The Remarkable Effect of Titanium Tetraisopropoxide in Diastereoselective Reaction of Carbaldehydes with Chiral Benzenesulfonamide Lithium Complexes

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Chiral benzenesulfonamide titanium ate-complexes (4 and 8) were prepared from the lithium complexes (2 and 6) by treatment with titanium tetraisopropoxide. The diastereoselective reactions of aromatic carbaldehydes with 4 and 8 were performed, and the chiral *o*-(1-aryl-1-hydroxymethyl)benzenesulfonamides (3a—d and 7a—e) were obtained in 80—87% yields. The diastereomeric excesses (d.e.) of these products were evaluated as 62—82%. These compounds were also prepared from the lithium complexes (2 and 6), but the d.e. values were only 6—14% in this case.

Keywords chiral benzenesulfonamide; chiral benzenesulfonylpyrrolidine; chiral *ortho*-lithiated benzamide; diastereoselective reaction; (*S*)-*N*-methylvalinol; organolithium complex; organotitanium ate-complex; (*S*)-prolinol; titanium tetraisopropoxide; transmetalation

The utility of *ortho*-metalation in the regiospecific synthesis of aromatic compounds has been the subject of a number of reviews,[1-3] and several papers have appeared on the preparation of phthalides *via* the *ortho*-lithiated benzamides[4] or phenyloxazolines.[5,6] Meyers and co-workers[7] reported that chiral 2-(*o*-lithiophenyl)-4-methoxymethyl-5-phenyloxazoline could be condensed with various carbonyl compounds to afford the chiral imino lactones in 60—70% yields, though with rather poor stereoselectivity (2—28% diastereoselectivities). In this paper, we wish to describe the stereoselective reaction of chiral *ortho*-metalated benzenesulfonamides with various carbaldehydes and the key role of titanium tetraisopropoxide in this reaction.

The synthesis of (*S*)-*N*-(2′-hydroxy-1′-isopropylethyl)-*N*-methylbenzenesulfonamide (**1**) was achieved by condensation of (*S*)-*N*-methylvalinol with benzenesulfonyl chloride in 75% yield, and the lithium 2-(*o*-lithiobenzenesulfonamido)-2-isopropylethoxide (**2**) was prepared from (*S*)-**1** by treatment with two equimolar amounts of *n*-butyllithium. The reaction of aromatic carbaldehydes such as benzaldehyde, *p*-tolualdehyde, *p*-anisaldehyde, and 1-naphthaldehyde with **2** gave diastereomeric mixtures of *o*-(1′-aryl-1′-hydroxymethyl)-*N*-(2-hydroxy-1-isopropylethyl)-*N*-methylbenzenesulfonamides (**3a—d**) in 79—84% yields. Two diastereomeric forms could be considered, depending on the configuration of the newly created asymmetric carbon atom of the 1′-aryl-1′-hydroxymethyl groups. The ratios of the two isomers were estimated by proton nuclear magnetic resonance (^{1}H-NMR) spectrometry, and the diastereomeric excesses (d.e.) of these products were evaluated to be 6—10%.

Recent work has demonstrated the utility of exchanging lithium for copper, magnesium, zinc,[8] and titanium,[9] and we have reported that lithium complexes are easily converted into titanium ate-complexes by treatment with titanium tetraisopropoxide.[9] Thus, the chiral benzenesulfonamide lithium complex (**2**) was converted into the chiral benzenesulfonamide titanium ate-complex (**4**) by treatment of an equimolar amount of titanium tetraisopropoxide. The diastereoselective reaction of aromatic carbaldehydes with **4** was performed in a similar manner to that employed for the reaction with **2** to give **3a—d** in 80—87% yields. The d.e. values of these products were estimated as 66—80% by ^{1}H-NMR spectrometry. A great improvement in the diastereoselectivity was thus achieved with the aid of titanium tetraisopropoxide. The major products of **3a—d**

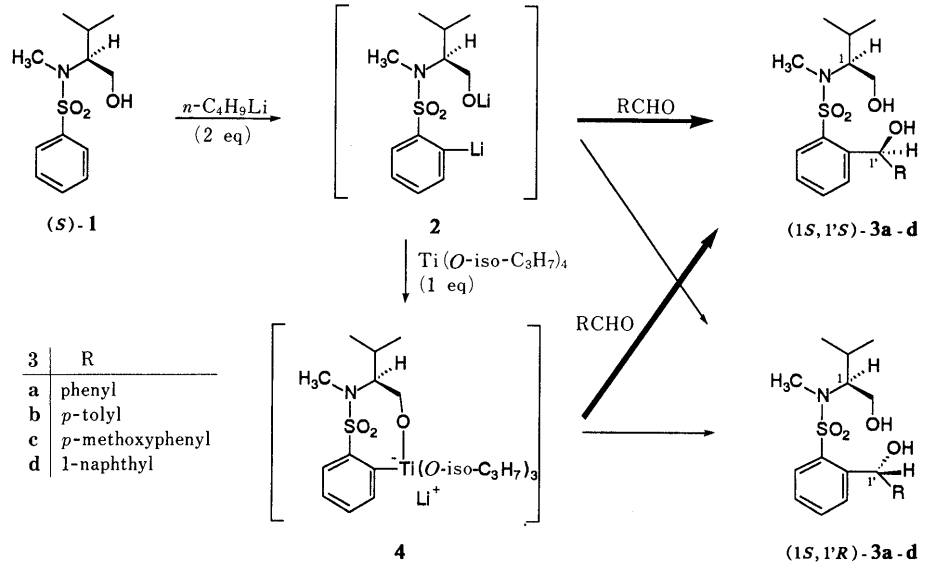
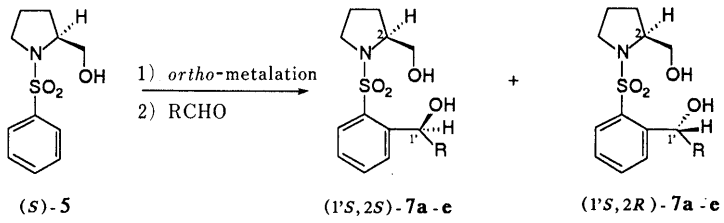


Chart 1

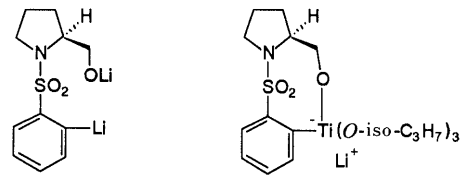
TABLE I. Reaction of Carbaldehydes with Chiral Benzenesulfonamide Metal Complexes

Carbaldehyde	Product	Lithium complex **2**[a] **6**[b]			Titanium complex **4**[a] **8**[b]		
		Complex	Yield[c] (%)	Ratio of isomers[d] (1′*S*) : (1′*R*)	Complex	Yield[c] (%)	Ratio of isomers[d] (1′*S*) : (1′*R*)
Phenyl	**3a**	**2**	82	54 : 46	**4**	85	83 : 17
p-Tolyl	**3b**	**2**	84	54 : 46	**4**	82	87 : 13
p-Methoxyphenyl	**3c**	**2**	81	53 : 47	**4**	80	90 : 10
1-Naphthyl	**3d**	**2**	79	55 : 45	**4**	87	89 : 11
Phenyl	**7a**	**6**	75	57 : 43	**8**	85	83 : 17
p-Tolyl	**7b**	**6**	82	56 : 44	**8**	80	84 : 16
p-Methoxyphenyl	**7c**	**6**	80	55 : 45	**8**	82	88 : 12
1-Naphthyl	**7d**	**6**	80	57 : 43	**8**	84	91 : 9
2-Furyl	**7e**	**6**	75	53 : 47	**8**	85	81 : 19

a) Run at −50°C for 4 h. *b*) Run at 0°C for 3 h. *c*) Isolated yield. *d*) Estimated by ^{1}H-NMR (270 MHz) spectral analysis.



(*S*)-**5** (1′*S*,2*S*)-**7a-e** (1′*S*,2*R*)-**7a-e**



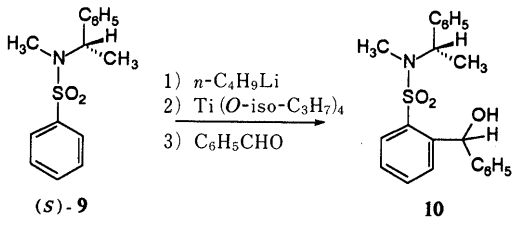
6 **8**

7	R
a	phenyl
b	*p*-tolyl
c	*p*-methoxyphenyl
d	1-naphthyl
e	2-furyl

Chart 2

prepared from **2** coincided with the major products prepared from **4** on the basis of ^{1}H-NMR spectral comparison, and the former minor products also coincided with the later minor products. The optically active compounds, *i.e.*, (1*S*,1′*S*)-**3a—d** (major products) and (1*S*,1′*R*)-**3a—d** (minor products), were isolated from the diastereomeric mixtures by recrystallization.

The preparation of (*S*)-*N*-benzenesulfonyl-2-hydroxymethylpyrrolidine (**5**) was achieved by condensation of (*S*)-prolinol with benzenesulfonyl chloride in 90% yield, and the reaction of **5** with two equimolar amounts of *n*-butyllithium gave chiral lithium *N*-(*o*-lithiobenzenesulfonyl)-pyrrolidinyl-2-methoxide (**6**). The condensation of aromatic carbaldehydes such as benzaldehyde, *p*-tolualdehyde, *p*-anisaldehyde, 1-naphthaldehyde, and 2-furaldehyde with **6** gave diastereomeric mixtures of *N*-[*o*-(1′-aryl-1′-hydroxymethyl)benzenesulfonyl]-2-hydroxymethylpyrrolidines (**7a—e**) in 75—82% yields. The d.e. values of these products were estimated as 6—14% by ^{1}H-NMR spectrometry. The chiral lithium complex (**6**) was converted into the chiral benzenesulfonylpyrrolidine titanium ate-complex (**8**) by treatment with an equimolar amount of titanium tetraisopropoxide, and the reaction of aromatic carbaldehydes with **8** was performed to give diastereomeric mixtures of **7a—e** in 80—85% yields. The d.e. values of these products were



(*S*)-**9** **10**

Chart 3

estimated as 62—82% by ^{1}H-NMR spectrometry. The major products of **7a—e** prepared from **6** coincided with the major products produced from **8** on the basis of ^{1}H-NMR spectral comparison, and the former minor products coincided with the later minor products. The major component of *N*-[*o*-(1′-hydroxy-1′-(α-naphthyl)methyl)benzenesulfonyl]-2-hydroxymethylpyrrolidine [(1′*S*,2*S*)-**7d**] was a solid, which was isolated by recrystallization from the isomeric mixture, but diastereomerically pure compounds could not be isolated from the oily diastereomeric mixtures (**7a—c** and **7e**).

The diastereoselective reactions of (*S*)-*N*-methyl-*N*-(1-phenylethyl)benzenesulfonamide (**9**) lacking the hydroxymethyl group at the chiral center were examined. Benzaldehyde was condensed with the corresponding lith-

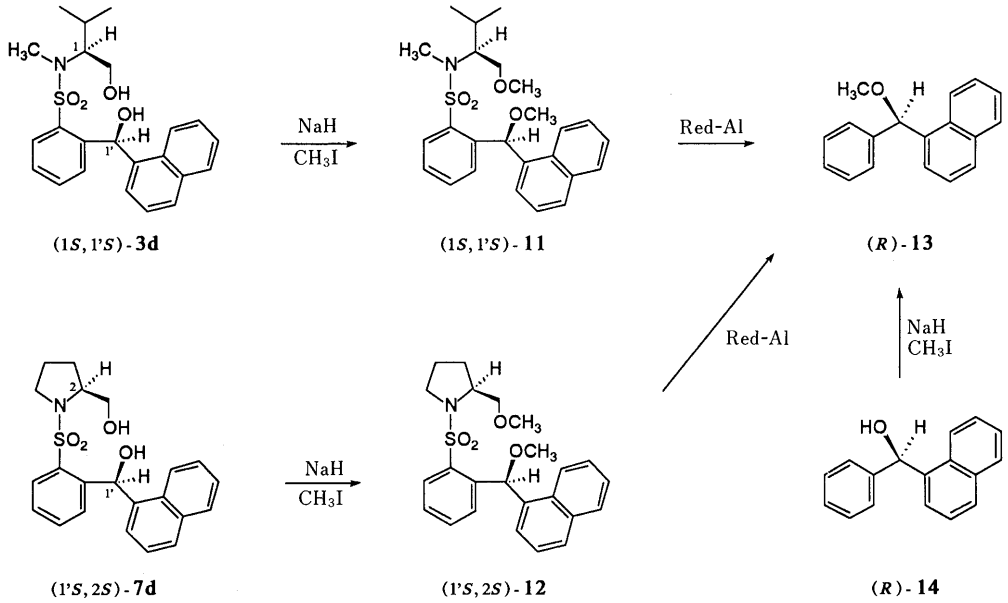


Chart 4

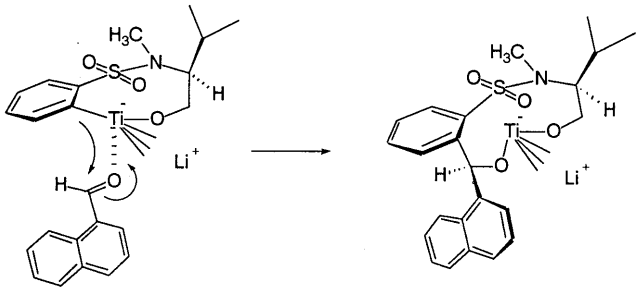


Chart 5

ium and titanium complexes to give a mixture of *o*-(1-hydroxy-1-phenylmethyl)-*N*-methyl-*N*-(1-phenylethyl)-benzenesulfonamide (**10**) in 85% and 82% yields, and the d.e. values of these products were estimated as 9% and 6% by ^{1}H-NMR spectrometry. It was suggested that the hydroxymethyl group is important for increasing the diastereoselectivity, because the titanium could be linked between the oxygen atom of the chiral hydroxymethyl group and the carbon atom at the *ortho*-position of the benzene ring.

The absolute configurations at the 1'-positions of **3d** and **7d** were elucidated as follows: The major products of **3d** and **7d** gave (1*S*,1'*S*)-*N*-(2-methoxy-1-isopropylethyl)-*o*-[1'-methoxy-1'-(α-naphthyl)methyl]-*N*-methylbenzenesulfonamide (**11**) and (1'*S*,2*S*)-*N*-[*o*-(1'-methoxy-1'-(α-naphthyl)-methyl)benzenesulfonyl]-2-methoxymethylpyrrolidine (**12**), respectively, upon *O*-methylation with sodium hydride and methyl iodide. The removal of the sulfonamide groups was performed by hydrogenolysis with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al) to give (*R*)-1-methoxy-1-(α-naphthyl)-1-phenylmethane (**13**). On the other hand, (*R*)-**13** was synthesized by *O*-methylation of (*R*)-1-(α-naphthyl)-1-phenylmethanol (**14**)[10,11] and the identical with the compounds prepared from **11** and **12**. Consequently, the absolute configurations of **3d** and **7d** were determined as (1*S*,1'*S*) and (1'*S*,2*S*), and those of **3a**—**c**, **7a**—**c**, and **7e** may be assumed to have the same configurations because these compounds are expected to be formed through a similar reaction mechanism.

It was found that the reaction of carbaldehydes with chiral benzenesulfonamide titanium ate-complexes by means of 1,6-asymmetric induction proceeds with high diastereoselectivity. Consequently, we propose a reaction mechanism in which the chiral benzenesulfonamide titanium ate-complex approaches the carbonyl carbon atom (a), and a chelated dialcoholatotitanium ate-complex intermediate (b) is formed, as shown in Chart 5.

Experimental

The ^{1}H-NMR spectra were obtained with a JEOL JNM-GSX270 spectrometer and the mass spectra (MS) were recorded with a JEOL JMS-D300 spectrometer by using the electron impact (EI) and the chemical ionization (CI) (isobutane) methods. The melting points were measured with a Yanagimoto micromelting-point apparatus and are uncorrected. The optical rotations were measured with a JASCO DIP-360 digital polarimeter.

(*S*)-*N*-(2'-Hydroxy-1'-isopropylethyl)-*N*-methylbenzenesulfonamide (1) Benzenesulfonyl chloride (17.7 g, 100 mmol) was added dropwise to a stirred solution of (*S*)-*N*-methylvalinol (12.3 g, 105 mmol) and Et_3N (11.1 g, 110 mmol) in CH_2Cl_2 (100 ml) at 0 °C, and stirring was continued at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure. The orange oily residue was dissolved in AcOEt (120 ml) and passed through a short column of silica gel. The solvent was evaporated off under reduced pressure to give a colorless solid (19.3 g, 75%). Colorless plates, mp 72—73 °C (pentane–CH_2Cl_2). $[\alpha]_D^{20}$ −16.9° (*c*=1.04, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{19}NO_3S$: C, 56.00; H, 7.44; N, 5.44. Found: C, 56.14; H, 7.54; N, 5.36. MS *m/z*: EI, 226 (M^+ −CH_2OH, 100%), 214 (M^+ −C_3H_7, 35%), 141 ($PhSO_2^+$, 50%); CI, 258 (M^+ +1, 100%), 226 (M^+ −CH_2OH, 24%). ^{1}H-NMR ($CDCl_3$) δ: 0.74 (3H, d, *J*=6.7 Hz, $CHC\underline{H}_3$), 0.94 (3H, d, *J*=6.7 Hz, $CHC\underline{H}_3$), 1.53 (1H, dd, *J*=4.9, 6.1 Hz, $CH_2O\underline{H}$), 1.72 (1H, double septet, *J*=6.7, 8.6 Hz, $CHC\underline{H}(CH_3)_2$), 2.79 (3H, s, NCH_3), 3.53 (1H, ddd, *J*=4.9, 8.6, 11.0 Hz, $NCHC\underline{H}_2OH$), 3.64 (1H, dt, *J*=3.1, 8.6 Hz, $NC\underline{H}CH_2OH$), 3.74 (1H, ddd, *J*=3.1, 6.1, 11.0 Hz, $NCHC\underline{H}_2OH$), 7.47—7.89 (5H, m, aromatic H).

Reaction of Carbaldehydes with Lithium Complex (2) *n*-BuLi (12.5 mmol, 7.8 ml of 1.6 M solution of hexane) was added dropwise to a stirred solution of (*S*)-**1** (1.29 g, 5 mmol) in tetrahydrofuran (THF) (25 ml) at 0 °C under a nitrogen atmosphere, and stirring was continued for 10 min. The resulting solution was placed on a cold bath at −50 °C and stirred for 20 min to form a lithium complex (**2**). A solution of a carbaldehyde

(benzaldehyde, *p*-tolualdehyde, *p*-anisaldehyde, or 1-naphthaldehyde, 6.5 mmol) in THF (8 ml) was slowly added dropwise to a stirred solution of **2** using an infusion pump at −50 °C, and stirring was continued for 4 h. The reaction mixture was treated with NH_4Cl saturated aqueous solution (1 ml) and dried over $MgSO_4$. The resulting white precipitate was filtered off, and the filtrate was concentrated under reduced pressure. The d.e. value of the residue thus obtained was estimated by ^{1}H-NMR spectrometry. The residue was subjected to column chromatography on silica gel with a solution of hexane–ether (2:3) to give the corresponding diastereomeric mixture (**3a—d**). The experimental data are summarized in Table I.

Reaction of Carbaldehydes with Titanium Complex (4) Ti(*O*-iso-C_3H_7)$_4$ (1.8 ml, 6 mmol) was added dropwise to a stirred solution of **2** prepared form (*S*)-**1** (5 mmol), and stirring was continued at −50 °C for 30 min to from a titanium complex (**4**). A solution of a carbaldehyde (6.5 mmol) in THF (8 ml) was slowly added dropwise to the stirred solution of **4** using an infusion pump at −50 °C, and stirring was continued for 4 h. The reaction mixture was worked up as described for the reaction of **2** to give the corresponding diastereomeric mixture (**3a—d**). The experimental data are summarized in Table I.

(1*S*,1′*S*)-*N*-(2-Hydroxy-1-isopropylethyl)-*o*-(1′-hydroxy-1′-phenylmethyl)-*N*-methylbenzenesulfonamide (**3a**) [Major Product]: This compound was isolated from the diastereomeric mixture (ratio, 83:17) by recrystallization from hexane–CH_2Cl_2 solution. Colorless plates, mp 105—106 °C (hexane–CH_2Cl_2). $[\alpha]_D^{22}$ −236.7° (*c*=0.39, $CHCl_3$). *Anal.* Calcd for $C_{19}H_{25}NO_4S$: C, 62.78; H, 6.93; N, 3.85. Found: C, 63.02; H, 7.03; N, 3.79. MS *m/z*: EI, 345 ($M^+ - H_2O$, 0.1%), 332 ($M^+ - CH_2OH$, 12%); CI, 364 ($M^+ + 1$, 0.4%), 346 ($M^+ - OH$, 100%), 332 ($M^+ - CH_2OH$, 5%). ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.03 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.78 (1H, double septet, *J*=6.7, 8.5 Hz, $CHCH(CH_3)_2$), 2.15 (1H, br, OH), 2.75 (3H, s, NCH_3), 3.47—3.56 (1H, m, $NCHCH_2OH$), 3.82—3.92 (2H, m, $NCHCH_2OH$), 4.15 (1H, br, OH), 6.88 (1H, s, PhCHOH), 7.20—8.01 (9H, m, aromatic H).

(1*S*,1′*R*)-**3a** [Minor Product]: This compound was isolated from the diastereomeric mixture (ratio, 54:46) by recrystallization from ether–hexane solution. Colorless plates, mp 139—140 °C (hexane–benzene). $[\alpha]_D^{21}$ +189.2° (*c*=0.25, $CHCl_3$). *Anal.* Calcd for $C_{19}H_{25}NO_4S$: C, 62.78; H, 6.93; N, 3.85. Found: C, 62.91; H, 7.01; N, 3.85. MS *m/z*: EI, 345 ($M^+ - H_2O$, 0.1%), 332 ($M^+ - CH_2OH$, 16%); CI, 364 ($M^+ + 1$, 3%), 346 ($M^+ - OH$, 100%), 332 ($M^+ - CH_2OH$, 9%). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, d, *J*=6.7 Hz, $CHCH_3$), 0.98 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.60 (1H, br, OH), 1.83 (1H, double septet, *J*=6.7, 9.2 Hz, $CHCH(CH_3)_2$), 3.01 (3H, s, NCH_3), 3.41 (1H, dt, *J*=3.7, 9.2 Hz, $NCHCH_2OH$), 3.58 (1H, dd, *J*=9.2, 12.2 Hz, $NCHCH_2OH$), 3.72 (1H, dd, *J*=3.7, 12.2 Hz, $NCHCH_2OH$), 3.95 (1H, br, OH), 6.66 (1H, s, PhCHOH), 7.20—8.08 (9H, m, aromatic H).

(1*S*,1′*S*)-*N*-(2-Hydroxy-1-isopropylethyl)-*o*-[1′-hydroxy-1′-(*p*-tolyl)-methyl]-*N*-methylbenzenesulfonamide (**3b**) [Major Product]: This compound was isolated from the diastereomeric mixture (ratio, 87:13) by recrystallization from hexane–CH_2Cl_2 solution. Colorless plates, mp 68.5—69.5 °C (hexane–CH_2Cl_2). $[\alpha]_D^{23}$ −191.8° (*c*=0.60, $CHCl_3$). *Anal.* Calcd for $C_{20}H_{27}NO_4S$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.73; H, 7.36; N, 3.46. MS *m/z*: EI, 359 ($M^+ - H_2O$, 12%), 346 ($M^+ - CH_2OH$, 8%); CI, 378 ($M^+ + 1$, 0.7%), 360 ($M^+ - OH$, 100%), 346 (M^+ -CH_2OH, 2%). ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.02 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.78 (1H, double septet, *J*=6.7, 8.6 Hz, $CHCH(CH_3)_2$), 2.09 (1H, br, OH), 2.32 (3H, s, $PhCH_3$), 2.76 (3H, s, NCH_3), 3.47—3.56 (1H, m, $NCHCH_2OH$), 3.81—3.90 (2H, m, $NCHCH_2OH$), 3.98 (1H, br, OH), 6.84 (1H, s, PhCHOH), 7.13—8.00 (8H, m, aromatic H).

(1*S*,1′*R*)-**3b** [Minor Product]: This compound was isolated from the diastereomeric mixture (ratio, 54:46) by recrystallization from ether. Colorless needles, mp 153.5—154.5 °C (ether). $[\alpha]_D^{24}$ +175.6° (*c*=0.52, $CHCl_3$). *Anal.* Calcd for $C_{20}H_{27}NO_4S$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.87; H, 7.33: N, 3.66. MS *m/z*: EI, 359 ($M^+ - H_2O$, 7%), 346 ($M^+ - CH_2OH$, 8%); CI, 378 ($M^+ + 1$, 0.6%), 360 ($M^+ - OH$, 100%), 346 ($M^+ - CH_2OH$, 4%). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, d, *J*=6.7 Hz, $CHCH_3$), 0.96 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.71 (1H, t, *J*=5.5 Hz, CH_2OH), 1.82 (1H, double septet, *J*=6.7, 9.2 Hz, $CHCH(CH_3)_2$), 2.35 (3H, s, $PhCH_3$), 3.00 (3H, s, NCH_3), 3.41 (1H, dt, *J*=3.7 9.2 Hz, $NCHCH_2OH$), 3.58 (1H, ddd, *J*=5.5, 9.2, 11.6 Hz, $NCHCH_2OH$), 3.71 (1H, ddd, *J*=3.7, 5.5, 11.6 Hz, $NCHCH_2OH$), 3.82 (1H, d, *J*=3.1 Hz, CHOH), 6.63 (1H, d, *J*=3.1 Hz, PhCHOH), 7.17—8.07 (8H, m, aromatic H).

(1*S*,1′*S*)-*N*-(2-Hydroxy-1-isopropylethyl)-*o*-[1′-hydroxy-1′-(*p*-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide (**3c**) [Major Product]: This compound was isolated from the diastereomeric mixture (ratio, 90:10) by recrystallization from ether. Colorless plates, mp 111.5—112.5 °C (benzene). $[\alpha]_D^{22}$ −225.9° (*c*=0.65, $CHCl_3$). *Anal.* Calcd for $C_{20}H_{27}NO_5S$: C, 61.05; H, 6.92; N, 3.56. Found: C, 61.33; H, 7.13; N, 3.45. MS *m/z*: EI, 375 ($M^+ - H_2O$, 0.4%), 362 ($M^+ - CH_2OH$, 9%); CI, 394 ($M^+ + 1$, 0.2%), 376 ($M^+ - OH$, 100%), 362 ($M^+ - CH_2OH$, 3%). ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.01 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.77 (1H, double septet, *J*=6.7, 9.2 Hz, $CHCH(CH_3)_2$), 2.16 (1H, br, OH), 2.74 (3H, s, NCH_3), 3.50 (1H, dd, *J*=10.4, 12.8 Hz, $NCHCH_2OH$), 3.78 (3H, s, OCH_3), 3.80—3.89 (2H, m, $NCHCH_2OH$), 4.01 (1H, br, OH), 6.81 (1H, s, PhCHOH), 6.83—7.99 (8H, m, aromatic H).

(1*S*,1′*R*)-**3c** [Minor Product]: This compound was isolated from the diastereomeric mixture (ratio, 53:47) by recrystallization in hexane–CH_2Cl_2 solution. Colorless needles, mp 149.5—150.5 °C (pentane–CH_2Cl_2). $[\alpha]_D^{25}$ +172.4° (*c*=0.41, $CHCl_3$). *Anal.* Calcd for $C_{20}H_{27}NO_5S$: C, 61.05; H, 6.92; N, 3.56. Found: C, 61.28; H, 7.05; N, 3.48. MS *m/z*: EI, 375 ($M^+ - H_2O$, 2%), 362 ($M^+ - CH_2OH$, 5%); CI, 394 ($M^+ + 1$, 0.3%), 376 ($M^+ - OH$, 100%), 362 ($M^+ - CH_2OH$, 1%). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, d, *J*=6.7 Hz, $CHCH_3$), 0.96 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.69 (1H, t, *J*=6.1 Hz, CH_2OH), 1.82 (1H, double septet, *J*=6.7, 9.2 Hz, $CHCH(CH_3)_2$), 3.00 (3H, s, NCH_3), 3.41 (1H, dt, *J*=3.7, 9.2 Hz, $NCHCH_2OH$), 3.58 (1H, ddd, *J*=6.1, 9.2, 12.2 Hz, $NCHCH_2OH$), 3.73 (1H, ddd, *J*=3.7, 6.1, 12.2 Hz, $NCHCH_2OH$), 3.81 (3H, s, OCH_3), 3.83 (1H, d, *J*=3.1 Hz, CHOH), 6.61 (1H, d, *J*=3.1 Hz, PhCHOH), 6.87—8.07 (8H, m, aromatic H).

(1*S*,1′*S*)-*N*-(2-Hydroxy-1-isopropylethyl)-*o*-[1′-hydroxy-1′-(α-naphthyl)methyl]-*N*-methylbenzenesulfonamide (**3d**) [Major Product]: This compound was isolated from the diastereomeric mixture (ratio, 89:11) by recrystallization from benzene. Colorless plates, mp 172—173 °C (benzene). $[\alpha]_D^{27}$ −215.1° (*c*=0.45, $CHCl_3$). *Anal.* Calcd for $C_{23}H_{27}NO_4S$: C, 66.80; H, 6.58; N, 3.39. Found: C, 66.89; H, 6.57; N, 3.24. MS *m/z*: EI, 395 ($M^+ - H_2O$, 0.2%), 382 ($M^+ - CH_2OH$, 6%); CI, 414 ($M^+ + 1$, 0.4%), 396 ($M^+ - OH$, 100%), 382 ($M^+ - CH_2OH$, 2%). ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.06 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.88 (1H, double septet, *J*=6.7, 8.5 Hz, $CHCH(CH_3)_2$), 2.51 (1H, dd, *J*=4.3, 6.7 Hz, CH_2OH), 2.83 (3H, s, NCH_3), 3.56 (1H, ddd, *J*=6.7, 9.8, 11.6 Hz, $NCHCH_2OH$), 3.88 (1H, dt, *J*=4.3, 11.6 Hz, $NCHCH_2OH$), 3.98 (1H, ddd, *J*=4.3, 8.5, 9.8 Hz, $NCHCH_2OH$), 4.34 (1H, d, *J*=4.3 Hz, CHOH), 7.10—8.08 (12H, m, NaphCHOH, and aromatic H).

(1*S*,1′*R*)-**3d** [Minor Product]: This compound was isolated from the diastereomeric mixture (ratio, 55:45) by recrystallization from hexane–CH_2Cl_2 solution. Colorless needles, mp 140—140.5 °C (CH_2Cl_2). $[\alpha]_D^{26}$ +211.6° (*c*=0.17, $CHCl_3$). *Anal.* Calcd for $C_{23}H_{27}NO_4S$: C, 66.80; H, 6.58; N, 3.39. Found: C, 66.54; H, 6.64; N, 3.28. MS *m/z*: EI, 395 ($M^+ - H_2O$, 1%), 382 ($M^+ - CH_2OH$, 3%); CI, 414 ($M^+ + 1$, 0.8%), 396 ($M^+ - OH$, 100%), 382 ($M^+ - CH_2OH$, 4%). ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.11 (3H, d, *J*=6.7 Hz, $CHCH_3$), 1.82 (1H, t, *J*=5.5 Hz, CH_2OH), 1.89 (1H, double septet, *J*=6.7, 8.6 Hz, $CHCH(CH_3)_2$), 3.08 (3H, s, NCH_3), 3.54—3.80 (3H, m, $NCHCH_2OH$), 4.17 (1H, d, *J*=2.4 Hz, CHOH), 7.07—8.19 (12H, m, NaphCHOH and aromatic H).

(*S*)-*N*-Benzenesulfonyl-2-hydroxymethylpyrrolidine (5) Benzenesulfonyl chloride (17.9 g, 101 mmol) was added dropwise to a stirred solution of (*S*)-prolinol (11.1 g, 110 mmol) and Et_3N (13.2 g, 130 mmol) in CH_2Cl_2 (100 ml) at 0°C, and strring was continued at room temperature for 2 h. The reaction mixture was worked up as described for the preparation of (*S*)-**1** to give a colorless oil (21.7 g, 90%). bp 160—162 °C (0.25 mmHg). $[\alpha]_D^{27}$ −58.8° (*c*=1.08, $CHCl_3$). *Anal.* Calcd for $C_{11}H_{15}NO_3S$: C, 54.75; H, 6.27; N, 5.80. Found: C, 54.87; H, 6.39; N, 5.74. MS *m/z*: EI, 223 ($M^+ - H_2O$, 25%), 210 ($M^+ - CH_2OH$, 100%), 141 ($PhSO_2^+$, 51%); CI, 242 ($M^+ + 1$, 100%), 224 ($M^+ - OH$, 53%), 210 ($M^+ - CH_2OH$, 18%). ^{1}H-NMR ($CDCl_3$) δ: 1.40—1.52 (1H, m, CH_2CH_2), 1.63—1.89 (3H, m, CH_2CH_2), 2.79 (1H, br, OH), 3.28 (1H, dt, *J*=6.7, 10.4 Hz, NCH_2), 3.48 (1H, dt, *J*=6.1, 10.4 Hz, NCH_2), 3.61—3.75 (3H, m, $NCHCH_2OH$), 7.52—7.89 (5H, m, aromatic H).

Reaction of Carbaldehydes with Lithium Complex (6) *n*-BuLi (2.4 mmol, 1.5 ml of 1.6 M solution of hexane) was added dropwise to a stirred solution of (*S*)-**5** (0.24 g, 1 mmol) in THF (5 ml) at 0 °C under a nitrogen atmosphere and the reaction mixture was stirred for 30 min to form a lithium complex (**6**). A solution of a carbaldehyde (benzaldehyde, *p*-tolualdehyde, *p*-anisaldehyde, 1-naphthaldehyde, or 2-furaldehyde, 1.3 mmol) in THF (1 ml) was slowly added dropwise to the stirred solution of **6** at 0 °C, and stirring was continued for 3 h. The reaction mixture was worked up as

described for the reaction of **2**. The d.e. value of the residue was estimated by ^{1}H-NMR spectrometry, and the residue was subjected to column chromatography on silica gel with the appropriate eluent to give the corresponding diastereomeric mixture (**7a—e**). The experimental data are summarized in Table I.

Reaction of Carbaldehydes with Titanium Complex (8) Ti(*O*-iso-C_3H_7)$_4$ (0.35 ml, 1.2 mmol) was added dropwise to a stirred solution of **6** prepared from (*S*)-**5** (1 mmol), and stirring was continued at 0 °C for 30 min to form the titanium complex (**8**). A solution of a carbaldehyde (1.3 mmol) in THF (1 ml) was slowly added dropwise to the stirred solution of **8** at 0 °C, and stirring was continued for 3 h. The reaction mixture was worked up as described for the reaction of **6** to give the corresponding diastereomeric mixture (**7a—e**). The experimental data are summarized in Table I.

N-[*o*-(1′-Hydroxy-1′-phenylmethyl)benzenesulfonyl]-2-hydroxymethylpyrrolidine (**7a**): Eluent, CH_2Cl_2–ether (10 : 1). MS *m/z*: EI, 329 ($M^+ - H_2O$, 0.1%), 316 ($M^+ - CH_2OH$, 43%); CI, 348 ($M^+ + 1$, 3%), 330 ($M^+ - OH$, 100%), 316 ($M^+ - CH_2OH$, 6%). ^{1}H-NMR ($CDCl_3$) δ: (1′*S*,2*S*)-**7a** (Major component); 1.77—2.02 (4H, m, CH_2CH_2), 2.48 (1H, t, J=4.3 Hz, $CH_2O\underline{H}$), 3.16 (1H, dt, J=6.1, 9.8 Hz, NCH_2), 3.37 (1H, dt, J=6.7, 9.8 Hz, NCH_2), 3.58 (1H, dt, J=11.6, 4.3 Hz, $NCHC\underline{H}_2OH$), 3.77 (1H, d, J=4.9 Hz, $CHO\underline{H}$), 3.83 (1H, dt, J=11.6, 4.3 Hz, $NCHC\underline{H}_2OH$), 4.09 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 6.93 (1H, d, J=4.9 Hz, $PhC\underline{H}OH$), 7.24—8.00 (9H, m, aromatic H). (1′*S*,2*R*)-**7a** (Minor component); 1.72—2.10 (4H, m, CH_2CH_2), 2.56 (1H, br, OH), 3.20—3.30 (1H, m, $NCHC\underline{H}_2OH$), 3.34—3.47 (2H, m, NCH_2 and $NCHC\underline{H}_2OH$), 3.70—3.80 (1H, m, NCH_2), 3.87—3.96 (1H, m, $NC\underline{H}CH_2OH$), 3.90 (1H, br, OH), 6.86 (1H, s, $PhC\underline{H}OH$), 7.20—8.07 (9H, m, aromatic H).

N-[*o*-(1′-Hydroxy-1′-(*p*-tolyl)methyl)benzenesulfonyl]-2-hydroxymethylpyrrolidine (**7b**): Eluent, CH_2Cl_2–AcOEt (5 : 1). MS *m/z*: EI, 343 ($M^+ - H_2O$, 0.03%), 330 ($M^+ - CH_2OH$, 16%); CI, 362 ($M^+ + 1$, 0.8%), 344 ($M^+ - OH$, 100%), 330 ($M^+ - CH_2OH$, 8%). ^{1}H-NMR ($CDCl_3$) δ: (1′*S*,2*S*)-**7b** (Major component); 1.78—2.01 (4H, m, CH_2CH_2), 2.34 (3H, s, $PhCH_3$), 2.45 (1H, t, J=4.3 Hz, $CH_2O\underline{H}$), 3.17 (1H, dt, J=6.1, 9.8 Hz, NCH_2), 3.36 (1H, dt, J=6.7, 9.8 Hz, NCH_2), 3.57 (1H, dt, J=11.6, 4.3 Hz, $NCHC\underline{H}_2OH$), 3.63 (1H, d, J=4.9 Hz, $CHO\underline{H}$), 3.82 (1H, dt, J=11.6, 4.3 Hz, $NCHC\underline{H}_2OH$), 4.07 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 6.89 (1H, d, J=4.9 Hz, $PhC\underline{H}OH$), 7.15 (2H, d, J=7.9 Hz, aromatic H), 7.31 (2H, d, J=7.9 Hz, aromatic H), 7.36—7.99 (4H, m, aromatic H). (1′*S*,2*R*)-**7b** (Minor component); 1.70—2.05 (4H, m, CH_2CH_2), 2.34 (3H, s, $PhCH_3$), 2.60 (1H, br, OH), 3.15—3.75 (5H, m, NCH_2, $NCHC\underline{H}_2OH$, and $PhCHO\underline{H}$), 3.85—3.95 (1H, m, $NC\underline{H}CH_2OH$), 6.83 (1H, s, $PhC\underline{H}OH$), 7.10—8.05 (8H, m, aromatic H).

N-[*o*-(1′-Hydroxy-1′-(*p*-methoxyphenyl)methyl)benzenesulfonyl]-2-hydroxymethylpyrrolidine (**7c**): Eluent, hexane–AcOEt (1 : 1). MS *m/z*: EI, 359 ($M^+ - H_2O$, 0.5%), 346 ($M^+ - CH_2OH$, 14%); CI, 378 ($M^+ + 1$, 1%), 360 ($M^+ - OH$, 100%), 346 ($M^+ - CH_2OH$, 2%). ^{1}H-NMR ($CDCl_3$) δ: (1′*S*,2*S*)-**7c** (Major component); 1.81—2.04 (4H, m, CH_2CH_2), 2.38 (1H, t, J=6.1 Hz, $CH_2O\underline{H}$), 3.18 (1H, dt, J=9.8, 6.1 Hz, NCH_2), 3.37 (1H, dt, J=9.8, 6.7 Hz, NCH_2), 3.56 (1H, d, J=4.9 Hz, $CHO\underline{H}$), 3.58 (1H, ddd, J=4.3, 6.1, 11.0 Hz, $NCHC\underline{H}_2OH$), 3.80 (3H, s, OCH_3), 3.83 (1H, ddd, J=4.3, 6.1, 11.0 Hz, $NCHC\underline{H}_2OH$), 4.07 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 6.87 (1H, d, J=4.9, $PhC\underline{H}OH$), 6.88 (2H, d, J=7.4 Hz, aromatic H), 7.35 (2H, d, J=7.4 Hz, aromatic H), 7.37—7.99 (4H, m, aromatic H). (1′*S*,2*R*)-**7c** (Minor component); 1.83—2.10 (4H, m, CH_2CH_2), 2.38 (1H, br, OH), 3.15—3.90 (5H, m, NCH_2, $NCHC\underline{H}_2OH$, and $PhCHO\underline{H}$), 3.80 (3H, s, OCH_3), 3.94 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 6.80 (1H, s, $PhC\underline{H}OH$), 6.87—8.03 (8H, m, aromaric H).

N-[*o*-(1′-Hydroxy-1′-(α-naphthyl)methyl)benzenesulfonyl]-2-hydroxymethylpyrrolidine (**7d**): Eluent, CH_2Cl_2–ether (10 : 1). MS *m/z*: EI, 379 ($M^+ - H_2O$, 0.4%), 366 ($M^+ - CH_2OH$, 15%); CI, 398 ($M^+ + 1$, 1%), 380 ($M^+ - OH$, 30%), 366 ($M^+ - CH_2OH$, 4%). The major product [(1′*S*,2*S*)-**7d**] was isolated from a diastereomeric mixture (ratio, 91 : 9) by recrystallization in benzene. Colorless needles, mp 113.5—114.5 °C (benzene). $[\alpha]_D^{20}$ −236.7° (c=1.04, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{23}NO_4S$: C, 66.50; H, 5.79; N, 3.46. Found: C, 66.48; H, 5.83; N, 3.52. ^{1}H-NMR ($CDCl_3$) δ: 1.90—2.12 (4H, m, CH_2CH_2), 2.40 (1H, t, J=5.2 Hz, $CH_2O\underline{H}$), 3.18 (1H, dt, J=10.4, 6.1 Hz, NCH_2), 3.41 (1H, dt, J=10.4, 6.7 Hz, NCH_2), 3.65 (1H, ddd, J=4.0, 5.2, 11.6 Hz, $NCHC\underline{H}_2OH$), 4.02 (1H, ddd, J=4.0, 5.2, 11.6 Hz, $NCHC\underline{H}_2OH$), 4.31 (1H, dq, J=7.9, 4.0 Hz, $NC\underline{H}CH_2OH$), 4.44 (1H, d, J=5.5 Hz, $NaphCHO\underline{H}$), 7.08—7.44 (5H, m, aromatic H), 7.47 (1H, d, J=5.5 Hz, $NaphC\underline{H}OH$), 7.58—8.08 (6H, m, aromatic H). (1′*S*,2*R*)-**7d** (Minor component); ^{1}H-NMR ($CDCl_3$) δ: 1.90—2.12 (4H, m, CH_2CH_2), 2.72 (1H, br, $CH_2O\underline{H}$), 3.27 (1H, dt, J=9.8, 6.7 Hz, NCH_2), 3.45—3.70 (3H, m, $NCHC\underline{H}_2OH$ and $NaphCHO\underline{H}$), 3.81 (1H, dt, J=6.7, 9.8 Hz, NCH_2), 4.15 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 7.05—8.12 (12H, m, $NaphC\underline{H}OH$ and aromatic H).

N-[*o*-(1′-(α-Furyl)-1′-hydroxymethyl)benzenesulfonyl]-2-hydroxymethylpyrrolidine (**7e**): Eluent, CH_2Cl_2–ether (1 : 1). MS *m/z*: EI, 319 ($M^+ - H_2O$, 0.1%), 306 ($M^+ - CH_2OH$, 9%); CI, 338 ($M^+ + 1$, 1%), 320 ($M^+ - OH$, 100%), 306 ($M^+ - CH_2OH$, 2%). ^{1}H-NMR ($CDCl_3$) δ: (1′*S*,2*S*)-**7e** (Major component); 1.74—1.90 (4H, m, CH_2CH_2), 2.25 (1H, t, J=6.1 Hz, $CH_2O\underline{H}$), 3.22—3.28 (2H, m, NCH_2), 3.41 (1H, d, J=4.9 Hz, $CHO\underline{H}$), 3.53 (1H, ddd, J=4.3, 6.1, 11.6 Hz, $NCHC\underline{H}_2OH$), 3.69 (1H, ddd, J=4.3, 6.1, 11.6 Hz, $NCHC\underline{H}_2OH$), 3.98 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 6.31 (1H, d, J=3.7 Hz, furyl H), 6.37 (1H, dd, J=1.8, 3.7 Hz, furyl H), 6.88 (1H, d, J=4.9 Hz, $C\underline{H}OH$), 7.40 (1H, d, J=1.8 Hz, furyl H), 7.44—8.02 (4H, m, aromatic H). (1′*S*,2*R*)-**7e** (Minor component); 1.72—2.04 (4H, m, CH_2CH_2), 2.58 (1H, br s, $CH_2O\underline{H}$), 3.20—3.30 (1H, m, NCH_2), 3.30—3.45 (1H, m, NCH_2), 3.47 (1H, br s, $CHO\underline{H}$), 3.50—3.60 (1H, m, $NCHC\underline{H}_2OH$), 3.64—3.75 (1H, m, $NCHC\underline{H}_2OH$), 3.90 (1H, dq, J=8.5, 4.3 Hz, $NC\underline{H}CH_2OH$), 6.27 (1H, dd, J=1.8, 3.1 Hz, furyl H), 6.35—6.36 (1H, m, furyl H), 6.83 (1H, s, $C\underline{H}OH$), 7.40—8.04 (5H, m, aromatic H).

(*S*)-*N*-Methyl-*N*-(1-phenylethyl)benzenesulfonamide (9) A solution of benzenesulfonyl chloride (3.54 g, 20 mmol) in CH_2Cl_2 (8 ml) was added dropwise to a stirred solution of (*S*)-*N*-methyl-1-phenylethylamine (2.74 g, 20.3 mmol) and Et_2N (2.98 g, 29.4 mmol) in CH_2Cl_2 (30 ml) at room temperature. The reaction mixture was refluxed for 20 min, then concentrated. The residue was dissolved in AcOEt (40 ml) and the solution was passed through a short column of silica gel. The solvent was evaporated off under reduced pressure to give a colorless solid (4.60 g, 84%). Colorless prisms, mp 71—72 °C (benzene–hexane). $[\alpha]_D^{25}$ −28.7° (c=1.51, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{17}NO_2S$: C, 65.43; H, 6.22; N, 5.09. Found: C, 65.36; H, 6.26; N, 5.04. MS *m/z*: EI, 275 (M^+, 1%), 260 ($M^+ - CH_3$, 26%), 141 ($PhSO_2^+$, 31%); CI, 276 ($M^+ + 1$, 100%), 260 ($M^+ - CH_3$, 12%). ^{1}H-NMR ($CDCl_3$) δ: 1.30 (3H, d, J=6.7 Hz, $CHC\underline{H}_3$), 2.59 (3H, s, NCH_3), 5.30 (1H, q, J=6.7 Hz, $C\underline{H}CH_3$), 7.22—7.89 (10H, m, aromatic H).

Reaction of Benzaldehyde with Lithium Complex of (*S*)-9 *n*-BuLi (1.3 mmol, 0.81 ml of 1.6 M solution of hexane) was added dropwise to a stirred solution of (*S*)-**9** (0.28 g, 1 mmol) in toluene (30 ml) at −20 °C under a nitrogen atmosphere, and stirring was continued for 30 min to form the lithium complex of (*S*)-**9**. A solution of benzaldehyde (0.14 g, 1.3 mmol) in toluene (1 ml) was added dropwise to stirred suspension of the lithium complex, and stirring was continued at −20 °C for 3 h. The reaction mixture was worked up as described for the reaction of (*S*)-**2**. The d.e. value was estimated as 9% by ^{1}H-NMR spectrometry. The residue was subjected to column chromatography on silica gel with a solution of hexane–ether (3 : 1) to give a diastereomeric mixture of (*S*)-*o*-(1-hydroxy-1-phenylmethyl)-*N*-methyl-*N*-(1-phenylethyl)benzenesulfonamide (**10**) (0.32 g, 85%) as a colorless oil. This product decomposed during distillation *in vacuo*. MS *m/z*: EI, 366 ($M^+ - CH_3$, 0.1%); CI, 382 ($M^+ + 1$, 0.2%), 366 ($M^+ - CH_3$, 1%). ^{1}H-NMR ($CDCl_3$) δ: 1.57 and 1.58 (3H, d, J=7.3 Hz, $CHC\underline{H}_3$), 2.67 and 2.71 (3H, s, NCH_3), 3.17 and 3.41 (1H, d, J=4.3 Hz, $CHO\underline{H}$), 5.26 and 5.31 (1H, q, J=7.3 Hz, $C\underline{H}CH_3$), 6.64 and 6.72 (1H, d, J=4.3 Hz, $PhC\underline{H}OH$), 7.16—8.00 (14H, m, aromatic H).

Reaction of Benzaldehyde with Titanium Complex of (*S*)-9 Ti(*O*-iso-C_3H_7)$_4$ (0.38 ml, 1.3 mmol) was added dropwise to a stirred suspension of the lithium complex (1 mmol) prepared from (*S*)-**9**, and stirring was continued at −20 °C for 30 min to form the titanium complex. A solution of benzaldehyde (0.14 g, 1.3 mmol) in toluene (1 ml) was added dropwise to the stirred solution of the titanium complex, and stirring was continued at −20 °C for 3 h. The reaction mixture was worked up as described for the reaction with the lithium complex to give a diastereomeric mixture of **10** (0.31 g, 82%). The d.e. value was estimated as 6% by ^{1}H-NMR spectrometry.

(1*S*,1′*S*)-*N*-(2-Methoxy-1-isopropylethyl)-*o*-[1′-methoxy-1′-(α-naphthyl)-methyl]-*N*-methylbenzenesulfonamide (11) NaH (17 mmol, 0.68 g of 60% NaH in liquid paraffin) was added to a stirred solution of (1*S*,1′*S*)-**3d** (2.01 g, 4.86 mmol) in THF (20 ml), and CH_3I (1.5 ml, 23 mmol) was added dropwise to the mixture. The reaction mixture was refluxed for 10 min, then treated with NH_4Cl aqueous solution, and the whole was extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated. The residue was subjected to column chromatography on silica gel with a solution of hexane–ether (3 : 1) to give a colorless solid (1.85 g, 86%). Colorless plates, mp 79—80 °C (hexane–benzene). $[\alpha]_D^{22}$ −39.0° (c=0.76, $CHCl_3$). *Anal.* Calcd for $C_{25}H_{31}NO_4S$: C, 68.05; H, 7.08; N, 3.17. Found: C, 67.97; H, 7.15; N, 3.09. MS *m/z*: EI, 441 (M^+, 0.2%), 396 ($M^+ - CH_2OCH_3$, 12%), 311 ($M^+ - C_7H_{16}NO$, 55%). ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, d, J=6.7 Hz, $CHC\underline{H}_3$), 0.94 (3H, d, J=6.7 Hz, $CHC\underline{H}_3$), 1.92 (1H, double septet, J=6.7, 9.8 Hz, $CHC\underline{H}(CH_3)_2$), 2.69 (3H, s, NCH_3),

3.18 (3H, s, OCH_3), 3.32 (1H, dd, J=3.1, 10.4 Hz, $NCHC\underline{H}_2O$), 3.42 (1H, dd, J=6.1, 10.4 Hz, $NCHC\underline{H}_2O$), 3.54 (3H, s, OCH_3), 3.70 (1H, ddd, J=3.1, 6.1, 9.8 Hz, $NC\underline{H}CH_2O$), 7.23 (1H, s, $NaphC\underline{H}OCH_3$), 7.32—8.16 (11H, m, aromatic H).

(1′*S*,2*S*)-*N*-[*o*-(1′-Methoxy-1′-(α-naphthyl)methyl)benzenesulfonyl]-2-methoxymethylpyrrolidine (12) NaH (18.3 mmol, 0.73 g of 60% NaH in liquid paraffin) was added to a stirred solution of (1′*S*,2*S*)-**7d** (2.12 g, 5.33 mmol) in THF (20 ml), and CH_3I (1.3 ml, 20 mmol) was added dropwise to the mixture. The reaction mixture was refluxed for 10 min, then worked up as described for the preparation of (1*S*,1′*S*)-**11** to give a colorless solid (1.86 g, 82%). Colorless needles, mp 96—97 °C (hexane–benzene). $[\alpha]_D^{21}$ +14.1° (c=0.46, $CHCl_3$). *Anal.* Calcd for $C_{24}H_{27}NO_4S$: C, 67.74; H, 6.40; N, 3.29. Found: C, 67.97; H, 6.45; N, 3.58. MS m/z: 425 (M^+, 0.2%), 380 ($M^+ - CH_2OCH_3$, 20%), 311 ($M^+ - C_6H_{12}NO$, 60%). ^{1}H-NMR ($CDCl_3$) δ: 1.14—1.70 (4H, m, CH_2CH_2), 3.10 (2H, dd, J=6.1, 7.3 Hz, NCH_2), 3.16 (1H, dd, J=7.3, 9.8 Hz, $NCHC\underline{H}_2O$), 3.18 (3H, s, OCH_3), 3.26 (1H, dd, J=4.3, 9.8 Hz, $NCHC\underline{H}_2O$), 3.54 (3H, s, OCH_3), 3.66—3.75 (1H, m, $NC\underline{H}CH_2O$), 7.18 (1H, s, $NaphC\underline{H}OCH_3$), 7.08—8.21 (11H, m, aromatic H).

(*R*)-1-Methoxy-1-(α-naphthyl)-1-phenylmethane (13) i) From (1*S*,1′*S*)-**11**: Red-Al (20 mmol, 10 ml of 2 M solution in toluene) was added dropwise to a stirred solution of (1*S*, 1′*S*)-**11** (2.45 g, 5.55 mmol) in toluene (16 ml). The reaction mixture was refluxed for 15 h, then poured into a 0.5 N HCl aqueous solution, and the whole was extracted with ether. The organic layer was washed with 0.5 N HCl and 20% K_2CO_3 aqueous solutions, dried over $MgSO_4$, and evaporated. The residue was subjected to column chromatography on alumina with a solution of hexane–ether (25 : 1) to give a colorless oil (0.45 g, 33%), bp 160—165 °C (0.8 mmHg) (bulb-to-bulb distillation). $[\alpha]_D^{22}$ +93.5° (c=1.83, benzene). *Anal.* Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49. Found: C, 87.02; H, 6.48. MS m/z: 248 (M^+, 100%), 217 ($M^+ - OCH_3$, 89%), 171 ($M^+ - C_6H_5$, 58%), 121 ($M^+ - C_{10}H_7$, 31%). ^{1}H-NMR ($CDCl_3$) δ: 3.46 (3H, s, OCH_3), 5.92 (1H, s, $PhC\underline{H}OCH_3$), 7.21—8.08 (12H, m, aromatic H).

ii) From (1′*S*,2*S*)-**12**: Red-Al (21 mmol, 10.5 ml of 2 M solution in toluene) was added dropwise to a stirred solution of (1′*S*,2*S*)-**12** (1.50 g, 3.52 mmol) in toluene (10 ml). The reaction mixture was refluxed for 9 h, then worked up as described for the reaction of (1*S*,1′*S*)-**11** to give a colorless oil (0.21 g, 24%). $[\alpha]_D^{28}$ +89.0° (c=0.41, benzene). This compound was identical with (*R*)-**13** prepared from (1*S*,1′*S*)-**11** on the basis of ^{1}H-NMR spectral comparison.

iii) From (*R*)-1-(α-Naphthyl)-1-phenylmethanol (**14**): NaH (2.5 mmol, 0.1 g of 60% NaH in liquid paraffin) was added to a stirred solution of (*R*)-**14** (73.4% e.e.)[11] (0.16 g, 0.68 mmol) in THF (6 ml), and CH_3I (0.5 ml) was added dropwise to the mixture. The reaction mixture was refluxed for 10 min, then worked up as described for the reaction of (1*S*,1′*S*)-**11**. The residue was subjected to column chromatography on silica gel with a solution of hexane–ether (25 : 1) to give a colorless oil (0.16 g, 93%). $[\alpha]_D^{22}$ +71.1° (c=1.45, benzene). This compound was identical with (*R*)-**13** on the basis of ^{1}H-NMR spectral comparison.

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References and Notes

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11) This compound showed $[\alpha]_D^{22}$ +43.7° (c=0.92, benzene) and the enantiomeric excess was estimated as 73.4% [lit.[10] $[\alpha]_D^{25}$ +59.5° (c=0.82, benzene)].