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(1*S*,2*R*,2′*S*)- and (1*S*,2*S*,2′*S*)-1-phenyl-2-phenylthio-2-(tetrahydropyran-2′-ylthio)ethanol diastereoisomers at 193 K

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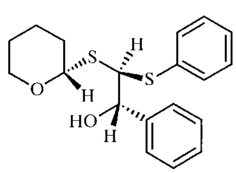
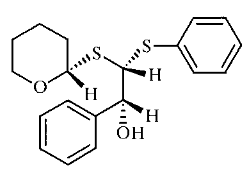
In the synthesis of 1-phenyl-2-phenylthio-2-(tetrahydropyran-2-ylthio)ethanol, $C_{19}H_{22}O_2S_2$, four diastereoisomers are formed. Two non-centrosymmetric enantiomeric forms which crystallize in space groups $P2_12_12_1$ and $Pna2_1$ are presented. The former has an intramolecular hydrogen bond between the hydroxyl group and the O atom of the tetrahydropyran ring. In the latter isomer, the hydroxyl group forms an intermolecular hydrogen bond to the O atom of the tetrahydropyranyl group of a neighbouring molecule, joining the molecules into chains in the *c*-axis direction; the O···O distances are 2.962 (4) and 2.764 (3) Å, respectively. The tetrahydropyran rings are in chair conformations in both isomers and the S side chain has an equatorial orientation in the former, but an axial orientation in the latter molecule.

Comment

The two title diastereoisomers may alternatively be named with configurations (1*R*,2*S*,15*S*), (I), and (1*S*,2*S*,15*S*), (II), using the atomic labelling presented in Figs. 1 and 2, and in accordance with the previously reported diastereomer with the configuration (1*S*,2*S*,15*R*), (III) (Kansikas *et al.*, 1996).



(I)



(II)

These three diastereoisomers crystallize as a conglomerate of enantiomeric crystals in non-centrosymmetric orthorhombic space groups; (I) and (III) in $P2_12_12_1$ (No. 19), and (II) in $Pna2_1$ (No. 33). The fourth diastereoisomer crystallizes as a racemate with the configuration (1*R**,2*S**,15*R**), (IV), and the structural details will be reported later. Previously, we presented a very closely related compound, 2-(1-phenylthio)-1-(tetrahydropyran-2-ylthio)propan-2-ol, $C_{20}H_{24}O_2S_2$, with the configuration (1*S**,2*S**,16*R**), (V), where C16 is the C atom of the tetrahydropyran ring bonded to S (Kansikas *et al.*, 1995). The conformation of (V) is nearly equal to that of the ethanol diastereoisomer (III), and molecules of (I), (III) and (V) possess an intramolecular hydrogen bond. However, though the structures of these three molecules are rather similar, compound (V) crystallizes in a centrosymmetric space group $P2_1/c$. The configurations of molecules (I) and (II) differ only at C1, but the conformations within the molecules are

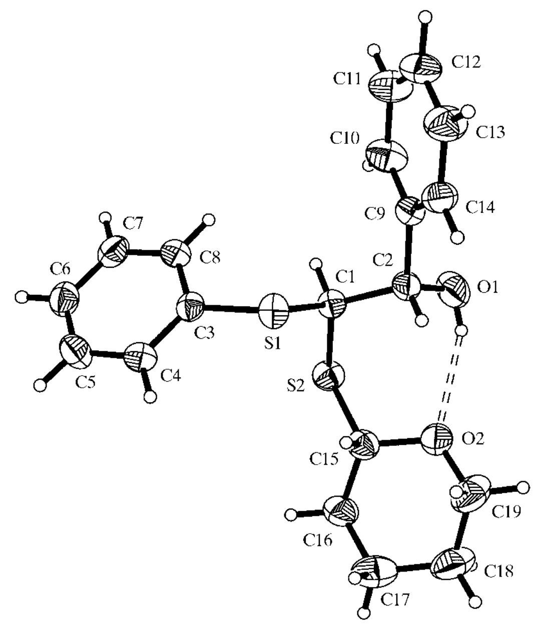


Figure 1
View of (I) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

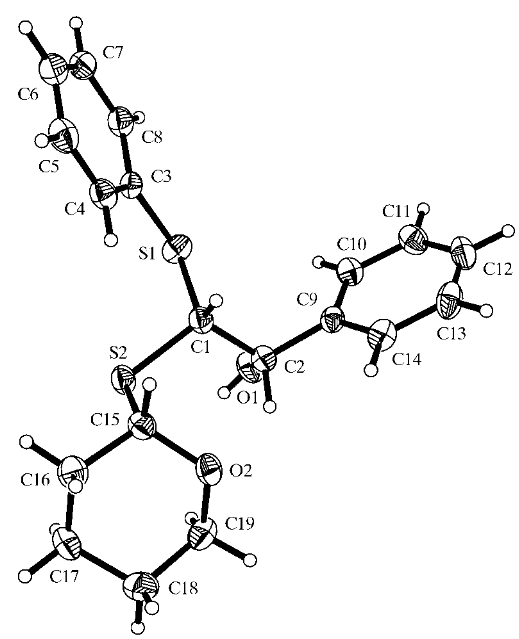


Figure 2
View of (II) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

quite different. In (I), there is an intramolecular hydrogen bond between the hydroxyl group and the O atom of the tetrahydropyran ring, with an O···O distance of 2.962 (4) Å (Table 2). This is remarkably longer than the respective hydrogen bonds of 2.719 (10) Å in (III) and 2.816 (3) Å in the propanol derivative (V). The stronger hydrogen bonding is probably the reason for the ready crystallizability of (III) and (V) compared with (I). In (II), the molecules are linked into chains in the *c*-axis direction by hydrogen bonds between the hydroxyl group and the O atom of the tetrahydropyran ring of a neighbouring molecule with the symmetry code ($x, y, z - 1$) (Table 4 and Fig. 3). The absence of intramolecular hydrogen bonding causes prolonged retention time in liquid chromatography, 10.9 min for (II), 6.6 min for (I) and 5.9 min for (III), and very slow crystallizability. Bond lengths and angles are normal in molecules (I) and (II), and the S atom distances to the aromatic rings are slightly shorter than the other S—C bonds (Tables 1 and 3). In structures (I) and (II), the tetrahydropyran ring is in a chair conformation as expected, and the S side chain at C15 is in an equatorial orientation in isomer (I), but axial in (II). Free rotations around the acyclic single bonds give rise to different conformations which can be described by the torsion angles where, for example, C1 is involved. Selected torsion angles are listed in Tables 1 and 3 and the conformational differences are also seen in Figs. 1 and 2. The measured ^{1}H NMR coupling constants of H15 for (I) (7.4 and 3.2 Hz) compared with those calculated (Still *et al.*, 1994) from the crystal data (11.4 and 2.9 Hz) indicate that in $CDCl_3$ solution also, the S side chain is mostly in the equatorial position. The axial S side chain at C15 of compound (II) is also predominant in solution according to the corresponding coupling constants (5.7 and 3.9 Hz measured, and 5.9 and 1.1 Hz calculated).

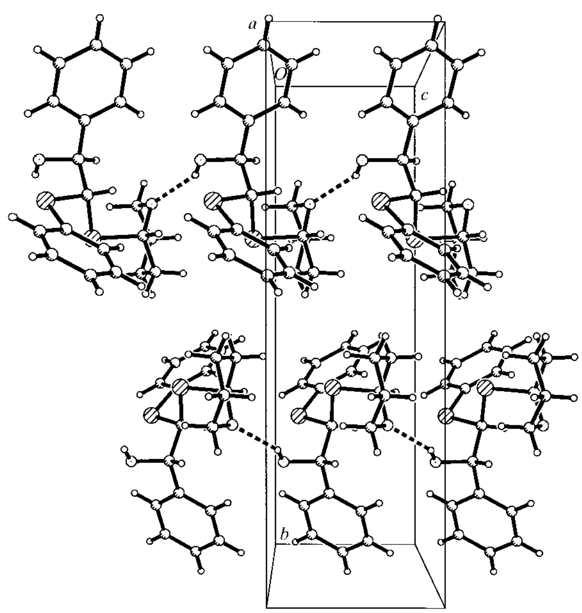


Figure 3
View of the molecular packing of (II) showing the hydrogen-bonding scheme in the *c*-axis direction seen perpendicular to the *bc* plane.

Experimental

1-Phenyl-2-phenylthio-2-(tetrahydropyran-2-ylthio)ethanol was synthesized from 2-(phenylthiomethylthio)tetrahydropyran and benzaldehyde as a mixture of four diastereomers according to the previously reported procedure of Kansikas *et al.* (1996). After evaporation of the solvent, the four diastereomers were separated by semi-preparative high-pressure liquid chromatography (HPLC). The crystals for the structure determinations were obtained after several slow recrystallizations from absolute ethanol. (1*S**,2*R**,2′*S**)-1-Phenyl-2-phenylthio-2-(tetrahydropyran-2′-ylthio)ethanol, (I) (m.p. 379–381 K), ^{1}H NMR: δ 1.5–1.9 (*m*, 3 × CH_2), 3.52–3.65 and 3.93–4.05 (*m*, OCH_2), 4.53 (*d*, 4.8 Hz, SCHS), 4.55 (*d*, 7.8 Hz, OH), 5.02 (*dd*, 4.8 and 7.5 Hz, PhCH), 5.09 (*dd*, 3.2 and 7.4 Hz, OCHS), 7.2–7.5 (*m*, aromatic H); ^{13}C NMR: δ 22.5 and 25.5 and 31.3 (CH_2), 63.8 (SCHS), 66.3 (OCH_2), 76.0 (PhCH), 80.2 (OCHS), 126.8–142.0 (aromatic C). (1*S**,2*S**,2′*S**)-1-Phenyl-2-phenylthio-2-(tetrahydropyran-2-ylthio)-ethanol, (II) (m.p. 359 K), ^{1}H NMR: δ 1.4–2.0 (*m*, 3 × CH_2), 3.36–3.50 and 3.75–3.92 (*m*, OCH_2), 3.60 (*d*, 5.2 Hz, OH), 4.60 (*d*, 5.2 Hz, SCHS), 4.94 (*t*, 5.2 Hz, PhCH), 5.10 (*dd*, 3.9 and 5.7 Hz, OCHS), 7.2–7.5 (*m*, aromatic H); ^{13}C NMR: δ 22.0, 25.7 and 30.9 (CH_2), 63.2 (SCHS), 64.9 (OCH_2), 75.4 (PhCH), 82.8 (OCHS), 127.4–140.4 (aromatic C).

Isomer (I)

Crystal data

$C_{19}H_{22}O_2S_2$
M_r = 346.49
Orthorhombic, $P2_12_12_1$
a = 5.3170 (11) Å
b = 16.642 (3) Å
c = 19.998 (4) Å
V = 1769.5 (6) Å^3
Z = 4
D_x = 1.301 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 4–10°
μ = 0.308 mm^{-1}
T = 193 (2) K
Prismatic, colourless
0.31 × 0.22 × 0.16 mm

Data collection

Rigaku AFC-7*S* diffractometer
$\omega/2\theta$ scans
2057 measured reflections
2057 independent reflections
1850 reflections with $I > 2\sigma(I)$
θ_{max} = 26.45°
$h = 0 \rightarrow 6$
$k = 0 \rightarrow 20$
$l = 0 \rightarrow 24$
3 standard reflections every 100 reflections intensity decay: none

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

S1—C3	1.779 (3)	O1—C2	1.408 (5)
S1—C1	1.814 (3)	O2—C15	1.424 (4)
S2—C15	1.794 (4)	O2—C19	1.433 (5)
S2—C1	1.816 (3)	C1—C2	1.554 (4)
C3—S1—C1	101.71 (15)	C2—C1—S2	114.8 (2)
C15—S2—C1	101.86 (16)	S1—C1—S2	114.20 (17)
C15—O2—C19	111.2 (3)	O1—C2—C1	110.8 (3)
C2—C1—S1	107.3 (2)	O2—C15—S2	108.4 (3)
C3—S1—C1—C2	164.2 (2)	S2—C1—C2—O1	43.6 (4)
C3—S1—C1—S2	−67.4 (2)	S1—C1—C2—C9	−68.3 (3)
C15—S2—C1—C2	58.9 (3)	S2—C1—C2—C9	163.6 (3)
C15—S2—C1—S1	−65.6 (2)	C1—S2—C15—O2	−80.0 (3)
S1—C1—C2—O1	171.7 (2)	C1—S2—C15—C16	159.1 (3)

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.105$
$S = 1.030$
2057 reflections
208 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0549P)^2 + 0.7649P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter = 0.22 (13)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*A*···O2	0.84	2.25	2.962 (4)	143

Isomer (II)

Crystal data

$C_{19}H_{22}O_2S_2$
$M_r = 346.49$
Orthorhombic, $Pna2_1$
$a = 16.699$ (3) Å
$b = 18.507$ (4) Å
$c = 5.6150$ (11) Å
$V = 1735.3$ (6) Å^3
$Z = 4$
$D_x = 1.326$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 4$–10°
$\mu = 0.314$ mm^{-1}
$T = 193$ (2) K
Prismatic, colourless
0.38 × 0.26 × 0.22 mm

Data collection

Rigaku AFC-7*S* diffractometer
$\omega/2\theta$ scans
7318 measured reflections
1955 independent reflections
1842 reflections with $I > 2\sigma(I)$
$R_{int} = 0.070$
$\theta_{max} = 26.51°$
$h = -20 \rightarrow 20$
$k = -23 \rightarrow 23$
$l = 0 \rightarrow 7$
3 standard reflections
every 100 reflections
intensity decay: none

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

S1—C3	1.783 (2)	O1—C2	1.425 (3)
S1—C1	1.816 (3)	O2—C15	1.420 (3)
S2—C1	1.834 (2)	O2—C19	1.431 (3)
S2—C15	1.843 (3)	C1—C2	1.550 (3)
C3—S1—C1	104.95 (12)	C2—C1—S2	111.34 (16)
C1—S2—C15	100.48 (12)	S1—C1—S2	109.22 (12)
C15—O2—C19	114.04 (18)	O1—C2—C1	110.7 (2)
C2—C1—S1	107.81 (18)	O2—C15—S2	113.66 (17)
C3—S1—C1—C2	−156.81 (15)	S2—C1—C2—O1	74.4 (3)
C3—S1—C1—S2	82.08 (15)	S1—C1—C2—C9	75.2 (2)
C15—S2—C1—C2	86.5 (2)	S2—C1—C2—C9	−165.03 (19)
C15—S2—C1—S1	−154.53 (13)	C1—S2—C15—O2	−64.06 (18)
S1—C1—C2—O1	−45.4 (2)	C1—S2—C15—C16	169.66 (17)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*B*···O2[i]	0.74 (3)	2.12 (4)	2.764 (3)	146 (4)

Symmetry code: (i) $x, y, z - 1$.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.032$
$wR(F^2) = 0.083$
$S = 1.027$
1955 reflections
212 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0535P)^2 + 0.1178P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.25$ e Å^{-3}
$\Delta\rho_{min} = -0.43$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter = 0.00 (8)

All H atoms in (I) were placed at calculated positions and were refined using a riding model with fixed distances and angles. In (II), all other H atoms were treated in a similar way to (I), except that the hydroxy H atom was located from the Fourier map and refined separately because the calculated position was not satisfactory for hydrogen bonding. The absolute configurations of the two isomers presented here are based on the values of the Flack (1983) parameters of 0.22 (13) for (I) and 0.00 (8) for (II); no Friedel reflections were used in these refinements.

For both compounds, data collection and cell refinement: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1996); data reduction: *TEXSAN* (Molecular Structure Corporation, 1993); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: OS1121). Services for accessing these data are described at the back of the journal.

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