1,2-Epimino-3,4-epoxybutane: A Versatile Chiral Building Block

Guido Harms,[a] Ernst Schaumann,*[a] Gunadi Adiwidjaja[b]

[a] Institut für Organische Chemie, Technische Universität Clausthal, Leibnizstraße 6, 38678 Clausthal-Zellerfeld, Germany

[b] Mineralogisch-Petrographisches Institut, Universität Hamburg, Grindelallee 48, 20146 Hamburg, Germany

Fax +49(5323)722858; E-mail: ernst.schaumann@tu-clausthal.de

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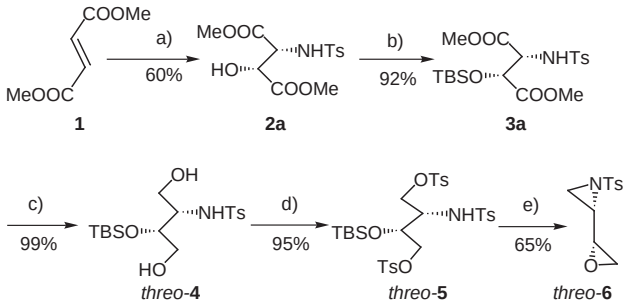
Abstract: The synthesis of enantiomerically pure 1,2-epimino-3,4-epoxy-(*N*-toluenesulfonyl)butane (**6**) in the *S,R*-(*erythro*) and *R,R*-(*threo*) configurations is described. This building block offers a new route to targets with an 1,2-aminohydroxy functionality. As an example, the new 1,4-biselectrophile is employed in a cyclopentane synthesis.

Key words: amino alcohols, domino reactions, epoxides, ring opening, cyclopentanes

A vicinal aminohydroxy unit is a frequently encountered feature in many natural products and in biologically active synthetic molecules. Therefore, the asymmetric Sharpless aminohydroxylation represents an important synthetic tool.[1] However, this approach gives access only to *cis* configured α-amino alcohols and yields vary depending on the type of C=C bond which is aminohydroxylated. For the synthesis of the corresponding *trans* compounds, ring opening reactions of an aziridine with an oxygen nucleophile[2] or of an epoxide with a suitable nitrogen nucleophile are recommended as methods of choice.[3] We now present an alternative where the vicinal arrangement of oxygen and nitrogen functionalities in an activated form is already present in the precursor as in **6**. Thus, reactions with a wide range of carbon nucleophiles are possible, and, because of the different reactivities of epoxides[4] and aziridines,[5] proceed with complete control of chemoselectivity. Moreover, the stereoisomers of **6** can be looked upon as 1,4-biselectrophiles and so invite to be submitted to our silicon-based domino cyclisation.[4]

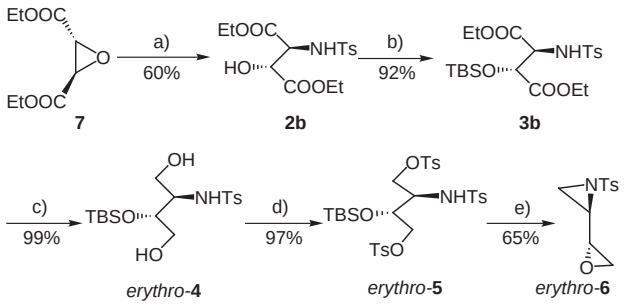
We aimed at a method which would allow access to both diastereomers of **6** in enantiomerically pure form and, for convenience, to use the diastereomers of the same precursor molecule. Actually, dialkyl 3-hydroxy-2-(tosyl)aminosuccinates **2** turned out to open a route to the diastereomers of **6**. Thus, *threo*-**6** is readily available in five steps from dimethyl fumarate (Scheme 1). Asymmetric aminohydroxylation of dimethyl fumarate **1** leads to aminohydroxylated succinate **2a**.[6] Silylation of **2a** with *tert*-butylchlorodimethylsilane under standard conditions provides **3a**, which is reduced in high yield with calcium borohydride to give *threo*-**4**.[7] For the tosylation of **4** the method of *Sakakura* et al.[8] turned out to be the only efficient way to give the precursor *threo*-**5** of the title compound. Subsequent treatment with tetrabutylammonium fluoride (TBAF) yields enantiomerically pure *threo*-**6** (Scheme 1). Thus, TBAF acts simultaneously as desilylating agent and as a base in the deprotonation of the sulfonamide.



Reagents and conditions: a) Chloramine T, $K_2OsO_4 \cdot 2H_2O$ $(DHQ)_2PHAL$, H_2O/MeCN (Ref. 6); b) TBSCl, imidazole; c) $Ca(BH_4)_2$, EtOH/THF; d) TsCl, $Me_3N \cdot HCl$, Et_3N; e) $TBAF \cdot 3H_2O$

Scheme 1

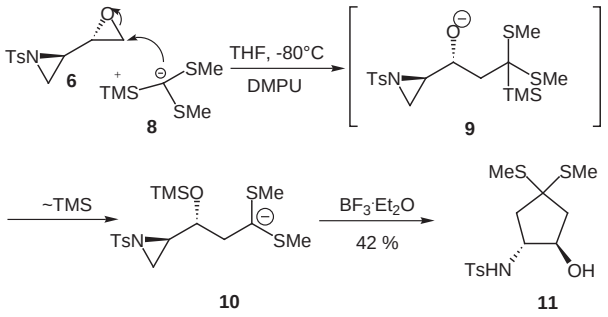
The synthesis of *erythro*-**6** starts from diethyl *threo*-2,3-epoxysuccinate (**7**), which is obtained from diethyl tartrate employing the method of Mori et al.[9] This functionalized epoxide is opened by chloramine T to give the *N*-protected amino alcohol **2b** in one step from epoxide **7** and not as usual in two steps.[10] The following steps proceed in equally good yields as for the *threo*-compound to give *erythro*-**6** in 32% overall yield (Scheme 2). Of course, use of the enantiomers of **2a** or **7**, respectively, would give the mirror image molecules making all four stereoisomers of **6** readily accessible.



Reagents and conditions: a) Chloramine T; H_2O/*t*-BuOH; b) TBSCl, imidazole; c) $Ca(BH_4)_2$, EtOH/THF; d) TsCl, $Me_3N \cdot HCl$, Et_3N; e) $TBAF \cdot 3H_2O$

Scheme 2

Building block *erythro*-**6** was successfully employed in a cyclopentane synthesis (Scheme 3). As expected based on the pronounced difference in the reactivity of the epoxide versus the aziridine ring, the formaldehyde equivalent **8** chemoselectively attacks the oxirane ring to give intermediate **9**. Alkoxide **9** is obviously in equilibrium with silyl ether **10** via a homo-Brook rearrangement. Contrary to our earlier experience,[4] intramolecular ring opening of the aziridine unit by the carbanion in **10** does not occur spontaneously, but requires Lewis-acid assistance to give the functionalized cyclopentane **11.**



Scheme 3

The constitution and expected configuration of **11** were confirmed by an X-ray structural investigation (Figure).[11,12]

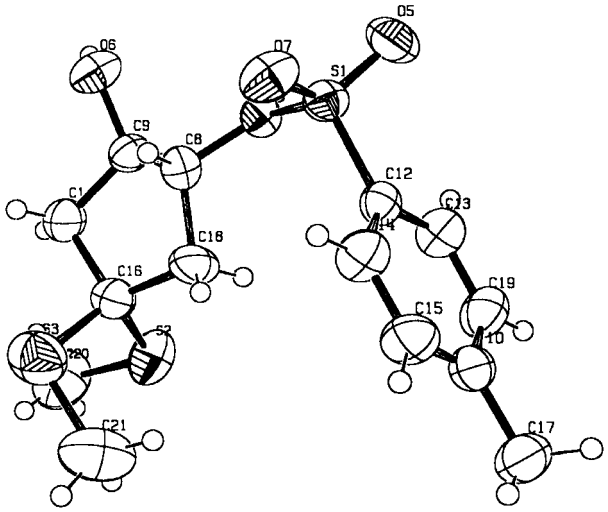


Figure Crystal structure of **11**

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DPX-200 and AMX-400 instruments in $CDCl_3$ as the solvent. Chemical shifts were measured in δ (ppm) and coupling constants *J* in Hz. TMS was used as reference for ^{1}H NMR spectra (δ = 0.00 ppm). The solvent peak was used as reference for ^{13}C spectra (δ = 77.00 ppm). For assignment of the number of substituents attached to the specified carbon, each carbon is described as +(secondary carbon), - (primary or tertiary carbon) or o (quarterny carbon), as determined by DEPT method. When necessary, NMR data were assigned using HH and CH correlated spectra. Melting points are uncorrected. Specific rotations were recorded on a Perkin-Elmer 43B polarimeter. IR spectra were recorded on a Bruker Vektor 22 FTIR spectrometer. Elemental analyses were performed by the Institut für Pharmazeutische Chemie, Braunschweig. TLC was performed on Merck 60 F_{254} precoated silica plates and spots were detected by spraying with a solution of 10% $KMnO_4$ and 0.5 M Na_2CO_3 in H_2O or 3% *p*-methoxybenzaldehyde and 1% H_2SO_4 in MeOH and heating. Flash chromatography was performed with silica gel 60 (Merck, 40−63 µm). Concentrations were performed on a rotary evaporator at 40 °C. Petroleum ether (PE) with the boiling range 60−70 °C was used in the seperations. All solvents were distilled before use.

Diethyl (2*R*,3*S*)-2-Hydroxy-3-[(4-methylphenyl)sulfonylamino]succinate (2b)

Diethyl (2*R*,3*R*)-*threo*-2,3-epoxysuccinate (**7**;[9] 1.09 g, 5.8 mmol) was dissolved in *t*-BuOH/H_2O (40 mL) and chloramine T trihydrate (8 g, 5 equiv) added. The solution was stirred for 7 d. When there was no more starting material left (detected by TLC), the *t*-BuOH was distilled from the reaction mixture under reduced pressure. The aqueous residue was extracted with CH_2Cl_2 (4 × 40 mL) and the combined organic layers washed with brine (2 × 20 mL) and dried ($MgSO_4$). The crude product was purified by flash chromatography (PE/EtOAc, 5:1) to give colorless crystals (970 mg, 47%); mp 96−98 °C; $[\alpha]_D^{20}$ +30.3 (*c* = 1.03, CH_2Cl_2).

IR (KBr) : ν = 3475, 3279, 2957, 1746, 1438, 1341, 1162, 1092 cm^{-1}.

^{1}H NMR (200 MHz): δ = 1.13 and 1.31 (t, 3 H, *J* = 7 Hz, CH_2CH_3), 2.42 (s, 3 H, $ArCH_3$), 3.31 (d, 1 H, *J* = 6 Hz, OH), 4.01 and 4.07 (dq, 1 H, *J* = 11, 7 Hz, CH_2CH_3), 4.27 (q, 2 H, *J* = 7 Hz, CH_2CH_3), 4.40 (dd, 1 H, *J* = 3, 8 Hz, C*H*NHTos), 4.49 (dd, 1 H, *J* = 3, 6 Hz, C*H*OH), 5.70 (d, 1 H, *J* = 8 Hz, NH), 7.31 (d, 2 H, *J* = 8 Hz, ArH), 7.77 (d, 2 H, *J* = 8 Hz, ArH).

^{13}C NMR (50 MHz): δ = 13.79 and 14.03 (+, CH_2CH_3), 21.52 (+, $ArCH_3$), 58.86 (+, *C*NHTos), 62.46 (−, CH_2CH_3), 72.41 (+, COH), 127.21 and 129.71 (+, C_{arom}), 136.58 and 143.87 (o, C_{arom}), 167.52 and 170.77 (o, CO_2Et).

Anal. calcd: C, 50.08; H, 5.84; N, 3.90; S, 8.93; found, C, 50.09; H, 5.82; N, 3.92; S, 8.90.

Dimethyl (2*R*,3*R*)-2-(*tert*-Butyldimethylsiloxy)-3-[(4-methylphenyl)sulfonylamino]succinate (3a); Typical Procedure

Compound **2a**[6] (950 mg, 2.6 mmol) was dissolved in DMF (5 mL) and imidazole (500 mg, 1.2 equiv) and TBDMSCl (471 mg, 1.2 equiv) were added. The mixture was stirred for 16 h at 35 °C. H_2O was added and the cloudy solution extracted with CH_2Cl_2 (5 × 20 mL), the combined CH_2Cl_2 layers were washed with H_2O (30 mL) and brine (30 mL), and dried ($MgSO_4$). Filtration and concentration gave a crude oil that was purified by column chromatography (PE/EtOAc, 3:1) to give the product as colorless crystals (1.13 g, 85%); mp 103−106 °C; $[\alpha]_D^{24}$ +12.9 (*c* = 0.96, CH_2Cl_2).

IR (film): ν = 3285, 2954, 2858, 761, 1742, 1163, 839, 664 cm^{-1}.

^{1}H NMR (200 MHz): δ = −0.07 and 0.07 [s, 3 H, $Si(CH_3)_2$], 0.82 (s, 9 H, SiC_4H_9-*t*), 2.34 (s, 3 H, $ArCH_3$), 3.54 and 3.56 (s, 3 H, OCH_3), 4.44 (dd, 1 H, *J* = 2, 11 Hz, C*H*NHTs), 4.64 (d, 1 H, *J* = 2 Hz, C*H*OTBS), 5.32 (d, 1 H, *J* = 11 Hz, NH), 7.26 (d, 2 H, *J* = 8 Hz, ArH), 7.69 (d, 2 H, *J* = 8 Hz, ArH).

^{13}C NMR (50 MHz): δ = −6.01 and −4.88 [+, $Si(CH_3)_2$], 18.11 (o, SiC_4H_9-*t*), 21.47 (+, $ArCH_3$), 25.39 (+, SiC_4H_9-*t*), 52.22 and 52.68 (+, OCH_3), 59.12 (+, *C*NHTos), 73.03 (+, *C*OTBS), 127.18 and 129.45 (+, C_{arom}), 137.20 and 143.50 (o, C_{arom}), 169.01 and 169.86 (o, CO_2Me).

Anal. calcd: C, 51.21; H, 7.01; N, 3.14; S, 7.20; found, C, 51.33; H, 7.45; N, 2.82; S, 7.18.

Diethyl (2*R*,3*S*)-2-(*tert*-Butyldimethylsiloxy)-3-[(4-methylphenyl)sulfonylamino]succinate (3b)

Compound **3b** was prepared from **2b** in an analogous manner; yield: 1.03 g (89%); oil $[\alpha]_D^{24}$ +66.4 (*c* = 1.12, CH_2Cl_2).

IR (film): ν = 3281, 2931, 2858, 1761, 1165, 840, 663 cm^{-1}.

^1H NMR (200 MHz): δ = 0.08 [s, 6 H, $Si(CH_3)_2$], 0.88 (s, 9 H, SiC_4H_9-*t*), 1.13 and 1.29 (t, 3 H, *J* = 7 Hz, CH_2CH_3), 2.42 (s, 3 H, $ArCH_3$), 4.01 (m, 4 H, CH_2CH_3), 4.41 (dd, 1 H, *J* = 3, 7 Hz, C*H*NHTs), 4.49 (d, 1 H, *J* = 3, 6 Hz, C*H*OTBS), 5.43 (d, 1 H, *J* = 7 Hz, NH), 7.30 (d, 2 H, *J* = 8 Hz, ArH), 7.76 (d, 2 H, *J* = 8 Hz, ArH)

^{13}C NMR (50 MHz): δ = −5.30 and −5.05 [+, $Si(CH_3)_2$], 13.82 and 14.08 (+, CH_2CH_3), 18.12 (o, *C*Me$_3$), 21.50 (+, Ar*C*H$_3$), 25.53 [+, $SiC(CH_3)_3$], 59.24 (+, *C*NHTos), 61.30 and 62.24 (−, CH_2CH_3), 74.59 (+, *C*OTBS), 127.24 and 129.73 (+, C_{arom}), 136.38 and 143.79 (o, C_{arom}), 167.88 and 170.04 (o, CO_2Et).

Anal. calcd.: C, 53.25; H, 7.45; N, 2.96; S, 6.77; found, C, 53.26; H, 7.64; N, 2.95 S, 6.77.

(2*R*,3*S*)-2-(*tert*-Butyldimethylsiloxy)-3-[(4-methylphenyl)sulfonylamino]butane-1,4-diol (*threo*-4); Typical Procedure

To a solution of **3a** (1.0 g, 2.24 mmol) in EtOH (20 mL) in a 100 mL flask was added a suspension of $CaCl_2$ (1.24 g, 5 equiv) in THF (30 mL) and the mixture was stirred virgorously. After 15 min, $NaBH_4$ (873 mg, 10 equiv) was added cautiously at r.t. After further 2 h, the mixture was hydrolyzed with aq citric acid (1 M, 20 mL) and ice. The mixture was then concentrated and the resulting aqueous suspension was diluted with H_2O (50 mL) and extracted with CH_2Cl_2 (5 × 40 mL). The combined organic layers were washed with aq sat. $NaHCO_3$ solution (3 × 30 mL) and brine (30 mL), and dried ($MgSO_4$). Filtration and concentration gave the product as colorless crystals (845 mg, 99%); mp 143 °C; $[\alpha]_D^{20}$ −41.0 (*c* = 1.03, CH_2Cl_2).

IR (film): ν = 3281, 2933, 2856, 1438, 1338, 1257, 1162, 1037, 833, 781, 673 cm^{-1}.

^1H NMR (200 MHz): δ = 0.09 and 0.10 [s, 3 H, $Si(CH_3)_2$], 0.88 (s, 9 H, *t*-C_4H_9), 2.44 (s, 3 H, $ArCH_3$), 3.19 (m, 2 H, CH_2OH), 3.59 (m, 1 H, TsNHC*H*), 3.69 (m, 2 H, CH_2OH), 3.91 (ddd, 1 H, *J* = 6, 3, 3 Hz, C*H*OTBS), 5.35 (d, 1 H, *J* = 8 Hz, NH), 7.32 (d, 2 H, *J* = 8 Hz, ArH), 7.77 (d, 2 H, *J* = 8 Hz, ArH).

^{13}C NMR (50 MHz): δ = −5.00 and −4.75 (+, $SiCH_3$), 17.89 (o, *C*Me$_3$), 21.52 (+, Ar*C*H$_3$), 25.68 [+, $C(CH_3)_3$], 55.37 (+, *C*HNHTos), 59.83 and 61.42 (−, CH_2OH) 71.80 (+, *C*OTBS), 126.99 and 129.81 (+, C_{arom}), 137.25 and 143.73 (o, C_{arom}).

(2*R*,3*R*)-2-(*tert*-Butyldimethylsiloxy)-3-[(4-methylphenyl)sulfonylamino]butan-1,4-diol (*erythro*-4)

Compound *erythro*-**4** was prepared analogously from **3b**; yield: 5.6 g (99%); $[\alpha]_D^{20}$ +10.9 (*c* = 1.0, CH_2Cl_2); mp 135 °C.

IR (film): ν = 3501, 3301, 2930, 2858, 1598, 1327, 1255, 1160, 1092, 838, 780, 668, 553 cm^{-1}.

^1H NMR (200 MHz): δ = 0.06 and 0.07 [s, 3 H, $Si(CH_3)_2$], 0.86 (s, 9 H, *t*-C_4H_9), 2.43 (s, 3 H, $ArCH_3$), 2.68 (s, 2 H, OH), 3.31−3.48 (m, 2 H, CHCH), 3.49−3.90 (m, 4 H, CH_2OH), 5.40 (d, 1 H, *J* = 8 Hz, NH), 7.31 (d, 2 H, *J* = 8 Hz, ArH), 7.77 (d, 2 H, *J* = 8 Hz, ArH).

^{13}C NMR (50 MHz): δ = −5.44 and −4.70 (+, $SiCH_3$), 17.91 (o, *C*Me$_3$), 21.48 (+, Ar*C*H$_3$), 25.69 [+, $C(CH_3)_3$], 56.05 (+, *C*HNHTos), 60.84 (−, CH_2OH), 63.22 (−, CH_2OH) 73.49 (+, *C*OTBS), 127.06 and 129.80 (+, C_{arom}), 137.05 and 143.71 (o, C_{arom}).

Anal. calcd.: C, 52.41; H, 8.02; N, 3.60; S, 8.23; found, C, 52.50; H, 8.28; N, 3.51; S, 7.93.

(2*R*,3*S*)-2-(*tert*-Butyldimethylsiloxy)-1,4-bis[(4-methylphenyl)sulfonyloxy]-3-[(4-methylphenyl)sulfonylamino)butane (*threo*-5); Typical Procedure

Compound *threo*-**4** (3.17 g, 8.1 mmol) was stirred in anhyd CH_2Cl_2 (130 mL) with Et_3N (5.6 mL, 5 equiv) at r.t. until a clear solution had formed. Then Me_3N•HCl (744 mg, 1 equiv) was added and the mixture stirred for a further 10 min before the solution was cooled to −10 °C. A solution of TsCl (6.17 g, 4 equiv) in anhyd CH_2Cl_2 (40 mL) was added dropwise over 30−45 min and the mixture was stirred at r.t. After no more starting material could be detected by TLC (ca 30 min), H_2O was added (50 mL) and the mixture stirred for 15 min. The aqueous layer was then extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine (30 mL) and dried ($MgSO_4$). Filtration and concentration gave the crude product as colorless solid. Purification by flash chromatography yielded the pure product (PE/EtOAc, 4:1); yield: 5.22 g (97%); mp 38−45 °C; $[\alpha]_D^{20}$ +12.5 (*c* = 1.04, CH_2Cl_2).

IR (film): ν = 3289, 2930, 2858, 1598, 1366, 1178 cm^{-1}.

^1H NMR (200 MHz): δ = −0.04 [s, 6 H, $Si(CH_3)_2$], 0.77 (s, 9 H, t-C_4H_9), 2.46, 2.47, 2.47 (s, 9 H, $ArCH_3$), 3.67 (dd, 1 H, *J* = 10, 6 Hz, TsNHC*H*), 3.80 (dd, 1 H, *J* = 9, 9 Hz, C*H*OTBS), 3.39−3.49 and 3.89−3.99 (m, CH_2OTs), 4.78 (d, 1 H, *J* = 9 Hz, NH), 7.80−7.60 and 7.40−7.20 (m, 12 H, ArH).

^{13}C NMR (50 MHz): δ = −5.32 and −4.69 (+, $SiCH_3$), 17.86 (o, *C*Me$_3$), 21.60 and 21.69 (+, Ar*C*H$_3$), 25.66 [+, $C(CH_3)_3$], 52.75 (+, *C*HNHTos), 66.84 and 67.81 (−, CH_2OTs), 68.91 (+, *C*OTBS), 126.93, 127.91, 128.03 and 129.98 (+, C_{arom}), 130.05, 132.34, 136.67, 144.15, 145.23 and 145.37 (o, C_{arom}).

Anal. calcd.: C, 53.35; H, 6.21; N, 2.01; S, 13.78; found, C, 53.41; H, 6.52; N, 1.76; S, 13.46.

(2*R*,3*R*)-*2*-(*tert*-Butyldimethylsiloxy)-1,4-bis[(4-methylphenyl)sulfonyloxy)-3-[(4-methylphenyl)sulfonylamino]butane (*erythro*-5)

This compound was prepared from *erythro*-**4** in an analogous manner as described above; oil; yield: 493 mg (98%); $[\alpha]_D^{25}$ +1.6 (*c* = 5.93, CH_2Cl_2).

IR (film): ν = 3287, 3066, 2930, 2858, 1737, 1599 cm^{-1}.

^1H NMR (200 MHz): δ = −0.04 and −0.01 [s, 3 H, $Si(CH_3)_2$)], 0.76 (s, 9 H, *t*-C_4H_9), 2.44−2.46 (s, 9 H, $ArCH_3$), 3.32−3.46 (m, 1 H, TsNHC*H*), 3.73 (dd, 1 H, *J* = 11, 4 Hz, C*H*OTBS), 3.81−3.94 and 3.98−4.05 (m, 2 H, CH_2OH), 4.84 (d, 1 H, *J* = 9 Hz, NH), 7.80−7.60 and 7.40−7.20 (m, 12 H, ArH).

^{13}C NMR (50 MHz): δ = −5.26 and −4.56 (+, $SiCH_3$), 17.87 [o, $C(CH_3)_3$], 21.58 and 21.68 (+, Ar*C*H$_3$), 25.63 (+,*C*Me$_3$), 53.94 (+, *C*HNHTos), 66.95 and 70.24 (−, CH_2OTs), 70.20 (+, *C*OTBS), 127.19, 127.99, 128.08, 129.94 and 130.02 (+, C_{arom}), 131.89, 132.34, 136.58, 144.00, 145.25 and 145.71 (o, C_{arom}).

Anal. calcd.: C, 53.35; H, 6.21; N, 2.01; S, 13.78; found, C, 53.41; H, 6.52; N, 1.76; S, 13.46.

(2*S*)-1-[(4-Methylphenyl)sulfonyl]-2-[(2*R*)-oxiran-2-yl]aziridine (*threo*-6); Typical Procedure

Compound *threo*-**5** (4.696 g, 6.73 mmol) was dissolved in anhyd THF (100 mL) and at −15 °C TBAF•3 H_2O (10.6 g, 5 mmol) in anhyd THF (40 mL) was added slowly. The solution was allowed to warm to r.t. overnight. After 16 h, the mixture was quenched by addition of Et_2O (60 mL)/aq sat. NH_4Cl solution (60 mL) and stirred for 15 min. H_2O was added until the precipitate dissolved. The organic layer was concentrated, diluted with Et_2O (200 mL), washed with brine (30 mL) and dried ($MgSO_4$). Purification by flash chromatography gave the poduct as colorless crystals (1.05 g, 65%); mp 108 °C; $[\alpha]_D^{25}$ −9.1 (*c* = 1.05, CH_2Cl_2).

IR (film): ν = 3000, 2925, 1598, 1324, 1162, 1094, 937, 817, 721 cm^{-1}.

^1H NMR (200 MHz): δ = 2.30 (d, 1 H, *J* = 4 Hz, CH_2N), 2.45 (s, 3 H, ArCH_3), 2.60 (dd, 1 H, *J* = 5, 2 Hz, CH_2O), 2.67 (d, 1 H, *J* = 7 Hz, CH_2N), 2.75 (dd, 1 H, *J* = 5, 4 Hz, CH_2O), 2.90 (dt, 1 H, *J* = 7, 4 Hz, CHN), 3.00 (dt, 1 H, *J* = 4, 2 Hz, CHO), 7.34 and 7.82 (d, 2 H, ArH).

^{13}C NMR (50 MHz): δ = 21.66 (+, ArCH_3), 30.69 (−, CH_2N), 38.58 (+, CHN), 45.51 (−, CH_2O), 49.16 (+, CHO), 127.97 and 129.74 (+, C_{arom}), 134.57 and 144.82 (o, C_{arom}).

(2*R*)-1-[4-Methylphenyl)sulfonyl]-2-[(2*R*)-oxiran-2-yl]aziridine (*erythro*-6)

Compound *erythro*-**6** was prepared from *erythro*-**5** in a similar manner as described above; yield: 66 mg (58%); mp 106 °C; $[\alpha]_D^{25}$ +44.8 (*c* = 1.03, CH_2Cl_2).

IR (Film): ν = 3072, 3020, 2924, 1595, 1310, 1166, 953, 874, 822, 719, 703 cm^{-1}.

^1H NMR (200 MHz): δ = 2.25 (d, 1 H, *J* = 4 Hz, CH_2N), 2.45 (s, 3 H, ArCH_3), 2.56 (dd, 1 H, *J* = 5, 2 Hz, CH_2O), 2.62 (d, 1 H, *J* = 7 Hz, CH_2N), 2.76 (dd, 1 H, *J* = 5, 2 Hz, CH_2O), 2.91 (ddd, 1 H, *J* = 7, 4, 4 Hz, CHN), 2.99 (ddd, 1 H, *J* = 4, 4, 2 Hz, CHO), 7.82 and 7.35 (d, 2 H, ArH).

^{13}C NMR (50MHz): δ = 21.68 (+, ArCH_3), 30.64 (−, CH_2N), 38.89 (+, CHN), 45.19 (−, CH_2O), 49.35 (+, CHO), 127.87 and 129.68 (+, C_{arom}), 134.43 and 144.78 (o, C_{arom}).

Anal. calcd.: C, 55.21; H, 5.48; N, 5.85; S, 13.40; found C, 55.23; H, 5.49; N, 5.50; S, 13.36.

***N*-[2-Hydroxy-4,4-bis(methylsulfanyl)cyclopentyl]-4-methylbenzenesulfonamide (11)**

Freshly distilled bis(methylthio)trimethylsilylmethane (90 mg, 1.1 equiv, 0.48 mmol) was dissolved in anhyd THF (2 mL). BuLi (0.34 mL, 1.2 equiv, 1.6 M in hexane) and DMPU (0.06 mL) were added slowly at −78 °C. The mixture was allowed to warm to 0 °C during 1 h and stirred for another hour at this temperature. The pale yellow solution was added via canula to a solution of *erythro*-**6** (100 mg, 1 equiv) in anhyd THF (4 mL) at −78 °C. After stirring for 1 h at −50 °C, freshly distilled BF_3•OEt_2 (0.18 mL, 10 equiv) was added slowly. After 10 min, aq sat. $NaHCO_3$ solution (1 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (4 × 20 mL). The combined organic layers were washed with brine (2 mL). Purification by flash chromatography gave the product as colorless crystals (69 mg 42%); mp 135 °C; $[\alpha]_D^{25}$ −15.1 (*c* = 1.00, $CHCl_3$).

IR (KBr): ν = 3373, 3277, 2923, 1655, 1330, 1160, 816, 666 cm^{-1}.

^1H NMR (200 MHz): δ = 1.76 (dd, 1 H, *J* = 14, 7 Hz, CNHTsCH_2), 1.96 (dd, 1 H, *J* = 14, 7 Hz, CHOHCH_2), 2.01 (s, 3 H, SCH_3), 2.00 (s, 3 H, SCH_3), 2.32 [dd, 1 H, *J* = 14, 7 Hz, C(NHTs)CH_2], 2.42 (dd, 1 H, *J* = 14, 7 Hz, CHOHCH_2), 2.44 (s, 3 H, ArCH_3), 3.56−3.70 (m, 1 H, C*H*NHTs), 4.29 (ddd, 1 H, *J* = 7, 7, 6 Hz, C*H*OH), 5.42 (d, 1 H, *J* = 8 Hz, NH), 7.33 and 7.79 (d, 2 H, *J* = 7 Hz, ArH).

^{13}C NMR (50 MHz): δ = 13.11 (+, SCH_3), 21.54 (+, ArCH_3), 44.40 (−, NCHCH_2), 46.17 (−, COHCH_2), 59.63 [o, *C*$(Sme)_2$], 60.88 (+, NCH), 77.20 (+, COH), 127.14 and 129.85 (+, C_{arom}), 136.81, 143.83 (o, C_{arom}).

Crystal Data of **11**

$C_{14}H_{21}NO_3S_3$ (347.50). Crystal size 0.54 × 0.23 × 0.21 mm. Orthorhombic. Space group $P2_12_12_1$. Unit cell dimensions a = 6.450(1) Å, b = 12.929(1) Å, c = 20.778(1) Å. Cell volume Z = 1732.7(3) $Å^3$. Method of collection: 'Collect Nonius', 'SIR-97,[11] 'SHELXL-97', Extinction coefficient = 0.084(7). Reflections collected = 3945.

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