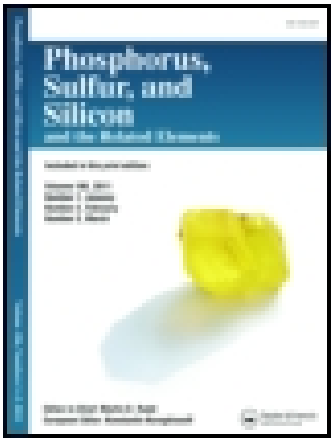

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ASYMMETRIC SYNTHESIS OF SULTAMS AND SULFONAMIDES VIA DIASTEREOSELECTIVE REDUCTION OF N-SULFONYLIMINES

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ASYMMETRIC SYNTHESIS OF SULTAMS AND SULFONAMIDES VIA DIASTEREOSELECTIVE REDUCTION OF N-SULFONYLIMINES

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Dedicated to Professor John G. Verkade on the occasion of his 60th birthday

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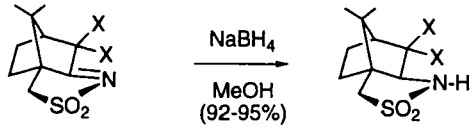
The diastereoselective reduction of both cyclic and acyclic camphor sulfonylimines was investigated. With cyclic camphor sulfonylimines **1**, reduction using $NaBH_4$ in methanol afforded the corresponding camphorsultams **2** in 92–95% yield as single diastereomers with the exception of **1c** where debromination occurred prior to reduction. For the large scale preparation of camphorsultam **1a** and its derivatives, important chiral auxiliaries in asymmetric synthesis, reduction with $NaBH_4$ is the reagent of choice. Reduction of acyclic camphor sulfonylimines **7** to camphorsulfonamides **8** with the bulky reducing reagent, $LiAl(OBu\text{-}i)_3H$ afforded the highest de's (>90% de) and yields 90–95%.

Key words: Asymmetric synthesis, diastereoselective reduction, chiral nonracemic sulfonamides, sultams, chiral auxiliaries.

In a project related to the development of new enantioselective electrophilic fluorinating reagents, we required access to large quantities of diastereopure camphorsultam auxiliaries **2b–d** (X = Cl, Br, OMe) and secondary sulfonamides **8**.[1] (−)-D-2,10-Camphorsultam (**2a**, X = H), widely known as Oppolzer's chiral auxiliary,[2] was previously prepared via the reduction of (−)-(camphorsulfonyl)imine (**1a**, X = H) with Raney nickel,[3] or lithium aluminum hydride (LAH).[4] Considering the potential for dehalogenation of imines **1b** and **1c** by these reducing reagents,[5] reduction of **1** with sodium boron hydride ($NaBH_4$) was explored.[6,7]



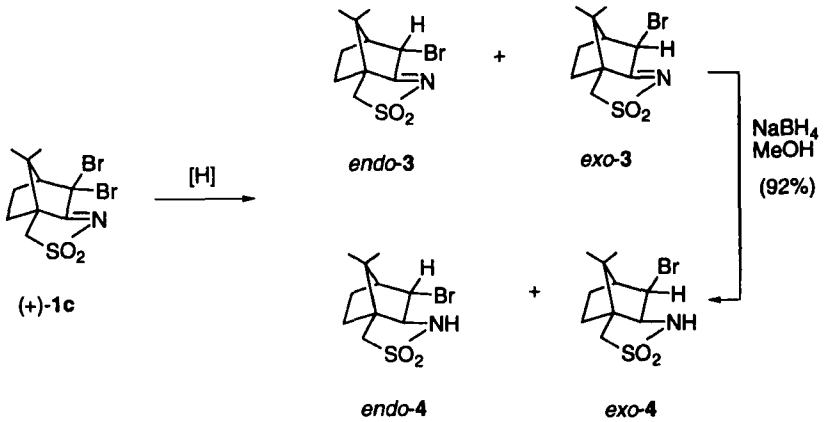
1 **2**

a) X = H, b) X = Cl, c) X = Br, d) X = MeO

Typically, sodium boron hydride was added portion-wise to a slurry of (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine (**1b**) in methanol at rt. As the reduction proceeded, imine **1b**, which was not very soluble in methanol, gradually dissolved and on com-

pletion (1–2 h) gave a clear solution. Following acidification the product was isolated by filtration affording (+)-3,3-dichloro-2,10-camphorsultam (**2b**) in 92% isolated yield. The expected *endo* reduction product **2b** was confirmed by an X-ray crystal structure of the corresponding N-fluoro derivative.[1] Dechlorination products were not detected. These conditions applied equally well to (+)-(camphorsulfonyl)imine (**1a**) and (+)-[(7,7-dimethoxycamphoryl)sulfonyl]imine (**1d**) giving sultams, **2a** and **2d** in 95 and 92% yield, respectively.

Similar reduction of (+)-[(7,7-dibromocamphoryl)sulfonyl]imine (**1c**), however, resulted in debromination, affording a mixture of monobromoimines **3** and monobromosultams **4** (Scheme I, Table I). The *exo*-**3**/*endo*-**3** mixture was readily separated from *exo*-**4**/*endo*-**4** by flash chromatography. The structures of **3** were assigned by comparison of their ^{1}H NMR spectra with reported values.[8] While attempts to separate the monobromosultams *exo*-**4**/*endo*-**4** by chromatography failed, crystallization from ethanol gave a ca. 35% of the *exo*-product. The *exo*/*endo* structures were as-



SCHEME I

TABLE I

Reduction of (+)-[(7,7-dibromocamphoryl)sulfonyl]imine (**1c**)

Entry	Conditions [H]/Solv./Temp.(°C)/Time (h)	% Yield[a] 3	4	Ratio[b]
1	$NaBH_4$/MeOH/rt/1.0h	0	93	0:0:50:50
2	$NaBH_4$/MeOH/-78°C/1.5h	7	85	4.5:4.5:41:45
3	$NaBH_4$/HOAc/0°C to rt/6.0h	no reaction		
4	$NaBH_3CN$/EtOAc/-78°C to rt/5.0h	60	29	32:33:18:17
5	BH_3/THF/-78°C to 65°C/4.5h	no reaction		
6	$LiAl(OBu^t)_3H$/THF/-78°C to rt/18h	55	36	30:30:20:20
7	H_2, Pd-C/EtOAc/rt/3.0h	19	71	11:12:44:43

[a]Isolated yield.

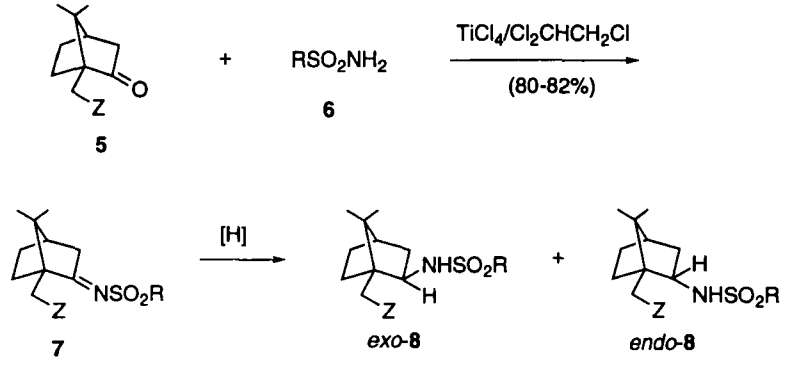
[b]Ratio of *exo*-**3**/*endo*-**3**/*exo*-**4**/*endo*-**4** as determined by ^{1}H NMR.

signed to **4** based on the reduction of *exo*-[(7-bromocamphoryl)sulfonyl]imine (**3**)[8] with $NaBH_4$/MeOH to give *exo*-**4** in 92% yield (Scheme I).

Several other reducing agents and reaction conditions were investigated in order to obtain the desired dibromocamphorsultam **2c** (Table I). No reduction was observed with sodium borohydride/acetic acid or borane-THF (Table I, entries 3 and 5) and debromination occurred with sodium cyanoborohydride, lithium tri-*tert*-butoxyaluminohydride and H_2/Pd (Table I, entries, 4, 6 and 7). The ratio of **3/4** was dependent on the reaction conditions. With $NaBH_4$, the major products were the monobromosultams **4** even at −78°C (Table I, entry 2). On the other hand sodium cyanoborohydride and lithium tri-*tert*-butoxyaluminohydride gave mostly **3**. These results suggested that debromination of **1c** is the first step in the reduction with the monobromoimine **3** being reduced to the monobromosultam **4**. We believe that the difference in behavior between **1b** and **1c** is due, in part, to the weaker C—Br bond vs. the C—Cl bond and the bulkier *endo*-bromine atom which inhibits reduction of the imine.

The reduction of camphor N-sulfonylimines **7**, prepared as previously described from 10-[(N,N-dialkylamino)sulfonyl]camphor **5** and methyl- and phenylsulfonamides **6**,[9] to the corresponding secondary sulfonamide **8** was also explored (Scheme II). However, reduction of **7a** with $NaBH_4$ in methanol at rt for 2 h gave **8** as a 64:36 *exo-endo*-mixture in 82% yield (Table II; entry 1). The *exo*/*endo*-ratio was determined by the integration of the C8/C9 camphor methyl absorption (*exo*: C8/C9 Me at δ 0.87/1.07 ppm, *endo*: C8/C9 Me at δ 0.95/0.98 ppm). These assignments were based on the assumption that the reducing reagent preferentially attacks the C—N double bond from the *endo*-direction. Similar observation has been made by Oppolzer *et al.* in the diastereoselective reduction of 10-[(N,N-dialkylamino)sulfonyl]-camphors **5**.[10]

Not surprisingly, when the reduction of **7** was carried out at a lower temperature the diastereoselectivity improved, although at the expense of the reaction time (Table II, compare entry 1 and 2). Use of the bulkier DIBAL reagent further increased the asymmetric induction (Table II, entry 3). The best results, however, were obtained with $LiAl(OBu\text{-}t)_3H$ affording *exo*-**8a** exclusively (Table II, entry 4). Similarly *exo*-



SCHEME II

TABLE II

Reduction of 10-[(N,N-dialkylamino)sulfonyl]camphors **7** to sulfonamide **8**

Entry	7	Z	R	Conditions [H]/Solv./Temp.(°C)/Time (h)	8 Yield(%)[a]	8 Ratio[b]
1	a	$SO_2N(c\text{-}C_6H_{11})_2$	Me	$NaBH_4$/MeOH/rt/2.0h	82	64:36
2	a			$NaBH_4$/MeOH/0°C/10h	80	73:27
3	a			DIBAL/THF/0°C/11h	79	80:20
4	a			LiAl(OBu-*i*)$_3$H/THF/0-25 °C/18h	92	>99:1
5	b	$SO_2N(c\text{-}C_6H_{11})_2$	Ph	LiAl(OBu-*i*)$_3$H/THF/0-25 °C/18h	90	>99:1
6	c	$SO_2N(i\text{-}Pr)_2$	Ph	LiAl(OBu-*i*)$_3$H/THF/0-25 °C/18h	95	>99:1

[a]Isolated yield.

[b]Ratio of *exo*-**8**/*endo*-**8** determined by ^1H NMR.

8b and *exo*-**8c** were obtained as single isomers in 90 and 95% yield, respectively (Table II, entries 5 and 6).

In summary useful methodology is reported for the asymmetric synthesis of camphorsultams and camphor sulfonamides, important chiral auxiliaries. From a preparative perspective, particularly on a large scale, $NaBH_4$/MeOH is preferable to LAH for the preparation of camphorsultams **2** because rigorously anhydrous conditions are not necessary and work-up is simpler. In addition, a highly diastereoselective preparation of camphor sulfonamides **8** from camphor imines **7** was developed.

EXPERIMENTAL

Details concerning the recording of spectra, the analytical instruments used, the determination of melting points, elemental analyses and the purification of solvents (freshly distilled) have been previously reported.[9] All reactions were performed under an argon/nitrogen atmosphere. (+)-/(−)-Camphorsulfonyl)imines (**1a**), (+)-/(−)-[(7,7-dichlorocamphoryl)sulfonyl]imines (**1b**) and (+)-/(−)-[(7,7-dimethoxycamphoryl)sulfonyl]imines (**1d**) were prepared according to literature procedures.[11]

(+)-[(7,7-Dibromocamphoryl)sulfonyl]imine (**1c**) was prepared via a modification of an earlier procedure using 1,3-dibromo-5,5-dimethylhydantoin.[8] The product **1c** was purified by crystallization from ethanol yield (90%), mp 194–196°C, $[\alpha]_D^{20}$ +4.7 (c 1.0, $CHCl_3$), [lit.[8] mp 195–196°C, $[\alpha]_D^{20}$ +4.7 (c 1.0, $CHCl_3$)]; the spectroscopic data were identical to those reported previously.[8]

10-[(N,N-Dialkylamino)sulfonyl]camphor N-(Alkylsulfonyl)imines **8** were prepared from the corresponding sulfonamides, 10-[(N,N-dialkylamino)sulfonyl]camphors **7**, titanium tetrachloride as previously described.[9]

(−)-10-[(N,N-Dicyclohexylamino)sulfonyl]camphor N-(Methylsulfonyl)imine (**7a**): yield 81%; mp 154–156°C; $[\alpha]_D^{20}$ −6.6° (c 0.8, $CHCl_3$); IR (KBr, cm^{-1}); 2940.3, 1640.2, 1451.6, 1311.9, 1142.1, 1045; ^1H NMR ($CDCl_3$) δ 3.38 (d, J = 14.3 Hz, 1H), 3.30 (m, 2H), 3.31 (s, 3H), 2.99 (m, 1H), 2.87 (d, J = 14.3 Hz, 1H), 2.57 (m, 2H), 1.00–2.10 (m, 24H), 1.14 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 197.7, 57.9, 57.4, 52.6, 48.9, 43.7, 41.8, 39.2, 32.6, 32.5, 27.1, 26.3, 25.0, 19.6, 19.4. Anal. Calcd. for $C_{23}H_{40}N_2O_4S_2$: C, 58.44; H, 8.52. Found: C, 58.44; H, 8.32.

(+)-10-[(N,N-Dicyclohexylamino)sulfonyl]camphor N-(Phenylsulfonyl)imine (**7b**): yield 80%; mp 185–187°C; $[\alpha]_D^{20}$ +0.78° (c 1.0, $CHCl_3$); IR (KBr, cm^{-1}); 2920.4, 1627.1, 1448.1, 1321.4, 1155.6, 1089.7; ^1H NMR ($CDCl_3$) δ 8.01–8.02 (m, 2H), 7.27–7.99 (m, 3H), 3.37 (d, J = 14.3 Hz, 1H), 3.04–3.25 (m, 3H), 2.80 (d, J = 14.3 Hz, 1H), 2.55–2.70 (m, 2H), 1.95–2.10 (m, 2H), 1.00–1.75 (m, 22H), 1.15 (s, 3H), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 198.5, 140.6, 132.8, 128.8, 127.0, 57.5, 52.6, 49.1, 43.9, 39.7, 32.8, 32.5, 27.4, 26.5, 26.3, 25.1, 19.8, 19.6. Anal. Calcd. for $C_{28}H_{42}N_2O_4S_2$: C, 62.89; H, 7.91. Found: C, 62.53; H, 8.15.

(−)-10-[(N,N-Diisopropylamino)sulfonyl]camphor N-(Phenylsulfonyl)imine (**7c**): yield 82%; mp 109–110°C; $[\alpha]_D^{20}$ −9.8° (c 1.1, $CHCl_3$); IR (KBr, cm^{-1}); 2973.2, 1645.8, 1445.6, 1329.4, 1302.1, 1150.4, 1092.1; ^1H NMR ($CDCl_3$) δ 7.92–7.96 (m, 2H), 7.43–7.58 (m, 3H), 3.52–3.63 (m, 2H), 3.28 (d, *J* = 14.3 Hz, 1H), 3.01–3.10 (m, 1H), 2.81 (d, *J* = 14.3 Hz, 1H), 2.49–2.62 (m, 2H), 1.89–2.07 (m, 2H), 1.68–1.71 (m, 1H), 1.18–1.39 (m, 1H), 1.13 (d, *J* = 6.8 Hz, 12H), 1.08 (s, 3H), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 197.8, 140.5, 132.7, 128.5, 126.9, 58.2, 52.0, 48.9, 48.0, 43.9, 39.5, 27.3, 26.2, 22.1, 21.9, 19.6, 19.3. Anal. Calcd. for $C_{22}H_{34}N_2O_4S_2$: C, 58.12; H, 7.54. Found: C, 58.28; H, 7.23.

Preparation of Camphorsultams **2a**, **2b** *and* **2d**

General procedure: In a 250 mL oven dried one-necked round bottomed flask fitted with a magnetic stirring bar were placed the appropriate (camphorylsulfonyl)imine **1** (20 mmol) in 100 mL of dry MeOH. The reaction flask was cooled to 0°C and 1.9 g (50 mmol, 2.5 equivalents based on the camphorsulfonylimine) of anhydrous $NaBH_4$ was added in small portions over 10 minutes. After addition the reaction mixture was warmed to rt, stirred for 1–2 h and quenched with 10% of HCl. The MeOH solvent was removed on a rotary evaporator and the residue was diluted with 50 mL of water. The mixture was brought to pH 3 with 10% HCl and the white precipitated collected, air dried and crystallized from $CHCl_3$/*n*-hexane.

(−)-2,10-Camphorsultam (**2a**): yield 95%; mp 182–184°C, $[\alpha]_D^{20}$ −31.5° (c 1.0, $CHCl_3$); {lit.[4] mp 183–184°C, $[\alpha]_D^{20}$ −31.8° (c 2.3, $CHCl_3$)}, its spectral properties are identical to those reported previously.[4]

(+)-2,10-Camphorsultam (**2a**): yield 95%; mp 182–184°C, $[\alpha]_D^{20}$ +31.5° (c 1.0, $CHCl_3$); its spectral properties are identical to (−)-**2a**.

(+)-3,3-Dichloro-2,10-camphorsultam (**2b**): yield 92%; mp 200°C, $[\alpha]_D^{20}$ +20.2° (c 2.6, $CHCl_3$); IR (KBr) cm^{-1} 3257.4, 2967.6, 1312.2, 1147.7, 1091.0; ^1H NMR ($CDCl_3$) δ 1.06 (s, 3H), 1.47 (s, 3H), 1.60–1.66 (m, 1H), 1.88–2.12 (m, 2H), 2.38–2.41 (m, 1H), 2.56 (d, *J* = 4.6 Hz, 1H), 3.23 (s, 2H), 3.96 (d, *J* = 5.3 Hz, 1H), 4.90 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 93.4, 77.1, 61.5, 55.8, 50.3, 49.7, 30.2, 25.6, 23.2, 22.9; Anal. Calcd. for $C_{10}H_{15}Cl_2NO_2S$: C, 42.26; H, 5.32; N, 4.93. Found: C, 42.01; H, 5.26; N, 4.78.

(−)-3,3-Dichloro-2,10-camphorsultam (**2b**): yield 93%; mp 200–201°C, $[\alpha]_D^{20}$ −20.4° (c 1.0, $CHCl_3$); its spectral properties were identical to (+)-**2b**.

(+)-3,3-Dimethoxy-2,10-camphorsultam (**2d**): yield 92%; mp 119–120°C, $[\alpha]_D^{20}$ +38.0° (c 2.0, $CHCl_3$); IR (KBr) cm^{-1} 3350.3, 2967.7, 1325.5, 1137.3, 1080.2; ^1H NMR ($CDCl_3$) δ 0.92 (s, 3H), 1.27 (s, 3H), 1.45–1.55 (m, 1H), 1.70–2.00 (m, 3H), 2.21 (d, *J* = 4.7 Hz, 1H), 3.10 (s, 2H), 3.22 (d, *J* = 10.2 Hz, 1H), 3.23 (s, 3H), 3.27 (s, 3H), 4.58 (d, *J* = 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 107.5, 69.2, 57.1, 50.0, 49.8, 49.4, 48.1, 47.1, 30.8, 22.1, 20.6, 20.2; Anal. Calcd. for $C_{12}H_{21}NO_4S$: C, 52.34; H, 7.69; N, 5.09. Found: C, 52.03; H, 7.88; N, 5.30.

(−)-3,3-Dimethoxy-2,10-camphorsultam (**2d**): yield 91%; mp 118.5–120°C, $[\alpha]_D^{20}$ −37.6°; its spectral properties are identical to (+)-**2d**.

Reduction of [(7,7-dibromocamphoryl)sulfonyl]imine (**1c**)

Typical procedure: In a 250 mL oven dried one-necked round bottomed flask fitted with a magnetic stirring bar were placed 7.4 g (20 mmol) of **1c** in 100 mL of dry MeOH. The reaction flask was cooled to 0°C and 1.9 g (50 mmol, 2.5 equivalents based on **1c**) of anhydrous $NaBH_4$ was added in small portions over 10 min. After the addition was complete the reaction mixture was warmed to rt, stirred for 1 h and quenched with 10% of HCl. The solvent was removed on a rotary evaporator, the residue was diluted with 50 mL of water and the mixture brought to pH 3 with 10% of HCl. The crude product was collected by filtration, air dried and crystallized from $CHCl_3$/*n*-hexane to give 5.4 g (93%) of *endo*-/*exo*-**4** (ratio 50:50 based on ^1H NMR). Crystallized from absolute EtOH afforded 2.1 g (35%) of (−)-3-*exo*-monobromo-2,10-camphorsultam (**4**): mp 200°C dec., $[\alpha]_D^{20}$ −55.9° (c 1.1, $CHCl_3$); IR (KBr) cm^{-1} 3254.5, 2958.0, 1345.5, 1306.8, 1139.2, 1118.2, 1071.7; ^1H NMR ($CDCl_3$) δ 0.94 (s, 3H), 1.24–1.52 (m, 1H), 1.44 (s, 3H), 1.84–2.29 (m, 3H), 3.25 (s, 2H), 3.63 (t, *J* = 7.6 Hz, 1H), 3.34 (d, *J* = 7.9 Hz, 1H), 4.46 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 65.9, 56.3, 52.4, 51.5, 51.3, 48.6, 30.3, 28.3, 21.9, 21.8; Anal. Calcd. for $C_{10}H_{16}BrNO_2S$: C, 40.83; H, 5.48; Found: C, 41.06; H, 5.31.

Reduction of exo-(−)-[(7-bromocamphoryl)sulfonyl]imine (**3**) *with* $NaBH_4$

In a 25 mL dried one necked round bottomed flask fitted with a magnetic stirring bar were placed 0.073 g (0.25 mmol) of *exo*-**3**[8] in 1 mL of dry MeOH. The reaction mixture was cooled to 0°C and 0.019 g (0.5 mmol, 2.0 equivalents based on *exo*-**3**) of anhydrous $NaBH_4$ was added in one portion. The reaction mixture was stirred for 1 h, quenched with 10% of HCl and the solvent removed on a rotary evaporator. The residue was

extracted with EtOAc (2 × 25 mL), combined, washed with 10 mL of brine, and dried ($MgSO_4$). Removal of the solvent gave 0.070 g (95%) of *exo*-(−)-**4**; mp 200°C dec., $[\alpha]_D^{20}$ −55.9° (c 1.1, $CHCl_3$); its physical and spectroscopic properties were identical to **1c** prepared earlier.

Preparation of (1R)-exo-(−)-N,N-Dicyclohexyl-2-(N-methanesulfonyl)amino-7,7-dimethyl-bicyclo[2,2,1]heptane-1-methanesulfonamide (**8a**)

Typical procedure: In a 100 mL oven dried one-necked round bottomed flask fitted with a magnetic stirring bar were placed sulfonylimine **7a** (3.15 g, 6.7 mmol) and anhydrous lithium tri-*tert*-butoxyaluminohydride [LiAl(OBu-*t*)$_3$H] (2.2 g, 13.4 mmol, 2.0 equivalents based on **7a**). The reaction flask was cooled to 0°C and 20 mL of freshly distilled THF was added. The reaction mixture was warmed to rt, stirred for 8 h, quenched with 20 mL of H_2O at 0°C and diluted with 20 mL of ethyl acetate. The solution was brought to pH 3 with 10% HCl and the aqueous layer was extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were washed with 20 mL of H_2O, 20 mL brine, dried ($MgSO_4$). Concentration gave a white solid which was crystallized from $CHCl_3$/*n*-pentane to give 2.9 g (92%) of *exo*-(−)-**8a**; mp 163–164°C; $[\alpha]_D^{20}$ −44.2° (c 0.7, $CHCl_3$); IR (KBr, cm^{-1}); 3264.9, 2936.0, 1457.1, 1318.7, 1164.9, 1134.8, 1049.2; ^1H NMR ($CDCl_3$) δ 5.20, (d, J = 4.5 Hz, 1H), 3.55–3.59 (m, 1H), 3.21–3.31 (m, 2H), 3.14 (d, J = 14.0 Hz, 1H), 3.01 (s, 3H), 2.75 (d, J = 14.0 Hz, 1H), 2.27–2.34 (m, 1H), 1.13–1.93 (m, 26H), 1.07 (s, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 59.5, 57.8, 55.0, 49.4, 44.7, 38.9, 38.2, 33.6, 33.0, 32.5, 27.1, 26.4, 25.1, 20.6, 20.4. Anal. Calcd. for $C_{23}H_{42}N_2O_4S_2$: C, 58.19; H, 8.92. Found: C, 58.38; H, 8.76.

(1R)-exo-(−)-N,N-dicyclohexyl-2-(N-benzenesulfonyl)amino-7,7-dimethyl-bicyclo[2,2,1]heptane-1-methanesulfonamide (**8b**): yield 90%; mp 75–77°C; $[\alpha]_D^{20}$ −21.0° (c 0.7, $CHCl_3$); IR (KBr, cm^{-1}); 3258.8, 2934.0, 1448.2, 1320.2, 1166.4, 1138.2, 1048.0; ^1H NMR ($CDCl_3$) δ 7.86–7.89 (m, 2H), 7.26–7.57 (m, 3H), 5.90 (d, J = 2.9 Hz, 1H), 3.23–3.45 (m, 2H), 3.20 (d, J = 14.0 Hz, 1H), 2.99–3.05 (m, 1H), 2.72 (d, J = 14.0 Hz, 1H), 2.48–2.55 (m, 1H), 1.00–1.80 (m, 26H), 1.12 (s, 3H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.5, 132.6, 128.9, 127.6, 59.4, 57.8, 55.1, 50.8, 49.4, 44.6, 34.4, 33.1, 32.9, 32.5, 27.0, 26.3, 25.0, 20.6, 20.0. Anal. Calcd. for $C_{28}H_{44}N_2O_4S_2$: C, 62.65; H, 8.26. Found: C, 62.38; H, 8.45.

(1R)-exo-(−)-N,N-diisopropyl-2-(N-benzenesulfonyl)amino-7,7-dimethyl-bicyclo[2,2,1]heptane-1-methanesulfonamide (**8c**): yield 95%; mp 118–119°C; $[\alpha]_D^{20}$ −44.7° (c 2.0, $CHCl_3$); IR (KBr, cm^{-1}); 3233.7, 2946.1, 1446.6, 1321.6, 1156.8, 1127.9; ^1H NMR ($CDCl_3$) δ 7.85–7.89 (m, 2H), 7.27–7.60 (m, 3H), 5.95 (d, J = 2.7 Hz, 1H), 3.72–3.82 (m, 2H), 3.20 (d, J = 13.9 Hz, 1H), 2.98–3.01 (m, 1H), 2.72 (d, J = 13.9 Hz, 1H), 2.53–2.60 (m, 1H), 1.41–1.76 (m, 4H), 1.34 (m, 12H), 1.22–1.28 (m, 1H), 1.13 (s, 3H), 1.07–1.09 (m, 1H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.4, 132.6, 128.9, 127.5, 59.4, 54.0, 49.4, 48.5, 44.6, 34.2, 33.1, 27.0, 22.5, 21.9, 20.5, 19.9. Anal. Calcd. for $C_{22}H_{36}N_2O_4S_2$: C, 57.86; H, 7.95. Found: C, 57.91; H, 7.47.

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