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Substituent Effects on the Spectroscopic and Structural Parameters of Several New 1,3,2-Diazaphosphorinanes. Syntheses, Spectroscopic Characterization, and X-ray Crystallography

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New 1,3,2-diazaphosphorinanes with the formula 4-X-$C_6H_4NHP(O)[NH(CH_2)_3NH]$ (X = F (**1**), Cl (**2**), Br (**3**), and I (**4**)) were synthesized and characterized by ^1H, ^{13}C, and ^{31}P NMR and IR spectroscopy, and elemental analysis. The structures have been determined for compounds **3** and **4** by X-ray crystallography.

1,3,2-Diazaphosphorinanes form an important part of phosphorus chemistry. These ring systems are analogous to antitumor drugs such as cyclophosphamide, isophosphamide, and trophophosphamide.[1] In contrast with 1,3,2-oxaza-[2] and dioxa-phosphorinanes[3] which have been extensively studied, less attention has been paid to the synthesis and stereochemistry of 1,3,2-diazaphosphorinanes.[4] The synthetic[5] and coordination chemistry[6] of 1,3,2-diazaphosphorinanes have already been investigated. So far, the crystal structures of only a few of the compounds of this series have been determined.[7] Herein, we synthesized, spectroscopically characterized, and determined the crystal structures of several new 1,3,2-diazaphosphorinanes to study how their spectroscopic and structural properties are affect by different substituents.

Results and Discussion

Spectroscopic Study. The spectroscopic data of molecules **1**–**4** and also of compound $C_6H_5NHP(O)[NH(CH_2)_3NH]$ (**5**)[8] are given in Table 1. In ^1H NMR spectra of compounds **1**–**5**, a doublet is observed due to the coupling of the endocyclic NH protons with phosphorus ($^2J(PNH) \approx 8.0$ Hz). The NH proton of exocyclic group in these molecules splits with phosphorus atom and $^2J(PNH) \approx 10.0$ Hz. Also, in the ^1H NMR spectra of compounds **1**–**5**, multiplets for the four protons of two CH_2 groups were observed; however, the H_{axial} and $H_{equatorial}$ atoms of CH_2 group with three bond distances from P atom have different chemical shifts. The unequivalent methylene protons in these compounds at room temperature suggest a single chair conformation for six-membered ring and exclude flexible boat forms in which pseudorotation would tend to average the chemical shifts and coupling constants.[9] This was confirmed by X-ray crystal structures of compounds **3** and **4** in which there are chair conformations (Figs. 1 and 2). $^3J(P,C)_{aliphatic}$ coupling constants in these molecules have larger values than $^2J(P,C)_{aliphatic}$ coupling constants. The phosphorus chemical shifts are upfield from each other due to the decreasing of electronegativity from fluorine to iodine atom at para position of aniline ring. The phosphorus atom in compounds **1**–**5** are deshielded in the order of F > H > Cl > Br > I.

X-ray Crystallography Investigation. The crystallographic data of compounds **3** and **4** are given in Table 2 and selected bond lengths and angles are listed in Table 3. Molecular structures of compounds **3** and **4** are shown in Figs. 1 and 2,

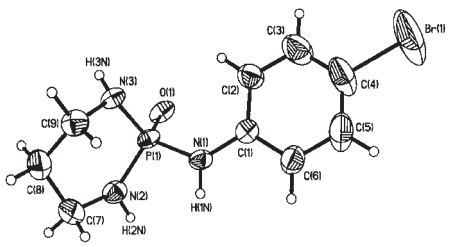

Fig. 1. ORTEP diagram and atom labeling scheme for compound **3** (50% probability ellipsoids).

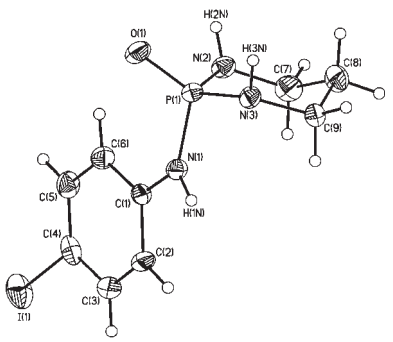

Fig. 2. ORTEP diagram and atom labeling scheme for compound **4** (50% probability ellipsoids).

Table 1. Spectroscopic Data of Compounds **1**–**5**

Compound	$\delta(^{31}P)$ /ppm	$^2J(PNH)_{endocyclic}$ /Hz	$^2J(PNH)_{exocyclic}$ /Hz	$^3J(PNCH)$ /Hz	$^2J(P,C)_{aliphatic}$ /Hz	$^3J(P,C)_{aliphatic}$ /Hz
1[a)]	5.82	8.0	10.1	—	3.3	7.8
2[a)]	5.50	7.8	10.2	—	3.8	7.6
3[a)]	5.51	8.1	10.3	—	3.3	7.6
4[a)]	5.39	7.9	10.2	—	3.3	7.8
5[b)]	5.60	8.0	10.2	—	3.3	7.7

a) This work. b) The spectroscopic data of compound **5**, $C_6H_5NHP(O)[NH(CH_2)_3NH]$, are presented in Ref. 8.

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Table 2. Crystallographic Data for Compounds **3** and **4**

	3	**4**
Empirical formula	$C_9H_{13}BrN_3OP$	$C_9H_{13}IN_3OP$
Formula weight	290.10	337.09
Temperature/K	230(2)	190(2)
Wavelength/Å	0.7173	0.7173
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Unit cell dimensions		
a/Å	13.225(4)	10.428(2)
b/Å	10.861(3)	11.583(2)
c/Å	8.915(3)	9.616(2)
α/deg	90.0	90.0
β/deg	97.789(7)	90.83(3)
γ/deg	90.0	90.0
V/Å^3	1268.7(7)	1161.3(4)
Z, Calculated density/Mg m^{-3}	4, 1.519	4, 1.928
Absorption coefficient/mm^{-1}	3.346	2.874
F(000)	584	656
Crystal size/mm^3	0.25 × 0.20 × 0.10	0.20 × 0.10 × 0.10
θ range for data collection/deg	2.44 to 28.17	2.63 to 26.00
Limiting indices	$-17 \le h \le 17$	$-12 \le h \le 12$
	$-14 \le k \le 14$	$-14 \le k \le 0$
	$-11 \le l \le 11$	$0 \le l \le 11$
Reflections collected/unique	12801/3059 [R(int) = 0.0361]	2347/2207 [R(int) = 0.0331]
Completeness to theta	98.0%	96.4%
Absorption correction	Semi-empirical from equivalents	None
Max. and min. transmission	0.7308 and 0.4940	—
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	3059/0/136	2207/0/136
Goodness-of-fit on F^2	1.050	0.972
Final R indices	$R_1 = 0.0507$, $wR_2 = 0.1353$	$R_1 = 0.0515$, $wR_2 = 0.1094$
R indices (all data)	$R_1 = 0.0738$, $wR_2 = 0.1519$	$R_1 = 0.0756$, $wR_2 = 0.1181$
Largest diff. peak and hole/e Å^{-3}	1.151; −0.989	2.114; −0.889

Table 3. Selected Bond Lengths (Å) and Angles (°) of Compounds **3** and **4**

3		**4**	
P(1)–O(1)	1.483(2)	P(1)–O(1)	1.472(5)
P(1)–N(1)	1.646(2)	P(1)–N(1)	1.654(6)
P(1)–N(2)	1.643(3)	P(1)–N(2)	1.649(6)
P(1)–N(3)	1.650(2)	P(1)–N(3)	1.651(6)
N(1)–C(1)	1.402(4)	N(1)–C(1)	1.392(9)
C(4)–Br(1)	1.894(4)	C(4)–I(1)	2.103(7)
O(1)–P(1)–N(1)	110.6(1)	O(1)–P(1)–N(1)	117.1(3)
O(1)–P(1)–N(2)	115.8(1)	O(1)–P(1)–N(2)	111.2(3)
O(1)–P(1)–N(3)	109.8(1)	O(1)–P(1)–N(3)	113.3(3)
N(1)–P(1)–N(2)	104.4(1)	N(1)–P(1)–N(2)	104.5(3)
N(1)–P(1)–N(3)	110.0(1)	N(1)–P(1)–N(3)	100.6(3)
N(2)–P(1)–N(3)	106.0(1)	N(2)–P(1)–N(3)	109.3(3)
C(1)–N(1)–P(1)	127.9(2)	C(1)–N(1)–P(1)	125.6(5)
C(1)–N(1)–H(1N)	116.6	C(1)–N(1)–H(1N)	109.6
P(1)–N(1)–H(1N)	115.5	P(1)–N(1)–H(1N)	124.7
C(7)–N(2)–P(1)	124.7(2)	C(7)–N(2)–P(1)	117.1(5)
C(7)–N(2)–H(2N)	113.5	C(7)–N(2)–H(2N)	116.2
P(1)–N(2)–H(2N)	116.7	P(1)–N(2)–H(2N)	110.8
C(9)–N(3)–P(1)	117.7(2)	C(9)–N(3)–P(1)	116.4(5)
C(9)–N(3)–H(3N)	114.1	C(9)–N(3)–H(3N)	108.0
P(1)–N(3)–H(3N)	110.0	P(1)–N(3)–H(3N)	108.2

respectively. The endocyclic nitrogen atoms in compounds **3** and **4** are distorted from planarity. Sum of the angles around the endocyclic N atoms in **3** are 341.84 and 354.87° for N(3) and N(2) atoms, respectively. The exocyclic nitrogen atoms of *p*-haloaniline groups are relatively planar. In the other words, the surrounding angles of exocyclic nitrogen atoms N(1) in compounds **3** and **4** are 359.99 and 359.95°, respectively. The P–N bonds in these molecules are smaller than the P–N single bond (1.77 Å[10]). The C–X bond length (X = halogen atom at para position of aniline ring) in compounds **3** and **4** are 1.894(4) and 2.103(7) Å, respectively. These data suggest that the C–X bond in compound **3** is smaller than in compound **4** because of more electronegativity of bromine than iodine and also fluorine than chlorine atom.

The P=O bond lengths in compounds **3** and **4** are 1.483(2) and 1.472(5) Å, respectively, and they are slightly longer than the typical P=O double bond length (1.45 Å).[10] This bond is in an equatorial position. The P atoms have slightly distorted tetrahedral configurations with the angles are in the range of 115.8(1)–104.4(1)° (in **3**) and 117.1(3)–100.6(3)° (in **4**). Compound **3** forms intermolecular N–H···O hydrogen bonds and produces a centrosymmetric dimmer, and this dimer is surrounded by four other intermolecular N–H···O hydrogen bonds that lead to a two-dimensional polymeric chain. In the structure of compound **4**, each molecule is connected to another one by intermolecular P–O···H–N hydrogen bonds.

Experimental

Spectroscopic Measurements. All reactions were performed under argon and using dry solvents. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance DRS 500 spectrometer. ^{1}H and ^{13}C chemical shifts were determined relative to internal TMS, ^{31}P chemical shifts are referenced to 85% H_3PO_4 as external standard. Infrared (IR) spectra were recorded on a Shimadzu model IR-60 spectrometer. Elemental analysis was performed using a Heraeus CHN-O-RAPID apparatus. Melting points were determined using an Electrothermal instrument.

X-ray Measurements. X-ray data of compound **3** was collected on a Bruker SMART 1000 with a CCD area detector and of compound **4** on a Siemens P3/PC single crystal diffractometer with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structures were refined with SHELXL-97[11] by full matrix least squares on F^2. The positions of hydrogen atoms were obtained from the difference Fourier map. Routine Lorentz and polarization corrections were applied and an absorption correction was performed using the SADABS program for compound **3**.[12] Crystallographic data for the structures **3** and **4** have been deposited with Cambridge Crystallographic Data Center as supplementary publication Nos. CCDC 292750 ($C_9H_{13}BrN_3OP$) and CCDC 286219 ($C_9H_{13}IN_3OP$). Copies of the data may be obtained, free of charge, on application to CCDC, 12, Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk/conts/retrieving.html).

Syntheses. Synthesis of compounds **1**–**4** were performed by the reaction of *N*-4-halophenylphosphoramidic dichloride[13] with 1,3-diaminopropane in 1:2 molar ratio. After about 10 h stirring, the solvent was removed and product was washed with distilled water and recrystallized from methanol/acetonitrile.

2-(4-Fluoroanilino)-1,3,2-diazaphosphorinane-2-oxide (1): Yield: 63%, mp 201 °C. ^{1}H NMR (500.13 MHz, DMSO-d_6, 25 °C, TMS) δ 1.45 (m, 1H, CH), 1.51 (m, 1H, CH), 3.01 (m, 4H, CH_2), 4.28 (td, ^{3}J(H,H) = 5.4 Hz, ^{2}J(PNH) = 8.0 Hz, 2H, NH(endocyclic)), 6.94 (t, ^{3}J[(H,H), (F,H)] = 9.0 Hz, 2H, Ar–H), 7.10 (dd, ^{4}J(F,H) = 4.9 Hz, ^{3}J(H,H) = 9.0 Hz, 2H, Ar–H), 7.13 (d, ^{2}J(PNH) = 10.1 Hz, 1H, NH(exocyclic)). ^{13}C NMR (125.77 MHz, DMSO-d_6, 25 °C, TMS) δ 156.09 (d, ^{1}J(F,C) = 234.6 Hz, 1C, C_{ipso}), 139.48 (d, ^{4}J(F,C) = 1.9 Hz, 1C, C_{para}), 118.40 (t, ^{3}J[(F,C), (P,C)] = 7.0 Hz, 2C, C_{ortho}), 114.76 (d, ^{2}J(F,C) = 22.0 Hz, 2C, C_{meta}), 41.81 (d, ^{2}J(P,C) = 3.3 Hz, 2C, CH_2), 27.00 (d, ^{3}J(P,C) = 7.8 Hz, 1C, CH_2). ^{31}P NMR (202.46 MHz, DMSO-d_6, 25 °C, H_3PO_4 external) δ 5.82 (m). IR (KBr, cm^{-1}): 3300 (νNH), 3175 (νNH), 2950, 1503, 1289, 1172 (νP=O), 1107, 951 (νP–N), 822 (νP–N), 638. Anal. Calcd for $C_9H_{13}FN_3OP$: C, 47.16; H, 5.72; N, 18.33%. Found: C, 47.13; H, 5.71; N, 18.32%.

2-(4-Chloroanilino)-1,3,2-diazaphosphorinane-2-oxide (2): Yield: 71%, mp 172 °C. ^{1}H NMR (500.13 MHz, DMSO-d_6, 25 °C, TMS) δ 1.43 (m, 1H, CH), 1.51 (m, 1H, CH), 3.02 (m, 4H, CH_2), 4.35 (td, ^{3}J(H,H) = 5.0 Hz, ^{2}J(PNH) = 7.8 Hz, 2H, NH(endocyclic)), 7.08 (d, ^{3}J(H,H) = 8.8 Hz, 2H, Ar–H), 7.14 (d, ^{3}J(H,H) = 8.8 Hz, 2H, Ar–H), 7.28 (d, ^{2}J(PNH) = 10.2 Hz, 1H, NH(exocyclic)). ^{13}C NMR (125.77 MHz, DMSO-d_6, 25 °C, TMS) δ 142.25 (s), 128.14 (s), 122.73 (s), 122.73 (s), 118.73 (d, ^{3}J(P,C) = 6.8 Hz, 2C, C_{ortho}), 41.78 (d, ^{2}J(P,C) = 3.8 Hz, 2C, CH_2), 26.91 (d, ^{3}J(P,C) = 7.6 Hz, 1C, CH_2). ^{31}P NMR (202.46 MHz, DMSO-d_6, 25 °C, H_3PO_4 external) δ 5.50 (m). IR (KBr, cm^{-1}): 3380 (νNH), 3225 (νNH), 3050, 2930, 1588, 1483, 1293, 1202, 1177 (νP=O), 1005, 987 (νP–N), 820 (νP–N), 570. Anal. Calcd for $C_9H_{13}ClN_3OP$ C, 44.00; H, 5.33; N, 17.11%. Found: C, 44.02; H, 5.32; N, 17.10%.

2-(4-Bromoroanilino)-1,3,2-diazaphosphorinane-2-oxide (3): Yield: 68%, mp 198 °C. ^{1}H NMR (500.13 MHz, DMSO-d_6, 25 °C, TMS) δ 1.42 (m, 1H, CH), 1.51 (m, 1H, CH), 3.03 (m, 4H, CH_2), 4.36 (td, ^{3}J(H,H) = 4.8 Hz, ^{2}J(PNH) = 8.1 Hz, 2H, NH(endocyclic)), 7.04 (d, ^{3}J(H,H) = 8.7 Hz, 2H, Ar–H), 7.26 (d, ^{3}J(H,H) = 8.7 Hz, 2H, Ar–H), 7.32 (d, ^{2}J(PNH) = 10.3 Hz, 1H, NH(exocyclic)). ^{13}C NMR (125.77 MHz, DMSO-d_6, 25 °C, TMS) δ 142.66 (s), 130.99 (s), 119.24 (d, ^{3}J(P,C) = 6.7 Hz, 2C, C_{ortho}), 110.45 (s), 41.77 (d, ^{2}J(P,C) = 3.3 Hz, 2C, CH_2), 26.91 (d, ^{3}J(P,C) = 7.6 Hz, 1C, CH_2). ^{31}P NMR (202.46 MHz, DMSO-d_6, 25 °C, H_3PO_4 external) δ 5.51 (m). IR (KBr, cm^{-1}): 3305 (νNH), 3135 (νNH), 2930, 1585, 1481, 1381, 1274, 1196, 1173 (νP=O), 1072, 948 (νP–N), 821 (νP–N), 480. Anal. Calcd for $C_9H_{13}BrN_3OP$: C, 37.26; H, 4.52; N, 14.48%. Found: C, 37.24; H, 4.52; N, 14.47%.

2-(4-Iodoanilino)-1,3,2-diazaphosphorinane-2-oxide (4): Yield: 54%, mp 220 °C. ^{1}H NMR (500.13 MHz, DMSO-d_6, 25 °C, TMS) δ 1.43 (m, 1H, CH), 1.49 (m, 1H, CH), 3.03 (m, 4H, CH_2), 4.34 (m, ^{3}J(H,H) = 5.3 Hz, ^{2}J(PNH) = 7.9 Hz, 2H, NH(endocyclic)), 6.92 (d, ^{3}J(H,H) = 8.2 Hz, 2H, Ar–H), 7.27 (d, ^{2}J(PNH) = 10.2 Hz, 1H, NH(exocyclic)), 7.41 (d, ^{3}J(H,H) = 8.2 Hz, 2H, Ar–H). ^{13}C NMR (125.77 MHz, DMSO-d_6, 25 °C, TMS) δ 143.15 (s), 136.80 (s), 119.81 (d, ^{3}J(P,C) = 6.8 Hz, 2C, C_{ortho}), 81.24 (s), 41.77 (d, ^{2}J(P,C) = 3.3 Hz, 2C, CH_2), 26.89 (d, ^{3}J(P,C) = 7.8 Hz, 1C, CH_2). ^{31}P NMR (202.46 MHz, DMSO-d_6, 25 °C, H_3PO_4 external) δ 5.39 (m). IR (KBr, cm^{-1}): 3310 (νNH), 3120 (νNH), 2925, 1580, 1477, 1379, 1270, 1196 (νP=O), 1072, 947 (νP–N), 823 (νP–N), 797, 480. Anal. Calcd for $C_9H_{13}IN_3OP$: C, 32.07; H, 3.89; N, 12.47%. Found: C, 32.05; H, 3.89; N, 12.46%.

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References

1 Z. Li, J. Han, Y. Jiang, P. Browne, R. J. Knox, L. Hu, *Bioorg. Med. Chem.* **2003**, *11*, 4171.

2 A. B. Ouryupin, M. I. Kadyko, P. V. Petrovskii, E. I. Fedin, *Tetrahedron: Asymmetry* **1995**, *6*, 1813.

3 R. Hernández, R. Ramos, N. Sastre, R. Meza, H. Hommer, M. Salas, B. Gordillo, *Tetrahedron* **2004**, *60*, 10927.

4 Z. Zalan, T. Martinek, L. Lázár, F. Fülöp, *Tetrahedron* **2003**, *59*, 9117.

5 J.-F. Peyronel, O. Samuel, J.-C. Fiaud, *J. Org. Chem.* **1987**, *52*, 5320.

6 S. E. Denmark, P. C. Miller, S. R. Wilson, *J. Am. Chem. Soc.* **1991**, *113*, 1468.

7 K. Gholivand, Z. Shariatinia, M. Pourayoubi, S. Farshadian, *Z. Naturforsch., B: Chem. Sci.* **2005**, *60*, 1021.

8 K. Gholivand, Z. Shariatinia, unpublished results.

9 E. Eliel, R. O. Hutchins, *J. Am. Chem. Soc.* **1969**, *91*, 2703.

10 D. E. C. Corbridge, *Phosphorus: An Outline of its Chemistry, Biochemistry and Technology*, Elsevier, The Netherlands, **1995**, p. 55; **1995**, p. 57.

11 G. M. Sheldrick, *SHELXL v. 5.10, Structure Determination Software Suit*, Bruker AXS, Madison, WI, U.S.A., **1998**.

12 G. M. Sheldrick, *SADABS v. 2.01, Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, U.S.A., **1998**.

13 K. Gholivand, S. Ghadimi, A. Forouzanfar, H. Naderimanesh, *Magn. Reson. Chem.* **2001**, *39*, 684.