

(S)-2-(Iodomethyl)-1-tosylpyrrolidine

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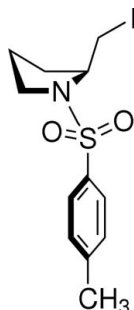
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Key indicators: single-crystal X-ray study; $T = 294$ K; mean $\sigma(\text{C}-\text{C}) = 0.009$ Å;
 R factor = 0.037; wR factor = 0.092; data-to-parameter ratio = 15.5.

In the title molecule, $\text{C}_{12}\text{H}_{16}\text{INO}_2\text{S}$, the pyrrolidine ring is in an envelope conformation. The dihedral angle between the four essentially coplanar atoms of the pyrrolidine ring and the benzene ring is 75.5 (4)°.

Related literature

For leading reviews, see: Allemann *et al.* (2004); List (2004); Notz *et al.* (2004); For related literature, see: Bahmanyar *et al.* (2003); List *et al.* (2000); Northrup & MacMillan, (2002); Sakthivel *et al.* (2001); Barbas *et al.* (1997); Dalko & Moisan (2004); Eder *et al.* (1971); Hajos & Parrish (1974); Machajewski & Wong (2000); Seayed & List (2005); Wagner *et al.* (1995).

**Experimental***Crystal data* $\text{C}_{12}\text{H}_{16}\text{INO}_2\text{S}$ $M_r = 365.22$ Monoclinic, $P2_1$ $a = 7.6345$ (16) Å $b = 7.7084$ (16) Å $c = 12.071$ (3) Å $\beta = 93.17$ (1)° $V = 709.3$ (3) Å³ $Z = 2$ Mo $K\alpha$ radiation $\mu = 2.40$ mm⁻¹ $T = 294$ (2) K $0.25 \times 0.16 \times 0.16$ mm*Data collection*

Bruker APEX CCD area-detector
diffractometer

Absorption correction: multi-scan
(*SADABS*; Sheldrick, 1996)

 $T_{\min} = 0.586$, $T_{\max} = 0.701$

4398 measured reflections

2424 independent reflections

1787 reflections with $I > 2\sigma(I)$ $R_{\text{int}} = 0.033$ *Refinement* $R[F^2 > 2\sigma(F^2)] = 0.037$ $wR(F^2) = 0.092$ $S = 1.02$

2424 reflections

156 parameters

1 restraint

H-atom parameters constrained

 $\Delta\rho_{\max} = 0.43$ e Å⁻³ $\Delta\rho_{\min} = -0.48$ e Å⁻³Absolute structure: Flack (1983),
with 664 Friedel pairs

Flack parameter: 0.02 (5)

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2000); software used to prepare material for publication: *SHELXTL*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH2560).

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(S)-2-(Iodomethyl)-1-tosylpyrrolidine**Ya-Wen Wang and Yu Peng****S1. Comment**

During the past few years, the field of asymmetric catalysis, previously dominated by biocatalysis, has been complemented by organocatalysis (List, 2004; Notz *et al.*, 2004; Allemann *et al.*, 2004) using small organic molecules as a third powerful tool. Organocatalysis reagents are usually non-toxic, highly efficient and selective, readily available, metal-free and robust, explaining the growing interest in their use for organic synthesis (Dalko & Moisan, 2004; Seayed & List, 2005). Considering the above features, low cost and availability in both enantiomeric forms, proline is attractive especially to synthetic chemists. Developed by two industrial laboratories in the early 1970 s (Hajos & Parrish, 1974; Eder *et al.*, 1971), a proline-catalyzed aldol reaction was reinvestigated recently and many novel results were obtained. For example, direct intermolecular asymmetric aldol reactions between aldehydes and the ketones (List *et al.*, 2000; Sakthivel *et al.*, 2001) or aldehydes (Northrup & MacMillan, 2002) afforded good to excellent enantioselectivity. The origin of stereoselectivity in this type of aldol reaction was examined in detail (Bahmanyar *et al.*, 2003) and it was generally accepted this involved enamine intermediates. Similar mechanisms are found in type-1 aldolases (Machajewski & Wong, 2000) and catalytic antibodies that are type-1 aldolase mimics (Wagner *et al.*, 1995; Barbas *et al.*, 1997).

The molecular structure of the title compound (Fig.1) contains a pyrrolidine ring, which exists in an envelope conformation. The dihedral angle between the plane of atoms N1–C1–C3–C5 and the benzene ring is 75.5 (4) °, which potentially provides enough space as a binding-site for substrates during asymmetric catalysis process.

S2. Experimental

The title compound was prepared by the cascade reaction of *p*-toluenesulfonyl chloride with (S)-prolinol (commercial available) and iodine. ¹H NMR (400 MHz, CDCl₃): 7.73 (d, J = 6.8 Hz, 2H), 7.34 (d, J = 6.8 Hz, 2H), 3.77–3.71 (m, 1H), 3.63–3.60 (m, 1H), 3.51–3.46 (m, 1H), 3.23 (t, J = 9.6 Hz, 2H), 2.44 (s, 3H), 1.90–1.77 (m, 3H), 1.56–1.50 (m, 1H) p.p.m.; ¹³C NMR (100 MHz, CDCl₃): 143.7, 134.2, 129.8 (2 C), 127.5 (2 C), 60.7, 50.0, 31.9, 23.8, 21.5, 11.5 p.p.m.. Single crystals suitable for X-ray determination were obtained by slow evaporation of a EtOAc solution over a period of several days.

S3. Refinement

All H atoms were placed geometrically (C—H distances were set to 0.98, 0.97, 0.96 and 0.93 Å for atoms CH, CH₂, CH₃, and CH (phenyl), respectively) and refined with a riding model, with $U_{\text{iso}}(\text{H}) = 1.2$ or 1.5 times $U_{\text{eq}}(\text{C})$.

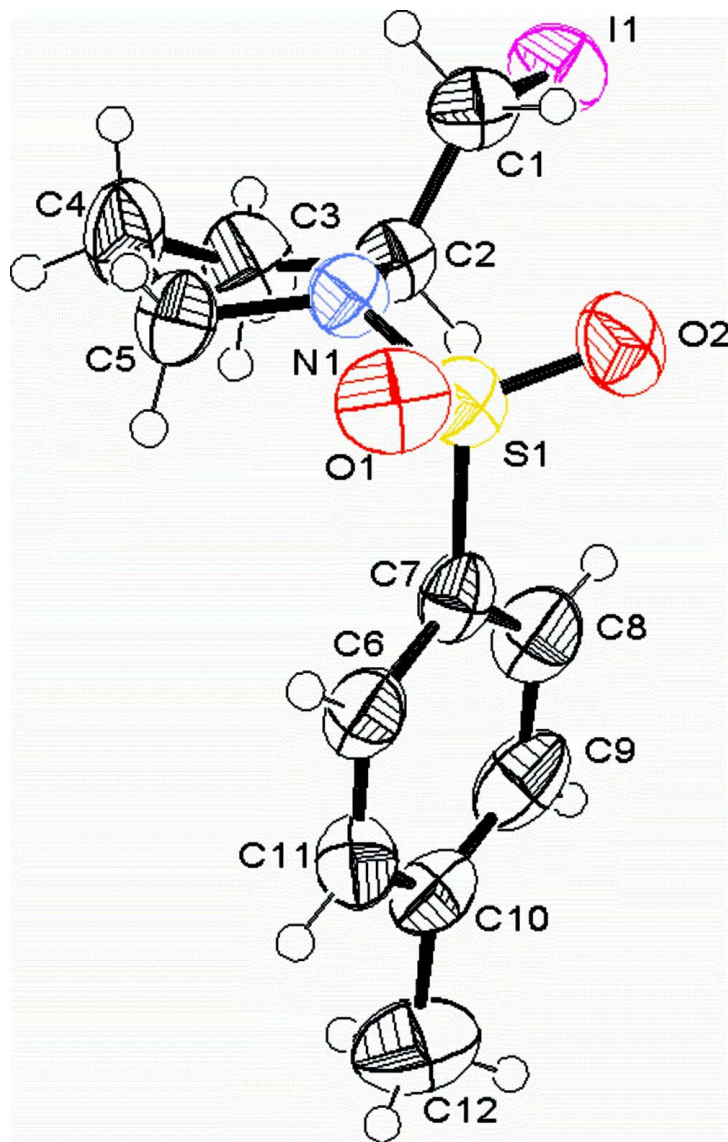


Figure 1

The molecular structure showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

(S)-2-(Iodomethyl)-1-tosylpyrrolidine

Crystal data

$C_{12}H_{16}INO_2S$

$M_r = 365.22$

Monoclinic, $P2_1$

Hall symbol: $P\ 2_1yb$

$a = 7.6345\ (16)\ \text{\AA}$

$b = 7.7084\ (16)\ \text{\AA}$

$c = 12.071\ (3)\ \text{\AA}$

$\beta = 93.17\ (1)^\circ$

$V = 709.3\ (3)\ \text{\AA}^3$

$Z = 2$

$F(000) = 360$

$D_x = 1.710\ \text{Mg m}^{-3}$

Mo $K\alpha$ radiation, $\lambda = 0.71073\ \text{\AA}$

Cell parameters from 1240 reflections

$\theta = 3.1\text{--}21.5^\circ$

$\mu = 2.40\ \text{mm}^{-1}$

$T = 294\ \text{K}$

Block, colorless

$0.25 \times 0.16 \times 0.16\ \text{mm}$

Data collection

Bruker APEX CCD area-detector
diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
 φ and ω scans
Absorption correction: multi-scan
(*SADABS*; Sheldrick, 1996)
 $T_{\min} = 0.586$, $T_{\max} = 0.701$

4398 measured reflections
2424 independent reflections
1787 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.033$
 $\theta_{\max} = 27.9^\circ$, $\theta_{\min} = 1.7^\circ$
 $h = -9 \rightarrow 9$
 $k = -6 \rightarrow 9$
 $l = -15 \rightarrow 15$

Refinement

Refinement on F^2
Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.037$
 $wR(F^2) = 0.092$
 $S = 1.02$
2424 reflections
156 parameters
1 restraint
Primary atom site location: structure-invariant
direct methods
Secondary atom site location: difference Fourier
map

Hydrogen site location: inferred from
neighbouring sites
H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.0387P)^2 + 0.1584P]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.43 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.48 \text{ e } \text{\AA}^{-3}$
Extinction correction: *SHELXL*,
 $F_c^* = kFc[1 + 0.001x\text{Fc}^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0027 (10)
Absolute structure: Flack (1983), 664 Friedel
pairs
Absolute structure parameter: 0.02 (5)

Special details

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
I1	0.74117 (5)	1.0996 (2)	0.25200 (3)	0.0737 (2)
S1	0.26704 (16)	0.6075 (3)	0.31530 (11)	0.0533 (3)
O2	0.4219 (6)	0.5601 (6)	0.2627 (4)	0.0703 (15)
C2	0.3980 (7)	0.9338 (7)	0.3147 (5)	0.0492 (14)
H2	0.3790	0.9188	0.2343	0.059*
C1	0.5919 (8)	0.9208 (9)	0.3477 (5)	0.0572 (16)
H1A	0.6320	0.8033	0.3355	0.069*
H1B	0.6108	0.9470	0.4260	0.069*
C3	0.3090 (8)	1.0976 (12)	0.3511 (5)	0.0749 (17)
H3A	0.2155	1.1311	0.2977	0.090*
H3B	0.3925	1.1922	0.3594	0.090*
C5	0.1722 (9)	0.8691 (9)	0.4444 (5)	0.0579 (16)
H5A	0.1685	0.8074	0.5143	0.069*
H5B	0.0566	0.8668	0.4068	0.069*
C4	0.2361 (10)	1.0518 (9)	0.4619 (6)	0.074 (2)
H4A	0.3265	1.0578	0.5214	0.089*

H4B	0.1406	1.1287	0.4788	0.089*
N1	0.3058 (6)	0.7944 (6)	0.3740 (4)	0.0484 (11)
O1	0.1979 (6)	0.4989 (6)	0.3981 (4)	0.0676 (12)
C6	−0.0698 (7)	0.5882 (12)	0.2289 (4)	0.0566 (15)
H6	−0.0957	0.5381	0.2962	0.068*
C7	0.1002 (8)	0.6359 (9)	0.2101 (4)	0.0491 (18)
C9	−0.0007 (11)	0.7369 (10)	0.0301 (5)	0.073 (2)
H9	0.0235	0.7888	−0.0369	0.088*
C11	−0.2011 (7)	0.6151 (13)	0.1476 (5)	0.0652 (16)
H11	−0.3147	0.5799	0.1605	0.078*
C10	−0.1693 (9)	0.6917 (9)	0.0491 (5)	0.0614 (17)
C8	0.1366 (10)	0.7067 (9)	0.1096 (5)	0.0651 (19)
H8	0.2514	0.7343	0.0944	0.078*
C12	−0.3186 (12)	0.7276 (15)	−0.0368 (7)	0.107 (3)
H12A	−0.3545	0.8465	−0.0315	0.160*
H12B	−0.4160	0.6532	−0.0233	0.160*
H12C	−0.2795	0.7057	−0.1097	0.160*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Il	0.0663 (3)	0.0651 (3)	0.0898 (3)	−0.0125 (3)	0.00491 (18)	0.0064 (3)
S1	0.0550 (7)	0.0350 (7)	0.0701 (8)	0.0009 (11)	0.0039 (6)	−0.0016 (12)
O2	0.062 (2)	0.042 (4)	0.107 (3)	0.006 (2)	0.007 (2)	−0.016 (2)
C2	0.060 (4)	0.032 (3)	0.056 (3)	0.001 (3)	0.000 (3)	0.003 (3)
C1	0.062 (4)	0.047 (4)	0.062 (4)	−0.006 (3)	−0.002 (3)	0.002 (3)
C3	0.079 (4)	0.036 (3)	0.111 (5)	−0.002 (5)	0.020 (3)	0.004 (6)
C5	0.067 (4)	0.050 (4)	0.058 (4)	0.002 (3)	0.009 (3)	−0.005 (3)
C4	0.082 (5)	0.050 (5)	0.094 (5)	0.000 (3)	0.022 (4)	−0.025 (4)
N1	0.052 (3)	0.035 (3)	0.058 (3)	0.000 (2)	0.003 (2)	−0.002 (2)
O1	0.084 (3)	0.042 (3)	0.076 (3)	−0.006 (2)	−0.004 (2)	0.016 (2)
C6	0.064 (3)	0.055 (4)	0.052 (3)	−0.013 (4)	0.014 (2)	−0.010 (4)
C7	0.062 (3)	0.036 (5)	0.050 (3)	−0.006 (3)	0.013 (2)	−0.004 (3)
C9	0.109 (6)	0.070 (5)	0.042 (4)	−0.012 (4)	0.007 (4)	−0.002 (3)
C11	0.059 (3)	0.067 (5)	0.070 (4)	0.004 (5)	0.011 (3)	−0.012 (5)
C10	0.075 (4)	0.056 (4)	0.053 (4)	−0.002 (3)	−0.002 (3)	−0.012 (3)
C8	0.074 (4)	0.063 (5)	0.061 (4)	−0.024 (4)	0.021 (3)	−0.005 (3)
C12	0.110 (7)	0.118 (8)	0.089 (6)	−0.007 (6)	−0.028 (5)	−0.001 (5)

Geometric parameters (Å, °)

Il—C1	2.163 (6)	C5—H5B	0.9700
S1—O2	1.420 (4)	C4—H4A	0.9700
S1—O1	1.427 (4)	C4—H4B	0.9700
S1—N1	1.625 (5)	C6—C11	1.379 (8)
S1—C7	1.762 (6)	C6—C7	1.380 (8)
C2—N1	1.490 (7)	C6—H6	0.9300
C2—C3	1.511 (10)	C7—C8	1.372 (8)

C2—C1	1.515 (8)	C9—C10	1.366 (10)
C2—H2	0.9800	C9—C8	1.401 (10)
C1—H1A	0.9700	C9—H9	0.9300
C1—H1B	0.9700	C11—C10	1.361 (9)
C3—C4	1.518 (9)	C11—H11	0.9300
C3—H3A	0.9700	C10—C12	1.523 (10)
C3—H3B	0.9700	C8—H8	0.9300
C5—N1	1.480 (7)	C12—H12A	0.9600
C5—C4	1.502 (9)	C12—H12B	0.9600
C5—H5A	0.9700	C12—H12C	0.9600
O2—S1—O1	120.8 (3)	C3—C4—H4A	111.1
O2—S1—N1	106.7 (3)	C5—C4—H4B	111.1
O1—S1—N1	106.3 (3)	C3—C4—H4B	111.1
O2—S1—C7	107.2 (3)	H4A—C4—H4B	109.1
O1—S1—C7	107.3 (3)	C5—N1—C2	110.8 (4)
N1—S1—C7	108.1 (3)	C5—N1—S1	118.7 (4)
N1—C2—C3	103.3 (5)	C2—N1—S1	120.6 (4)
N1—C2—C1	107.9 (5)	C11—C6—C7	119.7 (6)
C3—C2—C1	115.3 (5)	C11—C6—H6	120.1
N1—C2—H2	110.0	C7—C6—H6	120.1
C3—C2—H2	110.0	C8—C7—C6	119.3 (6)
C1—C2—H2	110.0	C8—C7—S1	120.8 (5)
C2—C1—I1	110.7 (4)	C6—C7—S1	119.8 (4)
C2—C1—H1A	109.5	C10—C9—C8	121.2 (6)
I1—C1—H1A	109.5	C10—C9—H9	119.4
C2—C1—H1B	109.5	C8—C9—H9	119.4
I1—C1—H1B	109.5	C10—C11—C6	122.0 (6)
H1A—C1—H1B	108.1	C10—C11—H11	119.0
C2—C3—C4	104.8 (6)	C6—C11—H11	119.0
C2—C3—H3A	110.8	C11—C10—C9	118.2 (6)
C4—C3—H3A	110.8	C11—C10—C12	120.7 (7)
C2—C3—H3B	110.8	C9—C10—C12	121.1 (7)
C4—C3—H3B	110.8	C7—C8—C9	119.4 (6)
H3A—C3—H3B	108.9	C7—C8—H8	120.3
N1—C5—C4	102.5 (5)	C9—C8—H8	120.3
N1—C5—H5A	111.3	C10—C12—H12A	109.5
C4—C5—H5A	111.3	C10—C12—H12B	109.5
N1—C5—H5B	111.3	H12A—C12—H12B	109.5
C4—C5—H5B	111.3	C10—C12—H12C	109.5
H5A—C5—H5B	109.2	H12A—C12—H12C	109.5
C5—C4—C3	103.1 (6)	H12B—C12—H12C	109.5
C5—C4—H4A	111.1		
N1—C2—C1—I1	173.7 (4)	C7—S1—N1—C2	−72.0 (5)
C3—C2—C1—I1	−71.5 (6)	C11—C6—C7—C8	−1.2 (12)
N1—C2—C3—C4	24.5 (7)	C11—C6—C7—S1	178.1 (7)
C1—C2—C3—C4	−92.9 (7)	O2—S1—C7—C8	−36.5 (7)

N1—C5—C4—C3	36.7 (7)	O1—S1—C7—C8	−167.6 (6)
C2—C3—C4—C5	−38.7 (7)	N1—S1—C7—C8	78.2 (6)
C4—C5—N1—C2	−22.3 (7)	O2—S1—C7—C6	144.1 (6)
C4—C5—N1—S1	−168.3 (5)	O1—S1—C7—C6	13.0 (7)
C3—C2—N1—C5	−1.4 (6)	N1—S1—C7—C6	−101.2 (7)
C1—C2—N1—C5	121.1 (5)	C7—C6—C11—C10	−1.5 (14)
C3—C2—N1—S1	143.9 (4)	C6—C11—C10—C9	2.3 (13)
C1—C2—N1—S1	−93.6 (5)	C6—C11—C10—C12	−177.0 (8)
O2—S1—N1—C5	−174.4 (4)	C8—C9—C10—C11	−0.3 (11)
O1—S1—N1—C5	−44.3 (5)	C8—C9—C10—C12	179.0 (7)
C7—S1—N1—C5	70.6 (5)	C6—C7—C8—C9	3.1 (11)
O2—S1—N1—C2	43.0 (5)	S1—C7—C8—C9	−176.3 (5)
O1—S1—N1—C2	173.1 (4)	C10—C9—C8—C7	−2.4 (11)
