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ORIGINAL PAPER

Synthesis and Crystal Structure of Diisopropyl Hydroxy (4-methoxyphenyl)methylphosphonate

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Abstract The title compound, $C_{14}H_{23}O_5P$, was synthesized by the reaction of 4-methoxybenzaldehyde and diisopropyl phosphite. Its structure was determined with X-ray crystallographic, NMR, MS, and elemental analysis (EA) techniques. The crystal belongs to monoclinic, space group $P\,2_{1/n}$ with the following crystallographic parameters: $a = 10.529$ (2) Å, $b = 8.424$ (2) Å, $c = 19.448$ (4) Å, $\alpha = 90°$, $\beta = 105.2$ (3)°, $\gamma = 90°$, $\mu = 0.180\ \mathrm{mm}^{-1}$, $V = 1664.1$ (6) Å^3, Z = 4, $Dx = 1.207\ \mathrm{mg/mm}^3$, $F\ (000) = 648$, $T = 293\ (2)$ K, $2.00° \leq \theta \leq 25.50°$. The final residual factor is 0.049 for 1933 reflections with $I > 2\sigma\ (I)$. Crystal packing is stabilized by interatomic hydrogen bond interactions between the doubly bonded phosphoryl O atom and the hydroxyl H atom which link the molecules into chains along the [011] plane of the unit cell.

Keywords Synthesis · Crystal structure · α-Hydroxyphosphonate

Introduction

α-Hydroxyphosphonic acids and their esters exhibit a variety of biological activities as enzyme inhibitors, antiviral, antibacterial and anticancer drugs [1–4]. α-Hydroxyphosphonates are easily synthesized from aldehydes and phosphites via the base-catalyzed the Pudovik reaction [5]. This reaction mainly proceeded in the presence of a basic catalyst [6, 7], acid catalyst [8] or a metal fluoride [9]. Recently we carried out the Pudovik reaction in 25% aqueous ammonia solution as a basic catalyst and discovered that the reaction proceeds smoothly under these conditions. In this paper we have synthesized a new α-hydroxyphosphonate and report its crystal structure. In this paper we report the X-ray structure of diisopropyl hydroxy(4-methoxyphenyl)methylphosphonate and intermolecular interactions.

Experimental

Materials and Methods

The melting point was obtained uncorrected with a Yanco micro melting point apparatus. Infrared-spectra were recorded on a Nicolet AVATR 360 FTIR spectrophotometer using KBr disks. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker 400 MHz spectrometer operating at 400, 100 and 160 MHz, respectively. The chemical shifts were reported in ppm with respect to the references and were stated relative to external tetramethylsilane (TMS) for ^{1}H and ^{13}C NMR, and to 85% phosphoric acid for ^{31}P NMR. Elemental analyses were performed with a Flash EA 1112. The mass spectrum was acquired with a Bruker ESQUIRE-3000 plus ion trap spectrometer equipped with a gas nebulizer probe in the positive ion mode.

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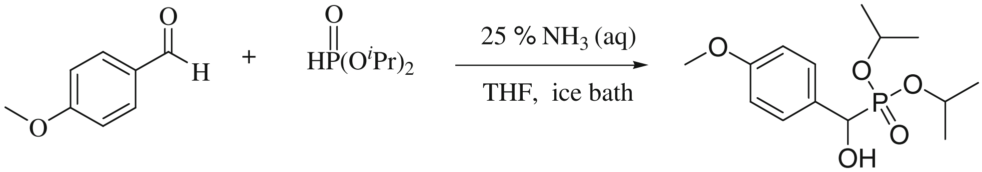
Scheme 1 Synthetic pathway of diisopropyl hydroxy(4-methoxyphenyl)methyl phosphonate



Synthesis of Diisopropyl Hydroxy(4-methoxyphenyl)methylphosphonate

To a solution of 4-methoxybenzaldehyde (5 mmol, 0.68 g) and diisopropyl phosphite (5 mmol, 0.83 g) in tetrahydrofuran (5 mL) at 0 °C was added aqueous ammonia (25%, 1.6 mL). The mixture was left to stand at ambient temperature for 2 h, during which time a precipitate separated (Scheme 1). The precipitate was filtered off and washed rapidly with cold diethyl ether [10]. Column chromatography of the solid using silica gel and 20% ethyl acetate in petroleum ether solution gave the title compound ($C_{14}H_{23}O_5P$; 1.29 g in 85.4% yield. m. p. 145–146 °C): ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43 (d, 2H, $J = 4.2$ Hz, ArH), 6.89 (d, 2H, $J = 4.2$ Hz, ArH), 4.90 (d, 1H, $^1J_{P–C\underline{H}} = 5$ Hz, CH), 4.65–4.60 (m, 2H, $2OC\underline{H}(CH_3)_2$), 3.81 (s, 3H, OCH_3), 3.72 (br, 1H, OH), 1.28–1.14 (m, 12H, $2OCH(C\underline{H}_3)_2$); ^{13}C NMR: 159.38, 128.93, 128.65, 128.59, 113.58, 113.56, 71.49 (d, $^1J_{P–\underline{C}H} = 161$ Hz, CH), 71.83, 71.55 ($2O\underline{C}H(CH_3)_2$), 55.25 (OCH_3), 23.62, 23.90 24.09, 24.19; ^{31}P NMR: 20.08; IR (KBr) υ (cm^{-1}): 3270, 1612, 1583, 1377; MS *m/z*: 303 $[M + H]^+$, 605 $[2M + H]^+$, 627 $[2M + Na]^+$; Anal. Calcd. for $C_{14}H_{23}O_5P$: C 55.62, H 7.67; Found C 55.65, H 7.69. The colorless single crystal was cultured from a mixture solution of dichloromethane/petroleum ether (v/v = 1/6) by slow evaporation at room temperature.

Crystal Structure Determinations and Refinements

X-ray data on a single crystal of dimensions 0.20 mm × 0.18 mm × 0.13 mm was collected on a Bruker SMART CCD X-ray area detector diffractometer at room temperature using Mo Kα radiation ($\lambda = 0.7173$ Å) with ϕ and ω scans. An absorption correction was applied using SADABS 2001 [11]. The structures were solved by direct methods using the SHELXL-97 program [12]. All H atoms were placed in geometrically idealized positions and treated as riding on their parent atoms, with C–H = 0.93 (aromatic), 0.96 (CH_3) or 0.98 (CH), O–H = 0.82 Å and $U_{iso}(H) = 1.2U_{eq}$ (aromatic C and CH) or $1.5U_{eq}$ (methyl C and O). Anisotropic temperature factors were introduced for all non-hydrogen atoms, and least-squares refinements were carried out by minimizing $\sum w\,(|F_o| - |F_c|)^2$, where F_o and F_c are the observed and calculated structure factors. The full crystallographic details are deposited in CCDC database under the reference number 659487 (see supplementary material).

Table 1 Crystal data and structure refinement details

CCDC nos.	659487
Empirical formula	$C_{14}H_{23}O_5P$
Formula weight	302.29
Crystal system, space group	Monoclinic, $P\,2_{1/n}$
Unit cell dimensions	$a = 10.529$ (2) Å
	$b = 8.424$ (2) Å
	$c = 19.448$ (4) Å
	$\alpha = 90°$
	$\beta = 105.2$ (3)°
	$\gamma = 90°$
Volume	1664.1 (6) Å^3
Z, Calculated density	4, 1.207 mg/mm^3
Density (calculated), mg/mm^3	1.207
Absorption coefficient	0.180 mm^{-1}
F (000)	648
Crystal size	0.20 × 0.18 × 0.13 mm^3
Theta range for data collection	2.00–25.50°
Limiting indices	$-10 \le h \le 12$, $-10 \le k \le 10$, $-23 \le l \le 22$
Reflections collected	4896
Independent/observed reflections	2897 [R(int) = 0.048]
Completeness to theta = 25.00	93.3%
Refinement method	Full-matrix least-squares on F^2
Max. and min. transmission	0.972 and 0.965
Data/restraints/parameters	2897/0/186
Goodness-of-fit on F^2	1.00
Final R indices ($I > 2$sigma(I))	$R_1 = 0.049$, $wR_2 = 0.102$
R indices (all data)	$R_1 = 0.092$, $wR_2 = 0.113$
Largest diff. peak and hole	0.24 and −0.22 e Å^{-3}

Results and Discussion

The crystal data and final refinement details of the title compound are given in Table 1, and the final geometrical parameters are given in Table 2. Table 3 gives the bond distances and bond angles of non-hydrogen atoms, respectively. The molecule consists of a phenyl ring at C(2). The average value of the bond distances (1.380(3) Å) and exocyclic bond angles (120.0(3)°) in the phenyl ring have normal values as compared to those of similar structure [13, 14]. The configuration around the phosphorus atom, which is *sp*^{3} hybridized, is that of a distorted tetrahedron with phosphorous at the center. The P–O bond lengths are P(1)–O(2) = 1.469 (2) Å, P(1)–O(3) = 1.573 (2) Å, P(1)–O(4) = 1.567 (2) Å and P(1)–C(1) = 1.820 (2) Å, respectively. The bond angles are ∠O(2)–P(1)–O(4) = 115.7 (1)°, ∠O(2)–P(1)–O(3) = 114.0 (2)°, ∠O(4)–P(1)–O(3) = 103.3 (2)°, ∠O(2)–P(1)–C(1) = 115.1 (1)°, ∠O(3)–P(1)–C(1) = 106.5 (1)° and ∠O(2)–P(1)–C(1) = 100.7 (6)°, respectively. Figure 1 represents an ORTEP [15, 16] diagram of the asymmetric unit of the molecule

Table 2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\times 10^3$Å^2) for the title compound

	x	y	z	*U*(eq)
P(1)	9,900(1)	7,653(1)	1,325(1)	41(1)
O(1)	9,575(2)	8,572(2)	2,534(1)	67(1)
O(2)	10,137(2)	5,964(2)	1,502(1)	50(1)
O(3)	8,429(2)	8,054(2)	932(1)	55(1)
O(4)	10,690(2)	8,368(2)	819(1)	51(1)
O(5)	15,860(2)	8,628(3)	3,446(1)	82(1)
C(1)	10,376(2)	9,005(3)	2,080(1)	48(1)
C(2)	11,845(2)	8,930(3)	2,440(1)	46(1)
C(3)	12,722(2)	9,905(3)	2,226(1)	57(1)
C(4)	14,070(3)	9,847(3)	2,538(1)	62(1)
C(5)	14,554(2)	8,796(4)	3,085(1)	58(1)
C(6)	13,696(3)	7,806(3)	3,308(2)	64(1)
C(7)	12,360(2)	7,871(3)	2,987(1)	57(1)
C(8)	7,299(2)	7,165(3)	1,037(2)	60(1)
C(9)	11,086(3)	7,464(3)	267(1)	63(1)
C(10)	6,330(3)	8,371(5)	1,143(2)	1,25(2)
C(11)	6,786(3)	6,130(5)	412(2)	1,27(2)
C(12)	12,330(3)	8,285(5)	187(2)	1,10(1)
C(13)	10,004(3)	7,472(4)	−402(2)	92(1)
C(14)	16,788(3)	9,638(4)	3,240(2)	99(1)

U(eq) is defined as one third of the trace of the orthogonalized *Uij* tensor

Table 3 Selected bond lengths (Å) and bond angles (°) of the title compound

Bond lengths	(Å)	Angles	(°)
P(1)–O(2)	1.469(2)	O(2)–P(1)–O(4)	115.7(1)
P(1)–O(4)	1.567(2)	O(2)–P(1)–O(3)	114.0(2)
P(1)–O(3)	1.573(2)	O(4)–P(1)–O(3)	103.3(4)
P(1)–C(1)	1.820(2)	O(2)–P(1)–C(1)	115.1(1)
O(1)–C(1)	1.420(3)	O(4)–P(1)–C(1)	100.7(6)
O(5)–C(5)	1.378(3)	O(3)–P(1)–C(1)	106.5(1)
O(5)–C(14)	1.430(3)	C(5)–O(5)–C(14)	117.4(2)
O(3)–C(8)	1.464(3)	C(8)–O(3)–P(1)	123.6(1)
O(4)–C(9)	1.464(3)	C(5)–C(4)–C(3)	119.2(2)
C(3)–C(2)	1.379(3)	C(4)–C(5)–O(5)	125.3(3)
C(3)–C(4)	1.391(3)	C(4)–C(5)–C(6)	119.5(3)
C(4)–C(5)	1.374(4)	O(5)–C(5)–C(6)	115.2(3)
C(5)–C(6)	1.381(4)	O(1)–C(1)–C(2)	113.6(2)
C(6)–C(7)	1.381(3)	O(1)–C(1)–P(1)	104.9(1)
C(7)–C(2)	1.386(3)	C(2)–C(1)–P(1)	112.1(1)
C(2)–C(1)	1.521(3)	O(3)–C(8)–C(11)	108.8(2)
C(8)–C(11)	1.478(4)	O(3)–C(8)–C(10)	106.3(2)
C(8)–C(10)	1.492(4)	C(11)–C(8)–C(10)	113.5(3)
C(9)–C(13)	1.486(4)	O(4)–C(9)–C(13)	109.8(2)
C(9)–C(12)	1.524(4)	O(4)–C(9)–C(12)	104.9(2)

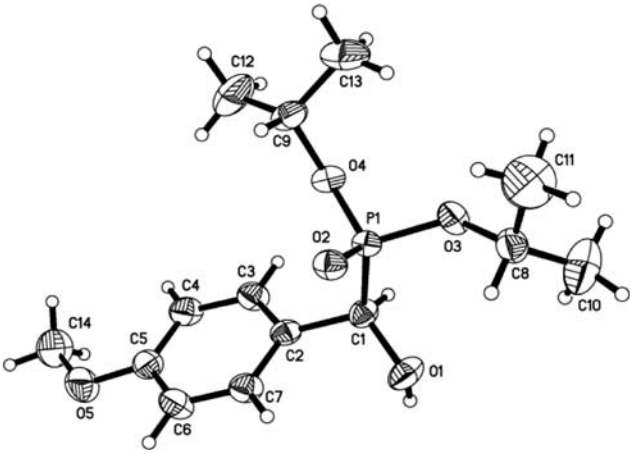


Fig. 1 ORTEP diagram of the molecule drawn at 50% probability

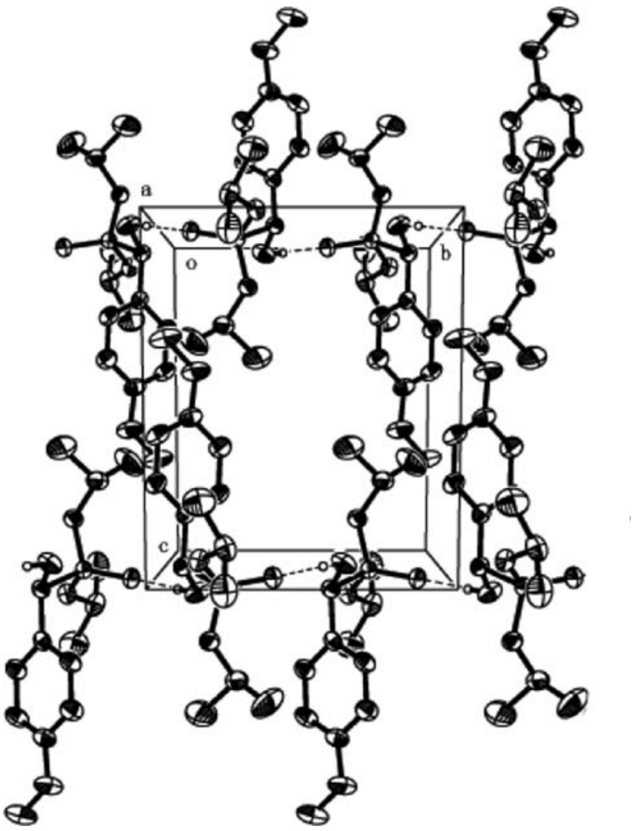


Fig. 2 The molecular packing for $C_{14}H_{23}O_5P$ viewed down the a axis with atoms drawn as 30% probability ellipsoids. Dashed lines indicate O–H···O intermolecular hydrogen bonds

Table 4 Hydrogen-bond geometry

D–H···A	d (D–H)	d (H···A)	d (D···A)	∠DHA
O1–H1···O2	0.82 Å	1.90 Å	2.715 (2) Å	173.9°

with thermal ellipsoids at 50% probability values. Crystal packing is stabilized by interatomic hydrogen bond interactions between the doubly bonded phosphoryl O atom and the hydroxyl H atom which link the molecules into chains along the [011] plane of the unit cell (Fig. 2, Table 4) (symmetry code: (i) 2 − x, −y + 1/2, −z + ½).

Supplementary Material

CCDC-659487 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033; email: deposit@ccdc.cam.ac.uk.

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