Inorganic Chemistry
Article

Inorg. Chem. **2010**, *49*, 9369–9379 **9369**
DOI: 10.1021/ic101079b

Synthesis and Reactivity of (Benzoxazol-2-ylmethyl)phosphonic Acid

Sylvie Pailloux,[†] Cornel Edicome Shirima,[†] Karen Ann Smith,[†] Eileen N. Duesler,[†]
Robert T. Paine,[*,†] Neil J. Williams,[‡] and Robert D. Hancock[‡]

[†]*Department of Chemistry and Chemical Biology, University of New Mexico, Albuquerque, New Mexico 87131, and*
[‡]*Department of Chemistry and Biochemistry, University of North Carolina-Wilmington, Wilmington,*
North Carolina 28403

Received May 28, 2010

An efficient three step synthesis of (benzoxazol-2-ylmethyl)phosphonic acid (**6-H$_2$**) is described along with IR, mass spectrometry (MS), and ^{1}H, ^{13}C, and ^{31}P NMR spectroscopic characterization data, and a single crystal X-ray diffraction structure determination. **6-H$_2$** is unstable in acidic aqueous solutions ($pH < 4$) undergoing ring-opening to give [(2-hydroxyphenylcarbamoyl)methyl] phosphonic acid (**7-H$_2$**) that is characterized by IR, MS, and NMR methods. The protonation constants (pK_a) for **7-H$_2$** have been measured, and crystal structure determinations for (NH_4)(**7-H**) and K(**7-H**)·DMF are described. Reactions of NaOH and KOH with **6-H$_2$** in MeOH/H_2O solutions led to isolation and crystal structure determinations of the salts [Na(**6-H**)·H_2O]$_2$, K(**6-H**), Na$_3$(**6**)(**6-H**)·H_2O, and [K$_2$(**6**)]$_2$·3H_2O. The complexation reactions of **7-H$_2$** with La(III), Nd(III), and Gd(III), as a function of pH, were also examined by titrametric methods, and a model for the 1:1 anion binding with Ln(III) cations is proposed.

Introduction

Phosphonate diesters, RP(O)(OR)$_2$, are known to undergo hydrolysis producing the corresponding phosphonic acids, RP(O)(OH)$_2$.[1] Under gentle physiological conditions these conversions are typically slow although rates may be enhanced by acid or base catalysis. This reactivity has attracted wide attention in the context of elucidating the mechanisms for phosphate diester hydrolysis and related enzyme catalyzed hydrolysis of RNA and DNA.[2−5] In inorganic and materials chemistry, the coordination properties of phosphonic acids have also attracted notice. In combination with p-, d-, and f-block metal ions, these species produce a wide array of amorphous, microporous solids as well as intricate, crystalline one-dimensional (1-D), two-dimensional (2-D), and three-dimensional (3-D) framework solids.[6] By variation of the steric size and functionality in the R group, chemically and physically diverse materials are generated that have unique ion exchange, proton conduction, nonlinear optic (NLO), sensor or catalyst properties.[6−8]

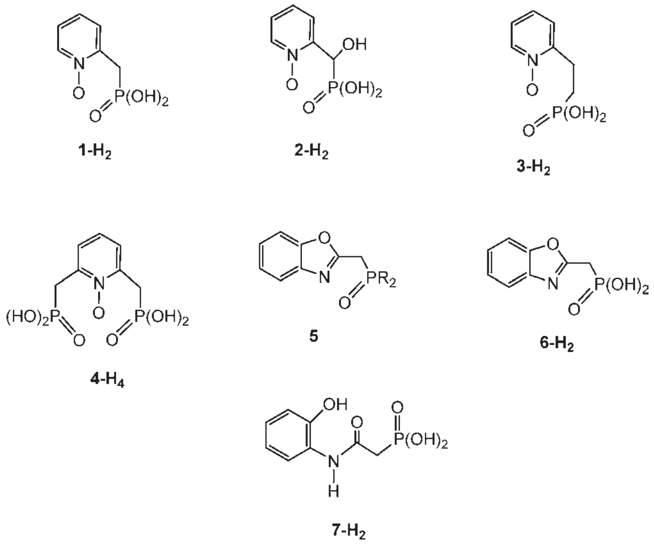
In our group, while defining new coordination environments for f-element ions using donor functionalized heterocyclic ring platforms, we have reported efficient routes for the formation of (phosphinoylalkyl)pyridine and pyridine N-oxide ligands.[9−12] These neutral ligands form chelate interactions with lanthanide(III)[9−11] and plutonium(IV)[12] ions, and they function as useful solvent extraction reagents for Ln(III)/An(III) ions in strongly acidic aqueous solutions.[13] During the course of this work, it was observed that, in some cases, phosphonate ester derivatives of alkyl and aryl (phosphinoylalkyl)pyridines and pyridine N-oxides undergo hydrolysis in strongly acidic aqueous solutions. Since the resulting phosphonic acids might be expected to interfere in extraction performance, it has become important to define the nature of the hydrolysis reactivity of the phosphonate esters as well as the coordination chemistry displayed by the resulting phosphonic acids with Ln(III) ions (Chart 1). In this regard, we have previously reported formation of 3-D or 1-D chain structures from lanthanides and **1-H$_2$**,[14] **2-H$_2$**,[14] **3-H$_2$**,[15] and **4-H$_2$**.[16]

---

*To whom correspondence should be addressed. E-mail: rtpaine@unm.edu.

(1) Quin, L. D. In *A Guide to Organophosphorus Chemistry*; J. Wiley & Sons: New York, 2000; pp 357−386.
(2) Engel, R. *Chem. Rev.* **1977**, *77*, 349 and references therein.
(3) Tsubouchi, A.; Bruice, T. C. *J. Am. Chem. Soc.* **1995**, *117*, 7399.
(4) Feng, G.; Tanifum, E. A.; Adams, H.; Hengge, A. C.; Williams, N. H. *J. Am. Chem. Soc.* **2009**, *131*, 12771.
(5) Hilderbrand, R. L. In *The role of phosphorus in living systems*; CRC Press: Boca Raton, FL, 1983; pp 97−104.
(6) Clearfield, A. *Prog. Inorg. Chem.* **1998**, *47*, 371 and references therein.
(7) Clearfield, A. *Dalton Trans.* **2008**, 6089 and references therein.
(8) Mao, J.-G. *Coord. Chem. Rev.* **2007**, *251*, 1493 and references therein.
(9) Rapko, B. M.; Duesler, E. N.; Smith, P. H.; Paine, R. T.; Ryan, R. R. *Inorg. Chem.* **1993**, *32*, 2164.
(10) Gan, X.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2001**, *40*, 4420. Gan, X.; Paine, R. T.; Duesler, E. N.; Nöth, H. *J. Chem. Soc., Dalton Trans.* **2003**, 153.
(11) Gan, X.; Rapko, B. M.; Duesler, E. N.; Binyamin, I.; Paine, R. T.; Hay, B. M. *Polyhedron* **2005**, *24*, 469.
(12) Matonic, J. H.; Neu, M. P.; Paine, R. T.; Scott, B. L. *J. Chem. Soc., Dalton Trans.* **2002**, 2388.
(13) Nash, K. L.; Lavallette, C.; Borkowski, M.; Paine, R. T.; Gan, X. *Inorg. Chem.* **2002**, *41*, 5849.
(14) Gan, X.; Binyamin, I.; Rapko, B. M.; Fox, J.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2004**, *43*, 2443.

Chart 1. Relevant Chemical Structures



Recently, we have also utilized additional heterocyclic platforms to develop new ligand environments, and this includes the formation of (phosphinoylmethyl)benzoxazoles, **5**.[17] In the course of that study, we examined the hydrolytic stability of phosphonate diester derivatives of **5** (R = OEt) and noted the formation of the phosphonic acid **6-H$_2$**. We report here an optimized synthesis of the phosphonic acid **6-H$_2$**, its neutralization chemistry, the acid-promoted ring-opening of the oxazole ring that produces **7-H$_2$**, the isolation and structural characterization of several NH_4^+, Na^+, and K^+ salts of **6-H$_2$** and **7-H$_2$**, and initial characterization of the solution complexation chemistry of **7-H$_2$** with Ln(III) cations.

Experimental Section

General Information. The 2-methylbenzoxazole (**8**) and other organic reagents employed in the ligand syntheses were purchased from Aldrich Chemical Co. and used without purification. Organic solvents were purchased from VWR. Infrared spectra were recorded on a Bruker Tensor 27 benchtop spectrometer, and solution NMR spectra were measured on Bruker FX-250 and Avance 500 spectrometers. The NMR standards were TMS (^{1}H, ^{13}C) and 85% H_3PO_4 (^{31}P), and downfield shifts were assigned as $+\delta$ (ppm). Elemental analyses were obtained from Galbraith Laboratory and mass spectra were recorded in the UNM Mass Spectroscopy Facility.

Synthesis of (Benzoxazol-2-ylmethyl)phosphonic Acid (6-H$_2$). A sample of 2-[(diethoxyphosphinoyl)methyl]benzoxazole[18] (**9**) (1.9 g, 7.1 mmol) was combined with Me_3SiBr (2.4 g, 15.6 mmol), stirred (23 °C, 4 h), and the reaction progress followed by TLC (EtOAc). Excess Me_3SiBr was vacuum evaporated leaving a pale pink oil, $[(Me_3SiO)_2P(O)CH_2]C_7H_4NO$ (**10**): yield, 2.4 g (92%). NMR ($CDCl_3$): ^{1}H (250 MHz) δ 0.28 (s, 18H, Si(CH_3)$_3$), 3.60 (d, 2H, J_{HP} = 22.3 Hz, CH_2), 7.3 (m, 2H, Ar), 7.5 (m, 1H, Ar), 7.7 (m, 1H, Ar); ^{13}C{^{1}H} (62.9 MHz) δ 0.5 (Si(CH$_3$)$_3$), 29.7 (d, J_{CP} = 143.1 Hz, CH$_2$), 109.7, 118.6, 123.9, 124.5, 139.5, 150.1, 159.0 (d, J_{CP} = 11.3 Hz, O-C=N); ^{31}P{^{1}H} (101.2 MHz) δ −1.4.

A sample of **10** (3.6 g, 10 mmol) was combined with distilled water (200 mL) and stirred (5 min). A white solid rapidly formed which was recovered by filtration, washed with $CHCl_3$ (50 mL), and dried leaving a white powder, $[(HO)_2P(O)CH_2]C_7H_4NO$ (**6-H$_2$**): yield, 1.5 g (70%); mp 228−230 °C. IR(KBr, cm^{-1}): 3436 (vs, br), 2925 (s), 2857 (m), 2358 (m), 1731 (m, sh), 1637 (sh,s), 1612 (s, ν_{CN}), 1568 (s), 1460 (s), 1398 (m), 1354 (m), 1310 (m), 1239 (vs, ν_{PO}), 1200 (s), 1132 (s), 1011 (s), 954 (vs), 852 (w), 809 (w), 746 (m), 685 (m), 650 (m), 544 (m), 506 (s). NMR (DMSO-d$_6$): ^{1}H (250 MHz) δ 3.43 (d, 2H, J_{HP} = 20.6 Hz, CH_2), 7.2−7.4 (m, 2H, Ar), 7.6−7.7 (m, 2H, Ar), 10.29 (2H, OH); ^{13}C{^{1}H} (62.9 MHz) δ 29.8 (d, J_{CP} = 129.9 Hz, CH$_2$), 110.3, 119.1, 124.1, 124.5, 140.9, 150.3, 160.8 (O-C=N); ^{31}P{^{1}H} (101.2 MHz) δ 15.4. ESI-MS: Found (Calcd.) m/z = 212.0109 (212.0113) $[M - H]^-$, 447.0121 $[(M - H)_2 + Na]^-$. Anal. Calcd. for $C_8H_8NO_4P$: C, 45.08; H, 3.78; N, 6.38. Found: C, 43.64; H, 3.96; N, 6.38.

Synthesis of [(2-Hydroxyphenylcarbamoyl)methyl]phosphonic Acid (7-H$_2$). A sample of **10** (4.2 g, 12 mmol) was combined with distilled water (200 mL) and stirred. A white solid (**6-H$_2$**) formed immediately; however, with continued stirring at 23 °C (3d), the solid redissolved completely. The resulting solution was extracted with $CHCl_3$ (3 × 50 mL), and the aqueous phase filtered and concentrated by vacuum evaporation. A white solid, $[(HO)_2P(O)CH_2C(O)N(H)]C_6H_4(OH)$ **7-H$_2$**, was recovered: yield, 2.1 g (77%), mp 180−182 °C. The solid was recrystallized from MeOH. IR(KBr, cm^{-1}): 3432 (s, br, ν_{OH}), 2250 (m), 2124 (m), 1675 (m, ν_{CO}), 1609 (w), 1535 (m), 1454 (m), 1380 (w), 1329 (w), 1246 (m, υ_{PO}), 1051 (vs), 1024 (vs), 824 (m), 762 (m), 623 (w). NMR (DMSO-d$_6$): ^{1}H (250 MHz) δ 2.9 (d, J_{HP} = 21 Hz, 2H, H_3), 6.7 (m, 1H, H_{11}), 6.8 (m, 1H, H_9), 6.9 (m, 1H, H_{10}), 7.4 (s, 3H, H_1, H_2, H_7) 7.9 (dd, J_{HH} = 8 Hz, J_{HH} = 1 Hz, 1H, H_{12}), 9.2 (s, 1H, H_5); ^{13}C{^{1}H} (62.9 MHz) δ 38.5 (d, J_{CP} = 125.5 Hz, C_3), 114.9 (C_9), 118.6 (C_{11}), 120.5 (C_{12}), 123.8 (C_{10}), 126.3 (C_8), 146.6 (C_6), 164.1 (C_4); ^{31}P{^{1}H} (101.2 MHz) δ 18.1. ESI-MS: Found (Calcd.) m/z = 230.0190 (230.0218) $[M - H]^-$. Anal. Calcd for $C_8H_{10}NO_5P$: C, 41.57; H, 4.36; N, 6.06. Found: C, 40.96; H, 4.24; N, 5.88.

Ligand pK_a and Complexation Constant Determinations. The protonation constants of **7-H$_2$** (pK_n) and formation constants (log K) for **7-H$_2$** with La(III), Nd(III), and Gd(III) were determined by UV−visible spectroscopy following procedures similar to those described by Choppin et al.[19] UV−visible spectra were recorded by using a Varian 300 Cary 1E UV−visible Spectrophotometer controlled by Cary Win UV Scan Application version 02.00(5) software. A VWR sympHony SR60IC pH meter with a VWR sympHony gel epoxy semimicro combination pH electrode was used for all pH readings. These were made in a thermostatted external titration cell, with N_2 bubbled through the cell to exclude CO_2. The pH meter was calibrated prior to every titration by means of an acid−base titration where measured potentials were fitted to calculated pH values to yield a Nernstian slope and $E°$ for the cell. The cell containing 50 mL of ligand/metal solution was placed in a temperature regulated water bath (25.0 ± 0.1 °C), and a peristaltic pump was used to circulate the solution through a 1 cm quartz flow cell situated in the spectrophotometer. The pH was altered in the range 2 to 7 by additions to the external titration cell of small amounts of $HClO_4$ or NaOH as required using a micropipet. After each adjustment of pH, the system was allowed to mix by operation of the peristaltic pump for 15 min prior to recording the spectrum.

7-H$_2$ has fairly intense bands in its UV spectrum because of $\pi-\pi^*$ transitions from the phenolic aromatic ring, and these were used to monitor complex-formation in solution. The variation of the spectra of **7-H$_2$** in 0.1 M $NaClO_4$ solutions as a function of pH at 25 °C are displayed in Figure 1. Three protonation constants were determined for **7-H$_2$** (Table 1) by the

---

[15] Gan, X.; Rapko, B. M.; Fox, J.; Binyamin, I.; Pailloux, S.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2006**, *45*, 3741.

[16] Gan, X.; Binyamin, I.; Rapko, B. M.; Fox, J.; Duesler, E. N.; Paine, R. T. *Polyhedron* **2006**, *25*, 3387.

[17] Shirima, C. E. Ph.D. Thesis, University of New Mexico, Albuquerque, NM, May, 2009 and references therein.

[18] Minami, T.; Isonaka, T.; Okada, Y.; Ichikawa, J. *J. Org. Chem.* **1993**, *58*, 7009.

[19] Xia, Y. X.; Chen, J. F.; Choppin, G. R. *Talanta* **1996**, *43*, 2073.

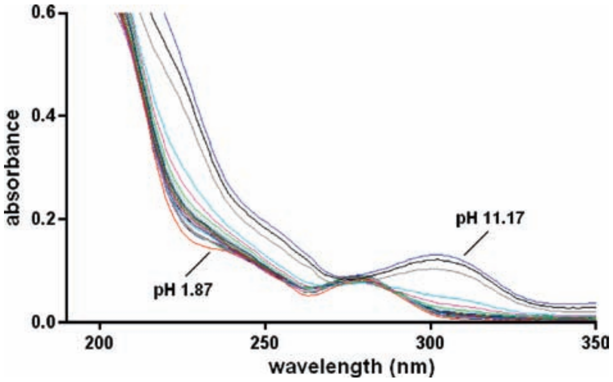


Figure 1. Absorption spectra of 2.00×10^{-5} M **7-H_2** in 0.1 M $NaClO_4$ as a function of pH. The variation of absorbance as a function of pH can be fitted[20] to yield the three protonation constants reported in Table 1.

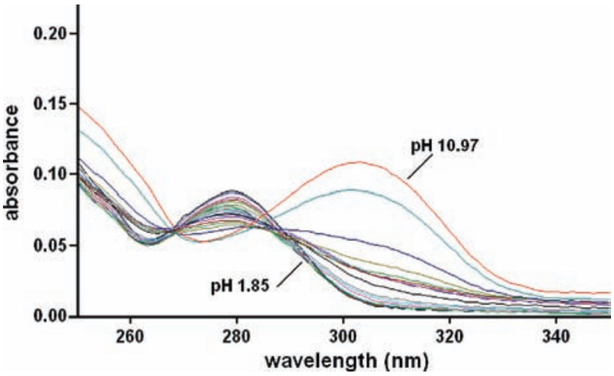


Figure 2. Absorption spectra of 2.00×10^{-5} M **7-H_2** plus 2×10^{-5} M Gd(III) in 0.1 M $NaClO_4$ as a function of pH. The initial spectrum was recorded at pH 1.85(lower spectrum), and the final pH was 10.97 (upper spectrum).

Table 1. Protonation Constants, and log $K_{(MLH)}$ Values for **7-H_2** (LH_3) with Lanthanide Ions, in 0.1 M $NaClO_4$ (25.0 ± 0.1 °C)

cation	equilibria	log *K*
H^+	$L^{3-} + H^+ \leftrightarrows LH^{2-}$	10.22(6)
	$LH^{2-} + H^+ \leftrightarrows LH_2^-$	7.39(3)
	$LH_2^- + H^+ \leftrightarrows LH_3$	2.2(4)
La(III)	$LaL + H^+ \leftrightarrows [LaLH]^{+1}$	10.14(5)
	$La^{3+} + LH^{2-} \leftrightarrows [LaLH]^{+1}$	6.5(1)
Nd(III)	$NdL + H^+ \leftrightarrows [NdLH]^{+1}$	9.71(5)
	$Nd^{3+} + LH^{2-} \leftrightarrows [NdLH]^{+1}$	6.5(1)
Gd(III)	$GdL + H^+ \leftrightarrows [GdLH]^{+1}$	10.08(5)
	$Gd^{3+} + LH^{2-} \leftrightarrows [GdLH]^{+1}$	6.2(1)

variation in absorbance as a function of pH at five different wavelengths. Fitting of theoretical absorbance versus pH curves was accomplished using the SOLVER module of EXCEL.[20] The standard deviations given in Table 1 were obtained using the SOLVSTAT macro.[20]

Formation constants with La(III), Nd(III), and Gd(III) as representative lanthanide (Ln) ions were measured by repeating the titrations with **7-H_2** in the presence of 1 equiv of the Ln(III) ion. The spectra of the 1:1 **7-H_2**/Gd(III) system as a function of pH are shown in Figure 2. From the displacement of the protonation equilibria to lower pH values, the formation constants were calculated[21] and the resulting values are displayed in Table 1. A continuous variation analysis (Job's method) was used to confirm the metal:ligand complex stoichiometry. An attempt was made to measure log $K_{(MLH)}$ for **7-H_2** with Lu(III) as the smallest of the Ln(III) ions, but precipitation of Lu(III) hydroxide prevented determination of a reliable value of log $K_{(MLH)}$.

Phosphonic Acid Neutralization Reactions. NaOH + (6-H_2). A sample of **6-H_2** (0.13 g, 0.62 mmol) was dissolved in MeOH (10 mL), and aqueous NaOH solution (0.1 M) was slowly added until the solution reached pH 7. The solution was then allowed to evaporate leaving a white powder, $Na\{[(HO)(O)_2PCH_2]C_7H_4NO\}\cdot H_2O$, **Na(6-H)·$H_2O$**, that was rinsed with acetone and allowed to dry: yield, 0.148 g (87%); mp > 250 °C. NMR (DMSO-d_6): $^{31}P\{^1H\}$ δ 12.2. Anal. Calcd. for $C_8H_9NO_5PNa$: C, 37.96; H, 3.58; N, 5.53. Found: C, 37.40; H, 2.76; N, 5.86.

NaOH + (6-H_2). In a second procedure, **6-H_2** (0.208 g, 0.976 mmol) in MeOH (20 mL) was treated with NaOH solution (0.1 M, 1.95 mmol) until the solution showed pH 12.7. The mixture was stirred (12 h), and the solution evaporated to dryness. The white solid residue was washed with MeOH (10 mL) and acetone (10 mL) and allowed to dry in air leaving a white powder, **Na_3(6)(6-H)·H_2O**. NMR (DMSO-d_6): $^{31}P\{^1H\}$ δ 13.1.

KOH + (6-H_2). A sample of **6-H_2** (0.11 g, 0.52 mmol) was dissolved in MeOH (20 mL) and slowly combined with aqueous KOH solution (0.1 M, 2.0 mmol). The mixture was stirred (12 h, 23 °C) and allowed to evaporate leaving a solid residue. This was dissolved in MeOH/CH_3CN, filtered and evaporated. The residue was extracted with dimethylformamide (DMF), the insoluble fraction recovered and recrystallized from hot MeOH leaving crystalline **[K_2(6)]$_2$·3H_2O**. The DMF filtrate was evaporated, and the residue recrystallized from MeOH/DMF giving **K(6-H)**.

KOH + (6-H_2). In a 2:1 stoichiometric combination, a sample of **6-H_2** (0.21 g, 0.98 mmol) in MeOH (25 mL) was combined with KOH (0.1 g, 1.95 mmol) in MeOH (15 mL), and the clear solution stirred under dry nitrogen (12 h). The final solution (pH 8) was allowed to slowly evaporate leaving a brown solid: yield, 0.22 g (44%, based on [**K_2(6)**]. NMR (DMSO-d_6): $^{31}P\{^1H\}$ δ 11.9. Anal. Calcd for $C_{16}H_{18}N_2O_{11}P_2K_4$: C, 30.38; H, 2.87; N, 4.43. Found: C, 30.69; H, 2.96; N, 4.43.

NH_4OH + (7-H_2) (2:1). A sample of **7-H_2** (0.25 g, 1.1 mmol) was dissolved in water (15 mL) resulting in a pH 1.5 solution. Aqueous 0.1 M NH_4OH solution was added dropwise until the mixture showed pH 9.2. The solution was then evaporated slowly leaving colorless needles, **NH_4 (7-H)**. NMR (DMSO-d_6): $^{31}P\{^1H\}$ δ 13.6.

KOH + (6-H_2). In a 1:1 stoichiometric combination a sample of **6-H_2** (0.13 g, 0.62 mmol) in MeOH (20 mL) was combined with KOH (0.035 g, 0.62 mmol) in water (100 mL), and the clear solution stirred (12 h) resulting in a pH 4 solution. This was allowed to evaporate leaving a white solid residue, **K(7-H)**: yield 0.156 g (93%); mp 140−141 °C. The solid was washed with DMF and recrystallized from MeOH by slow evaporation. The crystals were shown by X-ray crystallography to be **K(7-H)·DMF**. IR (KBr, cm^{-1}): 3440 (s, br, ν_{OH}), 2248 (m), 2121 (m), 1665 (m), 1536 (w), 1454 (w), 1382 (w), 1242 (w), 1044 (vs, ν_{PO}), 823 (m), 762 (m), 573 (m). NMR (DMSO-d_6): ^1H (250 MHz) δ 2.56 (d, J_{PH} = 18.7 Hz, 2H, CH_2), 4.46 (br, 4H), 6.60 (m), 6.79 (m), 7.81 (m), 7.88 (m), 10.07. $^{31}P\{^1H\}$ (101.3 MHz) δ 12.5. Anal. Calcd for $C_{11}H_{16}KN_2O_6P$: C, 38.59; H, 4.71; N, 8.18. Found: C, 37.78; H, 4.83; N, 7.69.

X-ray Diffraction Analyses. Crystals were placed in glass capillaries and mounted on a Bruker X8 Apex2 CCD-based X-ray diffractometer with a normal focus Mo-target X-ray tube ($\lambda = 0.71073$ Å), operated at 1500 W (50 kV, 30 mA), and an Oxford Cryostream 700 low temperature device. Full spheres of data were collected, and the frames integrated with the Bruker SAINT software package.[22] The data was processed with

---

(20) Billo, E. J. *EXCEL for Chemists*; Wiley-VCH: New York, 2001.

(21) Martell, A. E.; Motekaitis, R. J. *The Determination and Use of Stability Constants*; VCH Publishers: New York, 1989.

(22) Sheldrick, G. M. *SAINTPlus*, v.7.01; Bruker Analytical X-ray: Madison, WI, 2003.

Table 2. Crystallographic Data

	6-H$_2$	[Na(**6-H**)·(H$_2$O)]$_2$	Na$_3$(**6**)(**6-H**)·H$_2$O	K(**6-H**)	[K$_2$(**6**)]$_2$·3H$_2$O	NH$_4$(**7-H**)	K(**7-H**)·DMF
empirical formula	$C_8H_8NO_4P$	$C_{16}H_{18}N_2Na_2O_{10}P_2$	$C_8H_{7.5}NNa_{1.5}O_{4\cdot 5}P$	$C_8H_7KNO_4P$	$C_{16}H_{18}K_4N_2O_{11}P_2$	$C_8H_{13}N_2O_5P$	$C_{11}H_{16}KN_2O_6P$
formula weight	213.12	506.24	255.10	251.22	632.66	248.17	342.33
crystal system	orthorhombic	triclinic	monoclinic	monoclinic	orthorhombic	monoclinic	orthorhombic
space group	*Pca*2(1)	$P\bar{1}$	*P*2(1)/*c*	*P*2(1)/*c*	*Aba*2	*P*2(1)/*c*	*Pbca*
unit cell dimensions							
a, Å	19.883(2)	4.8192(3)	16.9793(9)	15.2517(7)	34.134(2)	19.8602(9)	7.4875(5)
b, Å	5.6194(6)	14.0855(7)	5.4083(3)	4.6921(2)	9.7662(6)	7.1524(3)	14.2950(8)
c, Å	7.814(1)	15.6805(9)	21.628(1)	14.1701(7)	7.1209(4)	8.1497(3)	28.810(2)
α, deg	90	80.514(3)	90	90	90	90	90
β, deg	90	81.492(3)	98.723(3)	98.359(2)	90	97.563(2)	90
γ, deg	90	85.122(3)	90	90	90	90	90
volume	873.1(2)	1036.3(1)	1963.1(2)	1003.28(8)	2373.8(2)	1147.58(8)	3083.6(3)
Z	4	2	8	4	4	4	8
T, K	228(2)	228(2)	183(2)	228(2)	228(2)	228(2)	228(2)
density, g cm^{-3}	1.621	1.622	1.726	1.663	1.770	1.436	1.475
absorption coeff, mm^{-1}	0.301	0.311	0.345	0.680	0.946	0.248	0.475
min/max transmission	0.850/0.970	0.8881/0.9789	0.890/0.972	0.834/0.944	0.6751/0.9446	0.8711/0.9875	0.8276/0.9474
reflection collected	21435	33065	42064	34844	36250	26858	62611
independent reflections [R_{int}]	2969[0.0239]	7917[0.0363]	6805[0.0298]	4403[0.0204]	4527[0.0226]	3477[0.0284]	4724[0.0280]
final *R* indices [$I > 2\sigma(I)$]							
R1 (wR2)	0.0243(0.0674)	0.0373(0.0950)	0.0496(0.1454)	0.0265(0.0727)	0.020190.0467)	0.0340/0.0937	0.0516/0.1332
final *R* indices (all data) R1(wR2)	0.0248(0.0679)	0.0554(0.1037)	0.0564(0.1489)	0.0324(0.0797)	0.0208(0.0470)	0.0418/0.0997	0.0644/0.1424

SADABS,[23] and the structures solved and refined with the Bruker SHELXTL software package.[24] Data collection and lattice parameters are summarized in Table 2. Specific comments related to each structure follow. **6-H$_2$**: Colorless prism (0.55 × 0.46 × 0.09 mm) recrystallized from MeOH/MeCN. The structure was solved and refined in the chiral orthorhombic space group *Pca*2(1). The presence of the P atom permitted determination of the absolute configuration (Flack x = 0.06(6)). All non-hydrogen atoms were refined anisotropically, and ring H atoms were placed in ideal positions with fixed $U_{iso} = 1.2\ U_{equiv}$ of the parent atom. H3 on O3 was placed in an ideal position with fixed $U_{iso} = 1.5U_{equiv}$ of O3. H2 on O2 and H1a and H1b on C1 were allowed to vary in position and U_{iso}. **[Na(6-H)·H$_2$O]$_2$**: Colorless needles (0.39 × 0.09 × 0.07 mm) recrystallized from MeOH. All non-hydrogen atoms were refined anisotropically and H-atoms on C-atoms were placed in idealized positions with fixed $U_{iso} = 1.2\ U_{equiv}$ of the parent atom. H-atoms on O-atoms were allowed to vary in position and U_{iso}. The initial assignment of the ring N and O atoms was tested by reversing the atom types. This led to increased R factors by 2−3%. **Na$_3$(6)(6-H)·H$_2$O:** Colorless plate (0.34 × 0.28 × 0.07 mm) recrystallized from MeOH. All non-hydrogen atoms were refined anisotropically, and H-atoms on C-atoms placed in idealized positions with $U_{iso} = 1.2U_{equiv}$ of the parent atom. The H-atom on O8 was located in a difference map, and it was allowed to vary in position and U_{iso}. The positions of H-atoms on O9 were deduced based on the likely H-bonding scheme: O9 has close approaches to N1[x, y, z] and O6[x, $y-1$, $z+1$]. The positions were fixed with O9−H 0.85 Å and $U_{iso} = 1.5U_{equiv}$ of O9. **K(6-H):** Colorless prism (0.28 × 0.16 × 0.09 mm) recrystallized from MeOH/DMF. All non-hydrogen atoms were refined anisotropically, and H-atoms on C-atoms were placed in idealized positions with fixed $U_{iso} = 1.2\ U_{equiv}$ of the parent atom. There is a small disorder in the N1/O1 positions: primary positions 86.5%; secondary positions 13.5%. The atom assignments of N1 and O1 were interchanged resulting in an increase of R1 by 5%. The H-atom on O4 was allowed to vary in position and U_{iso}. **[K$_2$(6)$_2$]$_2$·3H$_2$O:** Colorless plates (0.45 × 0.26 × 0.06 mm) recrystallized from hot MeOH. All non-hydrogen atoms were refined anisotropically, and H-atoms on ring C-atoms placed in idealized positions with fixed $U_{iso} = 1.2U_{equiv}$ of the parent atom. The H-atoms on C8 were placed in idealized positions with $U_{iso} = 1.5U_{equiv}$ of C8. The H-atoms on the water molecules were allowed to vary in position and U_{iso}. **NH$_4$(7-H):** Colorless plate (0.57 × 0.37 × 0.05 mm) recrystallized from H$_2$O/MeOH. All non-hydrogen atoms were refined anisotropically, and the H-atoms on all of the C-atoms were placed in idealized positions with $U_{iso} = 1.2U_{equiv}$ of the parent atom. The H-atoms on the N1, O2, and O5 atoms were allowed to vary in position and U_{iso}. **K(7-H)·DMF:** Colorless plate (0.41 × 0.39 × 0.16 mm) recrystallized from MeOH/DMF. The solvent DMF molecule was disordered over two sites with relative occupancies 72/28%. All non-hydrogen atoms except the minor site atoms C9A, C10A, and C11A were refined anisotropically. The H-atoms on the ring C-atoms were included in idealized positions with $U_{iso} = 1.2U_{equiv}$ of the parent atom. The H-atoms on C8 were placed in idealized positions with $U_{iso} = 1.5U_{equiv}$ of C8. The H-atoms on the O1, O3, and N1 atoms were allowed to vary in position and U_{iso}.

Results and Discussion

The synthesis of the target (benzoxazol-2-ylmethyl)phosphonic acid (**6-H$_2$**) employed a three-step sequence starting with commercially available 2-methyl benzoxazole (**8**) as summarized in Scheme 1. The conversion of **8** to 2-[(diethoxyphosphinyl)methyl] benzoxazole (**9**) has been previously described by Minami et al.[18] and others.[25] The Minami procedure was adopted in toto except it was performed with a

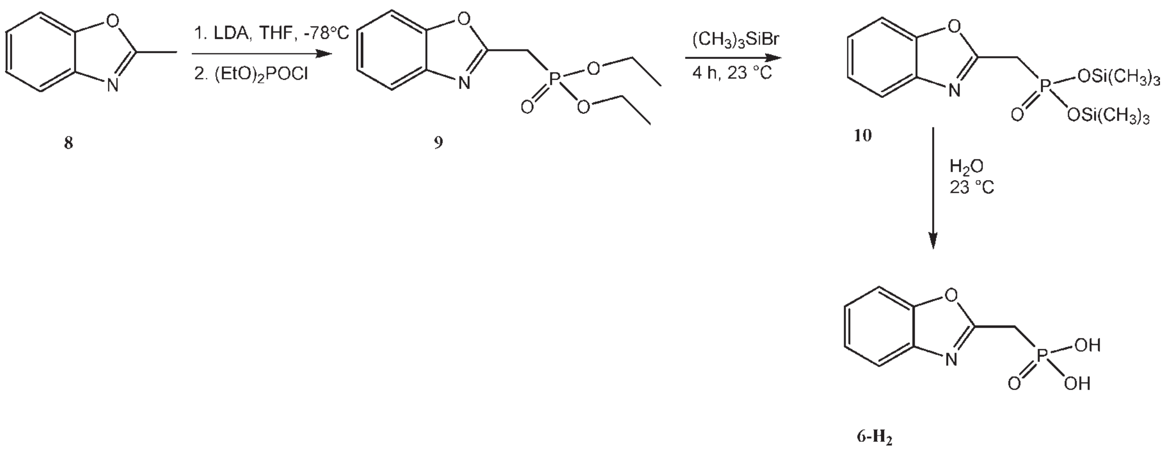
---

(23) Sheldrick, G. M. *SADABS, Program for Empirical Absorption Correction of Area Detector Data*, v.2.10; University of Göttingen: Göttingen, Germany, 2003.

(24) Sheldrick, G. M. *SHELXTL*, v.6.12; Bruker Analytical X-ray: Madison, WI, 2001.

(25) An alternative Arbusov synthesis of **9** has been reported involving the combination of 2-(bromomethyl)-1,3-benzoxazole and P(OEt)$_3$ at 150 °C. In our hands this synthesis was not as predictable as the approach described by Minami.[18]Kosaka, T.; Wakabayashi, T. *Heterocycles* **1995**, *41*, 1995. Anthony, N. D.; et al. *J. Med. Chem.* **2007**, *50*, 6116; Another alternative route may exist based upon a reaction involving alcohol elimination and subsequent condensation between R(R′O)P(O)CH$_2$CH(OR″)$_2$ and 2-aminophenol: Razumov, A. I.; Gurevich, P. A.; Liorber, B. G. *Zhur. Obsh. Khim.* **1969**, *39*, 392.

Scheme 1



10-fold scale-up. At that scale, **9** is obtained in 73% yield (81% lit.) as a colorless oil. Mass spectroscopic and ^{1}H NMR data are similar to data provided in the literature,[18] and additional IR and NMR spectra, recorded in the present study, are consistent with the proposed structure of **9**.[26]

Although some phosphonate esters undergo partial hydrolysis under relatively mild conditions,[14,16] more forcing conditions, for example, 6 M HCl with reflux,[27] are typically required for complete conversion. Such conditions are deleterious to the benzoxazole ring, vide infra; therefore, another synthetic approach was required to obtain **6-H$_2$**. We[15,28] and others[29−32] have reported that treatment of organyl phosphonate esters with Me$_3$SiCl or Me$_3$SiBr under mild conditions usually leads to formation of the corresponding silyl ester, and subsequent aqueous hydrolysis provides the desired phosphonic acid. In the present case, treatment of **9** with a slight excess of Me$_3$SiBr at 23 °C results in formation of a faintly pink oil, (benzoxazol-2-ylmethyl) phosphonic acid bis-(trimethylsilyl) ester, (**10**) in 92% yield. It is noted that the silylation reaction does not occur at a useful rate with Me$_3$SiCl. Compound **10** displays a strong IR band at 1240 cm^{-1}, that is tentatively assigned to the ν_{PO} stretching mode.[17] Several broad, overlapping adsorptions appear in the region 1650−1500 cm^{-1}, but confident assignment of one of these to ν_{CN} of an intact benzoxazole ring is not possible. The ^{1}H and ^{13}C{^{1}H} NMR spectra, however, provide ample evidence for the survival of the oxazole ring. For example, the ^{13}C{^{1}H} NMR spectrum contains a doublet resonance at δ 159.0 (J_{CP} = 11.3 Hz) assigned to the N = *C*-O unit of the oxazole fragment that closely compares with δ 158.2 (J_{CP} = 10 Hz) for the related carbon atom in **9**. The ^{1}H and ^{13}C{^{1}H} NMR resonances for the methylene group separating the P atom and benzoxazole ring in **10** appear at δ 3.60 (J_{PH} = 22.3 Hz) and δ 29.7 (J_{CP} = 143.1 Hz), respectively, and these data are similar to NMR data for **9**: ^{1}H δ 3.57 (J_{PH} = 21.7 Hz), ^{13}C{^{1}H} δ 27.6 (J_{CP} = 139.2 Hz). As expected for a silyl phosphonate ester,[14−16,28] the ^{31}P resonance for **10**, δ −1.4, is significantly upfield of the resonance in the ethyl ester **9**, δ 20.0.[26] The ^{31}P resonance for **10** is also upfield of the shifts recorded for (Me$_3$SiO)$_2$P(O)CH$_2$C(O)NEt$_2$, δ 2.8[28] and [(Me$_3$SiO)$_2$P(O)CH$_2$]$_2$, δ 11.6.[33]

The subsequent aqueous hydrolysis of **10** is rapid and quantitative providing **6-H$_2$** as a white solid. This compound was quickly recrystallized from cold water and recovered in 70% yield. The compound displays a parent ion species [M − H]$^{-1}$, as well as a dimer-sodium ion complex [(M − H)$_2$ + Na]$^{-1}$ in its negative ion mode ESI-MS. The infrared spectrum contains strong bands at 1612 and 1239 cm^{-1} that are tentatively ascribed to ν_{CN} and ν_{PO}, respectively, based upon IR data for **9**.[17,18,26] There is also a broad, strong band centered at 3436 cm^{-1} that is assigned to PO-H stretching modes that are not present in the spectra for the diesters **9** and **10**. As expected, the silyl group NMR resonances that were present in the ^{1}H and ^{13}C NMR spectra of **9** are now absent in **6-H$_2$**; however, resonances for the methylene group, ^{1}H δ 3.4 (J_{PH} = 20.6 Hz), ^{13}C{^{1}H} δ 29.8 (J_{CP} = 129.9 Hz) and the N = *C*-O unit, ^{13}C{^{1}H} δ 160.8, confirm the retention of the benzoxazole ring structure. In addition, a ^{1}H NMR resonance at δ 10.29 appears for the phosphonic acid protons. The ^{31}P{^{1}H} resonance for **6-H$_2$** in DMSO-d$_6$ appears at δ 15.4. This is slightly upfield from the value of δ 23.6 (CDCl$_3$) observed for 2-[(HO)$_2$P-(O)CH$_2$]C$_5$H$_4$NO (**11**)[14] and downfield from the value of δ 17.9 (CD$_3$CN/H$_2$O) in (HO)$_2$P(O)CH$_2$C(O)NEt$_2$.[28] It is noted that the ^{31}P NMR shifts for all of these compounds are very solvent and pH sensitive.

The spectroscopically deduced molecular structure of **6-H$_2$** was confirmed by a single crystal X-ray diffraction structure determination. A view of the molecule is shown in Figure 3, and selected bond lengths are provided in Table 3. As expected, the structure contains a 2-methyl benzoxazole fragment bonded to a -P(O)(OH)$_2$ unit. The P1−C1 bond length,

---

[26] Additional characterization data for **9**. IR(KBr, cm^{-1}): 2984(m), 2921(m), 1689(w), 1613(m, ν_{CN}), 1570(m), 1485(m), 1397(w), 1256(s, ν_{PO}), 1164(m), 1107(m), 1028(s), 967(s), 752(m), 653(w), 545(2), 507(w). ^{1}H NMR (250 MHz, CDCl$_3$): δ 1.31(t, J_{HH} = 7.2 Hz, 6H, OCH$_2$CH_3), 3.57(d, J_{HP} = 21.7 Hz, 2H, PCH_2), 4.15(q, J_{HH} = 6.4 Hz, 4H, OCH_2), 7.28(m, 2H, *Ar*), 7.66(m, 1H, *Ar*), 7.68(m, 1H, *Ar*). ^{13}C{^{1}H} NMR (62.9 MHz, CDCl$_3$): δ 15.8(d, J_{CP} = 5.8 Hz, C_1), 27.6(d, J_{CP} = 139.2 Hz, C_3), 62.5(d, J_{CP} = 6.4 Hz, C_2), 110.0(s), 119.4(s), 123.9(s), 124.5(s), 140.8(d, J_{CP} = 1.3 Hz), 150.6(s), 158.2(d, J_{CP} = 10 Hz, C_4). ^{31}P{^{1}H} NMR (101.2 Hz, CDCl$_3$): δ 20.0

[27] Engel, R. E. *Synthesis of Carbon-Phosphorus Bonds*; CRC Press: Boca Raton, FL, 1988; p 21.

[28] Conary, G. C.; McCabe, D. J.; Caudle, L. J.; Duesler, E. N.; Paine, R. T. *Inorg. Chim. Acta* **1993**, *207*, 213.

[29] Morita, T.; Okamoto, Y.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2169.

[30] McKenna, C. E.; Higa, M. T.; Cheng, N. H.; McKenna, M. *Tetrahedron Lett.* **1977**, 155.

[31] Rabinowitz, R. *J. Org. Chem.* **1963**, *38*, 2975.

[32] Neff, G. A.; Page, C. J.; Meintjes, E.; Tsuda, T.; Pilgrim, W.-C.; Roberts, N.; Warren, W. W., Jr. *Langmuir* **1996**, *12*, 238.

[33] Pudovik, M. A.; Terentéva, S. A.; Kibardina, L. K.; Pudovik, A. N. *Russ. J. Gen. Chem.* **2006**, *76*, 714.

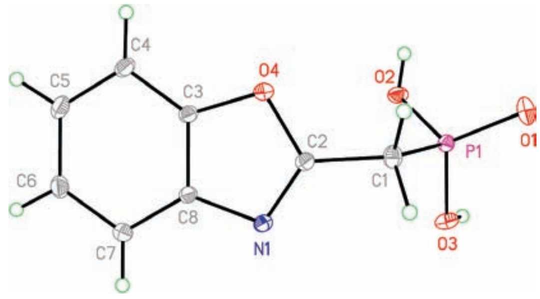


Figure 3. Molecular structure of $[(HO)_2P(O)CH_2]C_7H_4NO$, (**6-H$_2$**) (20% thermal ellipsoids).

1.818(1) Å, is similar to the P−C bond length in the related 2-[(diphenylphosphinoyl)methyl] benzoxazole, $2\text{-}[(Ph)_2P(O)CH_2]C_7H_4NO$ (**12**), 1.823(1) Å.[17] The P=O bond length in **6-H$_2$**, P1−O1, 1.4894(9) Å, is significantly shorter than the P−OH bond lengths, P1−O2, 1.5371(8) Å, and P1−O3, 1.5387(9) Å; however, it is similar to the P=O bond length in **12**, 1.4831(8) Å. The twist of the phosphonate P=O bond vector relative to the methyl benzoxazole fragment is indicated by the angle between the planes P1O1C1 and C1C2N1C8C7C6C5C4C3O4, 96.9°, and this can be compared with the related angle in **12**, 56.8°. The difference may, in part, result from the hydrogen bonding that takes place in **6-H$_2$** where the phosphonic acid H-atoms interact with a ring N atom and a phosphoryl O-atom in neighboring molecules.[34]

While attempting to determine the pK_a's and examining stoichiometric neutralization reactions of **6-H$_2$** it was noted that the compound, under some conditions, is subject to ring-opening chemistry that results in the formation of a white solid, [(2-hydroxyphenylcarbamoyl)methyl]phosphonic acid, **7-H$_2$**, in variable amounts. This was not entirely unexpected based upon literature reports of ring-opening for other benzoxazole compounds.[35−39] Therefore, an effort was made to devise an optimized synthesis for **7-H$_2$**. As depicted in Scheme 2, extending the reaction time for aqueous hydrolysis of **10** provides a suitable condition for obtaining **7-H$_2$** in high yield with analytical purity.[40] Conversion of **10** to **6-H$_2$**, as noted above, is very rapid as evidenced by immediate formation of a precipitate when water is added to neat samples of **10**. However, continued rapid stirring of the mixture over several days results in dissolution of the precipitate and formation of a clear solution from which **7-H$_2$** is isolated in good yield.

The conversion of **6-H$_2$** to **7-H$_2$** was followed by ^{31}P NMR. In water, **6-H$_2$** is only slightly soluble, but it displays a single resonance at δ 14 that disappears as the solid is consumed by hydrolysis. While the bulk of the solid is present, a resonance at δ 17 appears and increases in intensity as **7-H$_2$** is produced. The rate of this conversion reaction is increased with increasing temperature and decreasing aqueous solution pH caused by addition of a small amount of HCl.

Compound **7-H$_2$** displays a parent ion $[M - H]^-$ in its negative ion mass spectrum that confirms the addition of H and OH to **6-H$_2$**. The infrared spectrum for **7-H$_2$** has several of the same fingerprint features as **6-H$_2$**; however, the disappearance of a very strong bond at 1612 cm^{-1}, tentatively assigned to ν_{CN} in **6-H$_2$**, and appearance of a strong, sharp band at 1675 cm^{-1}, tentatively assigned to ν_{CO} in **7-H$_2$**, are consistent with the formation of the open ring structure.[17] The $^{13}P\{^1H\}$ NMR spectrum of **7-H$_2$** in DMSO-d$_6$ consists of a single resonance, δ 18.1, that is downfield of the resonance for **6-H$_2$** in DMSO-d$_6$, δ 15.4, and both chemical shifts are solvent and pH dependent. The ^{31}P NMR resonance for **7-H$_2$** is upfield of the resonance for the structurally related phosphonate diester, $(EtO)_2P(O)CH(CH_3)C(O)N(H)Ph$, δ 23.8.[41] The 1-D ^{1}H and $^{13}C\{^1H\}$, 2-D COSY, DEPT, ^{1}H - ^{13}C HMQC, ^{1}H - ^{13}C HMBC, ^{1}H - ^{15}N HMQC, and ^{1}H - ^{15}N HMBC NMR experiments[42] provide for complete assignments for the ring-opened structure, and representative spectra are included in the Supporting Information. It is noted that the ^{1}H and ^{13}C NMR resonances for the methylene group (C_3), ^{1}H δ 2.9; ^{13}C 38.5, are shifted from the values displayed by **6-H$_2$**.

Attempts to grow X-ray diffraction quality crystals of **7-H$_2$** failed. However, crystals of ammonium [(2-hydroxyphenylcarbamoyl)methyl]hydrogen phosphonate, $[NH_4^+][(HO)P(O)_2CH_2C(O)N(H)(C_6H_4OH)^-]$, **NH$_4$(7-H)**, were obtained from the 1:1 reaction of NH_4OH and **7-H$_2$** in water, and the molecular structure was determined by X-ray diffraction methods. A view of the molecule is shown in Figure 4, and selected bond distances are listed in Table 3. The structure determination confirms the ring-opened structure with bonding parameters similar to those reported for $[NH_2C(CH_3)_2CH_2C(O)CH_2C(CH_3)_2^+][(HO)(O)_2PCH_2C(O)NEt_4^-]$ (**13**).[28] The phosphorus atom adopts a pseudotetrahedral geometry with two shorter P−O bond lengths, P1−O1 1.4944(9) Å and P1−O3 1.5046(9) Å, and a longer P1−O2 bond length, 1.581(1) Å. The last belongs to the protonated P−OH group. Similar P−O and P−OH bond lengths appear in **13**. The P1−C1, C1−C2, C2−O4, and C2−N1 bond lengths in **NH$_4$(7-H)** 1.814(1), 1.508(2), 1.243(1), and 1.338(2) Å also are similar to the related parameters in **13**: (1.799(4) Å, 1.500(7) Å, 1.224(6) Å, and 1.340(6) Å. As expected, however, C2−N1 in **NH$_4$(7-H)** is significantly longer than C2−N1 in **6-H$_2$** 1.294(1) Å, and C2−O4 is much shorter than in **6-H$_2$**, 1.355(1) Å.[43] There are several hydrogen bonding interactions in the molecule that involve either the hydrogen phosphonate proton or the ammonium protons with the shortest being, O2−H2···O3A

---

[34] Hydrogen bonding interactions in **6-H$_2$** include O2-H2···N1A: O2-H2 0.77(2) Å, N1A···H2 1.81(2) Å, O2···N1A 2.560(1) Å, O2-H···N1A 163(3)°; O3-H3···O1B: O3-H3 0.83 Å, O1B···H3 1.67 Å, O3···O1B 2.473(1) Å, O3-H3···O1B 162.1°.

[35] Bruylants, A.; deMedicis, E. F. Cleavage of the Carbon-nitrogen double bond. In *The Chemistry of the Carbon-Nitrogen Double Bond*; Patai, S., Ed.; J. Wiley: New York, 1970.

[36] Werstiuk, N. H.; Ju, C. *Can. J. Chem.* **1989**, *67*, 812.

[37] Ono, M.; Yamakawa, K.; Kobayashi, H.; Itoh, I. *Heterocycles* **1988**, *27*, 881.

[38] Cole, E. R.; Crank, G.; Sumantu *Aust. J. Chem.* **1986**, *39*, 295.

[39] Hirota, T.; Koyama, T.; Basho, C.; Nauba, T.; Sasaki, K.; Yamato, M. *Chem. Pharm. Bull.* **1977**, *25*, 3056.

[40] Bookser, B. C.; Dong, Q.; Reddy, K. R. World Pat. Appl. WO 01/66553 A2. This document suggests that **7-H$_2$** may be obtained by combination of 2-hydroxyaniline and diethylphosphonoacetic acid with EDC/HOBT in DMF.

[41] Tay, M. K.; Abont-Jaudet, E.; Collignon, N.; Savignac, P. *Tetrahedron* **1989**, *45*, 4415.

[42] The long-range ^{1}H-^{15}N heteronuclear shift correlation NMR experiments using natural abundance ^{15}N were aided by literature reports: (a) Besse, P.; Combourieu, B.; Boyse, G.; Sancelme, M.; DeWever, H.; Deloit, A.-M. *Appl. Environ. Microbiol.* **2001**, *67*, 1412. (b) Barnwal, R. P.; Rout, A. K.; Chang, K. V. R.; Atreya, H. S. *J. Biomol. NMR* **2007**, *39*, 259.

[43] Examination of 79 structures listed in the Cambridge Crystallographic Data files that contain the benzoxazline fragment, reveals that 18 have the C−O bond length (C2-O4) in the range 1.360−1.369 Å and 25 in the range 1.370−1.379 Å. In addition, 32 structures have a C=N (C2-N1) bond length in the range 1.290−1.299 Å.

Table 3. Selected Bond Lengths (Å)

bond type	**6-H$_2$**		[Na(**6-H**)·(H$_2$O)]$_2$		Na$_3$(**6**)(**6-H**)·H$_2$O		K(**6-H**)		[K$_2$(**6**)]$_2$·3H$_2$O		NH$_4$(**7-H**)		K(**7-H**)·DMF	
P−O	P1−O1	1.4894(9)	P1−O1	1.4999(9)	P1−O1	1.540(2)	P1−O2	1.4918(7)	P1−O2	1.5110(8)	P1−O1	1.4944(9)	P1−O3	1.577(2)
	P1−O2	1.5371(8)	P1−O2	1.577(1)	P1−O2	1.508(2)	P1−O3	1.5118(7)	P1−O3	1.5215(8)	P1−O2	1.581(1)	P1−O4	1.498(1)
	P1−O3	1.5387(9)	P1−O3	1.487(1)	P1−O3	1.548(2)	P1−O4	1.5678(7)	P1−O4	1.5231(8)	P1−O3	1.505(9)	P1−O5	1.513(2)
			P2−O5	1.5034(9)	P2−O6	1.504(2)								
			P2−O6	1.586(1)	P2−O7	1.497(2)								
			P2−O7	1.486(9)	P2−O8	1.580(2)								
P−C	P1−C1	1.818(1)	P1−C1	1.822(1)	P1−C1	1.861(2)	P1−C8	1.8272(9)	P1−C8	1.857(1)	P1−C1	1.814(1)	P1−C8	1.809(2)
			P2−C9	1.819(1)	P2−C9	1.818(2)								
C−N	C2−N1	1.294(1)	C2−N1	1.292(2)	C2−N1	1.295(3)	C7−N1	1.298(1)	C7−N1	1.295(1)	C2−N1	1.338(2)	C7−N1	1.352(3)
	C8−N1	1.402(1)	C8−N1	1.401(2)	C8−N1	1.398(3)	C6−N1	1.398(1)	C6−N1	1.406(2)	C3−N1	1.424(2)	C6−N1	1.404(3)
			C10−N2	1.293(2)	C10−N2	1.288(3)								
			C16−N2	1.404(2)	C16−N2	1.403(3)								
C−O	C2−O4	1.355(1)	C2−O4	1.365(2)	C2−O4	1.374(3)	C1−O1	1.383(1)	C1−O1	1.379(2)	C2−O4	1.243(1)	C7−O2	1.213(3)
	C3−O4	1.386(1)	C3−O4	1.381(2)	C3−O4	1.377(3)	C7−O1	1.363(1)	C7−O1	1.377(2)	C4−O5	1.356(2)	C1−O1	1.375(3)
			C10−O8	1.367(2)	C10−O5	1.383(3)								
			C11−O8	1.383(2)	C11−O5	1.375(3)								
C−C	C1−C2	1.479(1)	C1−C2	1.481(2)	C1−C2	1.466(3)	C7−C8	1.478(1)	C7−C8	1.475(2)	C1−C2	1.508(2)	C7−C8	1.515(3)
			C9−C10	1.481(2)	C9−C10	1.476(3)								
M−O			Na1−O2	2.530(1)	Na1−O1	2.380(2)	K1−O3	2.8961(7)	K1−O3	2.7201(9)			K1−O1	3.180(2)
			Na1−O7	2.319(1)	Na1−O6	2.353(2)	K1−O4	2.8540(8)	K2−O3	2.7137(9)			K1−O4	2.762(2)
			Na1−O7(#1)	2.328(1)	Na1−O9	2.501(2)	K1−O2(#1)	2.6995(7)	K2−O3	2.9441(9)			K1−O6	2.776(2)
			Na1−O9	2.448(1)	Na1−O7(#1)	2.306(2)								
			Na1−O9(#2)	2.440(1)	Na1−O6(#2)	2.413(2)	K1−O2(#2)	2.7228(8)						
			Na2−O3	2.333(1)	Na1−O8(#2)	2.957(2)	K1−O3(#3)	2.8453(8)						
			Na2−O3(#)	2.397(1)	Na2−O2	2.369(2)								
			Na2−O10	2.385(1)	Na2−O3	2.303(2)								
			Na2−O10(#2)	2.540(1)	Na2−O8	2.304(2)								
			Na2−O6(#5)	2.669(1)	Na2−O7	2.461(2)								
					Na2−O1	2.588(2)								
					Na3−O2	2.327(2)								
					Na3−O9	2.345(2)								
					Na3−O1	2.395(2)								
					Na3−O3	2.398(2)								
					Na3−O7	2.821(2)								
					Na3−O8	2.856(2)								
M−N			Na1−N2	2.505(1)	Na2−N2	2.586(2)	K1−N1(#1)	2.8874(9)	K1−N1	3.016(1)				
			Na2−N1	2.510(1)										

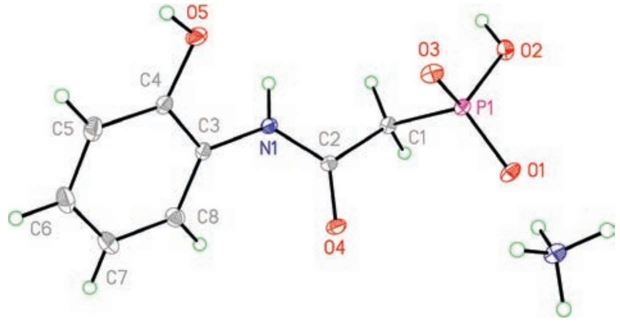
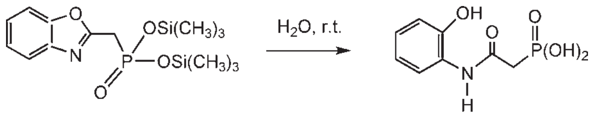


Figure 4. Molecular structure of $[NH_4^+][(HO)(O)_2PCH_2C(O)N(H)(C_6H_4OH)^-]$ **NH_4(7-H)** (20% thermal ellipsoids).

Scheme 2



10 **7-H_2**

(O2···O3, 2.52(1) Å). Additional hydrogen bond D···A approaches in the range 2.75−3.05 Å are listed in the Supporting Information.

The Bronsted acidity of **7-H_2** was evaluated by recording its absorption spectra in aqueous $NaClO_4$ solution as a function of pH, and representative spectra are shown in Figure 1. The protonation constants (p*K*) for **7-H_2**, summarized in Table 1, are much as would be expected from the structure of the ligand, and the values are comparable with those reported for 3-hydroxyphenylphosphonic acid: p*K*'s = 10.03, 7.24, and 1.8.[45] The first p*K* value for **7-H_2** at 10.08 corresponds to deprotonation of the phenolic hydroxyl group, and the remaining two p*K* values, 7.39 and 2.2, are assigned to the deprotonation of the hydroxyl groups of the phosphonic acid fragment. The assignment of the p*K* value of 10.08 for to the phenolic proton is supported by the fact that this protonation equilibrium is accompanied by a large change in the electronic spectrum (Figure 1). This is to be expected since the phenolic hydroxyl is directly attached to the aromatic ring whose $\pi-\pi^*$ transitions are being monitored in Figure 1. The protons of the phosphonic acid group that are involved in the second and third ionization processes are more distant from the aromatic ring, and so, as expected, they produce a much smaller change in the electronic spectrum.

Since we are also interested in having a water-soluble, storable salt form of **6-H_2** and **7-H_2** for subsequent metal coordination chemistry studies, we explored stoichiometric neutralization reactions of these phosphonic acids with NaOH and KOH in mixed MeOH/H_2O solutions and in MeOH. The reactions were performed in a manner analogous to a titration experiment by addition of aqueous base solution (0.1 M) to a MeOH solution of **6-H_2** or **7-H_2** or by combination of the reactants in MeOH solution. The reaction mixtures were stirred at 23 °C, and the products isolated by

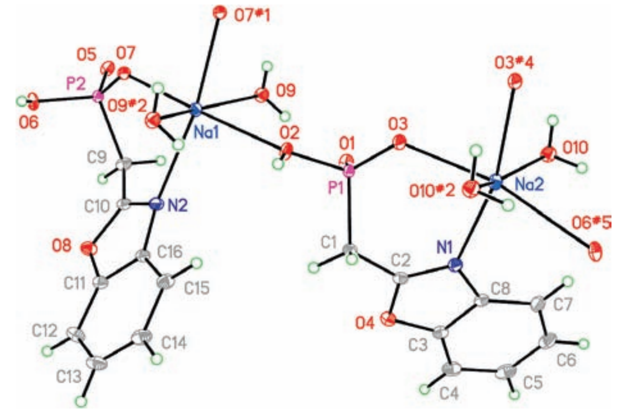


Figure 5. Molecular structure of $Na\{[(HO)(O)_2PCH_2]C_7H_4NO\}\cdot H_2O\}_2$ **[Na(6-H)·H_2O]$_2$** (20% thermal ellipsoids).

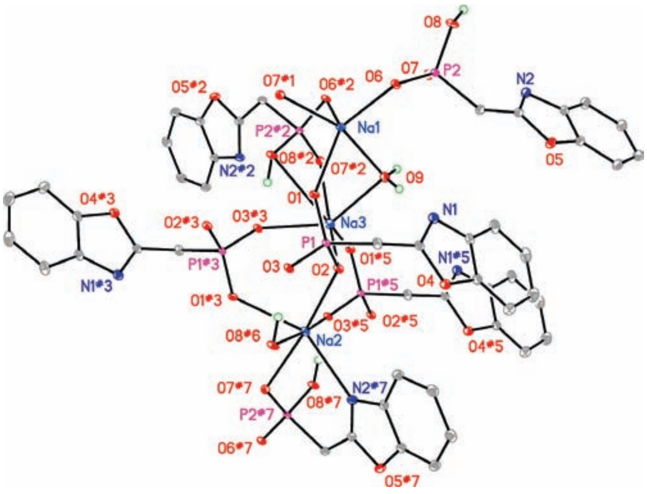


Figure 6. Molecular structure of $Na_3\{[O_3PCH_2]C_7H_4NO\}\{[(HO)(O)_2PCH_2]C_7H_4NO\}$ **[Na_3(6)(6-H)]**.

vacuum evaporation of the solvent followed by recrystallization of the residues in various solvent combinations. Elemental analyses of the residues indicate that the products are not obtained in analytically pure form. This is due in part to the dibasic ionization equilibria, the formation of loose solvates, and the competing ring-opening chemistry. Unfortunately, ^{31}P NMR spectroscopy does not provide a reliable probe for the compositional character of the salts because of the pH dependence of the chemical shifts. The species **(6-H)**$^-$ and **(6)**$^{2-}$ show similar chemical shifts (δ 11−13 ppm) that are concentration and solvent dependent, and these are only slightly upfield from **6-H_2** in DMSO, δ 15.4. Furthermore, the shifts for (**7-H**$^-$) and (**7**$^{2-}$) fall in the same region, δ 12.5−14 ppm. Nonetheless, single crystals of the salts **[Na(6-H)·H_2O]$_2$**, **Na_3(6)(6-H)·H_2O**, **K(6-H)**, **[K_2(6)]$_2$·3H_2O**, and **K(7-H)·DMF** were isolated and structurally characterized by X-ray diffraction methods. The syntheses and structural data for these compounds are discussed sequentially below. Views of the molecules are provided in Figures 5-9, and selected bond length data are listed in Table 3.

For the 1:1 reactions of **6-H_2** with NaOH in a mixed solvent MeOH/H_2O 3−5/1, the compound **Na(6-H)** was obtained in good yield. IR spectroscopic data suggest that (**6-H**$^-$) remains in the closed-benzoxazole ring form, and the single crystal X-ray diffraction analysis confirms this conclusion. The asymmetric

---

(44) A catalogue of structures in the Cambridge Crystallographic Data files provided 870 Na-N-sp^2 bond distances that fall in a range 1.280−3.115 Å with a mean value, 2.480 Å. A similar collection structure files provided 549 K-Nsp^2 bond distances that appear in the range 2.420−3.35 Å with a mean value, 2.844 Å.

(45) Martell, A. E.; Smith, R. M. *Critical Stability Constant Database, No. 46*; National Institute of Science and Technology (NIST): Gaithersburg, MD, 2003.

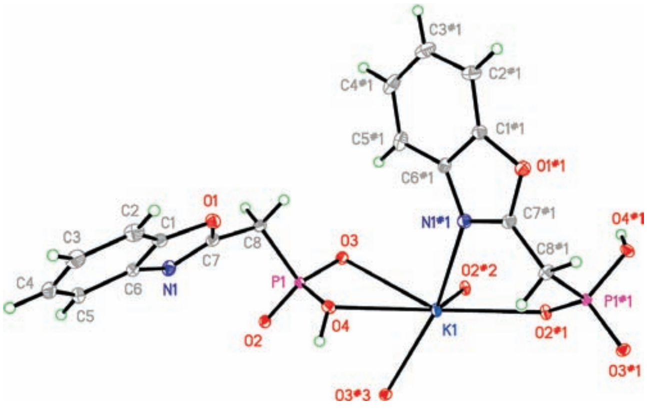


Figure 7. Molecular structure of K{[(HO)(O)$_2$PCH$_2$]C$_7$H$_4$NO} **K(6-H)** (20% thermal ellipsoids).

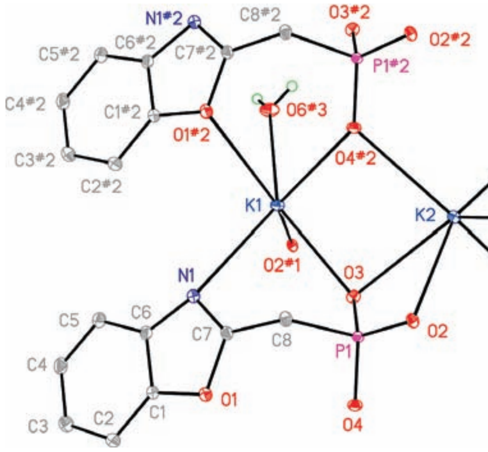


Figure 8. Molecular structure of [K$_2${[O$_3$PCH$_2$]C$_7$H$_4$NO}]$_2$·3H$_2$O **[K$_2$(6)]$_2$·3H$_2$O** (20% thermal ellipsoids).

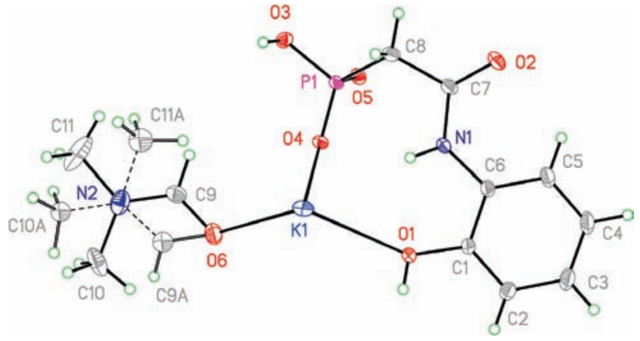


Figure 9. Molecular structure of [K$^+$][(HO)(O)$_2$PCH$_2$C(O)N(H)-(C$_6$H$_4$OH)$^-$], **K(7-H)·DMF** (20% thermal ellipsoids).

unit (Figure 5) contains two Na$^+$ cations, two water molecules, and two bidentate chelating hydrogen phosphonate anions, (**6-H**)$^-$. The chelate interaction employs one phosphonate oxygen atom and the N atom of the intact benzoxazole ring fragment. The unit cell is composed of infinite chains of dimers formed along the *b* axis via Na−O(H)P−O(molecule 1)-Na-(molecule 2) linkages. These chains are weakly associated above and below via hydrogen bonding of water molecules along the *a* axis. The Na$^+$ cations have distorted six coordinate coordination polyhedra with the polyhedron around Na2 more distorted than that around Na1. The vertices of the polyhedra are occupied by one N atom from a benzoxazole fragment, Na1−N2 2.505(1) Å and Na2−N1 2.510(1) Å, and five O atoms contributed by two water molecules, Na1−O9 2.448(1) Å, Na1−O9 (#2) 2.440(1) Å, Na2−O10 2.385(1) Å, Na2−O10 (#2) 2.540(1) Å, two phosphonate groups, Na1−O7 2.319(1) Å, Na1−O7 (#1) 2.328(1) Å, Na2−O3 2.333(1) Å, Na2−O3 (#4) 2.397(1) Å and a bridging P−O(H) group Na1−O2 2.530(1) Å and Na2−O6 (#5) 2.669(1) Å. The Na−N distances are slightly longer than the mean distance, 2.480 Å, derived from a large collection of compounds containing sodium-sp^2-nitrogen atom interactions.[44] The benzoxazole rings are planar with identical related bond lengths in the two ring fragments, and these are little changed from the bond lengths in the parent acid, (**6-H$_2$**). Most notable, the C2−N1and C8−N1 bond lengths, 1.292(2) Å and 1.401(2) Å, are identical to the respective values in the parent acid. The phosphonate groups have an asymmetric tetrahedral geometry with short, sodium coordinated P−O bond lengths, P1−O3 1.487(1) Å and P2−O7 1.486(1) Å, longer, terminal P−O bond lengths P1−O1 1.500(1) Å and P2−O5 1.503(1) Å, and P−O(H) bond lengths P1−O2 1.577(1) Å and P2−O6 1.586(1) Å. The P−O(H) group is also involved in the bridge bond between the monomer units making up the dimer.

The 2:1 reaction of aqueous NaOH solution (0.1 M) with **6-H$_2$** in MeOH was expected to produce **Na$_2$(6)**. This compound may form, but the only material that crystallized was found to be **Na$_3$(6)(6-H)·H$_2$O** in which the deprotonation of **6-H$_2$** is incomplete. The structure (Figure 6) contains three unique Na$^+$ cations, a (benzoxazole-2-ylmethyl) hydrogen phosphonate monoanion, (**6-H$^-$**), a (benzoxazole-2-ylmethyl) phosphonate dianion, (**6^{2-}**), and a water molecule. Each Na$^+$ cation resides in a distorted octahedral coordination environment. In the cases of Na1 and Na3, the polyhedral vertices are all occupied by oxygen atoms while for Na2 there are five oxygen atoms and a nitrogen atom in the vertex positions. The O-atoms surrounding Na1 are provided by an O-atom from one (**6^{2-}**) ligand, Na1−O1, an O-atom from each of two (**6-H$^-$**) anions, Na1−O6 and Na1−O7 #1, two O-atoms from an asymmetric bidentate P, O, O bonded (**6-H$^-$**) anion, Na1−O6 #2 and Na1−O8 #2(H), and an O-atom from a water molecule, Na1−O9, that bridges this unit to Na3. For Na3, the O-atoms are provided by the bridging water molecule O9, two O-atoms from a symmetric bidentate P, O, O bonded (**6-H$^-$**) anion, Na3−O7 #2 and Na3−O8 #2(H), and three O-atoms from three (**6^{2-}**) dianions, Na3−O2, Na3−O3 #3 and Na3 #01 #5. The Na−O (water) bond lengths are quite different: Na1−O9 2.501(2) Å and Na3−O9 2.345(2) Å. The Na−O(P) bond lengths fall in the ranges Na1 2.306(2)−2.413(2) Å (avg. 2.363 Å) and Na3 2.327(2)−2.821(2) Å (avg. 2.485 Å). The Na−O(H)P bond lengths, as expected, are longer: Na1−O8 #2(H) 2.957(2) Å and Na3−O8 #2(H) 2.856(2) Å. The O-atoms coordinated to Na2 originate from P−O groups in four (**6^{2-}**) dianions and a P−O(H) group O-atom in a (**6-H$^-$**) ligand. The last coordination position is provided by the N-atom of a bidentate (**6-H$^-$**) anion. The Na2−N2 distance, 2.586(2) Å, is longer than the value in **[Na(6-H)·H$_2$O]$_2$** suggestive of only a weak sodium-benzoxazole ring N-atom interaction.[44] The range of Na2−O(P) bond lengths is 2.303(2)−2.588(2) Å (avg. 2.430 Å). The benzoxazole ring fragments in (**6^{2-}**) and (**6-H$^-$**) are planar and each phosphorus atom is pseudo-tetrahedral. The P−O and P−C bond lengths in the (**6-H$^-$**) anion of **Na$_3$(6)(6-H)·H$_2$O** are similar to those found in the 1:1 **[Na(6-H)·H$_2$O]$_2$** structure: P2−O6 1.504(2) Å, P2−O7 1.497(2) Å, P2−O8(11) 1.580(2) Å and P2−C9 1.818(2) Å.

There are distinct changes, however, in the (**6^{2-}**) fragment. Two of the P−O bond lengths are essentially identical to the shorter distances in (**6-H$^-$**): P1−O1 1.514(2) Å and P1−O2 1.508(2) Å, but the third P−O bond length, P1−O3 1.548(2) Å, is much shorter as a result of the loss of the proton. Lastly, the P1−C1 bond length, 1.861(2) Å, is significantly elongated compared to P2−C9.

Stoichiometric 1:1 reactions of KOH and **6-H$_2$** in MeOH/H$_2$O mixtures and in pure MeOH, performed by slow combination of the reactants, produce solid residues that display a single ^{31}P NMR resonance at δ 12.4 in MeOH. Unfortunately, single crystals were not obtained from these samples. The 2:1 combinations of KOH and **6-H$_2$** were then explored in MeOH/H$_2$O solvent mixtures. Solid residues were obtained following solvent evaporation, and these were dissolved in MeOH/CH$_3$CN solution, filtered, and allowed to slowly evaporate. Crystals were not obtained; however, extraction of the solids with DMF led to partial dissolution. The soluble fraction was evaporated to dryness, recrystallized from MeOH/DMF mixtures and single crystals were obtained. X-ray diffraction analysis revealed that this compound is the salt **K(6-H)**. A view of the environment around K1 is shown in Figure 7. The asymmetric unit contains a K$^+$ cation and a **6-H$^-$** anion and the K$^+$ cation resides in a distorted octahedral coordination environment with vertices occupied by five oxygen atoms (O3, O4, O2 #1, O2 #2, O3 #3) and a nitrogen atom (N1 #1). The O2 #1 and N1 #1 atoms are provided by a molecule of **6-H$^-$** that binds in a bidentate fashion; the K1−O2 #1 bond length, 2.6995(7) Å, is the shortest of the K-donor atom bond lengths. The K1−N1 #1 bond length is 2.8874(9) Å.[44] A second **6-H$^-$** anion bonds to the K$^+$ as an asymmetric bidentate phosphonate with K1−O3 2.8961(7) Å and K1−O4 2.850(8) Å. The remaining two O-atoms in the coordination sphere are O2 #2 and O3 #3, with K−O bond lengths of 2.7228(8) Å and 2.8453(8) Å, respectively. The P-atom geometries in the benzoxazole fragments are distorted tetrahedral with P−O bond lengths in the range 1.4918(7)−1.5678(7) Å. The benzoxazole rings are planar, and the bond lengths are similar to those in **[Na(6-H)·H$_2$O]$_2$**.

The DMF insoluble fraction from the 2:1 KOH/**6-H$_2$** reaction was dissolved in hot MeOH, and the solution allowed to slowly cool. This provided single crystals of a second complex, and X-ray diffraction analysis revealed the structure of the expected 2:1 potassium complex, **[K$_2$(6)]$_2$·3H$_2$O**. A view of the molecule is shown in Figure 8. The asymmetric unit contains two K$^+$ cations, one phosphonate dianion (**6^{2-}**), and 11/2 water molecules. Each K$^+$ can be considered to reside in a highly distorted octahedral coordination environment in which the vertices for K1 are N1, O3, O1 #2, O4 #2, O6 #3, and O2 #1 and for K2 are O2, O3, O4 #2, O2 #4, O3 #5, and O5 #6. The range of K−O bond lengths involving K1, 2.676(9)−3.105(9) Å (avg. 2.828 Å) is slightly greater than the range of K−O bond lengths around K2: 2.714(9)−2.944(9) Å (avg. 2.721 Å). The K1−N1 bond length is fairly long, 3.016(9) Å, but still within the range observed in a collection of structures containing K-Nsp^2 interactions.[44] The longest K1−O bond length, K1−O6 #3, 3.105(9) Å, involves a potassium-water interaction. If this water is removed from the coordination sphere, leaving a five coordinate K1, then the range and average K−O distances about K1 and K2 become nearly identical. The six nearest neighbor atoms around K1 are provided by one bidentate N, O bound (**6^{2-}**) dianion (N1 and O3), one bidentate O, O bound (**6^{2-}**) dianion (O1 #2 and O4 #2), one O bound (**6^{2-}**) dianion, and a water molecule. It is noted that the benzoxazole ring O-atom, which is normally coordination silent in complexes formed with transition metal and lanthanide cations, is 3.105(1) Å from a K$^+$ cation. This may indicate a very weak K−O$_{\text{ring}}$ interaction. The nearest neighbors around K2 are provided by one bidentate phosphonate ligand (O2 and O3), one water molecule, and monodentate interactions with three additional (**6^{2-}**) dianions.

During the course of the studies of the KOH/**6-H$_2$** neutralization reactions it was noted that combination of the reagents under more dilute conditions (final solution pH ~4) led to a crystalline solid following recrystallization from DMF. Subsequent single crystal X-ray diffraction analysis revealed formation of another salt, **K(7-H)·DMF**. A view of the molecule is shown in Figure 9. The starting (benzoxazol-2-ylmethyl)phosphonic acid **6-H$_2$** has undergone ring-opening in a fashion noted earlier, vide supra. The K$^+$ can be considered to reside in a distorted monocapped trigonal prismatic coordination polyhedron. The trigonal face positions are occupied by the oxygen atoms O1(H) (K1−O1 3.180(2) Å), O1#1(H) (K1−O1#1 3.170(2) Å), O4(P) (K1-O4 2.762(2) Å) and O6 #1(K1−O6 #1 2.750(2) Å). The O6 and O6 #1 atoms originate from the disordered DMF solvent molecules. The seventh O atom, O3#2 (K1−O3#2 2.831(2) Å), belongs to a P−O(H) group in a third molecule of (**7-H$^-$**). The relatively long K1−O1 and K1−O1 #1 distances are consistent with the phenol group acting only as a very weak donor toward the potassium cation.

The lanthanide ion coordination chemistry of **6-H$_2$** and **7-H$_2$** is of interest, and numerous attempts were made to isolate and crystallize 1:1 and 2:1 ligand/Ln(III) complexes. Although it is apparent that complexes form, none were obtained analytically pure or as X-ray diffraction quality single crystals. However, titration of 1:1 mixtures of **7-H$_2$** and La(III), Nd(III), and Gd(III) in 0.1 M NaClO$_4$ solution as a function of pH were performed, and complex formation was monitored by UV-vis spectrophotometry (Figure 2). The spectra resemble those obtained from the free ligand alone (Figure 1). In particular, it is observed that the first protonation constant of **7-H$_2$**, in the presence of Ln(III) ions, is essentially unchanged. Therefore, it is concluded that the phenolic oxygen atom is probably not coordinating or only weakly coordinating to the Ln(III) ions. This is consistent with the structure of K(7-H)·DMF described above. In contrast, the equilibrium corresponding to the second protonation constant (pK_2) of the ligand is moved to lower pH as a result of competition between the proton and the metal ion for the anionic form of the ligand. From these equilibria, the formation constants were calculated, and the log $K_{(\text{MLH})}$ values are summarized in Table 1.[21] A continuous variation analysis (Job's method) was also performed by varying the ratio of La^{3+} to **7-H$_2$** at pH 6.0 with$\{[\text{La}^{3+}] + [\text{L}]\} = 2 \times 10^{-5}$ M, and this confirmed the proposed 1:1 metal/ligand complex stoichiometry. It is of interest that the log $K_{(\text{MLH})}$ values for the formation of the Ln(LH)$^{+1}$ complexes (LH^{2-} = **7^{2-}**) are very similar or decrease slightly going from La(III) to Gd(III). This is rather unusual since the stability of most lanthanide complexes increase significantly progressing from the lighter, larger ions to the heavier, smaller ions.[45]

Since we were unable to grow single crystals of Ln(III) complexes containing **7-H$^-$** or **7^{2-}**, one can only speculate on the structures of complexes based upon related systems.

For example, lanthanum(III) complexes with phenylphosphonic acid and benzylphosphonic acid, [ArP(O)(OH)$_2$], have been isolated and structurally characterized.[46] The complexes, La[O$_3$PAr][O$_2$(HO)PAr], contain both a dianionic ligand and a monoanionic ligand each bonded in a bidentate mode to La(III) through two of the phosphonic acid oxygen atoms. This results in four-membered La−O−P−O chelate rings. A rule of ligand design[47] indicates that four-membered chelate rings have a minimum steric strain with the largest metal ions. One could thus speculate that the small change in log *K* from La(III) to Gd(III) reflects a balancing of decreasing metal ion size and increasing steric requirements of the four-membered chelate ring formed by the anionic ligand. As mentioned above, the log *K* values obtained for the Ln(III) ions with **7-H$_2$** (Table 1) suggest that the phenolic group of the ligand is not coordinated to the metal ion, or at best is only weakly coordinated. This suggestion was examined further for a 1:1 complex fragment, [La(**7**)$^{+1}$], by MM (molecular mechanics) calculation[48] using the program HyperChem.[49] Such calculations using the default MM parameters, which include parameters for La(III), indicate a very high strain structure if the phenolic oxygen is coordinated to the Ln(III) ion. This is not unexpected as such coordination would involve formation of an energetically unfavorable 7-membered chelate ring, requiring considerable distortion of the **7-H$_2$** ligand. The calculated low strain structure generated by MM calculation formed with a non-coordinating and protonated phenolate group is shown in Figure 10. This structure features an asymmetric tripodal chelate interaction on La(III) by a **7**$^{2-}$ ligand binding through two La−O−P interactions and a La−O=C amide bond. Completion of charge neutralization might occur with a **7-H**$^-$ ligand (bound or unbound with La(III)) or by an appropriate simple anion, for example, ClO$_4^-$ or NO$_3^-$. The inner sphere coordination polyhedron of the computed cationic species was completed by addition of water molecules. Lastly, it is noted that attempts to measure log $K_{(MLH)}$ for the formation of the Lu(III) complex with **7-H$_2$** were prevented by precipitation of Lu(OH)$_3$ before significant complex-formation had occurred. This supports the idea that log $K_{(MLH)}$ for Lu(III) with **7-H$_2$** is even lower than for the larger Ln(III) ions such as La(III), Nd(III), and Gd(III).

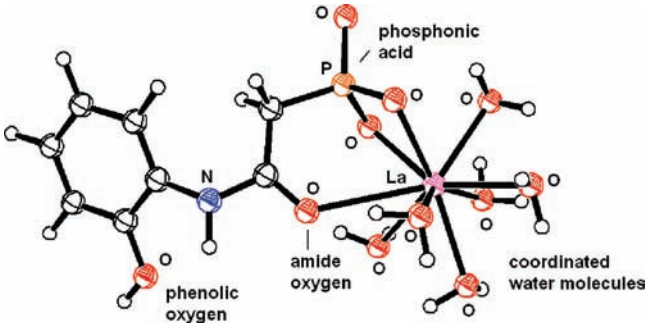


Figure 10. Proposed structure of a 1:1 complex [La(**7**)]$^{+1}$ {[LLH]$^{+1}$ in Table1}.

Conclusion

A convenient three step synthesis for the (benzoxazol-2-yl methyl)phosphonic acid, **6-H$_2$**, has been developed, and its subsequent ring-opening to give [(2-hydroxyphenylcarbamoyl) methyl]phosphonic acid, **7-H$_2$**, has been observed. Both phosphonic acids provide interesting possibilities as multifunctional ligands toward p-, d-, and f-block metal cations. It was desired to have well-defined Group 1 salts of **6-H$_2$** as reagents for metathetical syntheses of metal complexes; therefore, the neutralization reactions of **6-H$_2$** with NaOH and KOH were examined. These reactions revealed that the anions (**6-H**$^-$) and (**6**$^{2-}$) form complicated extended structures with Na$^+$ and K$^+$ cations. Further work is in progress that will reveal the coordination features of the phosphonates in complexes formed with alkaline earth, heavy p-block and f-block cations.

Supporting Information Available: Selected NMR spectra for **7-H$_2$** and CIF files for the crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(46) Wang, R.-C.; Zhang, Y.; Hu, H.; Frausto, R. R.; Clearfield, A. *Chem. Mater*. **1992**, *4*, 864.

(47) Hancock, R. D.; Martell, A. E. *Chem. Rev*. **1989**, *89*, 1875.

(48) Hancock, R. D. *Acc. Chem. Res*. **1990**, *26*, 875.

(49) *HyperChem program*, version 7.5; Hypercube, Inc.: Waterloo, Ontario, N2l 3X2, Canada.