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Reactions of cyclochlorotriphosphazatriene with 2-mercaptoethanol. Calorimetric and spectroscopic investigations of the derived products

Sedat Ture[a], Rafig Gurbanov[b], and Murat Tuna[c]

[a]Departments of Chemistry and Molecular Biology and Genetics, Bilecik Şeyh Edebali University, Bilecik, Turkey; [b]Departments of Chemistry, Faculty of Arts & Sciences, Bilecik Şeyh Edebali University, Bilecik, Turkey; [c]Department of Chemistry, Faculty of Arts & Sciences, Sakarya University, Sakarya, Turkey

ABSTRACT

The reactions of hexachlorocyclotriphosphazatriene, $N_3P_3Cl_6$ (**1**) with 2-mercaptoethanol, 2-HS-CH_2-CH_2-OH (**2**), in (1:1, 1:2 and 1:3) mole ratios, in excess of NaH, in THF and diethylether solutions yield a total of 6 novel products: one mono *spiro*, $N_3P_3Cl_4$[O-CH_2-CH_2-S] (**3**); one mono-substituted open chain, $N_3P_3Cl_5$[S-CH_2-CH_2-OH] (**4**); one *dispiro*, $N_3P_3Cl_2$[O-CH_2-CH_2-S]$_2$ (**5**); one tri-substituted open chain, $N_3P_3Cl_3$[S-CH_2-CH_2-OH]$_3$ (**6**); one tris-*spiro*, N_3P_3[O-CH_2-CH_2-S]$_3$ (**7**) and one disubstituted open chain, $N_3P_3Cl_4$[S-CH_2-CH_2-OH]$_2$ (**8**) derivatives. The *spiro* products (**3**, **5** and **7**) are formed as the major products in this system and all of the synthesized compounds are found to be stable at room temperature. The structures of the derived compounds were elucidated by elemental analysis, TLC-MS, ^{31}P and ^{1}H NMR spectral data. For evaluation of melting behavior of derivatives (**6**) and (**7**), thermal transition peaks and their corresponding enthalpies were determined via DSC technique.

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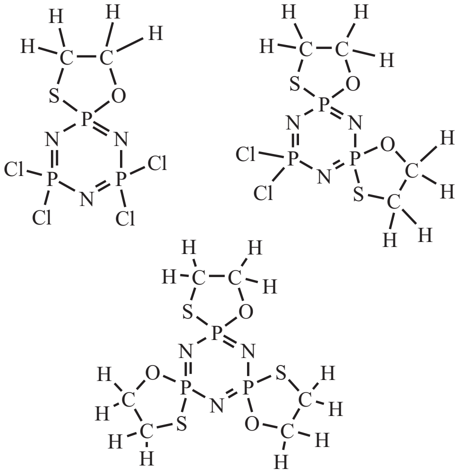
Hexachlorocyclotriphosphazene; 2-mercaptoethanol; spiro compounds; open chain compounds; DSC analysis

GRAPHICAL ABSTRACT



1. Introduction

The reactions of cylotriphosphazene (**1**) with difunctional nucleophilic reagents such as diamines and diols gave a great variety of different cyclophosphazene derivatives.[1–7] Cyclotriphosphazene (**1**), when reacting with difunctional reagents, can lead to the formation of different kind of products; an open chain (if only one of two functional groups react with **1**), *spiro*, *ansa* and bridged derivatives.[8–20] The selectivity of the nucleophilic substitution patterns and the formation of these products are strongly depended on temperature, solvent, base and the type of the nucleophilic reagent.[21–25] For example, the reactions of **1** with shorter chain length of the nucleophiles [-(CH_2-)$_n$, $n = 2$, 3, 4 moieties], when using pyridine as the base in diethylether or dichloromethane solution gave predominantly *spiro* formations.[1,8] On the other hand, the reaction of **1** with sodium tetraethyleneglycol in THF gave predominantly a *cis-ansa* structure.[13] The solvent effect plays an important role in determining the stereo and regio selective control on the cyclophosphazene rings.[21–24] However, reactions of **1** with longer chain length of nucleophiles gave overwhelmingly bridged

CONTACT Sedat Ture s.ture@yahoo.com; sedat.ture@bilecik.edu.tr Departments of Chemistry and Molecular Biology and Genetics, Bilecik Şeyh Edebali University, 1230 Bilecik, Turkey.

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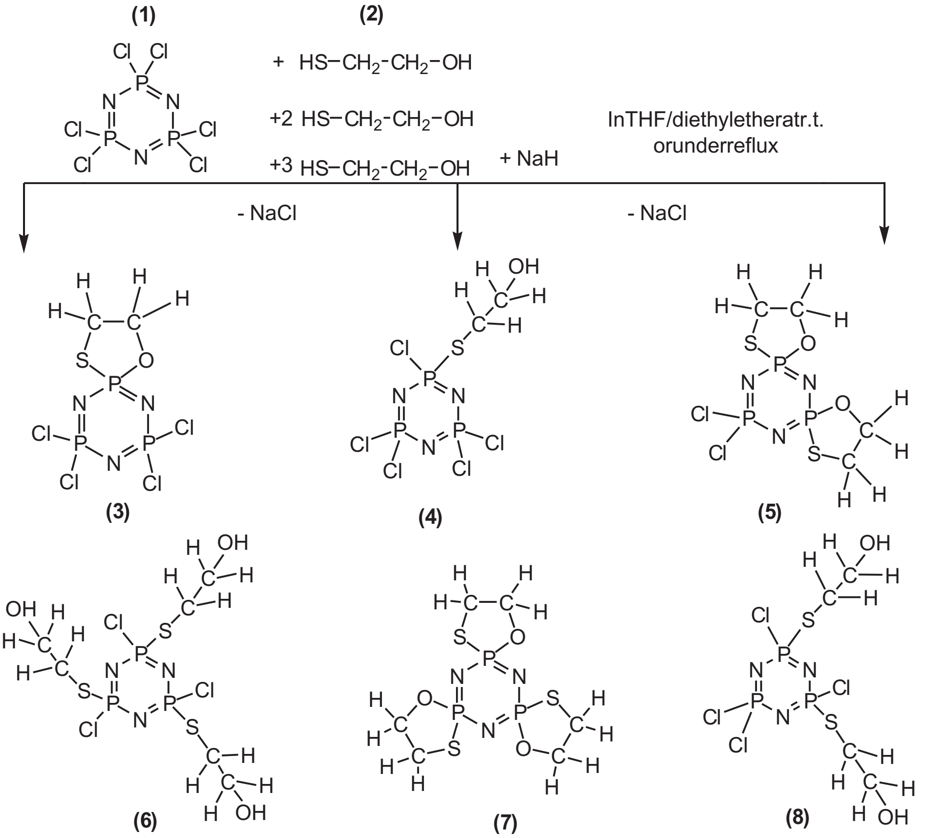


Figure 1. The reactions of cyclotriphosphazene (**1**) with 2-mercaptoethanol (**2**) and structures of the products.

derivatives, besides giving trace amounts of *ansa* formations.[1–3,24]

In this study, we wished to understand the reactivity and substitution patterns of cyclotriphosphazene (**1**) with shorter chain length of difunctional reagent (consist of HS- and –OH functional groups) and nucleophilic tendency to donate electrons or react at the electron-poor sites on the phosphorus atoms. On the one hand, 2-mercaptoethanol (**2**) is used as a chain transfer agent in processes where molecular weight control is critical and used for non-graphene synthesis for cellular imaging and drug delivery.[26a–c]

It is also used in the synthesis of multifunctional polymeric micelle employed in specific targeting of tumor degradation.[27a–d] On the other hand, cyclotriphosphazenes have a wide range of properties and applications such as electrical conductivity,[28] liquid crystals[29] and biomedical activities.[25,30] For this reason, in our next studies, we intend to examine the biological activities of the derived products (**3**-**8**). The structures of the cyclotriphosphazene derivatives are presented in Figure 1.

In THF/r.t. (1:1): **3**, **4** and **5**; in THF/under reflux (1:3): **5**, **6** and **7**; in diethylether/r.t. (1:2): **3**, **8** and **5**; in diethylether/r.t. (1:3): **3**, **5** and **6**.

In general, when an electrophile reacts with a difunctional nucleophile such as 2-mercaptoethanol (**2**), which contains both a thiol (HS-) and hydroxyl (HO-) group, and during the reaction, at first electrophile attack on the thiol moiety of the molecule. Reactions at the hydroxyl group is often not possible as long as the thiol group is not changed in a separate step using a protecting group to react previously.[31] As noted, it is presumed that the first substitution occurs on the HS- group and possibly later on the -OH group. However, the situation is different when working with phosphazenes. Due to the presence of chlorine groups (Cl or Cl_2) on the phosphorus atoms and since the phosphorus atoms are still open to new substitution reactions after the initial displacement (Cl with the HS- group), it remains possible for the hydroxyl group to attack on phosphorus atoms for second substitution.

The formation of the non-geminal product at the *ansa* stage would be anticipated from the steric effect, slower reactivity at low temperature as well as another term where the exocyclic substituent is too small and also weakly electron releasing of the both S_N1 and S_N2 pathways. Unless a very special changes in reaction conditions is made, it is unlikely to obtain the *ansa* type non-geminal cyclic structures with a shorter chain length of the nucleophile. Therefore, we were only able to obtain intramolecular geminal (*spirocyclic*) and non-geminal (open chain) products. Experimental details together with the product types are summarized in Figure 1 and ^{31}P and ^{1}H NMR data may be found in Tables 1 and 2.

2. Results and discussion

The reactions of $N_3P_3Cl_6$ (**1**) with one, two and three mole equivalents of 2-mercaptoethanol (**2**) were carried out in THF at 25°C and under reflux condition and in diethylether at 25°C. The following derivatives were synthesized and characterized: (**i**) mono *spiro* compound, $N_3P_3Cl_4$ [S-CH$_2$-

CH_2)-O] (**3**, in THF 0.82 g 48%); (**ii**) mono-substituted open chain compound, $N_3P_3Cl_5$[S-CH_2-CH_2)-OH] (**4**, in THF 0.33 g 22%); (**iii**) *dispiro* compound, $N_3P_3Cl_2$[S-CH_2-CH_2)-O]$_2$ (**5**, in diethylether 0.70 g 38%); (**iv**) tri-substituted open chain compound, $N_3P_3Cl_3$[S-(CH_2-CH_2)-OH]$_3$ (**6**, in THF 0.40 g 17%); (**v**) tris-*spiro* compound, N_3P_3[S-(CH_2-CH_2)-O]$_3$ (**7**, in THF 0.73 g 40%) and (**vi**) disubstituted open chain compound, $N_3P_3Cl_4$[S-CH_2-CH_2)-OH]$_2$ (**8**, in diethylether 0.35 g 16%). TLC-MS mass spectra of compounds (**3**) and (**4**) are presented as examples in Figures 2 and 3 respectively.

Table 1. Selected ^{31}P NMR parameters of hexachlorocyclotriphosphazene (**1**) derivatives (**3-8**)[a].

Compound	δPCl_2[b]	δP*spiro*[b]	δP(SROH)Cl [b]	^2J[P*spiro*-PCl_2][c]	^2J[P(SROH)-PCl_2][c]
$N_3P_3Cl_6$(**1**)	19.9				
(**3**)	24.7	18.8		44.8	
(**4**)	22.4		14.6		47.2
(**5**)	24.3	19.9		46.9	
(**6**)			17.6		
(**7**)		24.9			
(**8**)	25.2		22.2		48.2

[a] In $CDCl_3$ (with respect to 85% phosphoric acid external reference) at 202.38 MHz.
[b] In ppm.
[c] In Hz.

Table 2. Selected ^{1}H NMR parameters of compounds (**3-8**)[a].

Compound	$\delta POC\underline{H_2}$[b]	$\delta PSC\underline{H_2}$[b]	$\delta SCC\underline{H_2}$[b]	$\delta C\text{-}O\underline{H}$[b]	^3J(P-H)[c]
(**3**)	4.30	3.40	2.11	4.48	12.70
(**4**)		3.50			9.60
(**5**)	4.20	3.33	2.02	4.46	13.10
(**6**)		3.48			9.50
(**7**)	4.15	3.30	2.08	4.50	13.07
(**8**)		3.50			9.52

[a] In $CDCl_3$ (referenced to internal TMS) at 199.5 and 399.95 MHz. (room temperature).
[b] In ppm.
[c] In Hz.

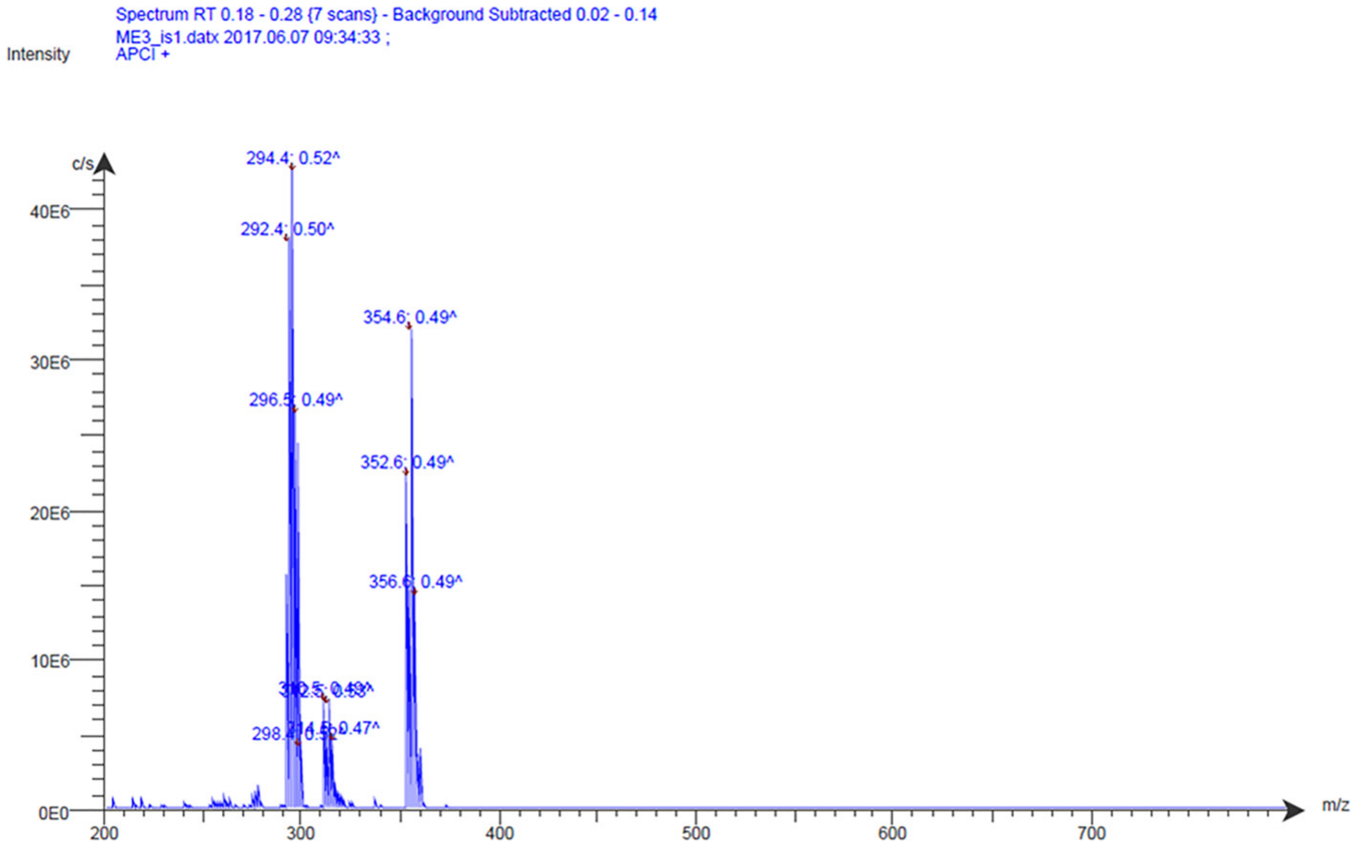


Figure 2. TLC-MS mass spectrum of compound **3**.

2.1. Characterization of the reaction products (3-8) by ^{31}P and ^{1}H NMR spectroscopy

2.1.3. ^{31}P NMR data

The ^{31}P NMR spectra of the resulting compounds formed by reaction with 2-mercaptoethanol showed the predominance of *spirocyclic* structures with A_2B (A_2X), AB_2 and A_3 spin systems.

Compound, $N_3P_3Cl_4$[S-CH_2-CH_2-O] (**3**), whose analysis and mass spectrum (Figure 2) showed that this can be either mono *spiro* or its *ansa* isomer. The *ansa* compound has an AX_2 type spectrum, whilst that of the *spiro* isomer is of the A_2B spin system tending to A_3, which can be readily assigned by consideration of signal intensities, chemical shifts and coupling patterns. ^{31}P (-H-) coupling affects the X_2 part of the former and A_2 part of the later giving further splitting on the spectrum. It was reported that shorter chain length of the nucleophilic reagents can hardly give *ansa* type structures.[22–24] We therefore assign a mono *spiro* structure (**3**) to this. The proton decoupled ^{31}P NMR spectrum of compound (**3**) is given in Figure 4.

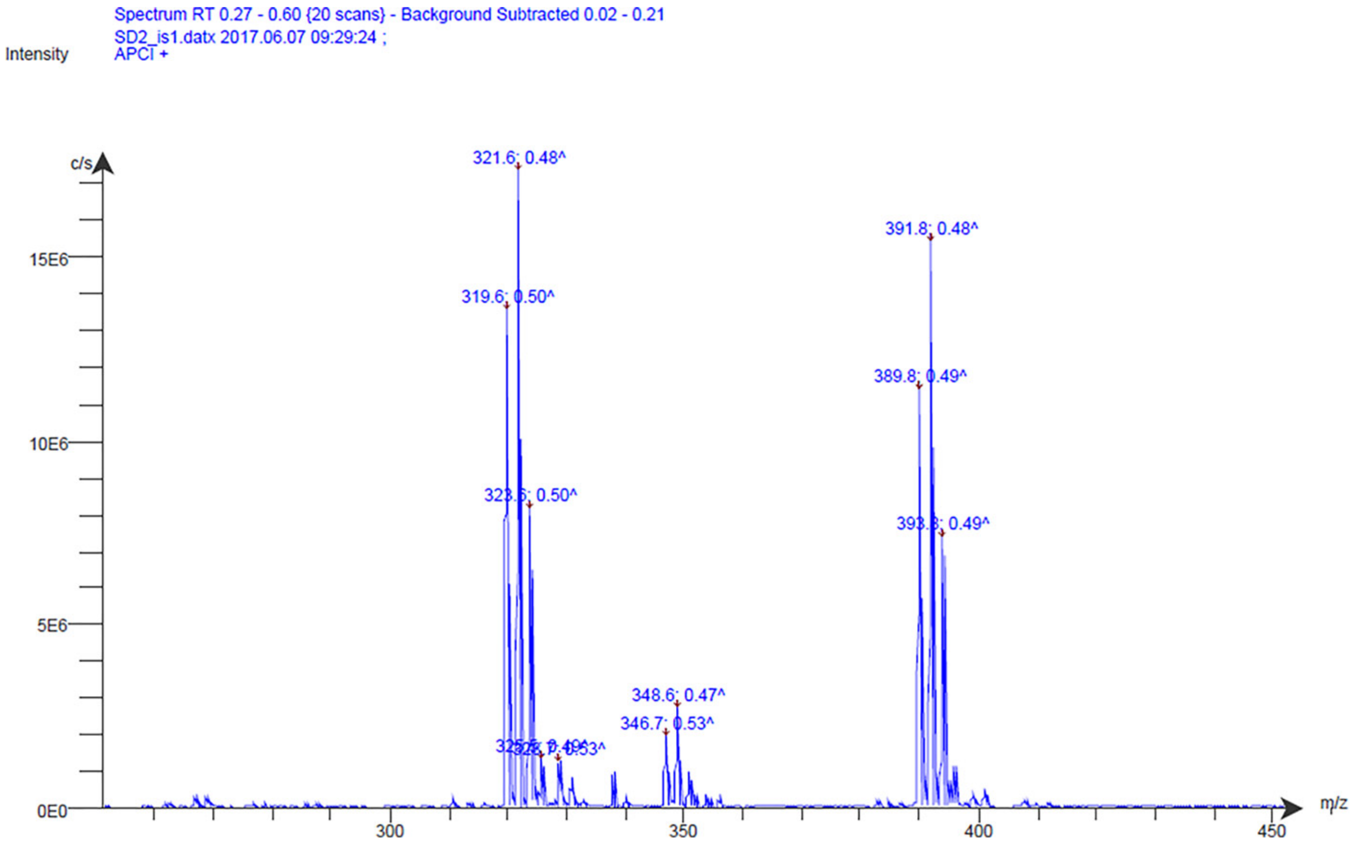


Figure 3. TLC-MS mass spectrum of compound **4**.

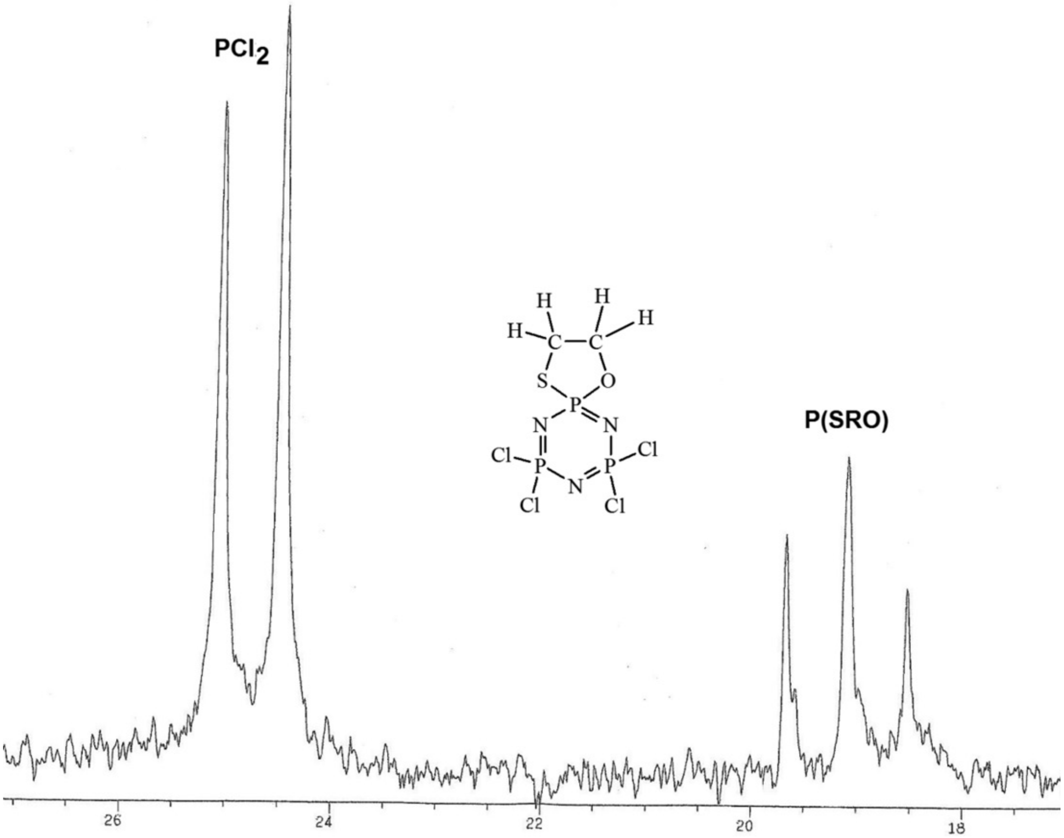
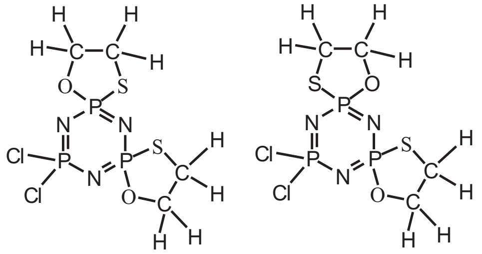


Figure 4. Proton decoupled ^{31}P NMR spectra of mono *spiro* compound (**3**): in $CDCl_3$, at 162.00 MHz, room temperature and referenced to external 85% H_3PO_4.

Compound **5** may give rise to two different types of isomeric structures depending on whether the exocyclic nitrogen atoms have *cis* or *trans* disposition (see below).



Which is (**5**) tentatively assigned to the *trans* structure due to its higher TLC R_f value. Previous reports show that the TLC R_f value of the *trans*-aminochlorocyclotriphosphazene derivative is greater than the *cis* analogue.[32]

The $^{31}P\ \{^1H\}$ NMR spectrum of compound **5** is AB_2 type and gives rise to a five line structure. ^{31}P NMR proton-coupled spectrum of the structure allows identification of the lines due to the ≡P*spiro* and ≡PCl_2 groups, where *spiro* group split into further lines. Proton coupling experiments as well as comparison with the analogues diols and diamine derivatives[21–33] allow precise assignment of the structure. The proton decoupled ^{31}P NMR spectrum of compound (**5**) is presented in Figure 5(b).

Compounds (**4**) and (**8**) give rise to A_2X and AB_2 type spin system respectively. MS (Figure 3 for compound **4**) and the ^{31}P NMR spectra of both compounds show conclusively that they possess open chain structures. The resonance of ≡PCl_2 groups for compound **4** appears as a doublet which is twice the integrated intensity of the triplet arising from the ≡P(SR)Cl group. Proton coupling effects the X part of the former and B_2 parts of the later (≡P(SR)Cl, where each group split into further lines). The spectra are quite facilitated by looking at the open chain derivatives of diols.[33] We therefore, with confidence assigned them to be open chain derivatives (**4** and **8**). The proton decoupled and coupled ^{31}P NMR spectra of compound (**4**) are presented in Figure 6. In the case of compounds (**6**) and (**7**), where the ^{31}P NMR spectrum is of the A_3 spin type. An A_3 spin system arises, when the phosphorus nuclei have identical or very similar environments.[9,24,33] In each structure, the ≡P(SRO), *spiro* groups and the ≡P(SR)Cl, open chain groups are in identical chemical environments and linked to similar groups; therefore, one single line is observed at 17.6 and 24.9 ppm respectively for these compounds. The proton decoupled ^{31}P NMR spectrum of compound (**6**) is exhibited in Figure 5(a). ^{31}P NMR data of the derived compounds are shown in Table 1.

2.1.4. ^1H NMR data

The ^1H NMR spectra of geminal *spirocyclic* and non-geminal open chain derivatives (**3-8**) are by far less complex and also the most interesting. The methylene protons of mono- (**3**), di- (**5**) and tris-*spiro* (**7**) derivatives show exceptional

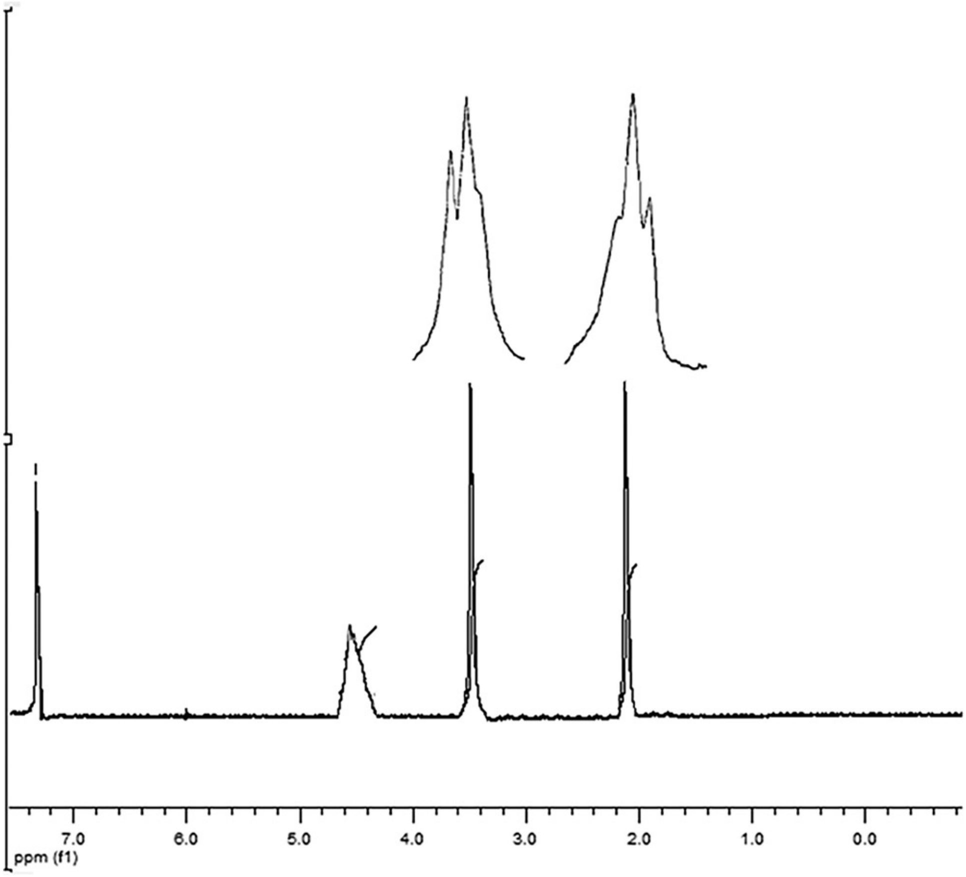


Figure 5. Proton decoupled ^{31}P NMR spectra of compounds (a) **6** and (b) **5**: in $CDCl_3$, at 162.00 MHz, room temperature and referenced to external 85% H_3PO_4.

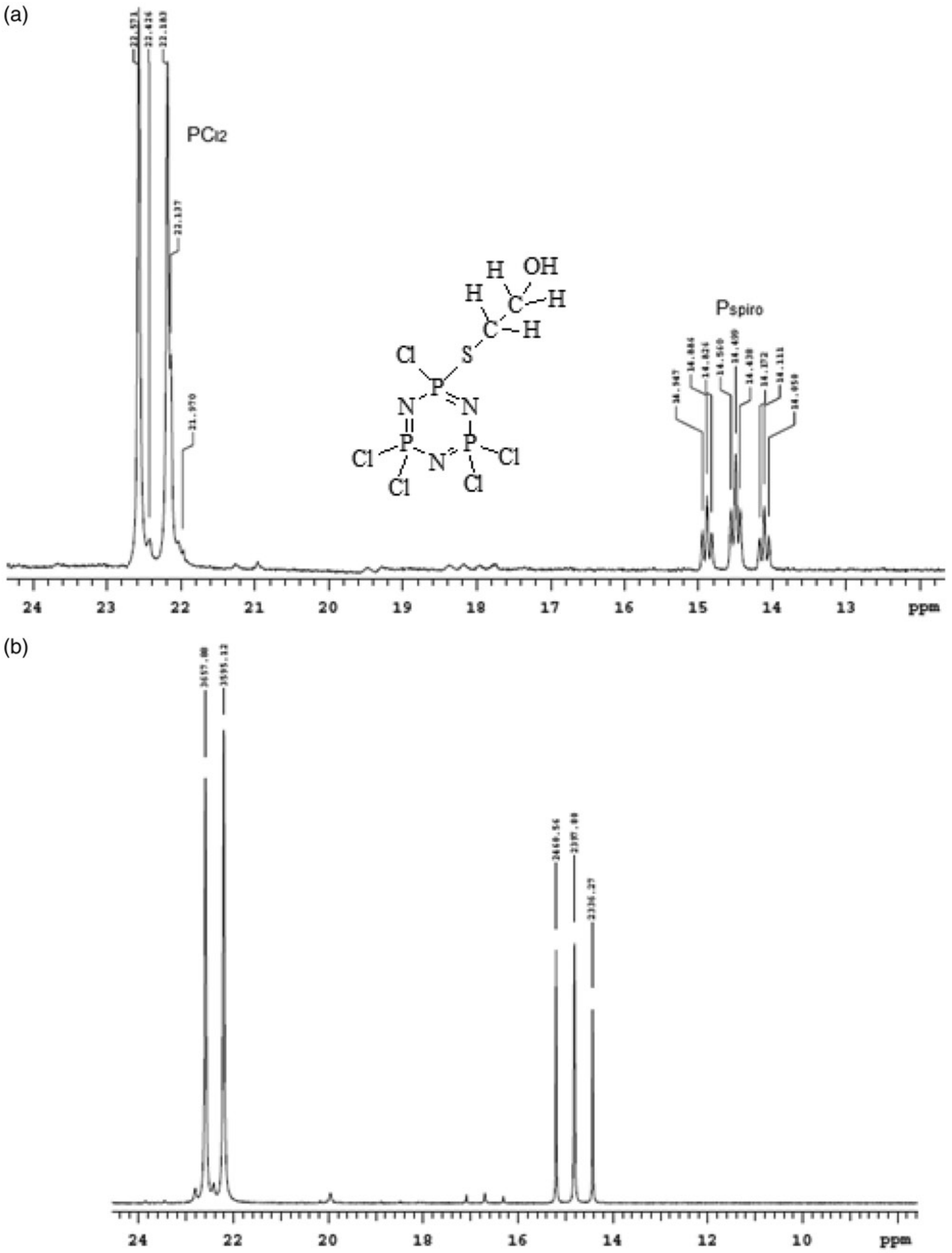


Figure 6. Proton decoupled (a) and proton coupled (b) ^{31}P NMR spectra of compound (**4**): in $CDCl_3$, at 162.00 MHz, room temperature and referenced to external 85% H_3PO_4.

similarity in -SC$\underline{H}_2$ and -OC$\underline{H}_2$ chemical shifts and fall into two distinct groups. The methylene protons of the -SC$\underline{H}_2$ and -OC$\underline{H}_2$, groups are non-equivalent due to being part of a cyclic and open chain moiety and existing in chemically and magnetically in different environments. As expected, we have observed intense virtual couplings for the -SCH_2 and -OC$\underline{H}_2$ protons in the spectrum of compound **5**. The ^1H NMR spectra of compound **4**, **6** and **8** are similar to each other and consistent with the suggested structures; the chemical shifts for C$\underline{H}_2$ protons adjacent to Oxygen and Sulfur atoms are observed in the ranges 4.15-4.30 and 3.40-3.50 ppm, respectively, and the signals for the C-O-$\underline{H}$ protons are also located at higher frequency (at 4.35-4.40 ppm) as a broad peak. The ^1H NMR spectrum of compound (**3**) is shown in Figure 7.

-SC$\underline{H}_2$ and -CC$\underline{H}_2$ protons appear as well resolved pairs and the phosphorus ^3J(P-H) proton coupling can be measured. ^{3J}(P-H) coupling constants have been subjected to closer scrutiny than chemical shifts, that they depend on the electro-negativity of the substituent and the electron density on the phosphorus atom (in derivatives of the type [-S-$(CH_2)_2$-NH_2], by inclusion of smaller coupling constants values for the substituents at the phosphorus atom). Therefore, ^{3J}(P-H) coupling constant values in the open chain derivatives are lower than the *spiro* compounds. Because of the high thermal vibrations of some of the substituent atoms, it is not possible to comment on the exact stereochemistry of all the substituent sulfur atoms. However, the sulfur atoms may have a very pronounced pyramidality in dangling formations [≡P(SROH)], and the sulfur atoms may be much

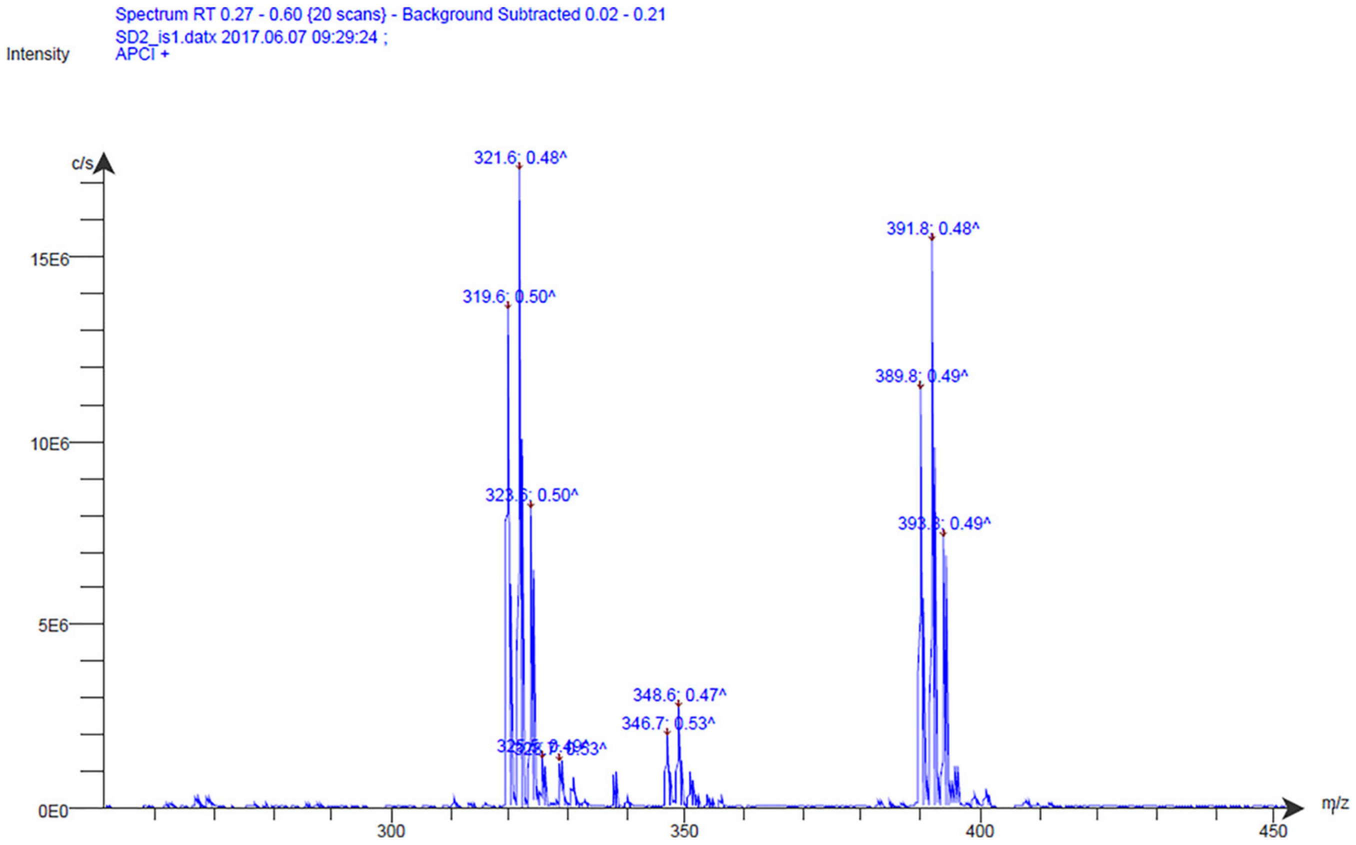


Figure 7. ^{1}H NMR spectrum of compound (**3**), at room temperature, in $CDCl_3$ (TMS as internal reference) and at 399.95 MHz.

more planer in the spiro formations [≡P(SRO)].[34] It is clear from the above that the deviation from planarity of the substituent atoms in question, together with the increase in the P-N bond lengths, cause a marked decrease in ^{3J}(P-H) coupling constant values in the dangling derivatives. Selected ^{1}H NMR parameters of compounds (3-8) are presented in Table 2.

2.2. Calorimetric characterization of compounds 6 and 8

2.2.1. DSC Results

In this study, we utilized DSC to identify thermal stabilities (thermally-induced events) i.e. heat of fusion in the chemical structure of compounds 6 and 7 as well as to determine their purities. The thermograms of the derivatives (**6** and **7**) and the assignments of the analyzed thermal peaks are shown in Figure 8 (**A**, **7** and **B**, **6**) and Table 3, respectively. The assigned peaks were also labeled on the thermograms. As demonstrated in Figure 8**A**, two endothermic peaks were found at the 113.87 °C (ΔH° 67.67 J/g) and 150.54 °C (ΔH° 130.30 J/g) positions for derivative **7**. The whole melting process was took place in two steps, in which, the first peak (#1) was assigned as first melting event, while the second one (#2) was considered as second melting event. No exothermic event was monitored for this compound.

In the case of second derivative (**6**), again the complete melting process was occurred with two steps. The peaks (#1 and 2) at the 109.83 °C (ΔH° 6.15 J/g) and 118.58 °C (ΔH° 9.14 J/g) positions were respectively assigned to first and second melting events. Further analysis of thermogram revealed three exothermic peaks (#3,4 and 5) at the 153.96° C (ΔH° 67.67 J/g), 187.12 °C (ΔH° 28.06 J/g) and 210.20° C (ΔH° 6.63 J/g) positions, respectively. These peaks were assigned to crystallization events most likely occurred due to the recrystallization processes after melting event (Figure 8**B**, Table 3).

In short, endothermic (heat consume due to melting) event were measured for compound **7** at two steps, while both endothermic and exothermic (heat release due to crystallization) events were measured for compound **6**, which is a typical observation for compounds in crystal form. Most common cause of two-step melting process is the existence of two different crystal morphologies in both derivatives. In this, first step comes from the melting of imperfect row-nucleated crystals, so called shish–kebab morphologies, while the second step comes from the melting of perfect spherulitic crystals where all the crystallites are roughly symmetric. These findings are also supported by the standard enthalpy changes (ΔH°), since they were calculated as being bigger for second step melting process than first step. It makes sense, because more energies are required to break the spherulitic crystals than row-nucleated ones. In case of exothermic peaks, already melted and/or disordered molecules attain more ordered crystal structures and release their excess free energy during the recrystallization process since they are no longer at random state. Another explanation for exothermic peaks can be chemical curing process, in which

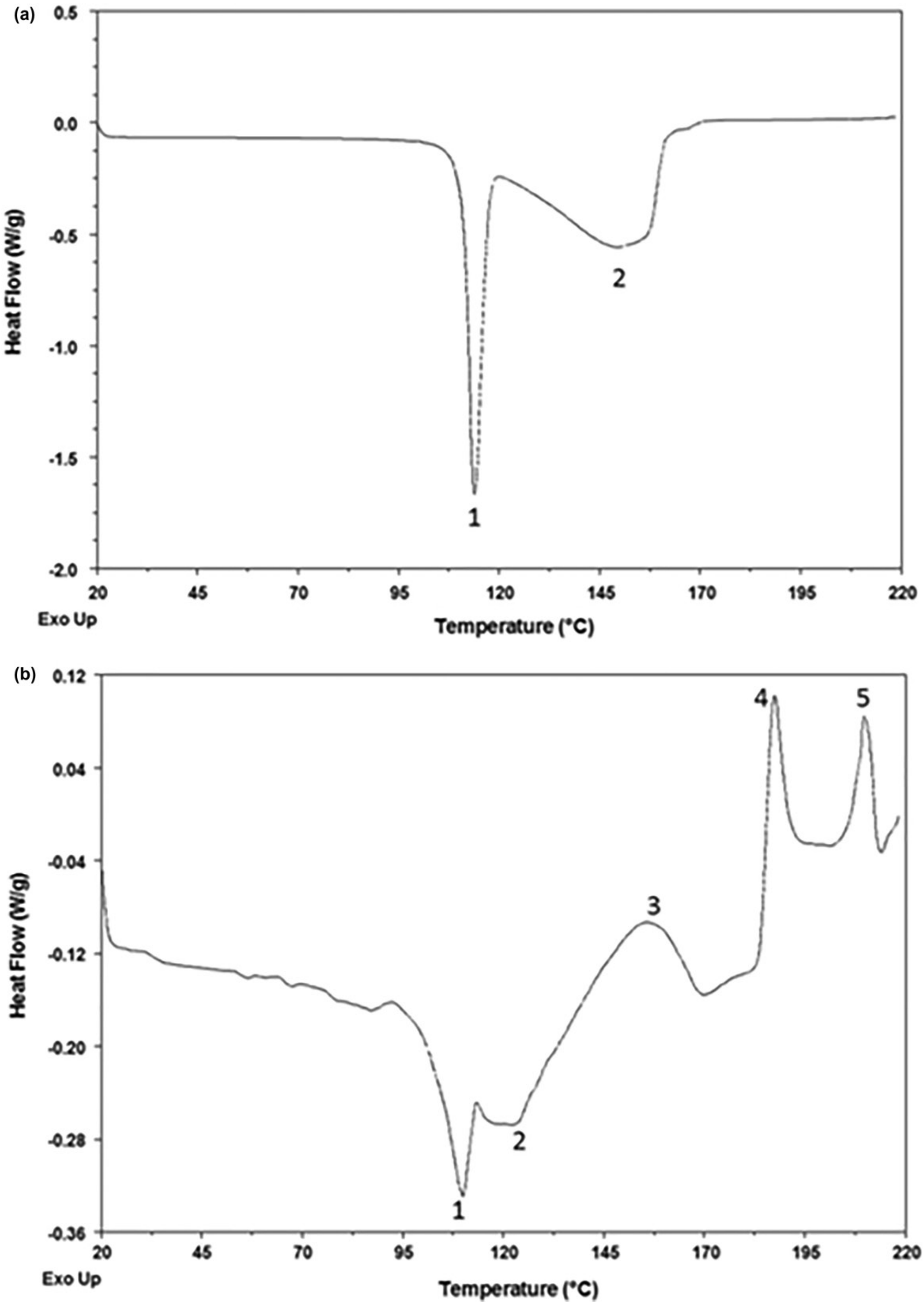


Figure 8. DSC thermograms of compounds 7(A) and 6B.

the disordered molecular fragments bind to each other though the stable interactions (bonds) and form tightly-linked and ordered networks in the system. Our DSC results indicated competent quality of purity for both derivatives, still the obtained thermal profiles were unique for each substance as presented and discussed above.

3. Experimental section

3.1. Materials

Reagent grade solvents were used throughout the work, benzene, light petroleum (b.p. 40–60° C), anhydrous diethyl ether, methanol, butanol, n-hexane (>96%), dichloromethane

Table 3. Calorimetric characterizations of 2-Mercaptoethanol (**2**) derivatives.

2-Mercaptoethanol	# Peaks	Peak character	Peak position (°C)	Standard enthalpy change-ΔH° (J/g)	Phase Transitions
Compound 7 (A)	1	Endothermic	113.87	67.67	First melting p.
	2	Endothermic	150.54	130.30	Second melting p.
Compound 6 (B)	1	Endothermic	109.83	6.15	First melting p.
	2	Endothermic	118.58	9.14	Second melting p.
	3	Exothermic	153.96	28.06	Recrystallization
	4	Exothermic	187.12	11.68	Recrystallization
	5	Exothermic	210.20	6.63	Recrystallization

(>99.0%), chloroform, acetonitrile (used for recrystallization), THF, acetone and hexachlorocyclotriphosphazatriene (Sigma Aldrich). Hexachlorocyclotriphosphazene was purified by fractional crystallization from hexane. THF was distilled over a sodium-potassium alloy under an argon atmosphere. $CDCl_3$, deuteriated solvent for NMR spectroscopy (Sigma Aldrich), Silica gel (60, 0.063–0.200 mm Merck) was used for column chromatography, Kieselgel 60° F_{254} (silica gel) precoated TLC plates (Merck).

The following materials were also obtained from Sigma Aldrich Chemicals: Ninhydrin (0,5%w/v), 2-mercapto-ethanol and $NaBH_4$ used as received, NaH (60% dispersion in mineral oil, which was removed by washing with dry n-heptane followed by decantation).

3.2. Methods

All reactions were monitored using Kieselgel 60° F_{254} (Merck Silica gel plates) precoated TLC plates and sprayed with Ninhydrin (0,5% w/v) in butanol solution, and developed at approximately 130° C. Separations of products were carried out by column chromatography using Kieselgel 60. (Merck 60, 0.063–0.200 mm; for 2 g crude mixture, 100 g silica gel was used in a column of 2.5 cm in diameter and 90 cm in length) Melting points were determined on a Hot Stage Microscopy at Southampton University and hot stage connected to a FP 800 central processor both fitted with a polarizing microscope. Elemental analyses were obtained using a ThermoFinnigan Flash 1112 instrument.^{1}H NMR spectra were recorded using a Varian INOVA 500 MHz spectrometer and (operating at 499 MHz.), a Bruker DRX 500 MHz spectrometer. Samples were dissolved in $CDCl_3$ and placed in 5mm NMR tubes. Measurements were carried out using a $CDCl_3$ lock, TMS as internal reference and sample concentrations of 15–20 mg cm^3. ^{31}P NMR spectra were recorded using a Varian INOVA 500 MHz spectrometer (operating at 202 MHz.); in $CDCl_3$ and 85% H_3PO_4 was used as an external reference. Mass spectra were recorded using a LC/MS (obtained by a Bruker MicrOTOF LC/MS spectrometer using electro spray ionization (ESI) method). DSC experiments were carried out using DSC Q2000instrument (TA Instruments, US), while the data analyses were conducted by thermal analysis software (Universal Analysis 2000, TA Instruments, US). Experimental details together with product types are summarized in Figure 1 and ^{31}P and ^{1}H NMR data may be found in Tables 1 and 2.

3.3. Synthesis

Reactions were carried out with one (36 h), two (42 h) and three (26 and 48 h) equivalents of 2-mercaptoethanol (**2**) in excess of NaH, in THF and diethylether solutions.

The effect of solvent on chemical reactivity of cyclophosphazene has generally been explained in literature,[1–24] especially with respect to the polarity scale (increasing or decreasing the polarity scale, which plays an important role in the reaction conditions, which reduces the efficiency of yielding the monomers and increases the amount of polymers).

It is usually decided on the choice of solvent after doing some sample experiments in polar and apolar solvents with using starting materials in small quantities (in 1:1; 1:2 and 1:3 mole ratios, sometimes in 1:6 mole ratio). After TLC experiments, the preferred solvent system and mole ratio are determined.

(a) One equivalent of 2-mercaptoethanol (2), at room temperature and in THF solution: Cyclotriphosphazene (**1**), (4 g, 11.5 mmol) and 2-mercaptoethanol (**2**, 0,9 g, 11.5 mmol) were dissolved in dry THF (110 mL) in a 250 mL three-necked round-bottom flask. This mixture was stirred approximately for 30 minutes at room temperature then two equivalents of NaH (60% oil suspension, 0,55 g, 23 mmol) in THF (30 mL) was added dropwise to the stirred solution under an argon atmosphere. The mixture was stirred (36 h) until TLC indicated the completion of the reaction. The reaction mixture was filtered to remove sodium chloride and any other insoluble materials. Then the reaction mixture was followed on TLC silica gel plates using dichloromethane-diethyl ether (3:1) as the eluent. The solvent was removed under reduced pressure and the resulting colourless solids and oils were subjected to column chromatography using the same solvent system, dichlomethane: diethyl ether (3:1) as the mobile phase. Products were recrystallized from benzene containing a few drops of light petroleum (b.p. 40–60° C). Three main fractions were synthesized: (**i**) The first phosphazene derivative was identified as mono *spiro* derivative, $N_3P_3Cl_4$ [S-CH_2-CH_2)-O] (**3**): m.p. 161-163° C, yield 0.82 g (48%). Anal. Calc. for $C_2H_4OSN_3P_3Cl_4$: C, 6.80; H, 1.13; N, 11.89%, (M, 353). Found: C, 6.81; H, 1.14; N, 11.89%; ([M + H]$^+$, 354.01). ^{1}H NMR ($CDCl_3$), $\delta POC\underline{H}_2$: 4.30, $\delta PSC\underline{H}_2$: 3.40, ^3J(P-H): 12.70 Hz. ^{31}P NMR ($CDCl_3$), δPCl_2:24.7, δP_{spiro}: 18.8, $^2J[P_{spiro}, PCl_2]$: 44.8 Hz. (**ii**) Second compound was identified as mono substituted open chain derivative, $N_3P_3Cl_5$ [S-CH_2-CH_2)-OH] (**4**): m.p. 157–158° C, yield 0.33 g (22%). Anal. calc. for $C_2H_5OSN_3P_3Cl_5$: C, 6.16; H, 1.28; N, 10.78%, (M, 389.5). Found: C, 6.16; H, 1.30; N, 10.78%; ([M + H]$^+$, 390.03). ^{1}H NMR ($CDCl_3$), $\delta PSC\underline{H}_2$: 3.50, $\delta SCC\underline{H}_2$: 2.11, $\delta C\text{-}O\underline{H}$: 4.48, ^3J(P-H): 9.60 Hz. ^{31}P NMR ($CDCl_3$), δPCl_2: 22.4, δP(SROH)Cl: 14.6, ^2J[P(SROH), PCl_2]: 47.2 Hz. (**iii**) Third compound was identified as *dispiro* derivative, $N_3P_3Cl_2$[S-CH_2-CH_2)-O]$_2$ (**5**): m.p. 184–186° C, yield 0.41 g (26%). Anal. calc. for $C_4H_8O_2S_2N_3P_3Cl_2$: C, 13.40; H, 2.23; N, 11.73%, (M, 358).

Found: C, 13.40; H, 2.25; N, 11.73%; ($[M+H]^+$, 359.01). ^1H NMR ($CDCl_3$), $\delta POC\underline{H}_2$: 4.20, $\delta PSC\underline{H}_2$: 3.33, ^3J(P-H): 13.10 Hz. ^{31}P NMR ($CDCl_3$), δPCl_2: 24.3, δP_{spiro}: 19.9, $^2J[P_{spiro}, PCl_2]$: 46.9 Hz.

(b) Three equivalents of 2-mercaptoethanol (2) in THF solution and under reflux: Cyclotriphosphazene (**1**), 4 g, 11.5 mmol) and 2-mercaptoethanol (**2**, 2.7 g, 34.5 mmol) were dissolved in dry THF (80 mL) in a 250 mL three-necked round-bottom flask. This mixture was stirred approximately for 30 minutes at room temperature then six equivalents of NaH (60% oil suspension, 1,66 g, 69 mmol) in THF (30 mL) was added dropwise as hydrogen chloride acceptor to the stirred solution under an argon atmosphere. The solution was heated for 26 h under reflux. The course of the reaction was followed by TLC with silica gel plates using benzene/dichloromethane (1:2) as the mobile phase. Heating was stopped and the apparatus was cooled to room temperature. Then the bulk of the reaction mixture was filtered off and the remaining was removed by column chromatography using a mixture of CH_2Cl_2/Et_2O (3:1). For the separation of the individual phosphazenes the mixture was re-chromatographed using benzene/dichloromethane (1:2) as the eluent. Products were recrystallized from benzene containing a few drops of light petroleum (b.p. 40–60° C). Three main phosphazene fractions were obtained: (**i**) *Dispiro* derivative, $N_3P_3Cl_2[S\text{-}CH_2\text{-}CH_2)\text{-}O]_2$ (**5**), yield 0.46 g 20%). (**ii**) Tri-substituted open chain derivative, $N_3P_3Cl_3[S\text{-}(CH_2\text{-}CH_2)\text{-}OH]_3$ (**6**): m.p. 210–211° C, yield 0.40 g (17%). Anal. calc. for $C_6H_{15}O_3S_3N_3P_3Cl_3$: C, 15.39; H, 3.17; N, 8.88%, (M, 472.5). Found: C, 15.40; H, 3.19; N,8.88%, ($[M+H]^+$, 473.07). ^1H NMR ($CDCl_3$), $\delta PSC\underline{H}_2$: 3.48, $\delta SCC\underline{H}_2$: 2.02, $\delta C\text{-}O\underline{H}$: 4.46, ^3J(P-H): 9.50 Hz. ^{31}P NMR ($CDCl_3$), δP(SROH)Cl: 17.6. (**iii**) Tris-*spiro* derivative, $N_3P_3[S\text{-}(CH_2\text{-}CH_2)\text{-}O]_3$ (**7**): m.p. 149–151° C, yield 0.73 g (40%). Anal. calc. for $C_6H_{12}O_3S_3N_3P_3$: C, 19.83; H, 3.30; N,11.57%, M, 363. Found: C,19.84; H, 3.31; N, 11.57%, (M^+, 363). ^1H NMR ($CDCl_3$), $\delta POC\underline{H}_2$: 4.15, $\delta PSC\underline{H}_2$: 3.30, ^3J(P-H): 13.07 Hz. ^{31}P NMR ($CDCl_3$), δP_{spiro}: 24.9.

(c) Two equivalents of 2-mercaptoethanol (2), at room temperature and in diethylether solution: Reaction procedure as for one equivalent of 2-mercaptoethanol (**2**). In excess of NaH, stirring time was approximately 42 h. Three main fractions were synthesized: (**i**) The first phosphazene derivative was identified as mono *spiro*, (**3**): yield 0.65 g (36%).

(**ii**) Second phosphazene derivative was identified as disubstituted open chain, $N_3P_3Cl_4[S\text{-}CH_2\text{-}CH_2)\text{-}OH]_2$ (**8**): recrystallized from n-hexane-acetonitril (5:1), m.p. 179–180° C, yield 0.35 g (16%). Anal. calc. for $C_4H_{10}O_2S_2N_3P_3Cl_4$: C, 11.13; H, 2.32; N, 9.74%; M, 431. Found: C, 11.14; H, 2.34;N, 9.74%; ($[M+H]^+$, 432.07). ^1H NMR ($CDCl_3$), $\delta PSC\underline{H}_2$: 3.50, $\delta SCC\underline{H}_2$: 2.08, $\delta C\text{-}O\underline{H}$: 4.50, ^3J(P-H): 9.52 Hz. ^{31}P NMR ($CDCl_3$), δPCl_2: 25.2, δP(SROH)Cl: 22.2, $^2J[P(SROH), PCl_2]$: 48,2 Hz.(**iii**) Third derivative was identified as *dispiro*, (**5**), yield 0.70 g (38%).

(d) Three equivalents of 2-mercaptoethanol (2), at room temperature (48 h) and in diethylether solution: Reaction procedure as for one equivalent of 2-mercaptoethanol (**2**). Three main fractions were synthesized: (**i**) Mono *spiro* derivative (**3**); yield 0.35 g (18%). (**ii**) *Dispiro* derivative (**5**), yield 0.25 g (14%). (**iii**) Tri-substituted open chain derivative (**6**), yield 0.30 g (16%).

3.3.1. DSC experiments

For DSC analyses samples were prepared in the aluminum hermetic pans and the pans were sealed before the test. An empty pan was sealed and placed in a particular position in DSC device next to the pan containing sample in order to eliminate calorimetric pan effect. Scan was performed at a thermal region from 20°C to 220°C with a scanning rate (ramp) of 5°C/min. This scanning rate was used to obtain thermal event temperatures in between the real thermodynamic value. The peak positions in temperature axis (°C) were evaluated for the calculation of the melting temperatures. Standard enthalpy changes ($\Delta H°$ J/g) were calculated by linearly dividing the integrating peak area to the sample weight.

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