# On the Use of *O*-Methylmandelic Acid for the Establishment of Absolute Configuration of α-Chiral Primary Amines

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The absolute configuration of α-chiral primary amines is correlated to the relative $^1$H NMR shifts (upfield or downfield) observed in the diastereomeric amides formed from (*S*)-*O*-methylmandelic acid. The amides are easily formed without racemization from either the amine or the amine salt. A model is described that explains the observed shifts and can be used to determine the absolute configuration of unknown α-chiral primary amines.

In today's scientific and regulatory environment, establishment of the enantiomeric purity and absolute configuration of a compound is of the utmost importance. Chiral amines, such as amino acids, have a central importance in both chemistry and biology. Accordingly, the development of techniques to address the issues of enantiomeric purity and configuration of α-chiral amines has attracted considerable attention. Spectroscopic methods, such as NMR, relying on covalent diastereomers,[1] chiral shift reagents,[2] and chiral solvating agents[3] have been developed. In addition, chromatographic techniques employing chiral stationary phases[4] and separation of diastereomers[5] have been successful. Rabin and Mislow[6] first described the use of *O*-methylmandelic acid to determine the enantiomeric purity of alcohols and amines. For secondary alcohols, models relating the $^1$H NMR chemical shift differences of the mandelate, *O*-methylmandelate, and α-(trifluoromethyl)-*O*-methylmandelate esters to the absolute configuration at the carbinol center have been established.[7] A similar procedure for amines using α-(trifluoromethyl)-*O*-methylmandelic acid has been developed in which the conformational model resembles that of the corresponding ester.[8]

During the course of our studies on asymmetric induction we had occasion to examine a series of related chiral allylic amines.[9] Using *O*-methylmandelic acid to determine the enantioselectivity of our reactions, we noted a trend in the chemical shifts of the diastereomers formed. Since the direction of the chemical shift differences between diastereomeric α-(trifluoromethyl)-*O*-methylmandelamides and esters is the same, the chemical shift differences of the diastereomeric *O*-methylmandelamides might similarly be expected to follow those of the *O*-methylmandelate esters.[10] However, the direction of the chemical shift differences between the diastereomeric *O*-methylmandelamides was *opposite* to that observed for esters of similar absolute configuration. Given the much lower cost of *O*-methylmandelic acid compared to α-(trifluoromethyl)-*O*-methylmandelic acid, we examined a more diverse group of amines to determine if this relation was in fact generally applicable. We wish to describe in this report the results of this investigation which led to a $^1$H NMR method employing *O*-methylmandelic acid to determine the absolute configuration of α-chiral (secondary alkyl) primary amines in which the conformational model used to predict the stereochemistry is *reversed* with respect to that of the corresponding esters.

## Results and Discussion

Preparation of diastereomeric amides from either the free amine or the amine salt and *O*-methylmandelic acid was accomplished by one of three methods: (1) DCC (method A); (2) DCC, DMAP, and triethylamine (method B), or (3) DMF and oxalyl chloride[11] (method C). The free amines were derivatized using either method A or, if racemization became a problem due to long reaction times, method C. The amine salts were derivitized using method B. In each case studied, samples of the enantiomerically pure amine and the racemic amine were coupled to (*S*)-*O*-methylmandelic acid. Using this protocol, the observation of a 1:1 mixture of diastereomers in the racemic case assured us that no kinetic resolution had occurred during the derivatization step, which would have compromised the measurement of the enantioselectivity in the amination reactions we were studying. The amines employed were either purchased as single enantiomers of known absolute configuration or, in the case of our allylic amines, the absolute configuration was established by chemical correlation with known compounds. The $^1$H NMR chemical shifts for each set of diastereomers are summarized in Table 1. The chemical shifts for the diastereomer not prepared from a single amine enantiomer were determined from the spectrum of the 1:1 diastereomeric mixture by comparison with the chemical shifts of the known diastereomer.

To relate the chemical shift differences to absolute configuration it is necessary to examine the conformation

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(4) (a) Rubinstein, H.; Feibush, B.; Gil-Av, E. *J. Chem. Soc., Perkin Trans. 2* **1973**, *15*, 2094. (b) *Chromatographic Chiral Separations;* Zief, M., Crane, L. J., Eds.; Marcel Decker: New York, 1988.

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(9) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089.

(10) The conformational models for α-(trifluoromethyl)-*O*-methylmandelate and *O*-methylmandelate esters predict opposite directions for the diastereomeric chemical shifts; see ref 7.

(11) Stadler, P. A. *Helv Chim. Acta* **1978**, *61*, 1675.

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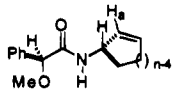
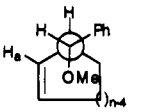
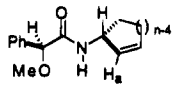
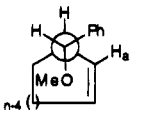
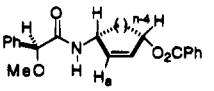
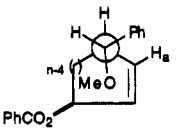
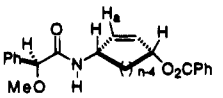
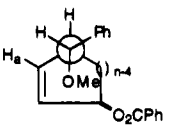
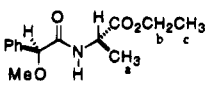
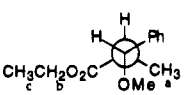
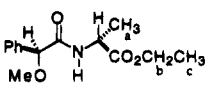
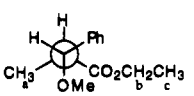
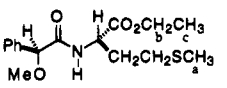
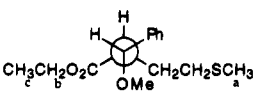
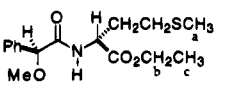
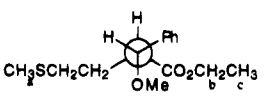
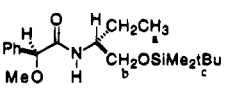
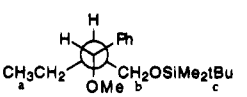
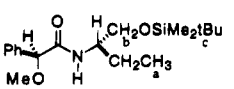
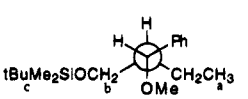
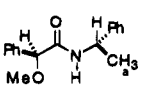
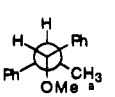
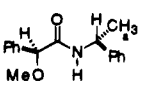
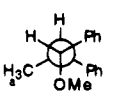
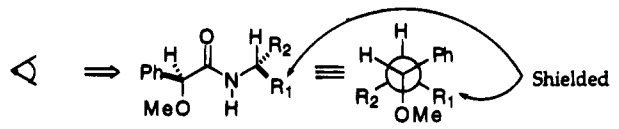
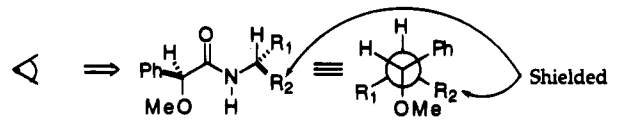
**Table 1. Correlation of *O*-Methylmandelic Amides**

| Entry | *O*-Methylmandelamide | Newman Projection | $H_a$ | $H_b$ | $H_c$ |
|---|---|---|---|---|---|
| |  |  | | | |
| 1a | n=5 | n=5 | 5.75 | | |
| 2a | n=6 | n=6 | 5.65 | | |
| 3a | n=7 | n=7 | 5.60 | | |
| |  |  | | | |
| 1b | n=5 | n=5 | 5.65 | | |
| 2b | n=6 | n=6 | 5.55 | | |
| 3b | n=7 | n=7 | 5.50 | | |
| |  |  | | | |
| 4a | n=5 | n=5 | 6.01 | | |
| 5a | n=6 | n=6 | 5.82 | | |
| 6a | n=7 | n=7 | 5.61 | | |
| |  |  | | | |
| 4b | n=5 | n=5 | 6.15[a] | | |
| 5b | n=6 | n=6 | 5.94 | | |
| 6b | n=7 | n=7 | 5.71 | | |
| 7a |  |  | 1.39 | 4.20 | 1.30 |
| 7b |  |  | 1.47 | 4.15 | 1.24 |
| 8a |  |  | 2.00 | 4.22 | 1.30 |
| 8b |  |  | 2.10 | 4.17 | 1.25 |
| 9a |  |  | 0.90 | 3.45<br>3.55[b] | 0.88 |
| 9b |  |  | 0.80 | 3.6 | 0.90 |
| 10a |  |  | 1.47 | | |
| 10b |  |  | 1.54 | | |

[a] Signal overlapped by other vinyl proton at 6.1−6.2 [b] Methylene protons separated (2 × dd).




1

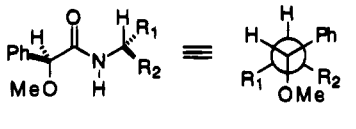



2

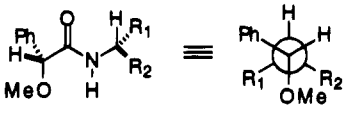
of the amides. The opposite sense of the differential anisotropy observed between esters and amides suggests two different conformations. The conformation depicted in structures **1** and **2** appears to be the most important conformation for amides of this type (for esters the methoxy group is *syn* periplanar to the carbonyl group). The amide NH stretching frequency in the IR (~3410 $cm^{-1}$) and the coupling constant between the amine proton and the α-proton ($J \sim 7-8$ Hz) support this contention. This proposed change in the rotamer populations between esters and amides may result from an intramolecular hydrogen bond between the amide hydrogen and the methoxy substitutent.[1a,12] The protons on the amine portion of the molecule, $R_1$ or $R_2$, feel an anisotropic magnetic shielding due to the phenyl ring on the *O*-methylmandelic acid moiety. When looking at this conformation, it is often convenient to view the amides via an "extended Newman projection" where the central amide linkage is omitted for clarity. The intervening amide linkage (O=C–N–H) defines a plane that divides the molecule into a right and left half when so viewed. In the extended Newman projection, the group ($R_1$ or $R_2$) located on the same side of that plane as the phenyl ring is thereby shielded with respect to the diastereomer in which the group ($R_1$ or $R_2$) is on the same side as the hydrogen. This effect can be observed by comparing the differences in the $^1H$ NMR chemical shifts of the diastereomers. In **1**, the protons of $R_1$ are shielded (shifted upfield) relative to the protons of $R_1$ in **2**. The reverse is true for protons of $R_2$. For example, in Table 1, the vinyl proton ($H_a$) of entry 1a (*S,S*) is on the same side as the hydrogen, and its chemical shift occurs at δ 5.75. In the opposite diastereomer, 1b (*S,R*), $H_a$ is on the same side of the molecule as the phenyl ring (shielded), and its chemical shift is upfield at δ 5.65. This conformational model as well as the chemical shift trends are consistent with previous literature observations for amides of this type.

It should be emphasized that this method is equally applicable when only a single amine enantiomer of unknown configuration is available. Coupling the amine to both (*S*)- and (*R*)-*O*-methylmandelic acid yields diastereomers **3** and **4**. Structure **3** is, in fact, the same as structure **2**, while structures **1** and **4** are enantiomers and therefore isochronous. Therefore, allowing for the fact that the structures are diastereomeric at the carboxylate center and not the amine center, the same reasoning (*vide supra*) can be used to establish the absolute configuration via the differences in the $^1H$ NMR shifts.

(12) Helmchen, G.; Ott, R.; Sauber, K. *Tetrahedron Lett.* **1972**, *37*, 3873 and references cited therein.



3



4

In summary, we report that *O*-methylmandelic acid, both enantiomers of which are available in optically pure form, can be used to determine the absolute configuration of α-chiral secondary amines via $^1H$ NMR spectroscopy. Amines and amine salts are easily derivatized without racemization. Subsequent examination of the difference in the $^1H$ NMR chemical shifts between diastereomers is related to the configuration of the amine through a model of opposite relative orientation to that of the *O*-methylmandelate esters. This is in contrast to the related α-(trifluoromethyl)-*O*-methylmandelamides and esters which follow similar conformational models. Simultaneously, the $^1H$ NMR spectra of the *O*-methylmandelamides provide a quantitative measure of the enantiomeric purities of the amines. This method appears to have general applicability to α-chiral primary amines in which the stereocenter contains a methine hydrogen.

## Experimental Section

**Method A. General Procedure.** (*S*)-*O*-Methylmandelic acid (1.15 equiv) and DCC (1.25 equiv) were added to a solution of the amine (1 equiv) in methylene chloride. The reaction was stirred at 25 °C until TLC indicated the disappearance of amine and filtered to remove the dicyclohexylurea and the product amide purified by flash chromatography.

**(1′*R*,4′*S*)-*N*-[4′-(Benzoyloxy)cyclohex-2′-enyl]-(*S*)-2-methoxy-2-phenylacetamide (Table 1, Entry 5a).** (*S*)-*O*-Methylmandelic acid (14 mg, 0.08 mmol) and 17 mg of DCC (0.087 mmol) were added to a solution of (1*R*,4*S*)-4-(benzoyloxy)-cyclohex-2-enyl amine (17.4 mg, 0.08 mmol) in 0.7 mL of methylene chloride. The reaction was stirred at 25 °C for 5 h and filtered to remove the dicyclohexylurea and the product amide purified by flash chromatography on silica gel (30% EtOAc/hexanes) to give 24.0 mg (89%) of the amide as a clear oil: $[\alpha]_D = +77.1°$ (*c* 3.04, $CH_2Cl_2$); $R_f$ 0.16 (30% EtOAc/hexanes); IR (film from $CDCl_3$) 3402, 1716, 1674 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.07 (d, $J = 7.0$ Hz, 2 H), 7.56 (m, 1 H), 7.48–7.33 (m, 7 H), 6.85 (d, $J = 8.7$ Hz, 1 H), 6.01 (ddd, $J = 10.0, 4.0, 2.0$ Hz, 1 H), 5.82 (dd, $J = 10.0, 2.0$ Hz, 1 H), 5.46 (d, $J = 4.0$ Hz, 1 H), 4.64 (s, 1 H), 4.54 (m, 1 H), 3.37 (s, 3 H), 2.02 (m, 3 H), 1.85 (m, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.9, 166.0, 136.9, 133.4, 133.0, 130.4, 129.6, 128.6, 128.5, 128.3, 127.0, 83.7, 67.1, 57.1, 44.3, 26.2, 25.6. Anal. Calcd for $C_{22}H_{23}NO_4$: C, 72.30; H, 6.35; N, 3.83. Found: C, 72.40; H, 6.36; N, 3.83.

**Method B. General Procedure.** Triethylamine (4 equiv) was added to a stirred solution of the amine salt (1 equiv), (*S*)-*O*-methylmandelic acid (1.1 equiv), DCC (1.3 equiv), and DMAP (0.05 equiv) in methylene chloride (0.2 M). The reaction was stirred overnight at 25 °C and filtered to remove the dicyclohexylurea and the product amide purified by flash chromatography.

**(*S*)-*N*-((*S*)-2-Methoxy-2-phenylacetyl)alanine Ethyl Ester (Table 1, Entry 7a).** Triethylamine (40.5 mg, 0.40 mmol) was added to a stirred solution of 15.4 mg of (*S*)-alanine ethyl ester hydrochloride (0.1 mmol), 18.3 mg of (*S*)-*O*-methylmandelic acid (0.11 mmol), 26.8 mg of DCC (0.13 mmol), and 1.2 mg of DMAP (0.01 mmol) in 0.5 mL of methylene chloride. The reaction was stirred overnight at 25 °C and filtered to

remove the dicyclohexylurea and the product amide purified by flash chromatography on silica gel (30% EtOAc/hexanes) to give 24.1 mg (91%) of the amide as a clear oil: $[\alpha]_D = +54.6°$ (c 2.36, $CH_2Cl_2$); $R_f$ 0.54 (50% EtOAc/hexanes); IR (solution, $CDCl_3$) 3412, 1739, 1679 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.2–7.4 (m, 6 H), 4.63 (s, 1 H), 4.58 (dq, J = 7.6, 7.2 Hz, 1 H), 4.2 (q, J = 7.1 Hz, 2 H), 3.4 (s, 3 H), 1.39 (d, J = 7.2 Hz, 3 H), 1.30 (t, J = 7.1 Hz, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 172.9, 170.2, 136.9, 128.5, 128.4, 126.9, 83.6, 61.5, 57.4, 47.5, 18.4, 14.1. Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.37; H, 7.22; N, 5.28. Found: C, 63.57; H, 7.29; N, 5.27.

**Method C. General Procedure.** (*S*)-*O*-Methylmandelic acid (1 equiv) was added to a stirred suspension prepared by the slow addition of oxalyl chloride (1.1 equiv) to DMF (1.5 equiv) in acetonitrile (0.3 M) at 0 °C. After 5 min, a solution of the amine (1.1 equiv) in pyridine (2.2 equiv) was slowly added. After being stirred for 30 min the reaction mixture was diluted with diethyl ether, washed twice with saturated aqueous copper sulfate, dried over magnesium sulfate, and purified by flash chromatography.

**(*S*)-*N*-(α-Methylbenzyl)-(*S*)-2-methoxy-2-phenylacetamide (Table 1, Entry 10a).** (*S*)-*O*-Methylmandelic acid (66.5 mg, 0.4 mmol) was added to a stirred suspension prepared by the slow addition of 55.8 mg of oxalyl chloride (0.44 mmol) to 43.9 mg of DMF (0.6 mmol) in 1.3 mL of acetonitrile at 0 °C. After 5 min, a solution of 53.3 mg of (*S*)-α-methylbenzylamine (0.44 mmol) in 70 μL of pyridine was slowly added. After being stirred for 30 min, the reaction mixture was diluted with 20 mL of diethyl ether, washed with 2 × 5 mL of saturated aqueous copper sulfate, dried over magnesium sulfate, and purified by flash chromatography on silica gel (30% EtOAc/hexanes) to give 82.8 mg (77%) of the amide as a white solid: mp 120–122 °C; $[\alpha]_D = +4.2°$ (c 4.14, $CH_2Cl_2$); $R_f$ 0.61 (50% EtOAc/hexanes); IR (solution, $CDCl_3$) 3413, 1671 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.2–7.4 (m, 10 H), 7.0 (d, J = 7.5 Hz, 1 H), 5.1 (dq, J = 7.5, 6.9 Hz, 1 H), 4.6 (s, 1 H), 3.3 (s, 3 H), 1.47 (d, J = 6.9 Hz, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.5, 143.0, 137.0, 128.6, 128.5, 128.3, 127.3, 126.9, 83.6, 57.1, 48.2, 21.6. Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.81; H, 7.11; N, 5.16.

**(*S*)-*N*-(2′-Cyclopentenyl)-(*S*)-2-methoxy-2-phenylacetamide (Table 1, entry 1a):** $[\alpha]_D = +37.0°$ (c 5.20, $CH_2Cl_2$); $R_f$ 0.52 (50% EtOAc/hexanes); IR (film from $CDCl_3$) 3413, 1680 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.3–7.4 (m, 5 H), 6.7 (d, J = 7.3 Hz, 1 H), 5.9 (m, 1 H), 5.7 (m, 1 H), 5.0 (m, 1 H), 4,6 (s, 1 H), 3.3 (s, 3 H), 2.4–2.5 (m, 1 H), 2.3 (m, 2 H), 1.5 (m, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.7, 137.1, 134.8, 130.9, 128.5, 128.3, 127.0, 83.7, 57.1, 54.9, 31.2, 31.1. Anal. Calcd for $C_{14}H_{17}NO_2$: 231.12592. Found: 231.12605.

**(*S*)-*N*-(2′-Cyclohexenyl)-(*S*)-2-methoxy-2-phenylacetamide (Table 1, entry 2a):** $[\alpha]_D = +30.6°$ (c 2.31, $CH_2Cl_2$); $R_f$ 0.53 (50% EtOAc/hexanes); IR (film from $CDCl_3$) 3413, 1666 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.3–7.4 (m, 5 H), 6.7 (d, J = 7.4 Hz, 1 H), 5.85–5.95 (m, 1 H), 5.65 (m, 1 H), 5.0 (m, 1 H), 4.6 (s, 1 H), 4.5 (m, 1 H), 3.35 (s, 3 H), 2.0–2.1 (m, 2 H), 1.8–1.9 (m, 1 H), 1.6–1.7 (m, 2 H), 1.5 (m, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.7, 137.2, 131.1, 128.5, 128.4, 127.5, 127.0, 83.8, 57.1, 44.1, 29.3, 24.8, 19.7. Anal. Calcd for $C_{15}H_{19}NO_2$: 245.14160. Found: 245.14146.

**(*S*)-*N*-(2′-Cycloheptenyl)-(*S*)-2-methoxy-2-phenylacetamide (Table 1, entry 3a):** mp 91–97 °C; $[\alpha]_D = +49.8°$ (c 1.88, $CH_2Cl_2$); $R_f$ 0.56 (50% EtOAc/hexanes); IR (solution, $CDCl_3$) 3413, 1670 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.3–7.4 (m, 5 H), 6.9 (bd, J = 7.8 Hz, 1 H), 5.8–5.9 (m, 1 H), 5.6 (dm, J = 11.5 Hz, 1 H), 4.6 (s, 1 H), 4.6 (m, 1 H), 3.4 (s, 3 H), 2.1–2.2 (m, 2 H), 1.8–1.9 (m, 1 H), 1.6–1.8 (m, 3H), 1.5–1.6 (m, 1 H), 1.3–1.4 (m, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.3, 137.2, 134.4, 132.5, 128.5, 128.3, 126.9, 83.8, 57.2, 49.8, 33.9, 28.5, 27.5, 26.7. Anal. Calcd for $C_{15}H_{19}NO_2$: 259.15723. Found: 259.15703.

**(1′*R*, 4′*S*)-*N*-[4′-(Benzoyloxy)cyclopent-2′-enyl]-(*S*)-2-methoxy-2- phenylacetamide (Table 1, entry 4a):** $[\alpha]_D = +61.7°$ (c 1.07, $CH_2Cl_2$); $R_f$ 0.18 (30% EtOAc/hexanes); IR (film from $CDCl_3$) 3408, 1715, 1674 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 7.0 Hz, 2 H), 7.58 (t, J = 7.6 Hz, 1 H), 7.48–7.32 (m, 7 H), 6.89 (d, J = 9.0 Hz, 1 H), 6.15 (m, 1 H), 6.01 (m, 1 H), 5.83 (m, 1 H), 5.03 (m, 1 H), 4.62 (s, 1 H), 3.34 (s, 3 H), 2.96 (m, 1 H), 1.79 (dt, J = 14.5, 3.9 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.7, 166.1, 136.8, 133.1, 132.9, 129.6, 128.6, 128.5, 128.4, 127.0, 83.7, 78.2, 57.1, 38.7. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.76; H, 6.03; N, 3.99. Found: C, 71.80; H, 6.22; N, 3.98.

**(1′*R*,4′*S*)-*N*-[4′-(Benzoyloxy)cyclohept-2′-enyl]-(*S*)-2-methoxy-2- phenylacetamide (Table 1, entry 6a):** $[\alpha]_D = +70.9°$ (c 1.28, $CH_2Cl_2$); $R_f$ 0.43 (50% EtOAc/hexanes); IR (solution $CDCl_3$) 3409, 1714, 1671 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 7.0 Hz, 2 H), 7.57 (appt, J = 7.3 Hz, 1 H), 7.47–7.32 (m, 7 H), 6.93 (d, J = 8.3 Hz, 1H), 5.84 (dt, J = 12, 2.8 Hz, 1H), 5.65–5.56 (m, 3H), 4.62 (m, 2H), 3.35 (s, 3H), 2.06–1.65 (m, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 169.4, 165.6, 136.8, 134.0, 133.3, 132.9, 130.3, 129.5, 128.5, 128.4, 128.3, 126.9, 83.6, 74.0, 57.1, 49.6, 33.7, 32.4, 23.6. Anal. Calcd for $C_{23}H_{25}NO_4$: C, 72.79; H, 6.64; N, 3.69. Found: C, 72.53; H, 6.77; N, 3.75.

**(*S*)-*N*-((*S*)-2-Methoxy-2-phenylacetyl)methionine Ethyl Ester (Table 1, entry 8a):** $[\alpha]_D = +56.9°$ (c 2.96, $CH_2Cl_2$); $R_f$ 0.56 (50% EtOAc/hexanes); IR (solution $CDCl_3$) 3406, 1736, 1679 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 6 H), 4.7 (dt, J = 7.98, 5.0 Hz, 1H), 4.6 (s, 1 H), 4.2 (q, J = 7.1 Hz, 2H), 3.4 (s, 3H), 2.3–2.4 (m, 2 H), 2.1–2.2 (m, 1H), 1.9–2.0 (m, 1 H), 2.0 (s, 3 H), 1.3 (t, J = 7.1 Hz, 3 H); $^{13}C$ NMR (50 MHz, $CDCl_3$) δ 171.7, 170.6, 136.9, 128.5, 128.4, 126.7, 83.7, 61.6, 57.4, 50.9, 31.9, 29.7, 15.38, 14.1. Anal. Calcd for $C_{16}H_{23}NO_4S$: C, 59.05; H, 7.12; N, 4.31. Found: C, 59.20; H, 7.25; N, 4.32.

**(*R*)-*N*-[1-[(*tert*-Butyldimethylsiloxy)methyl]propyl]-(*S*)-2-methoxy-2- phenylacetamide (Table 1, entry 9a):** $[\alpha]_D = +89.1°$ (c 5.08, $CH_2Cl_2$); $R_f$ 0.48 (30% EtOAc/hexanes); IR (solution $CDCl_3$) 3414, 1667 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 7.3 (m, 5 H), 6.85 (d, J = 8.8 Hz, 1 H), 4.5 (s, 1 H), 3.75 (m, 1 H), 3.55 (dd, J = 10.0, 2.8 Hz, 1H), 3.45 (dd, J = 10.0, 3.8 Hz, 1 H), 3.3 (s, 3 H), 1.5–1.6 (m, 2 H), 0.9 (t, J = 7.5 Hz, 3H), 0.88 (s, 9 H), −0.05 (s, 6 H); $^{13}C$ NMR (50 MHz, $CDCl_3$) δ 169.9, 137.2, 128.4, 128.2, 126.9, 83.8, 63.7, 57.1, 51.3, 25.7, 24.3, 18.1, 10.5, −5.6, −5.7. Anal. Calcd for $C_{19}H_{33}NO_3Si$: C, 64.91; H, 9.46; N, 3.99. Found: C, 64.73; H, 9.53; N, 4.20.

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**Supplementary Material Available:** $^{13}C$ NMR spectra for entries 1a, 2a, and 3a of Table 1 (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.