Application of Wallach's Rule in a Comparison of the X-ray Crystal Structures of the Racemate and the (S) Enantiomer of (1-Hydroxy-3-phenyl-2-propenyl) Dimethylphosphonate

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Abstract

The crystal structures of the racemate and the (*S*) enantiomer of (1-hydroxy-3-phenyl-2-propenyl) dimethylphosphonate, $C_{11}H_{15}O_4P$, were determined by X-ray diffraction. The crystal density of the racemate was found to be 6.2% greater than the crystal density of the (*S*) enantiomer. In both crystal structures the molecules form chains by hydrogen bonding between the OH of one molecule and the P=O of another. Observed differences in atomic displacement between the two structures are discussed in view of the C—H···O interactions.

1. Introduction

Wallach's rule (Wallach, 1895) states that racemic crystals tend to be denser than their chiral counterparts. More recently, an extensive survey of the Cambridge Crystallographic Database (Brock, Schweizer & Dunitz, 1991) identified 129 compounds for which the structures of both the racemic and single enantiomer crystals had been reported. A small, but significant, increase in the average density of the racemic crystals of resolvable chiral compounds was found.

We recently reported a method for the asymmetric synthesis of α-hydroxy phosphonates (Blazis, Koeller & Spilling, 1995), which afforded us the opportunity to validate Wallach's rule for a new crystal pair. Addition of the phosphorous diamide (1) to cinnamaldehyde gave the hydroxyphosphonamide (2) in 78% d.e. (diastereomeric excess).
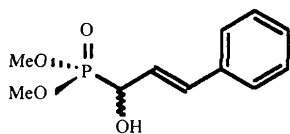

(±) (1-hydroxy-3-phenyl-2-propenyl) dimethylphosphonate
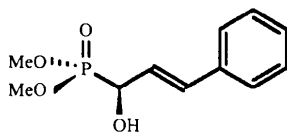
(*S*)-(1-hydroxy-3-phenyl-2-propenyl) dimethylphosphonate

The phosphonamide (2) was recrystallized to diastereoisomeric purity and hydrolyzed to the phosphonic acid, which was methylated with diazomethane to the (*S*)-hydroxyphosphonate (*S*)-(3) {>99% e.e. (enantiomeric excess) by HPLC, $[a]_D = -23.6°$ (c = 2.74 CHCl$_3$)}. Slow diffusion of hexanes into an ethyl acetate solution of (*S*)-(3) gave crystals, m.p. 371.9–372.6 K, suitable for X-ray diffraction studies. The racemate was prepared by Et$_3$N-catalyzed addition of dimethyl phosphite to cinnamaldehyde (Baraldi, Guarneri, Moroder, Pollini & Simoni, 1982). X-ray quality crystals, m.p. 374 K, were again prepared by the slow diffusion of hexanes into an ethyl acetate solution of (±)-(3).
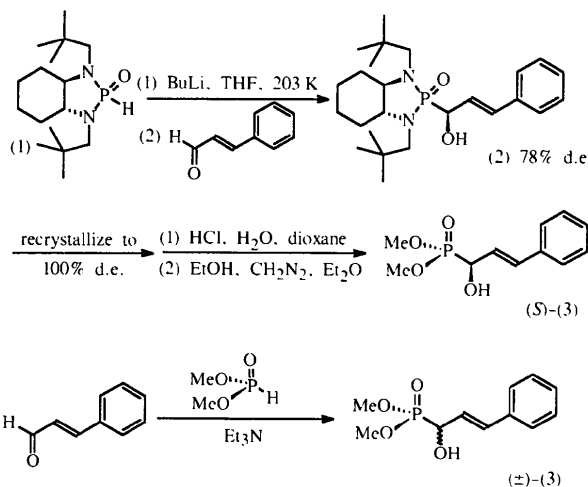
2. Experimental

Data were collected by the double-pass method using a CCD area detector system. The first 50 frames of data were recollected at the end of the data collection to monitor crystal decay.

The absolute structure was confirmed by Flack's parameter x [x = 0.05 (7)]. An earlier data collection on a crystal of the same compound using Cu $K\alpha$ radiation at room temperature also confirmed the absolute structure

[Flack x = 0.0 (7), R_1 = 0.076, wR_2 = 0.208 for θ_{max} = 50.0°].

Full-matrix least-squares refinement was carried out by minimizing $w(F_o^2 - F_c^2)^2$. Non-H atoms were refined anisotropically to convergence. H atoms were treated using the appropriate riding models (AFIX = *m*4; *SHELXTL-Plus*; Sheldrick, 1995), thus allowing refinement of the *X*—H distance without changing the *X*—H vector direction (1 parameter per each group of H's, total 11 parameters for 15 H's).

3. Discussion

The structures [Figs. 1, (*S*) enantiomer for (+/–) shown, and 2] showed bond angles and distances within the accepted ranges.† The molecules within the crystals of the racemate and the (*S*) enantiomer adopted similar conformations with respect to the O=P—C—OH arrangement [O1—P—C1—O4 torsion angles 61.6 (1) and 69.5 (1)° for the racemate and (*S*) enantiomer, respectively]. The density of the racemate

† Lists of atomic coordinates, anisotropic displacement parameters and structure factors have been deposited with the IUCr (Reference: BK1251). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.
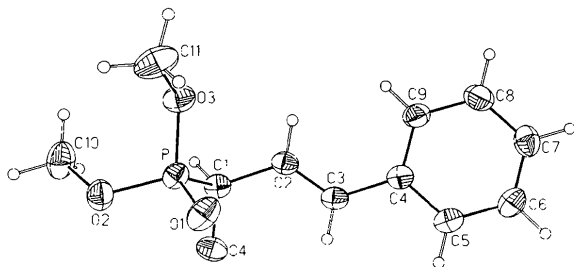
is 0.085 Mg m^{-3} (6.2%) greater than the (*S*) enantiomer. Thus, the hydroxy phosphonate crystal pair (*S*)-(3) and (±)-(3) provide a further example validating Wallach's rule.

Significantly larger atomic displacements were observed in the room-temperature data set of the (*S*) enantiomer compared with the racemate. In order to confirm this fact two new data sets were collected on both isomers at 193 K using freshly recrystallized samples. Similar differences were observed for the low-temperature data sets, suggesting different intermolecular interactions in the crystal lattices. Careful examination of the principle mean-square atomic displacement parameters and equivalent isotropic displacement parameters shows that the displacements of phenyl-ring C atoms are about twice as large for the (*S*) isomer as for the racemate. The methoxy O and C atoms also show significantly larger (60–80%) atomic displacement in the enantiomerically pure crystal. This difference can be attributed to differences in crystal packing between the two compounds (Figs. 3 and 4), in spite of the similarity of the O—H· · ·O hydrogen-bonded chains.

In both crystal structures the molecules pack in hydrogen-bonded chains. A hydrogen bond is formed between the P· · ·O of one molecule and the H—O of the next. The hydrogen-bonded chain in the racemate

Fig. 1. The molecular structure (*SHELXTL-Plus* plot; Sheldrick, 1995) of the (±) enantiomer of (1-hydroxy-3-phenyl-2-propenyl) dimethylphosphonate, shown with 50% probability ellipsoids.
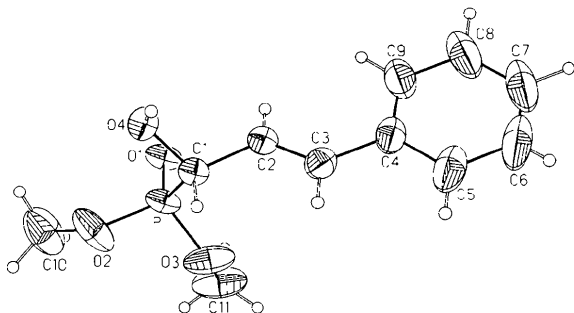

Fig. 2. The molecular structure (*SHELXTL-Plus* plot; Sheldrick, 1995) of the (*S*) enantiomer of (1-hydroxy-3-phenyl-2-propenyl) dimethylphosphonate, shown with 50% probability ellipsoids.
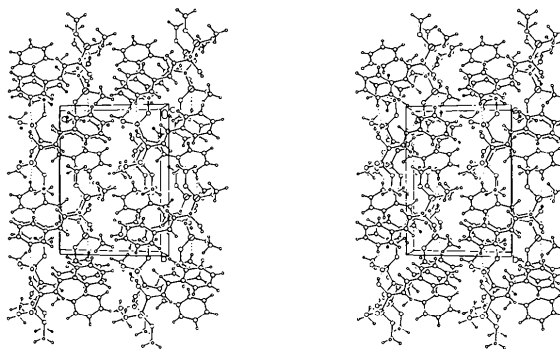

Fig. 3. The molecular packing diagram of (±)-(3) in stereo.
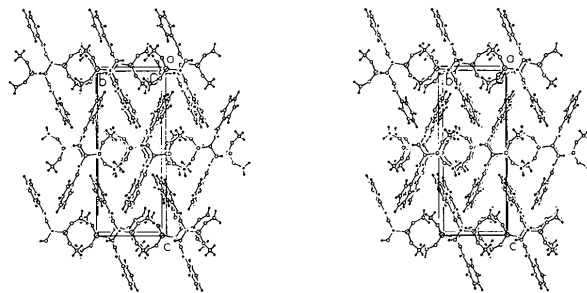

Fig. 4. The molecular packing diagram of (*S*)-(3) in stero.

Table 1. *Experimental details*

	(±) racemate	(S) enantiomer
Crystal data		
Chemical formula	$C_{11}H_{15}O_4P$	$C_{11}H_{15}O_4P$
Chemical formula weight	242.20	242.20
Cell setting	Monoclinic	Orthorhombic
Space group	$P2_1/c$	$P2_12_12_1$
a (Å)	10.1737 (1)	7.3601 (1)
b (Å)	13.9127 (1)	8.3440 (1)
c (Å)	8.7336 (1)	20.4292 (3)
β (°)	107.037 (1)	
V (Å^3)	1181.94 (2)	1254.61 (2)
Z	4	4
D_x (Mg m^{-3})	1.361	1.282
Radiation type	Mo $K\alpha$	Mo $K\alpha$
Wavelength (Å)	0.71073	0.71073
No. of reflections for cell parameters	8192	7124
θ range (°)	2.0–26.4	2.0–26.0
μ (mm^{-1})	0.229	0.215
Temperature (K)	193 (2)	193 (2)
Crystal form	Plates	Irregular
Crystal size (mm)	0.33 × 0.33 × 0.08	0.35 × 0.25 × 0.20
Crystal color	Colorless	Colorless
Data collection		
Diffractometer	Siemens CCD	Siemens CCD
Data collection method	ω scans	ω scans
Absorption correction	None	None
No. of measured reflections	17 306	21 347
No. of independent reflections	2855	3023
No. of observed reflections	2398	2692
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$
R_{int}	0.045	0.053
θ_{max} (°)	28.00	27.99
Range of h, k, l	$-13 \rightarrow h \rightarrow 12$	$-9 \rightarrow h \rightarrow 9$
	$0 \rightarrow k \rightarrow 18$	$0 \rightarrow k \rightarrow 11$
	$0 \rightarrow l \rightarrow 11$	$0 \rightarrow l \rightarrow 26$
Refinement		
Refinement on	F^2	F^2
$R[F^2 > 2\sigma(F^2)]$	0.033	0.040
$wR(F^2)$	0.097	0.107
S	1.04	1.04
No. of reflections used in refinement	2844	3023
No. of parameters used	156	156
H-atom treatment	Riding model, see text	Riding model, see text
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0533P)^2 + 0.2884P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0711P)^2 + 0.1111P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	−0.00	0.01
$\Delta\rho_{max}$ (e Å^{-3})	0.28	0.34
$\Delta\rho_{min}$ (e Å^{-3})	−0.38	−0.44
Extinction method	None	None
Source of atomic scattering factors	*International Tables for Crystallography* (1992, Vol. C)	*International Tables for Crystallography* (1992, Vol. C)
Computer programs		
Data collection	*SMART* (Siemens, 1995b)	*SMART* (Siemens, 1995b)
Cell refinement	*SAINT* (Siemens, 1995a)	*SAINT* (Siemens, 1995a)
Data reduction	*SAINT* (Siemens, 1995a)	*SAINT* (Siemens, 1995a)
Structure solution	*SHELXTL-Plus* (Sheldrick, 1995)	*SHELXTL-Plus* (Sheldrick, 1995)
Structure refinement	*SHELXTL-Plus* (Sheldrick, 1995)	*SHELXTL-Plus* (Sheldrick, 1995)
Preparation of material for publication	*SHELXTL-Plus* (Sheldrick, 1995)	*SHELXTL-Plus* (Sheldrick, 1995)

contains alternating (R) and (S) enantiomers (Fig. 5), with O1–O4^i and O1—H4^i [(i) = x, $\frac{3}{2} - y$, $z - \frac{1}{2}$] distances of 2.679 (1) and 1.86 (2) Å, respectively. The O1—H4′—O4′ angle is 162.8 (2)°. The (S) enantiomer, by definition, contains identical repeating unit with O1—O4^{ii} and O1—H4^{ii} [(ii) = $\frac{1}{2} + x$, $\frac{1}{2} - y$, $1 - z$] distances of 2.693 (2) and 1.88 (4) Å, respectively, and

an O1—H4^{ii}—O4^{ii} angle of 161.8 (14)°. The O—H···O bonds in the two structures are comparable.

In the racemate the phosphoryl O atom is also involved in linear hydrogen bonding with a phenyl H (H6) from a neighboring molecule [H6—O1^{iii} = 2.49 (1) Å, C6—H6—O1^{iii} = 168.5 (9)°; (iii) = 2 − x, $\frac{1}{2} + y$, $\frac{3}{2} - z$]. The significantly larger atomic displacements of

Table 2. *Fractional atomic coordinates and equivalent isotropic displacement parameters ($\mathring{A}^2$) for the ($\pm$) racemate*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	*y*	*z*	U_{eq}
P	0.74820 (3)	0.61485 (2)	1.01623 (4)	0.02763 (11)
O1	0.73111 (12)	0.61813 (7)	0.84361 (11)	0.0391 (3)
O2	0.60624 (10)	0.59241 (8)	1.04464 (12)	0.0375 (2)
O3	0.85381 (11)	0.53720 (7)	1.11083 (12)	0.0364 (2)
O4	0.72418 (10)	0.79733 (7)	1.06580 (12)	0.0344 (2)
C1	0.81847 (13)	0.72243 (9)	1.1289 (2)	0.0281 (3)
C2	0.96136 (13)	0.74285 (10)	1.1218 (2)	0.0288 (3)
C3	0.99761 (13)	0.82129 (10)	1.0582 (2)	0.0288 (3)
C4	1.13692 (13)	0.84310 (9)	1.0485 (2)	0.0285 (3)
C5	1.15417 (15)	0.91499 (10)	0.9441 (2)	0.0318 (3)
C6	1.2830 (2)	0.93475 (11)	0.9264 (2)	0.0367 (3)
C7	1.3968 (2)	0.88386 (11)	1.0141 (2)	0.0404 (3)
C8	1.3820 (2)	0.81399 (12)	1.1216 (2)	0.0435 (4)
C9	1.25393 (15)	0.79390 (11)	1.1387 (2)	0.0367 (3)
C10	0.5958 (2)	0.57041 (14)	1.2032 (2)	0.0487 (4)
C11	0.8478 (2)	0.43999 (12)	1.0505 (2)	0.0527 (5)

Table 3. *Selected geometric parameters ($\mathring{A}$, °) for the ($\pm$) racemate*

P—O1	1.4668 (10)	C2—C3	1.325 (2)
P—O2	1.5668 (10)	C3—C4	1.476 (2)
P—O3	1.5761 (10)	C4—C5	1.399 (2)
P—C1	1.8186 (13)	C4—C9	1.399 (2)
O2—C10	1.452 (2)	C5—C6	1.392 (2)
O3—C11	1.446 (2)	C6—C7	1.381 (2)
O4—C1	1.414 (2)	C7—C8	1.390 (2)
C1—C2	1.500 (2)	C8—C9	1.383 (2)
O1—P—O2	109.38 (6)	C3—C2—C1	124.43 (12)
O1—P—O3	114.67 (6)	C2—C3—C4	125.68 (13)
O2—P—O3	107.39 (6)	C5—C4—C9	117.93 (13)
O1—P—C1	116.11 (6)	C5—C4—C3	119.37 (12)
O2—P—C1	108.22 (6)	C9—C4—C3	122.69 (12)
O3—P—C1	100.42 (6)	C6—C5—C4	121.05 (13)
C10—O2—P	121.42 (10)	C7—C6—C5	120.05 (14)
C11—O3—P	120.04 (10)	C6—C7—C8	119.63 (14)
O4—C1—C2	113.52 (11)	C9—C8—C7	120.40 (15)
O4—C1—P	106.34 (8)	C8—C9—C4	120.89 (14)
C2—C1—P	111.43 (9)		

Table 4. *Fractional atomic coordinates and equivalent isotropic displacement parameters ($\mathring{A}^2$) for the (S) enantiomer*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U^{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	*y*	*z*	U_{eq}
P	0.78933 (6)	0.50678 (5)	0.48385 (2)	0.03721 (14)
O1	0.9892 (2)	0.51639 (14)	0.48390 (7)	0.0417 (3)
O2	0.6971 (2)	0.5711 (2)	0.54772 (10)	0.0693 (5)
O3	0.6968 (2)	0.5998 (2)	0.42615 (11)	0.0639 (5)
O4	0.7311 (2)	0.22265 (15)	0.53187 (6)	0.0372 (3)
C1	0.6917 (2)	0.3100 (2)	0.47352 (8)	0.0318 (3)
C2	0.7677 (3)	0.2283 (2)	0.41412 (8)	0.0345 (4)
C3	0.6668 (3)	0.1869 (2)	0.36332 (9)	0.0417 (4)
C4	0.7290 (3)	0.1051 (2)	0.30334 (9)	0.0494 (5)
C5	0.6046 (5)	0.0803 (3)	0.25311 (12)	0.0712 (8)
C6	0.6600 (4)	0.0009 (4)	0.19575 (13)	0.0939 (13)
C7	0.8319 (7)	−0.0522 (4)	0.18930 (13)	0.0975 (14)
C8	0.9585 (6)	−0.0276 (4)	0.23800 (13)	0.0854 (10)
C9	0.9066 (4)	0.0514 (3)	0.29493 (12)	0.0624 (6)
C10	0.7776 (4)	0.6797 (5)	0.5906 (2)	0.0861 (10)
C11	0.7722 (4)	0.7424 (3)	0.3985 (2)	0.0803 (9)

Table 5. *Selected geometric parameters ($\mathring{A}$, °) for the (S) enantiomer*

P—O1	1.4729 (12)	C2—C3	1.322 (2)
P—O2	1.566 (2)	C3—C4	1.475 (3)
P—O3	1.567 (2)	C4—C5	1.390 (3)
P—C1	1.805 (2)	C4—C9	1.392 (4)
O2—C10	1.392 (3)	C5—C6	1.406 (5)
O3—C11	1.429 (3)	C6—C7	1.347 (6)
O4—C1	1.427 (2)	C7—C8	1.379 (6)
C1—C2	1.500 (2)	C8—C9	1.391 (3)
O1—P—O2	114.44 (9)	C3—C2—C1	123.0 (2)
O1—P—O3	114.04 (9)	C2—C3—C4	126.8 (2)
O2—P—O3	105.58 (11)	C5—C4—C9	118.6 (2)
O1—P··C1	116.56 (7)	C5—C4—C3	118.5 (2)
O2—P—C1	103.70 (9)	C9—C4—C3	122.8 (2)
O3—P—C1	100.94 (8)	C4—C5—C6	119.6 (4)
C10—O2—P	124.2 (2)	C7—C6—C5	120.6 (3)
C11—O3—P	122.7 (2)	C6—C7—C8	121.0 (3)
O4—C1—C2	111.59 (13)	C7—C8—C9	119.2 (4)
O4—C1—P	106.62 (10)	C8—C9—C4	120.9 (3)
C2—C1—P	111.08 (11)		

the (S) enantiomer phenyl-group atoms can be attributed to the absence of this type of interaction. Fig. 5 shows the hydrogen bonding in the racemate.

In the (S) enantiomer weak intermolecular hydrogen bonding is observed between the H atom of the chiral center and the hydroxyl O of a neighboring molecule
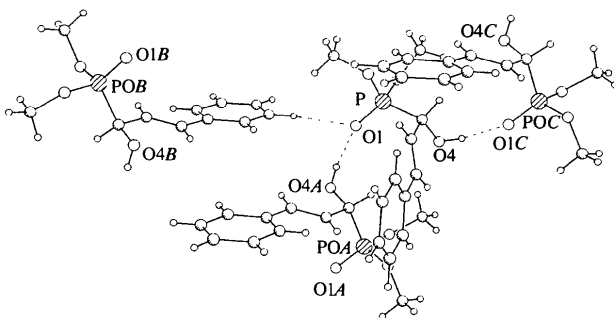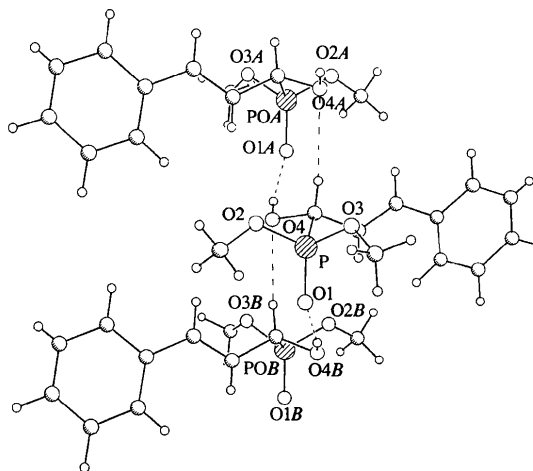

Fig. 5. The hydrogen-bonded chain of ($\pm$)-(3).

Fig. 6. The hydrogen-bonded chain of (S)-(3).

(Fig. 6). Eight-membered rings with approximate tetrahedral geometry around the hydroxyl oxygen are formed, as expected [O4—H1^{ii} = 2.52 (3) Å, C1^{ii}—H1^{ii}—O4 = 166 (2)°].

In both structures the phosphoryl and hydroxyl oxygens are involved in strong intermolecular interactions and show comparable atomic displacements. The difference in the atomic displacements of the methoxy groups probably reflects the generally looser packing in the S enantiomer.

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