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Syntheses and spectral characterizations of tetraspirocyclotetraphosphazenes containing bis(4-fluorobenzyl) pendant arms

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Abstract: The Cl exchange reactions of octachlorocyclotetraphosphazene, $N_4P_4Cl_8$ (1), with two equimolar amounts of N-(4-fluorobenzyl)-N'-ethylethane-1,2-diamine resulted in the formation of 4,4,8,8-tetrachloro-2-trans-6-bis-N-(4-fluorobenzyl)-N'-ethylethane-1,2-diaminocyclotetraphosphazene (2) in dry THF. The Cl substitution reactions of the starting compound 2 with excess amounts of sodium 2,2-dimethyl-1,3-propandioxide and 3-amino-1-propanoxide gave the bis(2,2-dimethyl-1,3-propandioxy) (2a) and 4-trans/cis-8-bis(3-amino-1-propanoxy) (*trans/cis* 2b) 2-trans-6-bis(4-fluorobenzyl)spirocyclotetra phosphazenes, respectively. The structures of tetraspiro products (2a and *trans/cis* 2b) were verified using elemental analyses, mass spectrometry (ESI-MS), FTIR, ^{1}H, ^{13}C $\{^{1}H\}$ and ^{31}P $\{^{1}H\}$ NMR spectroscopy. On the other hand, the possible conformation of the two five-membered and two six-membered rings in the spatial skeletons of the three compounds (2a and *trans/cis* 2b) ought to be considered. As it turns out, these structures can exist as stable conformational isomers at low temperature and possibly room temperature, depending on the orientation of the four spiro rings. These structures can also form structurally locked isomers at low temperatures.

Keywords: 2-*Trans*-6-bis-(4-fluorobenzyl), spirocyclotetraphosphazenes, replacement reactions, spectroscopy

Bis(4-florobenzil) pendant kollu tetraspirosiklotetrafosfazenlerin sentezi ve spektral karakterizayonu

Özet: Oktaklorosiklotetrafosfazen, $N_4P_4Cl_8$ (1)' in klor atomlarının iki eş molar miktarda N-(4-florobenzil)-N'-etiletan-1,2-diamin ile kuru THF içindeki değişim reaksiyonları 4,4,8,8-tetrakloro-2-trans-6-bis-N-(4-florobenzil)-N'-etiletan-1,2-diaminosiklotetrafosfazen (2) oluşumu ile sonuçlandı. Başlangıç bileşiği 2' nin aşırı miktarda sodyum 2,2-dimetil-1,3-propandioksit ve 3-amino-1-propanoksit ile Cl sübstitüsyon reaksiyonları, sırasıyla bis(2,2-dimetil-1,3-propandioksi) (2a) ve 4-trans/cis-8-bis(3-amino-1-propanoksi) (*trans/cis* 2b) 2-trans-6-bis(4-florobenzil)spirosiklotetrafosfazenleri verdi. Tetraspiro ürünlerinin (2a ve *trans/cis* 2b) yapıları, element analizi, kütle spektrometrisi (ESI-MS), FTIR, ^{1}H, ^{13}C $\{^{1}H\}$ ve ^{31}P $\{^{1}H\}$ NMR spektroskopisi kullanılarak doğrulandı. Öte yandan, üç bileşiğin (2a ve *trans/cis* 2b) uzaysal iskeletlerindeki iki beş üyeli ve iki altı üyeli halkanın olası konformasyonu dikkate alınmalıdır. Anlaşıldığı üzere, bu yapılar, dört spiro halkanın yönelimine bağlı olarak düşük sıcaklıkta ve muhtemelen oda sıcaklığında kararlı konformasyonel izomerler olarak var olabilir. Bu yapılar ayrıca düşük sıcaklıkta yapısal olarak kilitli izomerler oluşturabilir.

Anahtar Kelimeler: 2-*Trans*-6-bis-(4-florobenzil) spirosiklotetrafosfazenler, yer değiştirme reaksiyonları, spektroskopi

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1. INTRODUCTION

For long years, hexachlorocyclotriphosphazene (cyclic trimer, $N_3P_3Cl_6$) and octachlorocyclotetraphosphazene (cyclic tetramer, $N_4P_4Cl_8$) have been used largely as the beginning heterocyclic reagents for the preparation of the several substituted trimeric and tetrameric organocyclophosphazene derivatives [1-3]. The Cl replacement reactions of $N_3P_3Cl_6$ and $N_4P_4Cl_8$ with monofunctional ligands such as primary and/or secondary amines, alkyloxides and aryloxides continue to be extensively studied [4, 5]. Nevertheless, substitution reactions of $N_3P_3Cl_6$ and $N_4P_4Cl_8$ with the bifunctional ligands *e.g.* diamines, aminoalkoxides and dialkoxides are quite rare in the literature [6-8]. Depending on the reaction conditions, spiro, ansa, bino, dispiro, ansa-spiro, trispiro and tetraspiro products occur with these bifunctional ligands [9-11]. Besides, studies with the tetramer are much less common than with the trimer. The most important reason for this is the large number of exchangeable Cl atoms in the tetramer ring and the formation of a large number of geometric and chiral isomers due to the replacement reactions of Cl atoms with substituents. Moreover, these isomers are very difficult to separate from reaction mixtures.

On the other hand, some cyclophosphazenes have recently been potentially used as ionic liquids [12], organic light emitting diodes (OLEDs) [13], rechargeable lithium-ion batteries [14], fluorescent indicators [15], lubricants [16], biomaterials [17], dendrimers [18, 19] and synthetic bones [20]. Moreover, partially and/or fully substituted cyclophosphazene architectures have drawn great attention over the past two decades due to their potential for antituberculosis, antibacterial, antifungal, anticancer and DNA cleavage activities [21-23].

Eventually, the starting compound containing bis-(4-fluorobenzyl)-pendant arm (**2**) obtained from tetramer with two equimolar amounts of *N*-(4-fluorobenzyl)-*N'*-ethylethane-1,2-diamine was used in this research [24]. The present paper focuses on the Cl replacement reactions of **2** with excess amounts of the sodium 2,2-dimethyl-1,3-propandioxide and 3-amino-1-propanoxide (Figure 1), and the assessment of their spectroscopic properties.

2. MATERIAL AND METHOD

2.1. Physical measurements

The Cl exchange reactions have been pursued by thin-layer chromatography (TLC) on Merck DC Alufolien Kiesegel 60 B_{254} sheets in various solvents. Column chromatography has been carried out using Merck Kiesegel 60 (230-400 mesh ATSM) silica gel. Melting points were determined by a capillary tube with a Gallenkamp apparatus. Elemental analyses were realized with the Leco CHNS-932 instrument. Fourier transform infrared (FTIR) spectra of tetrakisspiro-(4-fluorobenzyl)cyclotetraphosphazenes (**2a** and ***trans* 2b**-***cis* 2b**) were enrolled with a Jasco FT/IR-430 spectrometer in KBr discs. Electron spray ionization-mass spectra (ESI-MS) were recorded using a Waters 2695 Alliance Micromass ZQ spectrometer. ^{1}H and ^{13}C $\{^{1}H\}$ NMR spectra were monitored on a Bruker DPX FT-NMR (500 MHz) spectrometer operating at 400.13 and 100.62 MHz, respectively. ^{31}P $\{^{1}H\}$ NMR spectra were obtained by a Bruker Avance III HD (600 MHz) spectrometer operating at 242.94 MHz. NMR spectrometers were equipped with the 5 mm PABBO BB inverse-gradient probe and standard Bruker pulse programs were employed [25]. Micro and spectral analyzes (FTIR, ESI-MS, ^{1}H, ^{13}C $\{^{1}H\}$ NMR and ^{31}P $\{^{1}H\}$ NMR) were determined using the microanalytical service of Ankara University and İnönü University.

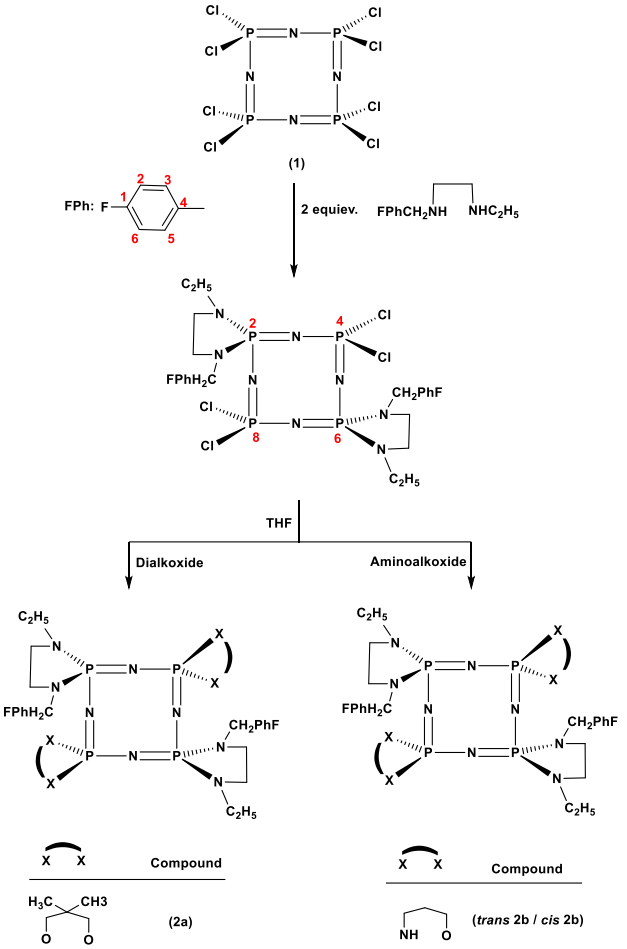

Figure 1. The syntheses of tetrakisspiro-(4-fluorobenzyl)cyclotetraphosphazenes (**2a** and ***trans* 2b**/***cis* 2b**).

2.2. Materials used for syntheses

The used organic solvents were distilled, dried and purified by common methods before use. The replacement reactions were fulfilled under Ar. $N_4P_4Cl_8$ (Otsuka Chemical Co. Ltd. and recrystallized from hot *n*-hexane), *N*-methylethane-1,2-diamine (Merck), 4-fluorobenzaldehyde (Aldrich), 3-amino-1-propanol (Merck) and 2,2-dimethyl-1,3-propandiol (Aldrich) were procured.

2.3. Experimental part

2.3.1. Syntheses of compounds

The starting reagent, *N*-(4-fluorobenzyl)-*N'*-ethylethane-1,2-diamine, was synthesized from the reactions of 4-fluorobenzaldehyde with *N*-methylethane-1,2-diamine in ethanol with respect to the published procedure [24]. The beginning cyclotetraphosphazene; 4,4,8,8-tetrachloro-2-*trans*-6-bis-*N*-(4-fluorobenzyl)-*N'*-ethylethane-1,3-diamino-cyclotetra phosphazene (**2**), was prepared with the reaction of $N_4P_4Cl_8$ (**1**) with two equimolar amounts of *N*-(4-fluorobenzyl)-*N'*-ethylethane-1,2-diamine in dry THF according to the procedure [24].

2.3.2. Synthesis of 2a

A solution of **2** (0.50 g, 0.70 mmol) in dry THF (100 mL) was slowly added into a solution of sodium 2,2-dimethyl-1,3-propandioxide (0.20 g, 1.55 mmol) in dry THF (50 mL) at -10 °C. The mixture was stirred for over 2 h at the same temperature. After the mixture was allowed to warm to ambient temperature, it was stirred and refluxed for 55 h under Ar. The sodium chloride was filtered off, and then the solvent was completely evaporated. The product was eluted by the column chromatography with toluene as eluent. Afterward, the separated white product (**2a**) was crystallized from toluene. Yield: 0.35 g (65 %). mp: 194 °C. Anal. Calcd. for $P_4N_8F_2C_{32}H_{50}O_4$, C, 49.74; H, 6.52; N, 14.50. Found: C, 50.17; H, 7.15; N, 15.09.ESI-MS (Ir %): *m/z* 773 ($[MH]^+$, 100). FTIR (KBr, cm^{-1}): *ν* 2928, 2870 (C-H aliph.), 1265 (asymm.) and 1179 (symm.) (P=N), 1048 (C-F). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): *δ* 7.26 (dd, 4H, $^3J_{HH}$= 7.6 Hz, $^4J_{FH}$= 6.0 Hz, H_3 and H_5), 6.97 (dd, 4H, $^3J_{FH}$= 8.4 Hz, $^3J_{HH}$= 8.8 Hz, H_2 and H_6), 4.10 (d, 4H, $^3J_{PH}$= 8.0 Hz, ArCH_2N), 3.77 (m, 8H, OCH_2C), 3.13 (m, 2H, $^3J_{PH}$= 10.4 Hz, $^2J_{HH}$= 7.2 Hz, NCH_2), 3.10 (m, 2H, $^3J_{PH}$= 10.8 Hz, $^2J_{HH}$= 7.6 Hz, NCH_2), 3.04 (m, 2H, $^3J_{PH}$= 10.8 Hz, $^2J_{HH}$= 6.8 Hz, CH_2NR), 3.00 (m, 2H, $^3J_{PH}$= 9.6 Hz, $^2J_{HH}$= 7.2 Hz, CH_2NR), 2.98 (m, 4H, $^2J_{HH}$= 7.2 Hz, NCH_2CH$_3$), 1.26 (s, 12H, C(CH_3)$_2$), 1.22 (t, 6H, $^2J_{HH}$= 6.0 Hz, NCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): *δ* 162.06 (d, $^1J_{FC}$= 245.3 Hz, C_1), 135.78 (dd, $^3J_{PC}$= 9.2 Hz, $^4J_{FC}$= 3.0 Hz, C_4), 129.59 (d, $^3J_{FC}$= 8.5 Hz, C_3 and C_5), 115.09 (d, $^2J_{FC}$= 21.4 Hz, C_2 and C_6), 67.11 (s, OCH$_2$C), 48.03 (d, $^2J_{PC}$= 4.0 Hz, ArCH$_2$N), 44.23 (d, $^2J_{PC}$= 14.6 Hz, NCH$_2$), 43.76 (d, $^2J_{PC}$= 13.2 Hz, CH$_2$NR), 39.38 (d, $^2J_{PC}$= 3.2 Hz, NCH$_2$CH$_3$), 29.65 and 29.61 (s, OCH$_2$C), 21.39 and 21.32 (s, C(CH$_3$)$_2$), 13.48 (d, $^3J_{PC}$= 6.1 Hz, NCH$_2$CH$_3$).

2.3.3. Syntheses of trans 2b/cis 2b

A solution of **2** (0.50 g, 0.70 mmol) in dry THF (100 mL) was slowly added into a solution of sodium 3-amino-1-propanoxide (0.15 g, 1.55 mmol) in dry THF (50 mL) at -10 °C. The mixture was stirred for over 2 h at the same temperature. After the mixture was allowed to warm to ambient temperature, it was stirred and refluxed for 60 h under Ar. The sodium chloride was filtered off, and the solvent was completely evaporated. The products were eluted by column chromatography with toluene. Afterward, the white products were the mixture of *trans* and *cis*-tetraspiro compounds (***trans* 2b** and ***cis* 2b**), and they could not be separated purely. The relative yields were calculated from the ^{31}P NMR spectrum of the mixture; ***trans* 2b** isomer: 59 % and ***cis* 2b** isomer: 41 %. Total yield of *trans*- and *cis*-isomer: 0.30 g (60 %). Anal. Calcd. for $P_4N_{10}F_2C_{28}H_{44}O_2$, ESI-MS (Ir %): *m/z* 715 ($[MH]^+$, 100). FTIR (KBr, cm^{-1}): *ν* 2917, 2849 (C-H aliph.), 1231 (asymm.) and 1177 (symm.) (P=N), 1051 (C-F).

***trans* 2b** isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm): *δ* 7.40 (dd, 4H, $^3J_{HH}$= 8.8 Hz, $^4J_{FH}$= 5.6 Hz, H_3 and H_5), 6.96 (dd, 4H, $^3J_{FH}$= 8.4 Hz, $^3J_{HH}$= 8.8 Hz, H_2 and H_6), 4.29 (m, 4H, OCH_2), 4.07 (d, 4H, $^3J_{PH}$= 6.4 Hz, ArCH_2N), 3.23 (m, 4H, $^3J_{PH}$= 9.6 Hz, $^2J_{HH}$= 5.6 Hz, NCH_2), 2.99 (m, 4H, $^3J_{PH}$= 13.6 Hz, $^2J_{HH}$= 7.2 Hz, CH_2NR), 2.95 (m, 4H, NH-CH_2), 2.91 (m, 4H, $^2J_{HH}$= 7.2 Hz, NCH_2CH$_3$), 2.26 (b, 2H, N*H*), 1.63 (m, 4H, NHCH$_2$CH_2), 1.13 (t, 6H, $^2J_{HH}$= 7.2 Hz, NCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): *δ* 161.84 (d, $^1J_{FC}$= 243.8 Hz, C_1), 135.08 (dd, $^3J_{PC}$= 9.2 Hz, $^4J_{FC}$= 3.1 Hz, C_4), 129.98 (d, $^3J_{FC}$= 8.0 Hz, C_3 and C_5), 114.91 (d, $^2J_{FC}$= 21.4 Hz, C_2 and C_6), 66.75 (d, $^2J_{PC}$= 6.8 Hz, OCH$_2$), 49.55 (d, $^2J_{PC}$= 4.6 Hz, ArCH$_2$N), 45.11 (d, $^2J_{PC}$= 12.3 Hz, NCH$_2$), 44.69 (d, $^2J_{PC}$= 10.7 Hz, CH$_2$NR), 42.08 (d, $^2J_{PC}$= 4.6 Hz, NH-CH$_2$), 40.61 (d, $^2J_{PC}$= 3.1 Hz, NCH$_2$CH$_3$), 27.93 (d, $^3J_{PC}$= 7.8 Hz, NHCH$_2$CH$_2$), 13.70 (d, $^3J_{PC}$= 6.8 Hz, NCH$_2$CH$_3$).

***cis* 2b** isomer: ^{1}H NMR (400 MHz, $CDCl_3$, ppm): *δ* 7.32 (dd, 4H, $^3J_{HH}$= 8.6 Hz, $^4J_{FH}$= 5.6 Hz, H_3 and H_5), 6.89 (dd, 4H, $^3J_{FH}$= 8.8 Hz, $^3J_{HH}$= 8.8 Hz, H_2 and H_6), 4.31 (m, 4H, OCH_2), 3.99 (d, 4H, $^3J_{PH}$= 6.7 Hz, ArCH_2N), 3.27 (m, 4H, $^3J_{PH}$= 9.6 Hz, $^2J_{HH}$= 5.2 Hz, NCH_2), 3.03 (m, 4H, $^3J_{PH}$= 14.0 Hz, $^2J_{HH}$= 6.8 Hz, CH_2NR), 2.94 (m, 4H, NH-CH_2), 2.88 (m, 4H, $^2J_{HH}$= 7.6 Hz, NCH_2CH$_3$), 2.26 (b, 2H, N*H*), 1.63 (m, 4H, NHCH$_2$CH_2), 1.18 (t, 6H, $^2J_{HH}$= 6.8 Hz, NCH$_2$CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): *δ* 161.87 (d, $^1J_{FC}$= 243.8 Hz, C_1), 135.02 (dd, $^3J_{PC}$= 9.4 Hz, $^4J_{FC}$= 3.2 Hz, C_4), 129.86 (d, $^3J_{FC}$= 7.8 Hz, C_3 and C_5), 114.69 (d, $^2J_{FC}$= 21.4 Hz, C_2 and C_6), 66.82 (d, $^2J_{PC}$= 7.2 Hz, OCH$_2$), 49.51 (d, $^2J_{PC}$= 3.8 Hz, ArCH$_2$N), 45.00 (d, $^2J_{PC}$= 14.6 Hz, NCH$_2$), 44.83 (d, $^2J_{PC}$= 11.5 Hz, CH$_2$NR), 41.98 (d, $^2J_{PC}$= 3.8 Hz, NH-CH$_2$), 40.70 (d, $^2J_{PC}$= 2.4 Hz, NCH$_2$CH$_3$), 27.85 (d, $^3J_{PC}$= 7.8 Hz, NHCH$_2$CH$_2$), 13.63 (d, $^3J_{PC}$= 7.7 Hz, NCH$_2$CH$_3$).

3. RESULTS AND DISCUSSION

3.1. Syntheses

Firstly, the Cl substitution reaction of $N_4P_4Cl_8$ (**1**) with two equimolar amounts of FPhCH$_2$NH(CH$_2$)$_2$NHCH$_2$CH$_3$, *N*-(4-fluorobenzyl)-*N*'-ethylethane-1,2-diamine, resulted in the formation of 2-*trans*-6-bis-spiro-cyclotetraphosphazene (**2**) in 55 % yield as the major product. However, mono-spiro and 2-*cis*-6-bis-spiro cyclotetraphosphazenes were obtained with the yields of 10 % and 7 %, respectively, as byproducts. The 2-*trans*-6-bis-spiro (**2**), mono-spiro and 2-*cis*-6-bis-spiro compounds were prepared with respect to our published paper [24]. Cyclotetraphosphazene **2** used in this study was eluted by column chromatography using toluene. Afterward, the exchange reaction of **2** with the an excess of

$Na_2[OCH_2C(CH_3)_2CH_2O]$, sodium 2,2-dimethyl-1,3-propandioxide, resulted in the formation of bis(2,2-dimethyl- 1, 3- propandioxide)- 2 - *trans* - 6- bis(4-fluorobenzyl)spiro compound (**2a**) with 65 % yield in dry THF (Figure 1). This product was eluted by column chromatography with toluene. Finally, as a result of the condensation reaction of **2** in dry THF with excess of $Na[OCH_2CH_2CH_2NH_2]$, sodium 3-amino-1-propanoxide, *trans*- and *cis*- bis(3-amino-1-propanoxy)-2-*trans*-6-bis(4-fluorobenzyl)spiro product mixture (***trans* 2b** and ***cis* 2b**) was formed in 60 % overall yield. The tetraspiro compounds; ***trans* 2b** and ***cis* 2b** could not be isolated in pure forms using column chromatography and preparative thin-layer chromatography (PTLC) methods. Therefore, were calculated as 59 % and 41 %, respectively, from the $^{31}P\ \{^1H\}$ NMR spectrum of the mixture of *trans*- and *cis*- cyclotetraphosphazenes. It has been found that the yield of ***trans* 2b** is larger than that of the ***cis* 2b** product, because of the large steric hindrances of *cis* product. In Figure 2, the $^{31}P\ \{^1H\}$ NMR spectrum of the mixture of ***trans* 2b** and ***cis* 2b** products was presented. The analytical and spectral data given in the Experimental Part are compatible with the suggested formulae of the tetraspiro structures. It is seen that the cyclotetraphosphazenes have $[MH]^+$ protonated molecular ion peaks in their ESI-MS spectra.

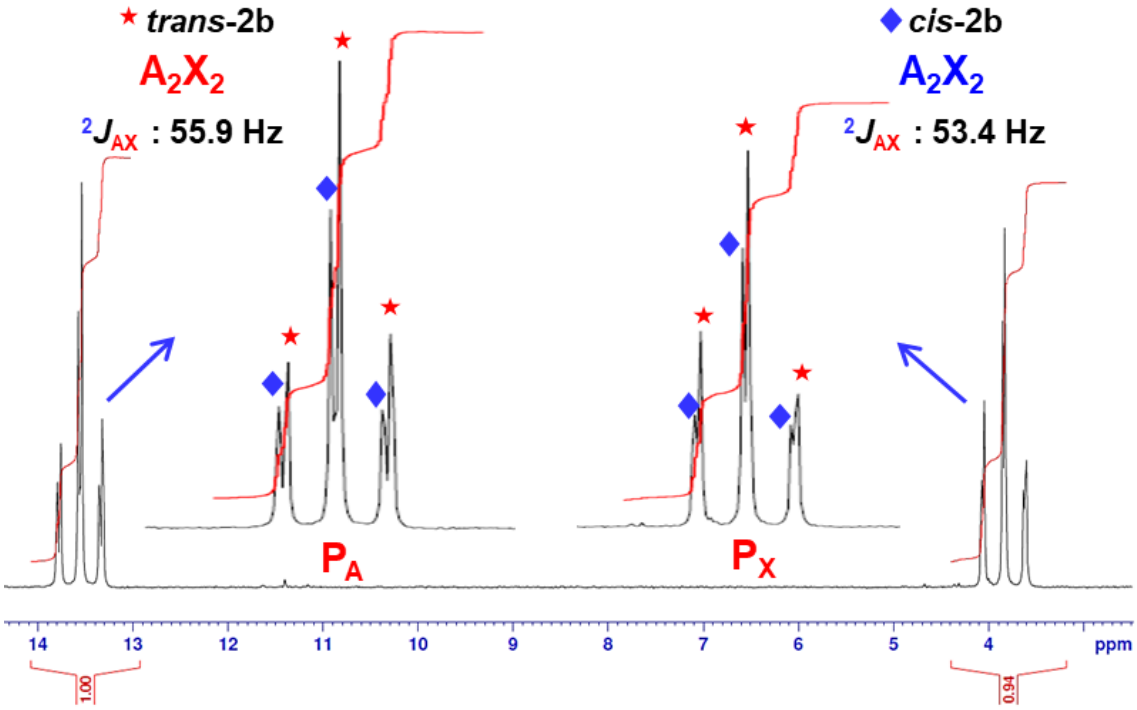

Figure 2. $^{31}P\ \{^1H\}$ NMR spectrum of the mixture of ***trans* 2b** and ***cis* 2b** products.

Table 1. $^{31}P\ \{^1H\}$ NMR data of bis(4-fluorobenzyl)cyclotetraphosphazenes (**2a**, ***trans* 2b** and ***cis* 2b**).

Comp.	Spin System	δ_{PNN} (ppm)	δ_{PCl2} (ppm)	δ_{PNO} (ppm)	$^2J_{PP}$ (Hz)
***2**	A_2X_2	P_A: 4.83	P_X: - 8.78	–	$^2J_{AX}$: 24.3
2a	A_2X_2	P_A: 14.09	–	P_X: 0.84	$^2J_{AX}$: 53.4
***trans* 2b**	A_2X_2	P_A: 13.54	–	P_X: 3.83	$^2J_{AX}$: 55.9
***cis* 2b**	A_2X_2	P_A: 13.58	–	P_X: 3.85	$^2J_{AX}$: 53.4

[a] ^{31}P NMR data for the compounds in $CDCl_3$ solutions at 293 K.
* $^{31}P\ \{^1H\}$ NMR value of **2** was taken from the literature 24

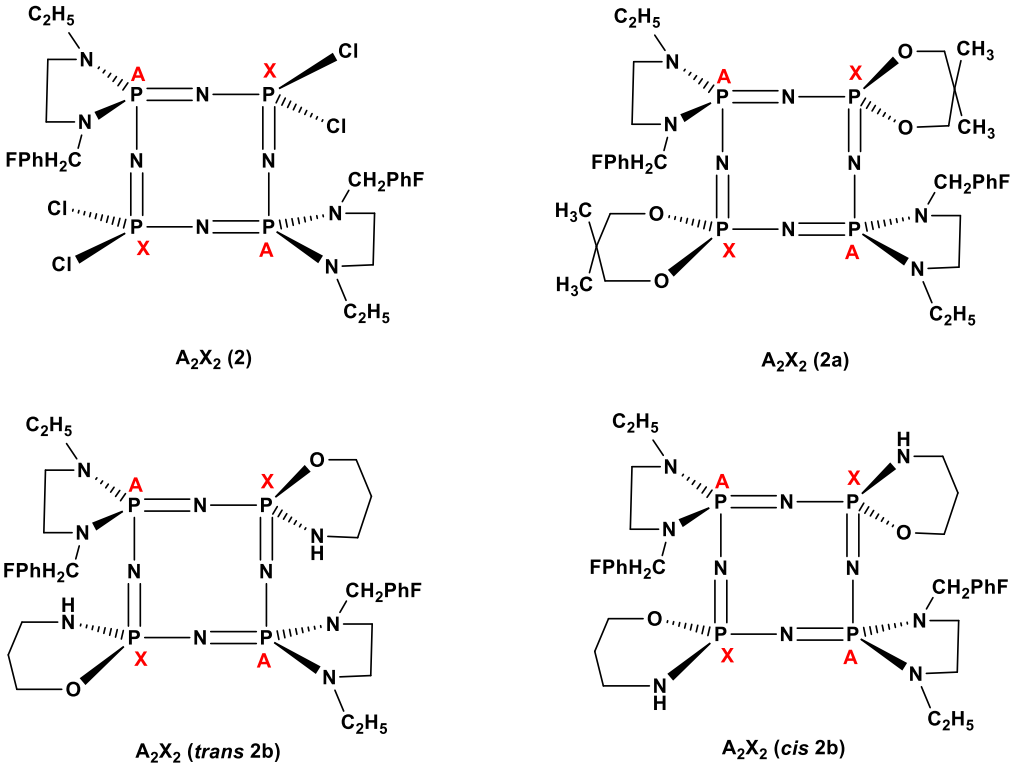

Figure 3. The spin systems of all the compounds.

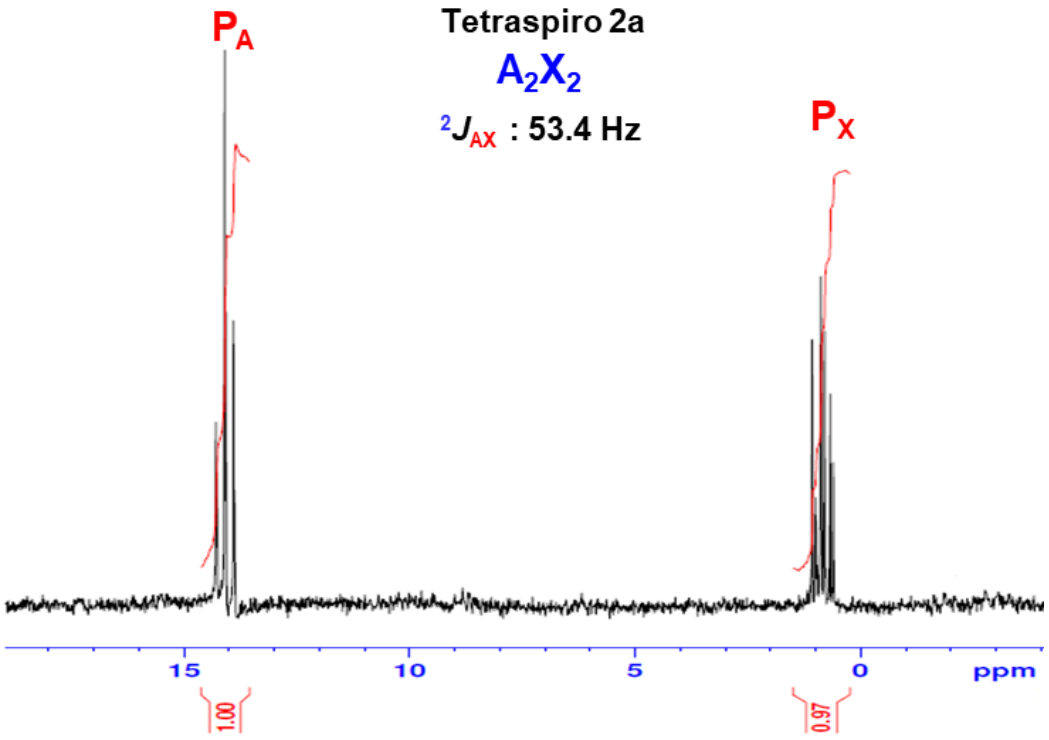

Figure 4. ^{31}P {^{1}H} NMR spectrum of **2a**.

3.2. NMR Spectroscopy

The ^{31}P $\{^1H\}$ NMR data of bis(4-fluorobenzyl)cyclotetraphosphazenes (**2a**, ***trans* 2b** and ***cis* 2b**) were listed in Table 1 along with the data of the starting tetrachloro compound (**2**) presented for comparison purpose. The spin systems of all the compounds were found to be as A_2X_2 owing to two different phosphorus environments in the cyclotetraphosphazene skeleton (Figure 3). It is noteworthy that the replacing of four Cl atoms with the propandioxide and/or aminopropanoxide groups significantly increases the chemical shifts (δ P) and coupling constant ($^2J_{PP}$) of **2a, *trans* 2b** and ***cis* 2b.**

The ^{31}P $\{^1H\}$ NMR spectrum of pure **2a** was illustrated in Figure 4, and the δ P chemical shifts and $^2J_{PP}$ coupling constants were assigned and written on the spectrum. Similarly, δ P and $^2J_{PP}$ values of ***trans* 2b** and ***cis* 2b** were written on the spectrum in Figure 2, as well.

Furthermore, in the starting cyclotetraphosphazene **2**, the four Cl atoms are diastereotopic and the unsubstituted P4 and P8 phosphorus atoms become prochiral centres (Figure 5.a). In bis-aminopropanoxy substituted compounds (***trans* 2b** and ***cis* 2b**), P4 and P8 phosphorus atoms have the same substituents, and their configurations are changeable because of the *trans*- and *cis*- orientations of the NH and O groups/atoms (Figure 6). However, optical isomers for both *trans* and *cis* orientations of the NH and O groups/atoms cannot be formed, since the two 4-fluorobenzyldiamine groups are bonded to the P2 and P6 phosphorus atoms in the *trans* position. On the other hand, the possible conformations of two five-membered and two six-membered rings in the spatial skeletons of three compounds (**2a**, ***trans* 2b** and ***cis* 2b**) are shown by drawing (Figures 5.b and 6). As understood, these structures can form stable conformational isomers at low temperatures and possibly also at room temperature, depending on the orientation of the four spiro rings. However, these structures may also be conformationally locked at low temperatures.

Based on the ^{13}C $\{^1H\}$ and ^1H NMR data, whole the carbon and proton signals were clearly interpreted. The δ chemical shifts, multiplicities and J coupling constants (J_{PC} and/or J_{FC} values) of aromatic *C1*, *C2/C6*, *C3/C5* and *ipso-C4* carbons of the 4-fluorobenzyl rings were evaluated with respect to the expected literature values [26] (Figure 1).

The average $^1J_{FC}$, $^2J_{FC}$, $^3J_{FC}$, and $^4J_{FC}$ values were calculated as $^1J_{FC}$= 244.3 Hz, $^2J_{\underline{F}C\underline{C}}$= 21.4 Hz, $^3J_{\underline{F}CC\underline{C}}$= 8.1 Hz and $^4J_{\underline{F}CCC\underline{C}}$= 3.1 Hz, respectively. Besides, the average J_{PC} value of *ipso-C*$_4$ carbons was estimated as $^3J_{\underline{P}NC\underline{C}}$=9.3 Hz. The average $^2J_{PC}$ values for the NC*H*$_2$ and C*H*$_2$NR carbons of three compounds (**2a**, ***trans* 2b** and ***cis* 2b**) were found to be 12.8 Hz. The most secure evidence from the exchange of the four Cl atoms of the starting compound (**2**) was the carbon signals of the propandioxy and aminopropanoxy substituents. As expected, the characteristic spiro O*C*H$_2$C, OCH$_2$*C* and C(*C*H$_3$)$_2$ carbon peaks of the propandioxy groups were seen at *ca*. 67.11 ppm, 29.63 ppm and 21.35 ppm, respectively. However, the characteristic spiro O*C*H$_2$, NH*C*H$_2$ and NHCH$_2$*C*H$_2$ carbon peaks of the aminopropanoxy groups were observed at *ca*. 66.80 ppm, 42.00 ppm and 27.90 ppm, respectively.

On the other hand, the integral ratios of ^1H NMR spectra for **2a**, ***trans* 2b** and ***cis* 2b** exhibited that two propandioxy and two aminopropanoxy groups were bonded to the P4 and P8 phosphorus atoms (Figure 1). The δ chemical shifts, multiplicities and J coupling constants (J_{FH} values) of aromatic H_2/H_6 and H_3/H_5 protons of 4-fluorobenzyl rings were elucidated in accordance with the given literature values [26] (Figure 1). The average values of $^3J_{FH}$ and $^4J_{FH}$ were determined as $^3J_{\underline{F}CC\underline{H}}$=8.5 Hz and $^4J_{\underline{F}CCC\underline{H}}$=5.7 Hz, respectively. In addition, the average value of $^3J_{PH}$ values for the NC*H*$_2$ and C*H*$_2$NR hydrogens of **2a**, ***trans* 2b** and ***cis* 2b** was figured out as 11.1 Hz.

Finally, characteristic FTIR vibrations of the bis(4-fluorobenzyl)cyclotetraphosphazenes were interpreted in their FTIR spectra. Stretching vibrations ($\nu_{P\text{-}Cl}$) of the starting tetrachlorophosphazene (**2**) appeared in 557 cm^{-1} and 507 cm^{-1}, and disappeared in the fully substituted ones (**2a**, ***trans* 2b** and ***cis* 2b**) [27]. The expected two kinds of asymmetric and symmetric $\nu_{P=N}$ stretching frequencies of these compounds were observed at *ca*. 1248 cm^{-1} and 1178 cm^{-1}, respectively, referring to the $\nu_{asymm.}$ and $\nu_{symm.}$ stretching bands of the P=N bonds of the cyclotetraphosphazene ring [28, 29]. Strong absorption band, *ca*. 1050 cm^{-1} attributed to $\nu_{C\text{-}F}$ frequencies of C-F bonds in the 4-fluorobenzyl skeletons, and this finding complies with the literature data of the 4-fluorobenzyl pendant armed cyclophosphazenes [24, 26].

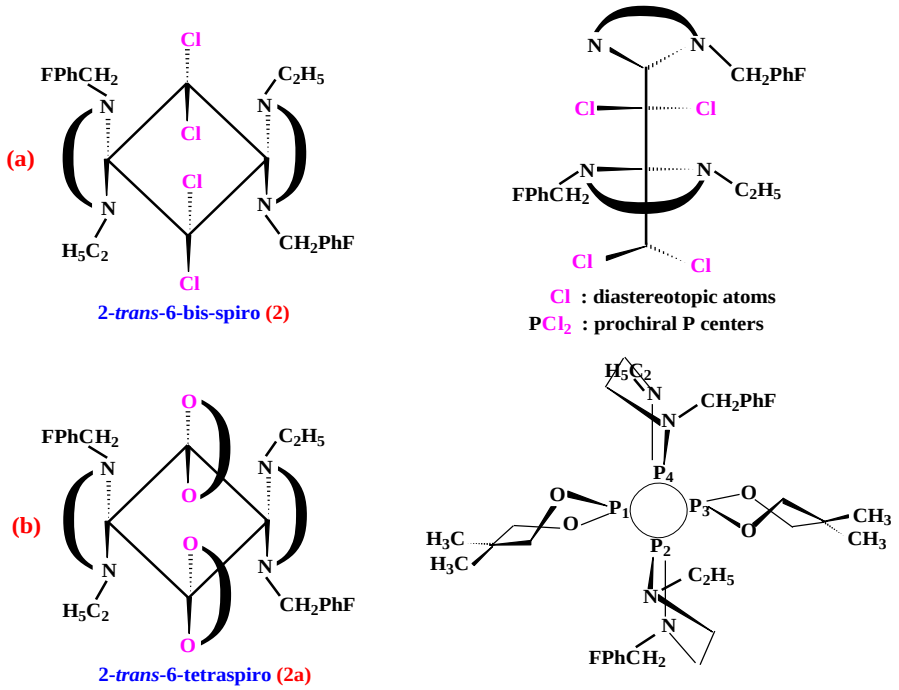

Figure 5. (**a**) The structure of 2-*trans*-6-bis-spiro (**2**) *via* stick diagram and spatial view and (**b**) the stick diagram of 2-*trans*-6-tetraspiro (**2a**) and one of its conformational isomers.

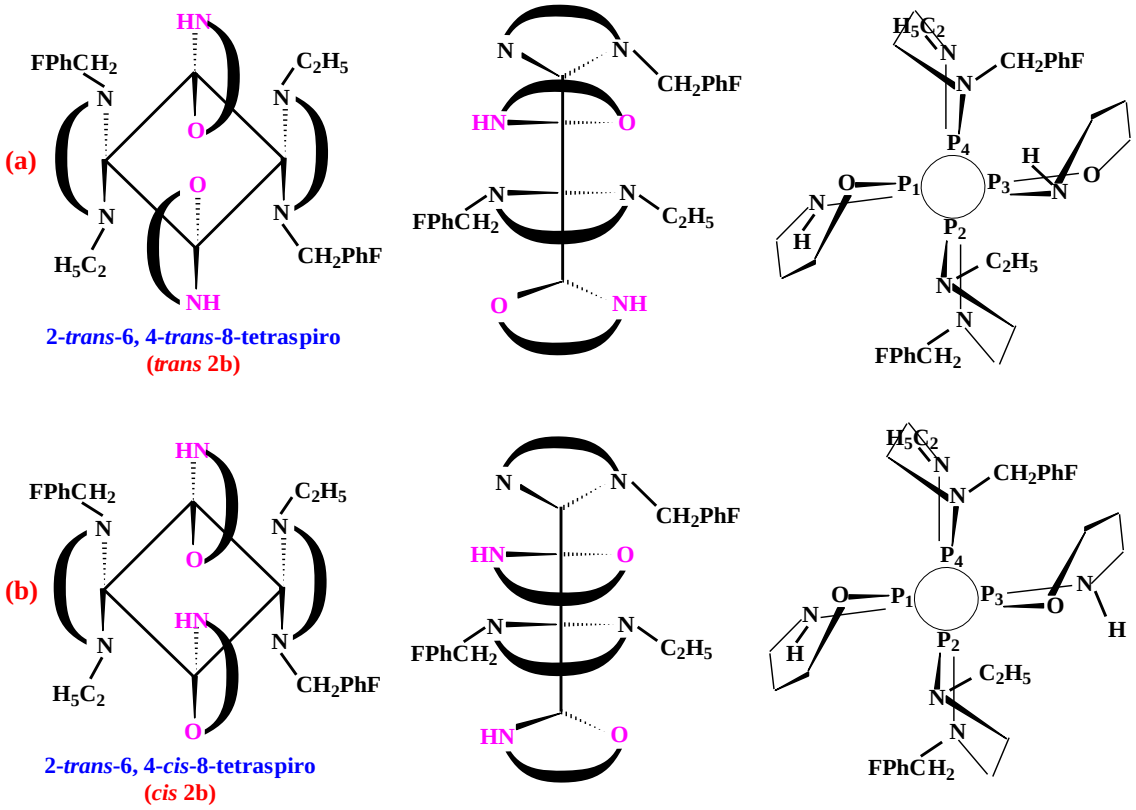

Figure 6. The stick diagram, spatial view and one of the conformational isomers of (**a**) 2-*trans*-6, 4-*trans*-8-tetraspiro (***trans* 2b**) and (**b**) 2-*trans*-6, 4-*cis*-8-tetraspiro (***cis* 2b**) cyclotetraphosphazenes.

4. CONCLUSIONS

In this research, the tetrachloro (**2**) carrying bulky bis(4-fluorobenzyl) pendant arms and its propandioxy and aminopropanoxy derivatives (**2a**, ***trans*** **2b** and ***cis*** **2b**) were prepared. All Cl atoms of **2** were replaced with sodium 2,2-dimethyl-1,3-propanoxide and 3-amino-1-propanoxide to obtain these completely multiple heterocyclic tetraspirocyclotetraphosphazenes. Structural investigations of new bis(4-fluorobenzyl)-tetraspiro products were carried out by ESI-MS, FTIR, ^{1}H, ^{13}C $\{^{1}H\}$ and ^{31}P $\{^{1}H\}$ NMR techniques. These structures may exist as stable conformational isomers at low temperatures and possibly room temperature, depending on the orientation of the two five-membered and two six-membered spiro rings. As expected, tetraspiro structures can create structurally locked conformational isomers at low temperatures. Tetraspiro compounds might also be strong phosphazene bases and can be used as starting materials in the preparation of phosphazenium salts (protic molten salts, PMOS).

5. Conflict of interest

The authors declare no competing financial interest.

Ethical Approval: Ethics Approval is not required for this study.

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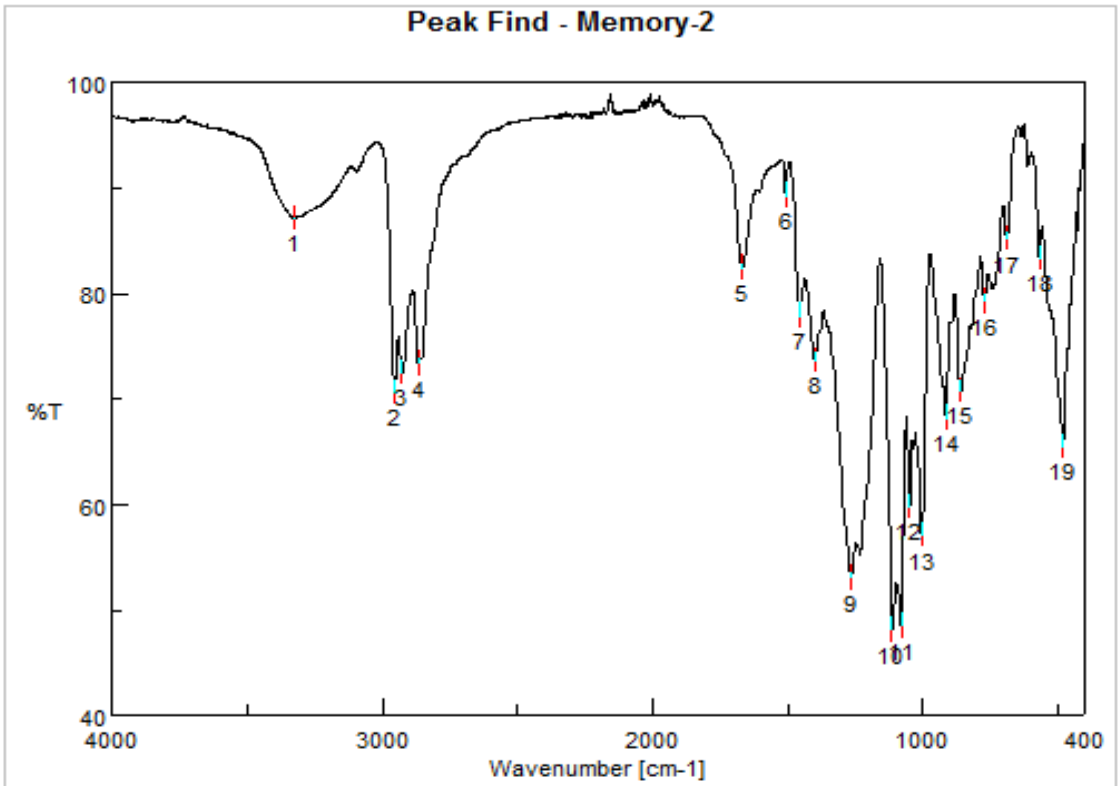
Supplamentery Materials

Contents



[Result of Peak Picking]

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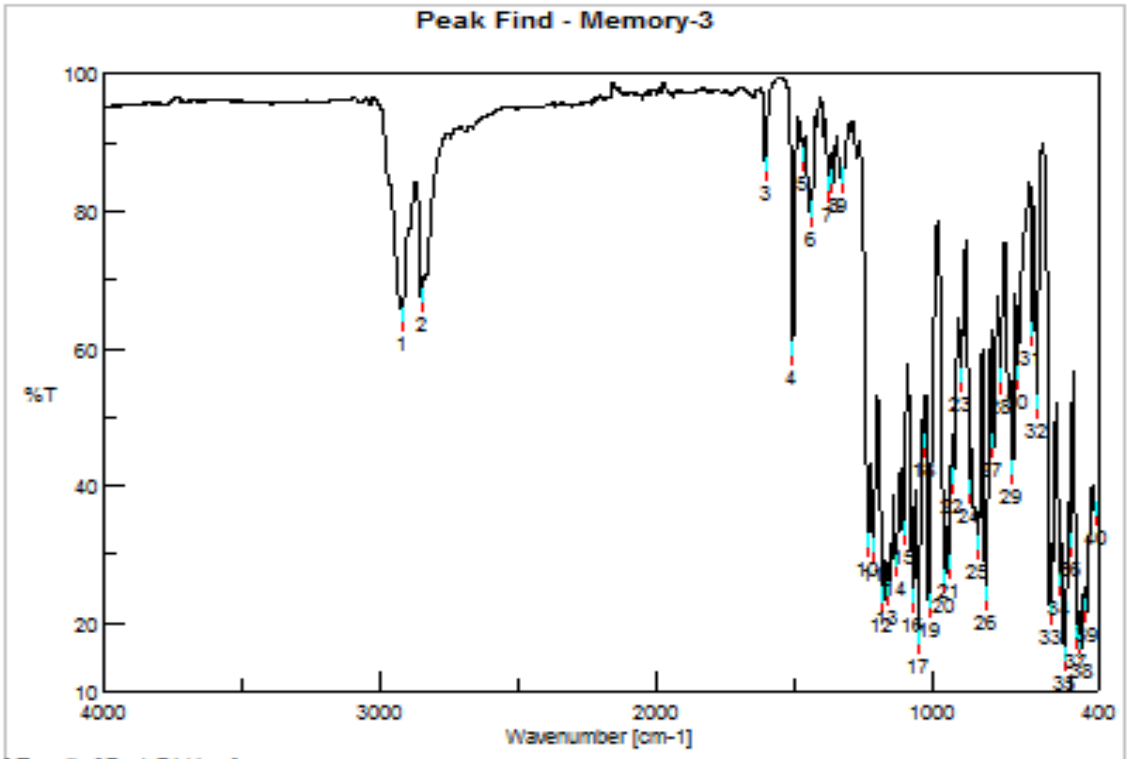
3	2928.38	72.5299	4	2869.56	73.4199
5	1667.16	82.446	6	1508.06	89.2996
7	1455.03	77.9196	8	1399.1	73.6287
9	1265.07	53.0791	10	1113.69	48.1359
11	1079.94	48.5395	12	1048.12	59.7861
13	1004.73	57.0985	14	914.093	68.2202
15	858.168	70.808	16	772.351	79.2973
17	688.463	85.2091	18	567.934	83.3878
19	480.188	65.5279			

Figure S1. FTIR spectrum of **2a.**



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	2916.81	64.1569	2	2849.31	66.9829	3	1603.52	85.8275
4	1505.17	59.2122	5	1463.71	87.4866	6	1440.56	79.3963
7	1376.93	82.9539	8	1360.53	84.0447	9	1324.86	84.3375
10	1231.33	31.313	11	1213.97	30.4783	12	1177.33	23.2224
13	1159.97	24.0049	14	1132.97	28.2417	15	1104.05	32.947
16	1072.23	22.9784	17	1051.01	17.0107	18	1029.8	45.7603
19	1012.45	22.4722	20	954.591	26.019	21	938.199	27.8786
22	923.736	40.5088	23	898.666	55.2914	24	863.953	38.9275
25	834.062	30.87	26	806.099	23.4146	27	779.101	45.7445
28	754.031	55.0279	29	709.676	41.7479	30	691.355	55.5066
31	639.287	62.0657	32	622.895	51.3733	33	573.719	21.1536
34	539.007	25.4572	35	519.722	14.5438	36	501.401	31.1161
37	474.403	17.6979	38	462.832	16.2045	39	441.619	21.6972
40	404.978	35.8594						

Figure S2. FTIR spectrum of the mixture of ***trans 2b*** and ***cis*** **2b.**

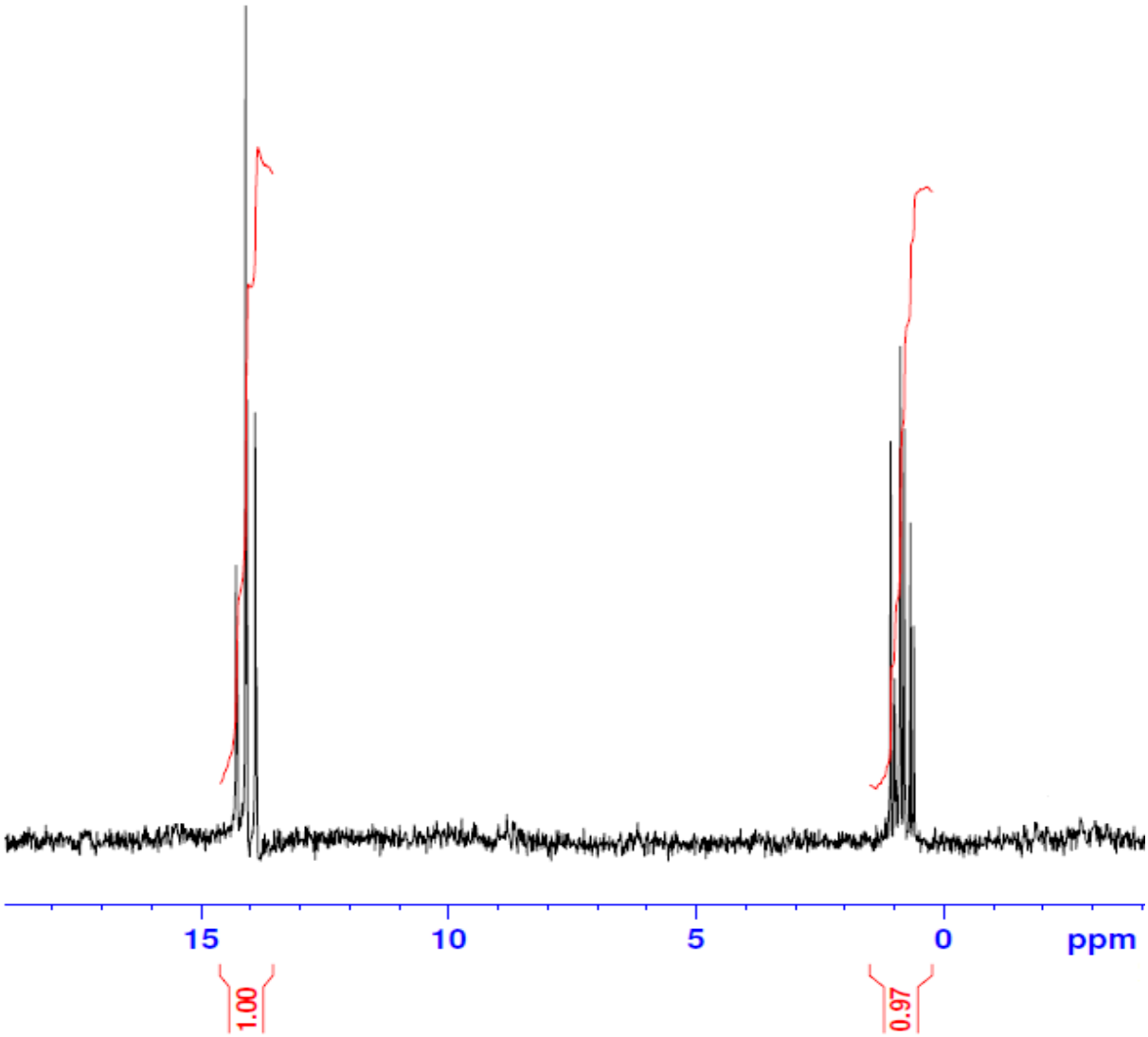


Figure S3. ^{31}P $\{^{1}H\}$ NMR spectrum of **2a.**

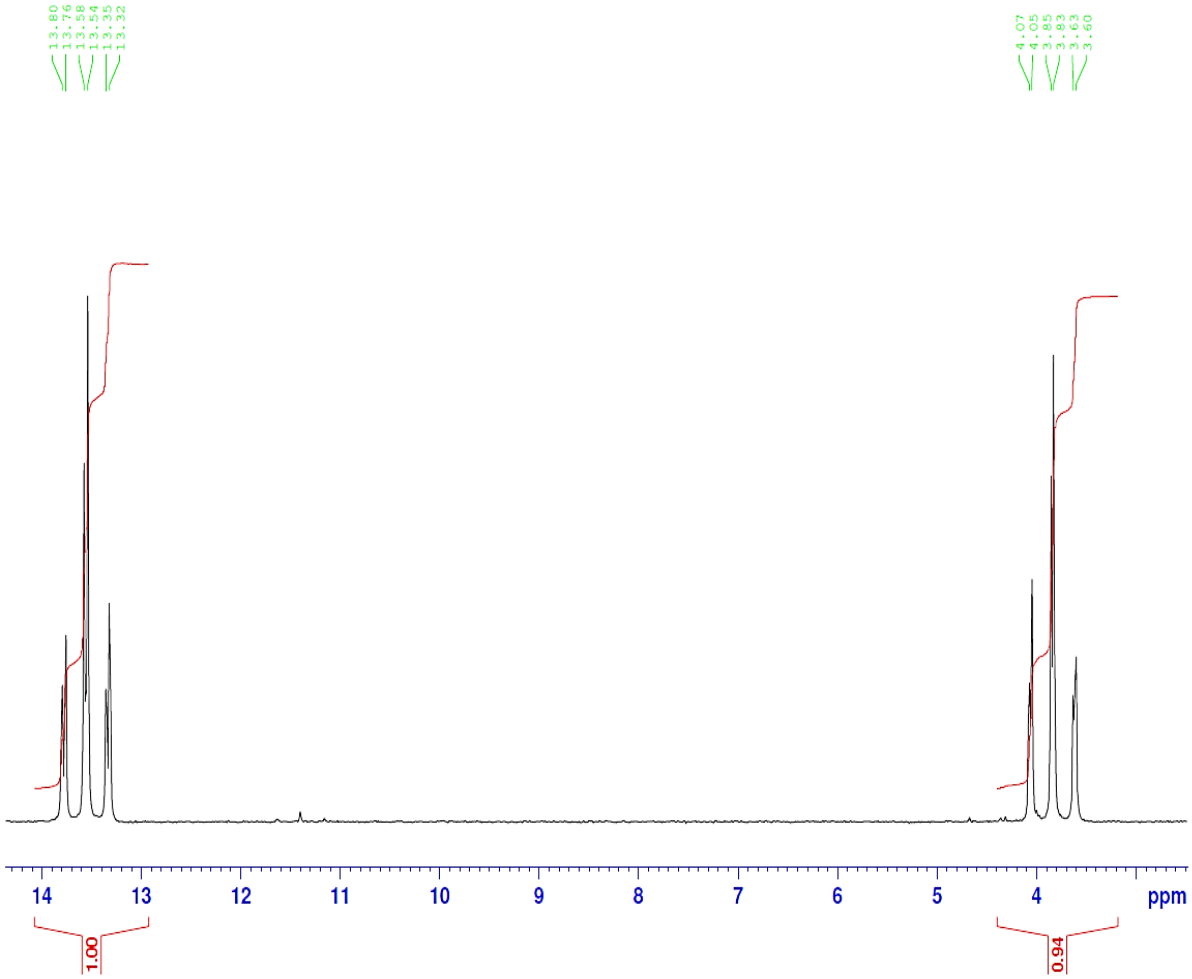


Figure S4. ^{31}P $\{^{1}H\}$ NMR spectrum of the mixture of ***trans*** **2b** and ***cis*** **2b.**

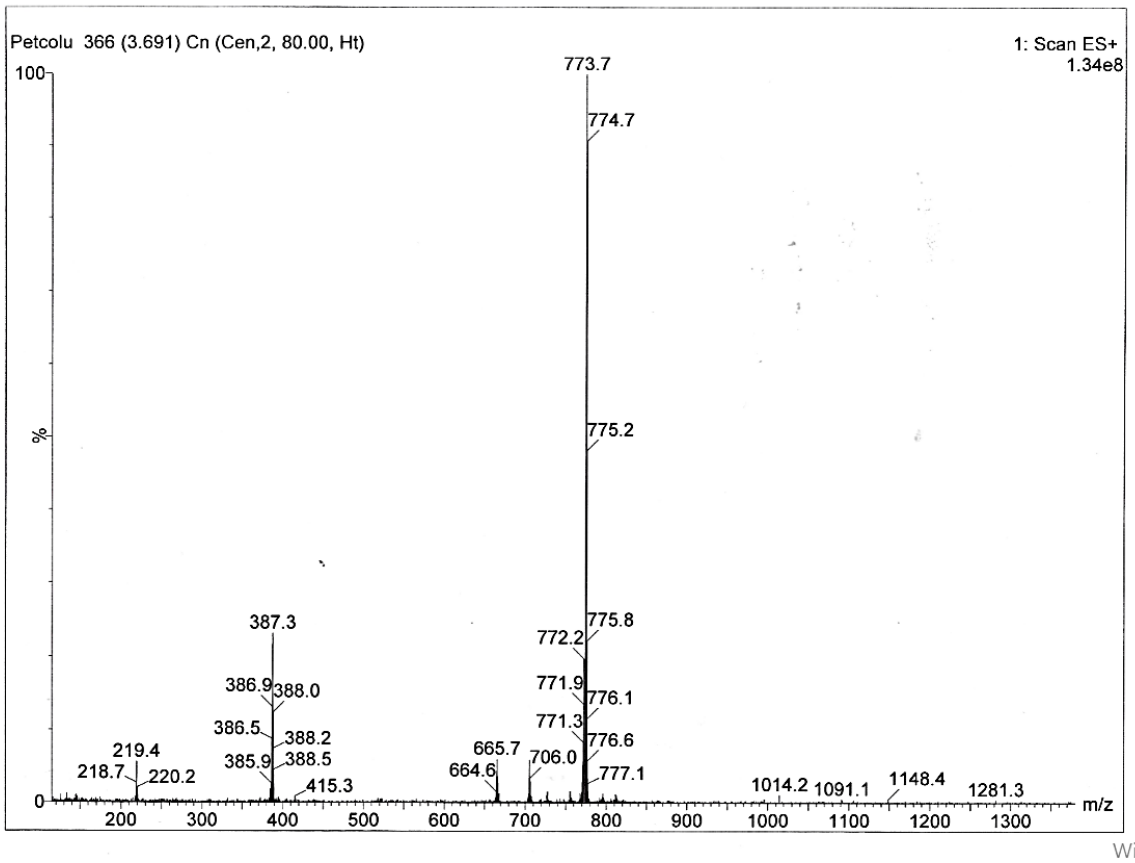


Figure S5. ESI-MS spectrum of **2a.**

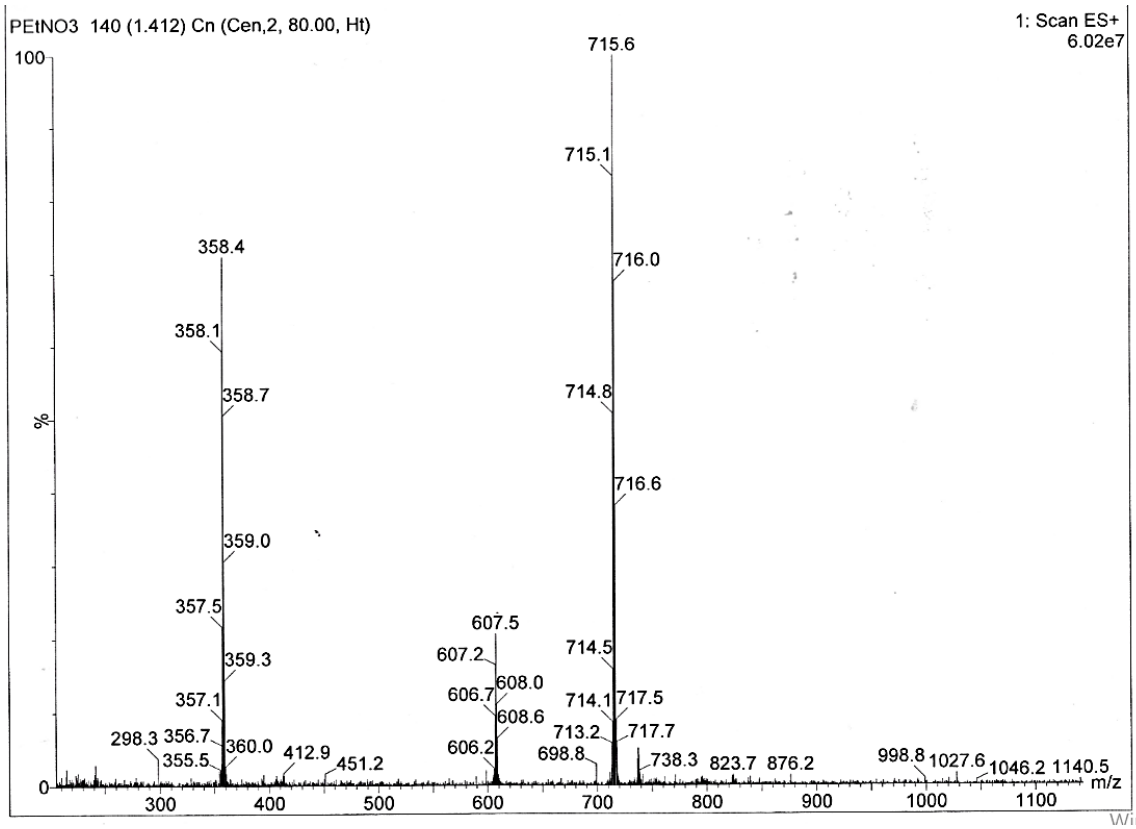


Figure S6. ESI-MS spectrum of the mixture of ***trans 2b*** and ***cis*** **2b.**

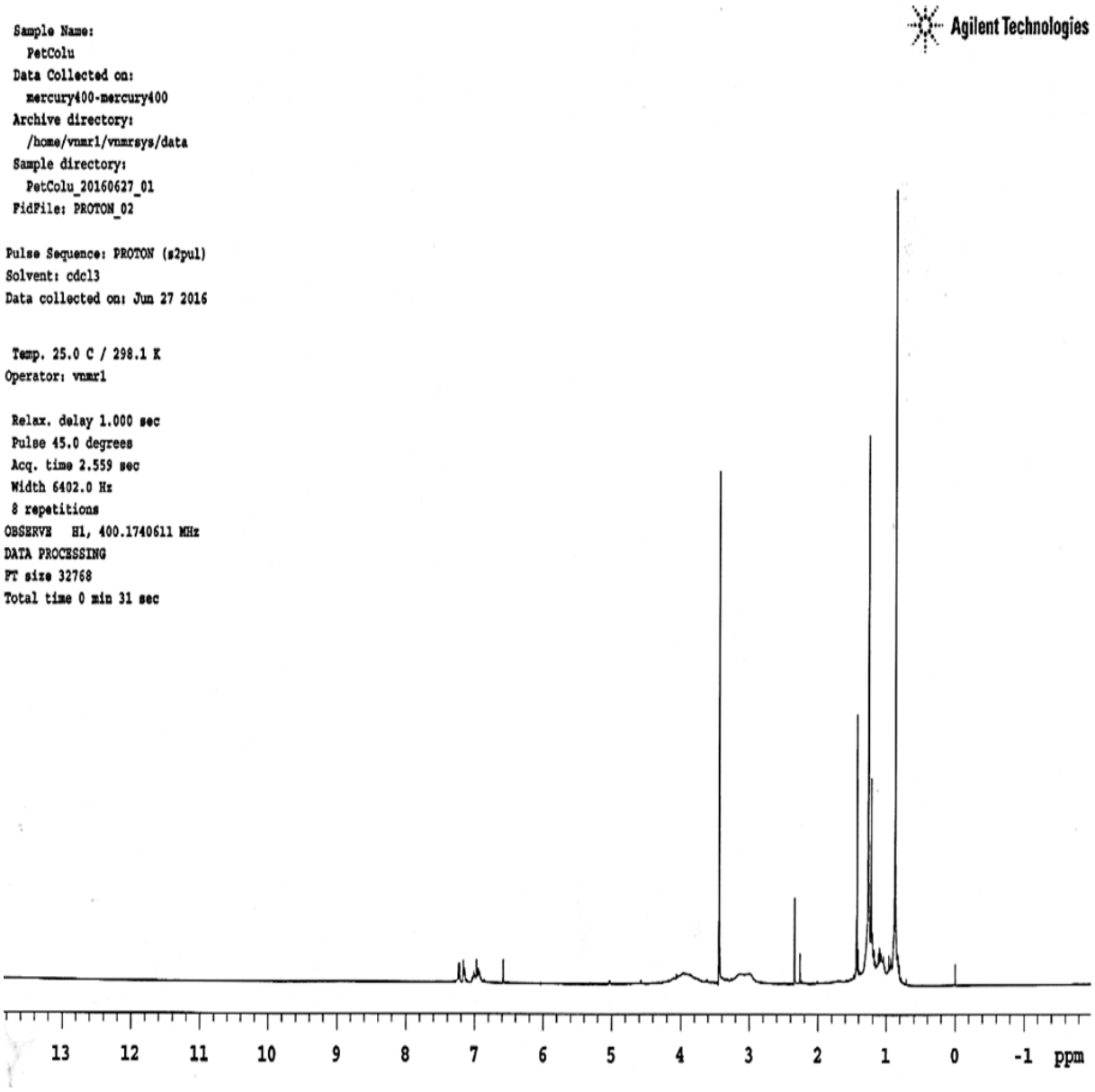


Figure S7. ^{1}H NMR spectrum of **2a.**

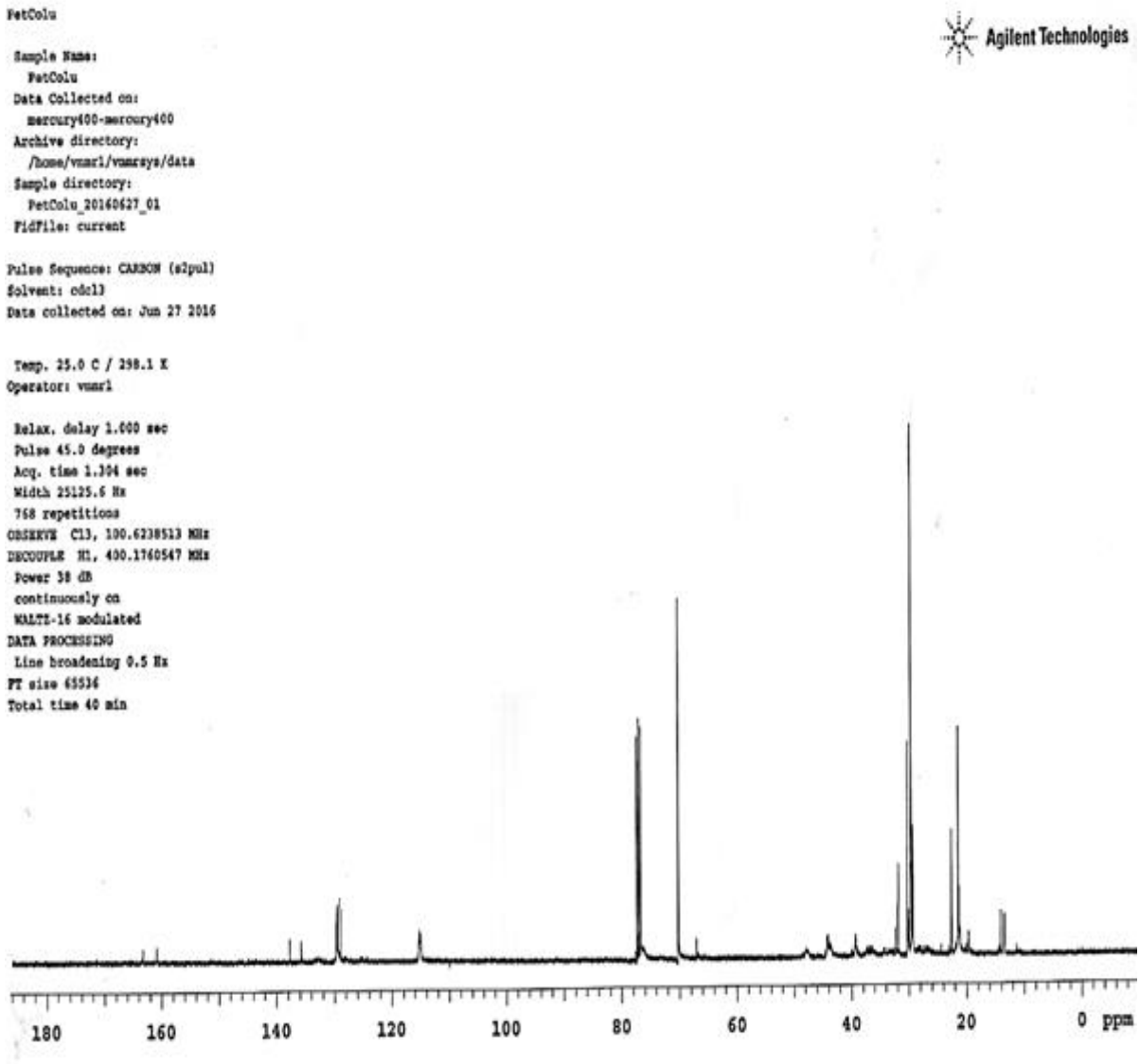


Figure S8. ^{13}C NMR spectrum of **2a.**

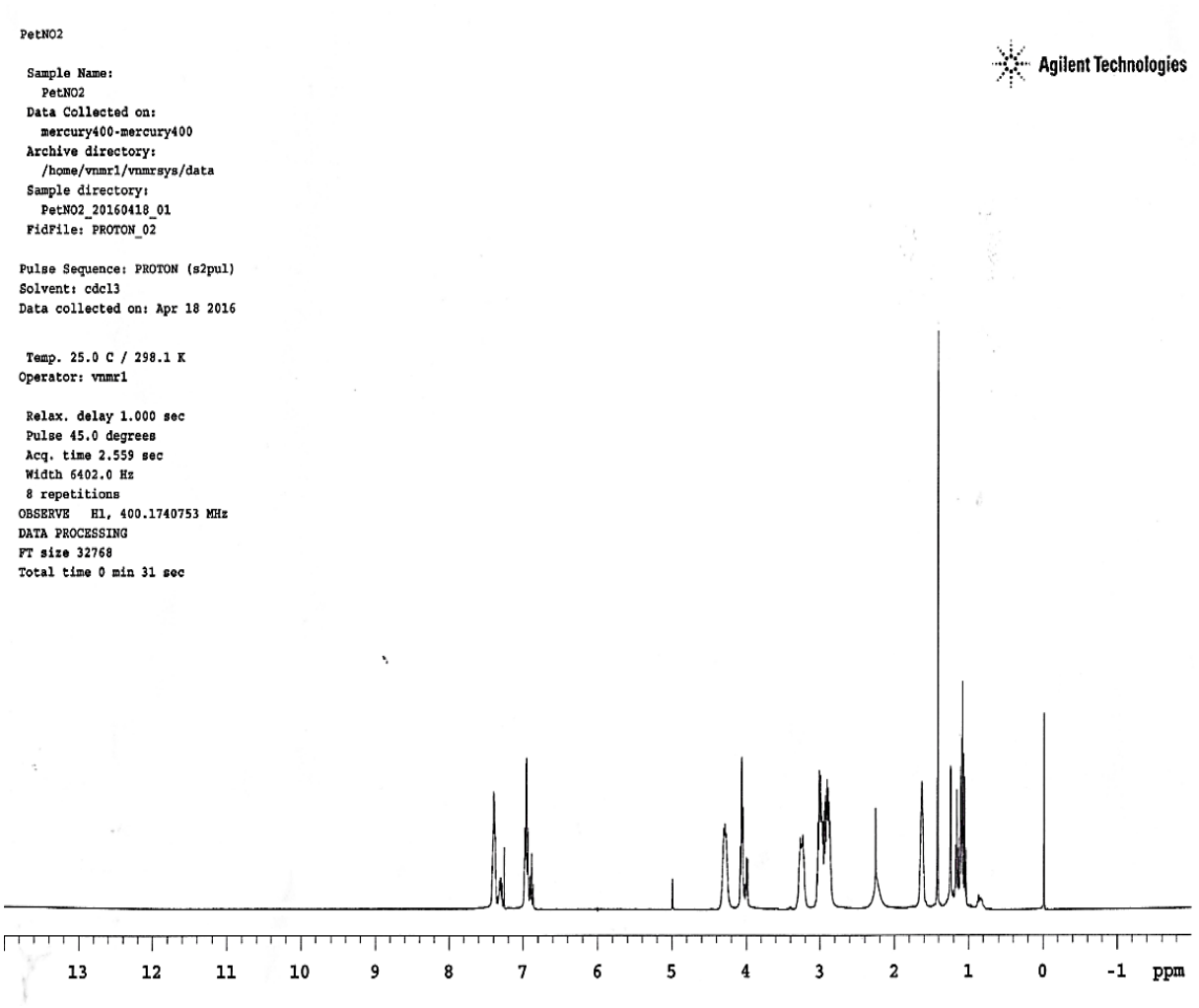


Figure S9. ^{1}H NMR spectrum of the mixture of ***trans 2b*** and ***cis*** **2b.**

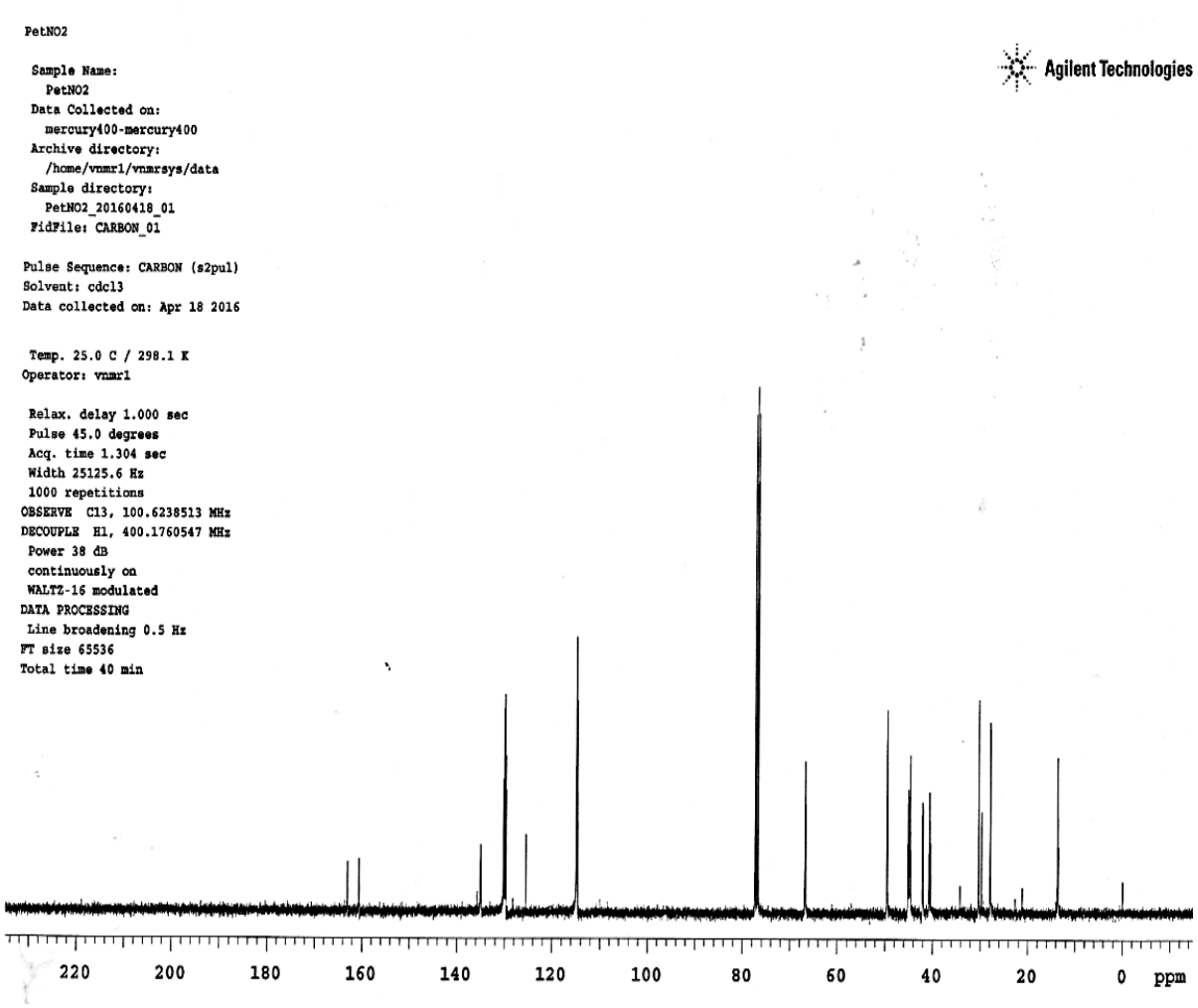


Figure S10. ^{13}C NMR spectrum of the mixture of ***trans 2b*** and ***cis*** **2b.**