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ORIGINAL PAPER

Synthesis, spectroscopic and configurational study, and ab initio calculations of new diazaphospholanes

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New 2-substituted diazaphospholane-2-oxides (*I–III*, *V–VIII*) and diazaphosphorinane-2-oxide (*IV*) were synthesised and characterised by ^{1}H, ^{13}C, and ^{31}P NMR, IR spectroscopy, and elemental analysis. The presence of chiral diamino groups in compounds *II* and *V–VIII* gives rise to various diastereomers so that the ^{31}P{^{1}H} NMR spectra demonstrated three and two peaks with different ratios, respectively. Also, the ^{1}H and ^{13}C{^{1}H} NMR spectra of compounds *II* and *V–VIII* revealed three and two sets of signals for the related conformers (diastereomers). Interestingly, the ^{31}P NMR spectrum of *V* in D_2O indicated a great upfield shift ($\Delta\delta$ = 19.0) for ^{31}P relative to the value obtained in DMSO-d_6 (solvent effect). The two signals in *V* split further to three signals in the presence of β-cyclodextrin. Moreover, conformational analysis of diazaphospholane *V* was studied by ab initio calculations at the HF and B3LYP levels of theory using the Gaussian 98 program. Results indicated that among four suggested diastereomers (C1–C4) of *V*, C1 and C3 containing methyl group in the equatorial position are the most stable forms.

Keywords: diazaphospholane, diastereomers, NMR, ab initio calculations

Introduction

1,3,2-Diazaphospholanes and 1,3,2-diazaphosphorinanes constitute a class of interesting mimetics of amino acids whose importance derives from their promising and diverse biological activity (Lucet et al., 1998; Saibabu Kotti et al., 2006; Wang et al., 2008; Olson & Du Bois, 2008). In fact, the vicinal diamino functionality is a significant structural unit that can make molecules biologically active (Du et al., 2008; Kim et al., 2008). This activity is usually based on the action of only one enantiomer of a diastereomer and thus in order to prepare efficient drugs in medicine it is of great significance to isolate the enantiomeric mixtures. The chiral α,β-diamino acid derivatives bearing vicinal diamino framework are widely found as antibiotics and natural products (Viso et al., 2005). Synthesis (Khaikin et al., 1988; Nifantiev et al., 1981; Peyronel et al., 1987; Zalán et al., 2003; De la Cruz et al., 1998), conformational analysis (Kranz et al., 1996; Denmark et al., 1991; Gholivand et al., 2009a; Setzer et al., 1989), and X-ray crystal structure of 1,3,2-diazaphosphorinanes and some diazaphospholanes (Dutasta et al., 1990; Gholivand et al., 2005a, 2005b, 2007a, 2009b) have been recently reported. NMR data can help to interpret the conformational equilibrium involving twist-envelope and half-chair conformations (Setzer et al., 1989). Although structures of 1,3,2-dioxa- (Dutasta et al., 1979; Nielsen & Dahl, 1984) and 1,3,2-oxaza-phospholane (Devillers et al., 1971; Hall et al., 1983) have been widely investigated, less attention has been paid to conformational analysis of 1,3,2-diazaphospholanes. Berlicki et al. (2003) studied the enantio differentiation of aminophosphonic and aminophosphinic acids using α- and β-cyclodextrins.

In this work, seven new 1,3,2-diazaphospholanes and one diazaphosphorinane were synthesised and characterised by multinuclear ^{1}H, ^{13}C, and ^{31}P NMR, and IR spectroscopy to investigate the effect of chiral-

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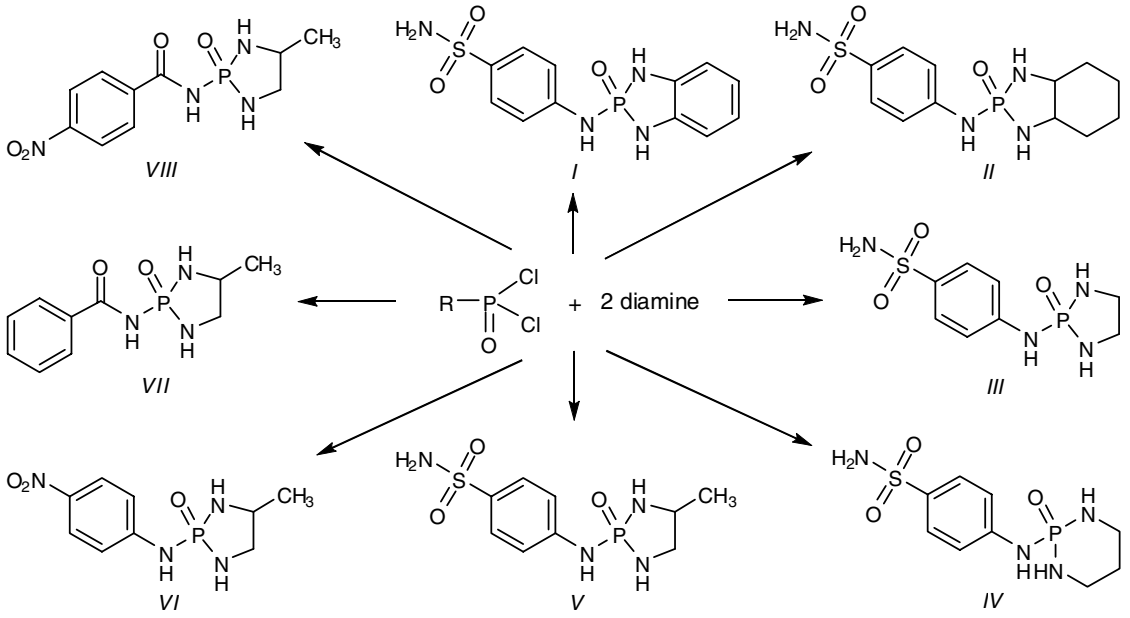

Fig. 1. Synthesis pathway for compounds *I–VIII*.

ity and different substituents on the structures. High temperature dynamic $^{31}P\{^{1}H\}$ NMR spectra of compounds *II* and *V* in DMSO-d_6 were also studied. In addition, quantum chemical calculations were done using the Gaussian 98 program to describe structures of four possible diastereomers of *V* including C1 (*RR*), C2 (*RS*), C3 (*SR*), C4 (*SS*) and their corresponding enantiomers C5 (*SS*), C6 (*SR*), C7 (*RS*), and C8 (*RR*).

Experimental

^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance DRS 500 spectrometer using TMS (for ^{1}H and ^{13}C) as the internal standard and 85 % H_3PO_4 (for ^{31}P) as the external standard. IR spectra (in KBr pellets) were recorded on a Shimadzu model IR-60 spectrometer. Elemental analyses were performed using a Heraeus CHN-O-RAPID apparatus. Melting points were obtained with an Electrothermal instrument.

2-(4-Sulphamoylphenylamino)-1,3,2-benzodiazaphospholan-2-one (I), 2-(4-sulphamoylphenylamino)-1,3,2-cyclohexodiazaphospholan-2-one (II), 2-(4-sulphamoylphenylamino)-1,3,2-diazaphospholan-2-one (III), 2-(4-sulphamoylphenylamino)-1,3,2-diazaphosphorinan-2-one (IV), 2-(4-sulphamoylphenylamino)-4-methyl-1,3,2-diazaphospholan-2-one (V), 2-(4-nitrophenylamino)-4-methyl-1,3,2-diazaphospholan-2-one (VI), 2-benzoylamino-4-methyl-1,3,2-diazaphospholan-2-one (VII), and 2-(4-nitrobenzoylamino)-4-methyl-1,3,2-diazaphospholan-2-one (VIII)

Compounds *I–VIII* were synthesised according to the general method as follows: To a solution of corresponding phosphoramidic dichloride (10 mmol) (4-sulphamoylphenylphosphoramidic dichloride for *I–V*; 4-nitrophenylphosphoramidic dichloride for *VI*; benzoylphosphoramidic dichloride for *VII*; 4-nitrobenzoylphosphoramidic dichloride for *VIII*) (Warnat, 1941; Amirkhanov et al., 1997) in dry acetonitrile, corresponding diamine (20 mmol) (benzene-1,2-diamine for *I*; cyclohexane-1,2-diamine for *II*; ethane-1,2-diamine for *III*; propane-1,3-diamine for *IV*; propane-1,2-diamine for *V–VIII*) was added dropwise at about 0 °C (in an ice bath) and the mixture was stirred for 8 h. The precipitate was filtered and the solvent was evaporated under diminished pressure to yield the product which was washed with distilled water and ethyl acetate and dried.

Results and discussion

In the present study, seven novel diazaphospholanes and one diazaphosphorinane were synthesised by the reaction of corresponding phosphoramidic dichloride and diamine (Fig. 1). Characterisation and spectral data of the prepared compounds *I–VIII* are summarised in Tables 1 and 2.

^{31}P NMR spectroscopy is a very convenient tool for the determination of the enantiomeric purity of organophosphorus compounds due to the large chemical shift dispersion and simplicity of the broad band in the ^{1}H decoupled spectra (Parker, 1991). In molecules *I* and *III–IV*, the diamino moiety is not chiral and there is only one signal for the phosphorus atom. Comparison of the $\delta(^{31}P)$ values of compounds *I* and *II* indicates that the phosphorus atom is deshielded when

Table 1. Characterisation data of newly prepared compounds

Compound	Formula	M_r	w_i(calc.)/mass % w_i(found)/mass %			Yield	M.p.
			C	H	N	%	℃
I	$C_{12}H_{13}N_4O_3PS$	324.29	44.40	4.04	17.30	69	192–194
			44.50	4.10	17.30		
II	$C_{12}H_{19}N_4O_3PS$	330.34	43.60	5.80	17.00	72	224–225
			43.60	5.85	16.88		
III	$C_8H_{13}N_4O_3PS$	276.25	34.80	4.74	20.30	69	219–221
			34.60	4.90	20.60		
IV	$C_9H_{15}N_4O_3PS$	290.28	37.20	5.21	19.30	69	192–194
			37.21	5.18	19.25		
V	$C_9H_{15}N_4O_3PS$	290.28	37.20	5.21	19.30	49	220–221
			37.60	5.15	19.80		
VI	$C_9H_{13}N_4O_3P$	256.20	42.20	5.11	21.90	63	210–212
			42.16	5.15	21.68		
VII	$C_{10}H_{14}N_3O_2P$	239.21	50.20	5.90	17.60	53	190–192
			50.21	5.92	17.56		
VIII	$C_{10}H_{13}N_4O_4P$	284.21	42.30	4.61	19.70	53	191–193
			42.16	4.70	19.68		

substituted by an aliphatic ring (δ = 11.63 in *I*, δ = 21.74, δ = 21.87, and δ = 23.30 in *II*). Endocyclic nitrogen atoms of the NH groups in compound *I* are bonded to carbon atoms with sp^2 hybridisation and to sp^3 carbon atoms in compound *II*. Therefore, as it was expected, the $^2J_{(P,NH)}$ in compound *I* (17.2 Hz) is higher than those in compound *II* (9.9 Hz, 10.0 Hz, 10.2 Hz, 10.7 Hz). The ring size affected both the phosphorus chemical shift and the $^2J_{(P,NH)}$ coupling constant. This means that the phosphorus atom is more shielded with the increasing ring size from a 5-membered ring in diazaphospholane *III* ($\delta(^{31}P)$ = 23.28) to a 6-membered one in diazaphosphorinane *IV* ($\delta(^{31}P)$ = 5.13). Conversely, $^2J_{(P,NH)}$ coupling constant increased from 11.7 Hz in *III* to 24.9 Hz in *IV*.

Chiral diamino groups in compounds *II* and *V–VIII* enable the formation of several diastereomers in the solution. In this respect, the $^{31}P\{^1H\}$ NMR spectra revealed three and two peaks with different ratios for *II* and *V–VIII*, respectively. Compounds *V*, *VII*, and *VIII* exhibited the ratio of diastereomers of 1 : 0.9 while the ratio of 1 : 0.4 was observed for *VI* indicating that synthesis of *VI* (containing the nitro group) is stereoselective. The ^{31}P NMR spectrum of *II* showed three separated signals (ratio of peaks of 3 : 1 : 0.8) at δ = 21.74, δ = 21.87, and δ = 23.3, respectively, with different $^2J_{(P,NH)}$ coupling constants in the range of 9.9–10.7 Hz. In addition, the ^1H and ^{13}C NMR spectra of *II* showed three sets of signals for individual stereoisomers. It was found that the *trans*-1,2-diaminocyclohexane of the C_2 symmetry is a chiral compound, whereas symmetrical *cis*-1,2-diaminocyclohexane is an optically inactive one. However, this compound can exist in chiral conformations which interconvert rapidly into each other through chair-antichair inversions of the cyclohexane ring. These findings confirm the presence of a *meso* form and *SSS* + *RRR* + *SSR* + *RRS* isomers (two diastereoisomeric mixtures) in compound *II*, which results in three peaks in the ^{31}P NMR spectrum. The high temperature dynamic $^{31}P\{^1H\}$ NMR spectra of compound *II* (Fig. 2) revealed only small differences in shifts and therefore, the signals overlapped at 333 K.

The situation with compound *V* is simpler as a mixture of two diastereoisomers was obtained (two peaks in ^{31}P NMR spectrum). The dynamic $^{31}P\{^1H\}$ NMR spectra of *V* did not reveal significant changes. Interestingly, the $^{31}P\{^1H\}$ NMR spectrum of *V* in D_2O showed a great upfield shift ($\Delta\delta \approx 19.0$) for $\delta(^{31}P)$ relative to the $\delta(^{31}P)$ value observed in DMSO-d_6 (solvent effect on the phosphorus shielding). Two signals at δ = 3.72 and δ = 2.17 with the ratio of 0.9 : 1 were observed in D_2O (Fig. 3). For enantiomeric resolution of the diastereomeric forms of compound *V*, β-cyclodextrin in a D_2O solution was used. In the presence of β-cyclodextrin, one of the two signals (at δ = 2.17) split to two signals indicating the separation of the two enantiomeric forms of one diastereomer. In this case, three signals at δ = 3.25, δ = 1.80, and δ = 1.76 were observed. The signal at δ = 3.25, corresponding to the second diastereotopic form, did not split further.

Replacement of the 4-sulphamoylphenyl group with 4-nitrophenyl, benzoyl, or 4-nitrobenzoyl did not change the stereochemistry of *VI–VIII*. In addition, comparing the spectra of compounds *I–V* with those of compounds *VI–VIII* it can be concluded that the conformational diversity originates from the chiral diamines only.

In the IR spectra of compounds *I–VIII*, ν(P═O)

Table 2. Spectral data of newly prepared compounds[a]

Compound	Spectral data
I	IR, $\tilde{\nu}$/cm^{-1}: 3160 (s, NH), 3035 (s, NH), 2640 (m), 1588 (m), 1488 (m), 1399 (w), 1299 (m), 1242 (w), 1179 (s, P═O), 1147 (s, SO_2), 1092 (m), 950 (s, PN), 898 (w), 828 (m), 739 (m, PN), 584 (m), 537 (m) ^{1}H NMR (DMSO-d_6), δ: 6.61 (d, 2H, ^3J = 8.4 Hz, ArH), 6.74 (s, 4H, ArH), 7.04 (s, 2H, NH_2), 7.88 (d, 2H, ^3J = 7.85 Hz, ArH), 8.40 (d, 1H, $^2J_{(P,NH)}$ = 8.1 Hz, NH), 8.59 (d, 2H, $^2J_{(P,NH)}$ = 17.2 Hz, NHP(O)NH) ^{13}C NMR (DMSO-d_6), δ: 109.59 (d, $^3J_{(P,C)}$ = 12.5 Hz), 116.39 (d, $^3J_{(P,C)}$ = 7.78 Hz), 119.13, 126.60, 131.75 (d, $^2J_{(P,C)}$ = 13.49 Hz), 135.35, 145.46 ^{31}P NMR (DMSO-d_6), δ: 11.63 (dt, $^2J_{(P,NH)}$ = 16.9 Hz, $^2J_{(P,NH')}$ = 8 Hz)
II	IR, $\tilde{\nu}$/cm^{-1}: 3385 (s, NH), 3215 (s, CH), 3070 (s, CH), 2940 (m), 1596 (m), 1499 (m), 1459 (m), 1301 (s), 1196 (m, P═O), 1173 (s, P═O), 1150 (s, SO_2), 1079 (m), 948 (m), 833 (m), 710 (m), 540 (m), 425 (w) ^{1}H NMR (DMSO-d_6), δ: 1.20 (m, 2H, CH_2), 1.29 (m, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 1.66 (m, 4H, CH_2), 1.80 (m, 2H, CH_2), 2.89 (m, 2H, CH), 3.40 (m, 2H, CH), 4.64 (d, 1H, $^2J_{(P,NH)}$ = 10.7 Hz, NH), 4.71 (d, 1H, $^2J_{(P,NH)}$ = 9.9 Hz, NH), 4.82 (d, 1H, $^2J_{(P,NH)}$ = 10.0 Hz, NH), 4.83 (d, 1H, $^2J_{(P,NH)}$ = 10.2 Hz, NH), 6.62 (s, 2H, NH_2), 6.64 (s, 2H, NH_2), 7.22 (d, 2H, ^3J = 8.8 Hz, ArH), 7.25 (d, 2H, ^3J = 8.8 Hz, ArH), 7.35 (d, 2H, ^3J = 8.9 Hz, ArH), 7.52 (d, 1H, $^2J_{(P,NH)}$ = 7.1 Hz, NH), 7.55 (d, 1H, $^2J_{(P,NH)}$ = 7.2 Hz, NH), 7.57 (d, 2H, ^3J = 8.8 Hz, ArH) ^{13}C NMR (DMSO-d_6), δ: 20.91, 20.94, 23.89, 23.97, 29.64 (d, $^3J_{(P,C)}$ = 6.6 Hz, CH_2), 30.10 (d, $^3J_{(P,C)}$ = 5.0 Hz, CH_2), 30.49 (d, $^3J_{(P,C)}$ = 12.2 Hz, CH_2), 30.72 (d, $^3J_{(P,C)}$ = 13.6 Hz, CH_2), 52.34 (d, $^2J_{(P,C)}$ = 8.3 Hz), 52.42 (d, $^2J_{(P,C)}$ = 8.4 Hz), 59.97 (d, $^2J_{(P,C)}$ = 7.8 Hz), 60.12 (d, $^2J_{(P,C)}$ = 6.7 Hz), 116.65 (d, $^3J_{(P,C)}$ = 6.7 Hz, C_{ortho}), 116.68 (d, $^3J_{(P,C)}$ = 6.6 Hz, C_{ortho}), 116.97 (d, $^3J_{(P,C)}$ = 6.6 Hz, C_{ortho}), 126.30, 126.33, 126.49, 134.36, 134.39, 134.45, 146.73, 146.88, 147.00 ^{31}P NMR (DMSO-d_6), δ: 21.74 (m), 21.87 (m), 23.30 (m)
III	IR, $\tilde{\nu}$/cm^{-1}: 3390 (s, NH), 3385 (s, NH), 3210 (m, CH), 3040 (w, CH), 2880 (w), 1595 (m), 1500 (m), 1418 (m), 1318 (m), 1283 (s), 1203 (m), 1178 (s, P═O), 1148 (s, SO_2), 1100 (s), 946 (m), 910 (m), 835 (m), 710 (m), 646 (m), 538 (m), 409 (w) ^{1}H NMR (DMSO-d_6), δ: 3.23 (d, 4H, $^3J_{(P,H)}$ = 9.8 Hz, CH_2), 4.60 (d, 2H, $^2J_{(P,NH)}$ = 11.7 Hz, NH), 7.01 (bs, 2H, NH_2), 7.12 (d, 2H, ^3J = 8.2 Hz, ArH), 7.54 (d, 1H, $^2J_{(P,NH)}$ = 9.8 Hz, NH), 7.57 (d, 2H, ^3J = 8.3 Hz, ArH) ^{13}C NMR (DMSO-d_6), δ: 41.00 (d, $^2J_{(P,C)}$ = 9.9 Hz, CH_2), 116.45 (d, 2C, $^3J_{(P,C)}$ = 6.9 Hz), 126.59, 134.40, 146.76 ^{31}P NMR (DMSO-d_6), δ: 23.28 (m)
IV	IR, $\tilde{\nu}$/cm^{-1}: 3320 (s, NH), 3195 (s, NH), 2930 (m), 1588 (m), 1490 (m), 1468 (w), 1332 (w), 1305 (w), 1178 (s, P═O), 1143 (s, SO_2), 1086 (m), 918 (m, PN), 825 (m, PN), 536 (m) ^{1}H NMR (DMSO-d_6), δ: 1.54 (s, 2H, CH_2), 3.04 (d, 2H, $^3J_{(P,H)}$ = 24.9 Hz, CH), 3.15 (s, 2H, CH), 4.46 (s, 2H, NH), 6.80 (bs, 2H, NH_2), 7.19 (d, 2H, ^3J = 8.45 Hz, ArH), 7.58 (d, ^3J = 8.35 Hz, ArH), 7.66 (d, 1H, $^2J_{(P,H)}$ = 9.85 Hz, NH) ^{13}C NMR (DMSO-d_6), δ: 26.78 (d, $^3J_{(P,C)}$ = 7.57 Hz, CH_2), 41.71, 116.45 (d, 2C, $^3J_{(P,C)}$ = 6.71 Hz), 126.49, 134.21, 146.63 ^{31}P NMR (DMSO-d_6), δ: 5.13 (m)
V	IR, $\tilde{\nu}$/cm^{-1}: 3390 (s, NH), 3325 (s, NH), 3207 (m, NH), 3052 (m, NH), 2975 (m, NH), 2973 (m, CH), 2874 (m, CH), 1499 (m, CH), 1473 (m, SO_2), 1299 (m, SO_2), 1179 (s, P═O), 1153 (s, SO_2), 1098 (m, CH), 900 (m, SN), 540 (m, SO_2) ^{1}H NMR (DMSO-d_6), δ: 1.12 (d, 3H, ^3J = 6.4 Hz, CH_3), 1.14 (d, 3H, ^3J = 6.4 Hz, CH_3), 2.50 (m, CH_2), 2.79 (m, CH_2), 3.35 (m, CH), 3.64 (m, CH), 4.55 (d, 1H, $^2J_{(P,NH)}$ = 10.3 Hz, NH), 4.61 (d, 1H, $^2J_{(P,NH)}$ = 10.9 Hz, NH), 4.73 (d, 1H, $^2J_{(P,NH)}$ = 10.6 Hz, NH), 4.76 (d, 1H, $^2J_{(P,NH)}$ = 10.3 Hz, NH), 7.04 (s, 2H, NH_2), 7.14 (d, 2H, ^3J = 8.8 Hz, ArH), 7.18 (d, 2H, ^3J = 8.8 Hz, ArH), 7.48 (d, 1H, $^2J_{(P,NH)}$ = 6.9 Hz, NH), 7.53 (d, 1H, $^2J_{(P,NH)}$ = 7.4 Hz, NH), 7.56 (d, 2H, ^3J = 8.5 Hz, ArH), 7.59 (d, 2H, ^3J = 8.5 Hz, ArH) ^{13}C NMR (DMSO-d_6), δ: 21.31 (d, $^3J_{(P,C)}$ = 10.4 Hz, CH_3), 22.14 (d, $^3J_{(P,C)}$ = 5.6 Hz, CH_3), 48.23 (d, $^2J_{(P,C)}$ = 10.0 Hz), 48.61 (d, $^2J_{(P,C)}$ = 6.0 Hz), 48.73 (d, $^2J_{(P,C)}$ = 5.8 Hz, CH_2), 48.83 (d, $^2J_{(P,C)}$ = 10.6 Hz, CH_2), 116.45 (d, $^3J_{(P,C)}$ = 7.0 Hz), 116.56 (d, $^3J_{(P,C)}$ = 7.0 Hz), 126.51, 126.58, 134.31, 134.37, 146.76, 146.82 ^{31}P NMR (D_2O), δ: 21.76 (m), 22.52 (m) ^{31}P NMR (DMSO-d_6), δ: 2.17 (m), 3.72 (m) ^{31}P NMR (D_2O with β-cyclodextrin), δ: 1.76 (m), 1.80 (m), 3.25 (m)
VI	IR, $\tilde{\nu}$/cm^{-1}: 3260 (m, NH), 2930 (w, CH), 1595 (s), 1516 (s, NO_2), 1340 (s, NO_2), 1295 (s, P═O), 1173 (s, P═O), 1110 (m, SO_2), 953 (m, PN), 835 (m, PN), 746 (m), 630 (m), 551 (w), 412 (w) ^{1}H NMR (DMSO-d_6), δ: 1.14 (m, CH_3), 2.81 (m, CH_2), 3.34 (m, CH), 3.67 (m, CH), 4.74 (d, 1H, $^2J_{(P,NH)}$ = 11.1 Hz, NH), 4.80 (d, 1H, $^2J_{(P,NH)}$ = 11.8 Hz, NH), 4.91 (d, 1H, $^2J_{(P,NH)}$ = 10.6 Hz, NH), 4.94 (d, 1H, $^2J_{(P,NH)}$ = 11.1 Hz, NH), 7.2 (d, 2H, ^3J = 9.1 Hz, ArH), 7.25 (d, 2H, ^3J = 9.3 Hz, ArH), 8.05 (m, 2H, ArH), 8.11 (d, 1H, $^2J_{(P,NH)}$ = 7.3 Hz, NH) ^{13}C NMR (DMSO-d_6), δ: 21.20 (d, $^3J_{(P,C)}$ = 9.8 Hz, CH_3), 22.02 (d, $^3J_{(P,C)}$ = 5.7 Hz, CH_3), 48.08 (d, $^2J_{(P,C)}$ = 9.7 Hz), 48.43 (d, $^2J_{(P,C)}$ = 8.8 Hz), 48.60 (d, $^2J_{(P,C)}$ = 9.0 Hz, CH_2), 48.70 (d, $^2J_{(P,C)}$ = 9.2 Hz, CH_2), 116.44 (d, $^3J_{(P,C)}$ = 7.0 Hz, ArC), 116.56 (d, $^3J_{(P,C)}$ = 6.9 Hz, ArC), 124.96, 125.02, 139.13, 139.19, 150.71, 150.75 ^{31}P NMR (DMSO-d_6), δ: 21.33 (m), 22.11 (m)

Table 2. (continued)

Compound	Spectral data
VII	IR, $\tilde{\nu}$/cm^{-1}: 3300 (m, NH), 3209 (m, NH), 2970 (m, CH), 2875 (m), 1657 (s, C═O), 1503 (m), 1458 (s), 1437 (s), 1196 (s, P═O), 1059 (s, PN), 711 (s), 542 (m) ^{1}H NMR (DMSO-d_6), δ: 1.12 (d, 6H, ^3J = 6.35 Hz, 2 × CH_3), 2.73 (m, 1H, CH), 3.17 (m, 1H, CH), 3.36 (m, 2H, CH_2), 3.63 (m, 2H, CH_2), 4.62 (d, 1H, $^2J_{(P,NH)}$ = 11.40 Hz, NH), 4.71 (d, 1H, $^2J_{(P,NH)}$ = 12.35 Hz, NH), 4.87 (d, 1H, $^2J_{(P,NH)}$ = 13.1 Hz, NH), 7.44 (t, 2H, ^3J = 7.6 Hz, ArH), 7.55 (t, 2H, ^3J = 7.30 Hz, ArH), 7.91 (d, 2H, ^3J = 7.30 Hz, ArH), 7.94 (d, 2H, ^3J = 7.8 Hz, ArH), 9.13 (s, 2H, NH) ^{13}C NMR (DMSO-d_6), δ: 21.13 (d, $^3J_{(P,C)}$ = 8.45 Hz, CH_3), 22.39 (d, $^3J_{(P,C)}$ = 7.1 Hz, CH_3), 48.33, 48.41, 48.47 (d, $^2J_{(P,C)}$ = 12.1 Hz, CH_2), 48.73 (d, $^2J_{(P,C)}$ = 11.56 Hz, CH_2), 127.37, 127.61, 127.95 (d, $^3J_{(P,C)}$ = 3.39 Hz), 128.11 (d, $^3J_{(P,C)}$ = 3.04 Hz), 131.73, 134.0 (d, $^3J_{(P,C)}$ = 7.55 Hz, C-1), 167.65 (s, C═O), 167.85 (s, C═O) ^{31}P NMR (DMSO-d_6), δ: 21.45 (m), 21.55 (m)
VIII	IR, $\tilde{\nu}$/cm^{-1}: 3402 (m), 3374 (m), 3313 (m, NH), 3065 (m, CH), 2904 (m, CH), 1665 (s, C═O), 1602 (m), 1519 (s, NO_2), 1494 (s), 1461 (s), 1349 (s, NO_2), 1200 (s, P═O), 1069 (s), 976 (m), 849 (m), 780 (m), 722 (s), 705 (m), 547 (m) ^{1}H NMR (DMSO-d_6), δ: 1.12 (d, 6H, ^3J = 5.8 Hz, 2 × CH_3), 2.75 (m, 1H, CH), 2.78 (m, 1H, CH), 3.42 (m, 2H, CH_2), 3.63 (m, 2H, CH_2), 4.73 (d, 1H, $^2J_{(P,NH)}$ = 11.8 Hz, NH), 4.82 (d, 1H, $^2J_{(P,NH)}$ = 11.8 Hz, NH), 4.84 (d, 1H, $^2J_{(P,NH)}$ = 11.9 Hz, NH), 4.98 (d, 1H, $^2J_{(P,NH)}$ = 13.5 Hz, NH), 8.14 (d, 4H, ^3J = 8.9 Hz, ArH), 8.26 (d, 4H, ^3J = 8.9 Hz, ArH), 9.11 (s, 2H, NH) ^{13}C NMR (DMSO-d_6), δ: 21.13 (d, $^3J_{(P,C)}$ = 8.4 Hz, CH_3), 22.40 (d, $^3J_{(P,C)}$ = 7.2 Hz, CH_3), 48.29, 48.38, 48.50 (d, $^2J_{(P,C)}$ = 12.1 Hz, CH_2), 48.72 (d, $^2J_{(P,C)}$ = 11.7 Hz, CH_2), 123.11, 123.26, 129.18, 129.45 (d, $^3J_{(P,C)}$ = 4.5 Hz), 139.70 (d, $^3J_{(P,C)}$ = 6.3 Hz, C-1 in Ar), 148.83 (d, $^3J_{(P,C)}$ = 7.5 Hz, C-4 in Ar), 166.25 (s, C═O), 166.47 (s, C═O) ^{31}P NMR (DMSO-d_6), δ: 21.04 (m), 21.17 (m)

a) Intensity of peaks in IR spectra: strong (s), medium (m), weak (w). In NMR spectra, Ar means aryl.

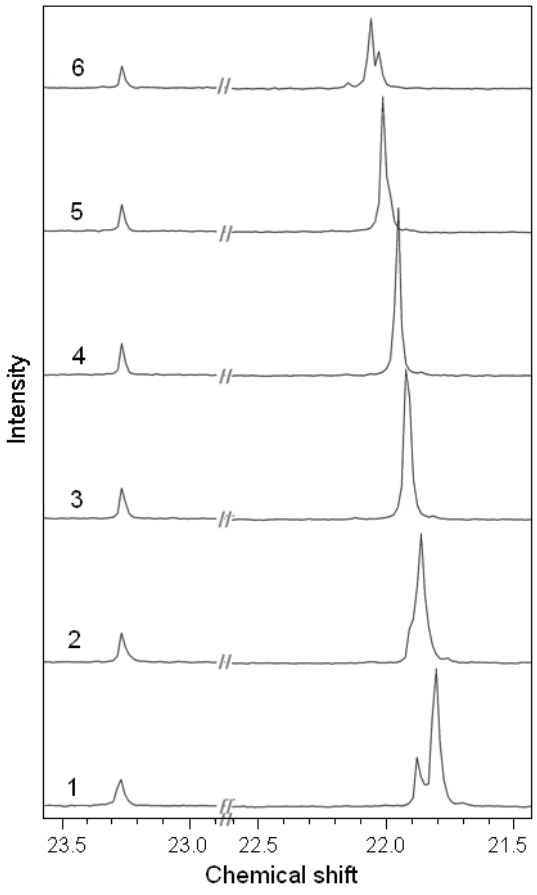

Fig. 2. High temperature dynamic ^{31}P{^{1}H} NMR spectra of compound *II* in DMSO-d_6 at temperatures: 313 K (1); 323 K (2); 333 K (3); 343 K (4); 353 K (5); 363 K (6).

vibrations were in the range of 1173–1205 cm^{-1}. For compounds containing a benzamide moiety, the ν(P═O) values appeared at higher wavenumbers than for those possessing an aniline moiety (Table 2). The value of ν(P═O) of *VIII* containing a 4-nitrobenzoyl moiety is the highest. It should be mentioned that the IR spectra of chiral diazaphospholanes *II* and *V*–*VIII* displayed only one or two peaks for ν(P═O). As the peaks are broad and with a shoulder, it is assumed that the other bands overlapped with the broad band.

In order to gain insight into the molecular structure and different conformations of the diazaphospholane *V*, ab initio calculations were performed using the Gaussian 98 software at the HF and B3LYP levels. Several conformations are feasible depending on the orientation of the methyl group in five-membered ring. The molecule of *V* has two chiral centres giving rise to four *RS*, *SR*, *RR*, and *SS* diastereomers. If the methyl group in *V* is in axial or equatorial positions with *trans* conformation of P═O and $NH_{exocyclic}$ bonds, then four diastereomers C1–C4 can be drawn. Four diastereomers, C1 (*RR*), C2 (*RS*), C3 (*SR*), C4 (*SS*), are presented in Fig. 4 for diazaphospholane *V*. These model molecules were optimised at the HF and B3LYP levels using the standard 6-311G* and 6-311+G** basis sets.

Energy differences for conformers C1–C4 and their corresponding enantiomers C5–C8 are small and vary at about 0.0–4.479876 kJ mol^{-1} (Table 3). The energies of conformers C1–C4 are equal to those of their corresponding enantiomers C5–C8. Conformers C3 and C1 are the most stable forms using the HF and

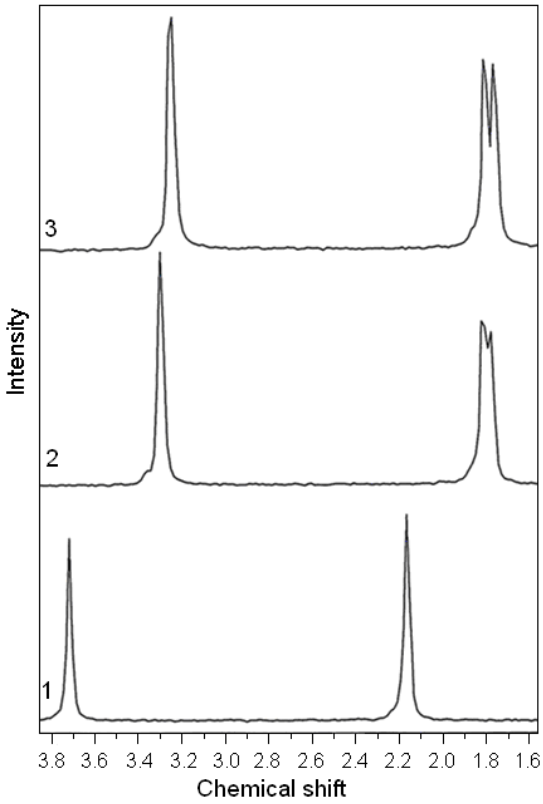

Fig. 3. $^{31}P\{^{1}H\}$ NMR spectra of compound *V*: in D_2O (1); with an addition of 5 mass % of β-cyclodextrin (2); with an addition of 25 mass % of β-cyclodextrin (3).

B3LYP methods. In both forms, the methyl group is located in the equatorial position. Differences in bond lengths, bond angles, and torsion angles of conformers C1–C4 are negligible but there are differences in their spatial arrangements. These results are also valid for corresponding enantiomers C5–C8.

The P═O bond lengths vary from 1.45 Å to 1.49 Å in the HF and B3LYP methods, corresponding to the P═O bond length (1.45 Å) (Corbridge, 1995). In conformers C1–C4, phosphorus atoms have distorted tetrahedral geometries. For example, surrounding angles around the P atom in C1 are in the range from 101.084° to 122.886°. The P—N bond lengths (ca. 1.68 Å) are shorter than the standard P—N bond length (1.78 Å) (Corbridge, 1995), suggesting the existence of partial multiple bond character between phosphorus and nitrogen atoms that has been confirmed by the crystallographic data of previous similar compounds (Gholivand et al., 2006, 2007b, 2007c).

Exocyclic nitrogen atoms as well as endocyclic nitrogen atoms of conformer C1 deviate from planarity. That is, the sum of the surrounding angles around $N_{exocyclic}$ and two $N_{endocyclic}$ atoms at HF/6-311G** are 357.38°, 347.33°, and 347.77°, with the averages of 119.1°, 115.8°, and 115.9°, respectively. It is clear that the two $N_{endocyclic}$ atoms have very distorted configurations and they are not planar which results in a puckered shape of the five membered rings. As suggested previously, the trigonal geometry around the N atoms and the small N—P—N angle caused by the cyclic structure (92–93°) enable stabilising the interactions between vacant *d* orbitals of phosphorus and the two 2*p* non-bonding orbitals of the nitrogen atoms in the ring. Similar results were obtained using the B3LYP/6-311G** method. This can be related to the strain of the five membered rings.

The analysis of calculated harmonic vibration frequencies can be useful in the assignment of vibration data. Assignment of vibration bands, obtained at the B3LYP/6-311+G** level for the four proposed conformers of compound *V* was carried out. The resulting vibration wavenumbers for optimised geometries of the C1–C4 conformers and the proposed assignments are given in Table 4. In the IR spectrum of compound *V*, strong absorptions in the range of 2975–3330 cm^{-1}

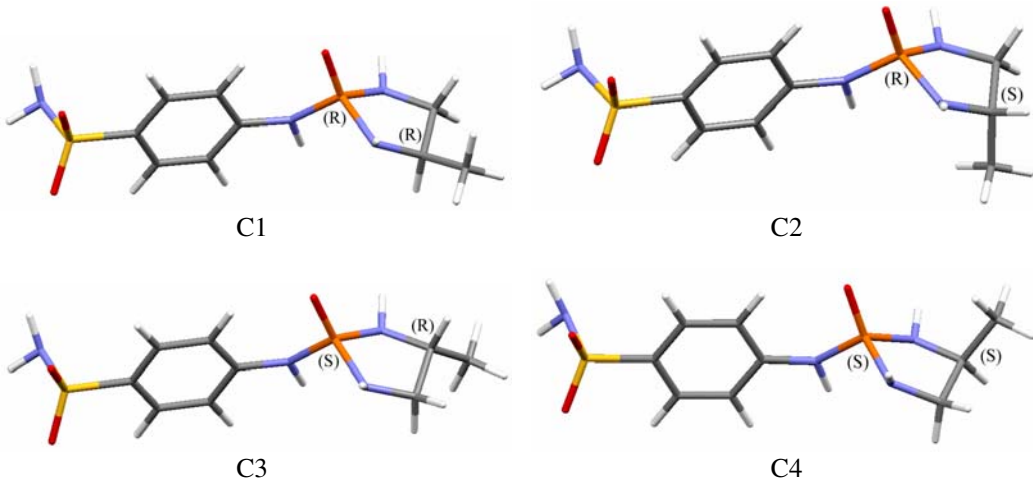

Fig. 4. Molecular structures of four diastereomers C1–C4 of compound *V* computed by HF and B3LYP methods.

Table 3. Calculated energies (E_h) and energy differences for eight conformers of compound *V*

Conformer	HF/6-311+G**		B3LYP/6-311+G**	
	$\sum E^a$/(kJ mol^{-1})	ΔE^b/(kJ mol^{-1})	$\sum E^a$/(kJ mol^{-1})	ΔE^b/(kJ mol^{-1})
C1 (*RR*)	−6406.378848	1.046700	−6431.920840	0.795492
C2 (*RS*)	−6406.373405	4.479876	−6431.914978	4.479876
C3 (*SR*)	−6406.380522	0.000000	−6431.922096	0.000000
C4 (*SS*)	−6406.375080	3.433176	−6431.917072	3.140100
C5 (*SS*)	−6406.378848	1.046700	−6431.920840	0.795492
C6 (*SR*)	−6406.373405	4.479876	−6431.914978	4.479876
C7 (*RS*)	−6406.380522	0.000000	−6431.922096	0.000000
C8 (*RR*)	−6406.37508	3.433176	−6431.917072	3.140100

a) $\sum E$ – sum of electronic and zero point energies; *b*) ΔE – energy differences; energies of other seven conformers were obtained relative to the most stable conformer C3.

Table 4. Selected observed (for *V*) and calculated (for C1–C4) wavenumbers of diazaphospholane *V* at B3LYP/6-311+G**

Wavenumber/cm^{-1}					Assignment[a]
V	C1	C2	C3	C4	
3390	3467	3472	3469	3471	$\nu_{as}(NH_2)_{sulph}$
3325	3459	3469	3465	3467	$\nu_{s}(NH)_{endo}$
3207	3450	3462	3451	3456	$\nu_{as}(NH)_{anil}$
3052	3447	3448	3450	3450	$\nu_{s}(NH)_{endo}$
2975	3365	3367	3366	3368	$\nu_{s}(NH_2)_{sulph}$
2973	3086	3085	3087	3086	$\nu(CH)_{arom}$
2874	3074	3075	3074	3074	$\nu(CH)_{arom}$
1499	1460	1464	1445	1451	$\delta(CH)$
1473	1433	1434	1439	1438	$\nu_{as}(SO_2)$
1299	1254	1253	1252	1254	$\nu_{as}(SO_2)$
1179	1178	1170	1164	1164	ν(P═O)
1153	1159	1157	1155	1155	$\nu_{s}(SO_2)$
1098	1080	1080	1079	1079	$\nu(CH)_{aliph}$
900	1043	1052	1047	1046	S—N
540	758	752	751	752	$\omega(SO_2)$

a) Assignment is approximate; as = antisymmetric; s = symmetric; sulph = sulphonamide; endo = endocyclic; anil = aniline; arom = aromatic ring; aliph = aliphatic.

dominate for the NH stretching modes. The peaks at 3390 cm^{-1} and 2975 cm^{-1} were assigned to the antisymmetric and symmetric N—H stretching modes of sulphonamide, respectively, which is in agreement with reported data (Topacli & Topacli, 2003; Varghese et al., 2003). Calculations showed that these vibrations are located in the range of 3364–3472 cm^{-1}. Therefore, theoretical calculations predict nearly similar values for the antisymmetric and symmetric N—H stretching mode. In addition, the strong intensity band near 1153 cm^{-1} can be assigned to the S═O stretching vibrations. The calculated values for the ν(S═O) mode were in the range of 1155–1159 cm^{-1}. At 1197–1164 cm^{-1}, the other characteristic modes of vibrations are the P═O stretching modes appearing in the region of 1208–1179 cm^{-1} as bands of medium intensity.

Conclusions

It can be concluded that the stereochemistry of diazaphospholane derivatives depends on the presence or absence of chirality in the diamine moiety. Stereochemical and conformational analyses were done using NMR spectroscopy ($^{31}P\{^1H\}$ spectra). In addition, computational methods were found to be a useful alternative for conformation studies since they revealed the most stable conformers of *V* as those bearing a methyl group in the equatorial position.

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