a 500 mL three-neck round-bottom flask. R-(−)-2-phenylglycinol (0.0144 mol, 1.97 g) and triethylamine (0.0288 mol, 2.91 g) were dissolved in THF (50 mL) and were added dropwise through an additional funnel to the phosphazene solution. The reaction mixture was stirred for two days at room temperature. The mixture solution was then filtered and the filtrate was concentrated. The crude product was purified *via* a silica gel column using a mobile phase of ethyl acetate:dichloromethane:hexanes (25 : 25 : 50). The resultant solid was recrystallized from ethyl acetate and hexanes to yield white crystals. The yield based on hexachlorocyclotriphosphazene was 63% (3.7397 g). δ_P ($CDCl_3$): 24.2 (2P, d, *P*Cl$_2$), 22.2 (1P, t). δ_H ($CDCl_3$): 7.45–7.26 (5H, m, C$_6$*H*$_5$), 4.91 (1H, br s, OC*H*H), 4.60 (1H, m, NC*H*), 4.13 (1H, q, OCH*H*), 3.35 (1H, d, N*H*).

Synthesis of dispiro phosphazene 3b

Hexachlorocyclotriphosphazene (8.00 mmol, 2.78 g) was dissolved in THF (150 mL) in a 500 mL three-neck round-bottom flask. Two equivalents of (R)-(−)-2-phenylglycinol (0.016 mol, 2.20 g) and four equivalents of triethylamine (0.0321 mol, 3.25 g) were dissolved in THF (100 mL) and introduced into an addition funnel. Aliquots of the phenylgylcinol and triethylamine solution (50 ml) were added dropwise as described for the synthesis of phosphazene **2**. The reaction solution was then stirred at room temperature for 5 days. The solution was filtered and concentrated. The resultant solid was recrystallized in chloroform and hexanes to give a white powder. The yield based on hexachlorocyclotriphosphazene was 38% (1.441 g). δ_P (*d*-THF): 29.8 (2P, dd), 26.8 (1P, t, *P*Cl$_2$). δ_H ($CDCl_3$): 7.39–7.26 (10H, m, C$_6$*H*$_5$), 4.92 (2H, br s, OC*H*H), 4.55 (2H, m, NC*H*), 4.11 (2H, m, OCH*H*), 3.19 (2H, m, N*H*). MS ESCI$^+$: *m*/*z* calcd 475; found 476 (M + H$^+$) and 498 (M + Na$^+$).

Synthesis of phosphazene 3

Hexachlorocyclotriphosphazene (0.0364 mol, 12.66 g) was dissolved in THF (150 mL) in a 500 mL three-neck round-bottom flask. Three equivalents of (R)-(−)-2-phenylglycinol (0.1092 mol, 14.98 g) and 6 equivalents triethylamine (0.2187 mol, 22.13 g) were dissolved in THF (300 mL) and placed in an addition funnel. Aliquots of the phenylglycinol and triethylamine solution (100 mL) were added dropwise as described for the synthesis of phosphazene **2**. The reaction mixture was stirred at room temperature for 5 days and the volume of the reaction solution was reduced to 50% by rotary evaporation. (R)-(−)-phenylgylcinol (0.0364 mol, 4.99 g) was then added to the reaction solution to force the formation of the trispiro product. After nine days of reaction at room temperature, the reaction solution was filtered and washed with THF. The filtrate was evaporated, and the resulting yellow adhesive residue was put under vacuum for two days. The product was then recrystallized from ethanol and hexanes to give white crystals. The yield based on hexachlorocyclotriphosphazene was 33% (6.5608 g). δ_P ($CDCl_3$): 33.88 (3P, s). δ_H ($CDCl_3$): 7.44–7.25 (15H, m, C$_6$*H*$_5$); 5.16 (3H, s, N*H*), 4.77 (3H, t, OC*H*H), 4.45–4.36 (3H, m, NC*H*), 3.99–3.95 (3H, t, OCH*H*).

Recrystallization methods

The crystals of phosphazene **2** and **3** were formed in three different ways, with the methods of crystallization detailed below. The crystal structure of these clathrates was determined by single crystal X-ray crystallography. ^{1}H NMR solution spectroscopy was also used as a secondary method to detect the presence of guest compounds. Crystals that formed were isolated from the mother

liquor and dissolved in $CDCl_3$. The selectivity of inclusion was determined from the intensity of the unique NMR peaks of the guest compounds to determine the ratio of included compounds.

Hot recrystallization. The host compound was dissolved in a solvent (*e.g.* benzene) at boiling temperature to achieve a clear, saturated solution. A non-solvent (*e.g.* hexanes) was added until the solution became cloudy. The solution was reheated to the boiling point and was filtered if the precipitate did not redissolve. The solution was then cooled slowly to room temperature. The resultant crystals were then washed with the non-solvent and were dried in air.

Cold recrystallization. A saturated solution was formed by dissolving the host compound in the guest liquid (*e.g.* propylene oxide) at room temperature. The solution was filtered if it was cloudy. The liquid was then placed in a capped vial and cooled slowly to −30 °C. If NMR spectroscopy was required, the resultant crystals were placed on a Buchner funnel filter and were washed with a non-solvent (*e.g.* ether) that was chilled to −30 °C. The crystals were dried briefly by passing air through the Buchner funnel.

Diffusion recrystallization. A saturated solution was produced by dissolving the host compound in the guest liquid (propylene sulfide) at room temperature. The saturated solution was filtered into a small vial and placed inside a larger jar containing a non-solvent (*e.g.* ether). The jar was capped and sealed to allow diffusion of the non-solvent from the larger jar into the vial. The crystals formed this way were washed with the non-solvent (ether) and dried.

X-Ray analysis

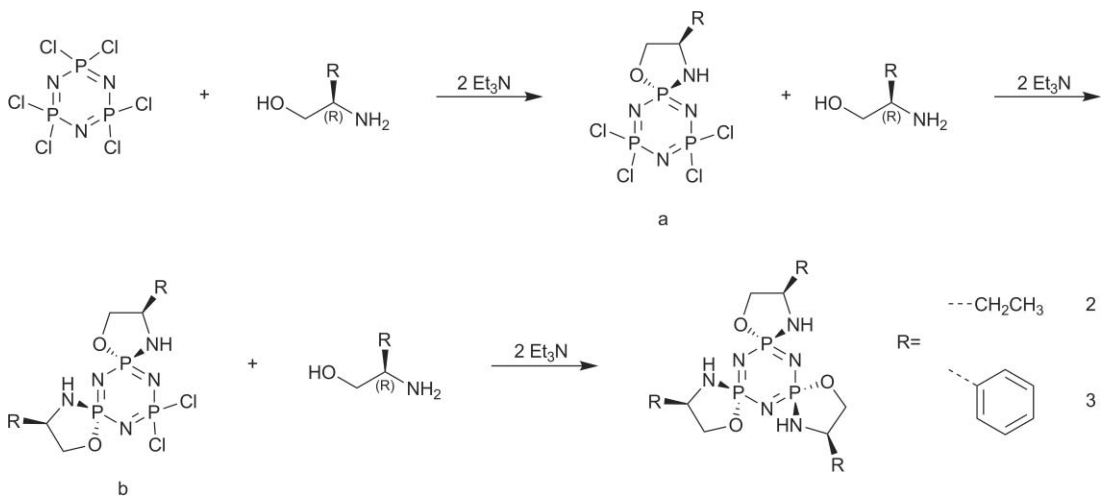
The X-ray intensity data were measured either at 298(2) K or at 113(2) K (cooled by Rigaku-MSC X-Stream 2000) on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube ($\lambda = 0.71073$ Å) operated at 1600 watts power (50 kV, 32 mA). The detector was placed at a distance of 5.8 cm from the crystal. A total of 1850 frames were collected with a scan width of 0.3° in ω and exposure times of 10–30 s/frame. The frames were integrated with the Bruker SAINT software package using a narrow-frame integration algorithm. The structure was solved and refined using the Bruker SHELXTL (Version 6.1) Software Package. PLATON software was used to identify higher symmetry and to transform coordinates from $P2_1$ to $P2_12_12_1$.[11] All non-hydrogen atoms were refined anisotropically and hydrogens rode on their parent atoms. Disorder in the structure was identified with the help of a difference-Fourier map.

Results and discussion

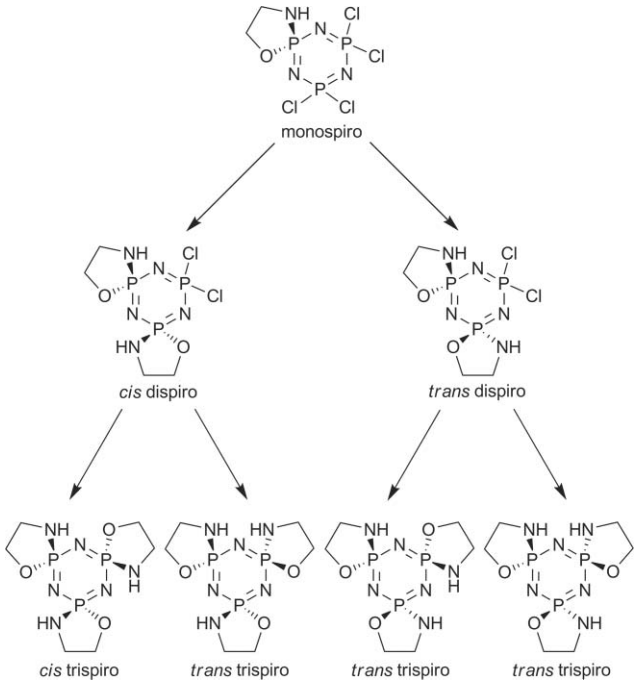
Synthesis and mechanism of *cis* isomer formation

Phosphazenes **2** and **3** were formed by nucleophilic replacement of the six chlorine atoms of hexachlorocyclotriphosphazene by three amino alcohol residues. The reactions were carried out at room temperature in tetrahydrofuran, and triethylamine was used as the hydrogen chloride acceptor (Scheme 1). Each charge of amino alcohol solution was added dropwise and stepwise to ensure that each equivalent of amino alcohol was consumed before the next equivalent was added. Synthesis of the phosphazenes in this manner maximized the formation of *cis* isomers. The formation of *cis* isomers was reduced if the amino alcohols were added too rapidly or if the reaction temperature was increased above room temperature. The ^{31}P NMR spectra of the reaction mixtures showed *cis*:*trans* isomer ratios of at least 7 : 3. A lack of stereoselectivity would cause the *cis*:*trans* ratio to be 1 : 3 (Scheme 2). The isolation of the *cis* isomers was achieved by column chromatography and/or recrystallization.

A similar unusual stereoselectivity for the formation of a *cis* product has been reported previously by Chandrasekar.[12] We believe that the first asymmetric ring attached to the phosphazene has a directing effect that influences the formation of subsequent spiro rings. First, consider the initial attachment of the amino alcohol residue to the phosphazene. Our preliminary experiments, which were reactions of $N_3P_3Cl_6$ with two equivalents of $HOCH_2CH_3$ and $NH_2CH_2CH_3$ in the presence of triethylamine, showed that amine groups are more nucleophilic than hydroxyl groups. All the amines were consumed within 12 h but only a few percent of the alcohol was consumed. Therefore, the amino group will



Scheme 1 Stepwise introduction of amino alcohol residues.



Scheme 2 Probability of non-selective isomer formation.

attach first to the phosphazene, followed by a rapid intramolecular reaction between the hydroxyl group and a phosphorus-chlorine bond to form the spiro ring. After the formation of the first spiro ring, the stereoselectivity of the next amino substitution will be crucial for the formation of the *cis* product. It appears that the substituent-solvating effect (SSE) proposed by Goldschmidt plays a crucial role in the preferential formation of the *cis* isomer.[13] These earlier kinetic studies by him indicated that *trans*-isomers of diaminocyclotriphosphazenes are generated preferentially due to formation of a six-membered ring stabilized transition state in which the departure of the chlorine atom is facilitated by solvation of a proton by the lone pair electrons on the exocyclic nitrogen atom (Scheme 3).

In the case of an asymmetric spirocyclic system, it would be expected that the same behavior would lead to amino substitution *trans* to the spirocyclic amine. This is because nitrogen is more basic than oxygen, and is thus more likely to donate its lone pair for proton solvation. Furthermore, substitution from the same side of the spiro amino unit is more sterically hindered. However, in the present work, the *trans*-isomer was not the major product. Closer examination of the experimental results revealed that the nitrogen lone pair on an existing spiro ring is partially delocalized over the spirocyclic P–N bond and is not readily available for donation to protons. This is evident from three observations. First, the X-ray crystallography of the monospiro phosphazene product showed that the spirocyclic P–N bond length is 1.62 Å (Fig. 2), which is much shorter than a conventional P–N single bond (1.77 Å).[14] Second, the spirocyclic C–N–P bond angle of 116° indicates that the spirocyclic nitrogen has more sp^2 trigonal-planar character than sp^3 tetrahedral characteristics. Finally, the ^{1}H NMR spectrum shows that the amine proton chemical shift is about 5 ppm, whereas a non-spirocyclic amine hydrogen is normally quoted to have a value near 2 ppm. The shortened bond length, the hybridization configuration, and the downfield proton shift all indicate delocalization of the nitrogen lone pair over the spirocyclic P–N bond, making it less available for solvating a proton. On the other hand, the spirocyclic oxygen atom maintains its tetrahedral configuration, and the P–O bond length of 1.6 Å is close to the normally quoted bond length of 1.573 Å. Therefore, the lone pair electrons of oxygen are available for solvating protons, which facilitates the detachment of a chlorine atom from the oxygen side of the phosphazene ring. This promotes the linkage of an amine group to the opposite side of the oxygen and on the same side as the amino group.

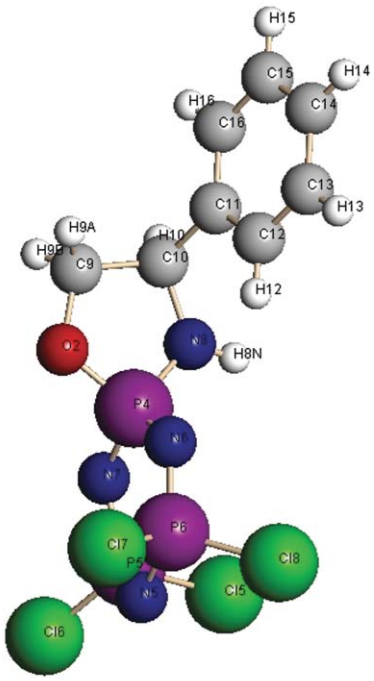
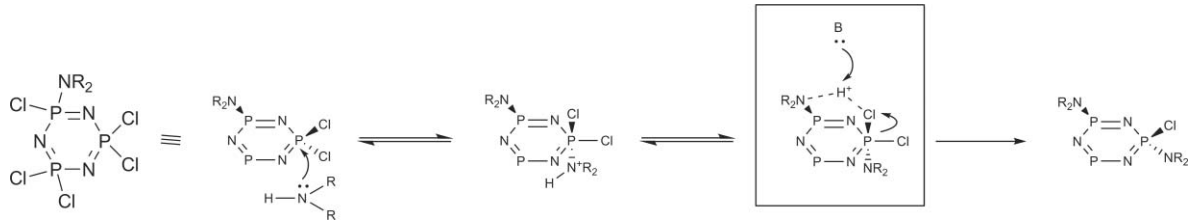
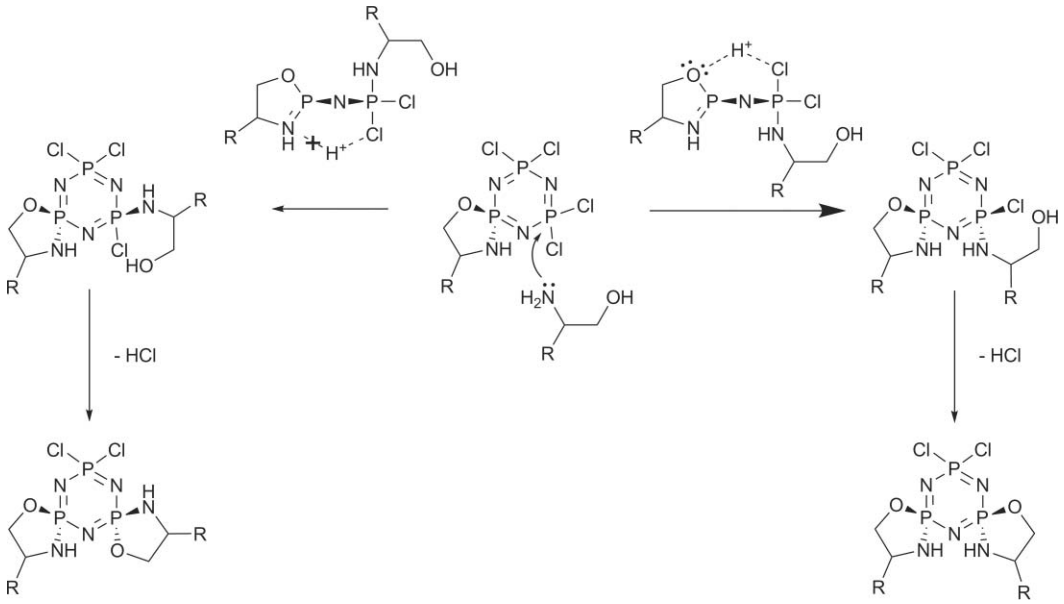


Fig. 2 The spiro cyclic P–N bond length is 1.62 Å and the P–N–C bond angle is 116°.

Scheme 4 shows the two possible routes for the formation of the second spiro ring. If the amine group on the second substituent



Scheme 3 Substituent solvating effect by Goldschmidt involving a six membered ring stabilized transition state.



Scheme 4 Preference for *cis*-isomer through substituent solvating effect.

attacked *trans* to the existing amino group, there would be no stabilizing six-member ring transition state due to the delocalized lone pair electrons of the spirocyclic nitrogen. On the other hand, if the second amine group attacks *cis* to the existing nitrogen on the spiro ring, then the departure of the chlorine is more favored due to the six-member ring transition state created with the lone pairs from the oxygen. This is in agreement with work by Shaw who also showed that, when a phosphazene with an asymmetric spiro ring reacts with pyrrolidine, substitution also occurred at the side opposite to the oxygen.[15]

Crystallization and inclusion behavior

Single crystal X-ray diffraction data for phosphazenes **2** and **3** were obtained to confirm the formation of the *cis* isomer (Fig. 3). Although the phosphazenes were soluble in most organic solvents, only a few solvents yielded crystals that were satisfactory for X-ray diffraction. The results of the diffraction experiments are summarized in Table 1.

Phosphazene **2** was recrystallized from hot solvents and could be obtained only in the form of clathrates that included guest molecules within channels of the crystal lattice (Fig. 4). Two examples shown in Table 1 are with benzene and ethanol as guests. Dichloromethane also formed clathrates with phosphazene **2**. The presence of dichloromethane was detected by ^{1}H NMR spectroscopy and by removal of the guest by vacuum extraction. However, the crystals obtained from dichloromethane were characterized by excessive disorder, and numerous attempts failed to produce a satisfactory crystal. Phosphazene **3** was also recrystallized using the hot recrystallization technique from various solvents such as benzene, xylene, dichloromethane, ethanol and dioxane. Crystallization from those different solvents yielded the same close-packed crystal structure with no included guest molecules (Fig. 5). However, phosphazene **3** formed inclusion complexes when crystallized from various epoxides and propylene sulfide. The cold recrystallization of phosphazene **3** from epoxides yielded crystals in which the presence of included epoxides was detected by ^{1}H NMR spectroscopy and by vacuum extraction. However, the crystals were too disordered to obtain a crystal structure. A satisfactory crystal structure was obtained only when

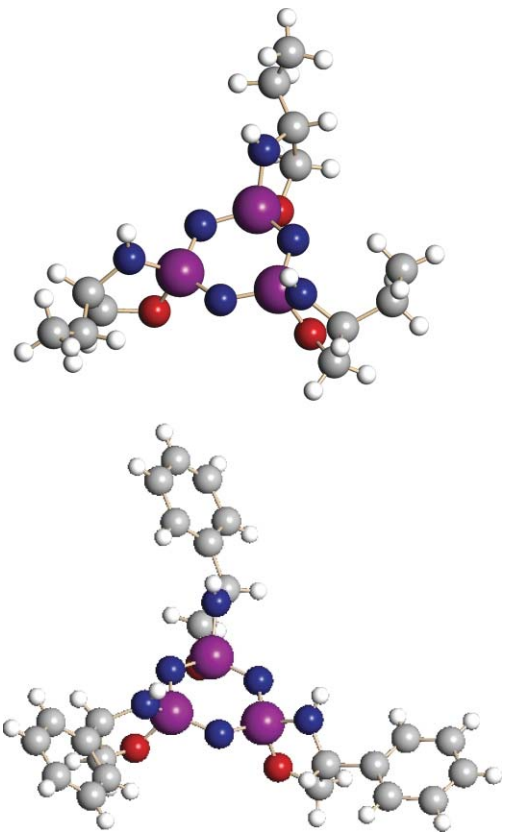


Fig. 3 Molecular structure of phosphazenes **2** (top) and **3** (bottom) obtained from X-ray crystallography.

Table 1 Summary of crystal structures

Species	Phosphazene **2**	Phosphazene **2**	Phosphazene **3**	Phosphazene **3**
Inclusion	Benzene	Ethanol	None	Propylene sulfide
Formula	$2(C_{12}H_{24}N_6O_3P_3)\cdot C_6H_6$	$4(C_{12}H_{24}N_6O_3P_3)\cdot (C_2H_5OH)$	$C_{48}H_{54}N_{12}O_6P_6$	$2(C_{24}H_{21}N_6O_3P_3)\cdot 0.56(C_3H_2S)$
Formula Weight	1741.44	1631.19	1080.85	1136.74
Host:Guest Ratio	2 : 1	4 : 1	N/A	~4 : 1
Crystal Habit	Colorless cubical	Colorless block	Colorless plate	Colorless pyramid
Crystal System	Triclinic	Orthorhombic	Orthorhombic	Rhombohedral
Space Group	*P*1	$P2_12_12_1$	$P2_12_12_1$	*R*3
a/Å	10.301(9)	10.0247(8)	9.4582(8)	30.844(4)
b/Å	13.723(12)	20.0725(16)	22.3485(18)	30.844(4)
c/Å	14.960(13)	38.752(3)	25.314(2)	16.089(4)
α/°	89.045(15)	90	90	90
β/°	81.827(15)	90	90	90
γ/°	88.721(15)	90	90	120
Volume/Å^3	2093(3)	7797.7(11)	5350.8(8)	13256(4)
Z	1	4	4	9
Reflections Measured	19196	68731	36694	26923
Independent Reflections	16021	19285	13241	9600
R_{int}(%)	3.56	4.54	2.99	11.57
R_1(%)	8.77	6.17	5.57	11.69
R_2(%)	19.64	14.17	13.98	29.73
Flack Parameter	0.11(12)	0.05(7)	–0.03(8)	0.51(8)

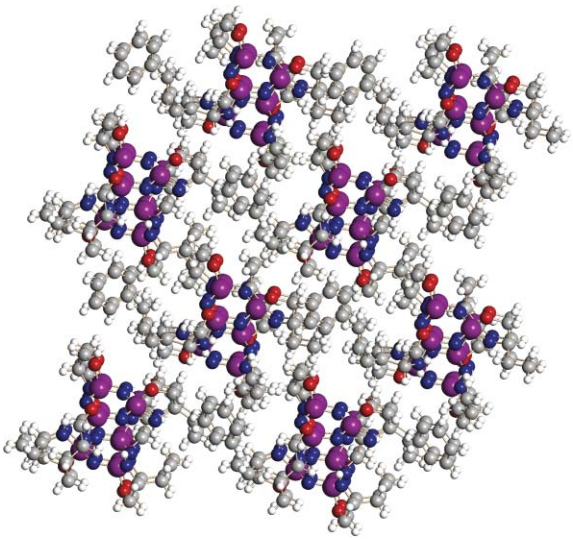


Fig. 4 Phosphazene **2** with benzene inclusion.

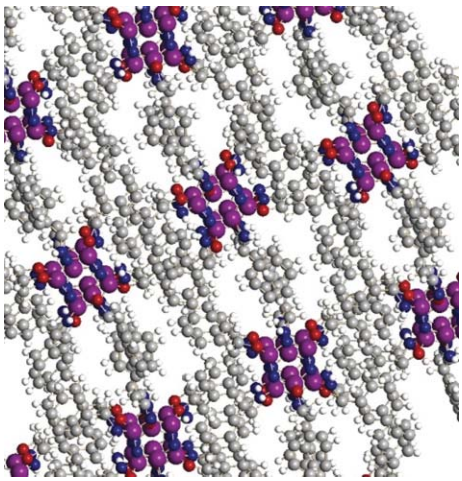


Fig. 5 Crystal structure of phosphazene **3** without inclusion.

phosphazene **3** was recrystallized from propylene sulfide using diffusion recrystallization (Fig. 6). The higher boiling point of propylene sulfide compared to propylene oxide is presumed to be the reason for the better crystals. These crystals still showed weak reflections at high resolution, and the R_{int} value of 11.57% reflects the disorder in the crystal lattice. For this reason, the structure refinement converged to a high R factor. This crystal structure serves as a good representation of how epoxides can be included within channels of the crystal lattice of phosphazene **3**. The channel structure of the clathrates formed from phosphazenes **2** and **3** allows the removal of guest molecules by placing the clathrates under vacuum. It appears that the incorporated guest molecules stabilize the channel structure of the clathrates because removal of guest molecules by vacuum results in the collapse of the crystal.

Every crystal structure obtained from phosphazenes **2** and **3** consists of dimers in which two phosphazene molecules are face to face with each other on the nitrogen side of the ring. These interdigitated dimers are the building blocks within the overall crystal structures. The formation of the dimer is due to hydrogen bonding interactions between the spirocylic amine with the phosphazene nitrogen units, and this bonding motif has been reported previously in crystals of cyclicphosphazenes that bear amine groups.[16] The distance between these two nitrogen atoms is about 3 Å, which is within the range for hydrogen bonding. Each dimer produces six hydrogen bonding interactions, which provides a strong driving force for interdigitation of two phosphazene molecules.

We examined the possibility that these phosphazenes with chiral side groups might be used for enantiometric separations, but crystallization of phosphazene **3** from racemic mixtures of chiral molecules, such as propylene sulfide, did not show enantiomeric

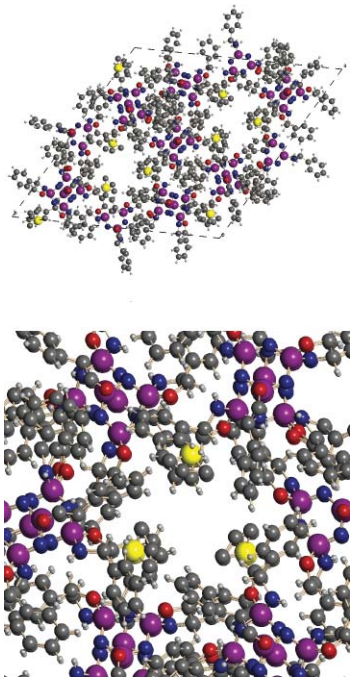


Fig. 6 Unit cell of phosphazene **3** with propylene sulfide (top) and a detailed view of the tunnel shaped clathrate (bottom).

selectivity. However, phosphazene **3** gave selectivity in the inclusion of epoxides as summarized in Table 2. Phosphazene **3** was first dissolved in a 50 : 50 molar ratio of 2 epoxides at room temperature to form a saturated solution. Crystals formed as the saturated solution was cooled slowly to −30 °C. The crystals were washed with cold ether and the selectivity of epoxide inclusion was determined by ^{1}H NMR spectroscopy.

The general inclusion behavior of phosphazene **3** is to incorporate the epoxide that has the smaller molar volume. This was apparent in all samples in which propylene oxide was present together with any other epoxide species. Molecules with shorter carbon chains were also preferentially included into the crystal structure in competition with molecules with longer chains and more disorder. Even though 1,2-epoxybutane and *cis*/*trans*-2,3-epoxybutane have the same molecular weight, both *cis* and *trans*-2,3-epoxybutane are preferentially included over 1,2-epoxybutane. Unfortunately, phosphazene **3** was not able to separate the *cis*-*trans* isomers of 2,3-epoxybutane. Thus, when phosphazene **3** was crystallized from a 1 : 1 mixture of *cis* and *trans*-2,3-epoxybutane, both 2,3-epoxybutane isomers were included equally in the crystal. The preference of *cis*-2,3-epoxybutane over 1,2-epoxybutane demonstrates that the clathrates of phosphazene **3** can be used to separate molecules with similar boiling points. The boiling point of *cis*-2,3-epoxybutane is 60–61 °C, while the boiling point of 1,2-epoxybutane is 63 °C. Another example of a successful separation of compounds with similar boiling points is that of propylene oxide and diethyl ether, which have boiling points of 34 °C and 34.6 °C respectively. The use of distillation to separate these two sets of compounds would be difficult. Thus, selective inclusion is an alternative option for chemical separations.

Table 2 Selectivity of epoxide inclusion

	Molar ratio	
Small molecule mixture	Solution	Adduct
Propylene oxide/1,2-Epoxybutane	50 : 50	63 : 37
Propylene oxide/*trans*-2,3-Epoxybutane	50 : 50	69 : 31
Propylene oxide/1,2-Epoxy-2-methylpropane	50 : 50	72 : 28
Propylene oxide/1,2-Epoxyhexane	50 : 50	75 : 25
Propylene oxide/Diethyl ether	50 : 50	83 : 17
cis-2,3-Epoxybutane/1,2-Epoxybutane	50 : 50	61 : 39
trans-2,3-Epoxybutane/1,2-Epoxybutane	50 : 50	56 : 44

Conclusions

Asymmetric spiro rings were formed when hexachlorocyclotriphosphazene reacted with chiral amino alcohols. A preferential formation of *cis* isomers was detected which was attributed to the delocalization of the spirocylic nitrogen lone pair, and its consequent unavailability for solvating a proton. Although oxygen is less basic than nitrogen, its lone pair electrons are not delocalized. Therefore, the spirocyclic oxygen facilitates the departure of the chlorine atom from the same side of the phosphazene ring and promotes the formation of a *cis* isomer. X-ray crystallography of the crystals confirmed the formation of *cis* isomers and showed the ability of these species to include guest molecules within their crystal lattices. Phosphazene **2** was able to include solvent molecules within channels in its crystal structure, whereas phosphazene **3** was capable of selective inclusion of epoxides which have similar structures and boiling points. The design and synthesis of related host molecules that can bring about selective isomeric and enantiometric separations is an ongoing objective.

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References

1 H. R. Allcock and L. A. Siegel, *J. Am. Chem. Soc.*, 1964, **86**, 5140–5144.
2 H. R. Allcock, *Acc. Chem. Res.*, 1978, **11**, 81–87.
3 H. R. Allcock, in, *Inclusion Compounds*, ed. J. L. Atwood, J. E. D. Davies and D. D. MacNicol, Academic Press, New York, 1984, vol. 1, ch. 8, 351-374.
4 H. R. Allcock, R. W. Allen, E. C. Bissell, L. A. Smeltz and M. Teeter, *J. Am. Chem. Soc.*, 1976, **98**, 5120–5125.
5 (*a*) H. R. Allcock, W. T. Ferrar and M. L. Levin, *Macromolecules*, 1982, **15**, 697–703; (*b*) H. R. Allcock and M. L. Levin, *Macromolecules*, 1985, **18**, 1324–1330; (*c*) H. R. Allcock, E. N. Silverberg and G. K. Dudley, *Macromolecules*, 1994, **27**, 1033–1038; (*d*) H. R. Allcock, G. K. Dudley and E. N. Silverberg, *Macromolecules*, 1994, **27**, 1039–1044; (*e*) H. R. Allcock, E. N. Silverberg, G. K. Dudley and S. R. Pucher, *Macromolecules*, 1994, **27**, 7550–7555.
6 T. Hertzsch, F. Budde, E. Weber and J. Hullinger, *Angew. Chem., Int. Ed.*, 2002, **41**, 2281–2284.
7 P. Sozzani, A. Comotti, S. Bracco and R. Simonutti, *Angew. Chem., Int. Ed.*, 2004, **43**, 2792–2797.
8 (*a*) H. Kobayashi, T. Ueda, K. Miyakubo, J. Toyoda, T. Eguchi and A. Tani, *J. Mater. Chem.*, 2005, **15**, 872–879; (*b*) H. Kobayashi, T. Ueda, K. Miyakubo, T. Eguchi and A. Tani, *Phys. Chem. Chem. Phys.*, 2008, **10**, 1263–1269.

9 G. Gahungu, B. Zhang and J. Zhang, *J. Phys. Chem. C*, 2007, **111**, 4838–4846.
10 A. Pangborn, M. Giardello, R. Grubbs, R. Rosen and F. Trimmers, *Organometallics*, 1996, **15**, 1518–1520.
11 A. L. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7–13.
12 V. Chandrasekhar, S. S. Krishnamurthy, H. Manohar, A. R. V. Murthy, R. A. Shaw and M. Woods, *J. Chem. Soc., Dalton Trans.*, 1984, (4), 621–625.
13 J. M. E. Goldschmidt and R. J. Goldstein, *J. Chem. Soc., Dalton Trans.*, 1981, (6), 1283–1288.
14 *CRC Handbook of Chemistry and Physics*, ed. D. R. Lide, CRC Press, 89th Edition, 2009.
15 S. Besli, S. J. Coles, D. B. Davies, M. B. Hursthouse, A. Kilic and R. A. Shaw, *Dalton Trans.*, 2007, (26), 2792–2801.
16 J. F. Bickley, R. Bonar-Law, G. T. Lawson, P. I. Richards, F. Rivals, A. Steiner and S. Zacchini, *Dalton Trans.*, 2003, (7), 1235–1244.

