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Hexa-arm star shaped hydrazone derivatives from hexakis(4-formylphenoxy)-cyclotriphosphazene core

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ABSTRACT

A series of novel hexasubstituted cyclophosphazene hydrazones [N_3P_3(—OC_6H_4—*p*—CH=N—NH—C(O)—C_6H_4—*p*—X)$_6$] (X = H, Br, Cl, F, OH, OCH_3, CH_3, NO_2, NH_2) were prepared by a sixfold condensation reaction of [N_3P_3(—OC_6H_4—*p*—CHO)$_6$] with *para*-substituted benzoic hydrazides [NH_2—NH—C(O)—C_6H_4—*p*—X] with excellent yields (91–98%). The structures of the compounds were confirmed by elemental analysis, FT-IR, ^{1}H, ^{13}C, ^{31}P, 2D-HSQC NMR and mass spectrometry (MALDI-TOF). All the synthesized cyclophosphazene hydrazones exhibit high thermal stability. The crystal structure of a homogeneously substituted hexakis(4-formylphenoxy)-cyclotriphosphazene was determined by X-ray diffraction analysis. The compound crystallizes in the monoclinic system, space group $P2_1/n$ with $a = 16.558(3)$ Å, $b = 10.250(2)$ Å, $c = 23.429(5)$ Å, $\alpha = \gamma = 90.00°$, $\beta = 90.461(4)°$, $V = 3976.5(14)$ Å^3 and $Z = 4$. The *R* value is 0.0823 for 4290 observed reflections. The conformations of the 4-formylphenoxy-groups are different at the three phosphorus atoms.

1. Introduction

Cyclophosphazenes containing alternate phosphorus and nitrogen atoms in their non-delocalized cyclic skeletons are an important family of inorganic ring systems [1,2]. In the past few decades a rich variety of cyclophosphazenes with interesting properties and applications are synthesized by easily replacing the chlorine of the chlorocyclotriphosphazenes with various nucleophiles [3–5]. The properties of cyclophosphazenes depend on the inorganic —P=N— skeleton as well as on the nature of the substituents attached to the phosphorus atoms [6,7]. Reactivity of the peripheral functionalities of the substituted cyclotriphosphazenes make them versatile precursors to synthesize supermolecular liquid crystals [8] and a wide range of star-shaped polymers possessing unique structures and properties arising from three dimensional compact shape [9,10]. The coordination chemistry of cyclophosphazene-based ligands is quite exciting and several structurally diverse metal complexes have been synthesized and characterized [11].

Hexakis(4-formylphenoxy)-cyclotriphosphazene (HFPC) (**1**) possessing six reactive peripheral aldehyde groups is used as a prototype system for the synthesis of polymer-bound chemotherapeutic agents [12]. More recently, it has been used as a core for the exploration of new dendritic structures [13–15]. Studies concerning cyclophosphazenes bearing oxime groups [16] and Schiff bases [17,18] prepared from HFPC are now well documented. Although some examples of formation of hydrazones by the condensation of aldehydes with cyclophosphazene hydrazides have been described [19], to our knowledge formation of hydrazones by the reaction of aromatic hydrazides with HFPC has not been reported and deserves further exploration.

Hydrazones containing an azometine (—NHN=CH—) group are important synthons for several transformations and have gained importance due to their broad spectrum of biological activities [20,21]. Metal complexes of hydrazones have been found to have therapeutic activity [22]. Hydrazone linkage provides a suitable system for pH-dependent release of drugs from drug-conjugates [23].

Here we present the synthesis of a series of cyclophosphazene hydrazones by the condensation of HFPC with *p*-substituted benzoic hydrazides. X-ray crystal structure of HFPC (**1**) was obtained for its molecular dimensions. The symbiosis that exists between cyclophosphazenes and the corresponding polymeric systems will ensure that small molecule developments will be readily translated to the more complex macromolecules [24].

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Table 1
Crystal data and structure refinement of HFPC (**1**).

CCDC deposit no.	678839
Crystal size	0.35 × 0.32 × 0.30 mm
Color/shape	Colorless/rectangular
Empirical formula	$C_{42}H_{30}N_3O_{12}P_3$
Formula weight	861.60
Temperature (K)	293(2)
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/n$
Cell dimensions	
	a = 16.558(3) Å
	b = 10.250(2) Å
	c = 23.429(5) Å
	α = 90.00°
	β = 90.461(4)°
	γ = 90.00°
Volume	3976.5(14) Å^3
Z	4
Density (calculated)	1.439 mg/m^3
Absorption coefficient	0.219 mm^{-1}
$F_{(000)}$	1776
θ range for data collection	2.17–26.5°
Reflections collected	8206
Independent reflections	4290 [R(int) = 0.0241]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4290/5/541
Goodness-of-fit on F^2	1.006
Final R indices [I > 2σ(I)]	R_1 = 0.0823, wR_2 = 0.2488
R indices (all data)	R_1 = 0.1553, wR_2 = 0.3177
$(\Delta/\sigma)_{max}$	0.069
$(\Delta\rho)_{max}$	0.661 e Å^{-3}
$(\Delta\rho)_{min}$	−0.417 e Å^{-3}
Measurement	Bruker Smart Apex CCD
Program system	SADABS
Structure determination	SHELXS-97
Refinement	SHELXL-97

Table 2
Selected bond lengths (Å) of HFPC (**1**).

Bond	Å	Bond	Å
P1—N1	1.568(3)	P1—O1	1.580(2)
P1—N3	1.587(3)	P1—O2	1.576(3)
P2—N1	1.571(3)	P2—O3	1.569(3)
P2—N2	1.584(3)	P2—O4	1.571(3)
P3—N2	1.578(3)	P3—O5	1.588(3)
P3—N3	1.571(3)	P3—O6	1.582(3)
C1—O1	1.396(4)	C7—O7	1.183(8)
C8—O2	1.399(4)	C14—O8	1.257(7)
C15—O3	1.410(5)	C21—O9	1.202(12)
C22—O4	1.389(4)	C28—O10	1.190(6)
C29—O5	1.391(5)	C35—O11	1.186(8)
C36—O6	1.404(5)	C42—O12	1.179(8)

Table 3
Selected bond angles (°) and torsion angles (°) of HFPC (**1**).

Bond angle	Degrees (°)	Torsion angle	Degrees (°)
P1—N1—P2	122.4(2)	N1—P1—N3—P3	6.2(3)
P2—N2—P3	122.4(2)	N1—P2—N2—P3	11.8(3)
P3—N3—P1	122.58(19)	N3—P3—N2—P2	−7.7(3)
N1—P1—N3	117.47(16)	N1—P1—O1—C1	−174.9(3)
N2—P2—N1	117.18(16)	N3—P1—O1—C1	−46.5(3)
N3—P3—N2	116.92(17)	N1—P1—O2—C8	70.9(3)
		N3—P1—O2—C8	−61.1(3)
O1—P1—O2	99.68(14)	N1—P2—O3—C15	68.8(4)
O3—P2—O4	98.68(14)	N2—P2—O3—C15	−62.5(4)
O5—P3—O6	94.07(15)	N1—P2—O4—C22	−172.1(3)
		N2—P2—O4—C22	−42.9(4)
P1—O1—C1	128.0(3)	N2—P3—O5—C29	−62.6(3)
P1—O2—C8	125.8(2)	N3—P3—O5—C29	69.5(3)
P2—O3—C15	125.6(3)	N2—P3—O6—C36	67.8(3)
P2—O4—C22	130.0(3)	N3—P3—O6—C36	−63.4(3)
P3—O5—C29	122.1(3)		
P3—O6—C36	120.8(3)	O3—P2—N1—P1	−133.9(2)
		O3—P2—N2—P3	140.1(2)
O7—C7—C4	106.3(7)	O4—P2—N1—P1	119.9(2)
O8—C14—C11	119.4(6)	O4—P2—N2—P3	−111.1(2)
O9—C21—C18	111.7(10)	O5—P3—N2—P2	121.0(2)
O10—C28—C25	125.9(5)	O5—P3—N3—P1	−131.1(2)
O11—C35—C32	114.1(8)	O6—P3—N3—P1	126.0(2)
O12—C42—C39	121.6(8)	O6—P3—N2—P2	−135.7(2)

2. Experimental

2.1. Materials and measurements

The ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded in DMSO-d_6 solvent on BRUKER AV-500 MHz High Resolution Multinuclear FT-NMR Spectrometer at room temperature. The ^{1}H and ^{13}C NMR chemical shifts were measured using $SiMe_4$ as an internal standard at δ = 0 ppm. The ^{31}P chemical shifts are reported in ppm relative to 85% H_3PO_4 at 0 ppm as an external standard. IR spectra were recorded in a KBr matrix using an Impact-410 Nicolet (USA) FT-IR spectrometer in 4000–400 cm^{-1} range. Single crystal X-ray analysis data was collected on a BRUKER SMART APEX CCD diffractometer. The electronic spectra of the compounds were recorded in HPLC grade DMSO solvent on a VARIAN CARY 50-BIO UV–visible spectrophotometer in the region of 200–1000 nm. Elemental analyses (C, H and N) were performed using Leco Model Truespec CHNS Analyser. The MALDI-TOF mass spectrum was measured with a Voyager-DE STR spectrometer with α-cyano-4-hydroxycinnamic acid as a matrix. Thermogravimetric analysis (TGA) curves were recorded on Perkin Elmer TGA7 ANALYSER at a heating rate of 10 °C per minute from room temperature to 800 °C under nitrogen atmosphere. Melting points were determined in an open capillary on a Gallenkamp melting point apparatus and are uncorrected.

All manipulations were carried out with standard high vacuum or dry nitrogen atmosphere techniques. Hexachlorocyclotriphosphazene (Aldrich) was re-crystallized from dry hexane. Solvents were purified by standard methods [25]. Tetrahydrofuran (Merck) was distilled from sodium-benzophenone. Sodium hydride as 60% dispersion in mineral oil (Loba) was used as received. All other chemicals (sd fine chemicals, India) were used as received. All compounds were routinely checked by thin-layer chromatography (TLC) on aluminum-backed silica gel plates.

2.2. Synthesis

2.2.1. Synthesis of Hexakis(4-formylphenoxy)-cyclotriphosphazene (1) [N_3P_3(—OC_6H_4—p—CHO)$_6$]

The synthesis and main characteristics of the title compound HFPC (**1**) were described earlier [12]. It was synthesized according to modified method [9] and its single crystals suitable for X-ray diffraction were obtained by slow evaporation of the ethylacetate solution at room temperature. Yield: 90%, M.P. 141–142 °C dec. Anal. Calc. for $C_{42}H_{30}N_3O_{12}P_3$: C 58.55, H 3.51, N 4.88%. Found: C 58.59, H 3.61, N 4.66%. ^{1}H NMR (DMSO-d_6, ppm): 7.15 (d, 12H, H^2). 7.77 (d, 12H, H^3), 9.92 (s, 6H, CHO),^{13}C NMR (DMSO-d_6, ppm): 121.92 (C^2), 132.35 (C^3), 134.45 (C^4), 154.47 (C^1), 192.55 (CHO) ppm. ^{31}P NMR (DMSO-d_6, ppm): δ 6.79 (s). IR (KBr, cm^{-1}): 3068 ν (w, C—H_{Ar}), 1704 (s, C=O) 1209, 1183 (s, P=N), 958 (s, P—O—C).

2.2.2. Synthesis of p-substituted benzoic hydrazides

Methyl benzoates were synthesized from their respective *p*-substituted benzoic acids, using excess dry methanol in the

Table 4
Physicochemical data for compounds **3a–i**.

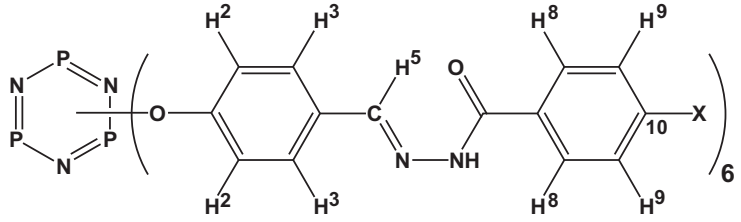
Compound	X	Formula	Yield (%)	M.P. (°C)	C%		H%		N%		Mass m/z $(M+Na)^+$	λ max (nm)
					Obsd	Calcd	Obsd	Calcd	Obsd	Calcd		
3a	H	$C_{84}H_{66}N_{15}O_{12}P_3$	96.75	292–297	64.39	64.24	4.41	4.24	13.21	13.38	1593.3322	308
3b	Br	$C_{84}H_{60}Br_6N_{15}O_{12}P_3$	98.02	312–315	49.22	49.36	2.81	2.96	10.44	10.28	2059.7886	305
3c	Cl	$C_{84}H_{60}Cl_6N_{15}O_{12}P_3$	98.01	308–313	56.91	56.77	3.62	3.40	11.69	11.82	1796.0886	310
3d	F	$C_{84}H_{60}F_6N_{15}O_{12}P_3$	91.71	306–310	60.26	60.11	3.44	3.60	12.38	12.52	1701.275	304
3e	OH	$C_{84}H_{66}N_{15}O_{18}P_3$	98.60	228–231	60.29	60.54	4.07	3.99	12.46	12.61	1689.3286	310
3f	OCH_3	$C_{90}H_{78}N_{15}O_{18}P_3$	97.76	288–292	61.69	61.75	4.42	4.49	12.04	12.00	1773.4981	307
3g	CH_3	$C_{90}H_{78}N_{15}O_{12}P_3$	97.63	295–299	65.19	65.33	4.91	4.75	12.61	12.70	1677.4917	306
3h	NO_2	$C_{84}H_{60}N_{21}O_{24}P_3$	98.05	195–198	54.66	54.82	3.15	3.29	16.11	15.98	1863.3178	275
3i	NH_2	$C_{84}H_{72}N_{21}O_{12}P_3$	96.45	217–220	60.66	60.76	4.48	4.37	17.85	17.71	1683.4203	309

Table 5
Characteristic IR vibrations (in cm^{-1}) of Compounds **3a–i**.

Compound	ν (N—H)	ν $(C—H)_{arom}$	ν (C=O)	ν (C=N)	ν (P=N)	ν (P—O—C)	Other
3a	3236	3062	1654	1604	1202–1173	955	–
3b	3236	3066	1654	1600	1204–1178	959	–
3c	3237	3067	1654	1600	1204–1178	958	–
3d	3239	3073	1654	1603	1200–1168	957	–
3e	N.O.	N.O.	1646	1606	1208–1166	956	**ν (OH)** 3425
3f	3236	3066	1652	1605	1211–1179	957	–
3g	3257	3074	1652	1607	1211–1182	957	–
3h	3247	3073	1661	1602	1197–1169	952	–
3i	3210	3069	1663	1608	1196–1177	960	**ν (NH_2)** 3466, 3339

N.O.: not observed.

Table 6
^1H NMR spectral data of **3a–i** compounds in DMSO-d_6.



Compound	X	NH (s, 6H)	H^2 (d, 12H)	H^3 (d, 12H)	H^5 (s, 6H)	H^8 (d, 12H)	H^9 (d, 12H)	Other
3a	H	11.93	7.11	7.68	8.58	7.94	7.51 (t)	$C^{10}H$ 7.62 (t, 6H)
3b	Br	11.85	7.04	7.60	8.47	7.76	7.66	–
3c	Cl	11.85	7.05	7.60	8.47	7.84	7.48	–
3d	F	11.87	7.06	7.63	8.49	7.94	7.29	–
3e	OH	11.71	7.02	7.59	8.51	7.82	6.82	—OH 10.14 (s, 6H)
3f	OCH_3	11.74	7.03	7.60	8.51	7.87	6.96	$C^{11}H$ 3.81 (s, 18H)
3g	CH_3	11.78	7.04	7.60	8.51	7.79	7.24	$C^{11}H$ 2.36 (s, 18H)
3h	NO_2	12.10	7.13	7.69	8.55	8.09	8.26	–
3i	NH_2	11.88	7.04	7.61	8.53	7.72	6.98	—NH_2 5.54 (s, 12H)

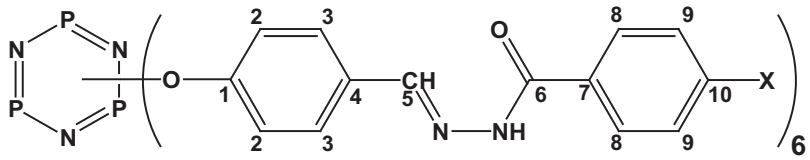
Chemical shifts (δ) are reported in ppm; s, singlet; d, doublet; t, triplet.

presence of H_2SO_4. *para*-Substituted benzoic hydrazides **(2a–i)** were prepared by reaction of the corresponding methyl benzoates (10 mmol) with hydrazine hydrate 99% (50 mmol) in methanol under reflux for 4–6 h. The excess solvent was removed under vacuum and the residue was filtered under suction, washed with water, and dried. The spectral and analytical data of benzoic hydrazide (**2a**) [26], 4-bromobenzoic hydrazide (**2b**) [27], 4-chlorobenzoic hydrazide (**2c**) [28], 4-fluorobenzoic hydrazide (**2d**) [26], 4-hydroxybenzoic hydrazide (**2e**) [29], 4-methoxybenzoic hydrazide (**2f**) [30], 4-methylbenzoic hydrazide (**2g**) [28], 4-nitrobenzoic hydrazide (**2h**) [28] and 4-aminobenzoic hydrazide (**2i**) [28] are in good agreement with literature values.

2.2.3. Synthesis of cyclophopshazene hydrazone

$[N_3P_3(—OC_6H_4—p—CH=N—NH—C(O)—C_6H_4—p—X)_6]$ {X = H **(3a)**; Br **(3b)**; Cl **(3c)**; F **(3d)**; OH **(3e)**; OCH_3 **(3f)**; CH_3 **(3g)**; NO_2

Table 7
^{13}C NMR (decoupled) spectral data of the compounds **3a–i** in DMSO-d_6.



Compound	X	C^1	C^2	C^3	C^4	C^5	C^6	C^7	C^8	C^9	C^{10}	C^{11}
3a	H	151.19	121.38	129.07	129.16	147.56	163.70	133.68	128.10	128.85	132.21	–
3b	Br	151.16	121.38	130.11	131.82	147.81	162.66	132.67	129.17	132.07	126.00	–
3c	Cl	151.18	121.37	129.95	132.68	147.8	162.53	132.31	129.18	128.87	137.04	–
3d	F	150.65	120.81	130.26	131.56	146.98	163.02	129.51	128.6	115.33	165.00	–
3e	OH	151.06	121.33	130.19	132.37	146.71	163.4	124.09	129.01	115.46	161.22	–
3f	OCH_3	151.06	121.34	130.02	132.3	146.96	162.43	125.67	129.04	114.06	163.13	55.82
3g	CH_3	151.10	121.35	130.77	132.24	147.28	163.52	129.35	128.11	129.05	142.22	21.49
3h	NO_2	151.32	121.40	129.60	131.90	148.55	161.80	139.17	129.31	123.84	149.52	–
3i	NH_2	151.08	121.38	130.06	132.33	147.53	162.68	123.57	128.41	115.24	152.32	–

Table 8
^{31}P NMR (decoupled) spectral data of the compounds **3a–i**.

Compound	ppm
3a	8.70
3b	8.66
3c	8.65
3d	8.69
3e	8.83
3f	8.76
3g	8.71
3h	8.59
3i	8.76

(3h); NH_2 **(3i)**}. These compounds were prepared in a similar manner. The following procedure is typical.

HFPC (**1**) (0.104 g, 0.12 mmol) was added to a solution of benzoic hydrazide (0.109 g, 0.8 mmol) in tetrahydrofuran (75 mL) and the reaction mixture was stirred under reflux for 18 h. The solvent was removed by evaporation under reduced pressure. The residue was filtered under suction and washed several times with hot tetrahydrofuran. The resulting solid (**3a**) was dried in vacuo at 40 °C for 8 h.

The analytical and physicochemical data of compounds **3a–i** are summarized in Table 4. The diagnostic IR bands are summarized in Table 5. Detailed assignment of ^{1}H, ^{13}C and ^{31}P NMR resonances are presented in Tables 6–8 respectively.

2.2.4. X-ray crystallography

A single crystal having dimensions of 0.35 × 0.32 × 0.30 mm was chosen for X-ray diffraction studies. The data were collected on a 'BRUKER SMART APEX CCD' diffractometer using graphite-monochromatized Mo Kα radiation (λ = 0.71073 Å); the scan modes were in the range 2.17–26.5°. The absorption correction was applied by the use of SADABS. The structure of the compound was solved by direct methods and refined by full-matrix least-squares techniques on F^2 by using SHELXS-97 [31]. All of the non-H atoms were refined anisotropically. The positions of hydrogen atoms were found in a difference Fourier map and refined with isotropic thermal parameters. Details of the data collection and structure refinement are given in Table 1.

3. Results and discussion

3.1. Synthesis of hexa-arm cyclophosphazene hydrazones

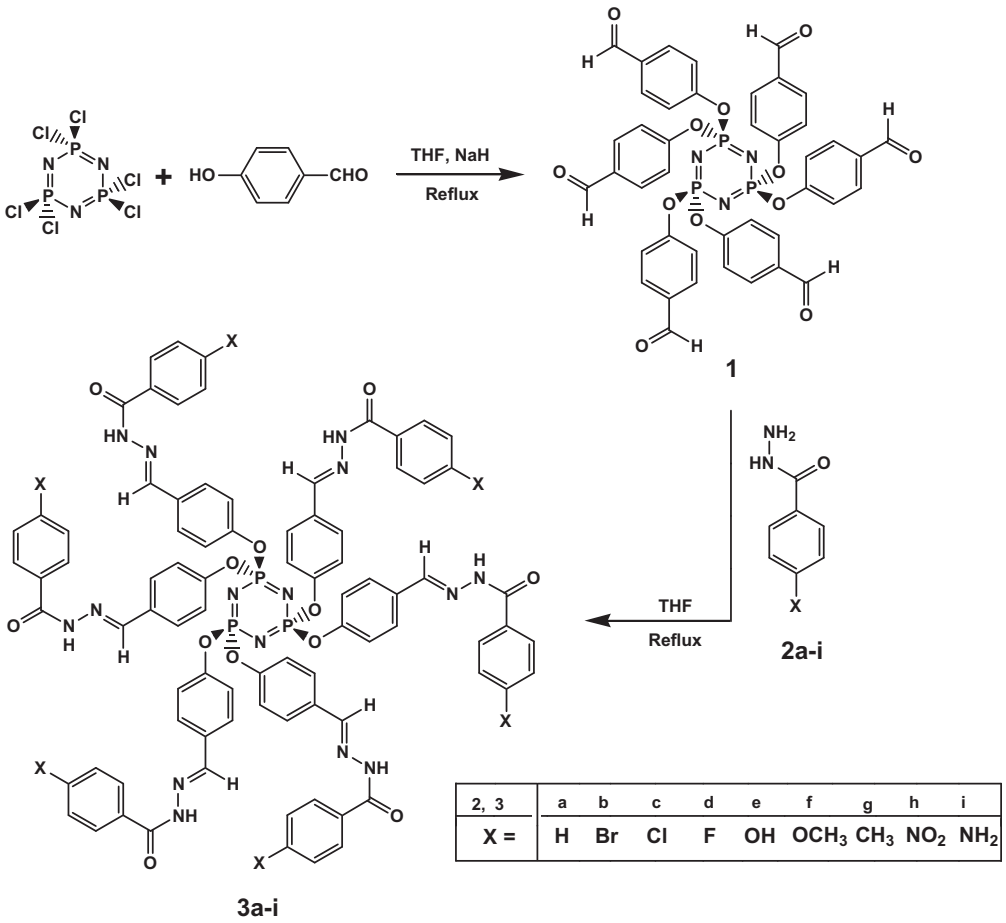
The first reaction for the synthesis of the hexa-arm star shaped hydrazones with different substitutions at para positions consists of the grafting of six hydroxybenzaldehyde groups onto the cyclotriphosphazene core. The reaction of hexachlorocyclotriphosphazene with the sodium salt of 4-hydroxybenzaldehyde in THF yielded hexakis(4-formylphenoxy)-cyclotriphosphazene. The second step consists of the condensation of 6 equivalents of benzoic hydrazide **2a–i** with the aldehyde functions of HFPC (**1**) in THF for 18–24 h at refluxing temperature and affords the corresponding hexafunctionalized hydrazones **3a–i**. The duration of the reaction for the synthesis of **3e** and **3h** is comparatively more perhaps due to the limited solubility of 4-hydroxybenzoic hydrazide and 4-nitrobenzoic hydrazide in THF. All products were generally obtained in high yields. General presentation of the reaction and structures of the compounds are shown in Scheme 1.

The structure of HFPC (**1**) has been confirmed by single crystal X-ray diffraction study. The synthesized cyclophosphazene hydrazone compounds were characterized by elemental analysis, FT-IR, ^{1}H, ^{13}C, ^{31}P and 2D-HSQC NMR spectroscopy and MALDI-TOF mass spectrometry.

*3.2. X-ray crystal structure HFPC (**1**)*

The HFPC molecule comprises a cyclotriphosphazene core and six 4-formylphenoxy groups. The X-ray crystallographic details are given in Table 1. An ORTEP of **1** with thermal ellipsoids drawn at 30% probability is shown in Fig. 1. It consists of a non-centrosymmetric, non-planar cyclic trimeric phosphazene ring with each phosphorus atom attached to two 4-formylphenoxy moieties. Three of the six 4-formylphenoxy substituents are on one side of the cyclophosphazene ring while the other three substituents are located on another side (Fig. 1). Selected bond distances are summarized in Table 2. A list of significant bond angles and torsion angles are given in Table 3.

The compound **1** crystallizes in $P2_1/n$ space group with z = 4. The six-membered phosphazene ring is slightly non-planar with a total puckering parameter of Q_T = 0.1104(2) Å. The conformation of the P_3N_3 ring is that of a twisted-boat with q_2 = 0.1071(2) Å, q_3 = −0.0269(2) Å, Φ_2 = −28.06(1)° and θ_2 = 104.08(1)°. Of the other molecules whose structures have been studied, the chloro



Scheme 1. Synthetic pathway and chemical structure for cyclophosphazene hydrazones **3a–i**.

derivative $[N_3P_3(Cl)_6]$ has slightly non-planar rings in the chair conformation [32] and phenoxy derivative $[N_3P_3(-OC_6H_5)_6]$ has slightly folded ring with approximate C_2 symmetry [33]. The deviations from planarity have been ascribed to intra- and inter-molecular steric effect [32,33].

The 4-formylphenoxy groups of the HFPC molecule show significant deviations from a symmetrical arrangement. The most notable of these distortions is the inequivalence of the orientation of the two 4-formylphenoxy groups bonded to each P atom. Fig. 2 shows orientations of these groups relative to the O—P—O planes. The arrangements are in fact different at the three phosphorus atoms, so that the molecule deviates from the threefold symmetry, at least, in the crystalline state.

The bond angles (Table 3) at phosphorus and nitrogen also show significant variations from threefold symmetry. The N—P—N angles in the ring are significantly smaller than the P—N—P angles. The N3—P3—N2 angle, 116.92(17)° is smaller than the N—P—N angles at Pl and P2. The P—N—P angles at N1, N2 and N3 are nearly equal. The most significant feature is that the O5—P3—O6 angle, 94.07(15)° is smaller than the O—P—O angles at Pl and P2. The O—P—N and P—O—C angles vary over several degrees, and these values are probably influenced by the orientation of the 4-formylphenoxy groups.

C—C—C bond angles of the phenyl ring are in the range 117.8(4)–122.7(4)° which is characteristic of the sp^2-hybridized carbons. O—C—C and O—C—H angles around the carbonyl carbon of the aldehyde group are in the range 106.3(7)–125.9(5)° and 117.1–126.8° respectively. As the O—C—C angle of the carbonyl carbon increases the O—C—H angle decreases. Crystal packing forces may explain this variation.

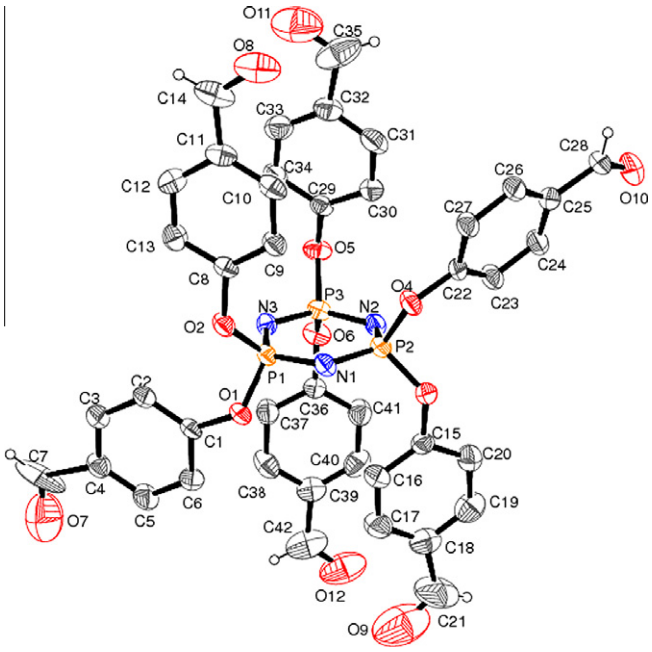


Fig. 1. ORTEP plot of HFPC (**1**) with the thermal ellipsoids drawn at the 30% probability level. Hydrogen atoms of the phenyl rings are omitted for clarity.

The P—N distances range from 1.568(3) to 1.587(3) Å, with a mean value of 1.576(3) Å which is essentially equal to the mean

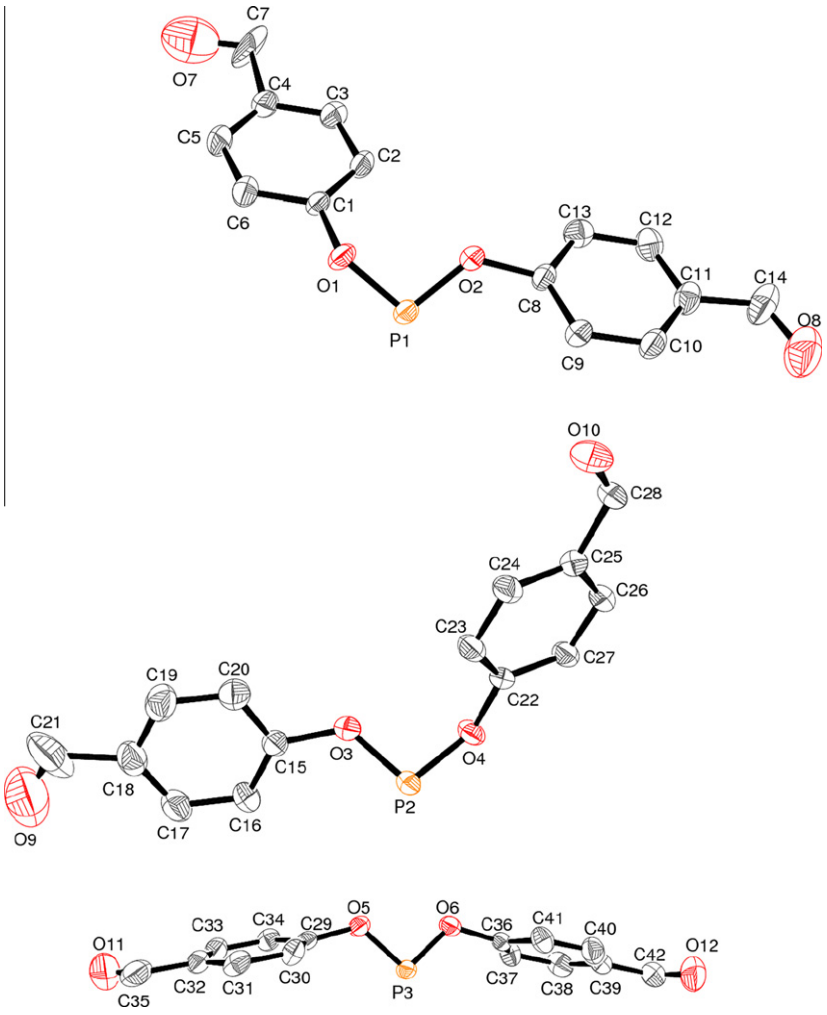


Fig. 2. Views along the O—P—O planes, showing arrangement of the *p*-formylphenoxy groups.

P—N distances of 1.575(2) in $N_3P_3(—OC_6H_4)_6$ molecule [33] and 1.578(3) in $N_3P_3(—OC_6H_4—o—OCH_3—p—CHO)_6$ molecule [34]. The P—O bonds are in the range 1.569(3)–1.588(3) Å, with a mean distance of 1.577(3) Å are 0.13 Å shorter than the single-bond distance [35], suggesting considerable exocyclic π-bonding. The distances of C—O bonds between the first carbon atom of each phenyl ring and the O atom attached to the P atom of the cyclophosphazene ring range from 1.389(4) to 1.410(5) Å and are higher than the value of 1.354(2) Å for the corresponding C—O bond in 4-hydroxybenzaldehyde [36]. It indicates that the conjugation of oxygen with the aromatic ring is decreased due to π-bond character of the O—P bonds.

The C—C bond distances of the phenyl ring are in the normal range of 1.354(7)–1.406(6) Å which is characteristic of the delocalized phenyl rings. The C—O bonds of the aldehyde group exhibits a typical double-bond character with bond distance ranging from 1.179(8) to 1.257(7) Å. The C—C bonds between the carbon of the aldehyde group and the carbon atom of phenyl ring are in the range 1.463(7)–1.646(8) Å. Most of the shorter contacts involve the 4-formylphenoxy groups.

There are no significant differences among chemically equivalent bond lengths. The angular deviations from threefold symmetry are probably a result of steric interactions among the bulky 4-formylphenoxy-groups. The observed molecular geometry is probably adopted to optimize both intra- and inter-molecular steric interactions.

3.3. IR spectral studies

The diagnostic IR bands are summarized in Table 5. The aldehyde carbonyl groups of the core (**1**) which were observed at 1704 cm^{-1} disappeared following hydrazone formation, accompanied by the appearance of C=N stretching frequencies in the 1600–1608 cm^{-1} region. A broad band at 3236–3257 cm^{-1} is due to N—H stretching frequency of the amide (—NH—C=O) moiety. In case of **3e** amide band was merged with O—H stretching frequency. A strong band at 1646–1663 cm^{-1} is ascribed to the amide carbonyl (—NH—C=O) stretching frequencies. A medium intensity absorption band at 3062–3074 cm^{-1} is attributed to the stretching vibrations of the aromatic C—H groups. The P=N stretching vibrations, which are observed between 1166 and 1211 cm^{-1} as sharp bands are characteristic of cyclophosphazenes. Furthermore, these cyclophosphazene derivatives show another important infrared band in the 952–960 cm^{-1} region attributed to P—O—R stretching. Thus, the IR spectral data results provide strong evidences for the formation of the cyclotriphosphazene hydrazones.

3.4. NMR investigations

The ^{1}H, ^{13}C and ^{31}P NMR spectra were obtained in dimethyl sulfoxide-d_6. According to the NMR spectral data, all the cyclophosphazene hydrazone (**3a–i**) molecules appear to have symmetric structures in the solution. The 2D-Heteronuclear Single Quantum

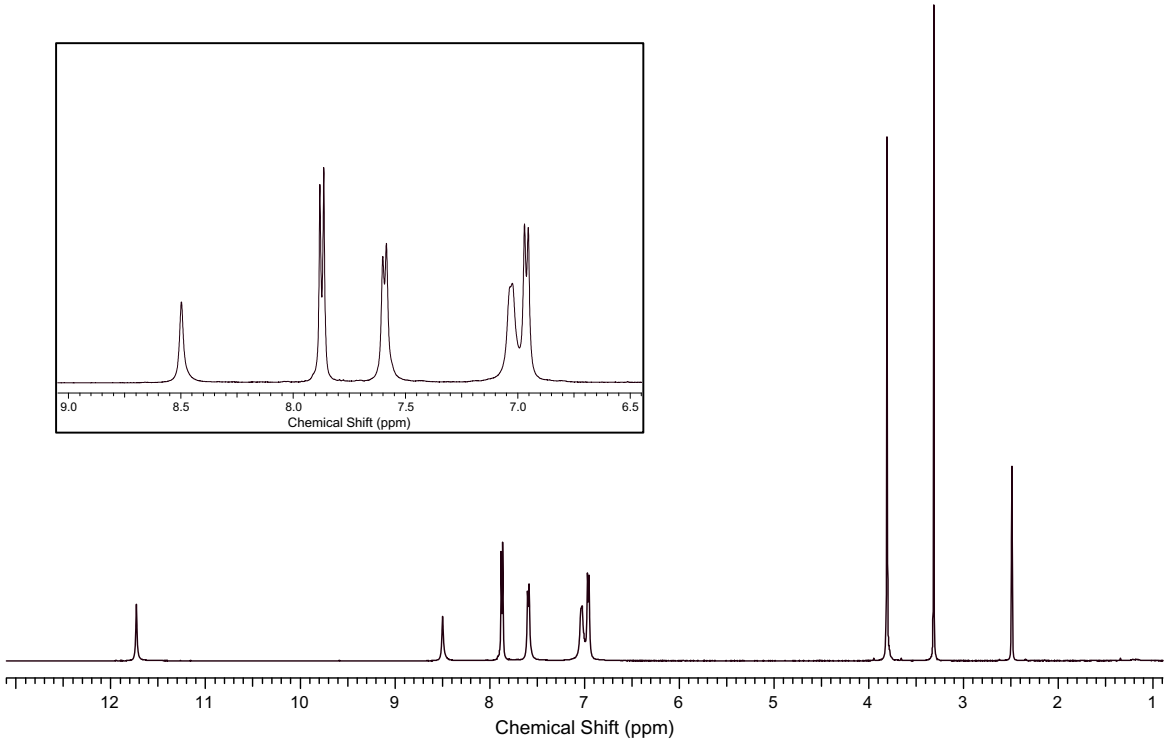


Fig. 3. ^{1}H NMR spectrum of **3f** in DMSO-d_6 (expansion of the aromatic region is shown in the box inset).

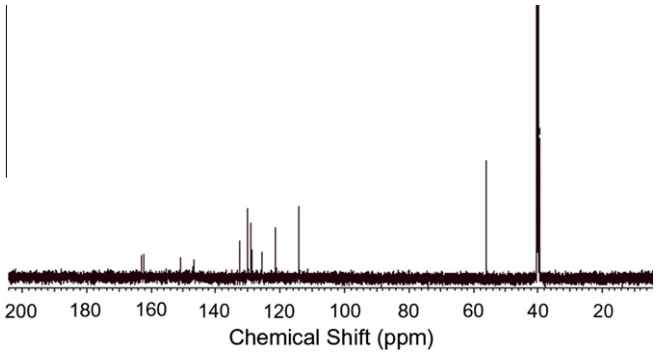


Fig. 4. The ^{13}C NMR spectra of **3f** in DMSO-d_6.

Coherence (HSQC) NMR study was undertaken to correlate chemical shifts of directly bound ^{1}H and ^{13}C nuclei and a representative spectrum of compound **3f** is displayed in Fig. 5. Detailed assignment of ^{1}H and ^{13}C NMR resonances presented in Tables 6 and 7 respectively was made based on the 2D-HSQC NMR analysis.

3.4.1. ^{1}H NMR studies

^{1}H NMR spectrum of **1** showed a singlet peak at 9.92 ppm for aldehyde protons in addition to the two doublet peaks at 7.15 and 7.77 ppm for the aromatic ring protons. The absence of the aldehydic proton resonance and the appearance of azomethine (—***H***C═N—N—) protons in the range 8.47–8.58 ppm integrating for six protons along with hydrazide (—CO—N***H***—N═C) protons as a broad singlet peak accounting for six protons in the downfield region 11.71–12.10 ppm confirms the formation of hydrazones compounds **3a**–**i**. The resonances due to 48 aromatic (H^2, H^3, H^8 and H^9) protons appear in the range 6.82–8.26 ppm as four doublets for the new compounds except for **3a** which exhibited two triplets and three doublets accounting for 54 (H^2, H^3, H^8, H^9 and H^{10}) protons. The six *para*-hydroxy (—OH) protons of **3e** resonate as a singlet in the downfield region 10.14 ppm. In case of **3f** and **3g** a singlet at 3.81 ppm and 2.36 ppm accounts for eighteen protons of *p*-methoxy (—OCH_3) and *p*-methyl (—CH_3) groups respectively. A representative ^{1}H NMR spectrum of compound **3f** is displayed in Fig. 3.

3.4.2. ^{13}C NMR spectral studies

^{13}C NMR analysis agreed with the ^{1}H NMR analysis in demonstrating the architecture of the star shaped hydrazones. In the ^{13}C NMR spectrum of compound **1**, the aldehyde carbon atoms are observed at 192.55, at the lowest downfield position of the carbon atoms. None of the ^{13}C NMR spectra of compounds **3a**–**i** exhibited any signal that could be attributed to unreacted aldehyde functions. ^{13}C NMR spectra of hydrazones showed resonance in the range 146.71–148.55 ppm due to the carbons (C^5) of the azomethine (H***C***═N—N) functions. 2D-HSQC NMR confirms that the signal observed in 161.8–163.7 ppm region is devoid of directly attached hydrogen and is assigned to amide carbonyl C^6.

From 2D HSQC NMR spectrum it is clear that the ^{13}C peaks of **3a–i** at δ values 150.65–151.32 and 129.16–132.68 ppm are due to carbons which do not bear directly attached hydrogen and are assigned to C^1 and C^4 respectively. The resonances arising from C^1 carbons are shifted upfield by 3.15–3.82 ppm compared to the corresponding signal at 154.47 ppm in **1**. The signals of C^2 and C^3 were observed in the range 120.81–121.40 and 129.07–130.77 ppm respectively. The resonances of these inner aromatic ring carbons remain almost unperturbed by the influence of the *para*-substituents at the periphery of the hydrazone arm.

C^7 and C^9 do not have directly attached protons hence does not exhibit contours in 2D HSQC NMR spectrum and the resonances of these carbons are influenced by the substituent at C^{10} carbon. Resonances in the range 128.10–129.31 ppm are attributed to C^8 carbons. The C^{10} carbons show large variation in their resonances depending upon the inductive and mesomeric effect of the substituent attached. In case of **3a**, carbons (C^{10}) bonded to hydrogen

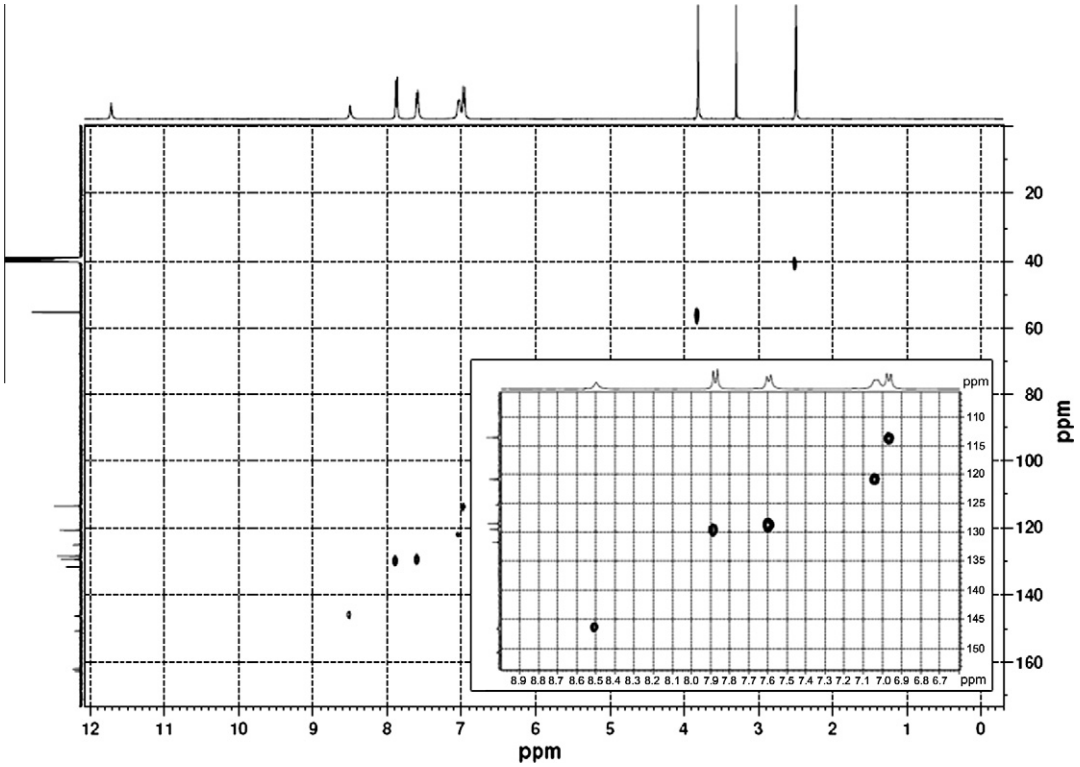


Fig. 5. 2D-HSQC-NMR spectra of **3f** in DMSO-d_6 (expanded form of the aromatic region is shown in the box inset).

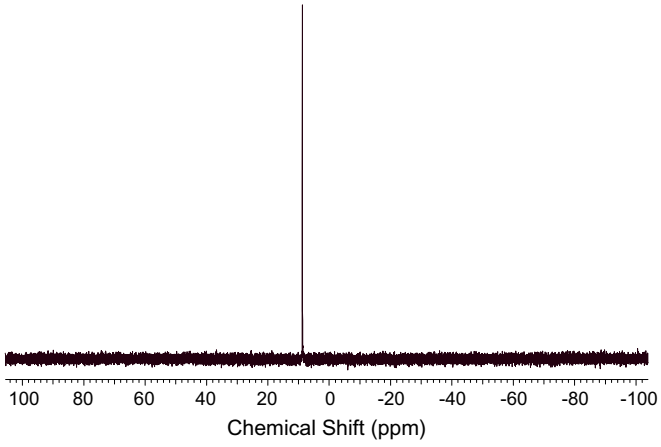


Fig. 6. ^{31}P NMR spectra of **3f** in DMSO-d_6.

show resonances at 132.21 while in **3g** they are attached to methyl group and resonates at 142.22 ppm. The signals due to the C^{10} attached to bromine (**3b**), chlorine (**3c**) and fluorine (**3d**) show downfield shift with increasing electronegativity of halogen substitutions and were observed at 126.00, 137.04 and 165.00 ppm respectively. The resonances arising from C^{10} attached to the hydroxy (**3e**), methoxy (**3f**) nitro (**3h**) and amino (**3i**) groups are observed at 161.22, 163.13, 149.52 and 152.32 ppm respectively. A representative ^{13}C NMR spectrum of **3f** is given at Fig. 4.

3.4.3. ^{31}P NMR spectral studies

The ^{1}H-decoupled ^{31}P NMR data of the cyclophosphazenes are given in Table 8. The ^{31}P NMR spectra of cyclophosphazene compounds **3a**–**i** bearing the six hydrazone arms exhibited a unique sharp singlet in the range 8.59–8.83 ppm indicating the symmetrically substituted phosphorus atoms in the cyclophosphazene ring. A deshielding effect of 1.8–2.04 ppm was detected in ^{31}P NMR when moving from aldehyde groups (δ ^{31}P = 6.79 ppm) to hydrazone groups. The *para*-substituents on the peripheral phenyl group are presumably too far from the cyclophosphazene center to influence the ^{31}P NMR shift to a larger extent. In the ^{31}P NMR spectrum of **3f** given as an example at Fig. 6, singlet appears at 8.76 ppm.

3.5. Electronic absorption

The electronic absorption spectra of **3a**–**i** in DMSO solvent were recorded at room temperature and the absorption band maxima assignments are listed in Table 1. Cyclotriphosphazene ring themselves do not absorb in near UV region. The UV–vis spectra of the hydrazone cyclphosphazene derivatives **3a–i** exhibit a band in the range 304–310 nm which can be attributed to $\pi \rightarrow \pi^*$ transitions according to absorption of similar molecules [18].

3.6. Mass spectrometry

The complete reaction of all peripheral aldehyde groups of **1** and the single molecular nature of the hydrazone trimers **3a**–**i** was also checked by MALDI-TOF mass spectrometry, which confirmed the expected chemical structures with *m*/*z* values corresponding to $(M+Na)^+$ ion (Table 1). MALDI-TOF mass spectrometry of **3f** is given as an example at Fig. 7.

3.7. Thermal decomposition studies

The high thermal stability of organophosphazenes is well-known [37] and has made these inorganic scaffolds good candidates for the preparation of thermally stable materials. The newly synthesized cyclophosphazene hydrazones are stable up to a temperature close to 310 °C as measured by TGA at a heating rate of 10 °C min^{-1}.

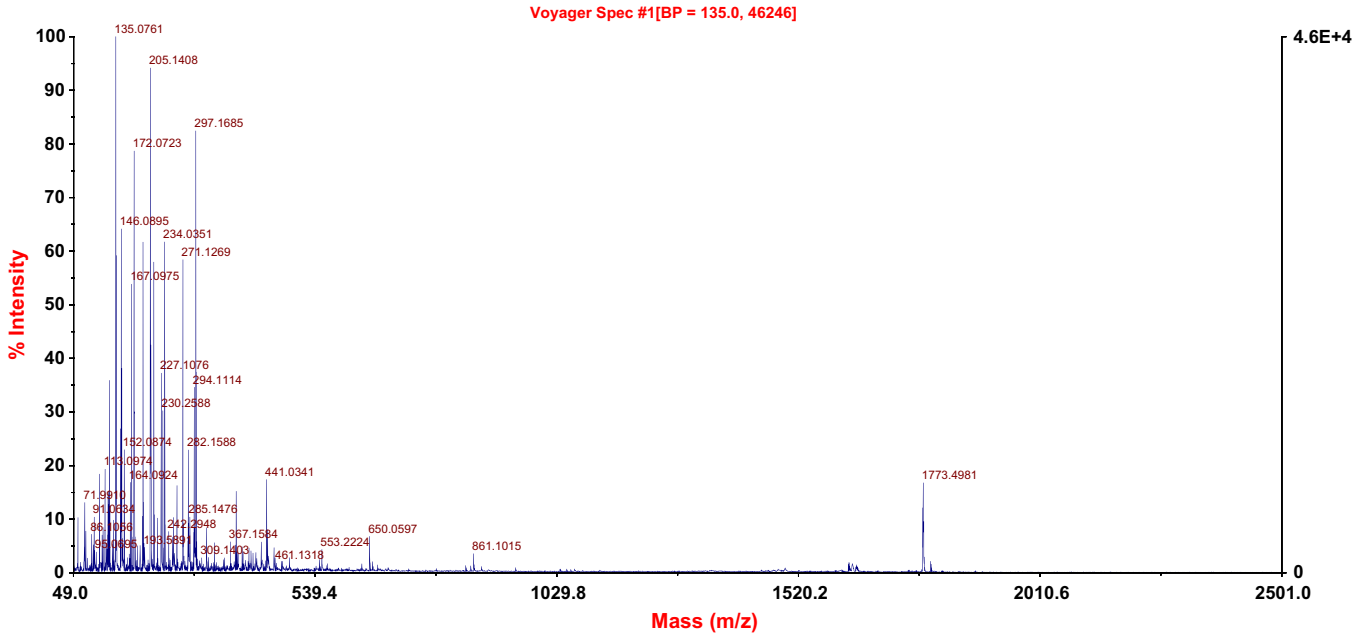


Fig. 7. MALDI-TOF mass spectrum of **3f**, *m*/*z* value 1773.4981 corresponds to $(M+Na)^+$ ion.

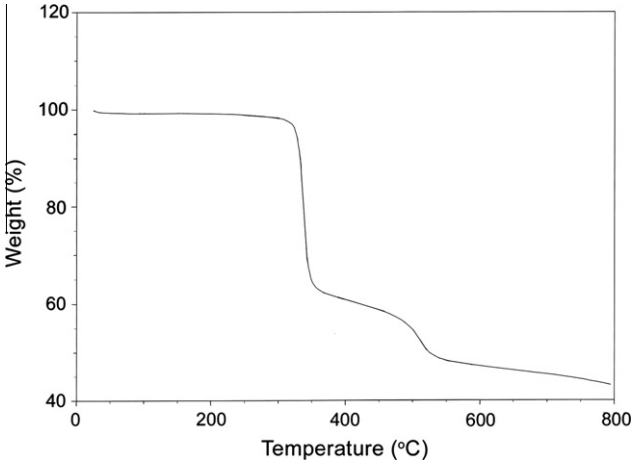


Fig. 8. TGA thermogram of **3f**.

Thermal decomposition of **3a–i** proceeds in two stages. The first stage loss in the temperature range of 329–345 °C is related to the volatilization of organic components arising from the peripheral phenyl groups. The second stage loss at higher temperature range of 489–528 °C is associated with the decomposition of the intermediate product. The final decomposition product (40–45%) at 800 °C is a pyrolitic residue [38]. A representative TGA thermogram of compound **3f** is displayed in Fig. 8.

4. Conclusion

A new general synthesis of the hexa-arm star shaped molecules bearing hydrazone functions is reported. Hexakis(4-formylphenoxy)-cyclotriphosphazene (**1**), a trimer which possesses six aldehydic functions on the side substituents was used as starting material. X-ray crystal analysis of the HFCP (**1**) was undertaken in order to determine the influences of the steric and electronic factors of the 4-formylphenoxy groups on the trimeric phosphazene ring system. The reactive terminal aldehyde groups in HFCP could be readily elaborated to the hexafunctionalized hydrazones by condensation with the benzoic hydrazides. Formation of the hydrazone moieties was corroborated by the absence of signals due to aldehyde groups and presence of hydrazone moieties in ^{1}H, ^{13}C and 2D-HSQC NMR as well as in IR spectroscopy. The constitutions and the structural homogeneities of the hexa-arm star shaped hydrazones were ascertained by ^{31}P NMR spectrum. MALDI-TOF mass spectrometry and microanalysis also confirmed the expected chemical structures. These cyclophosphazene hydrazones exhibit high thermal stability, as deduced from the thermogravimetric curves.

The compounds **3a–i** have been identified as fully substituted symmetric trimers and are important as synthetic and structural models for the reactions and molecular structure of the analogous high-polymeric phosphazenes [24]. Efforts on the synthesis and characterization of corresponding linear macromolecules and other cyclophosphazene hydrazones are in progress and will be reported in future communications.

Supplementary material

CCDC 678839 contains full crystallographic data for HFPC (**1**) molecule. Copies of this information may be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax:+44 1223 336033; email: deposit@ccdc.cam.ac.uk.

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