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Formation of novel spiro, spiroansa and dispiroansa derivatives of cyclotetraphosphazene from the reactions of polyfunctional amines with octachlorocyclotetraphosphazatetraene

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Abstract. Nucleophilic substitution reactions of $N_4P_4Cl_8$, with di-, tri-, and tetra-functional reagents such as N-methyl-1,3-propanediamine, N,N′-methyl-1,3-propanediamine, spermidine and spermine were investigated in this study. Six novel products were isolated whose structures have been characterized by elemental analysis, mass spectrometry, ^1H and ^{31}P NMR spectroscopy. The structure of (**11**) was investigated by X-ray crystallography.

Keywords. Cyclotetraphosphazenes; ^{31}P NMR spectroscopy; amino phosphazenes; spiro-phosphazene; X-ray.

1. Introduction

Phosphazenes are important compounds from which a large number of organophosphazenes can be derived by the reaction with nucleophiles. Organophosphazenes find a variety of applications in science and technology[1] including hydraulic fluids and lubricants,[2,3] electrical conductivity,[4] ionic liquids,[5] liquid crystalline materials,[6] tumour growth inhibitor,[7] ferroelectric and non-linear optical polymers,[8a] biomedical materials,[9] membrane polymer solid electrolytes, drug carrier, and flame retardents,[10,11] etc. Furthermore, chiral substituted cyclophosphazenes in principle should also be useful as bases in chiral catalysis and for chiral polymers.[8b] Some aminocyclophosphazenes such as octapyrrolidinocyclotetraphosphazene[12] have significant anticancer reagents[13] and some of them are also used as antimicrobial agents.[14] The reactions of hexachlorocyclotriphosphazatriene, $N_3P_3Cl_6$, with di-, tri- and tetra-functional amines have been extensively studied[15-18] and especially large difunctional diamines were reported for a potential value in cancer chemotherapy as selective carriers for delivering anticancer drugs to malignant target cells.[19,20] Although, a large number of octachlorocyclotetraphosphazatetraene (**1**), $N_4P_4Cl_8$, with monofunctional amines were prepared and studied,[21–31] discussion on a substitution with polyfunctional amines is relatively limited in the literature.[32–37]

We report here, the synthesis and structural characterization of six new cyclotetraphosphazene derivatives (scheme 1) and, to the best of our knowledge, there is no report so far of any derivative in this series that has been structurally characterized by any spectral data or x-ray crystallography.

2. Experimental

2.1 *Materials*

Octachlorocyclotetraphosphazatetraene (a gift from the Otsuka Chemical Co. Ltd.) was purified by fractional crystallization from *n*-hexane. Spermidine (Fluka 99·0%) and spermine (Fluka 99·0%), N,N′-Methyl-1,3-propanediamine (Fluka 97·0%), N-Methyl-1,3-pro-panediamine (Alfa Aesar 99·0%) were used as received. The following chemicals were obtained from Merck; CH_2Cl_2 (≥ 99·0%), *n*-hexane (≥ 99.0%), $CHCl_3$ (99·0–99·4%), THF

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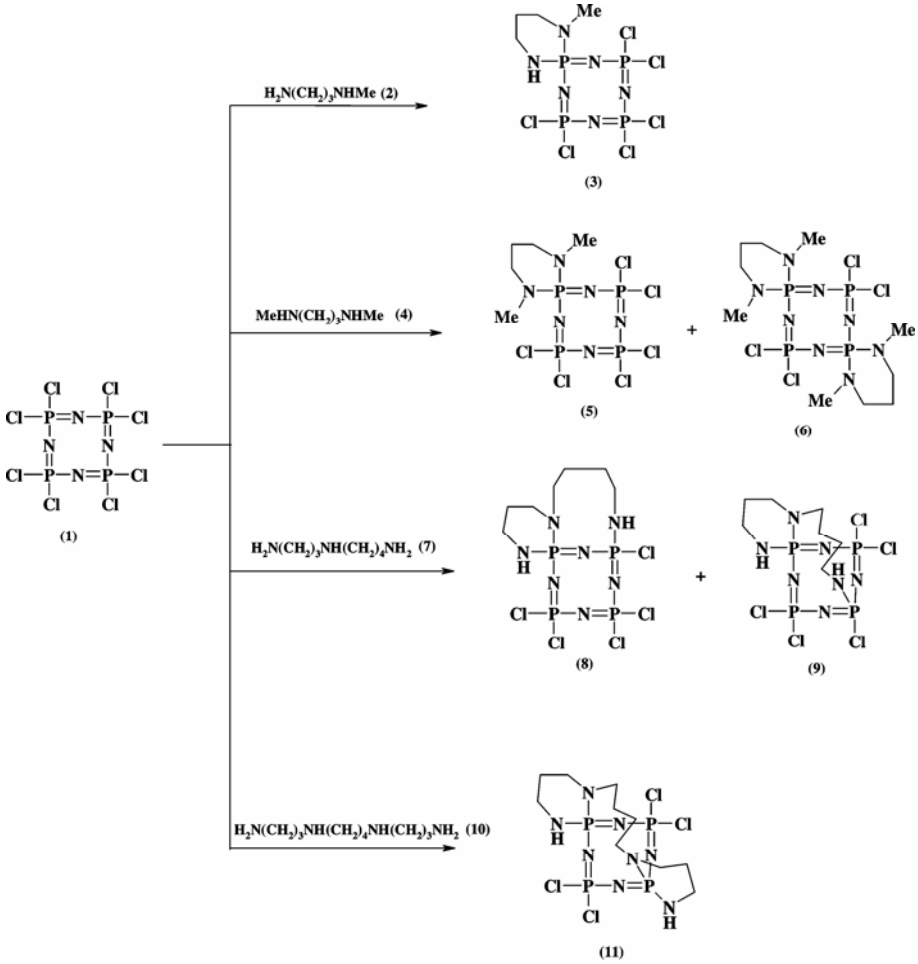


Scheme 1. The synthesis of cyclotetraphosphazene derivatives.

(≥ 99·0%). THF was distilled over a sodium–potassium alloy under an atmosphere of dry argon. All solvents used in this work were purified by conventional methods. The deuteriated solvent ($CDCl_3$) for NMR spectroscopy was obtained from Goss Scientific.

2.2 *Methods*

Elemental analyses were obtained using a Carlo Erba 1106 Instrument. Mass spectra were an Bruker MicrOTOF LC/MS spectrometer using Electro Spray Ionisation (ESI); ^{35}Cl values were used for calculated masses. Analytical thin layer chromatography (TLC) was performed on silica gel (Merck, Kieselgel 60, 0·25 mm thickness) with F_{254} indicator. Column chromatography was performed on silica gel (Merck, Kieselgel 60, 70–230 mesh; for 3 g crude mixture, 100 g silica gel was used in a column of 3 cm in diameter and 60 cm in length). ^1H and ^{31}P NMR spectra were recorded in $CDCl_3$ solutions on a Varian INOVA 500 MHz spectrometer using TMS as an internal reference for ^1H NMR and 85% H_3PO_4 as an external reference for ^{31}P.

2.3 *Synthetic procedures*

2.3a *Synthesis of 8, 8, 10, 10, 12, 12-hexachloro-1-methyl-1, 5, 7, 9, 11, 13-hexaaza-6λ⁵, 8λ⁵, 10λ⁵, 12λ⁵-tetraphosphaspiro [5.7]trideca-6, 8, 10, 12-tetraene (3)*: A solution of **(1)** (3 g, 6·4 mmol) in THF 70 mL was added drop-wise to a stirred solution of **(2)** (1·14 g, 12·8 mmol) in THF 30 mL. The reaction mixture was stirred under an atmosphere of argon at room temperature for a further 3 days and then N-methyl-1, 3-propanediamine dihydrochloride was filtered off and the solvent was removed under reduced pressure at 30°C, and the resulting colourless oil was subjected to column chromatography, using *n*-hexane-dichloromethane (1 : 3) as eluent.

Table 1. Analytical data of cyclotetraphosphazenes.

Comp.	Formula	Anal. data (%) Calculated N	C	H	Found N	C	H	MASS $[M+H]^+$	M
3	$C_4H_{10}Cl_6N_6P_4$	17·55	10·03	2·11	17·51	10·00	2·07	478·9	478
5	$C_5H_{12}Cl_6N_6P_4$	17·05	12·19	2·45	17·15	12·22	2·48	492·9	492
6	$C_{10}H_{24}Cl_4N_8P_4$	21·46	23·01	4·63	21·50	23·09	4·66	523·1	522
8	$C_7H_{16}Cl_5N_7P_4$	19·63	16·84	3·23	19·68	16·81	3·25	500·0	499
9	$C_7H_{16}Cl_5N_7P_4$	19·63	16·84	3·23	19·67	16·79	3·26	500·1	499
11	$C_{10}H_{22}Cl_4N_8P_4$	21·55	23·10	4·26	21·51	23·13	4·22	521·1	520

One product was **(3)** (yield 11%, m.p. 119–120°C) isolated as white powder. ^{1}H NMR: δ = 3·1 ppm (*m*, 2H, NCH_2 (spiro)), δ = 2·8–3·2 ppm (*m*, 2H, $NHCH_2$ (spiro)), δ = 2·7 ppm (*s*, 3H, CH_3), δ = 1·5 ppm (*m*, 2H, CH_2 (spiro)); 2·5 ppm (*s*, 1H, NH).

2.3b *Synthesis of 8, 8, 10, 10, 12, 12-hexachloro-1, 5-dimethyl-1, 5, 7, 9, 11, 13-hexaaza-6λ^5, 8λ^5, 10λ^5, 12λ^5-tetraphosphaspiro[5.7]trideca-6, 8, 10, 12-tetraene (***5***) and 8, 8, 17,17-tetrachloro-1,5,11,15-tetramethyl-1, 5, 7, 9, 11, 15, 16, 18-octaaza-6λ^5, 8λ^5, 10λ^5, 17λ^5-tetraphosphadispiro[5.3.5.3]octa-deca-6 (*18*), 7, 9, 16-tetraene (***6***)*: A solution of **(1)** (2 g, 4·3 mmol) in THF 70 mL was added drop-wise to a stirred solution of **(4)** (0·88 g, 8·6 mmol) in THF 30 mL. The reaction mixture was stirred under an atmosphere of argon at room temperature for a further 3 days and then N,N′-methyl-1,3-propanediamine dihydrochloride was filtered off and the solvent was removed under reduced pressure at 30°C and the resulting colourless oil was subjected to column chromatography, using CH_2Cl_2-*n*-hexane (3 : 1) as eluent. Compound **(5)** (yield 18%, m.p. >250°C) is white powder. ^{1}H NMR: δ = 3·1 ppm (*m*, 4H, NCH_2 (spiro)), δ = 2·7 ppm (*s*, 6H, CH_3), δ = 1·5 ppm (*m*, 2H, CH_2 (spiro)) and **(6)** (yield 6%) is viscous oil. ^{1}H NMR: δ = 3·1 ppm (*m*, 8H, NCH_2 (spiro)), δ = 2·7 ppm (*s*, 12H, CH_3), δ = 1·5 ppm (*m*, 4H, CH_2 (spiro)).

2.3c *Synthesis of 2, 2, 4, 4, 6-pentachloro-6, 8, 9, 10, 11, 14, 15, 16-octahydro-7H,13H-17, 6-epi-azeno-2λ^5, 4λ^5, 6λ^5, 17λ^5-[1, 3, 2]diazaphosphinino [1, 2-a][1, 3, 5, 7, 9, 2, 4, 6, 8]pentaazatetraphos-phacyclotridecine (***8***) and 2, 2, 4, 17, 17-penta-chloro-4, 6, 7, 8, 9, 12, 13, 14-octahydro-5H, 11H-15, 4-(epiazenophosphenoazeno)-2λ^5, 4λ^5, 15λ^5-[1, 3, 2]diazaphosp-hinino[1, 2-a][1, 3, 5, 7, 2, 4, 6]tetraazatriphosphacycloundecine (***9***)*: A solution of **(1)** (2 g, 4·31 mmol) in $CHCl_3$ 60 mL was added drop-wise to a stirred solution of **(7)** (1·25 g, 8·63 mmol) in $CHCl_3$ 60 mL. The reaction mixture was stirred under an atmosphere of argon at room temperature for a further 3 days and then spermidine trihydrochloride was filtered off and the solvent was removed under reduced pressure at 30°C, and the resulting colourless oil was subjected to column chromatography, using CH_2Cl_2-*n*-hexane (4 : 1) as eluent. Compound **(8)** (yield 21%, m.p. 177°C) was recrystallized from CH_2Cl_2-*n*-hexane (1 : 1). ^{1}H NMR: δ = 3·2 ppm (*m*, 4H, $NHCH_2$(bridge)), δ = 3·1 ppm (*m*, 4H, $NHCH_2$ (spiro) and NCH_2 (spiro)), δ = 2·3 ppm (*m*, 2H, NCH_2 (bridge)), δ = 1·5–1·1 ppm (*m*, 4H CH_2 (bridge)); 2·5 ppm (*s*, 2H, NH). Compound **(9)** (yield 3%) was isolated as viscous oil. ^{1}H NMR: δ = 3·2 ppm (*m*, 4H, $NHCH_2$ (bridge)), δ = 3·0 ppm (*m*, 4H, $NHCH_2$ (spiro) and NCH_2 (spiro)), δ = 2·4 ppm (*m*, 2H, NCH_2 (bridge)), δ = 1·5–1·3 ppm (*m*, 4H CH_2(bridge)); 2.5 ppm (*s*, 2H, NH).

2.3d *Synthesis of 17, 17, 19, 19-tetrachloro-1, 2, 3, 4, 7, 8, 11, 12, 13, 14-decahydro-6H, 9H-15, 21-epiazeno-15λ^5, 17λ^5, 19λ^5, 21λ^5-bis[1, 3, 2]diaza-phosphinino[1, 2-a : 2′, 1′-h][1, 3, 5, 7, 9, 2, 4, 6, 8]pentaazatetraphosphacyclotridecine (***11***)*: A solu-tion of **(1)** (2 g, 4·31 mmol) in $CHCl_3$ 60 mL was added dropwise to a stirred solution of **(10)** (1·75 g, 4·31 mmol) in $CHCl_3$ 60 mL. The reaction mixture was stirred under an atmosphere of argon at room temperature for a further 3 days and then spermine tetrahydrochloride was filtered off and the solvent was removed under reduced pressure at 30°C, and the resulting colourless oil was subjected to column

chromatography, using *n*-hexane-THF (2 : 1) as eluent. Compound (**11**) (Yield 15%, m.p.: >250°C) was recrystallized from CH_2Cl_2-*n*-hexane (1 : 1). ^{1}H NMR: δ = 3·1–3·2 ppm (*m*, 8H, NCH_2 (spiro)); 2·2–2·3 ppm (*m*, 4H, NCH_2 (bridge)); 1·5 ppm (*m*, 4H, CH_2 (bridge)); 1·4 ppm (*m*, 4H, CH_2 (spiro)); 2·5 ppm (*s*, 2H, NH). Analytical data of these compounds are given in table 1.

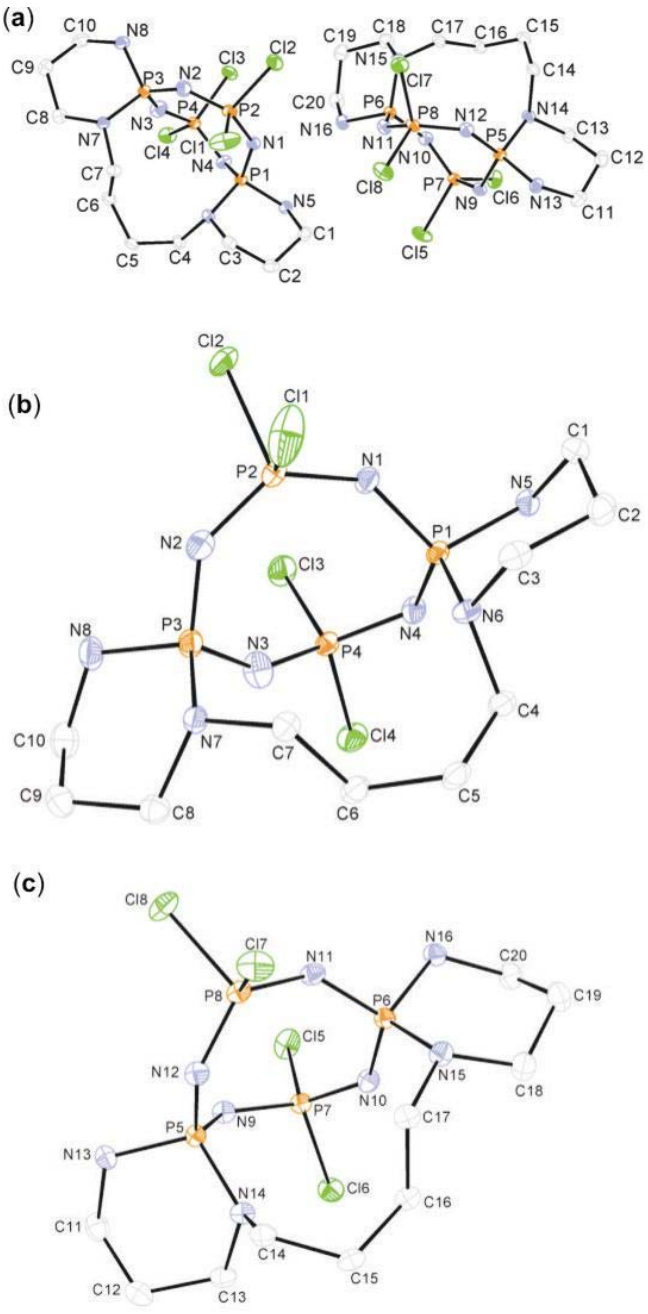


Figure 1. **a**. An ORTEP[40] drawing of the asymmetric unit with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. **b**, **c**, ORTEP[40] drawings of each molecules in the asymmetric unit with the atom -numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

2.4 *X-Ray crystallography*

Colourless crystals of (**11**) were crystallized from CH_2Cl_2-*n*-hexane. The molecular structure of compound along with the atom-numbering schemes are depicted in figures 1a–c, 2a and 2b. Crystallographic data are listed in table 2 and selected bond lengths and angles are given in table 3. Crystallographic data were collected on a Bruker Kappa APEXII diffractometer using MoK_α radiation (λ = 0·71073 Å) at T = 100(2) K. Absorption correction by multi-scan[38] was applied. Structure was solved by direct

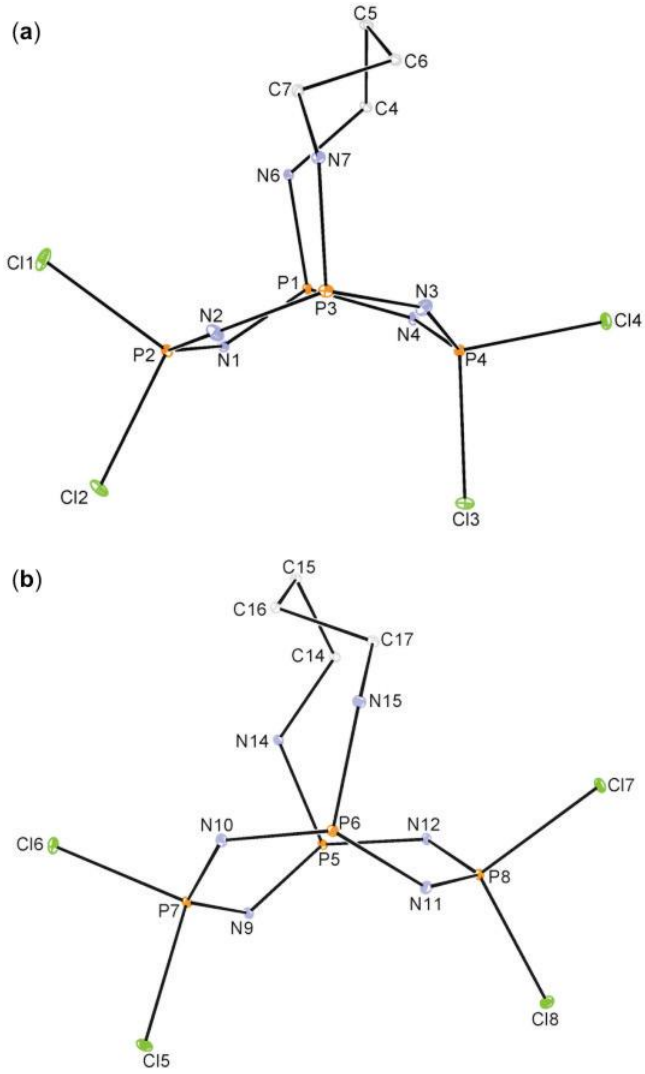


Figure 2. **a, b.** The conformations of the phosphazene and the macro ring for each molecule in the asymmetric unit with the atom-numbering scheme.

methods[39] and refined by full-matrix least squares against F^2 using all data.[39] All non-H atoms were refined anisotropically. The H atom positions were calculated geometrically at distances of 0·97 Å (CH_2) from the parent C atoms; a riding model was used during the refinement process and the U_{iso} (H) values were constrained to be 1·2 U_{eq} (carrier atom).

3. Results and discussion

3.1 *Synthesis*

The reactions of $N_4P_4Cl_8$ with polyfunctional (di-, tri- and tetra-functional) amines were studied in four sections:

(i) The compound **(3)** was synthesized from the reaction of $N_4P_4Cl_8$ with **(2)** at 1 : 2 molar ratio in dry THF for three days at room temperature under argon atmosphere;
(ii) Compounds **(5)** and **(6)** were obtained from the reaction of $N_4P_4Cl_8$ with **(4)** at the same experimental condition of (i).
(iii) The cyclotetraphosphazene derivatives **(8)** and **(9)** were synthesized from the reaction $N_4P_4Cl_8$ with **(7)** at 1 : 2 molar ratio at room temperature in $CHCl_3$ for three days;
(iv) The compound **(11)** was synthesized from the reaction of $N_4P_4Cl_8$ with **(10)** at the same experimental condition of (iii).

Table 2. Crystallographic data of (**11**).

Empirical formula	$C_{10}H_{20}Cl_4N_8P_4$
Fw	518·02
Crystal system	monoclinic
Space group	*Pn*
a (Å)	12·683(2)
b (Å)	12·777(4)
c (Å)	12·706(3)
α (°)	90·00
β (°)	92·86(3)
γ (°)	90·00
V (Å^3)	2056·5(9)
Z	4
μ (cm^{-1})	0·902 (MoK$_\alpha$)
ρ (calcd) (g cm^{-1})	1·673
Number of reflections total	121009
Number of reflections unique	10957
R_{int}	0·0407
$2\theta_{max}$ (°)	59·30
T_{min}/T_{max}	0·655/0·763
Number of parameters	470
R [$F^2 > 2\sigma(F^2)$]	0·0323
wR	0·0778

The preparation and spectral data of monospirobino-**(12)**, *bis*-spirobinospermidine **(13)** and dispirobinospermine cyclotetraphosphazene **(14)** derivatives have been reported elsewhere.[35] (iii) and (iv) are different methods which were employed for the synthesis of **(12)**, **(13)** and **(14)**.

In this work, the spectral data of **(12)**, **(13)** and **(14)** are given for comparison purposes in table 4.

Compounds **(3)**, **(5)**, **(8)** and **(11)** were obtained as white solids while **(6)** and **(9)** were obtained as viscous oils. In general, all products, especially the compounds **(6)** and **(9)**, were obtained in low yields after purification using a silica gel column. The reason for the low yield is attributed to the reactivity of the P–Cl bonds. After substitution of one of the chlorine atoms, the remaining P–Cl bonds become very reactive and give multiple substituted products. Also, due to the structural flexibility of $N_4P_4Cl_8$, the eight-membered ring is significantly more reactive than the planar six-membered trimer ring.[10,23,41] Although several minor multiple substituted products, which were detected by TLC using CH_2Cl_2-*n*-hexane (1 : 1) as mobile phase, were different from the main products **(3)**, **(5)**, **(6)**, **(8)**, **(9)** and **(11)**, separation of these minor products could not be achieved by column chromatography. Compounds **(3)**, **(5)** and **(6)** were found to be stable air whereas products obtained from the reaction of $N_4P_4Cl_8$ with *N*-methylethanolamine, 1, 2-diaminoethane were unstable in the earlier study.[33] **(8)**, **(9)** and **(11)** were also found to be stable air.

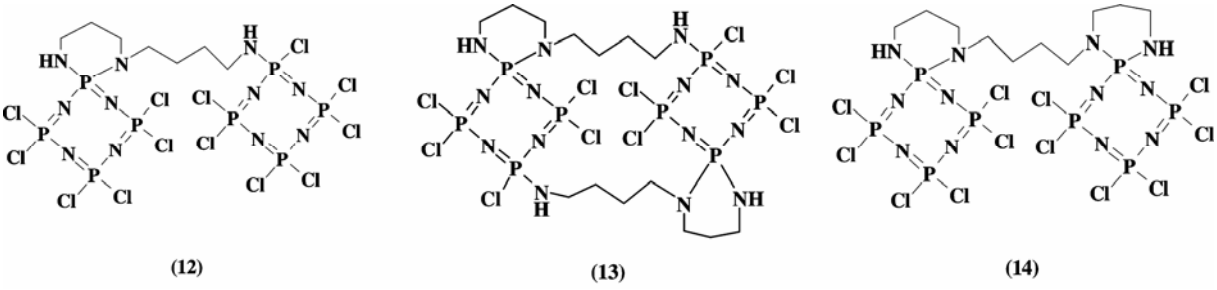
3.2 *Spectroscopy*

Compounds **(3)**, **(5)**, **(6)**, **(8)**, **(9)** and **(11)** were characterized by elemental analysis, mass spectrometry and ^{1}H and ^{31}P NMR spectroscopy. The MS spectra of phosphazene derivatives show the protonated $(M + H)^+$ peaks and the elemental analysis results are in good agreement with the proposed structures as shown in scheme 1 (table 1).

The ^{31}P NMR spectral data of **(3)**, **(5)**, **(6)**, **(8)**, **(9)**, **(11)** are given in table 4.

The proton decoupled ^{31}P NMR spectrum (A_4 type) of $N_4P_4Cl_8$ shows a singlet in figure 3a because of the chemical environment equivalence of all the phosphorus nuclei.

The proton decoupled ^{31}P NMR spectrum of the compound **(3)** in figure 3b exhibits an ABC_2 type spectrum due to three different phosphorus environments within the molecule. The chemical shifts and



(12) (13) (14)

Table 3. The selected bond lengths (Å) and angles (°) for (**11**).

P1-N1	1·604 (2)	P5-N9	1·600 (2)
P1-N4	1·594 (2)	P5-N12	1·588 (2)
P1-N5	1·665 (2)	P5-N13	1·661 (2)
P1-N6	1·647 (2)	P5-N14	1·655 (2)
P2-N1	1·557 (2)	P6-N10	1·600 (2)
P2-N2	1·546 (3)	P6-N11	1·589 (2)
P2-Cl1	2·0315 (12)	P6-N15	1·661 (2)
P2-Cl2	2·0051 (11)	P6-N16	1·652 (2)
P3-N2	1·579 (3)	P7-N9	1·562 (2)
P3-N3	1·606 (3)	P7-N10	1·554 (2)
P3-N7	1·659 (2)	P7-Cl5	2·0211 (10)
P3-N8	1·629 (2)	P7-Cl6	2·0299 (11)
P4-N3	1·532 (3)	P8-N11	1·546 (2)
P4-N4	1·567 (2)	P8-N12	1·565 (2)
P4-Cl3	2·0350 (10)	P8-Cl7	2·0276 (10)
P4-Cl4	2·0127 (11)	P8-Cl8	2·0132 (10)
N1-P1-N4	116·09 (12)	N9-P5-N12	119·09 (12)
N1-P1-N5	108·39 (12)	N9-P5-N14	108·57 (12)
N4-P1-N6	112·81 (12)	N12-P5-N13	105·85 (12)
N5-P1-N6	104·13 (12)	N13-P5-N14	108·71 (12)
N1-P2-N2	126·08 (13)	N10-P6-N11	116·15 (12)
N3-P3-N2	115·49 (14)	N10-P6-N15	109·12 (12)
N2-P3-N8	106·89 (14)	N11-P6-N16	105·36 (12)
N3-P3-N7	108·29 (13)	N15-P6-N16	105·39 (12)
N7-P3-N8	102·49 (12)	N9-P7-N10	124·16 (12)
N3-P4-N4	122·89 (13)	N11-P8-N12	123·75 (12)
P1-N1-P2	138·86 (12)	P5-N9-P7	129·15 (15)
P2-N2-P3	139·02 (17)	P6-N10-P7	133·42 (16)
P3-N3-P4	148·23 (19)	P6-N11-P8	137·36 (16)
P1-N4-P4	127·05 (15)	P5-N12-P8	132·28 (15)
C1-N5-P1	114·65 (17)	C11-N13-P5	113·35 (18)
C3-N6-P1	112·95 (17)	C13-N14-P5	112·57 (17)
C3-N6-C4	113·9 (2)	C14-N14-P5	122·70 (18)
C4-N6-P1	121·64 (18)	C13-N14-C14	115·4 (2)
C7-N7-P3	115·87 (17)	C18-N15-P6	117·48 (18)
C8-N7-P3	115·87 (17)	C17-N15-P6	117·10 (18)
C7-N7-C8	113·1 (2)	C17-N15-C18	114·1 (2)
Cl0-N8-P3	115·93 (19)	C20-N16-P6	115·14 (18)

the two coupling constant values of (Pspiro and PCl_2) are similar to that of (**12**) and (**13**) (table 4).[35] The proton coupled ^{31}P NMR spectrum (not shown) of (**3**) shows that the compound (**2**) replaces two the chlorine atoms in compound (**1**). The signals at ca. 0·78 ppm (P_A) are multiplet. The signals of P_B and P_C ($\delta = -4{\cdot}95$ and $-6{\cdot}11$ ppm) remain unchanged.

The proton decoupled ^{31}P NMR spectrum of the compound (**5**) in figure 3c exhibits an ABC_2 type spectrum similar to that of compound (**3**). The

Table 4. ^{31}P NMR parameters for cyclotetraphosphazenes.

Compd.	Ref.	δ (^{31}P NMR)[ppm]			^{2}J(PP) [Hz]			
		P(Nspiro)	P(NHR)Cl	PCl_2	P(Nspiro)–PCl_2	P(Nspiro)–P(NHR)	P(NHR)Cl PCl_2	PCl_2–PCl_2
1	This work	–	–	–5·4	–	–	–	–
3	This work	0·78	–	–4·95 –6·11	27·4	–	–	27·8
5	This work	3·08	–	–5·07 –8·54	27·3	–	–	26·6
6	This work	3·53	–	–8.94	27·1	–	–	–
8	This work	0·18	6·26	–1·37 –3·71	26·3	39·8	–	22·4
9	This work	8·38	–2·09	–3·73	31·2	–	31·8	–
1	This work	1·06	–	–3·34	28·5	–	–	–
12	35	–0·35	–5·2	–2·8 –6·9 –4·4 –7·1	27·6	–	27·3	38·8 33·3
13	35	6·1	–0·1	–1·6 –3·8	25·5	39·15	–	21·9
14	35	–0·6	–	–5·3 –7·3	28·0	–	–	26·85

chemical shift of P(spiro)(P_A) is 3·08 ppm and this value is more downfield in contrast to that of (**3**) (table 4). The proton coupled ^{31}P NMR spectrum (not shown) of (**5**) is similar to that for compound (**3**).

The proton decoupled ^{31}P NMR spectrum (A_2X_2 spin system) of (**6**) consisting of two triplets is shown in figure 3d. Based on the similar product, $N_4P_4Cl_4[N(i\text{-}Pr)(CH_2)_3N(i\text{-}Pr)]_2$, given in the literature,[32] we suggest that the compound (**6**) should be the most possible product. The proton coupled ^{31}P NMR spectrum (not shown) indicates that two different singlets appear as multiplets (P_A) and triplet (P_X).

The ^{2}J(P–N–P) values for compounds (**3**), (**5**), (**6**) are lower than that for $N_3P_3Cl_4(HN(CH_2)_3N(CH_3)]$.[42a] It appears that this is a general trend for (amino) cyclophosphazenes.[32,42b]

The proton decoupled ^{31}P NMR spectrum of the compound (**8**) in figure 4a gives an ABCD type spectrum because of four different phosphorus environments within the molecule. The compounds (**12**) and (**13**) had two A_2BC and two ABCD types spectra in earlier work, respectively.[35] The doublet at $\delta = -3{\cdot}71$ ppm is caused by PCl_2 group (P_D) in figure 4a and the coupling constant of this group was calculated as $^{2}JP_CP_D = 22{\cdot}4$ Hz (table 4). The proton coupled ^{31}P NMR spectrum of (**8**) show that the spermidine replaces three chlorine atoms in compound (**1**). The signals at ca. 0·18 ppm (P_A) and 6·26 ppm (P_B) are seen as multiplets and the signals of PCl_2 groups ($\delta = -1{\cdot}37$ and $-3{\cdot}71$ ppm) remain unchanged (figure 4b).

The proton decoupled ^{31}P NMR spectrum (ABC_2 spin system) of compound (**9**) possessing three sets of triplets corresponding to the Pspiro (P_A), P(NHR)Cl (P_B) and the PCl_2 groups (P_C) are shown in figure 5a. The proton coupled ^{31}P NMR spectrum (not shown) of (**9**) indicates that the multiplets corresponds to Pspiro group ($\delta = 8{\cdot}38$ ppm) and (NHR)Cl group ($\delta = -2{\cdot}09$ ppm). The signals of the PCl_2 groups ($\delta = -3{\cdot}73$ ppm) remain unchanged.

The proton decoupled spectrum of (**11**) in figure 5b has an A_2B_2 spectrum. The spin system of this spectrum is different from (**14**) (ABCD type)[35] since the two triplets are seen at ca. ($\delta = 1{\cdot}06$ (P_A) (PNspiro) and $-3{\cdot}34$ ppm (P_B)(PCl_2)), but the two coupling constant of P(Nspiro-PCl_2)(P_AP_B) is 28·5 Hz similar to that of (14).[35] The proton coupled ^{31}P NMR spectrum (not shown) of (**11**) shows that the spermine replaces four chlorine atoms in compound (**1**). Two different singlets are seen as multiplets (P_A) and triplet (P_B).

3.3 *X-ray analysis*

In order to further corroborate the structural assignments, single crystal X-ray structure of compound (**11**) is reported. The asymmetric unit contains two crystallographically independent molecules as given in figures 1a–c, respectively. The phosphazene con-

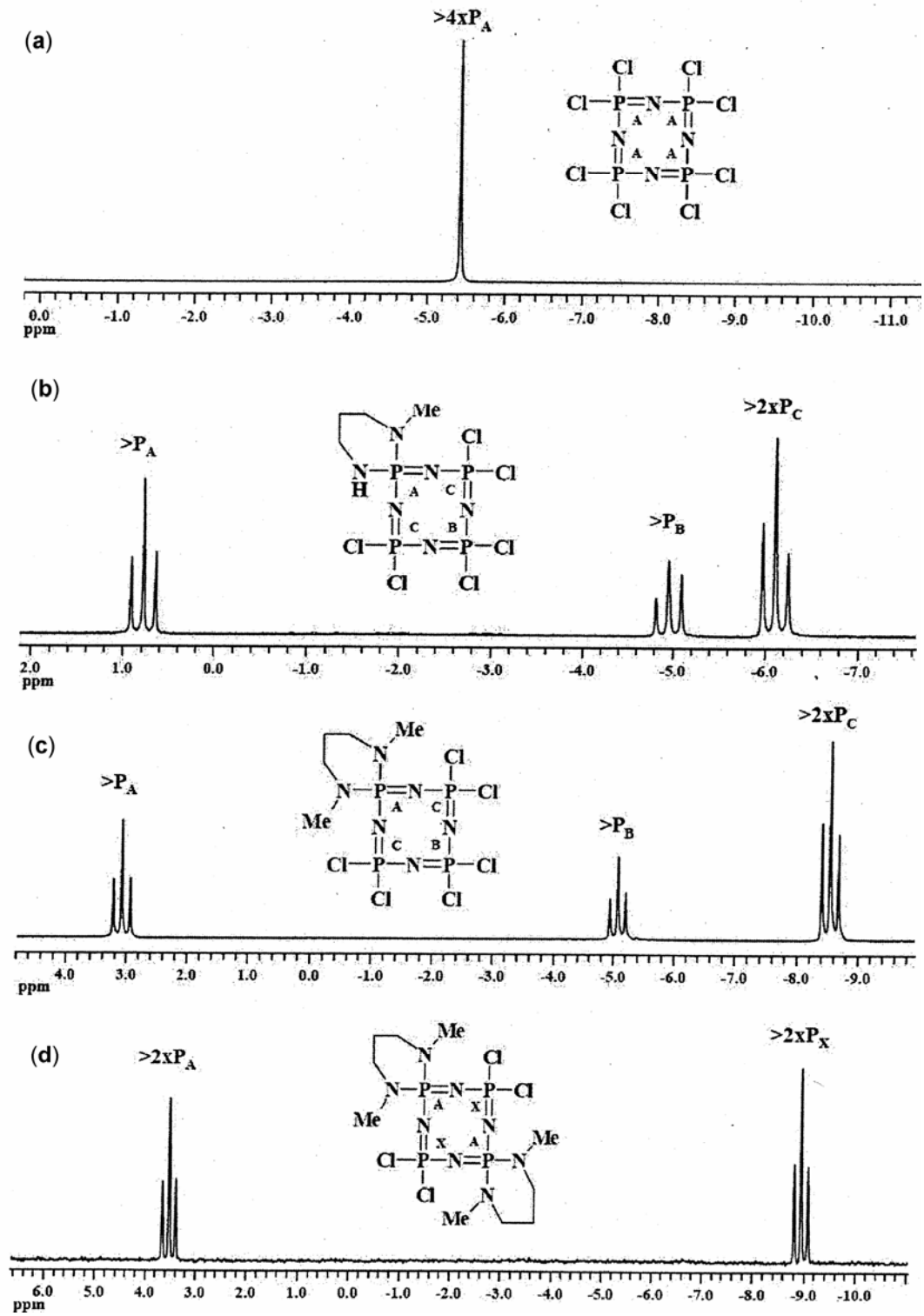


Figure 3. Proton decoupled ^{31}P NMR spectra of (**a**) (**1**); (**b**) (**3**); (**c**) (**5**) and (**d**) (**6**).

sists of an eight-membered ring, $(PN)_4$, with the two P atoms in the ring being bridged by a macro-ring. The other P atoms have chloride atoms attached. The maximum separations between the two non-bridged P atoms in each molecule are P2 … P4 3·902(3) Å and P7 … P8 3·973(3) Å. All other P … P distances in the two molecules are in the ranges 2·829(3)–4·070(3) and 2·856(3)–3·973(3) Å, with means of 3·161(3) and 3·105(3) Å, respectively. The N atoms are displaced above (+) and

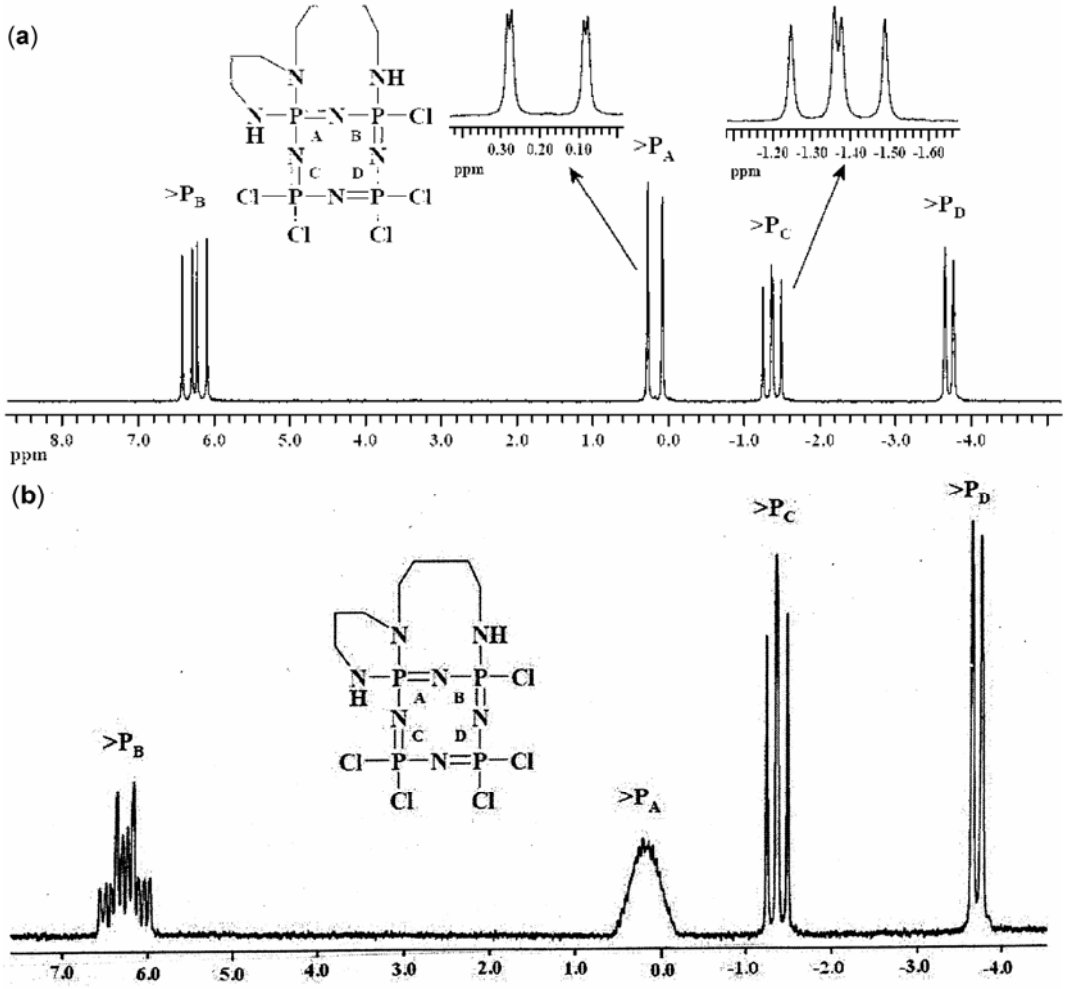


Figure 4. (**a**) Proton decoupled ^{31}P NMR spectrum of (**8**); (**b**) Proton coupled ^{31}P NMR spectrum of (**8**).

below (–) to the least-squares planes through the P atoms by the following distances: N1 0·394(2), N2 0·046(3), N3 –0·259(3), N4 0·023(2) and N9 0·555(2), N10 –0·380(2), N11 0·470(2), N12 –0·262(2) Å.

The phosphazene rings are not planar, and are twisted (figure 5a; $\varphi_2 = -177{\cdot}80$ (18)°, $\varphi_3 = -124{\cdot}26(32)°$, $\theta_2 = 69{\cdot}16(13)°$ and $\theta_3 = 111{\cdot}45(35)°$] and twisted [figure 5b; $\varphi_2 = 135{\cdot}05(15)°$, $\varphi_3 = 179{\cdot}15(9)°$, $\theta_2 = 38{\cdot}70(18)°$ and $\theta_3 = 95{\cdot}60(9)°$] conformations having total puckering amplitudes[43] Q_T of 0·871(2) Å and 1·465(6) Å, respectively. The six-membered rings (P1/N5/N6/C1–C3), (P3/N7/N8/C8–C10), (P5/N13/N14/C11–C13) and (P6/N15/N16/C18–C20) are in chair conformations [$Q_T = 1{\cdot}085(6)$ Å, $\varphi_2 = -32{\cdot}4$ (3)° and $\theta_2 = 122{\cdot}6(1)°$; $Q_T = 1{\cdot}095(8)$ Å, $\varphi_2 = 143{\cdot}9(3)°$ and $\theta_2 = 53{\cdot}2(1)°$; $Q_T = 1{\cdot}017(7)$ Å, $\varphi_2 = -32{\cdot}7(4)°$ and $\theta_2 = 126{\cdot}1(1)°$; $Q_T = 0{\cdot}098(7)$ Å, $\varphi_2 = -32{\cdot}1(4)°$ and $\theta_2 = 128{\cdot}5(1)°$, respectively]. As expected, the macrocyclic rings are non-planar with the puckering amplitudes Q_T of 2·233(2) Å and 1·501(2) Å; 1·964 (2) Å and 1·955(2) Å, respectively. The average P–N bond lengths in phosphazene rings are 1·573(3) and 1·576(2) Å, which are shorter than the average exocyclic P–N bonds of 1·650(2) and 1·657(2) Å, respectively. The sum of the bond angles around the N atoms in the eleven-membered *spiro*-cyclic rings are 348·49 (18)° and 346·07(18)°; 350·67(18) and 348·68(18)°, respectively, which approve that the N atoms in have pyramidal geometries.

According to spectral data of (**3**), (**5**), (**6**), (**8**), (**9**) and (**11**), the compounds (**3**), (**5**) and (**6**) contain a N_4P_4 ring with six-membered spiro ring, whereas compound (**11**) is dispiroansa. On the other hand, spiroansa compounds (**8**) is tricyclic systems based on a single tetramer unit, six-membered spiro ring and nine-membered ansa ring. Furthermore, the structure of (**9**) is spirobino.

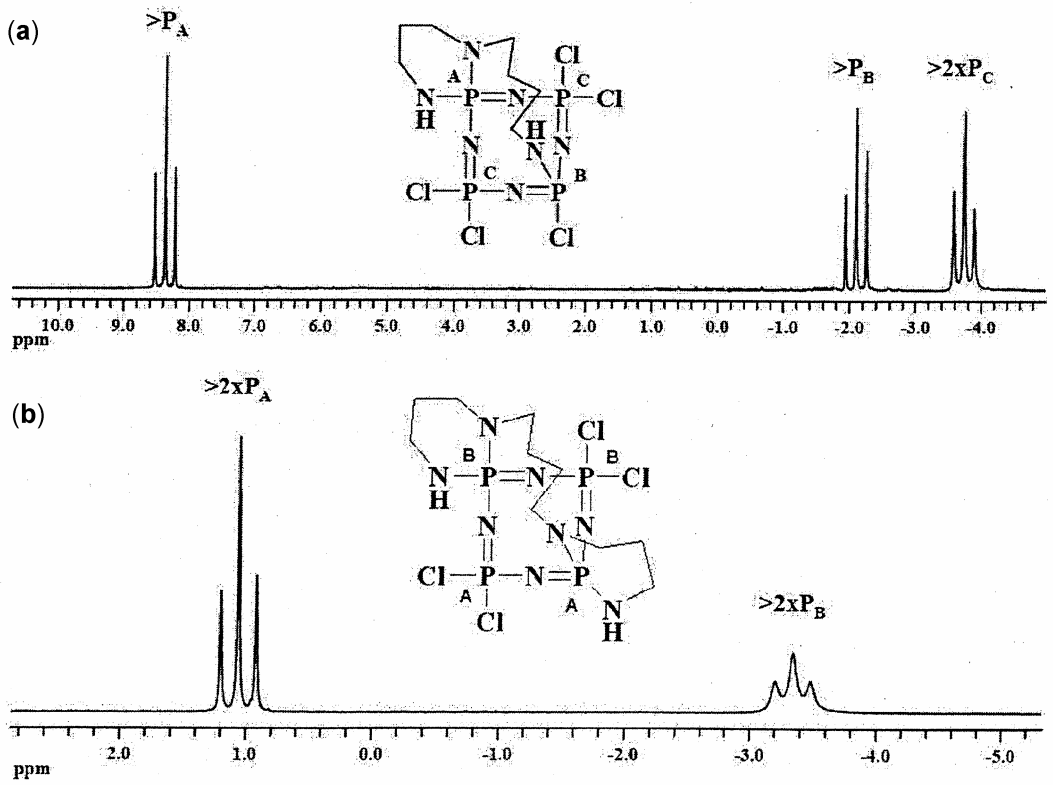


Figure 5. Proton decoupled ^{31}P NMR spectra of (**a**) (**9**), (**b**) (**11**).

4. Summary

The synthesis and characterization of novel mono-spiro N-methyl-propane-1,3-diamino (**3**), mono-(**5**), bis-spiro-N,N′-dimethyl- propane-1, 3-diamino-cyclotetraphosphazenes (**6**), two spiroansa phosphazenes (**8**) and (**9**) with spermidine and one dispiroansa cyclotetraphosphazene (**11**) with spermine were studied. These compounds could be useful as precursors for preparing other models of mixed-substituent phosphazenes since chiral systems and biological materials show chemotherapeutic or antimicrobial agent behaviours.

Supplementary data on crystallographic data for the structure reported here have been deposit at the CCDC as supplementary data, CCDC No 710330. Copies of the data can be on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK. e-mail: deposit@ccdc.cam.ac.uk.

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