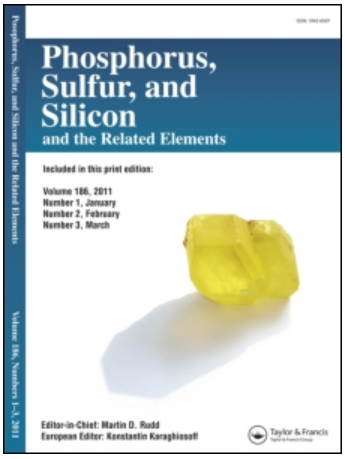

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PHOSPHORUS DERIVATIVES OF NITROGEN HETEROCYCLES. 5. CARBON AND PHOSPHORUS NUCLEAR MAGNETIC RESONANCE OF PYRIDYLPHOSPHONATES

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PHOSPHORUS DERIVATIVES OF NITROGEN HETEROCYCLES. 5. CARBON AND PHOSPHORUS NUCLEAR MAGNETIC RESONANCE OF PYRIDYLPHOSPHONATES

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The carbon (^{13}C) and phosphorus (^{31}P) nmr spectra of 14 pyridyl-2- and 4-phosphonic acids and corresponding esters are reported. the ^{13}C spectra show only small shielding effects (0–4.5 ppm) from the ester groups (PO_3R_2) on the pyridyl ring carbon atoms. The phosphonic acid mono- and dianions (PO_3H^- and PO_3^{2-}) show significant shielding (10–15 ppm) at the directly bonded carbon only. The C–P couplings, particularly in the diethyl pyridyl-2-phosphonates, are larger than in typical arylphosphonates. The C–P coupling in the phosphonic acids shows some variation with ionization state. The ^{31}P chemical shifts are unexceptional although the T_1 values for the 4-pyridylphosphonate esters are significantly shorter than for the 2-pyridyl esters.

Previous work in our laboratories has provided synthetic routes to a number of dialkyl pyridyl-2- and -4-phosphonates and the corresponding phosphonic acids.[1,2] From the mass spectral data of the esters and the dissociation constants of the acids it was concluded that pyridyl-4-phosphonates are typical arylphosphonates whereas pyridyl-2-phosphonates exhibit unusual properties.[3] In view of the insight obtained into C–P bonding by measurement ^{13}C nmr spectra in other studies[4] it seemed worthwhile to obtain ^{13}C spectra of the two families of pyridylphosphonates. The spectra herein reported extend ^{13}C nmr data in both organophosphorus compounds and nitrogen heterocycles.

^{13}C CHEMICAL SHIFTS

The chemical shifts for the series of diethyl pyridyl-2-phosphonates (**1**) are presented in Table I. The average shielding effect of the 2-PO_3Et_2 group, determined by comparison of the shifts with those of the parent pyridines,[5] is shown in Table V. The relatively small deshielding effect observed at all ring carbon atoms is consistent with the values recently reported for diethyl phenylphosphonate.[6] The deshielding is greatest at C_3 (4.6 ppm) as is the case in diethyl phenylphosphonate where deshielding at the ortho carbon is 3.6 ppm.

The chemical shifts for the pyridyl-2-phosphonic acids (**2**) are presented in Table II. The spectra were

TABLE I

^{13}C/nmr chemical shifts for diethyl pyridyl-2-phosphonates (**1**)[a] (Jp-c Hz)

Compound	R	C_2	C_3	C_4	C_5	C_6	Other
1a	H	151.0(220)	128.1(25)	136.2(12)	126.1(3.5)	150.5(23)	
1b	3-CH_3	150.2(223)	136.8(26)	138.8(12)	125.7(4)	146.9(23)	19.4(CH_3)
1c	4-CH_3	151.5(217)	128.9(25)	147.6(13)	126.9(4)	150.3(25)	20.9(CH_3)
1d	6-CH_3	151.0(218)	125.3(25)	136.3(13)	125.9(4)	159.7(23)	24.5(CH_3)
1e	4,6-CH_3	150.8(220)	126.5(25)	147.4(13)	126.6(3.5)	159.4(24)	20.9,24.3(CH_3)
1f	3,5-CH_3	147.6(217)	138.2(27)	139.2(13.5)	135.7(4)	147.7(24)	18.3,19.2(CH_3)
1g	3-Cl	149.6(234)	135.7(21)	138.2(9)	126.7(3.5)	147.5(22)	
1h	3-Br	152.4(222)	128.1(25)	136.2(12)	126.0(3.5)	150.5(23)	
1i	3-F	140.0(230) (15)*	161.7(16) (264)*	124.4(7) (20)*	128.3(4) (4)*	146.2(22) (4)*	

* Jc-f.

[a] Determined on 25% solutions in $CDCl_3$ using TMS as internal standard.

TABLE II

^{13}C/nmr chemical shifts for pyridyl-2-phosphonic acids (**2**)[a] (Jp-c Hz)

Compound	*R*	pH	C_2	C_3	C_4	C_5	C_6	Other
2a	H	<3	152.1(175)	130.2(12)	147.6(9)	128.9	142.5(8)	
2b	3-CH_3	<3	152.3(173)	139.4(8)	149.3(8)	128.4	142.3(10)	19.9(CH_3)
2c	4-CH_3	<3	150.1(179)	130.8(11)	162.2(10)	129.5	141.6(8)	22.8(CH_3)
2d	6-CH_3	<3	151.4(178)	127.5(11)	146.9(10)	129.8	156.1(8)	20.1(CH_3)
2e	4,6-CH_3	<3	158.3(167)	126.7(12)	156.6(9)	127.1	154.6(11)	21.1, 22.0(CH_3)
2g	3-Cl	<3	152.6(179)	137.0(10)	145.6(6)	128.6	142.9(–11)	
2h	3-Br	≈7	153.1(216)	123.9(12)	143.0(7)	125.9	147.3(16)	
2i	3-F	<3	b	163.2 (264)*	135.3(9) (4)*	131.1 (9)*	139.8(5) (4)*	
2j	3,6-CH_3	10	156.3(168)	137.0(13)	146.1(9)	126.7	151.6(10)	19.0, 19.6(CH_3)
2k	3-CH_2CH_3, 6-CH_3	12	b	140.1(21)	138.3(10)	124.2(3)	154.5(17)	15.5, 23.6, 25.6

[a] Determined on approximately 20% solutions in D_2O using dioxane as internal standard (δ 67.4 ppm).
[b] Low intensity resonance hidden by noise or stronger peaks.
* C–F coupling.

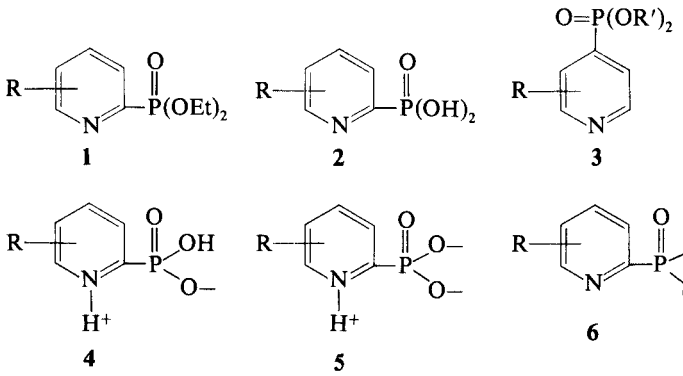


TABLE III

pH effects on chemical shifts (Jc-p Hz)

Compound	pH	C_2	C_3	C_4	C_5	C_6
2a	3	152.1(175)	130.2(12)	147.6(9)	128.9	142.5(8)
	6	157.4(166)	129.3(12)	145.4(8)	127.2	142.9(9)
	10	162.3(190)	126.9(19)	138.3(9)	124.9	148.5(17)
2b	3	152.3(173)	139.4(8)	149.3(8)	128.4	142.3(10)
	6	156.0(188)	141.3(10)	148.2(8)	127.1	138.3(9)
	12	161.2(192)	137.0(21)	139.5(9)	124.3(3)	145.9(19)
2c	3	150.1(179)	130.8(11)	162.2(10)	129.5	141.6(8)
	6	155.3(162)	130.1(10)	161.0(8)	128.0	140.8(8)
	10	161.2(186)	127.9(18)	151.2(10)	125.8(2)	147.6(17)
2g	3	152.6(179)	137.0(10)	145.6(6)	128.6	142.9(11)
	6	155.8(188)	136.7(14)	141.9(6)	127.1(2)	145.1(14)
	12	160.0(192)	134.8(16)	138.9(7)	125.5(3)	147.2(17)
3h	3	153.9(13)	126.2(9)	156.0(164)	126.2(9)	153.9(13)
	6	155.0(11)	124.5(11)	157.0(155)	124.5(8)	155.0(11)
	12	157.6(11)	122.8(8)	152.2(159)	122.8(8)	157.6(11)
		CH_2	CH_3			
Ethyl	1	20.2(135)	6.8(7)			
Phosphonic	5	21.6(134)	8.0(6)			
Acid	12	22.6(132)	9.1(5.5)			

TABLE IV

^{13}C nmr chemical shift for dialkyl pyridyl-4-phosphonates (**3**) (Jp-c Hz)

Compound	R'	R	C_2	C_3	C_4	C_5	C_6	Other
3a	iPr	H	150.0(12)	125.2(8)	137.8(188)	125.2(8)	150.0(12)	
3b	iPr	3-CH_3	153.0(12)	136.0(9)	138.2(188)	130.5(9)	148.6(12)	18.0(CH_3)
3c	iPr	3,5-CH_3	151.3(13)	137.1(9)	136.4(178)	137.1(9)	151.3(13)	19.9(CH_3)
3d	El-	2,6-Me	158.4(13)	121.7(8.5)	137.8(185)	121.7(8.5)	158.4(13)	24.4(CH_3)
3e	H	H	143.9(11)	130.9(9)	159.3(168)	130.9(9)	143.9(11)	
3f	H	3-Me	143.8(11)	147.1(9)	161.1(155)	134.1(9)	143.8(11)	22.9(CH_3)
3g	H	3,5-Me	144.9(11)	146.2(9)	160.1(163)	146.2(9)	144.9(11)	25.1(CH_3)
3h	H	2,6-Me	153.9(13)	126.2(9)	156.0(164)	126.2(9)	153.9(13)	19.7(CH_3)
3i	H	2,3,6-Me	150.0(14)	136.2(9)	153.9(163)	127.6(8)	152.9(14)	16.7, 18.5, 19.2(CH_3)

measured in D_2O without adjustment of pH (except as indicated) and thus are spectra of zwitterions **4**. The average shielding of the PO_3H^- in the pyridinium compounds **4** (see Table V) was calculated using ^{13}C chemical shifts for the parent pyridinium ions reported by Lapper *et al.*[7] A significant deshielding is observed (10.2 ppm) for C_2, the carbon bearing the substituent, but virtually no effect is observed on the other ring carbon atoms. The effect of protonation on the ^{13}C chemical shift of pyridines is well known[5,7] but the effect of the ionization state on ^{13}C nmr of phosphonic acids apparently has not been reported. By judicious choice of pH it is possible to obtain ^{13}C spectra of species **5** and **6** in addition to **4**. The results obtained for four pyridyl-2-phosphonic acids and one pyridyl-4-phosphonic acid are shown in Table III. In Table V are summarized shielding effects of PO_3^{2-} in the pyridinium form **5** and in pyridine form **6** again using the data from Lapper for the parent compounds. The deshielding effect is again most significant on C_2 the carbon bearing the substituent. The spectrum of ethylphosphonic acid is also included in Table III as a reference for the shielding effects of $—PO_3H_2$, PO_3H^- and PO_3^{2-}.[8] In this case the deshielding due to PO_3H^- is 15.9 ppm and for PO_3^{2-} 16.9 ppm, comparable to the results in the pyridylphosphonic acids. Table IV summarizes the ^{13}C nmr shifts for the pyridyl-4-phosphonic acids and esters (**3**). The phosphonate ester function again shows a minor deshielding effect (Table V). The acid **3e** shows a deshielding of 11.0 ppm for C_4, 2.3 ppm for C_3 and 1.7 ppm for C_2.

TABLE V

Shielding effects from phosphorus substituents

Substituent	C_2	C_3	C_4	C_5	C_6
2-PO_3Et_2	+0.6	+4.6	+0.7	+2.2	+0.3
2-PO_3H^- in **4**	+10.2	+1.5	0.0	+0.8	+1.7
2-PO_3^{2-} in **5**	+14.9	+1.4	−1.4	−0.7	0.0
2-PO_3^{2-} in **6**	+11.2	+2.6	+2.3	+0.3	−2.0
4-PO_3Pr_2	+1.3	+2.5	+1.2	+2.5	+1.3

C–P COUPLING

A summary of the C–P coupling of the various phosphonic acids and esters is provided in Table VI. The one-bond C–P coupling is significantly greater in the 2-phosphonate esters than in the 4-phosphonate esters (222 Hz *vs.* 185 Hz). A similar difference is seen in the ^{13}C–^1H coupling constants at C_2 (180 Hz) and C_4 (160 Hz) in pyridine.[9] This effect is due to the α-heteroatom and has been noted in the C–P coupling of aliphatic phosphonates.[10]

The two-bond and three-bond C–P coupling in the 4-phosphonates **3** are similar in magnitude to those observed in phenylphosphonate (10 Hz and 15 Hz).[6] On the other hand significantly larger two-bond C–P coupling of 24 Hz is found in 2-pyridylphosphonate esters **2**. The three-bond coupling in **2** to C_4 is 10 Hz and to C_6 23 Hz. This difference may also be due to the heteroatom effect.

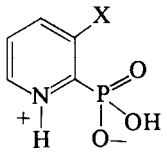
The C–P coupling constants of the phosphonic acids show variations (Table III) with pH as might be anticipated since different phosphorus functional groups are being generated. Apparently no reports have been made of the ^{13}C–^{31}P coupling for

TABLE VI

Summary of ^{13}C-^{31}P coupling (Hz)

	C_2	C_3	C_4	C_5	C_6
2-PO_3Et_2	222	24	10.2	3.8	23.2
2-PO_3H^- (pH < 3)	175	10.7	8.7	0	9.3
4-PO_3Pri_2	12.3	9	185		
2-PO_3H^- (pH < 3)	12	9	163		

$—PO_3H_2$, $—PO_3H^-$ and $—PO_3^{2-}$. As is shown in Table III these three functional groups give virtually identical couplings in ethylphosphonic acid. On the other hand we have found that for phenylphosphonic acid monoanion Jc–p is 186 Hz and for the dianion 167 Hz. In the pyridylphosphonic acids **2a** and **2c** a similar result is obtained comparing species **4** and **5** (pH3 and pH6, Table III). A similar trend is observed for the pyridyl-4-phosphonic acid **3h**. For compounds **2b** and **2g** a much different result is obtained; the magnitude of the coupling is much larger in ionization state **8** than in **7** (173 Hz



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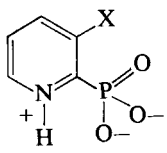

8

to 188 Hz for **2b** and 179 Hz to 188 Hz for **2g**). In studying the dissociation constants of pyridyl-2-phosphonic acids it was observed that the removal of a proton from **8** was much more difficult when X = H[3] (the pKa was 1.6 units greater). This difference was attributed to steric interference of solvation by the substituent (X) enhancing intramolecular hydrogen bonding. The geometrical constraints of this intramolecular hydrogen bonding can account for the increase in magnitude of the C–P coupling from 162 Hz in **8** (X = H) to 188 Hz in **8** (X = CH_3 or Cl). In the completely ionized form **6**, where PO_3^{2-} is attached to a neutral pyridine, the C–P couplings are unaffected by a 3-substituent and are similar to the esters **2** or in 6 with the exception of the coupling to C_4 which is unchanged (three-bond coupling).

TABLE VII

^{31}P nmr spectral data for dialkyl pyridyl phosphonates **1** and **3**

Compound	*Chemical shift δ^a	T_1 (sec)[a]
1a	+8.2	16.9
1b	+11.9	20.2
1c	+11.3	18.8
1d	+11.2	19.7
1e	+11.7	20.7
1f	+10.6	18.3
1g	+8.6	25.8
1h	+10.7	30.1
3a	+14.9	—
3b	+12.9	9.1
3c	+13.6	9.9
3d	+15.0	11.7

[a] 20% solutions in $CDCl_3$.

* Shifts downfield of 85% H_3PO_4 are reported as positive.

^{31}P NMR DATA

As noted earlier[3] ^{31}P chemical shifts of the pyridylphosphonates show no apparent correlation with changes in substituent (Table VII). Attachment of phosphorus at C_4 appears to result in a slight deshielding effect. On the other hand quite distinct differences were noted between the relaxation times (T_1) for the 4-phosphonate esters (**3**) and the 2-phosphonates (**2**). The values for the 2-phosphonates, 17-30 secs, are similar to literature values for phosphorus esters[11] while the 4-phosphonates are shorter, 9–12 secs.

EXPERIMENTAL SECTION

The synthesis of the pyridyl phosphonates has been previously described.[1,2,3] Ethylphosphonic acid was obtained from Richmond Organics.

The carbon-13 magnetic resonance spectra were obtained in the Fourier transform mode on a Jeol FX-60 spectrometer system equipped with 16K memory Texas Instruments computer. The spectra were obtained at an observing frequency of 15.03 MHz. General nmr spectral parameters were internal lock to the deuterium containing solvent ($CDCl_3$) for esters, D_2O for acids); spectral width 2500 Hz; pulse width 12 μs corresponding to a 75° pulse angle; and a pulse repetition time of 2.0 s.

The phosphorus-31 nmr spectra were obtained on the same instrument at an observing frequency of 24.6 MHz. Spectral width 2500 Hz; pulse width 12 μs corresponding to a 90° pulse angle; and a pulse repetition of 2.0. T_1 values were obtained by the inversion–recovery method, pulse sequence 180°–τ–90°, calculated by the Jeol software, which uses the semilogarithmic plot of $(A - A\tau)$ *vs.* τ.

SUMMARY

The ^{13}C spectral data show that the pyridylphosphonate esters exhibit no unusual C–P bonding by comparison with other arylphosphonates. The pyridyl-2-phosphonic acids do show some unexpected properties which can be correlated with hydrogen bonding properties.

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