Asymmetric Syntheses of Optically Active α,β-Disubstituted β-Amino Acids

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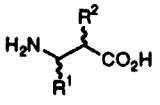
β-Amino acids 1 are potentially valuable for preparations of peptidomimetics,[1] functionalized β-lactams, and some naturally occurring materials.[2-4] These disubstituted amino acids are not easily prepared in stereochemically pure form, however. The most accessible members of this series of compounds are aspartic acid ($R^1 = CO_2H$, $R^2 = H$) derivatives obtained via enolate formation and alkylation at the β-carbon, reactions which can be made to be highly diastereoselective by judicious choice of *N*-protecting functionalities.[5-8] Compounds 1 not derived from aspartic acid are more difficult to make. For instance, one recently published procedure involves incorporating an optically active α-unsubstituted β-amino acid in a heterocyclic system (specifically, a perhydropyrimidinone), enolate formation, alkylation, and then vigorous hydrolysis.[9] This method has several limitations, not least of which being the availability of the starting material. Described here are syntheses of disubstituted systems 1 with high absolute and relative stereochemical purity, from naturally occurring α-amino acids. Some limitations of the methodology are also described.



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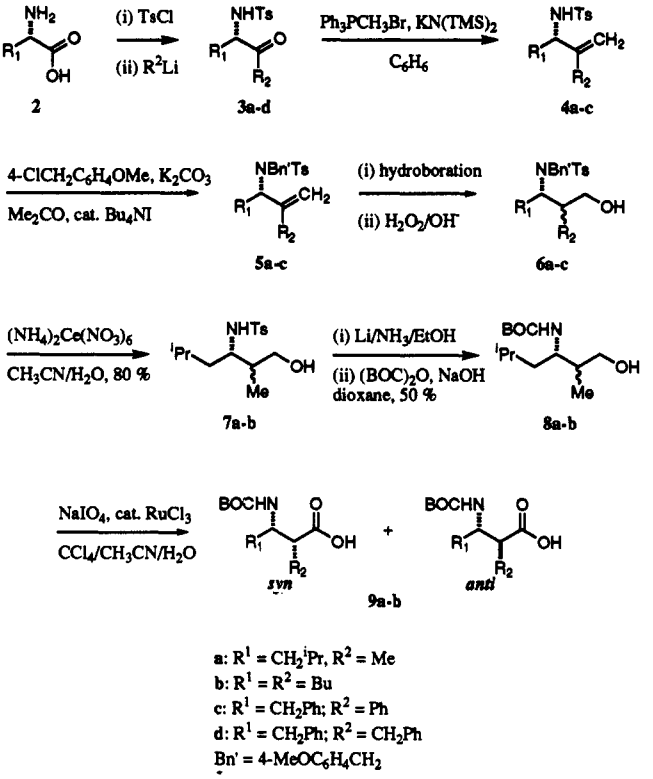
Scheme I outlines the route followed for the preparations of the BOC-protected target compounds. Leucine, norleucine, and phenylalanine (amino acids 2; $R^1 = CH_2{}^iPr$, n-Bu, and CH_2Ph) were *N*-tosylated and converted to the ketones **3a–c**[10-13] and then to the corresponding alkenes. The Wittig reaction in benzene is an improvement over the titanium-mediated methylenation[14-18] we previously used to form compound **4a** and related derivatives.[19] However, neither of these methods was suitable for the highly enolizable benzylic ketone **3d**. At this stage the optical purity of allylamines **4a–c** was measured via Eu(hfc)$_3$/^{1}H NMR; no racemization was detected for compounds **4a** and **4c**, and the norleucine derivative **4b** had an enantiomeric excess of 94%. Allylic amines **4a-c** then were converted to the *N*-(4-methoxybenzyl) derivatives **5a-c**, thus allowing oxidative deprotection later in the synthesis.

Hydroboration/oxidation of allylic amines **5a-c** is the key step in the syntheses described in this paper. We had previously reported that similar hydroborations were *anti*-selective if BH_3 was the hydroborating agent and *syn*-selective if 9-BBN or catecholborane/rhodium catalysis were used, and that use of two *N*-protecting groups increased the magnitude of the stereoselection in either

Scheme I. General Route to Syntheses of Compounds 9



2 3a-d 4a-c 5a-c 6a-c 7a-b 8a-b 9a-b

a: $R^1 = CH_2{}^iPr$, $R^2 = Me$
b: $R^1 = R^2 = Bu$
c: $R^1 = CH_2Ph$; $R^2 = Ph$
d: $R^1 = CH_2Ph$; $R^2 = CH_2Ph$
Bn' = 4-MeOC$_6$H$_4$CH$_2$

Table I. Diastereoselectivities for Hydroboration/Oxidation of Allylamine Derivatives 5a–c

entry	substrate	R^1	R^2	conditions[a]	*syn*/*anti*[b]	isolated yield of major isomer (%)
1	**5a**	$CH_2{}^iPr$	Me	BH_3	1.0:>20	60
2	**5a**	$CH_2{}^iPr$	Me	9-BBN	>20:1.0	85
3	**5b**	*n*-Bu	*n*-Bu	BH_3	1.0:16	77
4	**5b**	*n*-Bu	*n*-Bu	9-BBN	1.3:1.0	54 (86)[c]
5	**5c**	CH_2Ph	Ph	BH_3	1:>20	80
6	**5c**	CH_2Ph	Ph	9-BBN	*d*	0

[a] See Experimental Section for details. [b] The sense and magnitude of these diastereoselectivities were accessed via ^{1}H NMR, as described previously.[19] [c] Significant amount of starting material recovered; the yield in parentheses is that based on conversion. [d] No reaction.

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sense.[19] Diastereoselectivities observed for substrates **5a-c** are given in Table I.

The methyl-substituted alkene **5a** gave excellent and opposite selectivities with BH_3 and 9-BBN (Table I, entries 1 and 2). High diastereoselectivity was also observed for the *anti*-selective hydroboration of the dibutyl-substituted system **5b**. However, hydroboration of the same substrate by 9-BBN was incomplete even after 22 h at 25 °C and gave poor diastereoselectivity. This result perhaps reflects excessive steric hindrance about the alkene even though the only difference between the 2-substituent of substrates **5a** and **5b** is that between Me and *n*-Bu. Consistent with this, no reaction at all was observed for the phenyl-substituted compound in the presence of 9-BBN, even after long reaction times. Catalyzed hydroborations of compounds **5b** and **5c** {2 mol %, $RhCl(PPh_3)_3$, $HBO_2C_6H_4$, THF, 25 °C, 24 h} also failed to give any product. Consequently it appears that the stereoselectivities observed in the hydroboration of **5a** using 9-BBN (entry 2) is a fortunate consequence of selective steric retardation of reaction via one of the alternative transition states, but the balance between this effect and overall suppression of the reaction is a delicate one (entries 4 and 6).

The 4-methoxybenzyl substituent was removed under oxidative conditions to give the *N*-tosyl alcohols **7**. As far as we are aware there is no precedent for oxidative removal of 4-methoxybenzyl protecting groups from *N*-tosylamines. Reductive cleavage of the *N*-tosyl group with lithium in ammonia gave free amines which were not isolated, but were directly converted to BOC-protected systems **8a,b** instead. Curiously, CAN did not remove the 4-methoxybenzyl substituent from the phenyl-substituted derivative **7c**. Probe experiments indicated that this group could be cleaved from **7c** using HBr in acetic acid, but not in good yield. Ruthenium-mediated oxidation of alcohols[20] **7** gave the target acids **8a,b** in a protected form suitable for peptide syntheses. No epimerization was detected during the oxidation process (^1H NMR). In pilot experiments alcohols **7** also were oxidized to the corresponding acids before reductive cleavage of the *N*-tosyl group; however, the yields obtained via the route shown in Scheme I were superior.

In conclusion, this route to α,β-disubstituted amino acids can give products with high relative and absolute stereoselectivity. The key hydroboration step is extremely sensitive to steric effects; hydroboration of allylic amines **5** is highly stereoselective for some substrates whereas marginally more hindered systems do not react under the same conditions. Reductive removal of *N*-tosyl group masking functionalities may be unsuitable for some R^1 and R^2 substituents, but acid-labile sulfonamides like (2,2,5,7,8-pentamethylchromanyl)-6-sulfonyl (Pmc)[21,22] and (4-methoxy-2,3,6-trimethylphenyl)sulfonyl (Mtr)[23] presumably could be used in place of tosyl. Recognizing this, there is considerable scope for tailoring the route outlined in Scheme I to fit α,β-disubstituted amino acids other than the ones described here.

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Experimental Section

General Procedures. High-field NMR spectra were recorded on a Bruker AF300 (^1H at 300 MHz, ^{13}C at 75.4 MHz) or a Bruker AC250 (^1H at 250 MHz, ^{13}C at 62.9 MHz) in $CDCl_3$ unless otherwise indicated. ^1H chemical shifts are reported in δ (ppm) relative to $CHCl_3$ (7.25 ppm) as internal standard, and ^{13}C chemical shifts are reported in δ (ppm) relative to $CHCl_3$ (77.0 ppm) unless specified otherwise. Multiplicities in ^1H NMR are reported as (s) singlet, (d) doublet, (t) triplet, (q) quartet, and (m) multiplet. The carbon multiplicities are listed as (C) quaternary, (CH) methine, (CH_2) methylene, and (CH_3) methyl assigned via DEPT sequence experiments. Thin-layer chromatography was performed on silica gel 60 F_{254} plates from Whatman. 1,2-Dimethoxyethane and THF were distilled immediately before use from sodium benzophenone ketyl. We estimate that optical purities accessed using $Eu(hfc)_3$ are accurate to within ±2%.

(3*S*)-5-Methyl-3-(*N*-tosylamino)-2-hexanone (3a). An aliquot of *N,N,N,N*-tetramethylethylenediamine (TMEDA, 2.52 g, 21.7 mmol) was added to *N*-tosyl-L-leucine (2 g, 7.01 mmol) in 30 mL of THF and cooled to −78 °C. To this well-stirred mixture was added methyllithium (15.5 mL, 21.7 mmol) over 15 min. The mixture was stirred at −78 °C for 1 h and then allowed to warm to 25 °C and stirred for an additional 2 h. The reaction mixture was cooled and poured into ice-cold 2 M H_3PO_4 (200 mL) and extracted with EtOAc (3 × 50 mL). The EtOAc layer was washed with 3 × 50 mL of saturated $NaHCO_3$ solution followed by 2 × 50 mL of saturated brine. The EtOAc layer was dried (Na_2SO_4) and the solvent evaporated to yield 1.80 g of the crude product. Purification via flash chromatography over silica gel column eluting with hexane/EtOAc (2:1) gave 1.05 g (53%) of the product: mp 68-69 °C; R_f 0.3 (20% EtOAc/hexane); ^1H NMR δ 0.87 (m, 6H), 1.37 (m, 2H), 1.79 (m, 1H), 1.98 (s, 3H), 2.39 (s, 3H), 3.67 (m, 1H), 5.29 (d, J = 8.4 Hz, 1H), 7.27 (d, J = 8.7 Hz, 2H), 7.69 (d, J = 8.7 Hz, 2H); ^{13}C NMR δ 21.2 (CH/CH_3), 21.4 (CH/CH_3), 23.1 (CH/CH_3), 24.3 (CH/CH_3), 26.6 (CH/CH_3), 41.0 (CH_2), 60.5 (CH/CH_3), 127.2 (CH), 129.6 (CH), 136.7 (C), 143.6 (C), 206.3 (C); IR ($CHBr_3$) 3318 (md), 1602 (md), 1714 (st), 1335 (st) cm^{-1}; MS (EI) m/e 240 (32), 155 (36), 91 (100); $[\alpha]^{26}_D$ +77.7° (c = 1.54, $CHCl_3$). Anal. Calcd for $C_{14}H_{21}NO_3S$: C, 59.17; H, 7.24; N, 4.69. Found: C, 59.34; H, 7.47; N, 4.94.

(6*S*)-6-(*N*-Tosylamino)-5-decanone (3b). To a solution of *N*-tosyl-L-norleucine (3.5 g, 12.9 mmol) in 40 mL of dry THF at −78 °C was added 20 mL of butyllithium (2.1 M in hexane) slowly over a period of 20 min, and the reaction mixture was stirred at that temperature for 1.5 h and then for an additional 1 h at 25 °C. The reaction mixture was poured into ice-cold 1 M HCl (250 mL) and extracted with 3 × 75 mL of EtOAc. The EtOAc layers were combined and washed with 3 × 50 mL of saturated $NaHCO_3$ solution followed by brine (2 × 50 mL). The EtOAc layer was dried and the solvent evaporated to give an oil which was purified by flash chromatography using hexane/EtOAc (5:1) as the eluant. The yield of the product was 1.93 g (48%): R_f 0.58 (hexane/EtOAc (4:1)); ^1H NMR δ 0.78 (t, J = 7 Hz, 3H), 0.83 (t, J = 6.8 Hz, 3H), 1.07 (m, 1H), 1.3 (m, 8H), 1.72 (m, 1H), 2.16 (m, 1H), 2.29 (m, 1H), 2.38 (s, 3H), 3.84 (dd, J = 7.3, 4.2 Hz, 1H), 5.49 (d, J = 7.7 Hz, 1H), 7.27 (m, 2H), 7.68 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 13.6 (CH/CH_3), 13.7 (CH/CH_3), 21.4 (CH/CH_3), 21.9 (CH_2), 22.2 (CH_2), 25.4 (CH_2), 26.6 (CH_2), 32.0 (CH_2), 39.1 (CH_2), 61.2 (CH/CH_3), 127.2 (CH), 129.5 (CH), 136.7 (C), 143.5 (C), 208.0 (C); IR ($CHBr_3$) 3316 (st), 2950 (st), 1715 (st), 1596 (st) cm^{-1}; MS (EI, 70 eV) m/e 326 (0.08 (MH^+)), 240 (72), 155 (42), 91 (100); $[\alpha]^{26}_D$ +88.6° (c = 1.615, $CHCl_3$). Anal. Calcd for $C_{17}H_{27}NO_3S$: C, 62.68; H, 8.3; N, 4.3. Found: C, 62.26; H, 8.35; N, 4.15.

(2*S*)-1,3-Diphenyl-2-(*N*-tosylamino)-1-propanone (3c). To a stirred solution of 3.03 g of *N*-tosyl-L-phenylalanine in 40 mL of THF at −40 °C was added slowly 20 mL of 2.0 M of PhLi in cyclohexane/ether. The dark brown solution was stirred at 25 °C for 4 h and then quenched with 40 mL of 20% HCl at 0 °C. The resulting mixture was extracted with EtOAc several times, washed with saturated brine, dried, concentrated to dryness, and purified via flash chromatography (silica gel, 20% EtOAc in hexanes). After the viscous liquid had solidified, the product was recrystallized from EtOAc/hexanes to afford 2.26 g (63%) of the pale yellow solid: mp 101–102 °C; TLC R_f 0.425 (33% EtOAc in hexanes); IR (neat) 1684, 1559, 1456, 1339, 1157, 1092

cm^{-1}; ^{1}H NMR δ 7.71 (d, J = 7.2 Hz, 2 H), 7.65–7.50 (m, 3 H), 7.50–7.35 (m, 2 H), 7.25–7.15 (m, 3 H), 7.09 (d, J = 7.4 Hz, 2 H), 7.05–6.90 (m, 2 H), 5.56 (d, J = 8.8 Hz, 1 H), 5.20–5.05 (m, 1 H), 3.14 (dd, J = 5.7, 13.9 Hz, 1 H), 2.96 (dd, J = 5.9, 13.8 Hz, 1 H), 2.29 (s, 3 H); ^{13}C NMR δ 197.3 (C), 143.4 (C), 136.9 (C), 134.9 (C), 134.2 (C), 133.9 (CH), 129.62 (CH), 129.58 (CH), 128.8 (CH), 128.4 (CH), 127.1 (CH), 58.2 (CH), 40.2 (CH_2), 21.4 (CH_3); $[\alpha]_D$ +90.40° (c = 0.25, $CHCl_3$). Anal. Calcd for $C_{22}H_{21}NO_3S$: C, 69.63; H, 5.58; N, 3.69. Found: C, 69.45; H, 5.59; N, 3.59.

(2*S*)-1,4-Diphenyl-2-(*N*-tosylamino)-3-butanone (3d). To a stirred solution of 6.2 mL of TMEDA in 45 mL of toluene at 0 °C was added 19 mL of 2.1 M of *n*-BuLi in hexane. After stirring at 25 °C for 40 min, the solution was cooled in a ice bath and then 3.03 g of *N*-tosyl amino acid **2** (R^1 = CH_2Ph, 9.51 mmol) in 15 mL of THF was added slowly. The mixture was stirred overnight and then quenched with 10% HCl at 0 °C. The organic layer was extracted with EtOAc several times, washed with saturated brine, dried, and concentrated to dryness. The crude product was purified via flash chromatography (20% EtOAc in hexanes) and then recrystallized from EtOAc/hexanes. The mother liquor was purified again in silica gel to furnish a yellow viscous liquid 2.37 g (78%): mp 94–95 °C; TLC R_f 0.37 (33% EtOAc in hexanes); ^{1}H NMR δ 7.51 (d, J = 8.3 Hz, 2 H), 7.30–7.20 (m, 6 H), 7.17 (d, J = 8.1 Hz, 2 H), 7.10–6.90 (m, 2 H), 6.90–6.80 (m, 2 H), 5.25 (d, J = 8.0 Hz, 1 H), 4.19 (m, 1 H), 3.53 (s, 2 H), 2.96 (dd, J = 6.5, 14.0 Hz, 1 H), 2.91 (dd, J = 6.6, 14.0 Hz, 1 H), 2.40 (s, 3 H); ^{13}C NMR δ 205.5 (C), 143.5 (C), 136.4 (C), 135.0 (C), 132.5 (C), 129.7 (CH), 129.5 (CH), 129.3 (CH), 128.8 (CH), 128.6 (CH), 127.3 (CH), 127.2 (CH), 127.0 (CH), 61.3 (CH), 47.5 (CH_2), 38.8 (CH_2), 21.5 (CH_3); $[\alpha]_D$ +70.00° (c = 0.2, $CHCl_3$). Anal. Calcd for $C_{23}H_{23}NO_3S$: C, 70.20; H, 5.89; N, 3.56. Found: C, 70.27; H, 5.98; N, 3.51.

(3*S*)-2,5-Dimethyl-3-(*N*-tosylamino)-1-hexene (4a). A solution of potassium bis(trimethylsilyl)amide (7.40 g, 37.1 mmol, 3 equiv) and methyltriphenylphosphonium bromide (13.25 g, 37.1 mmol, 3 equiv) in 100 mL of benzene was cooled to 0 °C under nitrogen and to this ice cold solution was added **3a** (3.5 g, 12.36 mmol, 1 equiv) slowly over 15 min. The reaction mixture was allowed to warm to 25 °C over 30 min and then refluxed for 4 h. The reaction mixture was cooled and diluted with 250 mL of ether and washed three times with 50 mL of water. The ether layer was dried over anhydrous magnesium sulfate and the solvent evaporated to leave an oil which was purified by flash chromatography eluting with hexane/EtOAc (12:1 followed by 4:1) to yield 3.12 g (90%) of the product: mp 96–97 °C; R_f 0.13 (hexane/EtOAc (6:1)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.8 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.6 Hz, 3H), 1.29 (dd, J = 7.2 Hz, 2H), 1.52 (m, 1H), 1.56 (s, 3H), 2.4 (s, 3H), 3.6 (dd, J = 7.4 Hz, 1H), 4.38 (J = 7.2 Hz, 1H), 4.66 (s, 1H), 4.72 (s, 1H), 7.26 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.1 Hz, 2H); ^{13}C NMR δ 17.0 (CH/CH_3), 21.4 (CH/CH_3), 22.2 (CH/CH_3), 24.4 (CH/CH_3), 43.2 (CH_2), 57.9 (CH/CH_3), 113.2 (CH_2), 127.2 (CH), 129.2 (CH), 137.9 (C), 143.0 (C), 143.5 (C); IR ($CHBr_3$) 3300 (md), 1644 (wk) cm^{-1}; MS (EI) m/e 281 (0.2 (M^+)), 224 (48), 155 (40), 91 (100); $[\alpha]^{26}_D$ +26.8° (c = 1.155, $CHCl_3$). Anal. Calcd for $C_{15}H_{23}NO_2S$: C, 63.91; H, 8.04; N, 4.59. Found: C, 64.02; H, 8.24; N, 4.97.

(3*S*)-3-(*N*-Tosylamino)-2-*n*-butylhept-1-ene (4b). The procedure used was analogous to the one described for **4a**; **3b** was converted to **4b** to yield 1.24 g (56%) after purification by flash chromatography eluting with hexane/EtOAc (7:1): R_f 0.25 (hexane/EtOAc (7:1)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81 (m, 6H), 1.18 (m, 8H), 1.47 (m, 2H), 1.71 (t, J = 7.3 Hz, 2H), 2.39 (s, 3H), 3.72 (dd, J = 14.5, 7.2 Hz, 1H), 4.68 (s, 1H), 4.70 (d, J = 7.7 Hz, 1H), 4.78 (s, 1H), 7.25 (d, J = 7.6 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 13.8 (CH/CH_3), 13.9 (CH/CH_3), 21.4 (CH/CH_3), 22.2 (CH/CH_3), 22.4 (CH/CH_3), 27.7 (CH_2), 29.4 (CH_2), 31.0 (CH_2), 34.1 (CH_2), 59.0 (CH/CH_3), 111.0 (CH_2), 127.2 (CH), 129.2 (CH), 138.0 (C), 143.0 (C), 147.9 (C); IR ($CHBr_3$) 3369 (st), 3282 (st), 2930 (st), 1642 (st), 1589 (st) cm^{-1}; MS (EI) m/e 323 (0.5 (M^+), 266 (62), 155 (40), 91 (100); $[\alpha]^{26}_D$ +10.5 (c = 1.24, $CHCl_3$). Anal. Calcd for $C_{18}H_{29}NO_2S$: C, 66.77; H, 8.96; N, 4.33. Found: C, 66.63; H, 8.93; N, 4.61.

(3*S*)-2,4-Diphenyl-3-(*N*-tosylamino)-1-butene (4c). A suspension of 5.64 g of $(Ph_3P)_3PMeBr$ and 2.96 g of $KN(SiMe_3)_2$ in 50 mL of benzene was stirred at 25 °C for 1 h under nitrogen; this solution was cooled to 0 °C then 1.41 g of *N*-tosylamino ketone **3c** in 20 mL of THF was added slowly. The suspension was stirred at 25 °C for 14 h then diluted with an aliquot amount of EtOAc and filtered through 40 mL of silica gel. The solvent was removed, and the crude product was purified by flash chromatography (silica gel, 20% EtOAc/hexanes) to yield 1.40 g (99%) of **4c** as yellow viscous liquid which solidified on standing: mp 65–67 °C; TLC R_f 0.22 (20% EtOAc in hexanes); IR (neat) 1602, 1495, 1455, 1320, 1159, 1094, 1065, 699, 667 cm^{-1}; ^{1}H NMR δ 7.56 (d, J = 8.3 Hz, 2 H), 7.40–7.10 (m, 10 H), 7.00–6.90 (m, 2 H), 5.21 (s, 1 H), 5.06 (s, 1 H), 4.65–4.45 (m, 2 H), 2.89 (dd, J = 5.4, 14.2 Hz, 1 H), 2.67 (dd, J = 6.6, 14.2 Hz, 1 H), 2.39 (s, 3 H); ^{13}C NMR δ 148.1 (C), 143.1 (C), 139.9 (C), 137.4 (C), 136.2 (C), 129.48 (CH), 129.43 (CH), 128.49 (CH), 128.45 (CH), 127.8 (CH), 126.99 (CH), 126.92 (CH), 126.7 (CH), 115.0 (CH_2), 58.0 (CH), 41.0 (CH_2), 21.5 (CH_3); $[\alpha]_D$ +60.00° (c = 0.25, $CHCl_3$). Anal. Calcd for $C_{23}H_{23}NO_2S$: C, 73.18; H, 6.14; N, 3.71. Found: C, 72.88; H, 6.24; N, 3.63.

(3*S*)-2,5-Dimethyl-3-[*N*-(4-methoxybenzyl)-*N*-tosylamino]-1-hexene (5a). To a solution of **4a** (2.47 g, 8.79 mmol) in 50 mL of acetone was added 7.33 g (53.1 mmol, 6 equiv) of anhydrous potassium carbonate and catalytic tetra-*n*-butylammonium iodide. To this mixture was added 2.68 mL (4.16 g, 26.5 mmol, 3 equiv) of 4-methoxybenzyl bromide and the reaction mixture was stirred at 25 °C for 24 h. The solution was diluted with 300 mL of ether, washed with 3 × 50 mL of water, and then dried. Evaporation of the solvent gave the crude product which was purified by flash chromatography eluting with hexane/EtOAc (10:1) to give 3.23 g (92%) of the product: R_f 0.28 (hexane/EtOAc (6:1)); ^{1}H NMR δ 0.71 (d, J = 6.3 Hz, 3H), 0.82 (d, J = 6.3 Hz, 3H), 1.13 (m, 1H), 1.45 (m, 5H), 2.39 (s, 3H), 3.77 (s, 3H), 4.05 (d, J = 15.4 Hz, 1H), 4.28 (m, 1H), 4.39 (d, J = 15.4 Hz, 1H), 4.78 (s, 1H), 4.95 (s, 1H), 6.77 (d, J = 8.6 Hz, 2H), 7.15–7.24 (m, 4H), 7.64 (d, J = 8.2 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 21.4 (CH/CH_3), 22.0 (CH/CH_3), 22.2 (CH/CH_3), 22.9 (CH/CH_3), 24.7 (CH/CH_3), 40.1 (CH_2), 47.0 (CH_2), 55.2 (CH/CH_3), 60.0 (CH/CH_3), 113.3 (CH), 114.8 (CH_2), 127.3 (CH), 129.2 (CH), 129.8 (CH), 130.1 (CH), 138.4 (C), 142.0 (C), 142.7 (C), 158.8 (C); IR ($CHBr_3$) 1623 (st), 1518 (st), 1335 (st) cm^{-1}; MS (EI) m/e 401 (0.5 (M^+)), 290 (8), 121 (100), 91 (28); $[\alpha]^{26}_D$ −78.2° (c = 1.19, $CHCl_3$). Anal. Calcd for $C_{23}H_{31}NO_3S$: C, 68.86; H, 7.92; N, 3.97. Found: C, 68.79; H, 7.78; N, 3.49.

(3*S*)-3-[*N*-(4-Methoxybenzyl)-*N*-tosylamino]-2-*n*-butylhept-1-ene (5b). To a solution of **4b** (1.2 g, 3.71 mmol), K_2CO_3 (1.53 g, 11.1 mmol), and catalytic tetra-*n*-butylammonium iodide in 50 mL of acetone was added 4-methoxybenzyl chloride (1.74 g, 11.1 mmol) and the reaction mixture was refluxed for 10 h. The solution was cooled and diluted with 250 mL of ether and washed with 2 × 50 mL of water. The ether layer was dried and the solvent evaporated to leave an oil, which was purified by flash chromatography (hexane/EtOAc (20:1)) to give 1.47 g (89%) of the product: R_f 0.4 (hexane/EtOAc (6:1)); ^{1}H NMR δ 0.76 (t, J = 7 Hz, 3H), 0.8 (t, J = 7 Hz, 3H), 1.13 (m, 8H), 1.27 (m, 2H), 1.61 (m, 2H), 2.38 (s, 3H), 3.76 (s, 3H), 4.05 (d, J = 5.3 Hz, 1H), 4.20 (dd, J = 8.9, 5.3 Hz, 1H), 4.36 (d, J = 15.3 Hz, 1H), 4.83 (s, 1H), 4.96 (s, 1H), 6.77 (d, J = 8.6 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.62 (d, J = 8.2 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 13.8 (CH/CH_3), 21.3 (CH/CH_3), 22.2 (CH_2), 22.4 (CH_2), 28.9 (CH_2), 29.7 (CH_2), 30.8 (CH_2), 34.3 (CH_2), 46.8 (CH_2), 55.1 (CH/CH_3), 60.6 (CH/CH_3), 113.0 (CH/CH_3), 113.1 (CH_2), 127.1 (CH), 129.2 (CH), 129.8 (CH), 130.2 (C), 138.5 (C), 142.7 (C), 145.7 (C), 158.7 (C); IR ($CHBr_3$) 3329 (md), 2964 (st), 1649 (st), 1609 (st), 1596 (st), 1509 (st) cm^{-1}; MS (EI) m/e 443 (0.04 (M^+)), 290 (15), 155 (22), 121 (99), 91 (100); $[\alpha]^{26}_D$ −63.9° (c = 1.175, $CHCl_3$).

(3*S*)-2,4-Diphenyl-3-[*N*-(4-methoxybenzyl)-*N*-tosylamino]-1-butene (5c). To a suspension of 2.52 g of *N*-tosylamine **4c** in 25 mL of THF were added 2.75 mL of 4-methoxybenzyl chloride, 4.70 g of potassium carbonate, 0.05 g of 18-crown-6, and 0.01 g of tetra-*n*-butylammonium iodide, and the reaction mixture was stirred at room temperature for 5 days. The mixture was filtered through 20 mL of silica gel and washed with EtOAc. After removal of solvents, the crude product was purified by flash chromatography (silica gel, 20% EtOAc in hexanes) to afford 3.3 g (99% yield) of **5c** as a viscous liquid which solidified on standing; mp 121–123 °C; TLC R_f 0.32 (20% EtOAc in hexanes); IR (neat) 1612, 1513, 1496, 1456, 1332, 1247, 1154, 1091, 1033, 1010, 686

cm^{-1}; ^{1}H NMR δ 7.30–7.05 (m, 12 H), 6.97 (d, J = 7.3 Hz, 2 H), 6.92 (d, J = 8.1 Hz, 2 H), 6.77 (d, J = 8.5 Hz, 2 H), 5.42 (s, 1 H), 5.36 (s, 1 H), 5.33 (dd, J = 4.2, 10.9 Hz, 1 H), 4.46 (d, J = 15.4 Hz, 1 H), 4.19 (d, J = 15.4 Hz, 1 H), 3.80 (s, 3 H), 3.11 (dd, J = 4.2, 14.2 Hz, 1 H), 2.94 (dd, J = 10.7, 14.2 Hz, 1 H), 2.31 (s, 3 H); ^{13}C NMR δ 159.0 (C), 144.3 (C), 142.4 (C), 141.4 (C), 138.6 (C), 137.8 (C), 130.0 (CH), 129.8 (C), 129.12 (CH), 129.06 (CH), 128.3 (CH), 128.1 (CH), 127.4 (CH), 127.1 (CH), 126.8 (CH), 126.2 (CH), 119.0 (CH_2), 113.6 (CH), 61.8 (CH), 55.2 (CH_3), 47.7 (CH_2), 39.4 (CH_2), 21.3 (CH_3); $[\alpha]_D$ −106.00° (c = 0.10, $CHCl_3$). Anal. Calcd for $C_{31}H_{31}NO_3S$: C, 74.82; H, 6.28; N, 2.81. Found: C, 74.65; H, 6.29; N, 2.68.

(3*S*)-*syn*-2,5-Dimethyl-3-[*N*-(4-methoxybenzyl)-*N*-tosylamino]hexan-1-ol (*syn*-6a). Compound **5a** (2.91 g, 7.25 mmol) in 50 mL of THF was cooled to −78 °C and then 50 mL (25 mmol) of a 0.5 M solution of 9-BBN in THF was added with stirring. The mixture was allowed to warm to 25 °C over 2 h and then stirred for 16 h. The solution was cooled in ice, 20 mL of EtOH, 10 mL of 3 M NaOH, and 10 mL of 30% hydrogen peroxide were added in that order, and the reaction mixture was stirred at 25 °C for 6 h. The mixture was diluted with 250 mL of ether, washed with 2 × 60 mL of 1 M NaOH and 1 × 50 mL of saturated ammonium chloride, and then dried. Evaporation of the solvent gave the crude material which was purified by flash chromatography eluting with hexane/EtOAc (2:1) to give 2.6 g (85.5%) of the product as a clear viscous oil: R_f 0.5 (hexane/EtOAc (2:1)); ^{1}H NMR δ 0.54 (d, J = 7.2 Hz, 3H), 0.66 (d, J = 6.4 Hz, 3H), 0.78 (d, J = 6.2 Hz, 3H), 0.83 (m, 1H), 1.37 (m, 2 H), 1.72 (m, 1H), 2.4 (s, 3H), 2.85 (m, 1H), 3.35 (m, 1H), 3.64 (m, 1H), 3.77 (s, 3H), 4.0 (m, 1H), 4.14 (d, J = 16.1 Hz, 1H), 4.43 (d, J = 16.1 Hz, 1H), 6.81 (d, J = 8.6 Hz, 2H), 7.23–7.26 (m, 4H), 7.6 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 12.3 (CH/CH_3), 21.4 (CH/CH_3), 22.0 (CH/CH_3), 23.0 (CH/CH_3). 24.4 (CH/CH_3), 38.3 (CH/CH_3), 38.7 (CH_2), 48.0 (CH_2), 55.2 (CH/CH_3), 56.7 (CH/CH_3), 64.6 (CH_2), 113.6 (CH/CH_3), 127.4 (CH), 129.4 (CH), 129.5 (CH), 129.8 (C), 137.5 (C), 143.2 (C), 158.8 (C); IR ($CHBr_3$) 3528 (st), 1602 (st), 1503 (st), 1321 (st) cm^{-1}; MS (EI) m/e 419 (0.1 (M^+), 360 (24), 155 (11), 121 (98), 91 (100), $[\alpha]^{26}_D$ +48.6° (c = 1.225, $CHCl_3$).

(3*S*)-2,5-Dimethyl-3-[*N*-(4-methoxybenzyl)-*N*-tosylamino]hexan-1-ol (*anti*-6a). A solution of 4.76 g (11.8 mmol) of the alkene **5a** in 60 mL of THF was cooled to −78 °C and then 35 mL (35 mmol) of a 1.0 M solution of BH_3·THF in THF was added with stirring. The mixture was stirred at −78 °C for 5 min and stored at −26 °C for 24 h and then at 0 °C for another 24 h. The reaction was cooled with ice while 50 mL of ethanol, 25 mL of 3 M NaOH, and 25 mL of 30% hydrogen peroxide were added. The mixture was allowed to warm to 20 °C, stirred for 10 h, and then diluted with 250 mL of ether. The ether solution was washed with 5 × 60 mL of 1 M NaOH and 4 × 70 mL of saturated ammonium chloride solution and dried. Evaporation of the solvent gave 2.87 g (94.5%) of the crude alcohol which was purified by flash chromatography eluting with hexane–ethyl acetate (2:1) to give 2.97 g (60%) of the product: mp 72–73 °C; ^{1}H NMR δ 0.66 (d, J = 6.3 Hz, 3H), 0.71 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.98 (m, 1H), 1.22 (m, 2H), 1.41 (m, 1H), 2.4 (s, 3H), 2.60 (m, 1H), 3.16 (m, 1H), 3.75 (m, 2H), 3.77 (s, 3H), 4.0 (d, J = 15.2 Hz, 1H), 4.57 (d, J = 15.2 Hz, 1H), 6.80 (d, J = 8.6 Hz, 2H), 7.22–7.26 (m, 4H), 7.63 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 15.2 (CH/CH_3), 21.4 (CH/CH_3), 21.7 (CH/CH_3), 23.5 (CH/CH_3), 24.1 (CH/CH_3), 38.9 (CH_2), 47.0 (CH_2), 55.2 (CH/CH_3), 58.2 (CH/CH_3), 64.4 (CH_2), 113.7 (CH/CH_3), 127.2 (CH), 129.1 (CH), 129.3 (CH), 130.2 (CH), 138.0 (C), 143.1 (C), 159.1 (C); IR ($CHBr_3$) 3557 (md), 1616 (st), 1518 (st), 1328 (st) cm^{-1}; MS (EI) m/e 419 (0.1 (M^+)), 360 (36), 155 (18), 121 (98), 91 (100); $[\alpha]^{26}_D$ +18.5° (c = 1.225, $CHCl_3$). Anal. Calcd for $C_{23}H_{33}NO_4S$: C, 65.54; H, 7.74; N, 3.10. Found: C, 65.84; H, 7.93; N, 3.34.

(3*S*)-2-*n*-Butyl-3-[*N*-(4-methoxybenzyl)-*N*-tosylamino]heptan-1-ol (*anti*-6b). A solution of **5b** (1.42 g, 3.20 mmol) in 30 mL of THF was cooled to −78 °C and 16 mL (16 mmol) of 1.0 M BH_3·THF complex in THF was added with stirring. The mixture was stirred at −78 °C for 2 h and then stored at −26 °C for 24 h. To this well-stirred reaction mixture at 0 °C were added sequentially 15 mL of ethanol, 8 mL of 3 M NaOH, and 8 mL of 30% hydrogen peroxide. The mixture was allowed to warm to 25 °C, stirred for 10 h, and then diluted with 300 mL of ether. The ether solution was washed with 2 × 40 mL of 1 M NaOH and 2 × 40 mL of saturated aqueous ammonium chloride and dried. Evaporation of the solvent gave the crude alcohol which was purified by flash chromatography eluting with 20% EtOAc in hexane to give 1.14 g (77%) of the product. NMR of the crude material showed it to be >94% *anti*: R_f 0.3 (hexane/EtOAc (4:1)); ^{1}H NMR δ 0.67 (t, J = 7.2 Hz, 3H), 0.87 (t, J = 7.1 Hz, 3H), 1.16 (m, 8H), 1.38 (m, 4H), 2.47 (s, 3H), 2.83 (m, 1H), 3.27 (m, 1H), 3.76 (m, 2H), 3.86 (s, 3H), 3.94 (d, J = 14.9 Hz, 1H), 4.77 (d, J = 15.2 Hz, 1H), 6.89 (d, J = 8.6 Hz, 2H), 7.3 (d, J = 6.1 Hz, 2H), 7.4 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 13.6 (CH/CH_3), 13.7 (CH/CH_3), 21.1 (CH/CH_3), 22.5 (CH_2), 22.6 (CH_2), 27.3 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 43.9 (CH/CH_3), 46.7 (CH_2), 55.0 (CH/CH_3), 59.6 (CH_2), 59.7 (CH/CH_3), 113.4 (CH), 127.0 (CH), 129.2 (CH), 129.2 (CH), 130.26 (CH), 137.8 (C), 143.0 (C), 159.0 (C); IR ($CHBr_3$) 3528 (st), 2930 (st), 1609 (st), 1596 (st), 1582 (st), 1514 (st) cm^{-1}; MS (EI) m/e 461 (0.02 (M^+)), 360 (28), 155 (31), 121 (99), 91 (100); $[\alpha]^{26}_D$ +5.0° (c = 1.58, $CHCl_3$). Anal. Calcd for $C_{26}H_{39}NO_4S$: C, 67.58; H, 8.45; N, 3.03. Found: C, 67.76; H, 8.66; N, 3.16.

(3*S*)-2-*n*-Butyl-3-[*N*-(4-methoxybenzyl)-*N*-tosylamino]heptan-1-ol (*syn*-6b). A solution of 2.59 g (5.84 mmol) of compound **5b** in 30 mL of THF was cooled to −78 °C and then 44 mL (22 mmol) of a 0.5 M solution of 9-BBN in THF was added with stirring. The mixture was allowed to warm to 25 °C over 2 h and then stirred at 25 °C for 22 h. The solution was cooled to 0 °C, 20 mL of ethanol, 10 mL of 3 M NaOH, and 10 mL of 30% hydrogen peroxide were added in that order, and the reaction mixture was stirred at 25 °C for 6 h. The mixture was diluted with 250 mL of ether, washed with 3 × 50 mL of 1 M NaOH and 2 × 50 mL of saturated aqueous NH_4Cl, and then dried. Evaporation of the solvent gave the crude material which was purified by flash chromatography eluting with hexane/EtOAc (5:1) to give 86% (syn/anti, 1:1.3) of the product, based on the conversion of the starting material: R_f 0.26 (hexane/EtOAc (4:1)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (m, 6H), 0.88 (m, 8H), 1.40 (m, 1H), 1.51 (m, 1H), 2.39 (s, 3H), 3.47 (m, 1H), 3.61 (m, 1H), 3.76 (s, 3H), 3.8 (m, 1H), 3.97 (d, J = 16.1 Hz, 1H), 4.49 (d, J = 15.9 Hz, 1H), 6.61 (d, J = 8.6 Hz, 2H), 7.23–7.27 (m, 4H), 7.84 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 13.7 (CH/CH_3), 13.8 (CH/CH_3), 21.4 (CH/CH_3), 22.5 (CH_2), 22.8 (CH_2), 26.1 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 30.3 (CH_2), 44.3 (CH/CH_3), 47.8 (CH_2), 55.2 (CH/CH_3), 59.0 (CH/CH_3), 61.5 (CH_2), 113.6 (CH), 127.3 (CH), 129.4 (CH), 129.6 (CH), 129.9 (C), 137.6 (C), 143.2 (C), 158.9 (C); IR ($CHBr_3$) 3535 (md), 2957 (st), 1609 (st), 1596 (st) cm^{-1}; MS (EI) m/e 461 (0.02 (M^+)), 360 (22), 155 (21), 121 (99), 91 (100); $[\alpha]^{26}_D$ +38.3° (c = 1.09, $CHCl_3$). Anal. Calcd for $C_{26}H_{39}NO_4S$: C, 67.58; H, 8.45; N, 3.03. Found: C, 67.49; H, 8.82; N, 3.03.

(3*S*)-2,5-Dimethyl-3-(*N*-tosylamino)hexan-1-ol (*anti*-7a). To 1.92 g (4.58 mmol) of *anti*-**6a** in 20 mL of CH_3CN–H_2O (4:1) was added 8.79 g (0.16 mol) of ceric ammonium nitrate and the reaction mixture stirred vigorously at 25 °C for 10 min and then diluted with saturated aqueous NaCl (20 mL). The reaction mixture was extracted three times with 50 mL of EtOAc. The EtOAc layers were combined and dried, and the solvent was evaporated. The resulting oil was purified by flash chromatography eluting with hexane–EtOAc (2:1) and recrystallized from dichloromethane–hexane to give 1.1 g (80%) of the product: mp 86–87 °C; ^{1}H NMR δ 0.63 (d, J = 6.3 Hz, 3H), 0.75 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 7 Hz, 3H), 1.2 (m, 2H), 1.34 (m, 1H), 1.69 (m, 1H), 2.09 (m, 1H), 2.39 (s, 3H), 3.44 (m, 2H), 3.78 (m, 1H), 5.11 (d, J = 8.4 Hz, 1H), 7.27 (d, J = 7.8 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 13.5 (CH/CH_3), 21.4 (CH/CH_3), 21.8 (CH/CH_3), 23.0 (CH/CH_3), 24.2 (CH/CH_3), 38.8 (CH/CH_3), 41.9 (CH_2), 54.5 (CH/CH_3), 64.4 (CH_2), 126.9 (CH), 129.4 (CH), 138.3 (C), 143.0 (C); IR ($CHBr_3$) 3521 (md), 3374 (md), 3282 (md), 1609 (md), 1328 (st) cm^{-1}; MS (EI) m/e 299 (0.5 (M^+)), 240 (65), 155 (56), 91 (100); $[\alpha]^{26}_D$ −25.5° (c = 1.13, $CHCl_3$). Anal. Calcd for $C_{15}H_{25}NO_3S$: C, 59.93; H, 8.17; N, 4.40. Found: C, 60.17; H, 8.42; N, 4.68.

(3*S*)-2,5-Dimethyl-3-(*N*-tosylamino)-1-hexanol (*syn*-7a). The procedure described above was applied using 2.59 g (6.18 mmol) of *syn*-**6a** to give 1.32 g (71%) of the product: mp 106–107 °C; ^{1}H NMR δ 0.64 (m, 9H), 0.9 (m, 1H), 1.22 (m, 2H), 1.77 (m, 1H), 2.41 (s, 3H), 2.92 (bs, 1H), 3.51 (m, 2H), 3.64 (t, J = 10.8 Hz, 1H), 4.92 (d, J = 9.3 Hz, 1H), 7.3 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 8.2 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 9.7 (CH/CH_3),

21.4 (CH/CH_3), 21.9 (CH/CH_3), 22.5 (CH/CH_3), 24.1 (CH/CH_3), 37.3 (CH/CH_3), 41.3 (CH_2), 51.6 (CH/CH_3), 64.3 (CH_2), 127.0 (CH), 129.5 (CH), 137.7 (C), 143.4 (C); IR ($CHBr_3$) 3521 (md), 3289 (md), 2959 (st), 1609 (st), 1330 (st) cm^{-1}; MS (EI) *m/e* 299 (0.2 (M^+)), 240 (59), 155 (44), 91 (100); $[\alpha]^{26}_D$ −4.4° (*c* = 1.18, $CHCl_3$). Anal. Calcd for $C_{15}H_{25}NO_3S$: C, 60.06, H, 8.14; N, 4.53. Found: C, 60.17; H, 8.42; N, 4.68.

(3*S*)-2-*n*-Butyl-3-(*N*-tosylamino)heptan-1-ol (*anti*-7b). The procedure described above was applied using ***anti*-6b** (1.05 g, 2.27 mmol) to give 0.54 g (70%) of the product: R_f 0.16 (hexane/EtOAc (4:1)); ^1H NMR δ 0.7 (m, 6H), 1.1 (m, 10H), 1.4 (m, 2H), 1.7 (m, 1H), 2.4 (s, 3H), 3.31 (m, 1H), 3.5 (m, 1H), 3.8 (m, 1H), 5.2 (d, *J* = 8.4 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ 13.7 (CH/CH_3), 13.8 (CH/CH_3), 21.3 (CH/CH_3), 22.3 (CH_2), 22.7 (CH_2), 27.7 (CH_2), 27.77 (CH_2), 29.4 (CH_2), 33.1 (CH_2), 42.3 (CH/CH_3), 55.9 (CH/CH_3), 61.6 (CH_2), 126.8 (CH), 129.3 (CH), 138.3 (C), 142.8 (C); IR ($CHBr_3$) 3501 (md), 3289 (md), 2930 (st), 1597 (st) cm^{-1}; MS (EI) *m/e* 342 (0.1 (MH^+)), 240 (66), 155 (55), 91 (100); $[\alpha]^{26}_D$ −1.2° (*c* = 1.14, $CHCl_3$).

(3*S*)-2-*n*-Butyl-3-(*N*-tosylamino)heptan-1-ol (*syn*-7b). The procedure described above was applied using ***syn*-6b** (0.25 g, 0.54 mmol) to give 0.17 g (92%) of the product: R_f 0.19 (hexane/EtOAc (4:1)); ^1H NMR (300 MHz, $CDCl_3$) δ 0.6 (t, *J* = 6.3 Hz, 3H), 0.8 (m, 3H), 1.1 (m, 12H), 1.5 (m, 1H), 2.3 (s, 3H), 2.9 (m, 1H), 3.3 (m, 1H), 3.5 (d, *J* = 7.0 Hz, 2H), 5.6 (d, *J* = 9.0 Hz, 1H), 7.2 (d, *J* = 8 Hz, 2H), 7.7 (d, *J* = 8 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 13.6 (CH/CH_3), 13.7 (CH/CH_3), 21.2 (CH/CH_3), 22.0 (CH_2), 22.5 (CH_2), 25.9 (CH_2), 28.1 (CH_2), 29.5 (CH_2), 30.5 (CH_2), 42.7 (CH/CH_3), 54.5 (CH/CH_3), 62.8 (CH_2), 126.9 (CH), 129.3 (CH), 138.0 (C), 142.9 (C); IR ($CHBr_3$) 3508 (st), 3289 (st), 2957 (st), 1589 (st) cm^{-1}; MS (EI) *m/e* 342 (0.2 (MH^+)), 240 (52), 155 (40), 91 (70), 28 (100); $[\alpha]^{26}_D$ +2.4° (*c* = 1.265, $CHCl_3$).

(3*S*)-2,5-Dimethyl-3-[*N*-(*tert*-butoxycarbonyl)amino]hexan-1-ol (*anti*-8a). Lithium metal was added to a solution of ***anti*-7a** (1.5 g, 5.01 mmol) in 5 mL of THF and 200 mL of liquid NH_3 and the resulting dark blue solution was stirred for 1 h and then quenched with 1 mL of absolute ethanol. The ammonia was evaporated and $(BOC)_2O$ (3.28 g, 15 mmol) with 5 mL of 1 M NaOH were added to the resulting residue in 30 mL of dioxane–water (2:1) at 0 °C. The reaction mixture was allowed to warm to 25 °C, stirred at that temperature for 14 h, and then evaporated to one-half its volume. The mixture was acidified with potassium hydrogen sulfate, diluted with saturated aqueous NaCl (30 mL), and extracted four times with EtOAc (20 mL). The combined EtOAc layer was dried and the solvent evaporated. The resulting oil was flash chromatographed using hexane–EtOAc (4:1) to give 0.61 g (49.6%) of the pure compound: mp 57–58 °C; ^1H NMR δ 0.88 (d, *J* = 6.6 Hz, 3H), 0.9 (d, *J* = 6.9 Hz, 3H), 1.0 (d, *J* = 6.8 Hz, 3H), 1.19 (m, 1H), 1.36 (m, 2H), 1.41 (s, 9H), 1.67 (m, 1H), 3.49 (m, 1H), 3.53 (m, 1H), 3.76 (m, 1H), 4.39 (d, *J* = 9.3 Hz, 1H); ^{13}C NMR δ 14.6 (CH/CH_3), 21.3 (CH/CH_3), 23.6 (CH/CH_3), 24.9 (CH/CH_3), 28.3 (CH/CH_3), 40.8 (CH/CH_3), 41.9 (CH_2), 50.4 (CH/CH_3), 64.6, (CH_2), 79.9 (C), 158.6 (C); IR ($CHBr_3$) 3430 (st), 2966 (st) 1693 (st) cm^{-1}; MS (EI) *m/e* 245 (0.15 (M^+)), 186 (6), 130 (28), 57 (100); $[\alpha]^{26}_D$ −31.8° (*c* = 1.11, $CHCl_3$). Anal. Calcd for $C_{13}H_{27}NO_3$: C, 63.36; H, 10.83; N, 5.48. Found: C, 63.63; H, 11.09; N, 5.71.

(3*S*)-2,5-Dimethyl-3-[*N*-(*tert*-butoxycarbonyl)amino]-1-hexanol (*syn*-8a). The procedure used was analogous to the one described for ***anti*-8a**; ***syn*-7a** was converted to ***syn*-8a** to yield 0.48 g (48%) of the pure product after flash chromatography using hexane/EtOAc (4:1): mp 94–95 °C; ^1H NMR δ 0.63 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 2.9 Hz, 3H), 0.91 (d, *J* = 3 Hz, 3H), 1.15 (m, 1H), 1.37 (s, 1H), 1.41 (s, 9H), 1.60 (m, 1H), 1.75 (m, 1H), 3.19 (m, 1H), 3.36 (m, 1H), 3.97 (m, 1H), 4.11 (dd, *J* = 4.1 Hz, 1H), 4.33 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR δ 9.2 (CH/CH_3), 22.1 (CH/CH_3), 22.9 (CH/CH_3), 25.1 (CH/CH_3), 28.2 (CH/CH_3), 39.4 (CH/CH_3), 42.0 (CH_2), 47.2 (CH/CH_3), 64.8 (CH_2), 79.8 (C), 157.3 (C); IR ($CHBr_3$) 3437 (st), 1693 (st) cm^{-1}; MS (EI) *m/e* 245 (0.05 (M^+)), 215 (0.1), 186 (6), 130 (22), 57 (100); $[\alpha]^{26}_D$ −25.3° (*c* = 1.11, $CHCl_3$). Anal. Calcd for $C_{13}H_{27}NO_3$: C, 63.54; H, 10.97; N, 5.61. Found: C, 63.63; H, 11.09; N, 5.71.

(3*S*)-2-*n*-Butyl-3-[*N*-(*tert*-butoxycarbonyl)amino]heptan-1-ol (*anti*-8b). The procedure used was analogous to the one described for ***anti*-8a.** Thus ***anti*-7b** was converted to ***anti*-8b** to yield 0.14 g (36%) of the product after flash chromatography by eluting with hexane/EtOAc (4:1): R_f 0.45 (hexane/EtOAc (4:1)); ^1H NMR δ 0.8 (m, 6H), 1.3 (m, 12H), 1.4 (s, 9H), 2.5 (m, 1H), 3.5 (m, 2H), 3.7 (m, 1H), 4.6 (d, *J* = 9.6 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 13.9 (CH/CH_3), 22.5 (CH_2), 22.8 (CH_2), 27.6 (CH_2), 28.3 (CH/CH_3), 29.6 (CH_2), 32.8 (CH_2), 44.3 (CH/CH_3), 51.6 (CH/CH_3), 61.4 (CH_2), 79.1 (C), 156.8 (C); IR ($CHBr_3$) 3435 (st), 2930 (st), 1689 (st) cm^{-1}; MS (EI) *m/e* 130 (42), 86 (46), 57 (100); $[\alpha]^{26}_D$ −21.6° (*c* = 1.04, $CHCl_3$). Anal. Calcd for $C_{16}H_{33}NO_3$: C, 66.79; H, 11.48. Found: C, 66.87; H, 11.58.

(3*S*)-2-*n*-Butyl-3-[*N*-(*tert*-butoxycarbonyl)amino]heptan-1-ol (*syn*-8b). The procedure used was analogous to the one described for ***anti*-8a.** Thus ***syn*-7b** was converted to ***syn*-8b** to yield 0.48 g (48%) of the pure product after flash chromatography with hexane/EtOAc (4:1): mp 94–95 °C; ^1H NMR δ 0.63 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 2.9 Hz, 3H), 0.91 (d, *J* = 3 Hz, 3H), 1.15 (m, 1H), 1.37 (s, 1H), 1.41 (s, 9H), 1.60 (m, 1H), 1.75 (m, 1H), 3.19 (m, 1H), 3.36 (m, 1H), 3.97 (m, 1H), 4.11 (dd, *J* = 4.1 Hz, 1H), 4.33 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR δ 9.2 (CH/CH_3), 22.1 (CH/CH_3), 22.9 (CH/CH_3), 25.1 (CH/CH_3), 28.2 (CH/CH_3), 39.4 (CH/CH_3), 42.0 (CH_2), 47.2 (CH/CH_3), 64.8 (CH_2), 79.8 (C), 157.3 (C); IR ($CHBr_3$) 3437 (st), 1693 (st) cm^{-1}; MS (EI) *m/e* 245 (0.05 (M^+)), 215 (0.1), 186 (6), 130 (22), 57 (100); $[\alpha]^{26}_D$ −25.3° (*c* = 1.11, $CHCl_3$). Anal. Calcd for $C_{13}H_{27}NO_3$: C, 63.54; H, 10.97; N. 5.61. Found: C, 63.63; H, 11.09; N, 5.71.

(3*S*)-2,5-Dimethyl-3-[*N*-(*tert*-butoxycarbonyl)amino]hexanoic Acid (*anti*-9a). To a solution of ***anti*-8a** (0.43 g, 1.75 mmol) in 16 mL of $CCl_4/CH_3CN/H_2O$ (5:5:6) were added $RuCl_3$ (20 mg, 0.076 mmol) and 1.05 g $NaIO_4$ (4.9 mmol, 2.8 equiv), and the reaction mixture was stirred at 25 °C for 1.5 h. It was then diluted with saturated NaCl solution (25 mL) and extracted four times with 20 mL of EtOAc. The combined EtOAc layers were dried, and the solvent was evaporated to leave an oil. It was flash chromatographed using hexane/EtOAc (3:1) to give 0.43 g (95%) of the product: ^1H NMR δ 0.88 (m, 9H), 1.2 (m, 2H), 1.41 (s, 9H), 1.64 (m, 1H), 2.64 (m, 1H), 3.85 (m, 1H), 5.06 (d, *J* = 9.9 Hz, 1H), 5.78 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR δ 13.9 (CH/CH_3), 22.0 (CH/CH_3), 23.0 (CH/CH_3), 24.6 (CH/CH_3), 28.3 (CH/CH_3), 42.9 (CH_2), 43.3 (CH/CH_3), 50.4 (CH/CH_3), 79.1 (C), 156.0 (C), 180.6 (C); IR ($CHBr_3$) 3430 (st), 3346 (md), 2959 (st), 1707 (st) cm^{-1}; $[\alpha]^{26}_D$ −28.2° (*c* = 1.19, $CHCl_3$). Anal. Calcd for $C_{13}H_{25}NO_4$: C, 60.31; H, 9.79; N, 5.50. Found: C, 60.21; H, 9.72; N, 5.40.

(3*S*)-2,5-Dimethyl-3-[*N*-(*tert*-butoxycarbonyl)amino]hexanoic Acid (*syn*-9a). To a solution of ***syn*-8a** (0.48 g, 1.95 mmol) in $CH_3N/CCl_4/H_2O$ (16 mL, 1:1:1.2) were added sodium periodate (1.17 g, 5.48 mmol) and $RuCl_3$ (20 mg, 0.076 mmol), and the reaction mixture was stirred at 25 °C for 0.5 h. The reaction mixture was dilute with water (30 mL) and extracted with EtOAc (4 × 30 mL). The combined EtOAc layers were dried, and the solvent was evaporated to leave an oil which was chromatographed using hexane/EtOAc (3:1) to give 0.32 g (63%) of the pure product: ^1H NMR δ 0.86 (m, 9H), 1.11 (m, 2H), 1.37 (s, 9H), 1.6 (m, 1H), 2.6 (m, 1H), 2.58 (m, 1H), 3.6 (m, 1H), 4.85 (d, *J* = 9.4 Hz, 1H), 6.04 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR δ 12.4 (CH/CH_3), 13.3 (CH/CH_3), 21.2 (CH/CH_3), 23.4 (CH/CH_3), 24.6 (CH/CH_3), 28.2 (CH/CH_3), 40.5 (CH_2), 44.2 (CH/CH_3), 50.7 (CH/CH_3), 79.2 (C), 155.6 (C), 178.6 (C); IR ($CHBr_3$) 3444 (md), 2966, (st), 1707 (st) cm^{-1}; $[\alpha]^{26}_D$ −43.3° (*c* = 1.14, $CHCl_3$); MS (FAB) *m/e* 260.3 (M + 1).

(3*S*)-2-*n*-Butyl-3-[*N*-(*tert*-butoxycarbonyl)amino]heptanoic Acid (*anti*-9b). To a solution of ***anti*-8b** (0.12 g, 0.41 mmol) in $CH_3CN/CCl_4/H_2O$ (16 mL, 1:1:1.2) were added sodium periodate (0.25 g, 1.17 mmol) and $RuCl_3$ (0.005 g, 0.019 mmol), and the reaction mixture was stirred at 25 °C for 4 h. The reaction mixture was filtered through silica and the solvent evaporated. The crude residue was flash chromatographed, eluting with 20% EtOAc in hexane to yield 0.11 g (89%) of the product: R_f 0.22 (80:20 hexane/EtOAc); ^1H NMR δ 0.85 (m, 6H), 1.2 (m, 12H), 1.4 (s, 9H), 3.5 (m, 2H), 3.7 (d, *J* = 11 Hz, 1H), 4.8 (d, *J* = 9 Hz, 1H); ^{13}C NMR δ 13.7 (CH/CH_3), 13.9 (CH/CH_3), 22.4 (CH_2), 28.3 (CH/CH_3), 29.6 (CH_2), 34.2 (CH_2), 50.8 (CH/CH_3), 78.0 (C), 156.0 (C), 180.3 (C); IR ($CHBr_3$) 3435 (md), 2957 (st), 1702 (st) cm^{-1}; $[\alpha]^{27}_D$ −23.8° (*c* = 1.35, $CHCl_3$); MS (FAB) *m/e* 302.4 (M + 1).

(3*S*)-2-*n*-Butyl-3-[*N*-(*tert*-butoxycarbonyl)amino]heptanoic Acid (*syn*-9b). To a solution of ***syn*-8b** (0.050 g, 0.17 mmol) in $CH_3CN/CCl_4/H_2O$ (16 mL, 1:1:1.2) were added sodium periodate (0.104 g, 0.48 mmol) and $RuCl_3$ (0.005 g, 0.019 mmol),

and the reaction mixture was stirred at 25 °C for 2 h. The reaction mixture was filtered through silica and the solvent evaporated to leave behind an oily residue which was purified by flash chromatography, eluting with 20% EtOAc in hexane to give 0.045 g (90%) of the product: ^{1}H NMR δ 0.8 (m, 6H), 1.2 (m, 12H), 1.4 (s, 9H), 1.6 (m, 1H), 2.4 (m, 1H), 3.7 (m, 1H), 4.7 (d, J = 9.7 Hz, 1H), 5.8 (d, J = 7.6 Hz, 1H); ^{13}C NMR δ 13.8 (CH/CH_3), 13.9 (CH/CH_3), 22.3 (CH_2), 22.6 (CH_2), 28.3 (CH/CH_3), 29.7 (CH_2), 31.6 (CH_2), 50.4 (CH/CH_3), 51.8 (CH/CH_3), 79.2 (C), 155.7 (C), 178.6 (C); IR ($CHBr_3$) 3349 (st), 2957 (st), 1702 (st), 1682 (st) cm^{-1}; $[\alpha]^{27}_D$ −8.63° (c = 1.35, $CHCl_3$); MS (FAB) m/e 302.4 (M + 1).

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