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# Two types of monoethyl *α*-anilinobenzylphosphonates: a zwitterion and a molecular compound

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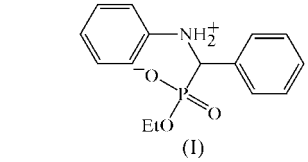
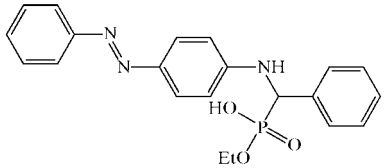
The crystal structures of the potential antitumour agents monoethyl (*α*-anilinobenzyl)phosphonate, $C_{15}H_{18}NO_3P$, (I), and its 4-azobenzene-substituted derivative monoethyl {*α*-[4-(phenyldiazenyl)anilino]benzyl}phosphonate, $C_{21}H_{22}N_3O_3P$, (II), are described. A zwitterionic form of (I) and a neutral molecular form of (II) are observed, which is fully in accordance with previously reported spectroscopic studies. In both structures, hydrogen bonding induces the formation of zigzag head-to-head double layers parallel to the crystallographic *b* axis.

## Comment

There has been continued interest in the chemistry of *α*-aminophosphonic acids and their derivatives, since these compounds exhibit a wide range of biological properties with potential applications in the agrochemical and pharmacological fields. A number of these compounds possess herbicidal (Kafarski *et al.*, 1995), fungicidal (Rodriguez *et al.*, 1999), antibiotic (Du *et al.*, 1999), antitumour (Lavielle *et al.*, 1991) and antiviral (Krize & Stella, 1996) activity. Another interesting aspect regarding this class of compounds arises from their metal-binding properties, which enable the application of selected derivatives as catalysts, extractants, ion exchangers,




(I)




(II)

*etc*. (Ohto *et al.*, 1997; Dzygiel *et al.*, 2003). On the other hand, some aminophosphonate complexes of Pt-group metals have shown antitumour activity (Bloemink *et al.*, 1999; Ćurić *et al.*, 1996; Tušek-Božić *et al.*, 2003, and references therein).

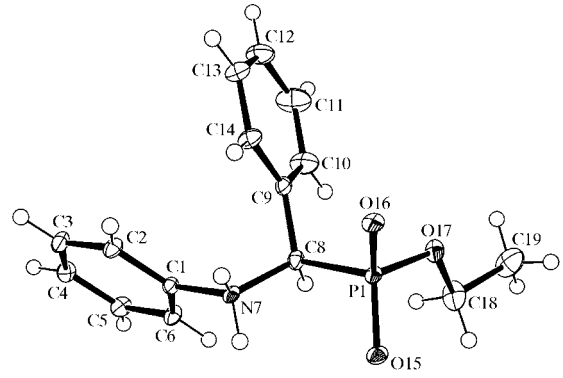



**Figure 1**
A view of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

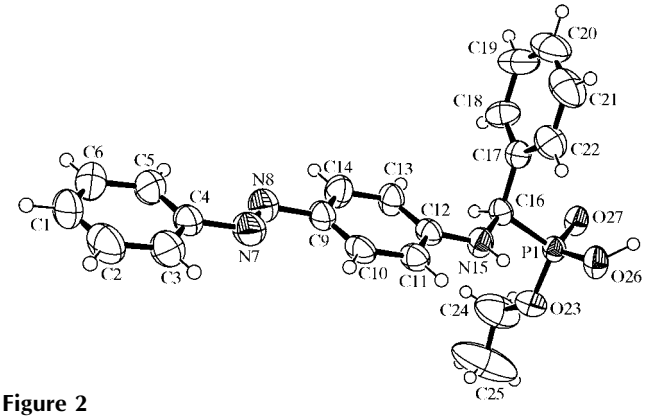



**Figure 2**
A view of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

Our interest in this field is aimed at dialkyl and monoalkyl esters of aniline- and quinoline-based aminophosphonic acids, as well as their palladium(II) and platinum(II) complexes, as potential antitumour agents. In the present work, the crystal structures of monoethyl (*α*-anilinobenzyl)phosphonate, (I), and its 4-azobenzene-substituted derivative monoethyl {*α*-[4-(phenyldiazenyl)anilino]benzyl}phosphonate, (II), are described.

Recent IR and $^1$H NMR spectroscopic studies on these compounds (Tušek-Božić *et al.*, 2000; Tušek-Božić & Lyčka, 2002; Tušek-Božić, 2002) have shown that monoester (I) has inner-salt character, with the aniline group being protonated and the phosphonic acid group being ionized, while monoester (II) possesses a neutral structure. Thus, in the spectra of (I), the $NH_2^+$ and $PO_2^-$ absorptions were observed, while in (II), those associated with the NH and P—O—H groups were present. The position and complexity of these absorptions indicate hydrogen bonding in both monoesters, which is in accordance with the results obtained for single-crystal X-ray studies of these compounds. The differences in the structure of these two types of anilinobenzylphosphonates could be

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ascribed to the relatively low basicity of the aniline N atom in (II) compared with that in (I), caused by the participation of its electron pair in resonance with the adjacent azobenzene $\pi$-system. In general, a zwitterionic structure has been determined for a large number of various aminophosphonic acids and their monoesters by IR, NMR and X-ray crystallographic studies (Appleton *et al.*, 1984; Gałdecki & Wolf, 1990; Fernández & Vega, 2003*a*,*b*; Fernández *et al.*, 2003; Tušek-Božić & D'Alpaos, 1998).

The molecular structures of (I) and (II) are given in Figs. 1 and 2, respectively. The bond lengths around P1 are considerably different in these two monoesters, as a consequence of the deprotonation of the P—O—H O atom in (I). In (II), a significant difference between the bond lengths P1—O26 [1.539 (3) Å] and P1—O27 [1.479 (2) Å] suggests double-bond character for the latter; in the Cambridge Structural Database (CSD, Version 5.25 of November 2003; Allen, 2002), among the 258 ethyl phosphonate derivatives with an unspecified substituent at the remaining singly bonded O atom, the average values of the analogous P—O bonds are 1.560 (1) and 1.465 (1) Å, respectively. However, only one monoethyl-phosphonate derivative was found in the current version of the CSD having a hydroxyl group bonded to P [as in (II)] (Hu *et al.*, 2000).

In (I), the deprotonation induces an overall charge delocalization around P, thus equating these two bond lengths [P1—O15 = 1.4959 (19) Å and P1—O16 = 1.4895 (19) Å]. A similar situation was observed among the six monoethyl phosphonate structures with a deprotonated hydroxyl group found in the CSD, where the average lengths of the analogous P—O bonds are 1.496 (5) and 1.489 (4) Å, respectively.

If the CSD search is extended to the 279 ethyl phosphonate structures with unspecified P—O bond types, a bond length scattergram of P—O1 *versus* P—O2 shows that, in the majority of such structures, non-delocalized P—O bonds are present (Fig. 3). In the two clearly revealed clusters on the scattergram, the average values of the P—O bonds are: *x* (P—O1) = 1.566 (1) Å, *y* (P—O2) = 1.460 (1) Å in one of the clusters, and *x* (P—O1) = 1.482 (1) Å, *y* (P—O2) = 1.555 (1) Å in the other. A third, less populated, cluster reveals approximately equal average values of *x* and *y* [1.48 (1) Å] and represents the small set of ethyl phosphonate structures with delocalized P—O bonds [as in (II), not as in (I)].

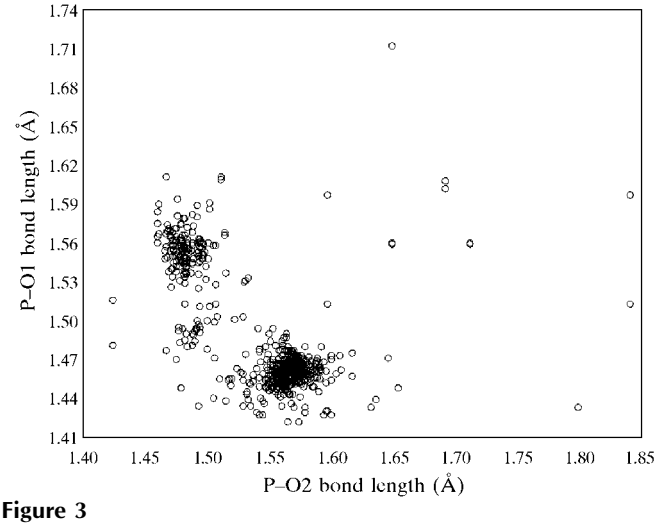


**Figure 3**
A scattergram of bond lengths P—O1 *versus* P—O2 in 279 ethyl phosphonate derivative structures found in the CSD (Version 5.25 of November 2003).

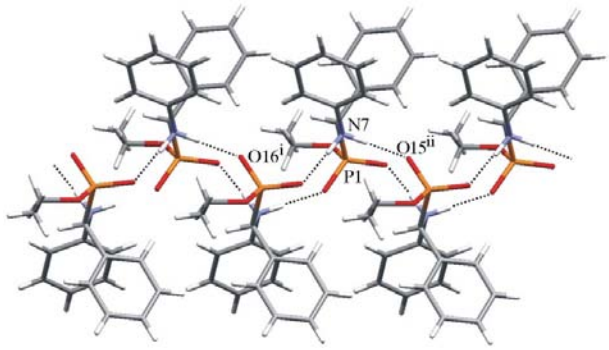


**Figure 4**
A crystal-packing diagram for (I) [symmetry codes: (i) $\frac{3}{2}-x, y+\frac{1}{2}, \frac{1}{2}-z$; (ii) $\frac{3}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$].

The P1—C and P1—$O_{ether}$ bonds are considerably longer in (I) [1.844 (3) and 1.588 (2) Å, respectively] than in (II) [1.805 (3) and 1.558 (3) Å, respectively]. The set of 258 CSD ethyl phosphonate structures reveals average values for these bonds of 1.797 (1) and 1.563 (1) Å, respectively. These values are comparable with those of (II). If, however, we analyse the set of six deprotonated structures, then the values for the analogous bonds are 1.841 (1) and 1.591 (4) Å, respectively, which are close to the corresponding values revealed by the structure of (I).

The (atom1)—P1—(atom2) bond angles reveal that the atoms attached to P1 form an almost perfect tetrahedron in both (I) and (II). An unusually short $Csp^3$—$Csp^3$ contact was observed for the terminal ethyl group in (II) [1.393 (6) Å], as a consequence of the disorder of this part of the molecule. It was not possible to resolve the disordered positions of the terminal ethyl group. In (I), the analogue bond has an expected value [1.504 (5) Å].

The interplanar angle between the aniline moiety and the phenyl ring bonded to the stereogenic centre C6 in (I) is 68.2 (1)°. The same angle in (II) is 85.7 (2)° and the angle between the phenyl ring attached to the stereogenic centre C16 and the least-squares plane calculated through 15 atoms of the phenyldiazenylaniline moiety in (II) is 84.4 (2)° [the maximum deviation from this least-squares plane is 0.096 (3) Å for atom N15]. The difference in the values of these two analoguous interplanar angles is due to the N—$C_{chiral}$ single-bond free rotation [the torsion angle C9—C8—N7—C1 in (I) is 53.9 (3)° and C17—C16—N15—C12 in (II) is −72.0 (4)°] (Figs. 1 and 2). The torsion angles around the $C_{Ph}$—$C_{chiral}$ bond [45.0 (3)° in (I) and −45.3 (4)° in (II)] suggest that the phenyl moiety has a particular preferred orientation with respect to the remainder of the molecule, which is maintained in both structures.

In both structures, the molecular chains formed by intermolecular hydrogen bonding are parallel to the *b* axis and

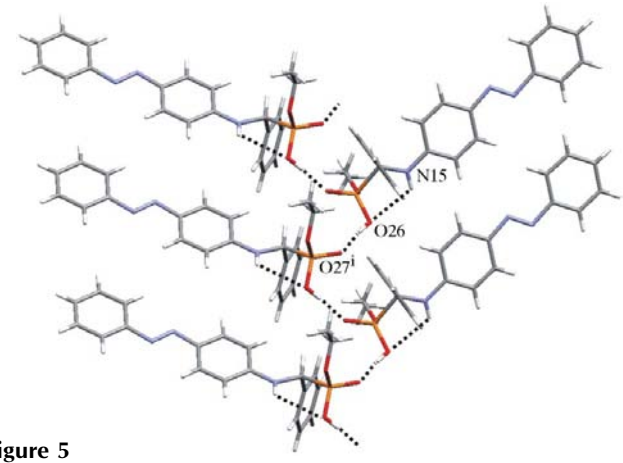


**Figure 5**
A crystal-packing diagram for (II), viewed down the *b* axis [symmetry code: (i) $\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$].

coincide with the four $P2_1$ screw axes perpendicular to the monoclinic plane. In (I), atom N7 engages both of its H atoms in intermolecular hydrogen bonding, connecting the parent molecule to two of its neighbours *via* atoms O16$^{i}$ and O15$^{ii}$ (Fig. 4; symmetry codes as in Fig. 4). At the same time, atom O15 of the parent molecule is the acceptor in the N7$^{i}$—H···O15 hydrogen bond, and atom O16 is the acceptor in the N7$^{ii}$—H···O16 hydrogen bond. The molecules are thus connected into doubly bonded zigzag chains parallel to the *b* axis. The elongation of the *a* axis in (II) relative to (I) is caused by the orientation of the bulky phenyldiazenylaniline moiety along this axis. In the structure of (II), the O atoms play a major role in the intermolecular hydrogen bonding (Fig. 5). Molecules are oriented head-to-head and intermolecular O26—H···O27$^{i}$ hydrogen bonds are observed creating molecular zigzag chains along the four twofold screw axes which are perpendicular to the *ac* plane (Fig. 5). In addition, there is an intramolecular N15—H···O26 hydrogen bond, making atom O26 a donor and an acceptor at the same time.

## Experimental

Compounds (I) and (II) were prepared by an acidification reaction from the corresponding sodium monoalkyl phosphonates, according to published methods (Jagodić, 1960; Jagodić & Tušek, 1972). Both monoesters were purified by repeated recrystallization from absolute ethanol and dried by heating to about 323 K under high vacuum. Crystals suitable for X-ray diffraction were obtained by slow evaporation from concentrated solutions in absolute ethanol, at 293 K for (I) and at 315 K for (II).

### Compound (I)

*Crystal data*

$C_{15}H_{18}NO_3P$
$M_r$ = 291.29
Monoclinic, $C2/c$
$a$ = 23.448 (2) Å
$b$ = 6.3510 (5) Å
$c$ = 20.790 (3) Å
$\beta$ = 109.94 (1)°
$V$ = 2910.4 (6) Å$^3$
$Z$ = 8
$D_x$ = 1.329 Mg m$^{-3}$
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta$ = 9.2–20.5°
$\mu$ = 1.74 mm$^{-1}$
$T$ = 293 (2) K
Needle, yellow
0.35 × 0.08 × 0.05 mm

*Data collection*

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: $\psi$ scan (North *et al.*, 1968)
$T_{min}$ = 0.862, $T_{max}$ = 0.914
3121 measured reflections
3029 independent reflections
2177 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.030
$\theta_{max}$ = 76.1°
$h = -27 \rightarrow 29$
$k = -7 \rightarrow 0$
$l = -26 \rightarrow 0$
3 standard reflections
frequency: 120 min
intensity decay: 1%

*Refinement*

Refinement on $F^2$
$R(F)$ = 0.050
$wR(F^2)$ = 0.133
$S$ = 1.04
3029 reflections
194 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.068P)^2 + 1.6186P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.30 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.54 e Å$^{-3}$

**Table 1**
Selected geometric parameters (Å, °) for (I).

| | | | |
|---|---|---|---|
| C1—N7 | 1.468 (3) | O15—P1 | 1.4959 (19) |
| C8—C9 | 1.510 (4) | O16—P1 | 1.4895 (19) |
| C8—N7 | 1.516 (3) | O17—P1 | 1.588 (2) |
| C8—P1 | 1.844 (3) | | |
| | | | |
| O16—P1—O15 | 118.16 (11) | O16—P1—C8 | 109.78 (12) |
| O16—P1—O17 | 107.58 (11) | O15—P1—C8 | 106.92 (12) |
| O15—P1—O17 | 111.28 (11) | O17—P1—C8 | 101.92 (11) |
| | | | |
| N7—C8—C9—C10 | −135.5 (3) | P1—C8—C9—C14 | −78.3 (3) |
| P1—C8—C9—C10 | 101.1 (3) | C9—C8—N7—C1 | 53.9 (3) |
| N7—C8—C9—C14 | 45.1 (3) | | |

**Table 2**
Hydrogen-bonding geometry (Å, °) for (I).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N7—H7$A$···O16$^{i}$ | 0.99 (4) | 1.71 (4) | 2.674 (3) | 161 (3) |
| N7—H7$B$···O15$^{ii}$ | 0.88 (4) | 1.81 (4) | 2.690 (3) | 175 (4) |

Symmetry codes: (i) $\frac{3}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $\frac{3}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$.

### Compound (II)

*Crystal data*

$C_{21}H_{22}N_3O_3P$
$M_r$ = 395.39
Monoclinic, $C2/c$
$a$ = 35.20 (2) Å
$b$ = 6.419 (4) Å
$c$ = 22.86 (1) Å
$\beta$ = 127.42 (4)°
$V$ = 4102 (4) Å$^3$
$Z$ = 8
$D_x$ = 1.28 Mg m$^{-3}$
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta$ = 12.0–17.1°
$\mu$ = 1.41 mm$^{-1}$
$T$ = 293 (2) K
Prism, orange
0.15 × 0.12 × 0.10 mm

*Data collection*

Enraf–Nonius CAD-4 diffractometer
Non-profiled $\omega/2\theta$ scans
Absorption correction: $\psi$ scan (North *et al.*, 1968)
$T_{min}$ = 0.788, $T_{max}$ = 0.862
4545 measured reflections
4261 independent reflections
2567 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.040
$\theta_{max}$ = 76.2°
$h = 0 \rightarrow 44$
$k = -8 \rightarrow 0$
$l = -28 \rightarrow 22$
3 standard reflections
frequency: 500 min
intensity decay: none

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.062P)^2 + 2.9216P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $R(F) = 0.061$ | $(\Delta/\sigma)_{max} < 0.001$ |
| $wR(F^2) = 0.161$ | $\Delta\rho_{max} = 0.37$ e Å$^{-3}$ |
| $S = 1.01$ | $\Delta\rho_{min} = -0.27$ e Å$^{-3}$ |
| 4261 reflections | |
| 255 parameters | |
| H atoms treated by a mixture of independent and constrained refinement | |

**Table 3**
Selected geometric parameters (Å, °) for (II).

| | | | |
|---|---|---|---|
| C4—N7 | 1.444 (5) | N7—N8 | 1.219 (4) |
| C9—N8 | 1.439 (4) | O23—P1 | 1.558 (3) |
| C12—N15 | 1.386 (4) | O26—P1 | 1.539 (3) |
| C16—N15 | 1.449 (4) | O27—P1 | 1.479 (2) |
| C16—P1 | 1.804 (3) | | |
| | | | |
| O27—P1—O26 | 113.53 (13) | O27—P1—C16 | 112.35 (14) |
| O27—P1—O23 | 114.70 (15) | O26—P1—C16 | 106.49 (15) |
| O26—P1—O23 | 102.59 (15) | O23—P1—C16 | 106.32 (15) |
| | | | |
| N15—C16—C17—C18 | 135.2 (3) | C11—C12—N15—C16 | 168.0 (3) |
| N15—C16—C17—C22 | −45.4 (4) | C17—C16—N15—C12 | −72.0 (4) |
| C13—C12—N15—C16 | −13.4 (5) | | |

**Table 4**
Hydrogen-bonding geometry (Å, °) for (II).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O26—H26···O27$^{i}$ | 0.93 (5) | 1.54 (5) | 2.476 (3) | 175 (5) |
| N15—H15···O26 | 0.84 (4) | 2.61 (5) | 2.99 (4) | 109 (6) |

Symmetry code: (i) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z$.

H atoms involved in hydrogen bonding were located directly from a Fourier map and refined freely. The positions of the remaining H atoms were determined in accordance with the relevant geometry and refined as a riding model, with C—H distances in the range 0.93–0.98 Å and with $U_{iso}(H) = 1.2U_{eq}(C)$.

For both compounds, data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *XCAD*4 (Harms & Wocadlo, 1995). For compound (I), program(s) used to solve structure: *SIR*2002 (Burla *et al.*, 2003). For compound (II), program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999). For both compounds, program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ1006). Services for accessing these data are described at the back of the journal.

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