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Phosphoric Amides. ^{15}N NMR Study of the P—N Bonding in Acyclic and Cyclic Compounds

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^{31}P and ^{15}N NMR spectra of 11 cyclic and non-cyclic phosphoramidates were measured. Comparison of the closely related structures demonstrated correlation between the bond angles at nitrogen and the ^{15}N NMR chemical shifts and the ^{1}J(P,N) coupling constants. ^{15}N NMR parameters allowed the exo- and endocyclic nitrogens to be distinguished and could be related to the hydrolytic stability of the P—N bonds. © **1997 John Wiley & Sons, Ltd.**

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INTRODUCTION

Nitrogen NMR spectroscopy has developed into a powerful tool for the study of the structure and reactivity of organic and bioorganic systems containing that element in their molecular framework.[1] Since phosphorus–nitrogen compounds represent one of the most important classes of organophosphorus derivatives,[2] and since the nuclei of both elements show the NMR receptivity, NMR (both ^{15}N and ^{31}P) spectroscopy seems to be an ideal method to study phosphoric amides and related systems. Classical work by Gray and Albright[3] revealed a correlation between the one-bond ^{15}N–^{31}P coupling and the bond order; in further contributions the ^{15}N and ^{31}P NMR spectroscopic characteristics were discussed in terms of changes in nitrogen hybridization,[4] delocalization of the N lone pair,[5] geometrical orientation of the P—N bond[6] and quantum chemical calculations.[7] We have recently found that the ^{15}N NMR chemical shift values are a good indication of the relative basicities of nitrogen atoms in phosphoramidates, as demonstrated by the rates of the acid-catalysed cleavage of the P—N bond in cyclic substrates.[8] Because of our interest in structure and chemistry of phosphoric amides and amido esters,[9] we report in this paper NMR (^{15}N and ^{31}P) spectroscopic data on selected phosphoric amides. The compounds used in this study were chosen from the point of view of the following structural variables: (i) the number of nitrogen atoms in the molecule (diesteramidates, **1**, esterdiamidates, **2**; triamidates, **3**), (ii) *N*-alkyl *vs.* *N*-aryl substitution of the amidate nitrogens; and (iii) exo- *vs.* endocyclic location of the nitrogen atoms in cyclic substrates. Whenever possible, the observed NMR characteristics are related to the known reactivity of the P—N bond in systems studied.

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RESULTS AND DISCUSSION

^{15}N and ^{31}P NMR spectroscopic data obtained for compounds **1**–**3** (Scheme 1) are given in Table 1. The first obvious conclusion concerns the values of the ^{31}P NMR chemical shift. Although they span a range of more than 28 ppm, there is no direct correlation between the number of the electronegative substituents at phosphorus (oxygen *vs.* nitrogen) and the shielding of the phosphorus nuclei. Similarly, the substitution of the phenyl for the alkyl group in the *N*-substituent (e.g. **1a** → **1c** or **1b** → **1d**) does not result in any deshielding of phosphorus due to the p_π–p_π donation from nitrogen into the aromatic ring,[5] but the most dramatic changes in the δ_P values seem to result from the changes in the σ-bond angles at the phosphorus tetrahedron. Gorenstein[10] emphasized the importance of the angular changes and developed an empirical correlation between ^{31}P NMR chemical shift and the O—P—O bond angles in phosphates. We believe that our results give further evidence for the importance of that structural factor, as can be seen by comparing the ^{31}P and ^{15}N NMR spectroscopic data for the closely related members of the series **1**, **2** and **3**. The ^{31}P NMR chemical shift for *N*,*N*-dimethyl diethylphosphoramidate, $(EtO)_2P(O)NMe_2$, is $\delta_P = 10.0$;[11] incorporation of the ester functions into a five-membered ring (**1a**) results in a significant deshielding of the ^{31}P nucleus ($\Delta\delta_P = 17.9$ ppm). On the other hand, rearranging the substituents at phosphorus in the same framework (**1a** → **1b**) or substituting one oxygen for a second nitrogen (**1a** → **2a**)

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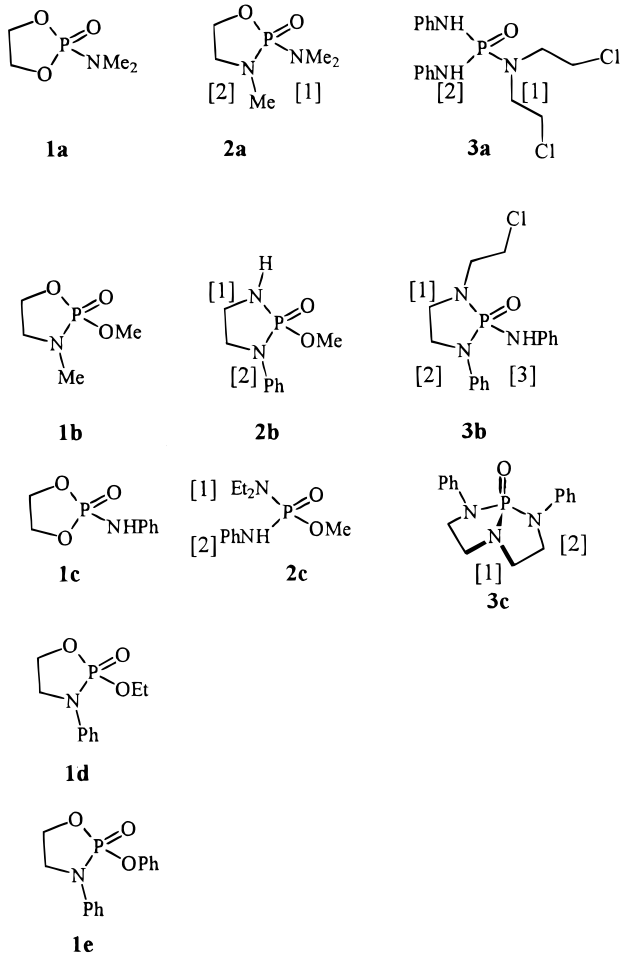

Scheme 1

does not significantly affect the δ_P value. The deshielding effect of the incorporation of the phosphorus into a five-membered ring can be also seen in the **2c**–**2b** pair ($\Delta\delta_P = 12.7$ ppm) and, most clearly, in the cyclization sequence: **3a** → **3b** → **3c**. Gorenstein's conclusions about the high-frequency shift effect caused by the decrease in the smallest X—P—X bond angle in phosphoryl compounds[12] can be illustrated by many other examples taken from the abundant ^{31}P NMR data on organophosphorus compounds.[13] According to Letcher and van Wazer,[14] the ^{31}P chemical-shift differences, $\Delta\delta_P$, are determined by

$$\Delta\delta_P = -C\Delta\chi + k\Delta n_\pi + A\Delta\Theta$$

where $\Delta\chi$ = difference in electronegativity in the P—X bond, Δn_π = change in π electron overlap, $\Delta\Theta$ = change in σ-bond angle and C, k and A are constants. When comparing the isomeric pair **1a**–**1b**, or the closely

Table 1. ^{15}N and ^{31}P NMR data[a] for the phosphoramidates 1, 2 and 3

Compound	δ_P	δ_N [^1J(P,N)][b] [N1]	[N2]	[N3]
1a	27.9	−360.5 (47.4)		
1b	23.1	−354.6 (33.6)		
1c	21.1	−314.4 (43.3)		
1d	13.9	−312.2 (38.5)		
1e	9.0	−312.5 (37.5)		
2a	28.2	−358.9 (36.6)	−353.8 (30.1)	
2b	23.9	−344.8 (23.9)	−310.4 (32.9)	
2c	11.2	−328.8 (37.3)	−307.2 (37.9)	
3a	5.1	−327.2 (28.6)[c]	−299.6 (65)[c]	
3b	13.4	−335.9 (29.1)	−309.2 (31.5)	−309.3 (28.5)
3c	33.5	−333.2 (5.7)	−300.8 (18.1)	

[a] In $CDCl_3$ (0.5 M) at 27 °C; ^1J(P,N) given in Hz.
[b] Following the argument by Gray and Albright,[3] all ^1J(P,N) values should be taken as negative.
[c] Broad singlets; band width given in Hz.

related pair **1c**–**1d**, it is clear that the electronegativity difference is approximately constant within each pair, and so are the X—P—X bond angles at the phosphorus centre. Nevertheless, the ^{31}P NMR chemical shift moves to high frequency in both cases (for **1a** → **1b**, $\Delta\delta_P = 4.8$ ppm; for **1c** → **1d**, $\Delta\delta_P = 7.2$ ppm). The observed change in the ^{31}P shielding suggests, therefore, that the structural changes are followed by the changes in the Δn_π values, i.e. that the degree of the π overlap of the nitrogen lone pair with the phosphoryl centre depends also on the exo- or endocyclic location of the nitrogen. In the discussion given below, we intend to demonstrate that the ^{15}N NMR spectroscopy of substrates **1**, **2** and **3** supports the conclusions based on the ^{31}P NMR data. Moreover, the NMR spectroscopy of the ^{15}N nuclei offers better insight into the bonding characteristics of the P—N bond and can, when the reactivity data are available, be correlated with the chemical behaviour of the compounds studied. In the most comprehensive reviews on the ^{15}N NMR spectroscopy,[15,16] it is shown for the family of tertiary amines, enamines and carboxyamides that increasing involvement of the N lone pair in the conjugation is followed by the shift of δ_N towards less negative values (high-frequency shift). Examination of the data in Table 1 shows that in each case the endocyclic nitrogen is characterized by a less negative δ_N value than the corresponding exocyclic nitrogen in the most structurally related compound. As a consequence of that effect, the endocyclic nitrogen should be less basic than its exocyclic counterpart, the conclusion remaining in full agreement with the interpretation of the rates of the acid-catalysed P—N bond cleavage in **1**, **2** and **3**.[8,17] We were also able to demonstrate before that the hydrolysis of **1c** and **1d** involves the pre-equilibrium protonation of the phosphoryl oxygen atom,[18] a consequence of the low basicity of the nitrogen atoms in those substrates—a conclusion corroborated now by the relatively high-frequency ^{15}N NMR chemical shift observed for these substrates.

The interpretation of the one-bond ^{15}N, X coupling available in the literature links the magnitude of $^1J(N,X)$ to the hybridization of nitrogen. According to Gray and Albright,[3] as well as Gorenstein,[19] increasing s character of the nitrogen bonding orbital results in the increase in the absolute value of $^1J(P,N)$. Similar conclusions were reached in the study of the *N*-phosphorylated cyclic amines, where the theoretical values for the $^1J(P,N)$ coupling involving 'pure' p^3 and 'pure' sp^2 nitrogens were estimated as -12 and -39 Hz, respectively.[4] The same trend was observed for the one-bond N—C coupling; for example, the average value of the three $^1J(N,C)$ coupling constants for nitrogen-5 (pyramidal, p^3) and nitrogen-10 (planar, sp^2) in the molecule of 5,10-methylenetetrahydrofolic acid are 5.4 and 12.2 Hz, respectively.[15] When a phosphoramidate nitrogen in a non-cyclic substrate or in an exocyclic position of a cyclic substrate is moved to the endocyclic location of the 1,3,2-oxazaphospholidine skeleton (**1a** → **1b**; **1c** → **1d** or **1e**; **2c** → **2b**), the bond angle requirements of the ring force the nitrogen into a more pyramidal geometry (smaller endocyclic C—N—P angle), thus reducing the s character of the N—P bonding orbital. In all such cases we observe a decrease in the absolute value of the $^1J(P,N)$ coupling constant, irrespective whether the nitrogen is substituted by an alkyl or by the phenyl group. Compound **2a** provided us with the opportunity of a direct comparison of the exo- and endocyclic nitrogens, very similar from the point of view of their substitution pattern. The endocyclic nitrogen is deshielded ($\Delta\delta_N = 5.1$ ppm), and its one-bond N–P coupling constant is reduced by 6.5 Hz. The hydrolytic behaviour of **2a** indicates lower basicity of the endocyclic nitrogen;[17] one of the possible reasons for that effect is that the protonation of the nitrogen would result in the hybridization change from pyramidal (p^3) to tetrahedral (sp^3) with unfavourable bond angles consequences. The gas-phase proton affinity of ammonia is 24.4 kcal mol^{-1} (1 kcal = 4.184 kJ) lower than that of NMe_3;[20] the NH_3 molecule is also more pyramidal (H—N—H bond angle of 106.5°) than the molecule of NMe_3 (C—N—C bond angle of 108.7).[21]

In the triamidate series **3a**, **3b**, **3c**, each cyclization results in a drastic reduction of the $^1J(P,N)$ value for both *N*-alkyl, and *N*-phenyl nitrogens. It is interesting that for the bicyclic compound **3c**, the bridgehead nitrogen is characterized by an unusually small $^1J(P,N)$ value, lower than any value reported for the nitrogen-containing phosphoryl compounds[1] and than the value of $^1J(P,N) = -12$ Hz calculated for the 'pure' p^3 nitrogen atom bonded to the phosphoryl centre.[4] For **3c** the N—P—N bond angles, determined by x-ray diffraction, are 96.2°, 95.7° and 114.4°,[22] still greater than the values expected for an ideal pyramidal geometry of a p^3, non-hybridized nitrogen derivative. It seems, therefore, that the calculations that led to the value of $^1J(P,N) = -12$ Hz underestimate the range of the variations of the one-bond N–P coupling as a function of the molecular geometry.

This study shows that the ^{15}N NMR spectroscopy is a useful technique for the probing of the bonding in the organophosphorus compounds of nitrogen, and the investigations of other phosphoramidic systems are in progress.

EXPERIMENTAL

Compounds

The preparation of the following substrates has been described previously: **1a**, **1b**, **2a**;[17] **1c**, **1d**;[18] **3a**, **3b**, **3c**.[23] 3-Phenyl-2-phenoxy-2-oxo-oxazaphospholidine (**1e**) was prepared from phenyl phosphorodichloridate and 2-anilinoethanol in toluene, in the presence of 2 mol equiv. of triethylamine; yield 45%; m.p. 64–66 °C [from CCl_4–hexane (1 : 1)]; δ_H ($CDCl_3$), 3.50 (1H, m), 3.76 (1H, m), 4.19 (1H, m), 4.46 (1H, m), 7.02–7.37 (10H, m). Analysis: calculated for $C_{14}H_{14}NO_3P$ (275.24), C 61.09, H 5.13, N 5.09; found, C 60.90, H 5.26, N 5.00%. 1-Phenyl-2-methoxy-2-oxo-diazaphospholidine (**2b**) was prepared from methyl phosphorodichloridate and *N*-phenyl-1,2-ethylenediamine in dioxane in the presence of 2 mol equiv. of triethylamine; yield 52%; m.p. 127–129 °C (from dioxane); δ_H ($CDCl_3$), 3.41 (2H, m), 3.51–3.72 (3H, m), 3.60 [3H, d, J(H,P) 11.2 Hz], 6.93 [1H, t, J(H,H) 7.5 Hz], 7.11 [2H, d, J(H,H) 6.0 Hz], 7.26 [2H, dd, J(H,H) 6.0, 7.5 Hz]. Analysis: calculated for $C_9H_{13}N_2O_2P$ (212.18), C 50.95, H 6.19, N 13.20; found, C 50.66, H 6.40, N 13.11%. *N*-Phenyl-*N*′,*N*′-diethyl methylphosphorodiamidate (**2c**) was prepared from *N*,*N*-diethyl methylphosphoroamidochloridate and 2 mol equiv. of aniline in acetonitrile; yield 82%; oil; δ_H ($CDCl_3$), 1.03 (6H, t, J(H,H) 7.0 Hz), 3.09 (4H, m), 3.67 [3H, d, J(H,P) 11.3 Hz], 5.29 (1H, br, s), 6.94–7.24 (5H, m). Analysis: calculated for $C_{11}H_{19}N_2O_2P$, C 54.54. H 7.91, N 11.56; found, C 55.44, H 7.83, N 11.53%.

NMR spectra

^{31}P NMR spectra were recorded on a Varian Gemini 200 spectrometer in $CDCl_3$ and δ values are given relative to 85% H_3PO_4 as an external standard. The ^{15}N NMR measurements were taken on a Bruker AM 500 instrument operating at 50.698 MHz for solutions in $CDCl_3$ at 300 K. For the compounds where nitrogen atoms were directly bonded to hydrogens, INEPT experiments optimized for $^1J = 100$ Hz were applied, otherwise long-range couplings of *ca.* 2–5 Hz were used for the polarization transfer procedure. Refocusing and proton broadband decoupling during acquisition were applied. Typical operating parameters were spectral width 17 000 Hz, acquisition time 1 s, 32K data points with zero-filling up to 64K to obtain better digital resolution for estimation of coupling constants and number of scans between 150 and 2000 to obtain a sufficient signal-to-noise ratio. The chemical shifts are given relative to nitromethane as an external standard.

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