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Syntheses and spectroscopic investigations of 2-pyridyl(N/N)spirocyclotriphosphazenes

Gamze Elmas
Ankara University, 06100, Ankara, Turkey

Abstract: The Cl substitution reaction of $N_3P_3Cl_6$ (**1**) with *N*-(2-pyridyl)-methyl-*N*'-methylpropane-1,3-diamine (**2**) afforded the partly substituted 2-pyridyl(N/N)spirocyclotriphosphazene (**3**) (with a yield of 57%) in dry THF. When the Cl replacement reactions of **2** carried out with excess pyrrolidine, morpholine, and 1,4-dioxa-8-azaspiro[4,5]decane (DASD), the corresponding 2-pyridyl(N/N)spirotetrapyrrolidino (**3a**), tetramorpholino (**3b**) and tetra(1,4-dioxa-8-azaspiro[4,5]decano) (**3c**) cyclotriphosphazenes were prepared in moderate yields. The structures of four cyclotriphosphazene derivatives were elucidated by the elemental analyses, Fourier transform infrared (FTIR), heteronuclear mass spectrometry (ESI-MS), heteronuclear multiple-bond correlation (HMBC), single quantum coherence (HSQC), ^{1}H, ^{13}C, and ^{31}P NMR techniques.

Keywords: 2-Pyridyl(N/N)spirocyclotriphosphazenes, Replacement reactions, Spectroscopy

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***Corresponding author. E-mail:** gegemen@ankara.edu.tr

Tel: +90 0312 2126720/1195.

INTRODUCTION

Cyclophosphazenes are inorganic heterocyclic ring systems consisting of a backbone that contains the repeating unit $[N=PX_2]_n$ (n=3,4,5,…) with nitrogen and phosphorus atoms and two organic, inorganic and/or organometallic side groups (X), linked covalently to each phosphorus atom (1,2). Hexachlorocyclotriphosphazene, $N_3P_3Cl_6$, is the best-known starting compound used for the preparation of the new phosphazene derivatives in the field of phosphazene chemistry (3). Hence, its Cl substitution reactions with monodentate (4,5) and bidentate reagents (6,7) have been thoroughly examined for years on account of the formation of various structural isomers and stereoisomers. The replacement reactions of $N_3P_3Cl_6$ with monoamines and diamines led to the formation of partly and fully substituted aminocyclotriphosphazenes (8). For instance, in the literature, there are many studies on the reactions of $N_3P_3Cl_6$ with various N/N donor typed difunctional ligands, *e.g.* containing 4-fluorobenzyl, ferrocenyl, and 4-nitrobenzyl pendant arms for the formation of the partly substituted (N/N)spirocyclotriphosphazenes (9-11). The fully substituted cyclophosphazenes are also obtained with the reactions of these products with excess monoamines (9-11).

On the other hand, the prepared cyclotriphosphazenes are used as liquid crystalline materials (12), ionic liquids (13), organic light emitting diodes (OLEDs) (14), photosensitizers (15), fluorescence chemosensors (16) and Langmuir–Blodgett thin films (17).

Besides, aziridino, pyrrolidino, morpholino and tetra(1,4-dioxa-8-azaspiro[4,5]decano) phosphazenes have revealed significant antibacterial, antifungal, and anticancer activities, and they were determined to be efficient in changing the mobility of the DNA (18-21). In such a manner, that some of the cyclophosphazenes were also found to be active in the different tumor cells; *e.g.* Hep2, HT-29, Hela, C6, Vero, DLD1 and A549 cells (22-24).

In addition, the pyridine derivatives are quite essential compounds with the incredible biological applications (25,26). The new compounds, which contain a trimeric phosphazene ring with 2-pyridyl pendant arm, may be considered to have possibly antimicrobial, anticancer, antituberculosis, and antiproliferative activities.

Consequently, this paper reports herein the salient features of the synthetic and spectroscopic properties of the partly (**3**) and fully heterocyclic amine substituted *spiro*-phosphazene derivatives (**3a-3c**).

EXPERIMENTAL PART

Materials and Methods

The starting compound, $N_3P_3Cl_6$ (Aldrich) was recrystallized from n-hexane. The solvents and reagents were purified using the standard methods before use. N-methylpropane-1,3-diamine, pyridine-2-carboxaldehyde, pyrrolidine, morpholine and 1,4-dioxa-8-azaspiro[4,5]decane (DASD) were supplied by Merck. The reactions were performed under Ar and monitored by TLC on Merck DC Alufolien Kiesegel 60 B254 sheets using various solvents. The melting points of the phosphazenes were designated on a Gallenkamp apparatus by capillary tubes. The elemental analyses of the compounds were carried out using a Leco CHNS-932 instrument in microanalytical service of Ankara University. The FTIR spectra were obtained from Jasco FT/IR-430 spectrometer in KBr disks and reported in cm^{-1} units. Mass spectra (ESI-MS) of the products were recorded on the Waters 2695 Alliance Micromass ZQ spectrometer. The ^1D (^1H and ^{13}C NMR) and ^2D (HSQC and HMBC) spectra were monitored on a Varian Mercury FT-NMR (400 MHz) spectrometer using $SiMe_4$ as an internal standard operating at 400.13 and 100.62 MHz (at Ankara University). $^{31}P\{^1H\}$ NMR spectra were saved on a Bruker Avance III HD (600 MHz) spectrometer using 85% H_3PO_4 as an external standard operating at 242.94 MHz (at Inönü University). The spectrometer was fitted with a 5 mm PABBO BB inverse-gradient probe, and standard Bruker pulse programs (27) were used.

Synthesis of 2-pyridyldiamine (2). *N*-(2-Pyridyl)-methyl-*N*'-methylpropane-1,3-diamine (**2**) was obtained from the reaction of pyridine-2-carboxyaldehyde with *N*-methylpropane-1,3-diamine in ethanol at -10 °C concerning to the published procedure (28).

Synthesis of 2-pyridyl(N/N)spirocyclotriphosphazene (3). A solution of **2** (2.20 g, 12.30 mmol) in THF (100 mL) and triethylamine (5.70 mL, 40.00 mmol) was added to a solution of $N_3P_3Cl_6$ (3.56 g, 10.00 mmol) in THF (50 mL) at -10 °C under Ar. The mixture was stirred for three days at room temperature, and then it was refluxed for two days. The precipitated triethylamine hydrochloride was filtered off, and the solvent was evaporated at reduced pressure. The product was purified by column chromatography using toluene:THF (2:1) as eluent, and an off-white powder of **3** crystallized from toluene. Yield: 2.59 g (57%). mp: 120 °C. Anal. Calcd. for $P_3N_6Cl_4C_{10}H_{15}$: C, 26.46; H, 3.33; N, 18.51. Found: C, 25.98; H, 3.67; N, 18.41. ESI-MS (fragments are based on ^{35}Cl, Ir %, Ir designates the fragment abundance percentage): *m/z* 455 ($[M+H]^+$, 100). FTIR (KBr, cm^{-1}): *v* 2924, 2855 (C-H aliph.), 1220 (asymm.), 1169 (symm.) (P=N), 579 (asymm.), 510

(symm.) (PCl). ^{1}H NMR (400 MHz, $CDCl_3$, ppm, numberings of protons are given in Figure 1): δ 8.59 (d, H, $^{3}J_{HH}$=5.2 Hz, H_5), 7.89 (dd, H, $^{3}J_{HH}$=7.6 Hz, $^{3}J_{HH}$=8.0 Hz, H_3), 7.73 (d, H, $^{3}J_{HH}$=8.0 Hz, H_2), 7.38 (dd, H, $^{3}J_{HH}$=5.2 Hz, $^{3}J_{HH}$=7.6 Hz, H_4), 4.31 (d, 2H, $^{3}J_{PH}$=11.2 Hz, Py-CH_2-N), 3.20 (t, 2H, $^{3}J_{PH}$=12.0 Hz, $^{2}J_{HH}$=6.0 Hz, Py-CH_2-N-CH_2), 3.15 (t, 2H, $^{3}J_{PH}$=11.6 Hz, $^{2}J_{HH}$=5.6 Hz, CH_3-N-CH_2), 2.63 (d, 3H, $^{3}J_{PH}$=14.0 Hz, N-CH_3), 1.92 (m, 2H, $^{3}J_{HH}$=6.0 Hz, $^{3}J_{HH}$=5.2 Hz, N-CH_2-CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, ppm, numberings of carbons are given in Figure 1): δ 156.79 (d, $^{3}J_{PC}$=8.5 Hz, C_1), 147.02 (s, C_5), 138.96 (s, C_3), 123.18 (s, C_2), 122.94 (s, C_4), 51.44 (d, $^{2}J_{PC}$=3.8 Hz, Py-CH_2-N), 50.03 (s, Py-CH_2-N-CH_2), 47.16 (s, CH_3-N-CH_2), 34.98 (d, $^{2}J_{PC}$=1.5 Hz, N-CH_3), 25.09 (d, $^{3}J_{PC}$=3.0 Hz, N-CH_2-CH_2).

Synthesis of 2-pyridyl(N/N)spirotetrapyrrolidino-cyclotriphosphazene (3a). A solution of **3** (0.80 g, 1.80 mmol) and triethylamine (1.00 mL, 7.20 mmol) in dry THF (100 mL) was added slowly to a solution of pyrrolidine (1.19 mL, 14.40 mmol) in dry THF (50 mL) under Ar. The mixture was stirred for two days at ambient temperature, and then it was refluxed for two days. The crude product was purified by column chromatography using toluene-THF (2:1) as eluent, and an off-white powder of **3a** was crystallized from toluene. Yield: 0.68 g (64%). mp: 169 °C. Anal. Calcd. for $P_3N_{10}C_{26}H_{47}$. 0.5 C_7H_8: C, 55.50; H, 8.05; N, 21.94. Found: C 55.66; H, 8.28; N, 21.48. ESI-MS (Ir %): *m/z* 593 ([M+H]$^+$, 100). FTIR (KBr, cm^{-1}): *v* 2958, 2851 (C-H aliph.), 1225 (asymm.), 1172 (symm.) (P=N). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.48 (d, H, $^{3}J_{HH}$=4.2 Hz, H_5), 7.72 (d, H, $^{3}J_{HH}$=8.0 Hz, H_2), 7.63 (dd, H, $^{3}J_{HH}$=7.6 Hz, $^{3}J_{HH}$=8.0 Hz, H_3), 7.12 (dd, H, $^{3}J_{HH}$=6.0 Hz, $^{3}J_{HH}$=7.6 Hz, H_4), 4.20 (d, 2H, $^{3}J_{PH}$=7.6 Hz, Py-CH_2-N), 3.16 (m, 2H, CH_3-N-CH_2), 3.08 [m, 16H, N-CH_2 (pyrr)], 3.07 (m, 2H, Py-CH_2-N-CH_2), 2.60 (d, 3H, $^{3}J_{PH}$=13.6 Hz, N-CH_3), 1.79 (m, 2H, $^{3}J_{HH}$=5.2 Hz, N-CH_2-CH_2), 1.78 [m, 8H, N-CH_2-CH_2 (pyrr)], 1.64 [m, 8H, N-CH_2-CH_2 (pyrr)]. ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 161.16 (d, $^{3}J_{PC}$=11.6 Hz, C_1), 148.68 (s, C_5), 136.45 (s, C_3), 121.72 (s, C_2), 121.61 (s, C_4), 52.78 (d, $^{2}J_{PC}$=2.9 Hz, Py-CH_2-N), 50.99 (s, Py-CH_2-N-CH_2), 47.09 (s, CH_3-N-CH_2), 46.20 and 46.18 [s, N-CH_2 (pyrr)], 36.36 (m, N-CH_3), 26.29 [(d, $^{3}J_{PC}$=6.9 Hz, N-CH_2-CH_2 (pyrr)], 26.22 [(d, $^{3}J_{PC}$=6.1 Hz, N-CH_2-CH_2 (pyrr)], 25.01 (d, $^{3}J_{PC}$=2.9 Hz, N-CH_2-CH_2).

Synthesis of 2-pyridyl(N/N)spirotetramorpholino-cyclotriphosphazene (3b). The experimental procedure was carried out as in **3a**, using **3** (0.80 g, 1.80 mmol), triethylamine (1.00 mL, 7.20 mmol) and morpholine (1.25 mL, 14.40 mmol). The mixture was stirred for two days at ambient temperature, and then it was refluxed for three days. The crude product was purified by column chromatography using toluene-THF (2:1) as eluent, and an off-white powder of **3b** crystallized from toluene. Yield: 0.66 g (56%). mp: 145 °C. Anal. Calcd. for $P_3N_{10}O_4C_{26}H_{47.}$ 0.5 C_7H_8: C, 50.45; H, 7.32; N, 19.94. Found: C, 50.93; H, 7.38; N, 20.05. ESI-MS (Ir %): *m/z* 657 ([M+H]$^+$, 100). FTIR (KBr, cm^{-1}): *v*

2918, 2851 (C-H aliph.), 1248 (asymm.), 1159 (symm.) (P=N). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.55 (d, H, $^{3}J_{HH}$=4.8 Hz, H_5), 7.45 (d, H, $^{3}J_{HH}$=8.0 Hz, H_2), 7.30 (dd, H, $^{3}J_{HH}$=8.0 Hz, $^{3}J_{HH}$=8.0 Hz, H_3), 7.18 (dd, H, $^{3}J_{HH}$=4.4 Hz, $^{3}J_{HH}$=8.0 Hz, H_4), 4.32 (d, 2H, $^{3}J_{PH}$=9.6 Hz, Py-CH_2-N), 3.69 [m, 8H, O-CH_2 (morp)], 3.65 [m, 8H, O-CH_2 (morp)], 3.21 (t, 2H, $^{3}J_{PH}$=12.0 Hz, $^{2}J_{HH}$=6.0 Hz, Py-CH_2-N-CH_2), 3.16 [m, 16H, N-CH_2 (morp)], 3.12 (t, 2H, $^{3}J_{PH}$=11.2 Hz, $^{2}J_{HH}$=5.6 Hz, CH_3-N-CH_2), 2.69 (d, 3H, $^{3}J_{PH}$=11.6 Hz, N-CH_3), 1.97 (m, 2H, $^{3}J_{HH}$=7.2 Hz, $^{3}J_{HH}$=7.2 Hz, N-CH_2-CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 157.45 (d, $^{3}J_{PC}$=6.1 Hz, C_1), 149.45 (s, C_5), 137.17 (s, C_3), 122.77 (s, C_2), 121.66 (s, C_4), 67.10 [(d, $^{3}J_{PC}$=7.7 Hz, O-CH_2 (morp)], 66.87 [(s, O-CH_2 (morp)], 52.18 (d, $^{2}J_{PC}$=2.8 Hz, Py-CH_2-N), 50.49 (s, Py-CH_2-N-CH_2), 46.99 (s, CH_3-N-CH_2), 44.96 and 44.70 [s, N-CH_2 (morp)], 35.61 (d, $^{2}J_{PC}$=3.1 Hz, N-CH_3), 25.07 (d, $^{3}J_{PC}$=3.1 Hz, N-CH_2-CH_2).

Synthesis of 2-pyridyl(N/N)spirotetra-DASD-cyclotriphosphazene (3c). The experimental procedure was carried out as in **3a**, using **3** (0.80 g, 1.80 mmol), triethylamine (1.00 mL, 7.20 mmol) and DASD (1.85 mL, 14.40 mmol). The mixture was stirred for two days at ambient temperature, and then it was refluxed for two days. The crude product was purified by column chromatography using toluene-THF (2:1) as eluent, and an off-white powder of **3c** crystallized from toluene. Yield: 0.95 g (60%). mp: 177 °C. Anal. Calcd. for $P_3N_{10}O_8C_{38}H_{63}$: C, 51.84; H, 7.21; N, 15.91. Found: C, 51.49; H, 7.33; N, 15.46. ESI-MS (Ir %): *m/z* 881 ([M+H]$^{+}$, 100). FTIR (KBr, cm^{-1}): *v* 2918, 2851 (C-H aliph.), 1216 (asymm.), 1152 (symm.) (P=N). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 8.49 (d, H, $^{3}J_{HH}$=4.8 Hz, H_5), 7.68 (dd, H, $^{3}J_{HH}$=6.0 Hz, $^{3}J_{HH}$=7.6 Hz, H_3), 7.65 (d, H, $^{3}J_{HH}$=7.6 Hz, H_2), 7.13 (dd, H, $^{3}J_{HH}$=6.0 Hz, $^{3}J_{HH}$=7.6 Hz, H_4), 4.11 (d, 2H, $^{3}J_{PH}$=7.6 Hz, Py-CH_2-N), 3.95 [s, 8H, O-CH_2 (DASD)], 3.89 [s, 8H, O-CH_2 (DASD)], 3.22 [m, 16H, N-CH_2 (DASD)], 3.14 (m, 2H, Py-CH_2-N-CH_2), 3.05 (m, 2H, CH_3-N-CH_2), 2.54 (d, 3H, $^{3}J_{PH}$=13.6 Hz, N-CH_3), 1.81 (m, 2H, N-CH_2-CH_2), 1.65 [m, 8H, N-CH_2-CH_2 (DASD)], 1.52 [m, 8H, N-CH_2-CH_2 (DASD)]. ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 160.16 (d, $^{3}J_{PC}$=7.5 Hz, C_1), 148.64 (s, C_5), 136.57 (s, C_3), 125.45 (s, C_2), 121.74 (s, C_4), 107.79 and 107.52 [s, O-*C*-O (DASD)], 64.16 and 64.07 [s, O-CH_2 (DASD)], 52.63 (d, $^{2}J_{PC}$=3.0 Hz, Py-CH_2-N), 50.83 (s, Py-CH_2-N-CH_2), 47.16 (s, CH_3-N-CH_2), 42.77 and 42.68 [s, N-CH_2 (DASD)], 36.31 (m, N-CH_3), 35.65 and 35.44 [m, N-CH_2-CH_2 (DASD)], 25.16 (d, $^{3}J_{PC}$=3.0 Hz, N-CH_2-CH_2).

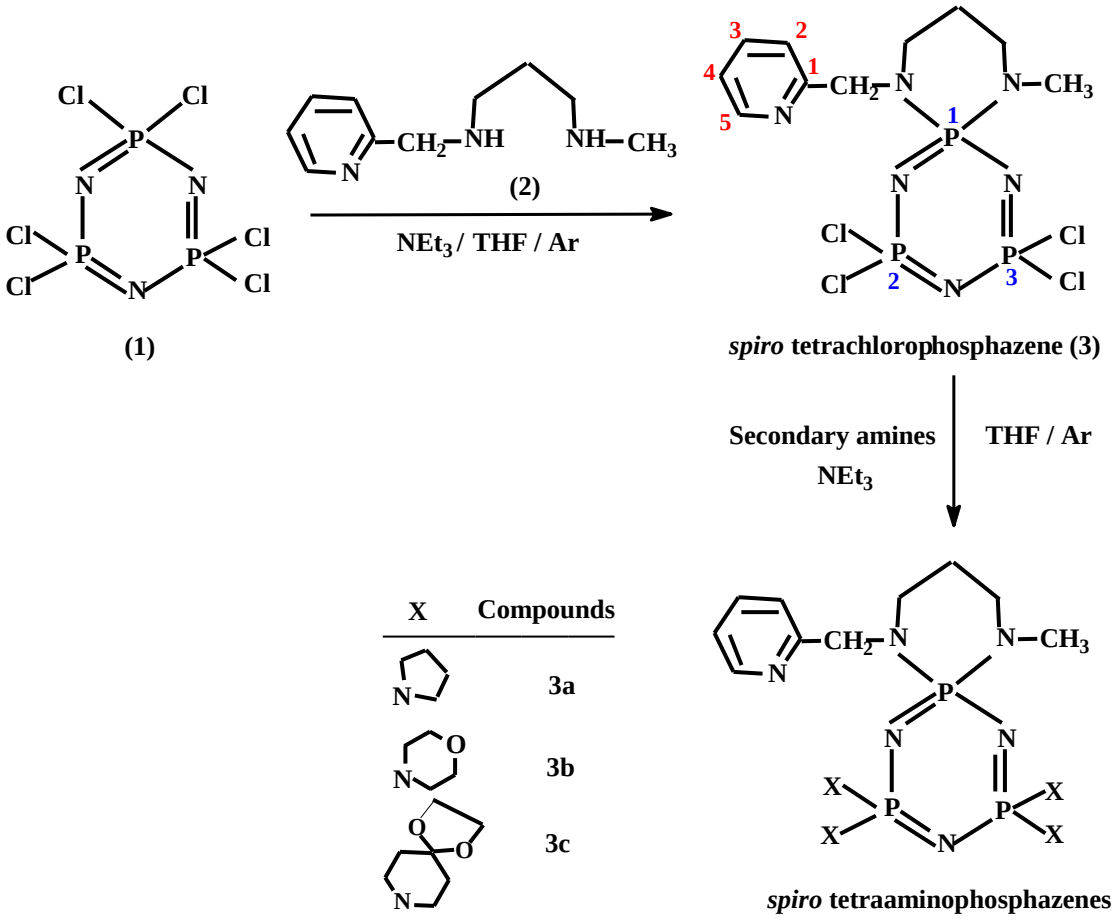


Figure 1. The synthesis of 2-pyridylspiro(N/N)cyclotriphosphazene (**3**) and its tetraamino derivatives (**3a-3c**).

RESULTS AND DISCUSSION

Syntheses

The reaction of pyridine-2-carboxyaldehyde with *N*-methylpropane-1,3-diamine led to the formation of the intermediate Schiff base. This product was reduced with $NaBH_4$ in ethanol to produce the difunctional ligand, *N*-(2-pyridyl)-methyl-*N*'-methylpropane-1,3-diamine (**2**), in accordance with the literature (28). The preliminary spiro cyclotriphosphazene; 2-pyridyl(N/N)spiro cyclotriphosphazene (**3**), was prepared from the reaction of $N_3P_3Cl_6$ with one equimolar amount of the 2-pyridyldiamine (**2**) with a yield of 57% in dry THF. The condensation reactions of **3** with excess pyrrolidine, morpholine and 1,4-dioxa-8-azaspiro[4,5]decane (DASD) afforded the fully amino substituted cyclotriphosphazenes (**3a-3c**). The estimating yields of these products were found to be 64, 56 and 60%, respectively (Figure 1).

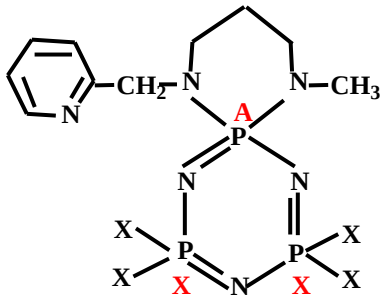
The structures of the 2-pyridylspiro(N/N)cyclotriphosphazenes with a half mole of toluene for **3a** and **3b**, were characterized by the elemental analyses, ESI-MS, FTIR, HSQC, HMBC, ^{1}H, ^{13}C and ^{31}P NMR techniques. The analytical and NMR results are given in the "Experimental Part". The ESI-MS spectra of all the trimeric phosphazenes exhibit the protonated molecular $[MH]^{+}$ ion peaks. The first leaving group in the ESI-MS spectra of the fully substituted compounds (**3a-3c**) was determined as 2-pyridyl-methyl [M-C_5H_4N-CH_2, 92].

NMR and IR Spectroscopy

The ^{31}P $\{^{1}H\}$ NMR chemical shifts and the coupling constants of 2-pyridylspiro(N/N)cyclotriphosphazenes (**3** and **3a-3c**) are tabulated in Table 1. The ^{31}P spectra of all the compounds display AX_2 type spectra on account of two different phosphorus environments within the structures, and they appear as one doublet (P_X) and one triplet (P_{spiro}, P_A). It is determined that the δ P_{spiro} chemical shifts of all the tetraamino-2-pyridylspiro(N/N)cyclotriphosphazenes (**3a-3c**) are higher than the compound **3**. As known, in compound **3**, the Cl atoms are withdrawing the electrons of the phosphazene ring. Hence, electrons are releasing from the nitrogen atoms of the spiro ring to the phosphazene skeleton and negative hyperconjugation occurs on the spiro phosphorus atom (29). This is reversed for the amino phosphazenes (**3a-3c**). On the contrary, the coupling constants of all the phosphazenes are nearly the same.

As examples, ^{31}P $\{^{1}H\}$ NMR spectra of the beginning spiro compound (**3**) and its morpholine substituted derivative (**3b**) are depicted in Figure 2. In the spectra of **3** and **3b**, the δ P_A of spiro (P_{NN}) and δ P_X (P_{Cl2} or P_{NN}) are 11.66 and 23.25 ppm, and 22.02 and 20.14 ppm, respectively. The $^{2}J_{PP}$ values of both are calculated as 38.9 Hz.

X: Cl, Pyrrolidine, Morpholine, DASD



AX_2 (3, 3a, 3b and 3c)

Compound	Spin Systems	P_A (P_{NN})	P_X (P_{NN})	P_X (P_{Cl2})	$^2J_{PP}$ (Hz)
3	AX_2	11.66 (t)	-	22.02 (d)	$^2J_{AX}$ 38.9
3a	AX_2	23.79 (t)	17.39 (d)	-	$^2J_{AX}$ 38.9
3b	AX_2	23.25 (t)	20.14 (d)	-	$^2J_{AX}$ 38.9
3c	AX_2	23.00 (t)	20.33 (d)	-	$^2J_{AX}$ 36.4

Table 1. ^{31}P {^1H} NMR data of 2-pyridyl(N/N)spirocyclotriphosphazenes.[a]

[a]242.925 MHz ^{31}P NMR measurements in $CDCl_3$ solutions at 298 K, and the chemical shifts referenced to external standard H_3PO_4.

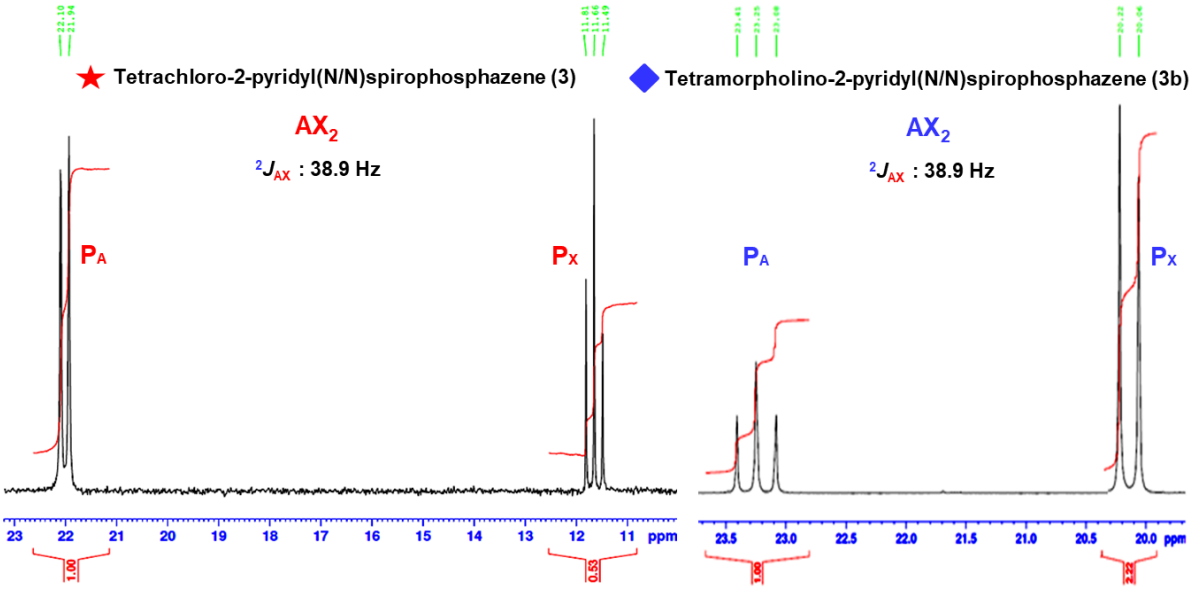


Figure 2. ^{31}P {^1H} NMR spectra of the compounds **3** and **3b**.

The interpretations of the δ chemical shifts, multiplicities, and J coupling constants are elucidated from the ^{13}C and ^1H NMR spectra of the new 2-pyridyl(N/N)spirocyclotriphosphazenes (**3** and **3a-3c**), and presented in "Experimental Part". The HSQC [using values corresponding to $^1J_{CH}$] and HMBC [using values corresponding to $^2J_{CH}$, $^3J_{CH}$ and $^4J_{CH}$ between the protons and carbons] are also quite useful for the assignments of the signals. The HMBC and HSQC spectra of **3a** are given in Figures 3a and 3b, respectively, as examples.

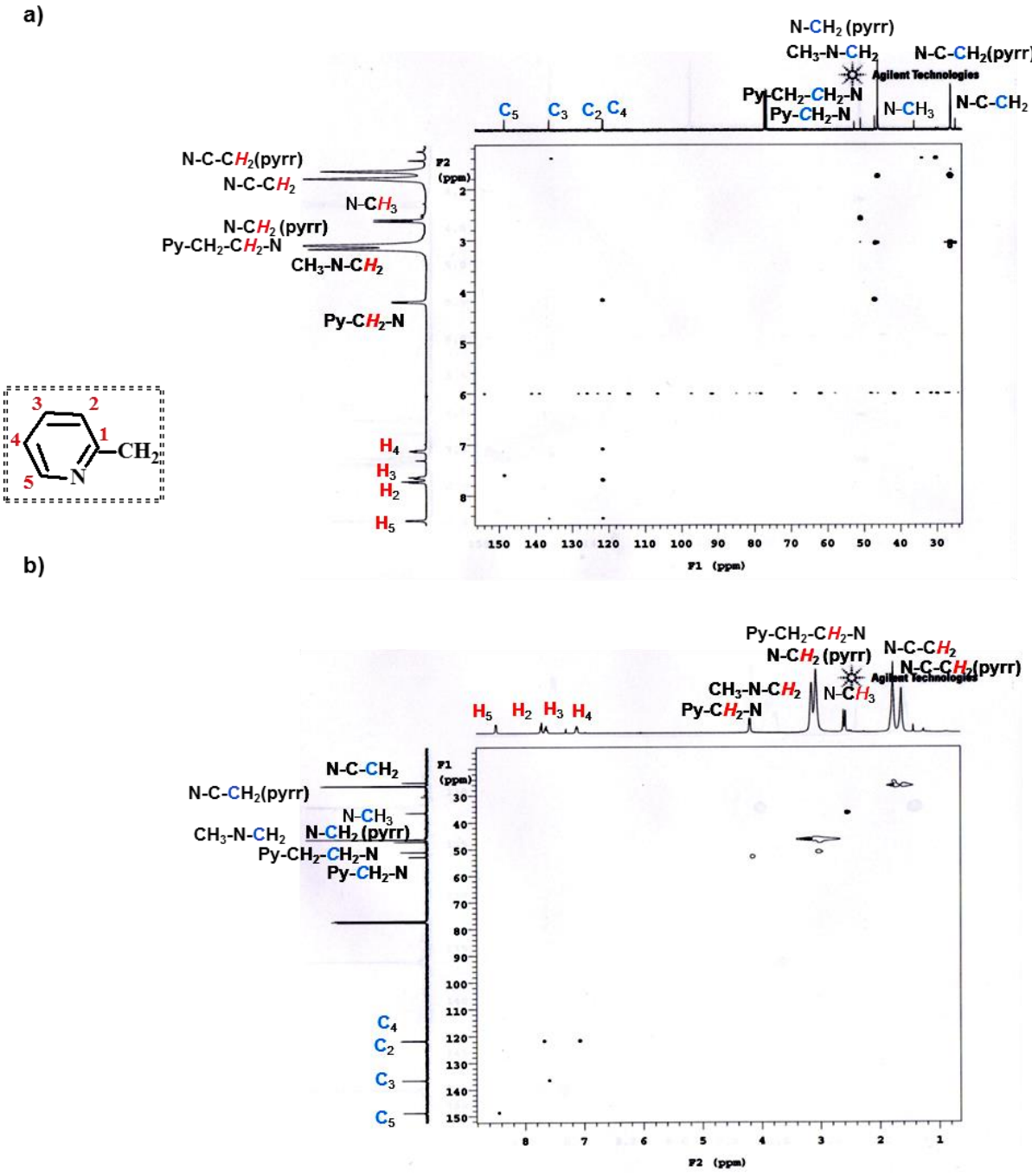


Figure 3. The (**a**) HMBC and (**b**) HSQC spectra of **3a**.

The signals of all the carbons of the 2-pyridyl(N/N)spirocyclotriphosphazenes are interpreted in the ^{13}C NMR spectra. The N-$\underline{C}$H$_3$ carbons of the phosphazenes are observed in the range of 34.98-36.36 ppm, and the average value is 35.88 ppm. The average values of $^{3}J_{\underline{P}NC\underline{C}}$, for the N-CH$_2$-$\underline{C}H_2$ carbons of the cyclotriphosphazene derivatives are 6.5 Hz (for pyrrolidine rings), 7.7 Hz (for morpholine) and 3.0 Hz (for six-membered NN spiro rings). In contrast with, the $^{2}J_{\underline{P}N\underline{C}}$, for the Py-$\underline{C}H_2$-N-$\underline{C}H_2$ and CH$_3$-N-$\underline{C}$H$_2$ carbons of the compounds are not observed. As expected, the *geminal* amine substituents in the ^{13}C spectra of the tetraaminocyclotriphosphazenes (**3a**-**3c**) displayed two small separated peaks for N-$\underline{C}$H$_2$,

N-CH_2-$\underline{C}H_2$, O-$\underline{C}H_2$ and O-$\underline{C}$-O groups, because two *geminal* groups were not equivalent to each other. The O-$\underline{C}$-O and C-O-$\underline{C}H_2$ carbon signals of **3c** are very characteristic, and they are observed at *ca*. 107 and 64 ppm as four separate singlets. The O-$\underline{C}H_2$ carbons of tetramorpholino-2-pyridyl(N/N)spirocyclotriphosphazene (**3b**) also appear at *ca*. 67 ppm as two separate singlets. On the other hand, the expected carbon peaks (C_1-C_5) of the pyridyl ring are assigned from the ^{13}C NMR spectra of all the compounds, and the obtained results are consistent with the literature findings of 2-pyridyl substituted derivatives (28).

The $^3J_{PNCC}$ values of the tetrapyrrolidino-2-pyridyl(N/N)spirocyclotriphosphazenes (**3a**) reveal to triplets of the N-CH_2-$\underline{C}H_2$ carbons on account of the second-order effects that have also been observed previously for some of the cyclotriphosphazenes (30,31) (Figure 4). The $^3J_{PNCC}$ values were estimated using the external transitions of the triplet peaks.

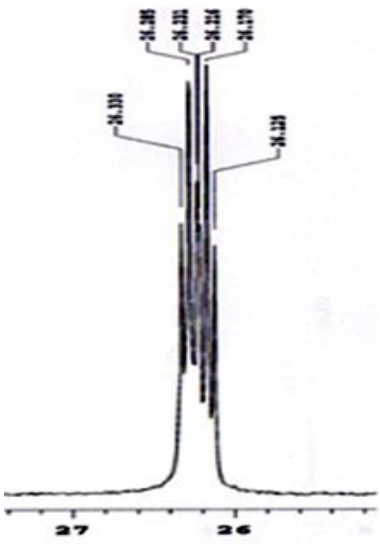


Figure 4. The second order effect in ^{13}C {^1H} NMR spectrum of **3a.**

The signals of the protons of the 2-pyridyl(N/N)spirocyclotriphosphazenes are evaluated in the ^1H NMR spectra. The ^1H NMR spectra of the fully substituted phosphazenes (**3a-3c**) show that four secondary monoamines (pyrrolidine, morpholine and DASD) were bonded to the P2 and P3 atoms (see numbering of trimer in Figure 1). The average values of N-CH_2-C$\underline{H}_2$, Py-CH_2-N-C$\underline{H}_2$ and CH_3-N-C$\underline{H}_2$ spiro protons of the phosphazenes (**3a-3c**) were found to be at 1.86 ppm, 3.14 ppm and 3.12 ppm, respectively, in comparison to the values (1.92 ppm, 3.20 ppm and 3.15 ppm) of the starting phosphazene (**3**). Furthermore, the δ_H shift of the protons of Py-C$\underline{H}_2$-N of the compounds was observed in the range of 4.11-4.32 ppm, and the average $^3J_{PH}$ value is 9.0 Hz. On the other hand, the expected proton peaks (H_2-H_5) of the pyridyl ring were determined from the ^1H NMR spectra of all the compounds, and the finding data are in accordance with the literature (28). The N-CH_3

protons of the cyclotriphosphazenes were observed in the range of 2.54-2.69 ppm, and the average $^{3}J_{PH}$ value, 13.2 Hz, was very large.

The characteristic FTIR bands of the 2-pyridyl(N/N)spirocyclotriphosphazenes are given in "Experimental Part". The compounds exhibited intense asymmetric and symmetric stretching vibrations between 1216-1248 cm^{-1} and 1152-1172 cm^{-1}, ascribed to the P=N bonds of the P_3N_3 skeletons (32). As expected, the asymmetric and symmetric vibrations of ν_{PCl2} for the partly substituted phosphazene (**3**) emerged at 579 cm^{-1} and 510 cm^{-1}, respectively (33). In other compounds (**3a-3c**), these peaks disappeared.

CONCLUSIONS

The reactions of $N_3P_3Cl_6$ (**1**) with one equimolar amount of the 2-pyridyl substituted N/N donor-type bidentate ligand (**2**) produced 2-pyridyl(N/N)spirocyclotriphosphazene (**3**) regioselectively in dry THF. The partly substituted spiro compound (**3**) reacted with excess secondary amines in THF to afford the fully substituted cyclotriphosphazenes (**3a-3c**). The obtained 2-pyridyl(N/N)spirocyclotriphosphazenes (**3** and **3a-3c**) are the first examples of the pyridyl pendant armed cyclotriphosphazenes. The spectroscopic features of the cyclophosphazenes were scrutinized using one and two dimensional NMR techniques in $CDCl_3$ solution. The synthetic and spectroscopic properties of the compounds were compared to each other. As known, the aminospirocyclotriphosphazenes are strong bases. Thus, the tetraamino-2-pyridyl(N/N)spirocyclotriphosphazenes synthesized in this paper ought to be used as heterocyclic ligands for the transition metal cations, and they may be produced phosphazenium salts with biologically active bulky organic acids. Moreover, 2-pyridyl-diamine (**2**), which is a pyridine derivative, is very essential chemical with great biological applications. Hence, the obtained new phosphazene derivatives (**3** and **3a-3c**), which contain a trimeric phosphazene ring with 2-pyridyl pendant arm, are considered to have probably anticancer, antituberculosis, antimicrobial, antiviral and antiproliferative activities.

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