Crystallographic and spectroscopic characterization of (R)-O-acetylmandelic acid

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The title compound [systematic name: (R)-$(-)$-2-acetoxy-2-phenylacetic acid], $C_{10}H_{10}O_4$, is a resolved chiral ester derivative of mandelic acid. The compound contains an acetate group and a carboxylic acid group, which engage in intermolecular hydrogen bonding, forming chains extending parallel to [001] with a short donor–acceptor hydrogen-bonding distance of 2.676 (2) Å.

1. Chemical context

Chiral, resolved carboxylic acids have played an important role as chiral NMR shift reagents (Lovely & Wenzel, 2008; Parker, 1991). The title compound, (R)-$(-)$-2-acetoxy-2-phenylacetic acid (I), commonly known as (R)-O-acetyl-mandelic acid, is a chiral, resolved derivative of mandelic acid. The compound may be synthesized by acetylation of the parent α-hydroxy acid with acetic anhydride in pyridine (Ornelas et al., 2013). When racemic, resolution of the compound with free amino acids has been demonstrated (Szeleczky et al., 2015). The title compound has been employed as a chiral NMR shift reagent (Parker, 1991).
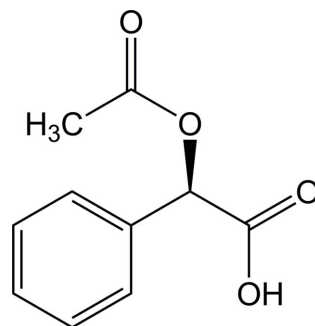

2. Structural commentary

The molecular structure of the title compound (Fig. 1) shows the R configuration about carbon atom C1, and that the molecule does not engage in intramolecular or pairwise hydrogen bonding. The absolute structure parameters confirm the R assignment, with Flack $x = -0.01$ (4) and Hooft $y = -0.02$ (4), calculated with PLATON (Spek, 2009).

3. Supramolecular features

The molecules pack together in the solid state via van der Waals forces and hydrogen bonding between the carboxylic acid OH group and the carbonyl oxygen atom of the ester on a
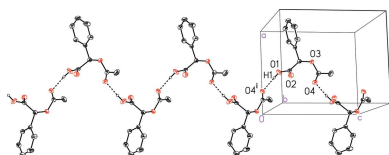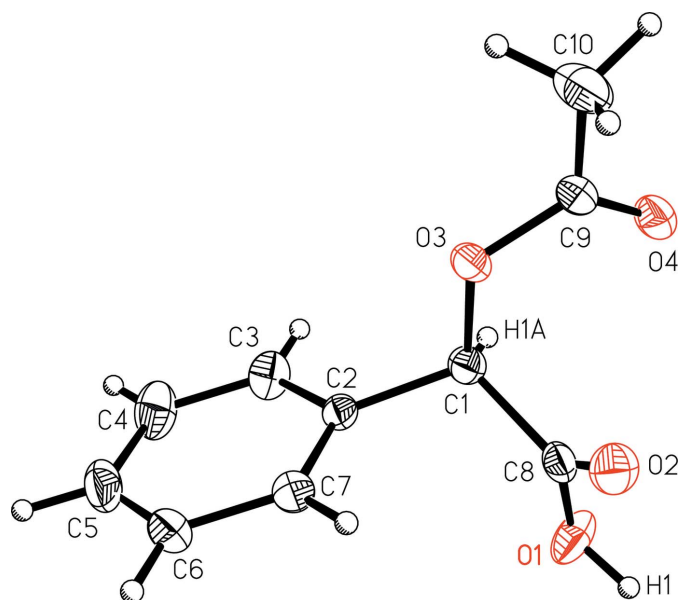

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Figure 1
A view of (*R*)-(−)-2-acetoxy-2-phenylacetic acid (I) with the atom-numbering scheme. Displacement ellipsoids are shown at the 50% probability level.

neighboring molecule, O1—H1···O4^i [symmetry code (i) $-x + \frac{1}{2}, -y + 1, z - \frac{1}{2}$] with a donor–acceptor distance of 2.676 (2) Å (Table 1). These interactions create zigzag hydrogen-bonded chains that extend parallel to the *c* axis of the unit cell (Fig. 2). Notably, there is no face-to-face or edge-to-face π-stacking.

4. Database survey

The Cambridge Structural Database (Groom *et al.*, 2016) contains several related mandelic acid ester structures.

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O4^i	0.85 (2)	1.84 (2)	2.6761 (16)	165 (2)

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

Related structures of resolved mandelic acid esters that differ by the nature of the ester group include (*2S*)-[(*2S*)-2-hydroxy-2-phenylethanoyloxy]phenylacetic acid (Mughal *et al.*, 2004) and (1*R*,2*R*,3*S*,4*S*)-2-[(*R*)-mandeloxycarbonyl]bicyclo(2.2.1)-heptane-3-carboxylic acid (Ohtani *et al.*, 1991). The hydrogen bonding in the former differs from (I), forming an inter-molecular chain with the carboxylic acid groups further cross-linked by hydrogen bonding of the alcohol moiety with the ester, whereas the latter compound exhibits pairwise dimer-ization of the carboxylic acid groups. A related structure with a *tert*-butyl ester and substituents on the phenyl ring, (*S*,*E*)-2-[2-(3-methoxy-3-oxoprop-1-en-1-yl)-4-(trifluoromethyl)-phenyl]-2-(pivaloyloxy)acetic acid (Xiao *et al.*, 2016), exhibits a similar one-dimensional intermolecular carboxylic acid OH···ester carbonyl hydrogen-bonding motif to that found in the title compound.

5. Synthesis and crystallization

(*R*)-(−)-2-acetoxy-2-phenylacetic acid (99%) was purchased from Aldrich Chemical Company, USA, and was used as received.

6. Analytical data

^{1}H NMR (Bruker Avance 300 MHz, CDCl$_3$): δ 2.19 (*s*, 3 H, C*H$_3$*), 5.93 (*s*, 1H, C*H*), 7.36–7.42 (*m*, 3 H, C$_{aryl}$*H*), 7.45–7.51
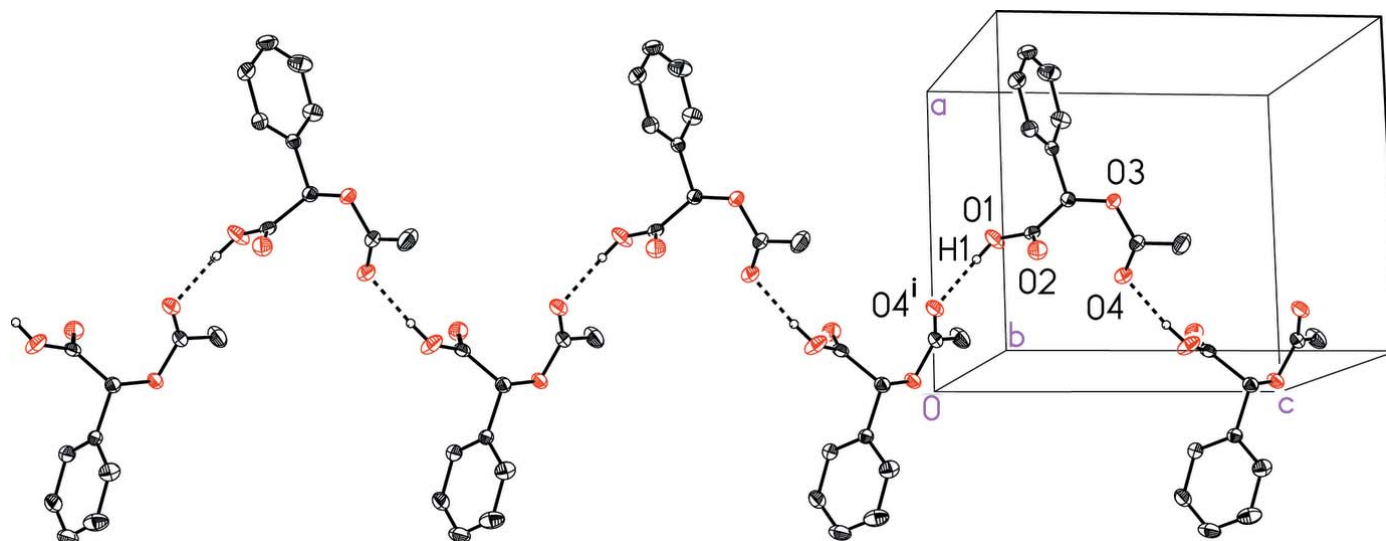

Figure 2
A view of the intermolecular hydrogen bonding in (*R*)-(−)-2-acetoxy-2-phenylacetic acid (I) that forms a one-dimensional chain. Symmetry code: (i) $-x + \frac{1}{2}, -y + 1, z - \frac{1}{2}$.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{10}H_{10}O_4$
M_r	194.18
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	125
a, b, c (Å)	9.1047 (10), 10.0086 (11), 10.5871 (11)
V (Å^3)	964.75 (18)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.88
Crystal size (mm)	$0.26 \times 0.26 \times 0.17$
Data collection	
Diffractometer	Bruker APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2013)
T_{min}, T_{max}	0.74, 0.86
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	8953, 1698, 1693
R_{int}	0.030
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.595
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.025, 0.062, 1.10
No. of reflections	1698
No. of parameters	131
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}, \Delta\rho_{min}$ (e Å^{-3})	0.19, −0.19
Absolute structure	Flack x determined using 691 quotients [$(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013); Hooft y calculated with *PLATON* (Spek, 2009)
Absolute structure parameter	−0.01 (4)

Computer programs: *APEX2* and *SAINT* (Bruker, 2013), *SHELXT* (Sheldrick, 2015*a*), *SHELXL2014* (Sheldrick, 2015*b*), *SHELXTL* (Sheldrick, 2008), *OLEX2* (Dolomanov *et al.*, 2009), *Mercury* (Macrae *et al.*, 2008) and *PLATON* (Spek, 2009).

(m, 2H, C$_{aryl}H$), 11.76 (*br s*, 1H, O*H*). ^{13}C NMR (^{13}C{^{1}H}, 75.5 MHz, CDCl$_3$): δ 20.59 (*C*H$_3$), 74.02 (*C*H), 127.62 (*C*$_{aryl}$H), 128.86 (*C*$_{aryl}$H), 129.49 (*C*$_{aryl}$H), 132.98 (*C*$_{aryl}$), 170.38 (*C*O), 174.55 (*C*O). IR (Thermo Nicolet iS50, ATR, cm^{-1}): 3483 (*w*), 3014 (*v b*r, O—H *str*), 2708 (*w*), 2588 (*w*), 1752 (*v s*, C=O *str*), 1686 (*v s*, C=O *str*), 1498 (*w*), 1461 (*w*), 1412 (*m*), 1382 (*s*), 1321 (*m*), 1277 (*s*), 1259 (*s*), 1206 (*s*), 1182 (*s*), 1045 (*s*), 996 (*m*), 967 (*m*), 919 (*m*), 888 (*m*), 767 (s), 734 (*s*), 700 (*s*), 642 (*m*), 616 (*w*), 603 (*w*), 583 (*w*), 525 (*s*), 487 (*w*). GC/MS (Hewlett-Packard MS 5975/GC 7890): *M*-18$^+$ = 176 (calc. exact mass 194.06 - water = 176).

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms on carbon were included in calculated positions and refined using a riding model with C–H = 0.95, 0.98 and 1.00 Å and $U_{iso}(H)$ = 1.2, 1.5 and 1.2 × $U_{eq}(C)$ of the aryl, methyl and methine C atoms, respectively. The position of the carboxylic acid hydrogen atom was found in the difference map and the atom refined semi-freely using a distance restraint $d(O—H)$ = 0.84 Å, and $U_{iso}(H)$ = 1.2$U_{eq}(O)$.

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supporting information

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Computing details

Data collection: *APEX2* (Bruker, 2013); cell refinement: *SAINT* (Bruker, 2013); data reduction: *SAINT* (Bruker, 2013); program(s) used to solve structure: SHELXT (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015b); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008), *OLEX2* (Dolomanov *et al.*, 2009), *Mercury* (Macrae *et al.*, 2008) and *PLATON* (Spek, 2009).

(*R*)-(-)-2-Acetoxy-2-phenylacetic acid

Crystal data

$C_{10}H_{10}O_4$	$D_x = 1.337$ Mg m^{-3}
$M_r = 194.18$	Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
Orthorhombic, $P2_12_12_1$	Cell parameters from 8300 reflections
$a = 9.1047$ (10) Å	$\theta = 4.2$–66.6°
$b = 10.0086$ (11) Å	$\mu = 0.88$ mm^{-1}
$c = 10.5871$ (11) Å	$T = 125$ K
$V = 964.75$ (18) Å^3	Block, colourless
$Z = 4$	$0.26 \times 0.26 \times 0.17$ mm
$F(000) = 408$	

Data collection

Bruker APEXII CCD diffractometer	8953 measured reflections
Radiation source: Cu IuS micro-focus source	1698 independent reflections
Detector resolution: 8.3333 pixels mm^{-1}	1693 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.030$
Absorption correction: multi-scan (SADABS; Bruker, 2013)	$\theta_{max} = 66.6°$, $\theta_{min} = 6.1°$
$T_{min} = 0.74$, $T_{max} = 0.86$	$h = -10 \rightarrow 10$
	$k = -11 \rightarrow 11$
	$l = -12 \rightarrow 12$

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
Least-squares matrix: full	
$R[F^2 > 2\sigma(F^2)] = 0.025$	$w = 1/[\sigma^2(F_o^2) + (0.0336P)^2 + 0.1385P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.062$	
$S = 1.10$	$(\Delta/\sigma)_{max} < 0.001$
1698 reflections	$\Delta\rho_{max} = 0.19$ e Å^{-3}
131 parameters	$\Delta\rho_{min} = -0.19$ e Å^{-3}
1 restraint	
Hydrogen site location: mixed	

Absolute structure: Flack x determined using
691 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*,
2013); Hooft y calculated with *PLATON* (Spek,
2009)
Absolute structure parameter: −0.01 (4)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	$U_{iso}*/U_{eq}$
O1	0.42132 (13)	0.46237 (13)	0.08956 (12)	0.0329 (3)
H1	0.355 (2)	0.479 (2)	0.035 (2)	0.039*
O2	0.35211 (12)	0.66275 (12)	0.16115 (11)	0.0286 (3)
O3	0.50941 (12)	0.63319 (11)	0.37499 (9)	0.0235 (3)
O4	0.29716 (12)	0.53107 (12)	0.42058 (10)	0.0273 (3)
C1	0.53382 (16)	0.53625 (15)	0.27588 (13)	0.0200 (3)
H1A	0.5199	0.4438	0.3097	0.024*
C2	0.69072 (15)	0.55447 (14)	0.23211 (13)	0.0184 (3)
C3	0.79939 (18)	0.47071 (16)	0.27844 (16)	0.0272 (4)
H3A	0.7744	0.3988	0.3329	0.033*
C4	0.94513 (18)	0.49242 (17)	0.2450 (2)	0.0346 (4)
H4A	1.0198	0.4358	0.2776	0.042*
C5	0.98206 (18)	0.59621 (18)	0.16417 (17)	0.0326 (4)
H5A	1.0818	0.6109	0.1418	0.039*
C6	0.87356 (18)	0.67809 (18)	0.11641 (16)	0.0303 (4)
H6A	0.8985	0.7482	0.0599	0.036*
C7	0.72770 (17)	0.65833 (17)	0.15078 (14)	0.0242 (3)
H7A	0.6534	0.7157	0.1187	0.029*
C8	0.42388 (15)	0.56275 (15)	0.16993 (14)	0.0201 (3)
C9	0.38220 (17)	0.62321 (16)	0.43773 (14)	0.0237 (3)
C10	0.3600 (2)	0.7365 (2)	0.52655 (17)	0.0364 (4)
H10A	0.4523	0.7555	0.5707	0.055*
H10B	0.2842	0.7128	0.5883	0.055*
H10C	0.329	0.8158	0.4792	0.055*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0273 (6)	0.0350 (6)	0.0363 (6)	0.0053 (5)	−0.0144 (5)	−0.0139 (5)
O2	0.0270 (6)	0.0289 (6)	0.0298 (6)	0.0060 (5)	−0.0008 (5)	−0.0001 (5)
O3	0.0209 (5)	0.0298 (6)	0.0198 (5)	−0.0061 (4)	0.0051 (4)	−0.0055 (4)
O4	0.0232 (5)	0.0335 (6)	0.0253 (6)	−0.0066 (5)	0.0058 (4)	0.0003 (5)
C1	0.0197 (7)	0.0209 (7)	0.0193 (7)	−0.0032 (6)	0.0012 (6)	−0.0020 (6)
C2	0.0171 (7)	0.0207 (7)	0.0173 (7)	−0.0019 (6)	−0.0001 (5)	−0.0046 (6)

C3	0.0249 (8)	0.0232 (8)	0.0334 (8)	0.0001 (7)	−0.0030 (7)	0.0014 (7)
C4	0.0214 (7)	0.0329 (9)	0.0496 (11)	0.0066 (7)	−0.0035 (8)	−0.0042 (8)
C5	0.0184 (7)	0.0424 (9)	0.0370 (9)	−0.0037 (7)	0.0061 (7)	−0.0119 (8)
C6	0.0276 (8)	0.0394 (9)	0.0238 (8)	−0.0093 (8)	0.0042 (7)	0.0016 (7)
C7	0.0215 (7)	0.0301 (8)	0.0210 (7)	−0.0005 (6)	−0.0010 (6)	0.0037 (6)
C8	0.0149 (7)	0.0237 (7)	0.0216 (7)	−0.0034 (6)	0.0036 (5)	−0.0010 (6)
C9	0.0213 (7)	0.0315 (8)	0.0184 (7)	−0.0036 (7)	0.0033 (6)	0.0021 (6)
C10	0.0390 (10)	0.0389 (10)	0.0311 (9)	−0.0082 (9)	0.0139 (8)	−0.0076 (8)

Geometric parameters (Å, º)

O1—C8	1.3168 (19)	C3—H3A	0.95
O1—H1	0.852 (19)	C4—C5	1.387 (3)
O2—C8	1.1989 (19)	C4—H4A	0.95
O3—C9	1.3389 (18)	C5—C6	1.380 (3)
O3—C1	1.4463 (17)	C5—H5A	0.95
O4—C9	1.218 (2)	C6—C7	1.391 (2)
C1—C2	1.5128 (19)	C6—H6A	0.95
C1—C8	1.527 (2)	C7—H7A	0.95
C1—H1A	1.0	C9—C10	1.487 (2)
C2—C3	1.386 (2)	C10—H10A	0.98
C2—C7	1.391 (2)	C10—H10B	0.98
C3—C4	1.391 (2)	C10—H10C	0.98
C8—O1—H1	107.2 (15)	C4—C5—H5A	120.1
C9—O3—C1	116.28 (11)	C5—C6—C7	120.22 (16)
O3—C1—C2	106.65 (11)	C5—C6—H6A	119.9
O3—C1—C8	108.41 (11)	C7—C6—H6A	119.9
C2—C1—C8	111.91 (12)	C6—C7—C2	119.95 (14)
O3—C1—H1A	109.9	C6—C7—H7A	120.0
C2—C1—H1A	109.9	C2—C7—H7A	120.0
C8—C1—H1A	109.9	O2—C8—O1	125.26 (14)
C3—C2—C7	119.87 (14)	O2—C8—C1	124.01 (14)
C3—C2—C1	119.51 (13)	O1—C8—C1	110.72 (12)
C7—C2—C1	120.54 (13)	O4—C9—O3	122.18 (14)
C2—C3—C4	119.76 (15)	O4—C9—C10	125.84 (14)
C2—C3—H3A	120.1	O3—C9—C10	111.98 (13)
C4—C3—H3A	120.1	C9—C10—H10A	109.5
C5—C4—C3	120.37 (16)	C9—C10—H10B	109.5
C5—C4—H4A	119.8	H10A—C10—H10B	109.5
C3—C4—H4A	119.8	C9—C10—H10C	109.5
C6—C5—C4	119.83 (15)	H10A—C10—H10C	109.5
C6—C5—H5A	120.1	H10B—C10—H10C	109.5
C9—O3—C1—C2	−172.13 (12)	C4—C5—C6—C7	1.1 (3)
C9—O3—C1—C8	67.21 (15)	C5—C6—C7—C2	−1.0 (3)
O3—C1—C2—C3	98.10 (15)	C3—C2—C7—C6	−0.2 (2)
C8—C1—C2—C3	−143.51 (14)	C1—C2—C7—C6	176.71 (15)

O3—C1—C2—C7	−78.78 (16)	O3—C1—C8—O2	13.69 (19)
C8—C1—C2—C7	39.62 (18)	C2—C1—C8—O2	−103.65 (16)
C7—C2—C3—C4	1.1 (2)	O3—C1—C8—O1	−167.43 (12)
C1—C2—C3—C4	−175.84 (16)	C2—C1—C8—O1	75.23 (15)
C2—C3—C4—C5	−0.9 (3)	C1—O3—C9—O4	6.3 (2)
C3—C4—C5—C6	−0.2 (3)	C1—O3—C9—C10	−173.19 (13)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O4[i]	0.85 (2)	1.84 (2)	2.6761 (16)	165 (2)
C10—H10*B*···O1[ii]	0.98	2.56	3.312 (2)	133

Symmetry codes: (i) −*x*+1/2, −*y*+1, *z*−1/2; (ii) −*x*+1/2, −*y*+1, *z*+1/2.