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The absolute configuration of (2*S*,4*S*)- and (2*R*,4*R*)-2-*tert*-butyl-4-methyl-3-(4-tolylsulfonyl)-1,3-oxazolidine-4-carbaldehyde

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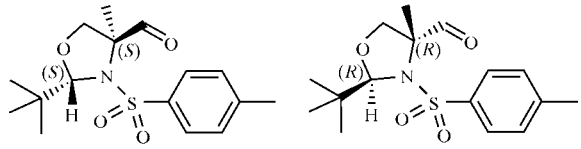
The title enantiomorphic compounds, $C_{16}H_{23}NO_4S$, have been obtained in an enantiomerically pure form by crystallization from a diastereomeric mixture either of (2*S*,4*S*)- and (2*R*,4*S*)- or of (2*R*,4*R*)- and (2*S*,4*R*)-2-*tert*-butyl-4-methyl-3-(4-tolylsulfonyl)-1,3-oxazolidine-4-carbaldehyde. These mixtures were prepared by an aziridination rearrangement process starting with (*S*)- or (*R*)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine. The crystal structures indicate an envelope conformation of the oxazolidine moiety for both compounds.

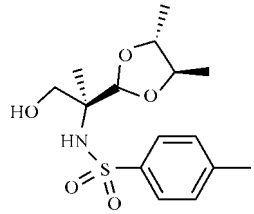
Comment

Aziridination of alkenes is an attractive process for the preparation of biologically active compounds (Tanner, 1994). Several aziridination methods are described in the literature, particularly for substituted alkenes (Evans *et al.*, 1994). However, less is known about the aziridination of functionalized alkenes, for example, enol ethers and related compounds. Recently, we have investigated the aziridination of cyclic vinyl acetals. We found that these compounds undergo an *in situ* aziridination rearrangement process to give 1,3-oxazolidine-4-carbaldehydes (Flock & Frauenrath, 2001). For example, treatment of (*S*)-(−)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (92% ee), prepared by $NiBr_2$[(−)-Diop]/$LiBHEt_3$-catalyzed isomerization of 2-*tert*-butyl-5-methylene-1,3-dioxane [Diop is 2,2-dimethyl-4,5-bis(diphenylphosphinomethyl)-1,3-dioxolane] (Frauenrath *et al.*, 1998; Flock *et al.*, 2005), with [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) in the presence of CuOTf benzene complex (10 mol%; OTf is trifluoromethanesulfonate) led in a one-step procedure to a 70:30 mixture of (2*S*,4*S*)- and (2*R*,4*S*)-2-*tert*-butyl-4-methyl-3-(4-tolylsulfonyl)-1,3-oxazolidine-4-carbaldehyde (Flock, 2003). After purification of the crude reaction product and recrystallization from *tert*-butyl methyl ether, the major diastereomer, (2*S*,4*S*)-(I), was obtained in a crystalline form. For the determination of the optical purity by NMR spectroscopy, the crystalline solid was reacted with (2*R*,3*R*)-(−)-butanediol to give *N*-[1-(4,5-dimethyl-1,3-dioxolan-2-yl)-2-hydroxy-1-methylethyl]-4-methylbenzenesulfonamide, (III). Surprisingly, only one diastereomer could be detected in the NMR spectra of the crude reaction mixture, indicating that



(I) (II)

the crystalline diastereomer, (I), was obtained in an enantiomerically pure form. The opposite enantiomer, (2*R*,4*R*)-(II), was prepared by the same procedure from (*R*)-(+)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (91% ee). The latter compound was readily obtained by asymmetric double-bond isomerization of 2-*tert*-butyl-5-methylene-1,3-dioxane using $NiBr_2$[(+)-Diop]/$LiBHEt_3$ as a catalyst (Flock *et al.*, 2005). Compounds (I) and (II) are useful chiral building blocks, for example, for the synthesis of unnatural amino acids bearing a quaternary chiral center, and a knowledge of the absolute configuration of these compounds is important for gaining more insight into the diastereoselective course of the intermediate aziridination process. For this reason, the structures and absolute configurations of compounds (I) and (II) have been established by X-ray crystallography.



(III)

The molecular structures and correct absolute configurations, as confirmed by refinement of the absolute structure parameter (Flack, 1983), of compounds (I) and (II) are shown in Figs. 1 and 2, respectively. In both structures, the bond distances and angles agree with the expected values and no unusual intermolecular interactions could be found. For (I), the closest intermolecular contacts to neighboring molecules are C4···C3^{i} and C5···O4^{ii} [3.2369 (16) and 3.2252 (19) Å; symmetry codes: (i) $-x, y-\frac{1}{2}, -z+\frac{3}{2}$; (ii) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$]. The C11···O1^{iii} distance of 3.3863 (17) Å [symmetry code: (iii) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$] may be regarded as an extremely weak C—H···O hydrogen bridge. The corresponding contact distances in compound (II) are almost identical. The oxazolidine moieties of (I) and (II) adopt the same envelope conformation, with atom C2 lying 0.479 (2) Å (mean value) above the plane formed by atoms C1, C3, O1 and N1. The deviation of atoms C1, C3, O1 and N1 from the ring plane [the mean values are −0.035 (1), −0.022 (1), 0.022 (1) and 0.035 (1) Å, respectively] and the distance of atom C2 from this plane are identical within 3σ for the two structures.

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Oxazolidine rings preferably adopt envelope conformations in the crystalline state, but with different atoms lying out of the plane. In the archetypal unsubstituted *p*-tosyl-1,3-oxazolidine (Gálvez-Ruiz *et al.*, 2004), the O atom lies out of the molecular plane, a conformation typically found for *p*-tosyl-1,3-oxazolidine derivatives with only Csp^3 atoms and a CH_2 group in the non-acetalic position α to the ring O atom. However, *p*-tosyl-1,3-oxazolidines with this CH_2 group out of the molecular plane (as found for the present structures) are not unusual. Twisted five-membered rings or conformations with N or other C atoms out of the plane exist but are rare exceptions. Therefore, we assume that, in the present case, the envelope conformation is mostly influenced by the substitution pattern of the quarternary C atom in the position (C3) α to the N atom. A closely related envelope conformation was found for 3-(*tert*-butyloxycarbonyl)-2,2-dimethyl-4-methyl-1,3-oxazolidine-4-carbaldehyde, which has a comparable substitution pattern in the C3 position (Avenoza *et al.*, 2003). The absolute value of the N1—C3—C4—O2 torsion angle is 156.63 (13)° in (I) and 156.80 (13)° in (II), which are also identical within 3σ and indicate a *gauche* orientation of the carbonyl group (C4═O2) with respect to the methyl group at atom C5. Obviously, this orientation of the C4═O2 carbonyl group leads to a minimization of the interaction of carbonyl atom O2 with atoms O1 and O4.

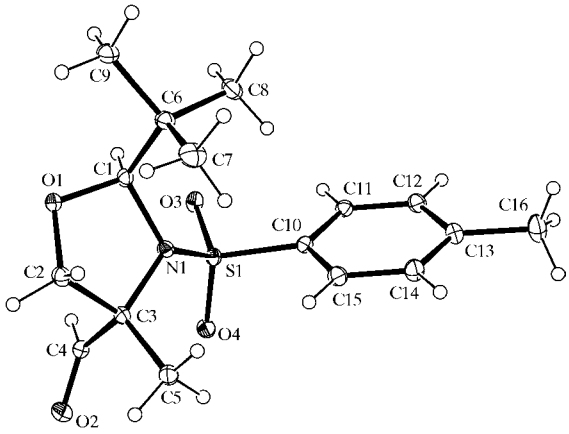

Figure 1
The molecular structure of (I), showing the atom-labeling scheme. Displacement ellipsoids for non-H atoms are drawn at the 30% probability level and H atoms are drawn as circles of arbitrary radii.

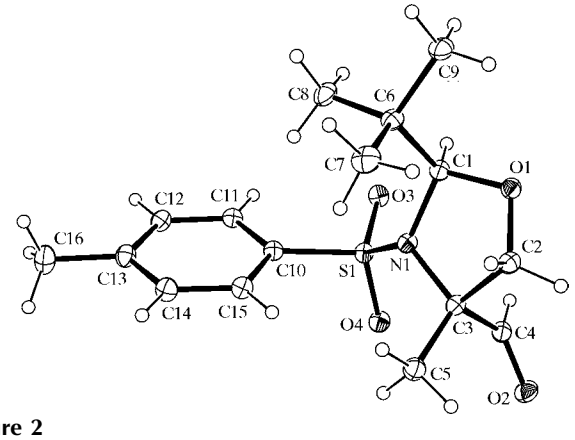

Figure 2
The asymmetric unit of (II), showing the atom-labeling scheme. Displacement ellipsoids for non-H atoms are drawn at the 30% probability level and H atoms are drawn as circles of arbitrary radii.

Experimental

For the preparation of (I) and (II), under an inert atmosphere, PhI═NTs (15 mmol, 5.598 g) was added in small portions over a period of 3 h to a solution of (−)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (10 mmol, 1.562 g, 92% ee) or (+)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (91% ee), respectively, and CuOTf benzene complex (0.503 g, 10 mol%) in dry *tert*-butyl methyl ether (25 ml). After complete conversion (monitored by gas chromatography), the solvent was evaporated under reduced pressure and the oily residue was purified by column chromatography (silica, light petroleum/diethyl ether, 5:1) to afford a diastereomeric mixture (70:30) of the oxazolidinecarbaldehyde as a colorless solid. Recrystallization from *tert*-butyl methyl ether led to single crystals of the main diastereomers, (I) and (II) (m.p. 398–399 K). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.84 [*s*, 9H, $C(CH_3)_3$], 1.63 (*s*, 3H, CH_3), 2.44 (*s*, 3H, Ph—CH_3), 4.04 (*d*, 1H, ^2J = 10.0 Hz, O—CH_2), 4.10 (*d*, 1H, ^2J = 10.0 Hz, O—CH_2), 5.44 (*s*, 1H, O—C*H*—N), 7.32 (*m*, 2H, CH aromatic), 7.76 (*m*, 2H, CH aromatic), 9.87 (*s*, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.6 (1C, CH_3), 21.5 (1C, Ph—CH_3), 26.3 [3C, $C(CH_3)_3$], 38.0 [1C, $C(CH_3)_3$], 71.9 (1C, N—C—CH_3), 73.2 (1C, OCH_2), 100.5 (1C, O—CH*R*—N), 127.5 (2C, C2 + 6 aromatic), 129.9 (2C, C3 + 5 aromatic), 138.0 (1C, C1 aromatic), 144.0 (1C, C4 aromatic), 198.4 (1C, CHO). IR (ATR, cm^{-1}): δ 2962, 2927, 2852, 1737, 1451, 1334, 1259, 1160, 1090, 1012, 812, 705, 665, 594, 547. Analysis calculated for $C_{16}H_{23}NO_4S$: C 59.05, H 7.12, N 4.30%; found: C 59.03, H 7.07, N 4.28%. For (I): $[\alpha]_D^{20} = -76.1$ (*c* 2.95, $CHCl_3$); for (II): $[\alpha]_D^{20} = +73.03$ (*c* 1.65, $CHCl_3$).

Enantiomorph (I)

Crystal data

$C_{16}H_{23}NO_4S$
M_r = 325.41
Orthorhombic, $P2_12_12_1$
a = 8.5175 (6) Å
b = 11.3011 (8) Å
c = 17.0503 (13) Å
V = 1641.2 (2) Å^3
Z = 4
D_x = 1.317 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 16746 reflections
θ = 2.2–27.0°
μ = 0.21 mm^{-1}
T = 100 (2) K
Plate, colorless
0.30 × 0.20 × 0.10 mm

Data collection

Stoe IPDS-II diffractometer
ω scans
Absorption correction: integration (*X-RED*; Stoe & Cie, 2004)
T_{min} = 0.923, T_{max} = 0.980
9743 measured reflections
3518 independent reflections
3192 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 27.0°
h = −10 → 10
k = −14 → 14
l = −21 → 21

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.025
$wR(F^2)$ = 0.059
S = 0.95
3518 reflections
205 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0374P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0103 (10)
Absolute structure: Flack (1983), 1486 Friedel pairs
Flack parameter: −0.04 (5)

Enantiomorph (II)

Crystal data

$C_{16}H_{23}NO_4S$
M_r = 325.41
Orthorhombic, $P2_12_12_1$
a = 8.5276 (6) Å
b = 11.3090 (11) Å
c = 17.0624 (12) Å
V = 1645.5 (2) Å^3
Z = 4
D_x = 1.314 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 17010 reflections
θ = 1.9–27.8°
μ = 0.21 mm^{-1}
T = 100 (2) K
Plate, colorless
0.35 × 0.30 × 0.20 mm

Data collection

Stoe IPDS-II diffractometer
ω scans
Absorption correction: integration (*X-RED*; Stoe & Cie, 2004)
T_{min} = 0.941, T_{max} = 0.971
13910 measured reflections
3772 independent reflections
3554 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 27.6°
$h = -10 \rightarrow 11$
$k = -14 \rightarrow 14$
$l = -21 \rightarrow 21$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.028
$wR(F^2)$ = 0.076
S = 1.02
3772 reflections
205 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0579P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.012
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.028 (2)
Absolute structure: Flack (1983), 1617 Friedel pairs
Flack parameter: −0.04 (5)

The methyl H atoms were constrained to an ideal geometry, with C—H distances of 0.96 Å and U_{iso}(H) values of $1.5U_{eq}$(C), but were allowed to rotate freely about the C—C bonds. All other H atoms were positioned geometrically and refined using a riding model, with C—H distances in the range 0.93–0.98 Å and U_{iso}(H) values of $1.2U_{eq}$(C).

For both compounds, data collection: *X-AREA* (Stoe & Cie, 2004); cell refinement: *X-AREA*; data reduction: *X-RED* (Stoe & Cie, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN1192). Services for accessing these data are described at the back of the journal.

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