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The structures of phenylphosphonic-acid-mono-(2-hydroxyphenyl)ester and phenylphosphonic-acid-mono-(3-hydroxynaphthalen-2-yl)ester – A combined experimental and theoretical study

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ABSTRACT

Two ester derivatives of phenylphosphonic acid were prepared from vicinal aromatic diols and phenylphosphonic dichloride in one-step procedures. The products were characterized by means of multi-nuclear NMR spectroscopy (¹H, ¹³C, ³¹P), mass spectrometry, elemental analysis, UV-Vis spectroscopy, and melting point as well as vibrational spectroscopy. Their molecular structures were determined by single crystal X-ray diffraction and found to be open-chain half-esters of the respective diols. Intermolecular contacts and hydrogen bonding were analyzed. Born-Haber-cycles based on DFT calculations were conducted for the partial hydrolysis of the assumed cyclic phenylphosphonates to assess the reaction energies for the partial P-O-C cleavage of the chelate rings. The observed partial hydrolysis was rationalized on grounds of molecular orbital considerations. Experimental data were correlated to DFT data. The bonding situation of the two compounds was described by means of NBO analyses.

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1. Introduction

Phosphorus plays a key-role in biochemistry as an important part of the deoxyribonucleic acid, adenosine triphosphate and many other compounds in living organisms. The metabolism of nutrients involves several phosphorylation steps [1]. Founding on the work of Westheimer and co-workers [2,3], the possible intermediary pentavalency of phosphorus during phosphotransferyl reactions has been a vivid point of discussion in the literature [4,5]. Recently, the structure of an intermediate from a phosphoryl transfer reaction containing a pentacoordinate phosphorus compound was elucidated by means of a single crystal X-ray study [6]. Being ubiquitous in cellular environments, carbohydrates appear as tempting bonding partners for pentavalent phosphorus. However, sound proof for the structure of such compounds based on data from single crystal X-ray studies was lacking completely in the literature up to several years ago. Important progress was made by Holmes and co-workers upon the integration of phosphorus into a macrocyclic framework, and the structures of several carbohydrate-supported λ^5 -phosphanes were elucidated [7–9].

Considerable work was done on the field of the "precursors" of λ^5 -phosphanes – i.e. the phosphates themselves – where structural

information about cyclic phosphates of nucleosides and some carbohydrate derivatives is well-established [10-14]. Several studies concerning the hydrolytic stability and cleavage of the cyclic motif at different pH-values were conducted [15].

The formation of cyclic esters has also been reported for phenylphosphonic acid. Yet, structural information about this class of molecules is scant and has been focused on the question of the chelate rings' conformations [16-21]. Only few work has been done on the field of hydrolytic stability of these compounds, except for the ethane-1,2-diol-derived phenylphosphonate [22].

An interesting behaviour has been claimed for the cyclic phenylphosphonates derived from the aromatic diols benzene-1,2-diol [23] and naphthalene-2,3-diol [24]. These were reported to undergo P-O-C-cleavage of the chelate ring and the formation of open-chain half-esters upon contact with air or even prolonged storage in a desiccator. The confirmation of this heightened sensitivity to moisture and the structures of the respective reaction products were solemnly based on the acidic behaviour of the compound and the products of acidic hydrolysis. A thorough characterization of these supposed half-esters was not conducted, the only physical constant reported being the melting points for both compounds.

Since this uncertainty about the molecular structures of these two compounds is an unacceptable starting point for a systematic study about the hydrolytic stability of cyclic phenylphosphonates,



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the formation of these half-esters was re-investigated and their molecular structures were determined.

2. Experimental

2.1. Reagents and instrumentation

Phenylphosphonic dichloride (Merck, synthesis grade), pyrocatechol (UNILAB, 98.5%) and 2,3-dihydroxynaphthalene (Aldrich, 98.0%) were used as received without further purification. Toluene (Merck, analytical grade) and triethylamine (Met-U-Ed Laboratory Supplies, 99%) were dried over molecular sieves (4 Å) and potassium hydroxide pellets, respectively. All operations were carried out under an atmosphere of dry nitrogen applying standard Schlenk techniques. A detailed description of the experimental procedures is given due to the partial scarce descriptions in the literature.

¹H and ¹³C NMR spectra were recorded on a Bruker Ultrashield 400 Plus spectrometer at 25 °C at 400 MHz and 101 MHz, respectively, and are referenced to internal TMS or the solvent residual peak of the deuterated solvent [25]. ³¹P NMR spectra were recorded on a Bruker Ultrashield 400 Plus spectrometer at 25 °C at 109 MHz and are referenced to external H₃PO₄ (w = 85% in water). IR spectra were recorded on a Bruker Platinum ATR unit. Mass spectra were obtained on a Waters Synapt G2 instrument. Elemental analyses were conducted on a Vario Elementar Microcube ELIII system. UV–Vis spectra were recorded on a Perkin Elmer Lambda 35 spectrometer. Melting points were determined on a Stuart Melting Point SMP30 apparatus and are uncorrected.

2.2. DFT calculations and NBO analyses

The structures of **1** and **2** were optimized with GAUSSIAN 09 [26] on the B3LYP/6-311++G(2d,p) level of theory with an ultrafine integration grid and very tight convergence criteria as singlet molecules under exclusion of symmetry in point group C_1 applying a solvent model for chloroform. The starting geometry was obtained by means of GaussView [27]. Frequency analyses were performed on the optimized structures to ensure that these represent minima on the global electronic potential hypersurface. Optimization of the cyclic phenylphosphonates as well as the other compounds needed for calculations in the Born-Haber-cycles were treated in the same manner. Calculations of NMR shifts were conducted on the PBE1PBE/6-311++G(2d,p) level of theory using the GIAO method [28] based on the optimized structures. A solvent model for chloroform was used in this step as well. The analysis and visualization of the molecular orbitals was conducted by the Avogardo [29] as well as the CHEMCRAFT program suite [30].

2.3. Crystallography

The diffraction studies on single crystals were performed at 200(2) K on a Bruker Kappa APEX-II CCD diffractometer (Mo K α , $\lambda = 0.71073$ Å). Structure solutions and refinement procedures were conducted by means of the SHELX program suite [31]. Crystallographic details of the structures are summarized in Table 1. Carbon-bound hydrogen atoms were calculated using the riding-model approximation and were included in the refinement with their $U_{\rm H}$ values set to $1.2U_{\rm eq}(\rm C)$. The hydrogen atoms of the hydro-xyl groups were located on a DFM and refined freely. Metrical parameters discussed for the crystal structures were obtained using PLATON [32], graphical presentations were prepared using Mercury [33] and ORTEP-III [34].

Table 1

Crystallographic data for the structure determinations of 1 and 2.

	1	2
Chemical formula	C ₁₂ H ₁₁ O ₄ P	C ₁₆ H ₁₃ O ₄ P
$M_{\rm r}/{ m g}~{ m mol}^{-1}$	250.18	300.23
Crystal system	orthorhombic	orthorhombic
Spacegroup	Pbca	P2 ₁ 2 ₁ 2 ₁
a (Å)	7.6833(2)	5.3893(2)
b (Å)	16.5277(3)	12.4298(4)
<i>c</i> (Å)	17.7383(3)	20.8061(8)
$V(Å^3)$	2252.54(8)	1393.76(9)
Ζ	8	4
$ ho$ (g cm $^{-3}$)	1.475	1.431
μ (mm ⁻¹)	0.243	0.210
Crystal size (mm)	$0.422\times0.119\times0.117$	$0.535\times0.172\times0.071$
θ -Range (°)	2.30-28.36	1.96-28.31
Reflections for metrics	9207	8002
Absorption correction	numerical	numerical
Transmission factors	0.9169-1.0000	0.9422-1.0000
Measured reflections	20228	13691
Independent reflections	2812	3450
R _{int}	0.0210	0.0180
Mean $\sigma(I)/I$	0.0134	0.0182
Reflections with $I \ge 2\sigma(I)$	2461	3249
x, y (weighting scheme)	0.0479, 0.7459	0.0368, 0.2618
Flack parameter	-	-0.03(7)
Parameter	162	198
Restraints	0	0
$R(F_{\rm obs})$	0.0298	0.0281
$R_{\rm w}(F^2)$	0.0863	0.0705
S	1.069	1.068
Shift/error _{max}	0.001	0.001
Maximum residual	0.330	0.268
density (e Å ⁻³)		
Minimum residual	-0.357	-0.240
density (e Å ⁻³)		

2.4. Preparation of phenylphosphonic-acid-mono-(2-hydroxy-phenyl)ester, PhPO(OH)OC₆H₄OH ($\mathbf{1}$)

In a three-necked round-bottomed flask (500 mL) equipped with a dropping funnel and a pressure-equalizing valve benzene-1,2-diol (2.75 g, 25.0 mmol) and triethylamine (6.95 mL, 5.06 g, 50.0 mmol) were dissolved in toluene (100 mL). Under external cooling with an ice-bath phenylphosphonic acid dichloride (3.51 mL, 4.87 g, 25.0 mmol) was added with vigorous stirring over the course of 30 min. In a slightly exothermic reaction the precipitation of a colourless solid was observed. After completion of addition, stirring was continued at room temperature overnight. The reaction mixture was filtered and the colourless filtrate was evaporated to dryness on a rotary evaporator. A colourless oil was obtained that solidified upon storage in an open flask at room temperature overnight, yield 5.33 g, 21.3 mmol, 85.2%. Crystals suitable for the diffraction study were obtained upon recrystallization from boiling toluene.

¹H NMR (DMSO-d₆): δ = 11.43 (s, 1 H, OH), 9.06 (s, 1 H, OH), 7.85–7.76 (m, 2 H, H_{ar}), 7.59–7.39 (m, 3 H, H_{ar}), 7.13–7.09 (m, 1 H, H_{ar}), 6.94–6.83 (m, 2 H, H_{ar}), 6.71–6.64 (m, 1 H, H_{ar}) ppm. ¹³C NMR (DMSO-d₆): δ = 148.5 (d, *J* = 4.8 Hz), 139.0 (d, *J* = 7.0 Hz), 131.9 (d, *J* = 3.2 Hz), 131.4 (d, *J* = 10.0 Hz), 128.3 (d, *J* = 14.7 Hz), 124.9 (d, *J* = 1.2 Hz), 121.5 (d, *J* = 3.2 Hz), 119.1 (d, *J* = 1.2 Hz), 117.3, 113.0 (d, *J* = 10.3 Hz) ppm. ³¹P NMR (DMSO-d₆): δ = 14 ppm. Elemental analysis found (calculated for C₁₂H₁₁O₄P): C, 57.81% (57.61%); H, 4.52% (4.43%). ICP-AES, found (calculated for C₁₂H₁₁O₄P): P, 12.11% (12.38%). HRMS (ESI⁺): *m/z* = found 251.0473 (calculated for C₁₂H₁₂O₄P⁺₁: 251.0473). HRMS (ESI⁻): *m/ z* = found 249.0316 (calculated for C₁₂H₁₀O₄P₁⁻: 249.0317). IR (neat): *v* = 3367 (m, OH), 3069 (w, CH), 3055 (w, CH), 3029 (w, CH), 1602 (m), 1591 (m), 1494 (s), 1467 (m), 1438 (m), 1395 (w), 1351 (w), 1316 (w), 1290 (w), 1265 (m), 1207 (s), 1182 (m), 1144 (s), 1098 (s), 1072 (m), 1031 (m), 1005 (m), 995 (m), 987 (s), 942 (m), 924 (s), 877 (m), 828 (m), 761 (m), 750 (s), 721 (m), 700 (m), 690 (m), 617 (w), 595 (m), 568 (m), 554 (m), 526 (s), 484 (m), 459 (m), 426 (m) cm⁻¹. UV–Vis (acetonitrile): $\lambda_{max} = 211, 213, 215,$ 267, 272 nm; UV–Vis (cyclohexane): no distinct absorption maxima in the range between 195 and 1100 nm. Melting point: 119– 123 °C (lit.: 123–124 °C [23]).

2.5. Preparation of phenylphosphonic-acid-mono-(3-hydroxynaphthalene-2-yl)ester, PhPO(OH)OC₁₀H₆OH (**2**)

In a three-necked round-bottomed flask (500 mL) equipped with a dropping funnel and a pressure-equalizing valve naphthalene-2,3-diol (4.00 g, 25.0 mmol) and triethylamine (6.95 mL, 5.06 g, 50.0 mmol) were dissolved in toluene (100 mL). Under external cooling with an ice-bath phenylphosphonic acid dichloride (3.51 mL, 4.87 g, 25.0 mmol) was added with vigorous stirring over the course of 30 min. In a slightly exothermic reaction the precipitation of a colourless solid was observed. After completion of addition, stirring was continued at room temperature overnight. The reaction mixture was filtered and stored in an open flask at ambient conditions over night. A colourless crystalline solid precipitated from the filtrate, yield 5.28 g, 17.6 mmol, 70.4%.

¹H NMR (DMSO-d₆): δ = 9.07 (s, 1 H, OH), 8.25 (s, 1 H, OH), 7.90– 7.81 (m, 2 H, H_{ar}), 7.67–7.61 (m, 3 H, H_{ar}), 7.58–7.43 (m, 3 H, H_{ar}), 7.35–7.21 (m, 3 H, H_{ar}) ppm. ¹³C NMR (DMSO-d₆): δ = 148.3 (d, J = 4.9 Hz), 140.5 (d, J = 7.3 Hz), 132.1, 131.9 (d, J = 2.9 Hz), 131.4 (d, J = 10.1 Hz), 131.2, 129.4, 128.3 (d, J = 14.8 Hz), 127.5 (d, I = 0.8 Hz), 126.8, 125.4 (d, I = 27.0 Hz), 123.3, 117.8 (d, I = 3.6 Hz), 111.0 ppm. ³¹P NMR (DMSO-d₆): δ = 14 ppm. Elemental analysis found (calculated for C₁₆H₁₃O₄P): C 64.24% (64.00%), H 4.28% (4.36%). ICP-AES, found (calculated for C₁₆H₁₃O₄P): P 10.41% (10.32%). HRMS (ESI⁻): *m*/*z* = found 299.0480 (calculated for $C_{16}H_{12}O_4P^-$: 299.0473). IR (neat): v = 3387 (m, OH), 3062 (w, CH), 2962 (w, CH), 1638 (w), 1594 (w), 1510 (s), 1471 (s), 1458 (m), 1438 (m), 1400 (w), 1366 (w), 1348 (w), 1320 (w), 1273 (m), 1260 (m), 1205 (m), 1193 (m), 1168 (m), 1135 (s), 1097 (s), 1071 (m), 1029 (m), 1001 (s), 986 (s), 949 (m), 922 (m), 892 (s), 880 (m), 867 (s), 808 (m), 756 (m), 744 (s), 718 (m), 691 (m), 655 (m), 619 (m), 590 (m), 550 (m), 525 (s), 496 (s), 473 (s), 445 (m), 423 (m), 413 (s), 357 (w) cm^{-1} . UV–Vis (acetonitrile): λ_{max} = 266, 272, 313, 327 nm; UV–Vis (cyclohexane): λ_{max} = 213 nm. Melting point: 139–142 °C (lit: 145–147 °C [24]).

3. Results and discussion

3.1. Crystal structure analysis

Phenylphosphonic-acid-mono-(2-hydroxy-phenyl)ester (1) was first prepared by Berlin and Nagabhushanam upon the attempted synthesis of the cyclic ester of phenylphosphonic acid and benzene-1,2-diol. According to an infrared analysis conducted immediately after the workup the desired cyclic ester was claimed to have been isolated by the authors. The compound was then reported to undergo hydrolytic cleavage of the chelate ring even upon storage in a desiccator [23]. A similar behaviour was observed by these authors for the naphthalene-2,3-diol-derived phenylphosphonate **2** (*cf.* Scheme 1) [24].

The results of a single crystal X-ray analysis on the solidified compound, **1**, obtained after reacting phenylphosphonic dichloride and benzene-1,2-diol confirmed the findings by Berlin and Nagabhushanam [23]. In the molecule, a benzene-1,2-diol moiety acts as a monodentate ligand and is esterified with phenylphosphonic acid by only one of its hydroxyl groups (Fig. 1). The second

hydroxyl group on the aromatic diol as well as the hydroxyl group on phosphorus remain unaffected.

The coordination polyhedron around the central atom can be described as tetrahedral. P–O bond lengths for all oxygen atoms are found in the range that was reported for two comparable monoesters derived from phenol [35] and ethanol [36] and substituted phenylphosphonic acids. The values are also in good agreement with the most common values reported for other derivatives of phenylphosphonic acids whose metrical parameters have been deposited with the Cambridge Structural Database [37].

The least-squares planes through the aromatic moieties enclose an angle of approximately 57°. Hydrogen bonding is a prominent feature in the crystal structure of **1**. The hydroxyl groups furnish the formation of infinite strands along [100]. In terms of graph-set analysis [38,39], two different patterns were observed. On the unary level, two antidromic chains intercross at the - formally - doublebonded oxygen atom on phosphorus. The pattern exclusively supported by the hydroxyl group of the aromatic diol necessitates a $C_1^1(7)$ descriptor while the chain involving the phosphorus-bonded hydroxyl groups can be described by means of a $C_1^1(4)$ descriptor. On the binary level, these chains form rings with a $R_2^2(11)$ descriptor. In addition, three C–H... π contacts stemming from two hydrogen atoms on the pyrocatechol's aromatic system and one hydrogen atom of the phosphorus-bonded phenyl group as donors and both aromatic systems as acceptors can be observed. π -Stacking does not contribute to the stabilization of the crystal structure as the shortest intercentroid distance between two centers of gravity was measured at 4.6299(8) Å in between the two different aromatic systems in neighbouring molecules.

An X-ray analysis of the reaction product **2** obtained from phenylphosphonic acid dichloride and naphthalene-2,3-diol yielded a similar picture for the coordination environment around phosphorus (Fig. 2). P–O bond lengths are in good agreement with the values apparent in **1**. The phosphorus atom is present in the center of a tetrahedral coordination polyhedron.

The least-squares planes through the aromatic moieties enclose an angle slightly below 45°. The hydrogen bonding system in the crystal structure of **2** slightly differs from the one observed in the crystal structure of 1. In the naphthalene-2,3-diol-supported phenyphosphonate, two homodromic chains were observed with a $C_1^{1}(4)$ and a $C_1^1(7)$ descriptor on the unitary level of graph-set analysis[38,39]. Both chains intercross at the - formally - double-bonded oxygen atom on phosphorus and furnish the formation of cyclic patterns with a $R_3^2(13)$ descriptor on the binary level. In total, strands along [100] are formed. In addition, two C-H...O contacts whose range falls by more than 0.1 Å below the sum of van-der-Waals radii of the atoms participating in them can be observed in the crystal structure of 2. The latter are exclusively supported by one of the hydrogen atoms in ortho and in meta position on the phosphorus-bonded phenyl group and exclusively apply the oxygen atom of the free hydroxyl group of the aromatic diol as acceptor. No C–H... π contacts are observed, however, the shortest intercentroid distance between two centers of gravity found in between the two different ring systems of the aromatic diol in neighbouring molecules - is measured at a slightly shorter value than in **1**, at 4.5491(12) Å.

3.2. Physical and spectroscopic properties

¹³C NMR spectra of crystals of **1** and **2** dissolved in DMSO- d_6 show the expected number of resonances in the aromatic region. ¹³C-³¹P coupling is observed for most of the resonances. ¹H NMR spectra of both compounds exhibit signals indicative for the presence of acidic hydroxyl groups. For both compounds, a ³¹P resonance at +14 ppm is detected. IR spectra confirm the presence of free hydroxyl groups.



Scheme 1. Synthetic pathways for compound 1 and 2.



Fig. 1. Structure of PhPO(OH)O-C₆H₄OH (**1**) (50% probability ellipsoids). Selected individual bond lengths (in Å), angles and torsional angles (in °): P1–O1 1.5398(9), P1–O2 1.4884(9), P1–O21 1.5890(9), P1–C11 1.7791(12), O2–P1–O1 115.35(5), O2–P1–O21 106.69(5), O1–P1–O21 104.34(5), O2–P1–C11 112.04(6), O1–P1–C11 108.39(6), O21–P1–C11 109.65(5), C11–P1–O21–C21 –44.71(10).



Fig. 2. Structure of PhPO(OH)O-C₁₀H₆OH (**2**) (50% probability ellipsoids). Selected individual bond lengths (in Å), angles and torsional angles (in °): P1–O1 1.5314(11), P1–O2 1.4935(10), P1–O21 1.6041(10), P1–C11 1.7744(13), O2–P1–O1 116.29(6), O2–P1–O21 110.41(6), O1–P1–O21 102.56(6), O2–P1–C11 11.94(6), O1–P1–C11 108.38(6), C11–P1–O21–C21 69.81(11).

Both compounds were found to be strong acids in water. The pH value for a saturated aqueous solution of **1** was measured at approximately 1.0, the corresponding value for **2** was found at around 1.5 (both determinations were observed by means of a colour-changing indicator stick). The solubility of **1** – where a concentration slightly below 0.1 m can be obtained – in water is markedly higher than that of **2**.

3.3. ³¹P NMR study

To assess the course of the reaction and the role the absence and presence of water plays, the reaction between phenylphosphonic acid dichloride and benzene-1,2-diol was repeated as described in the experimental section, however, under inert conditions, i.e. a blanket of dry nitrogen in flame-dried glassware and the use of scrupulously dried solvents (toluene) and reagents (triethylamine). ³¹P NMR spectra were recorded on samples taken directly from the reaction mixture as well as an aliquot of the reaction mixture spiked with several drops of water in the NMR sample tube. While the anhydrous sample showed a single resonance at 48 ppm, the sample that was mixed with several drops of water lacked this signal entirely. Instead, a resonance at 30 ppm was recorded in this case. The latter is in agreement with ³¹P NMR spectra of compound 1 recorded in the same solvent. The findings for the reaction mixture remain unchanged over the course of several weeks of storage at room temperature if inert conditions are maintained. A sample of the reaction mixture stored in a beaker with contact to the atmosphere, however, shows the disappearance of the resonance at 48 ppm and the emergence of the resonance at 30 ppm within 24 h. Therefore, it can be concluded that, as an intermediate of the reaction described in the experimental section, a phosphorus compound sensitive to hydrolysis is formed that undergoes hydrolytic cleavage to yield compound **1**. Although no parallel experimental sequence was conducted for the reaction between naphthalin-2,3-diol and phenylphosphonic dichloride under inert conditions as just described for benzene-1,2-diol, a corresponding behaviour ought to be expected on grounds of the similar openchain reaction product 2.

3.4. Quantum chemical calculations

3.4.1. Geometric parameters and NMR shifts

Starting from a geometry whose atomic coordinates resemble the structures obtained by X-ray diffraction, the optimized structures of **1** and **2** were found to closely maintain the found conformations in the solid state. The geometric parameters calculated for **1** and **2** are in good agreement with the experimentally-found values (*cf.* Table 2). The slight deviations apparent can be rationalized by taking into account packing effects in the crystal that are not accounted for by the DFT calculations applying a solvent model.

The optimized structures were analyzed by computational methods with regards to their isotropic NMR shielding tensors at the PBE1PBE/6-311++G(2d,p) level of theory applying a solvent model for chloroform. The calculated NMR shifts for phosphorus were found at +16 ppm for compound **1** and at +17 ppm for compound **2**. Taking into account the marked solvent effect apparent in ³¹P NMR spectroscopy, these values are in good agreement with the ones found experimentally for both compounds dissolved in DMSO-d₆ (+14 ppm).

3.4.2. Bonding situation

To assess the bonding situation in 1 and 2 – especially with regard to the P=O bond – NBO analyses were conducted for both

Table 2Comparison of selected averaged experimental bond lengths and angles (XRD) in 1and 2 with the corresponding parameters calculated at the B3LYP/6-311++G(2d,p)level of theory applying a solvent model for chloroform (DFT).

	1		2	
	XRD	DFT	XRD	DFT
d(P=O) (Å)	1.488	1.473	1.494	1.474
d(P-OH) (Å)	1.540	1.607	1.531	1.598
d(P-OC) (Å)	1.589	1.619	1.604	1.634
d(P-C) (Å)	1.779	1.797	1.774	1.791
∠(O–P–OH) (°)	115.35	116.01	116.29	116.65
∠(O–P–OC) (°)	106.69	109.84	110.41	113.84
∠(HO–P–OC) (°)	104.34	100.45	102.56	98.64

compounds. In both molecules, the d orbital contribution to the bonds established in between the phosphorus atom and the atoms it is bonded to, respectively, is small. The hybridization of the phosphorus atom is found at $sp^{2.04}d^{0.04}$ (1) and $sp^{1.96}d^{0.04}$ (2) for the P=O bond. The latter finding is also corroborated by the respective natural electronic configuration of phosphorus – $s^{0.78}p^{1.71}d^{0.09}$ (1) and $s^{0.79}p^{1.71}d^{0.09}$ (2) – that shows the negligible participation of diffuse orbitals in the bonds established by it. Invariably, the P=O bond shows around 26% phosphorus character with a $sp^{1.77}d^{0.02}$ hybridization on the oxygen atom. While the natural charge for the phosphorus atom is positive and nearly identical in value in 1 and 2, all other atoms bonded to the phosphorus atom bear a negative natural charge (*cf.* Table 3).

If Rydberg orbitals as well as core-centered electrons are neglected, second order perturbation theory calculations invariably show the interaction of one lone pair stemming from the phosphorus-bonded oxygen atom of the respective aromatic diol in **1** and **2** with the central atom to be the most stabilizing electronic factor within each compound. For **1**, the stabilization energy is calculated at 1420 kJ/mol while for **2** a lower value of 1330 kJ/ mol is predicted.

3.4.3. Thermochemistry

To estimate the ease of hydrolytic cleavage of the P–O–C chelate ring, Born–Haber-cycles for both compounds were calculated for the partial hydrolysis of the cyclic precursor compounds on grounds of the vibrational analyses calculated at the B3LYP/6-311++G(2d,p) level of theory for all molecular entities involved.

Table 3

Natural charges of the phosphorus atom and the atoms it is bonded to in **1** and **2** with the corresponding parameters calculated at the B3LYP/6-311++G(2d,p) level of theory applying a solvent model for chloroform (DFT).

	1	2
	*	-
Р	+2.39	+2.38
P=O	-1.10	-1.10
P-O(Catechol)	-0.84	-0.84
P-O(H)	-1.00	-0.99
P-C	-0.46	-0.46

Table 4

Calculated reaction energies for the hydrolytic cleavage of the respective cyclic precursors to **1** and **2** upon addition of one molecule of water ("Partial") as well as the full hydrolysis to phenylphosphonic acid and the respective aromatic diol ("Full"). All values are given in kJ/mol.

Esterified diol	Catechol		Naphthalin-2,3-diol	
	Partial (to 1)	Full	Partial (to 2)	Full
$\Delta E_{\rm tot}$	-23.7	-48.4	-27.0	-48.2
ΔE_0	-13.2	-32.6	-16.5	-32.1
ΔH_{298}	-15.8	-39.3	-19.0	-39.1

For **1** as well as for **2**, the break-up of the chelate ring upon the addition of one molecule of water was found to be exothermic as was the full hydrolysis to phenylphosphonic acid and the respective aromatic diol (*cf.* Table 4).

On grounds of these values, the full hydrolysis of the cyclic precursors of 1 and 2 should, therefore, be even more favourable than the cleavage of only one P-O-C bond which is in contradiction to the experimental findings as the two compounds can be stored at ambient conditions without further modification. To explain this behaviour, it is instructive to consider the mechanism of the hydrolysis reactions observed in the light of the respective molecular orbitals found in the individual compounds. For both - the partial as well as the full hydrolysis via a stepwise process – one necessary step will be the addition of a molecule of water to the phosphorus atom. As can be seen from Fig. 3 depicting the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) of the cyclic precursor of **1**, the LUMO is centered on the phosphorus atom. This allows for the attack of a molecule of water on the phosphorus atom, therefore facilitating the hydrolysis.

A different picture is apparent for the HOMO and the LUMO of **1** shown in Fig. 4. While the HOMO is centered on the aromatic system of the catechol moiety and neither engulfs the phosphorus atom nor the phenyl group bonded to it, the LUMO exclusively spans the phosphorus-bonded phenyl group, excluding the phosphorus atom. The addition of another molecule of water to the latter – that would be a crucial step in the second stage of hydrolysis to effect the split into phenylphosphonic acid and catechol – is hampered as a consequence.

A similar situation is at hand for the HOMO and the LUMO in the cyclic precursor of **2** (Fig. 5) as well as **2** (Fig. 6) itself, therefore explaining the identical behaviour of partial hydrolysis with the cleavage of only one P–O–C bond. While the HOMO in **2** is centered on the – formally – double-bonded oxygen atom, the LUMO in **2** is centered on the hydroxyl group bonded to the phosphorus atom. Both molecular orbitals do not extend to the phosphorus atom.

The energetic gap between the respective HOMO and the LUMO is calculated to 492 kJ/mol in **1** and 437 kJ/mol in **2**. Within a margin of 3% these values are in good agreement with the values calculated for the corresponding energetic gaps for the respective cyclic precursors of **1** and **2** therefore ruling out the observed partial hydrolysis to be caused purely on grounds of differing activation barriers.

The general exothermicity for the partial and full hydrolysis reactions is in accordance with the observations made for the base-catalyzed hydrolysis of the cyclic phenylphosphonate derived from ethane-1,2-diol. In this case, this behaviour was attributed to ring tension among the five-membered chelate ring [22]. Taking into account the preparative procedure for the synthesis of this compound given by Holý [40] where the organic phase containing the cyclic ester derived from this aliphatic diol was washed with water, the cyclic phenylphosphonate derived from ethane-1,2-diol seems to be inert against water at least for a short time. DFT calculations on the cyclic phenylphosphate of ethane-1,2-diol as well as its half-ester corresponding to the two title compounds allowed an assessment of the reaction energies for the partial as well as the full hydrolysis of this ester derived from the simplest vicinal aliphatic diol (cf. Table 5). An inspection of the pertaining HOMO and LUMO in the cyclic phenylphosphate of ethane-1.2-diol supports its observed persistence in water as both molecular orbitals of this compound do not span its phosphorus atom.

The reason for the heightened sensitivity of the respective cyclic precursors of **1** and **2** towards atmospheric moisture in comparison to the cyclic phenylphosphonic acid ester of ethane-1,2-diol could also be explained on grounds of the higher acidity of the hydroxyl groups on the aromatic systems in aqueous solution (pK_{a1})



Fig. 3. The highest occupied (HOMO) as well as the lowest unoccupied (LUMO) molecular orbital in the cyclic precursor of 1. The isocontour surfaces were drawn at the 0.005 cut-off level.



HOMO

LUMO

Fig. 4. The highest occupied (HOMO) as well as the lowest unoccupied (LUMO) molecular orbital in 1. The isocontour surfaces were drawn at the 0.002 and the 0.07 cut-off level.



Fig. 5. The highest occupied (HOMO) as well as the lowest unoccupied (LUMO) molecular orbital in the cyclic precursor of 2. The isocontour surfaces were drawn at the 0.002 and 0.003 cut-off level.



Fig. 6. The highest occupied (HOMO) as well as the lowest unoccupied (LUMO) molecular orbital in 2. The isocontour surfaces were drawn at the 0.02 cut-off level.

Table 5

Calculated (B3LYP/6-311++G(2d,p) level of theory applying solvent models for chloroform) reaction energies for the hydrolytic cleavage of the cyclic diester of phenylphosphonic acid and ethane-1,2-diol to the respective monodentate ester upon addition of one molecule of water to PhPO(OH)-OCH₂CH₂OH ("Partial") as well as the full hydrolysis to phenylphosphonic acid and ethane-1,2-diol ("Full"). All values are given in kJ/mol.

	Partial	Full
$\begin{array}{c} \Delta E_{\rm tot} \\ \Delta E_0 \\ \Delta H_{298} \end{array}$	-17.7 -10.4 -10.9	-15.1 -3.1 -7.4

benzene-1,2-diol: 10.87 [41] or 9.85 [42], pK_{a1} naphthalene-2,3diol 8.6 [43], pK_{a1} ethane-1,2-diol: 14.22 [42]). This denotes the precursors of 1 and 2 to more closely resemble mixed acid anhydrides instead of cyclic esters of phenylphosphonic acid, therefore explaining a heightened degree of hydrolytic sensitivity.

4. Conclusion

The X-ray structure analyses on 1 and 2 confirm the correct formulation of Berlin's and Nagabhushanam's reaction sequences. For both compounds, the supposed hydrolytic cleavage of the respective cyclic precursors was found to have occurred. Upon Born-Haber-cycles based on DFT calculations this partial hydrolysis was found to be exothermic. In contrast to a cyclic ester of phenylphosphonic acid derived from the simplest aliphatic vicinal diol. the P-O-C cleavage among the chelate ring of the corresponding compounds applying aromatic vicinal diols is already induced by atmospheric moisture while no further hydrolysis is observed. The latter experimental findings can be rationalized on grounds of molecular orbital considerations that explain the (non-)feasibility of the addition of a molecule of water to the central phosphorus atom in the various compounds. With this knowledge at hand a concise study about the formation and hydrolytic stability of cyclic esters of phenylphosphonic acid can be conducted.

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Appendix A. Supplementary data

CCDC 1024667 and CCDC 1024668 contain the supplementary crystallographic data for compound 1 and compound 2. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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