Supporting Information

“Novel Fragmentation Reaction of 2-Alkyl- and 2,4-Dialkyl-3-iodo-1-oxocyclohexan-2,4-carbolactone”

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All reported reactions were performed in flame-dried glassware under a dry nitrogen atmosphere. Reaction mixtures were stirred magnetically. Unless otherwise noted, all reagents were obtained from commercial sources and used without further purification. Hygroscopic liquids were transferred via syringe or cannula. Anhydrous solvents and reagents were obtained by distillation from the indicated reagents: dimethyl sulfoxide (DMSO) from CaH_2 , N,N-dimethylformamide (DMF) from CaH_2 , diethyl ether from sodium/benzophenone ketyl, pentane from CaH_2 , tetrahydrofuran (THF) from sodium/benzophenone ketyl, methylene chloride (CH_2Cl_2) from P_2O_5 or CaH_2 , carbon tetrachloride (CCl_4) from P_2O_5 , benzene from P_2O_5 or CaH_2 , toluene from P_2O_5 or CaH_2 , triethyl amine (Et_3N) from CaH_2 , pyridine from CaH_2 , acetonitrile from CaH_2 , and diisopropylamine from CaH_2 . Analytical thin-layer chromatography was performed on silica gel 60 (F-254). Visualization of spots was effected by iodine (I_2) vapor and if necessary, treatment of the plate with 25% (w/w) phosphomolybdic acid hydrate solution in 95% ethanol solution or with a 2.5% solution of anisaldehyde in ethanol containing 6% H_2SO_4 and 2% acetic acid followed by charring on a hot plate. Flash column chromatography was performed on silica gel 60 (230-400 mesh). Gravity-driven column chromatography was performed on silica gel 60 (70-230 mesh).

Melting points were measured in open capillaries and are uncorrected. ^1H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded in CDCl_3 solution unless otherwise noted. ^{19}F NMR spectra (470 MHz) were recorded in CDCl_3 and trifluoroacetic acid (TFA) was used as an external standard. Infrared (IR) spectra were obtained on a FT-IR spectrometer. The samples were prepared as neat oils or thin film. Bands are in units of cm^{-1} . Optical rotations were obtained on a polarimeter. Optical rotations ($[\alpha]$) were reported in degrees times 100 per centimeter at the specified temperature, and the concentration (c) was given in grams per 100 mL in CHCl_3 unless otherwise noted. Low resolution mass spectra (CI, isobutane) were reported as m/z and relative intensity.

(S)-2-Methoxy-1-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (5). This compound was prepared by literature methods (Schultz, A. G.; Macielag, M.; Sundararaman, P.; Taveras, A. G.; Welch, M. *J. Am. Chem. Soc.* **1988**, *110*, 7828).

(S)-2-Methoxy-1-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-5-methylbenzene (6). This compound was prepared by literature methods (Schultz, A. G.; Macielag, M.; Sundararaman, P.; Taveras, A. G.; Welch, M. *J. Am. Chem. Soc.* **1988**, *110*, 7828).

(S)-5-Benzyl-2-Methoxy-1-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]benzene (7).
1-(4'-Methoxyphenyl)-1-phenylmethanol. To a solution of PhMgBr (10 mL, 1 M in THF, 10 mmol) in diethyl ether (15 mL) was added *p*-anisaldehyde (0.60 mL, 5.00 mmol) in diethyl ether (5 mL) and heated at reflux for 6 h. The reaction mixture was quenched with water and extracted with CH₂Cl₂. The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography (hexanes/EtOAc, 7:1) of the crude residue gave alcohol (0.97 g, 92%) as a white solid. ¹H NMR 7.36-7.26 (m, 7H), 6.87 (dd, *J* = 8.9, 3.0 Hz, 2H), 5.82 (s, 1H), 3.79 (s, 3H); ¹³C NMR 143.8, 136.0, 128.6, 127.7, 127.1, 123.9, 126.2, 113.7, 75.6, 55.1; IR 3300 cm⁻¹.

4-Benzyl-1-methoxybenzene. To a solution of alcohol (6.00 g, 28.0 mmol) in 95% ethanol (150 mL) was added Raney Nickel (ca. 5 g). The reaction mixture was heated at reflux for 5 h. After filtration of the catalyst, the solvent was evaporated. The residue was dissolved in CH₂Cl₂, washed with brine, dried over Na₂SO₄, and concentrated to give anisole (5.25 g, 94%) as a yellow oil. ¹H NMR 7.31-7.13 (m, 7H), 6.85 (d, *J* = 6.6 Hz, 2H), 3.95 (s, 2H), 3.79 (s, 3H); ¹³C NMR 157.8, 141.5, 133.1, 129.7, 128.7, 128.6, 128.3, 127.0, 125.8, 113.7, 55.1, 40.9; IR 2931 cm⁻¹.

5-Benzyl-2-methoxybenzoic acid. To a solution of anisole (0.36 g, 11.9 mmol), TMEDA (*N,N,N',N'*-tetramethylethylenediamine, 1.70 mL, 11.9 mmol) in THF (75 mL) was added *s*-BuLi (38.0 mL, 1.3 M in cyclohexane, 30.0 mmol) dropwise at -78 °C and the resulting mixture

was stirred for 8 h. The reaction solution was then transferred to excess amount of dry ice in diethyl ether. After complete evaporation of dry ice, the solution was acidified with 1 N HCl solution. The resulting mixture was extracted with CH₂Cl₂ and the combined organic layers were dried over Na₂SO₄ and concentrated in vacuo to give benzoic acid (2.12 g, 75%) as a light yellow solid. ¹H NMR 8.06 (d, *J* = 2.2 Hz, 1H), 7.36 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.34-7.15 (m, 5H), 6.97 (d, *J* = 8.5 Hz, 1H), 4.04 (s, 3H), 3.97 (s, 2H); ¹³C NMR 156.4, 140.3, 135.3, 133.8, 128.7, 128.5, 126.2, 117.2, 56.6, 40.6; IR 3300, 1650 cm⁻¹.

(2S')-5-Benzyl-1-[2'-(hydroxymethyl)pyrrolidinyl]carbonyl-2-methoxybenzene. A solution of acid (1.88 g, 7.77 mmol) in SOCl₂ (10.0 mL, 0.13 mmol) was heated at reflux for 3 h. The excess SOCl₂ was evaporated. The residue was dissolved in CH₂Cl₂ (50 mL) and cooled to 0 °C. Et₃N (2.70 mL, 19.5 mmol) and (*S*)-prolinol (0.94 g, 9.32 mmol) was added to the solution and the stirred for 3 h at 0 °C. The reaction mixture was stirred additional 12 h at room temperature. The reaction mixture was quenched with water and extracted with CH₂Cl₂. The combined organic layers were washed with saturated NaHCO₃ and brine, dried over MgSO₄ and concentrated in vacuo to give amide (2.46 g, 97%) as a light yellow solid. ¹H NMR 7.30-6.83 (m, 8H), 4.33 (m, 1H), 3.92 (s, 2H), 3.82 (s, 3H), 3.68 (q, *J* = 7.3 Hz, 2H), 3.28 (m, 2H), 2.15 (m, 1H), 1.82 (m, 1H), 1.74 (m, 1H), 1.64 (1H).

(2S')-5-Benzyl-2-methoxy-1-[2'-(methoxymethyl)pyrrolidinyl]carbonylbenzene. To a solution of acid (2.46 g, 7.56 mmol) and MeI (0.94 mL, 15.1 mmol) in THF (150 mL) was added NaH (0.45 g, 18.9 mmol) portionwise at 0 °C. The reaction solution was stirred at for 3 h at 0 °C and then additional 12 h at room temperature. The reaction mixture was quenched with water and extracted with CH₂Cl₂. The combined organic layers were washed with brine, dried over MgSO₄ and concentrated in vacuo. Flash column chromatography (hexanes/EtOAc, 1:1) gave amide **7** (1.95 g, 76%) as a yellow sticky oil. ¹H NMR 7.29-6.81 (m, 8H), 4.40 (m, 1H), 3.91 (s, 2H), 3.80 (s, 3H), 3.72 (m, 1H), 3.53 (m, 1H), 3.40 (s, 2H), 3.20 (m, 1H), 2.98 (s, 1H),

2.00 (m, 2H), 1.93 (m, 2H), 1.75 (m, 1H); ^{13}C NMR 161.8, 156.4, 133.3, 130.3, 128.6, 128.2, 127.9, 125.9, 111.1, 72.1, 58.9, 56.0, 28.4

(S)-2-Methoxy-1-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-5-[(2'-methoxy)phenyl]benzene (8). To a solution of anisole (10.0 mL, 92.0 mmol) in THF (200 mL) at room temperature was added *n*-BuLi solution of 2.5 M in hexane (40.5 mL, 101.0 mmol). After stirring for 5 h the reaction mixture was cooled to $-78\text{ }^{\circ}\text{C}$, trimethyl borate (12.5 mL, 110.0 mmol) was added and the mixture was stirred for an additional 30 min at $-78\text{ }^{\circ}\text{C}$, then warmed to room temperature and stirred overnight. The reaction mixture was quenched with 10% HCl, diluted with EtOAc, and extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine (100 mL), dried over MgSO_4 , and concentrated to give colorless oil. Recrystallization from petroleum ether gave pure *o*-anisole boronic acid (8.95 g, 64%) as a pale white solid: ^1H NMR 7.84 (d, $J = 7.3\text{ Hz}$, 1H), 7.44 (t, $J = 7.3\text{ Hz}$, 1H), 7.02 (t, $J = 7.3\text{ Hz}$, 1H), 6.90 (d, $J = 7.3\text{ Hz}$, 1H), 6.27 (br, 2H), 3.90 (s, 3H),

To a solution of 5-iodosalicylic acid (2.64 g, 10.0 mmol) in acetone (150 mL) was added K_2CO_3 (5.52 g, 40.0 mmol) and dimethylsulfate (3.78 mL, 40.0 mmol). The solution was refluxed overnight, cooled to room temperature and then H_2O was added. Solvent was evaporated under reduced pressure and saturated aqueous NaHCO_3 solution was added until the mixture tested basic. The solution was then extracted with CH_2Cl_2 three times. The combined organic extracts were dried over Na_2SO_4 , concentrated, and purified by flash column chromatography (hexanes/EtOAc, 2:1) to give methyl 3-iodosalicylate as a white solid (2.86 g, 98%): ^1H NMR 8.02 (d, $J = 1.5\text{ Hz}$, 1H), 7.68 (dd $J = 7.6\text{ Hz}$, 1.5 Hz, 1H), 6.69 (d, $J = 7.6\text{ Hz}$, 1H), 3.83 (s, 3H), 3.80 (s, 3H); ^{13}C NMR 164.7, 158.6, 141.6, 139.6, 121.7, 114.3, 55.8, 51.9; IR (film) 1718 cm^{-1} ; CIMS 293 ($\text{M}^+ + 1$, 100%). Anal. Calcd for $\text{C}_9\text{H}_9\text{IO}_3$: C, 37.01; H, 3.11. Found: C, 37.28; H, 3.25.

Na_2CO_3 (1.80 g, 17.12 mmol) in water (18 mL) and *o*-anisole boronic acid (2.01 g, 13.15 mmol) in MeOH (18 mL) was added to a stirred solution of methyl 3-iodosalicylate (2.50 g, 8.56

mmol) and tetrakis(triphenylphosphine)palladium(0) (0.30 g, 0.26 mmol) in toluene (20 mL). The reaction mixture was refluxed overnight then cooled to room temperature and quenched with concentrated NH_4OH (6.0 mL) and saturated Na_2CO_3 solution (20 mL). The reaction mixture was then extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous MgSO_4 , and concentrated to give yellow oil. Flash column chromatography (hexanes/EtOAc, 5:1) of the crude residue provided methyl 2-methoxy-5-[(2'-methoxy)phenyl]benzoate (1.95 g, 7.20 mmol, 84%): ^1H NMR 7.83 (dd, $J = 7.9$ Hz, 1.8 Hz, 1H), 7.44 (dd, $J = 7.6$ Hz, 1.8 Hz, 1H), 7.38 (dt, $J = 7.6$ Hz, 1.8 Hz, 1H), 7.29 (dd, $J = 7.6$ Hz, 1.8 Hz, 1H), 7.20 (t, $J = 7.9$ Hz, 1H), 7.02 (m, 3H), 3.93 (s, 3H), 3.78 (s, 3H), 3.52 (s, 3H); ^{13}C NMR 166.8, 157.6, 156.5, 135.6, 133.5, 131.1, 130.2, 128.9, 126.5, 124.9, 122.9, 120.2, 110.7, 61.4, 55.4, 51.9; CIMS 273 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{O}_4$: C, 70.59; H, 5.92. Found: C, 69.95; H, 5.82.

A solution of potassium hydroxide (5.5 g, 98 mmol) in water (10.0 mL) was added to a solution of methyl 2-methoxy-5-[(2'-methoxy)phenyl]benzoate (2.66 g, 9.8 mmol) in MeOH (50 mL) at room temperature. The resultant reaction mixture was refluxed overnight then cooled to room temperature and concentrated. Water (10 mL) was added and extracted with CH_2Cl_2 (3×100 mL). The combined aqueous layers were acidified with 10% HCl (17 mL), and extracted with ethyl acetate (3×100 mL). The combined ethyl acetate layers were washed with brine (100 mL), dried over anhydrous MgSO_4 , and concentrated to give 2-methoxy-5-[(2'-methoxy)phenyl]benzoic acid (2.35 g, 93 %) as a pale white solid: ^1H NMR 8.09 (dd, $J = 7.9$ Hz, 1.9 Hz, 1H), 7.49 (dd, $J = 7.6$ Hz, 1.8 Hz, 1H), 7.39 (dt, $J = 7.6$ Hz, 1.8 Hz, 1H), 7.26 (dd, $J = 7.6$ Hz, 1.8 Hz, 1H), 7.24 (t, $J = 7.9$ Hz, 1H), 7.02 (m, 3H), 3.77 (s, 3H), 3.50 (s, 3H); ^{13}C NMR 166.8, 157.2, 156.2, 137.6, 132.1, 131.5, 130.8, 129.4, 125.4, 123.9, 121.8, 120.3, 110.8, 61.6, 55.3; CIMS 259 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{O}_4$: C, 69.76; H, 5.46. Found: C, 69.66; H, 5.49.

Oxalyl chloride (4.77 mL, 53.6 mmol) was added followed by DMF (0.20 mL, 2.50 mmol) to the stirred solution of 2-methoxy-5-[(2'-methoxy)phenyl]benzoic acid (13.2 g, 51.0 mmol) in CH₂Cl₂ (300 mL) at 0 °C. The reaction mixture was allowed to stir at room temperature for 5 h then cooled to -40 °C; a solution of (*S*)-prolinol (5.67 g, 56.1 mmol) in CH₂Cl₂ (20 mL) was added followed by triethylamine (14.3 mL, 102 mmol). The mixture was slowly warmed to room temperature and then stirred overnight. The mixture was washed with water and brine, and then the organic layer was dried and concentrated. The residue was dissolved in THF (100 mL) then cooled to 0 °C and treated with NaH (3.06 g, 76.5 mmol). After 30 min at room temperature, the mixture was cooled with an ice bath and iodomethane (MeI, 9.53 mL, 153.00 mmol) in THF (10 mL) was added dropwise. The mixture was stirred at 0 °C for 30 min followed by warming at room temperature for 30 min and then refluxed for additional 5 h. After cooling to 0 °C, the reaction mixture was quenched with saturated ammonium chloride and the solution was extracted with ethyl acetate (3×100 mL). The combined ethyl acetate layers were washed with brine (100 mL), dried over anhydrous MgSO₄, and concentrated to give very viscous pale colorless oil. Flash column chromatography (hexanes/EtOAc, 1:2) afforded **8** as a colorless viscous oil (11.38 g, 63 %): $[\alpha]_D^{24} -74.7$ (*c* 1.7); ¹H NMR (measured at 60 °C, a set of rotamers) 7.52 (m, 1H), 7.41 (m, 1H), 7.28 (m, 2H), 6.99 (t, *J* = 7.9 Hz, 1H), 6.94 (m, 2H), 3.77 (s, 3H), 3.50 (s, 3H); ¹³C NMR (measured at 60 °C, a set of rotamers) 167.8, 156.3, 154.2, 131.0, 130.9, 130.4, 130.3, 129.5, 128.7, 128.2, 127.1, 120.7, 111.3, 110.8, 73.3, 72.29, 58.84, 57.04, 56.1, 55.6, 55.5, 55.3, 48.4, 27.6, 24.1; IR (film) 3520, 3481, 2857, 2933, 1628, 1600, 1262 cm⁻¹; CIMS 356 (M⁺+1, 100). Anal. Calcd for C₂₁H₂₅NO₄: C, 70.96; H, 7.09. Found: C, 70.81; H, 7.15.

General Procedure for the Birch Reduction-Alkylation Reactions (5→9). Preparation of (2'*S*,6*S*)-1-Methoxy-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-6-methyl-1,4-

cyclohexadiene (9a). To a solution of the chiral benzamide **5** (2.63 g, 10.6 mmol) and *tert*-BuOH (1.0 mL, 10.6 mmol) in THF (10 mL) was condensed NH₃ (ca. 200 mL) at $-78\text{ }^{\circ}\text{C}$. Potassium metal (K) was added until the reaction solution became dark blue. The resulting solution was stirred for 0.5 h. Pipyrene was added until the solution turned to pale yellow. The resulting solution was stirred for 0.5 h. Methyl iodide (MeI, 2 mL, 11.8 mmol) was added dropwise via syringe. The solution was stirred for 4 h and quenched with solid NH₄Cl at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was stirred overnight at room temperature until NH₃ was completely evaporated. The resulting viscous residue was treated with water and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated to give **9a** (2.66 g, 95%). The crude residue was directly used for the next reaction without further purification: colorless oil; $[\alpha]_{\text{D}}^{27} -47.5$ (*c* 0.8); ¹H NMR 5.74 (dtd, *J* = 9.7, 3.4, 1.0 Hz, 1H), 5.49 (dt, *J* = 9.7, 2.0 Hz, 1H), 4.63 (br t, *J* = 3.4 Hz, 1H), 4.29 (m, 1H), 3.65-3.57 (m, 2H), 3.51 (s, 3H), 3.3 (s, 3H), 3.33-3.22 (m, 2H), 2.90 (dm, *J* = 22.4 Hz, 1H), 2.78 (dm, *J* = 22.4 Hz, 1H), 1.89-1.78 (m, 3H), 1.76-1.69 (m, 1H), 1.42 (s, 3H); ¹³C NMR 170.6 (s), 155.8 (s), 128.7 (d), 124.0 (d), 90.5 (d), 71.9 (t), 58.9 (q), 58.0 (d), 54.2 (q), 48.1 (s), 46.2 (t), 26.5 (t), 26.4 (t), 26.3 (q), 24.9 (t); IR 3483, 1682, 1633 cm⁻¹; CIMS 266 (M⁺+1, 100).

(2'S,6S)-6-[(3'-Chloro)propyl]-1-methoxy-6-[[2'-

(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (9b): colorless oil; $[\alpha]_{\text{D}}^{26} -32.2$ (*c* 0.9); ¹H NMR 5.87 (dt, *J* = 9.8, 3.5 Hz, 1H), 5.32 (dt, *J* = 9.8, 1.7 Hz, 1H), 4.75 (t, *J* = 3.5 Hz, 1H), 4.29-4.25 (m, 1H), 3.59-3.51 (m, 2H), 3.48 (s, 3H), 3.51-3.46 (m, 2H), 3.31 (s, 3H), 3.29-3.21 (m, 2H), 2.88 (dq, *J* = 22.7, 2.7 Hz, 1H), 2.76 (dq, *J* = 22.7, 3.7 Hz, 1H), 2.16-2.08 (m, 1H), 1.89-1.48 (m, 8H); ¹³C NMR 170.0, 152.6, 126.4, 126.3, 92.9, 71.9, 58.8, 58.1, 54.1, 51.5, 45.9, 45.3, 33.6, 27.7, 26.7, 26.2, 24.8; IR 1684, 1636 cm⁻¹; CIMS 330 (M⁺+1, 34), 328 (M⁺+1, 100).

(2'S,6S)-6-[(4'-Chloro)butyl]-1-methoxy-6-[[2'-

(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (9c): colorless oil; $[\alpha]_{\text{D}}^{26} -27.3$ (*c* 0.22); ¹H NMR 5.85 (br dt, *J* = 9.9, 3.3 Hz, 1H), 5.30 (br d, *J* = 9.9 Hz, 1H), 4.73 (br s, 1H),

4.27 (m, 1H), 3.60-3.55 (m, 2H), 3.50-3.48 (m, 2H), 3.47 (s, 3H), 3.30 (s, 3H), 3.22-3.21 (m, 1H), 2.87 (br dd, $J = 22.4, 2.1$ Hz, 1H), 2.76 (br d, $J = 22.4$ Hz, 1H), 2.03 (dt, $J = 12.6, 4.8$ Hz, 1H), 1.92-1.63 (m, 8H), 1.30-1.20 (m, 1H), 1.18-1.09 (m, 1H); ^{13}C NMR 170.4, 152.8, 126.5, 126.1, 92.9, 71.9, 58.8, 58.0, 54.1, 51.8, 45.9, 45.1, 35.0, 32.7, 26.7, 26.3, 24.8, 20.9; IR 1638 cm^{-1} ; CIMS 344 ($\text{M}^+ + 1$, 33), 342 ($\text{M}^+ + 1$, 100).

(2'S,6S)-6-[[2'-(2''-Bromo)phenyl]ethyl]-1-methoxy-6-[[2'-

(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (9d): colorless oil; $[\alpha]_{\text{D}}^{26} -30.0$ (c 0.2); R_f 0.67 (hexanes/EtOAc, 1:1); ^1H NMR 7.50 (dd, $J = 7.8, 0.7$ Hz, 1H), 7.21 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.16 (br t, $J = 7.8$ Hz, 1H), 6.98 (dt, $J = 7.8, 1.8$ Hz, 1H), 5.97 (dt, $J = 9.7, 3.3$ Hz, 1H), 5.47 (br d, $J = 9.7$ Hz, 1H), 4.84 (br t, $J = 3.3$ Hz, 1H), 4.33-4.28 (m, 1H), 3.84-3.60 (m, 2H), 3.54 (s, 3H), 3.33 (s, 3H), 3.31-3.24 (m, 2H), 2.99 (dq, $J = 22.6, 2.8$ Hz, 1H), 2.83 (dq, $J = 22.6, 3.7$ Hz, 1H), 2.58 (dt, $J = 13.2, 4.7$ Hz, 1H), 2.48 (dt, $J = 13.2, 4.7$ Hz, 1H), 2.33 (dt, $J = 13.2, 4.7$ Hz, 1H), 1.98 (dt, $J = 13.2, 4.7$ Hz, 1H), 1.95-1.71 (m, 4H); ^{13}C NMR 170.2, 152.7, 142.1, 132.4, 130.4, 127.2, 127.1, 126.5, 126.4, 124.5, 93.0, 71.9, 58.8, 54.1, 52.0, 46.0, 36.1, 30.7, 26.8, 26.3, 24.9; IR 1683, 1633 cm^{-1} ; CIMS 436 ($\text{M}^+ + 1$, 23), 142 (100).

(2'S,6S)-6-[[3'-(Benzyloxy)propyl]-1-methoxy-6-[[2'-

(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (9e): yellow oil; $[\alpha]_{\text{D}}^{25} -72.8$ (c 3.1); ^1H NMR 7.35 (m, 4H), 7.22 (m, 1H), 5.90 (dt, $J = 9.8, 3.1$ Hz, 1H), 5.38 (dt, $J = 9.8, 2.0$ Hz, 1H), 4.78 (m, 1H), 4.48 (s, 2H), 4.35 (m, 1H), 3.78 (m, 1H), 3.65 (dm, $J = 9.5$ Hz, 1H), 3.63 (d, $J = 11.8$ Hz, 1H), 3.55 (s, 3H), 3.48 (d, $J = 11.8$ Hz, 1H), 3.35 (s, 3H), 3.24 (m, 3H), 2.92 (dm, $J = 19.5$ Hz, 1H), 2.81 (dm, $J = 19.5$ Hz, 1H), 2.11 (dt, $J = 13.2, 4.7$ Hz, 1H), 1.90-1.60 (m, 6H), 1.50 (m, 1H), 1.39 (m, 1H); ^{13}C NMR 170.2, 152.8, 130.5, 128.4, 128.0, 127.8, 126.1, 97.9, 73.2, 72.1, 71.5, 71.2, 59.5, 58.4, 54.1, 46.0, 33.8, 27.9, 27.0, 25.5; IR 1632 cm^{-1} ; CIMS 400 ($\text{M}^+ + 1$, 100).

(2'S,6S)-1-Methoxy-6-[[2'-(methoxymethyl)-pyrrolidinyl]carbonyl]-6-[[2'-

trimethylsilyl)ethoxy]methyl]-1,4-cyclohexadiene (9f): yellow oil; $[\alpha]_{\text{D}}^{25} -82.8$ (c 7.2); ^1H

NMR 5.91 (dt, $J = 9.7, 3.0$ Hz, 1H), 5.47 (d, $J = 9.7$ Hz, 1H), 4.79 (m, 1H), 4.30 (m, 1H), 3.84 (d, $J = 9.5$ Hz, 1H), 3.76 (d, $J = 9.5$ Hz, 1H), 3.52 (m, 3H), 3.50 (s, 3H), 3.25 (m, 1H), 2.90 (dm, $J = 19.4$ Hz, 1H), 2.75 (dm, $J = 19.4$ Hz, 1H), 1.90-1.65 (m, 6H), 0.87 (m, 2H), -0.05 (s, 9H); ^{13}C NMR 169.8, 152.0, 127.0, 125.8, 93.8, 73.5, 72.0, 68.9, 58.4, 57.9, 54.2, 52.8, 45.7, 27.2, 26.4, 24.8, 18.0, -1.4; IR 1628 cm^{-1} ; CIMS 382 ($\text{M}^+ + 1$, 100).

(2'S,6S)-4,6-Dimethyl-1-methoxy-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (9g): light yellow oil; R_f 0.60 (hexanes/EtOAc, 1:1); $[\alpha]_D^{25} -24.2$ (c 1.2); ^1H NMR 5.16 (d, $J = 1.5$ Hz, 1H), 4.59 (t, $J = 3.4$ Hz, 1H), 4.26 (m, 1H), 3.60 (m, 1H), 3.48 (s, 3H), 3.31 (s, 3H), 3.28 (m, 3H), 2.65 (AB q, $J = 22.0$ Hz, 2H), 1.90 (m, 3H), 1.89 (s, 3H), 1.36 (s, 3H); ^{13}C NMR 171.2, 156.1, 131.6, 123.7, 90.7, 72.2, 59.0, 58.1, 54.5, 49.1, 46.3, 31.5, 26.6, 26.5, 25.1, 22.5; IR 1633 cm^{-1} ; CIMS 280 ($\text{M}^+ + 1$, 100).

(2'S,6S)-6-Ethyl-1-methoxy-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-4-methyl-1,4-cyclohexadiene (9h): light yellow oil; R_f 0.65 (hexanes/EtOAc, 1:1); ^1H NMR 5.0 (s, 1H), 4.75 (t, $J = 3.5$ Hz, 1H), 4.30 (s, 1H), 3.62 (dd, $J = 10.0, 4.0$ Hz, 1H), 3.50 (s, 1H), 3.49 (s, 3H), 3.33 (s, 3H), 3.29-3.26 (m, 2H), 2.77 (d, $J = 20.0$ Hz, 1H), 2.66 (d, $J = 20.0$ Hz, 1H), 2.05 (m, 2H), 1.84-1.75 (m, 2H), 1.74 (s, 3H), 1.73-1.66 (m, 2H), 0.66 (t, $J = 7$ Hz, 3H); ^{13}C NMR 171.0, 152.6, 133.4, 121.2, 92.8, 71.8, 58.6, 57.8, 54.0, 53.0, 45.6, 31.4, 28.6, 26.1, 24.7, 22.0, 13.9, 7.7; CIMS 294 ($\text{M}^+ + 1$, 100).

(2'S,6S)-6-(4'-Pentenyl)-1-methoxy-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-4-methyl-1,4-cyclohexadiene (9i): colorless oil; $[\alpha]_D^{23} -32.6$ (c 4.2); ^1H NMR 5.80-5.75 (m, 1H), 5.01 (s, 1H), 4.96-4.86 (m, 2H), 4.71 (m, 1H), 4.28-4.26 (m, 1H), 3.60-3.58 (m, 1H), 3.47 (s, 3H), 3.45-3.32 (m, 1H), 3.31 (s, 3H), 3.29-3.22 (m, 2H), 2.80-2.75 (d, $J = 22.0$ Hz, 1H), 2.64-2.60 (d, $J = 22.0$ Hz, 1H), 2.05-2.00 (m, 3H), 1.85-1.76 (m, 3H), 1.71 (s, 3H), 1.70-1.65 (m, 2H), 1.17-1.07 (m, 2H); ^{13}C NMR 170.4, 152.7, 138.8, 132.8, 121.2, 113.4, 92.1, 71.4, 58.3, 57.5, 53.7, 52.1, 45.2, 35.4, 33.5, 31.0, 25.8, 24.4, 22.8, 21.7; IR 2929, 1634 cm^{-1} ; CIMS 334 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_{20}\text{H}_{31}\text{NO}_3$ ($\text{M}^+ + 1$) 334.2382, found 334.2389.

(2'S,6S)-1-Methoxy-6-[[2'-(4''-methoxy)benzyloxy]ethyl]-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-4-methyl-1,4-cyclohexadiene (9j): colorless oil; R_f 0.50 (hexanes/EtOAc, 1:1); $[\alpha]_D^{30}$ -36.0 (c 1.0); ^1H NMR 7.22 (d, $J = 8.5$ Hz, 2H), 6.84 (d, $J = 8.5$ Hz, 2H), 5.12 (s, 1H), 4.67 (t, $J = 3.5$ Hz, 1H), 4.37 (s, 2H), 4.30 (m, 1H), 3.79 (s, 3H), 3.60 (dd, $J = 9.5, 3.2$ Hz, 1H), 3.46 (s, 3H), 3.43 (m, 2H), 3.33 (s, 3H), 3.28 (m, 2H), 2.65 (dq, $J = 21.9, 3.5$ Hz, 2H), 2.40 (m, 1H), 2.06 (m, 1H), 1.80 (m, 2H), 1.71 (s, 3H); ^{13}C NMR 170.5, 159.1, 153.3, 133.5, 131.2, 129.4, 121.7, 113.8, 92.6, 72.19, 72.16, 67.2, 59.1, 58.3, 55.4, 54.4, 51.4, 46.0, 36.0, 31.7, 26.5, 25.1, 22.4; IR 1632 cm^{-1} ; CIMS 430 ($\text{M}^+ + 1$, 100).

(2'S,6S)-4-Benzyl-6-ethyl-1-methoxy-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-1,4-cyclohexadiene (9k): light yellow oil; R_f 0.80 (hexanes/EtOAc, 1:1); ^1H NMR 7.29-7.14 (m, 5H), 5.17 (s, 1H), 4.70 (t, $J = 3.5$ Hz, 1H), 4.3 (m, 1H), 3.62 (dd, $J = 9.5, 3.2$ Hz, 1H), 3.51 (m, 1H), 3.46 (s, 3H), 3.33 (s, 3H), 3.30 (m, 1H), 3.15 (m, 1H), 2.74 (d, $J = 21.8$ Hz, 1H), 2.59 (dd, $J = 21.8, 3.5$ Hz, 1H), 2.06 (m, 1H), 1.81 (m, 3H), 1.78 (m, 1H), 1.65 (m, 1H), 0.68 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR 170.6, 152.3, 139.1, 136.8, 128.4, 128.0, 126.0, 122.5, 92.6, 71.8, 58.6, 57.7, 53.9, 53.0, 45.7, 43.0, 29.7, 28.6, 26.7, 25.3, 24.7, 7.8; IR 2900, 1600 cm^{-1} .

(2'S,6S)-1-Methoxy-6-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-4-[(2'-methoxy)phenyl]-6-methyl-1,4-cyclohexadiene (9l): colorless oil; $[\alpha]_D^{24}$ -152.3 (c 1.0); ^1H NMR 7.24-7.20 (ddd, $J = 7.9, 2.1, 1.5$ Hz, 1H), 7.09 (dd, $J = 7.9, 1.5$ Hz, 1H), 6.91 (dd, $J = 7.9, 1.5$ Hz, 1H), 6.84 (d, $J = 7.9$ Hz, 1H), 5.50 (s, 1H), 4.71 (t, $J = 0.8$ Hz, 1H), 4.38 (m, 1H), 3.89 (m, 1H), 3.76 (s, 3H), 3.63 (dd, $J = 9.5, 1.5$ Hz, 1H), 3.54 (s, 3H), 3.35 (m, 4H), 3.20 (m, 2H), 3.08 (m, 1H), 1.96-1.65 (m, 4H), 1.49 (s, 3H); ^{13}C NMR 170.4, 156.6, 155.1, 134.1, 130.9, 129.1, 128.3, 127.4, 120.4, 110.6, 90.9, 71.8, 58.6, 57.8, 55.1, 54.2, 48.6, 46.1, 29.8, 26.3, 25.9, 24.8; IR 2933, 1684 cm^{-1} ; CIMS 372 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_4$: C, 71.13; H, 7.87. Found: C, 70.93; H, 7.97.

General Procedure for the Hydrolysis of 9. Preparation of (2S,2'S)-2-Methyl-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10a). To a solution of the

crude **5a** (2.66 g, 10 mmol) in MeOH (10 mL) was added 6 N aqueous HCl solution (10 mL) at room temperature. The resulting solution was stirred for 3 h. The reaction mixture was extracted with CH₂Cl₂. The separated organic layers were dried over anhydrous Na₂SO₄ and concentrated. Flash column chromatography (hexanes/EtOAc, 1:1) of the crude residue gave **10a** (2.4 g, 90% for two steps): colorless oil; $[\alpha]_D^{24}$ -84.4 (*c* 0.45); ¹H NMR 5.89 (m, 2H), 5.60 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.59 (dd, *J* = 9.3, 3.4 Hz, 1H), 3.30 (s, 3H), 3.29-3.21 (m, 2H), 3.02-2.98 (m, 1H), 2.61-2.42 (m, 4H), 1.90-1.67 (m, 4H), 1.39 (s, 3H); ¹³C NMR 130.5, 126.8, 71.6, 58.8, 57.6, 57.5, 46.3, 35.7, 26.6, 25.7, 24.3, 24.0; IR 1711, 1634 cm⁻¹; CIMS 252 (M⁺+1, 100); HRMS calcd for C₁₄H₂₁NO₃ (M⁺+1) 252.1599, found 252.1597.

(2*S*,2'*S*)-2-[(3'-Chloro)propyl]-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10b): colorless oil; $[\alpha]_D^{24}$ -48.5 (*c* 0.33); ¹H NMR 5.97 (br dt, *J* = 9.8, 4.5 Hz, 1H), 5.65 (dm, *J* = 9.8 Hz, 1H), 4.22 (m, 1H), 3.59 (dd, *J* = 9.4, 3.3 Hz, 1H), 3.56-3.44 (m, 2H), 3.38-3.24 (m, 2H), 3.32 (s, 3H), 3.18-3.02 (m, 1H), 2.54-2.44 (m, 4H), 2.09-2.00 (m, 1H), 1.94-1.79 (m, 5H), 1.77-1.67 (m, 2H); ¹³C NMR 207.7, 168.2, 129.2, 127.9, 110.2, 71.8, 60.9, 58.9, 57.9, 46.7, 45.3, 36.6, 34.0, 28.1, 26.7, 25.9, 24.5; IR 1708, 1633 cm⁻¹; CIMS 316 (M⁺+1, 33), 314 (M⁺+1, 100); HRMS calcd for C₁₆H₂₄ClNO₃ (M⁺+1) 314.1523, found 314.1515.

(2*S*,2'*S*)-2-[(4'-Chloro)butyl]-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10c): colorless oil; $[\alpha]_D^{25}$ -53.8 (*c* 0.13); ¹H NMR 5.97 (br dt, *J* = 9.8, 4.2 Hz, 1H), 5.64 (br d, *J* = 9.8 Hz, 1H), 4.25-4.20 (m, 1H), 3.60 (dd, *J* = 9.4, 3.3 Hz, 1H), 3.54-3.46 (m, 2H), 3.32 (s, 3H), 3.33-3.22 (m, 2H), 3.06-3.01 (m, 1H), 2.60-2.46 (m, 4H), 1.96-1.69 (m, 8H), 1.45-1.36 (m, 2H); ¹³C NMR 208.1, 168.3, 129.2, 127.6, 71.7, 61.1, 58.9, 57.8, 46.5, 44.6, 36.7, 35.9, 32.8, 26.6, 25.9, 24.4, 22.2; IR 1708, 1635 cm⁻¹; CIMS 330 (M⁺+1, 33), 328 (M⁺+1, 100). Anal. Calcd for C₁₇H₂₆ClNO₃: C, 62.28; H, 7.99. Found: C, 62.41; H, 8.07.

(2*S*,2'*S*)-2-[[2'-(2''-Bromo)phenyl]ethyl]-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10d): colorless oil; *R_f* 0.58 (hexanes/EtOAc, 1:1); $[\alpha]_D^{25}$ -9.0 (*c* 1.0); ¹H NMR 7.47 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.33 (dd, *J* =

7.6, 1.8 Hz, 1H), 7.22 (dt, $J = 7.5, 1.2$ Hz, 1H), 7.03 (dt, $J = 7.6, 1.7$ Hz, 1H), 6.03 (br dd, $J = 9.8, 4.4$ Hz, 1H), 5.78 (br d, $J = 9.8$ Hz, 1H), 4.31-4.27 (m, 1H), 3.65 (br dd, $J = 9.3, 3.2$ Hz, 1H), 3.36 (s, 3H), 3.40-3.32 (m, 2H), 3.16-3.12 (m, 1H), 2.81-2.51 (m, 6H), 2.22-2.16 (m, 1H), 2.08-2.02 (m, 1H), 1.98-1.81 (m, 3H), 1.79-1.71 (m, 1H); ^{13}C NMR 207.8, 168.2, 141.3, 132.6, 130.1, 129.4, 128.0, 127.7, 124.1, 71.8, 61.3, 60.3, 59.0, 57.9, 46.8, 36.7, 36.3, 31.6, 26.6, 26.1, 24.6; IR 1707, 1635 cm^{-1} ; CIMS 421 ($\text{M}^+ + 1$, 64), 420 ($\text{M}^+ + 1$, 66), 142 (100). Anal. Calcd for $\text{C}_{12}\text{H}_{26}\text{BrNO}_3$: C, 60.01; H, 6.23. Found: C, 60.05; H, 6.24.

(2*S*,2'*S*)-2-[(3'-Benzyloxy)propyl]-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10e): colorless oil; $[\alpha]_{\text{D}}^{25} -147.8$ (c 3.2); ^1H NMR 7.38 (m, 4H), 7.24 (m, 1H), 5.92 (dm, $J = 9.7$ Hz, 1H), 5.65 (d, $J = 9.7$ Hz, 1H), 4.55 (s, 2H), 4.30 (m, 1H), 3.79 (d, $J = 13.2$ Hz, 1H), 3.62 (m, 1H), 3.58 (d, $J = 13.2$ Hz, 1H), 3.48 (m, 2H), 3.34 (m, 1H), 3.30 (m, 1H), 3.25 (m, 1H), 3.08 (m, 1H), 2.61-2.44 (m, 3H), 2.06 (m, 1H), 1.95-1.84 (m, 4H), 1.76 (m, 1H), 1.63 (m, 1H); ^{13}C NMR 207.6, 169.0, 139.1, 133.0, 129.5, 128.5, 128.0, 73.9, 72.4, 70.8, 70.2, 59.8, 58.5, 47.8, 44.1, 34.4, 32.5, 26.8, 26.0, 24.3; IR 1706, 1620 cm^{-1} ; CIMS 386 ($\text{M}^+ + 1$, 100).

(2*S*,2'*S*)-2-[[2'-(Methoxymethyl)pyrrolidinyl]-2-[[2'-trimethylsilyl]ethoxy]methyl]-carbonyl]-cyclohex-3-en-1-one (10f): colorless oil; $[\alpha]_{\text{D}}^{25} -145.2$ (c 5.8); ^1H NMR 6.07 (m, 1H), 5.64 (d, $J = 8.3$ Hz, 1H), 4.21 (m, 1H), 3.81 (d, $J = 13.2$ Hz, 1H), 3.77 (s, 2H), 3.75 (d, $J = 13.2$ Hz, 1H), 3.58 (dd, $J = 8.5, 4.4$ Hz, 1H), 3.45 (m, 2H), 3.31 (s, 3H), 3.25 (m, 1H), 2.93 (m, 1H), 2.73-2.56 (m, 3H), 2.41 (m, 1H), 1.90-1.78 (m, 2H), 1.68 (m, 1H), -0.35 (s, 9H); ^{13}C NMR 208.8, 167.9, 129.5, 126.8, 75.1, 72.0, 69.2, 61.9, 59.6, 59.0, 45.8, 38.3, 26.8, 25.5, 24.6, 17.8, -1.35; CIMS 368 ($\text{M}^+ + 1$, 100).

(2*S*,2'*S*)-2,4-Dimethyl-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10g): yellow oil; R_f 0.60 (hexanes/EtOAc, 1:1); $[\alpha]_{\text{D}}^{25} -39.7$ (c 1.3); ^1H NMR 5.30 (s, 1H), 4.20 (m, 1H), 3.60 (dd, $J = 9.5, 3.2$ Hz, 1H), 3.32 (s, 3H), 3.28 (m, 2H), 3.02 (m, 1H), 2.62 - 2.40 (m, 4H), 1.85 (m, 3H), 1.76 (s, 3H), 1.72 (m, 1H), 1.38 (s, 3H); ^{13}C NMR 209.2, 169.4, 135.0, 124.7, 71.5, 58.8, 57.5, 57.1, 46.2, 35.4, 30.3, 26.5, 24.3, 23.9, 22.8; IR 1705, 1625 cm^{-1} .

Anal. Calcd. for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74. Found: C, 67.65 H, 8.69.

(2'S,2S)-2-Ethyl-2-[[2'-methoxymethyl]pyrrolidinyl]carbonyl]-4-methyl-cyclohex-3-en-1-one (10h): light yellow oil; R_f 0.60 (hexanes/EtOAc, 1:1); $[\alpha]^{26}_D -57.0$ (c 1.0); 1H NMR 5.28 (s, 1H), 4.18 (m, 1H), 3.55 (dd, $J = 9.3, 2.9$ Hz, 1H), 3.27 (s, 3H), 3.20 (m, 1H), 3.00 (m, 1H), 2.35 (m, 4H), 1.80 (m, 4H), 1.75 (s, 3H), 1.66 (m, 1H), 0.82 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR 208.6, 168.8, 135.5, 123.6, 71.7, 61.1, 58.8, 57.6, 46.4, 36.6, 30.5, 29.6, 26.5, 24.4, 22.9, 9.3; IR 1710, 1635 cm^{-1} ; EI-HRMS calcd for $C_{16}H_{25}NO_3$ ($M^+ + 1$) 279.1834, found 279.1837.

(2'S,2S)-2-[[2'-Methoxymethyl]pyrrolidinyl]carbonyl]-4-methyl-2-(4'-pentenyl)-cyclohex-3-en-1-one (10i): light yellow oil; $[\alpha]^{23}_D -11.5$ (c 2.5); 1H NMR 5.78-5.73 (m, 1H), 5.34 (s, 1H), 4.99-4.90 (m, 2H), 4.24-4.23 (m, 1H), 3.61-3.59 (d, $J = 4.4$ Hz, 1H), 3.33 (s, 3H), 3.28-3.22 (m, 2H), 3.05-3.04 (m, 1H), 2.57-2.47 (m, 2H), 2.43-2.42 (m, 2H), 2.04-1.91 (m, 2H), 1.89-1.81 (m, 4H), 1.76-1.71 (m, 2H), 1.39-1.30 (m, 2H); ^{13}C NMR 189.0, 168.8, 138.3, 135.3, 123.7, 114.5, 71.6, 60.7, 58.8, 57.6, 46.3, 36.4, 36.1, 33.9, 30.4, 26.4, 24.4, 23.9, 22.8; IR 2924, 1710, 1638 cm^{-1} ; CIMS 320 ($M^+ + 1$, 100). Anal. Calcd for $C_{17}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.31; H, 9.07; N, 4.32.

(2S,2'S)-2-[2'-[(4''-Methoxy)benzyloxy]ethyl]-2-[[2'-(methoxymethyl)pyrrolidinyl]carbonyl]-4-methyl-cyclohex-3-en-1-one (10j): yellow oil; R_f 0.50 (hexanes/EtOAc, 1:1); $[\alpha]^{30}_D -36.4$ (c 1.4); 1H NMR 7.21 (d, $J = 8.3$ Hz, 2H), 6.84 (d, $J = 8.3$ Hz, 2H), 5.34 (s, 1H), 4.29 (AB q, $J = 11.0$ Hz, 2H), 4.26 (m, 1H), 3.78 (s, 3H), 3.62 (dd, $J = 8.5, 6.8$ Hz, 1H), 3.52 (m, 1H), 3.35 (s, 3H), 3.31 (m, 2H), 3.05 (m, 1H), 2.60-1.80 (m, 7H), 1.79 (s, 3H), 1.70 (m, 1H); ^{13}C NMR 208.1, 169.1, 159.1, 136.5, 130.6, 129.3, 123.4, 113.6, 72.4, 71.8, 67.0, 59.7, 58.9, 57.8, 55.2, 46.6, 36.9, 36.2, 30.2, 26.6, 24.5, 23.0; IR 1710, 1632 cm^{-1} ; CIMS 416 ($M^+ + 1$, 100). Anal. Calcd for $C_{24}H_{33}NO_5$: C, 69.37; H, 8.00. Found: C, 69.13; H, 8.15.

(2S,2'S)-4-Benzyl-2-ethyl-2-[[2'-methoxymethyl]pyrrolidinyl]carbonyl]-cyclohex-3-en-1-one (10k): pale yellow oil; $[\alpha]^{28}_D -26.2$ (c 1.7); R_f 0.80 (hexanes/EtOAc, 1:1); 1H NMR 7.28-7.18 (m, 5H), 5.45 (s, 1H), 4.25 (m, 1H), 3.60 (dd, $J = 9.3, 3.0$ Hz, 1H), 3.39 (s, 2H), 3.31 (s,

3H), 3.19 (m, 1H), 3.21 (m, 1H), 2.55 (m, 1H), 2.40 (m, 3H), 2.02 (m, 1H), 1.85 (m, 3H), 1.64 (m, 1H), 0.88 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR 207.9, 168.5, 138.8, 128.4, 128.3, 126.3, 124.9, 71.7, 61.1, 58.7, 57.4, 46.3, 43.5, 36.5, 29.5, 28.1, 24.4, 9.4; IR 1711, 1633 cm^{-1} ; CIMS 356 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_3$: C, 74.33; H, 8.22. Found: C, 74.06; H, 8.30.

(2*S*,2'*S*)-2-Ethyl-2-[[*(2'*-methoxymethyl)pyrrolidinyl]carbonyl]-4-[(2'-methoxy)phenyl]-cyclohex-3-en-1-one (10l): pale yellow oil; $[\alpha]_{\text{D}}^{24} -72.3$ (c 1.3) ^1H NMR 7.24-7.21 (ddd, $J = 7.9, 2.1, 1.5$ Hz, 1H), 7.09 (dd, $J = 7.9, 1.5$ Hz, 1H), 6.91 (dd, $J = 7.9, 1.5$ Hz, 1H), 6.84 (d, $J = 7.9$ Hz, 1H), 5.62 (s, 1H), 4.38 (m, 1H), 3.76 (s, 3H), 3.63 (dd, $J = 9.5, 1.5$ Hz, 1H), 3.35 (m, 5H), 2.82-2.61 (m, 5H), 1.94-1.65 (m, 4H), 1.49 (s, 3H); ^{13}C NMR 208.9, 169.1, 156.5, 138.9, 130.5, 128.8, 128.3, 127.7, 120.5, 110.6, 71.7, 58.8, 57.5, 55.1, 46.3, 35.6, 28.7, 26.6, 24.4, 23.2; IR 1711, 1632 cm^{-1} ; CIMS 358 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{21}\text{H}_{27}\text{NO}_4$: C, 70.56; H, 7.61. Found: C, 70.64; H, 7.70.

General Procedure for the Iodolactonization of 10a to 1a. (2R,3R,4R)-3-Iodo-2-methyl-1-oxocyclohexan-2,4-carbolactone (1a). To a solution of cyclohexenone **10a** (2.2 g, 8.8 mmol) in a 1:1 mixture of THF/H₂O (100 mL) was added I₂ (13 g, 52.8 mmol). The resulting solution was stirred overnight at room temperature. The reaction mixture was titrated with saturated aqueous Na₂S₂O₃ solution until the solution turned to light brown. The reaction mixture was extracted with ethyl acetate. The organic layers were isolated, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Flash column chromatography (hexane/EtOAc, 1:1) of the crude residue gave the desired product **1a** (2.2 g, 90%) as a white solid: mp 97–99 °C; $[\alpha]^{24}_{\text{D}} -300$ (c 0.27); ¹H NMR 4.98(m, 1H), 4.64 (dd, *J* = 5.2, 1.8 Hz, 1H), 2.77-2.60 (m, 3H), 2.50-2.42 (m, 1H), 1.29(s, 3H); ¹³C NMR 198.0, 170.5, 77.5, 60.1, 32.8, 27.6, 27.3, 12.3; IR 1782, 1724 cm⁻¹; MS (CI) 281 (M⁺+1, 100). Anal. Calcd for C₈H₉IO₃: C, 34.31; H, 3.24. Found: C, 34.43; H, 3.22.

(2R,3R,4R)-2-(3'-Chloropropyl)-3-iodo-1-oxocyclohexan-2,4-carbolactone (1b): white solid; mp 139–140 °C; $[\alpha]^{24}_{\text{D}} -250$ (c 0.12); ¹H NMR 4.97(br s, 1H), 4.70(dm, *J* = 5.2 Hz, 1H), 3.59-3.48(m, 2H), 2.73-2.57(m, 3H), 2.47-2.40(m, 1H), 2.04-1.98(m, 1H), 1.91-1.85(m, 1H), 1.73-1.66(m, 2H); ¹³C NMR 197.7, 169.4, 77.4, 63.1, 44.3, 33.0, 27.2, 26.2, 23.4, 22.8; IR 1780, 1725 cm⁻¹; MS (CI) 345 (M⁺+1, 32), 343 (M⁺+1, 100). Anal. Calcd for C₁₀H₁₂ClIO₃: C, 35.06; H, 3.53. Found: C, 34.99; H, 3.52.

(2R,3R,4R)-2-(3'-Chlorobutyl)-3-iodo-1-oxocyclohexan-2,4-carbolactone (1c): white solid; mp 86–87 °C; $[\alpha]^{24}_{\text{D}} -178$ (c 0.14); ¹H NMR 5.00-4.98(m, 1H), 4.77-4.76(m, 1H), 3.58-3.50(m, 2H), 2.73-2.57(m, 3H), 2.48-2.40(m, 1H), 1.95-1.74(m, 4H), 1.36-1.23(m, 2H); ¹³C NMR 198.0, 169.5, 108.7, 63.6, 44.5, 33.0, 32.3, 27.3, 23.7, 23.1, 20.2; IR 1783, 1724 cm⁻¹; MS (CI) 359 (M⁺+1, 31), 357 (M⁺+1, 100). Anal. Calcd for C₁₁H₁₄ClIO₃: C, 37.05; H, 3.96. Found: C, 36.77; H, 3.88.

(2R,3R,4R)-2-[2'-(2''-Bromophenyl)ethyl]-3-iodo-1-oxocyclohexan-2,4-carbolactone (1d): white solid; 87–89 °C; $[\alpha]^{27}_{\text{D}} -200$ (c 0.03); ¹H NMR 7.53-7.52(m, 1H), 7.31-7.24(m, 2H),

7.10-7.06(m, 1H), 5.04(m, 1H), 4.92(dd, $J = 5.4$ Hz, 1H), 2.79-2.57(m, 6H), 2.21(ddd, $J = 14.8$, 12.5, 4.6 Hz, 1H), 2.10(ddd, $J = 14.8$, 12.5, 5.2 Hz, 1H); ^{13}C NMR 197.7, 169.4, 139.9, 132.9, 130.5, 128.1, 127.8, 124.3, 77.4, 63.5, 33.0, 29.6, 27.3, 25.2, 23.2; IR 1782, 1725 cm^{-1} ; MS (CI) 451 ($\text{M}^+ + 1$, 94), 448 ($\text{M}^+ + 1$, 100). Anal Calcd for $\text{C}_{15}\text{H}_{14}\text{BrIO}_3$: C, 40.12; H, 3.14. Found: C, 39.97; H, 3.21.

(2R,3R,4R)-2-(3'-Benzyloxypropyl)-3-iodo-1-oxocyclohexan-2,4-carbolactone (1e):

colorless oil; $[\alpha]_D^{25} -123.3$ (c 1.2); ^1H NMR 7.38(m, 4H), 7.30(m, 1H), 4.91(s, 1H), 4.90(s, 1H), 4.49(d, $J = 12.0$ Hz, 1H), 4.43(d, $J = 12.0$ Hz, 1H), 3.54(m, 2H), 2.66(m, 1H), 2.62(m, 1H), 2.46(m, 4H), 2.02(m, 1H), 1.93(m, 1H), 1.56(m, 2H); ^{13}C NMR 198.1, 169.6, 138.2, 128.2, 127.6, 127.4, 76.7, 72.6, 69.9, 63.3, 32.8, 27.3, 23.4, 23.2, 21.7; IR 1758, 1705 cm^{-1} ; MS (CI) 415 ($\text{M}^+ + 1$). Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{IO}_4$: C, 49.28; H, 4.59. Found: C, 49.04; H, 4.59.

(2R,3R,4R)-3-Iodo-1-oxo-2-([1'-trimethylsilylethoxy]methyl)cyclohexan-2,4-

carbolactone (1f): white solid; mp 78–80 °C; $[\alpha]_D^{25} -57.5$ (c 0.80); ^1H NMR 5.02(t, $J = 3.7$ Hz, 1H), 4.98(s, 1H), 3.83(d, $J = 10.5$ Hz, 1H), 3.61(d, $J = 10.5$ Hz, 1H), 3.53(ddd, $J = 15.3$, 9.0, 7.3 Hz, 2H), 2.66(m, 1H), 2.56(dd, $J = 18.3$, 7.8 Hz, 2H), 2.39(m, 1H), 0.85(t, $J = 8.3$ Hz, 2H), -0.05(s, 9H); ^{13}C NMR 197.3, 168.2, 77.0, 69.0, 64.3, 62.5, 32.7, 27.0, 21.8, 17.6, -1.55; IR 1792, 1725 cm^{-1} ; MS (CI) 397 ($\text{M}^+ + 1$). Anal. Calcd for $\text{C}_{13}\text{H}_{21}\text{IO}_4\text{Si}$: C, 39.39; H, 5.30. Found: C, 39.26; H, 5.27.

(2R,3R,4R)-2,4-Dimethyl-3-iodo-1-oxocyclohexan-2,4-carbolactone (1g): white solid; mp

134–136 °C; $[\alpha]_D^{25} -218$ (c 1.3); ^1H NMR 4.36(s, 1H), 2.55-2.35(m, 4H), 1.52(s, 3H), 1.16(s, 3H); ^{13}C NMR 198.6, 170.9, 84.8, 70.0, 62.1, 35.4, 33.2, 33.0, 22.5, 12.7; IR 1781, 1685 cm^{-1} ; MS (CI) 295 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_9\text{H}_{11}\text{IO}_3$ ($\text{M}^+ + 1$) 294.9831, found 294.9826.

(2R,3R,4R)-2-Ethyl-3-iodo-5-methyl-1-oxocyclohexan-2,4-carbolactone (1h): white

solid; mp 91–92 °C; $[\alpha]_D^{25} -216.0$ (c 1.2); ^1H NMR 4.48 (s, 1H), 2.63 (m, 2H), 2.45 (m, 2H), 2.02 (m, 1H), 1.70 (m, 1H), 1.63 (s, 3H), 0.82 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR 198.5, 169.7, 84.1,

65.8, 33.4, 32.8, 30.4, 22.5, 17.6, 6.9; IR 1775, 1722 cm^{-1} ; MS (CI) 309 ($\text{M}^+ + 1$, 56), 183 (100); HRMS calcd for $\text{C}_{10}\text{H}_{13}\text{IO}_3$ ($\text{M}^+ + 1$) 308.9988, found 308.9984.

(2*R*,3*R*,4*R*)-3-Iodo-4-methyl-1-oxo-2-(pent-4'-ene-1-yl)cyclohexan-2,4-carbolactone

(1i): yellow solid; mp 64–65 °C; $[\alpha]_D^{23}$ –196.8 (*c* 1.6); ^1H NMR 5.76–5.73 (m, 1H), 5.03–4.93 (m, 2H), 4.45 (s, 1H), 2.60–2.46 (m, 2H), 2.44–2.39 (m, 2H), 2.10–2.06 (m, 2H), 1.89–1.86 (m, 1H), 1.71–1.65 (m, 1H), 1.59 (s, 3H), 1.23–1.18 (m, 2H); ^{13}C NMR 198.8, 169.5, 137.2, 114.8, 83.9, 65.1, 33.1, 33.0, 32.5, 30.8, 23.8, 22.2, 21.6; IR 1783, 1724 cm^{-1} ; MS (CI) 349 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_{13}\text{H}_{17}\text{IO}_3$ ($\text{M}^+ + 1$) 349.0301, found 349.0299.

(2*R*,3*R*,4*R*)-3-Iodo-2-[(4-methoxy)benzyloxy]ethyl-4-methyl-1-oxocyclohexan-2,4-carbolactone (1j):

yellow oil; $[\alpha]_D^{30}$ –90.0 (*c* 1.6); ^1H NMR 7.21 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.74 (s, 1H), 4.33 (AB q, *J* = 11.5 Hz, 2H), 3.78 (s, 3H), 3.55 (m, 2H), 2.60–2.02 (m, 6H), 1.51 (s, 3H); ^{13}C NMR 198.3, 170.2, 159.2, 130.0, 129.3, 113.8, 84.5, 72.5, 64.9, 64.7, 55.2, 33.3, 33.2, 32.5, 24.2, 22.4; IR 1783, 1612 cm^{-1} ; MS (CI) 325 ($\text{M}^+ + 1$ –120, 2), 121 (100). Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{IO}_5$: C, 48.66; H, 4.76. Found: C, 48.43; H, 4.75.

(2*R*,3*R*,4*S*)-4-Benzyl-2-ethyl-3-iodo-1-oxocyclohexan-2,4-carbolactone (1k):

pale yellow oil; $[\alpha]_D^{25}$ –128.3 (*c* 1.8); ^1H NMR 7.35–7.26 (m, 5H), 4.25 (s, 1H), 3.09 (AB q, *J* = 14.6 Hz, 2H), 2.65 (m, 2H), 2.43 (m, 2H), 1.95 (m, 1H), 1.65 (m, 1H), 0.60 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR 198.7, 169.5, 133.5, 130.1, 128.5, 127.5, 85.0, 65.3, 40.6, 33.5, 31.8, 28.1, 28.0, 17.5, 6.6; IR 1784, 1725 cm^{-1} ; MS (CI) 385 ($\text{M}^+ + 1$, 34), 259 (100); HRMS calcd for $\text{C}_{16}\text{H}_{17}\text{IO}_3$ ($\text{M}^+ + 1$) 385.0301, found 385.0294.

(2*R*,3*R*,4*S*)-3-Iodo-4-(2'-methoxy)phenyl-2-methyl-1-oxocyclohexan-2,4-carbolactone

(1l): off-white solid; mp 110–111 °C; $[\alpha]_D^{24}$ –173.5 (*c* 1.6); ^1H NMR 7.44 (ddt, *J* = 7.2, 6.7, 2.1 Hz, 1H), 7.36 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.05 (m, 2H), 5.04 (d, *J* = 1.5 Hz, 1H), 3.28 (m, 1H), 3.06 (m, 1H), 2.79 (dd, *J* = 15.5, 6.9 Hz, 1H), 2.63 (dt, *J* = 15.5, 6.9 Hz, 1H); ^{13}C NMR 198.9, 170.8, 158.2, 131.2, 128.1, 123.5, 120.6, 112.7, 85.2, 67.9, 55.9, 34.0, 33.4, 31.8, 12.4; IR 1783 cm^{-1} ; MS (CI) 387 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{15}\text{H}_{15}\text{IO}_4$: C, 46.65; H, 3.92. Found: C, 45.95;

H, 3.74. The foregoing combustion analysis of this sample indicates that the sample was probably wet. A sample of compound **11** sufficient for re-analysis is no longer available.

General Procedure for the Fragmentation of 1 with Lithium Hydroxide. To a solution of **1a** (255 mg, 0.9 mmol) in THF/H₂O (12 mL, 5:1) was added LiOH·H₂O (76 mg, 1.8 mmol). The resulting solution was stirred overnight at room temperature. The reaction mixture was neutralized with 10% aqueous HCl solution and extracted with diethyl ether. The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. Flash column chromatography (hexanes/EtOAc, 3:1) of the crude residue gave **11a** (34 mg, 27%) and **12a** (53 mg, 58%). **(5R)-[3-Methyl-5-(2'-hydroxycarbonyl)ethyl]furan-2(5H)-1-one (11a):** white solid; mp 82–84 °C; $[\alpha]_D^{25} -35.8$ (*c* 0.67); ¹H NMR 7.03 (d, *J* = 1.4 Hz, 3H), 5.00–4.97 (m, 1H), 2.58–2.49 (m, 2H), 2.22–2.15 (m, 1H), 1.93–1.91 (m, 3H), 1.87–1.79 (m, 1H); ¹³C NMR 177.9, 173.9, 147.9, 130.7, 79.6, 29.0, 28.2, 10.6; IR 3467, 2931, 1736 cm⁻¹; MS (CI) 171 (M⁺+1, 100); HRMS calcd for C₈H₁₁O₄ (M⁺+1) 171.0657, found 171.0657. **(4R)-4-Hydroxy-2-methyl-2-cyclohexen-1-one (12a):** colorless liquid; $[\alpha]_D^{28} +48.0$ (*c* 0.98); ¹H NMR 6.09 (m, 1H), 4.52 (m, 1H), 2.60–2.54 (m, 2H), 2.36–2.26 (m, 2H), 1.97–1.89 (m, 1H), 1.75 (m, 3H); ¹³C NMR 199.3, 147.9, 135.6, 66.4, 35.3, 32.7, 15.6; IR 3411, 1669 cm⁻¹; MS (CI) 127 (M⁺+1, 100); HRMS calcd for C₇H₁₀O₂ (M⁺+1) 127.0759, found 127.0759.

(5R)-[3-(3'-Chloropropyl)-5-(2'-hydroxycarbonyl)ethyl]furan-2(5H)-1-one (11b): white solid; mp 60–62 °C; $[\alpha]_D^{26} -66.7$ (*c* 0.03); ¹H NMR 7.09 (d, *J* = 1.4 Hz, 1H), 5.05–5.02 (m, 1H), 3.58–3.55 (m, 2H), 2.60–2.47 (m, 4H), 2.24–2.17 (m, 1H), 2.07–2.01 (m, 2H), 1.89–1.82 (m, 1H); ¹³C NMR 178.2, 173.3, 148.3, 133.5, 79.7, 43.9, 29.8, 28.9, 28.1, 22.6; IR 3630, 2962, 1742 cm⁻¹; MS (CI) 235 (M⁺+1, 34), 233 (M⁺+1, 100); HRMS calcd for C₁₀H₁₄ClO₄ (M⁺+1) 233.0580, found 233.0569.

(4R)-2-(3'-Chloropropyl)-4-hydroxy-2-cyclohexen-1-one (12b): colorless oil; $[\alpha]_D^{27} +50.0$ (*c* 0.06); ¹H NMR 6.72 (m, 1H), 4.58 (m, 1H), 3.56–3.51 (m, 2H), 2.64–2.58 (m, 1H), 2.40–2.31 (m, 4H), 1.99–1.87 (m, 3H); ¹³C NMR 198.2, 147.9, 138.2, 66.7, 44.4, 35.5, 32.7, 30.9, 26.8; IR

3404, 2957, 2871, 1667 cm^{-1} ; MS (CI) 191 ($M^+ + 1$, 31), 189 ($M^+ + 1$, 100); HRMS calcd for $\text{C}_9\text{H}_{13}\text{ClO}_2$ ($M^+ + 1$) 189.0682, found 189.0691.

(5R)-[[3-[2'-(2'Bromophenyl)ethyl]-5-(2'-hydroxycarbonyl)ethyl]furan-2(5H)-1-one

(11d): white sticky semi-solid; $[\alpha]_D^{26} -7.69$ (c 0.13); ^1H NMR 7.54 (br d, $J = 8.1$ Hz, 1H), 7.27-7.10 (m, 2H), 7.09-7.06 (m, 1H), 6.93 (br s, 1H), 4.98 (br m, 1H), 3.02-2.99 (m, 2H), 2.66-2.63 (m, 2H), 2.55-2.42 (m, 2H), 2.18-2.10 (m, 1H), 1.84-1.77 (m, 1H); ^{13}C NMR 178.2, 173.3, 148.2, 139.6, 133.7, 132.9, 130.5, 128.1, 127.6, 124.4, 79.7, 33.6, 29.0, 28.0, 25.2; IR 3630, 2933 cm^{-1} ; MS (CI) 341 ($M^+ + 1$, 96), 339 ($M^+ + 1$, 100); HRMS calcd for $\text{C}_{15}\text{H}_{13}\text{BrO}_4$ ($M^+ - 2$) 335.9997, found 335.9996.

(4R)-2-[2'-(2''Bromophenyl)ethyl]-4-hydroxy-2-cyclohexen-1-one (12d): colorless oil;

$[\alpha]_D^{21} +22.5$ (c 0.71); ^1H NMR 7.49 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.21 (dt, $J = 7.6, 1.2$ Hz, 1H), 7.16 (dd, $J = 1.9$ Hz, 1H), 7.05 (dt, $J = 7.6, 1.9$ Hz, 1H), 6.54 (q, $J = 1.2$ Hz, 1H), 4.49-4.46 (m, 1H), 2.83 (t, $J = 7.8$ Hz, 2H), 2.59 (dt, $J = 16.6, 4.5$ Hz, 1H), 2.53-2.43 (m, 2H), 2.38-2.25 (m, 2H), 1.95-1.88 (m, 1H); ^{13}C NMR 198.6, 148.2, 140.6, 138.2, 132.7, 130.6, 127.7, 127.4, 124.5, 66.5, 35.5, 34.6, 32.5, 29.5; IR 3420, 1672 cm^{-1} ; MS (CI) 297 ($M^+ + 1$, 91), 295 ($M^+ + 1$, 100). Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{BrO}_2$: C, 56.97; H, 5.12. Found: C, 56.69; H, 5.17.

(5R)-[3-(3'-Benzyloxy)propyl-5-(2'-hydroxycarbonyl)ethyl]furan-2(5H)-1-one (11e):

colorless oil; $[\alpha]_D^{25} -40.5$ (c 4.5); ^1H NMR 7.37 (m, 4H), 7.31 (m, 1H), 6.93 (s, 1H), 4.93 (m, 1H), 4.52 (s, 2H), 3.51 (t, $J = 6.1$ Hz, 2H), 2.47 (m, 2H), 2.39 (t, $J = 7.6$ Hz, 2H), 2.11 (m, 1H), 1.87 (m, 2H), 1.78 (m, 1H); ^{13}C NMR 177.3, 173.4, 147.6, 137.8, 133.9, 128.1, 127.7, 127.5, 127.4, 79.6, 72.5, 68.7, 28.7, 27.7, 27.0, 21.7; IR 3460, 1748, 1652 cm^{-1} ; MS (CI) 305 ($M^+ + 1$). Anal. Calcd for $\text{C}_{17}\text{H}_{20}\text{O}_5$: C, 67.11; H, 6.58. Found: C, 66.47; H, 6.57. The foregoing combustion analysis of this sample indicates that the sample was probably wet. A sample of compound **11e** sufficient for re-analysis is no longer available.

(4R)-2-(3'-Benzyloxy)propyl-4-hydroxy-2-cyclohexen-1-one (12e): colorless oil; $[\alpha]^{25}_{\text{D}}$ +15.4 (*c* 6.1); ^1H NMR 7.31 (m, 4H), 7.26 (m, 1H), 6.61 (s, 1H), 4.46 (s, 2H), 4.41 (m, 1H), 3.46 (t, *J* = 6.4 Hz, 2H), 3.08 (br s, 1H), 2.52 (dt, *J* = 16.6, 4.1 Hz, 1H), 2.30-2.17 (m, 1H), 2.24 (t, *J* = 7.8 Hz, 2H), 1.85 (m, 1H), 1.70 (m, 2H); ^{13}C NMR 198.6, 147.8, 138.5, 138.1, 128.1, 127.5, 127.4, 72.6, 69.4, 66.1, 35.4, 32.3, 27.9, 25.7; IR 3424, 1675 cm^{-1} ; MS (CI) 261 (M^+ +1). Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_3$: C, 73.85; H, 7.69. Found: C, 73.91; H, 7.83.

(5R)-[5-(2'-Hydroxycarbonyl)ethyl-3-([2'-trimethylsilyl]ethoxy)methyl]furan-2(5H)-1-one (11f): colorless oil; $[\alpha]^{25}_{\text{D}}$ -8.8 (*c* 4.0); ^1H NMR 10.56 (br s, 1H), 7.27 (s, 1H), 5.04 (m, 1H), 4.17 (s, 2H), 3.58 (t, *J* = 7.3 Hz, 2H), 2.51 (m, 2H), 2.16 (m, 1H), 1.84 (m, 1H), 0.96 (t, *J* = 7.5 Hz, 2H), -0.01 (s, 9H); ^{13}C NMR 177.6, 171.8, 148.9, 132.5, 80.4, 68.7, 63.6, 29.0, 27.9, 17.9, -1.61; IR 3495, 1757, 1713 cm^{-1} ; MS (CI) 287 (M^+ +1). Anal. Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_5\text{Si}$: C, 54.55, H, 7.69. Found: C, 54.32; H, 7.58.

(4R)-4-Hydroxy-2-([2'-trimethylsilyl]ethoxy)methyl-2-cyclohexen-1-one (12f): colorless oil; $[\alpha]^{25}_{\text{D}}$ +16.4 (*c* 0.55); ^1H NMR 6.85 (s, 1H), 4.53 (m, 1H), 4.01 (d, *J* = 6.1 Hz, 2H), 3.49 (t, *J* = 8.0 Hz, 2H), 2.51 (m, 1H), 2.30 (m, 1H), 2.24 (m, 1H), 1.89 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR 192.9, 147.0, 136.3, 68.4, 66.5, 66.0, 35.5, 32.4, 18.1, -1.5; IR 3420, 1676 cm^{-1} ; MS (CI) 243 (M^+ +1). Anal. Calcd for $\text{C}_{12}\text{H}_{22}\text{O}_3\text{Si}$: C, 59.50; H, 9.09. Found: C, 59.48; H, 9.00.

(5R)-[3,5-Dimethyl-5-(2'-hydroxycarbonyl)ethyl]furan-2(5H)-1-one (11g): yellow oil; $[\alpha]^{25}_{\text{D}}$ -27.0 (*c* 1.0); ^1H NMR 6.91 (s, 1H), 2.36-2.01 (m, 4H), 1.89 (s, 3H), 1.44 (s, 3H); ^{13}C NMR 178.6, 173.8, 152.4, 129.7, 85.6, 32.9, 28.5, 24.5, 10.6; IR 3489, 1742 cm^{-1} ; MS (CI) 185 (M^+ +1, 100). Anal. Calcd for $\text{C}_9\text{H}_{12}\text{O}_4$: C, 58.69, H, 6.57. Found: C, 58.58; H, 6.78.

(4R)-2,4-Dimethyl-4-Hydroxy-2-cyclohexen-1-one (12g): yellow oil; $[\alpha]^{25}_{\text{D}}$ +7.0 (*c* 1.0); ^1H NMR 6.49 (s, 1H), 2.62 (br s, 1H), 2.60-2.04 (m, 4H), 1.70 (s, 3H), 1.38 (s, 3H); ^{13}C NMR 199.6, 150.3, 134.4, 68.8, 37.6, 35.0, 29.5, 27.6, 15.8; IR 1669 cm^{-1} .

(5R)-[3-Ethyl-5-(2'-hydroxycarbonyl)ethyl-5-methyl]furan-2(5H)-1-one (11h): yellow solid; mp 66–68 °C; $[\alpha]^{25}_{\text{D}}$ -20.7 (*c* 1.3); ^1H NMR 11.0 (br s, 1H), 6.87 (s, 1H), 2.27-2.00 (m,

6H), 1.38 (s, 3H), 1.06 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR 178.0, 173.0, 150.6, 135.3, 85.4, 32.5, 28.1, 24.1, 18.1, 11.4; IR 3030, 1747, 1730 cm^{-1} ; MS (CI) 199 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{O}_4$: C, 60.59; H, 7.12. Found: C, 60.63; H, 7.09.

(4*R*)-2-Ethyl-4-hydroxy-4-methyl-2-cyclohexen-1-one (12h): yellow oil; $[\alpha]_{\text{D}}^{25} -2.9$ (c 1.4); ^1H NMR 6.40 (s, 1H), 2.54 (m, 1H), 2.32 (m, 1H), 2.07 (m, 2H), 2.00 (m, 2H), 1.35 (s, 3H), 0.90 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR 199.1, 148.7, 139.0, 68.3, 37.0, 34.9, 27.2, 21.6, 12.0; IR 3421, 1677 cm^{-1} ; MS (CI) 155 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_9\text{H}_{14}\text{O}_2$ ($\text{M}^+ + 1$) 155.1072, found 155.1066.

(5*R*)-[5-(2'-Hydroxycarbonyl)ethyl-3-(pent-4'-en-1-yl)-5-methyl]furan-2(5*H*)-1-one (11i): colorless oil; $[\alpha]_{\text{D}}^{23} -26.3$ (c 1.6); ^1H NMR 6.89 (s, 1H), 5.78-5.74 (m, 1H), 5.03-4.95 (m, 2H), 2.35-2.32 (m, 1H), 2.27-2.19 (m, 3H), 2.18-2.13 (m, 1H), 2.10-2.00 (m, 3H), 1.65-1.59 (m, 2H), 1.44 (s, 3H); ^{13}C NMR 178.3, 172.8, 151.2, 137.5, 133.9, 115.1, 85.2, 32.9, 32.5, 28.1, 26.3, 24.3, 24.2; IR 2934, 1754 cm^{-1} ; MS (CI) 239 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_{13}\text{H}_{18}\text{O}_4$ ($\text{M}^+ + 1$) 239.1282, found 239.1277.

(4*R*)-4-Hydroxy-4-methyl-2-(pent-4'-en-1-yl)-2-cyclohexen-1-one (12i): colorless oil; $[\alpha]_{\text{D}}^{23} +7.6$ (c 1.1); ^1H NMR 6.47 (m, 1H), 5.78-5.77 (m, 1H), 5.01-4.93 (m, 2H), 2.64-2.59 (m, 1H), 2.43-2.37 (m, 1H), 2.17-2.14 (m, 2H), 2.10-2.02 (m, 4H), 1.97 (br s, 1H), 1.51-1.45 (m, 2H), 1.43 (s, 3H); ^{13}C NMR 198.9, 149.2, 138.9, 137.9, 114.6, 64.2, 37.3, 35.0, 33.1, 28.3, 27.4, 27.2; IR 3430, 2359, 1666 cm^{-1} ; MS (CI) 195 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_{12}\text{H}_{18}\text{O}_2$ ($\text{M}^+ + 1$) 195.1385, found 195.1382.

(5*R*)-[5-(2'-Hydroxycarbonyl)ethyl-3-[2'-(4''-methoxy)benzyloxy]ethyl-5-methyl]furan-2(5*H*)-1-one (11j): yellow oil; $[\alpha]_{\text{D}}^{30} -7.3$ (c 1.1); ^1H NMR 7.20 (d, $J = 8.4$ Hz, 2H), 6.99 (s, 1H), 6.85 (d, $J = 8.4$ Hz, 2H), 4.42 (s, 2H), 3.77 (s, 3H), 3.61 (t, $J = 6.0$ Hz, 2H), 2.52 (t, $J = 6.0$ Hz, 2H), 2.18 (m, 3H), 1.98 (m, 1H), 1.40 (s, 3H); ^{13}C NMR 182.8, 178.0, 163.9, 158.3, 135.5, 134.7, 134.1, 118.5, 90.8, 77.2, 71.7, 59.9, 37.9, 33.8, 30.2, 28.9; IR 3300, 1751 cm^{-1} ; MS (CI) 335 ($\text{M}^+ + 1$, 1), 121 (100).

(4*R*)-4-Hydroxy-2-[2'-(4''-methoxy)benzyloxy]ethyl-4-methyl-2-cyclohexen-1-one

(12j): yellow oil; $[\alpha]_D^{25} -12.5$ (*c* 1.2); ^1H NMR 7.20 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.52 (s, 1H), 4.38 (s, 2H), 3.77 (s, 3H), 3.48 (m, 2H), 2.62-2.02 (m, 6H), 1.38 (s, 3H); ^{13}C NMR 198.9, 159.4, 151.4, 135.1, 130.4, 129.5, 113.9, 72.4, 68.7, 68.2, 55.4, 37.4, 35.2, 29.6, 27.6; IR 1674 cm^{-1} ; MS (CI) 291 ($\text{M}^+ + 1$, 3), 121 (100).

(5*R*)-[5-Benzyl-3-ethyl-5-(2'-hydroxycarbonyl)ethyl]furan-2(5*H*)-1-one (11k):

yellow solid; mp 77–78 °C; ^1H NMR 10.0 (br s, 1H), 7.29-7.10 (m, 5H), 6.78 (s, 1H), 3.03 (AB q, *J* = 4.0 Hz, 2H), 2.25 (m, 1H), 2.23 (m, 2H), 2.14 (m, 3H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR 178.2, 148.8, 137.1, 134.1, 130.2, 128.2, 127.0, 87.3, 44.3, 31.0, 27.8, 18.2, 11.6; IR 3050, 2971, 1748, 1740 cm^{-1} ; MS (CI) 275 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_4$: C, 70.06; H, 6.61. Found: C, 69.97; H, 6.63.

(4*R*)-4-Benzyl-4-Hydroxy-2-ethyl-2-cyclohexen-1-one (12k): yellow oil; $[\alpha]_D^{31} -22.2$

(*c* 1.4); ^1H NMR 7.36-7.23 (m, 5H), 6.41 (s, 1H), 2.92 (AB q, *J* = 13.4 Hz, 2H), 2.62 (m, 1H), 2.45 (m, 1H), 2.22 (m, 2H), 2.18 (m, 1H), 2.03 (m, 1H), 1.00 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR 198.6, 146.6, 140.4, 135.4, 130.4, 128.5, 127.1, 70.2, 46.1, 34.9, 34.6, 21.9, 12.2; IR 3429, 1670 cm^{-1} ; MS (CI) 231 ($\text{M}^+ + 1$, 81), 213 ($\text{M}^+ + 1 - \text{H}_2\text{O}$, 100); HRMS calcd for $\text{C}_{15}\text{H}_{18}\text{O}_2$ ($\text{M}^+ + 1$) 231.1385, found 231.1381.

(5*R*)-[5-(2'-Hydroxycarbonyl)ethyl-5-(2'-methoxy)phenyl-3-methyl]furan-2(5*H*)-1-

one (11l): colorless oil; $[\alpha]_D^{24} -43.3$ (*c* 1.1); ^1H NMR 9.10 (br s, exchangeable with D_2O , 1H), 7.69 (d, *J* = 1.5 Hz, 1H), 7.49 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.28 (dt, *J* = 6.5, 2.0 Hz, 1H), 6.93 (dt, *J* = 6.5, 2.0 Hz, 1H), 6.89 (d, *J* = 7.0 Hz, 1H), 3.78 (s, 3H), 2.65 (m, 1H), 2.40 (m, 1H), 2.20 (m, 2H), 1.85 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR 173.6, 155.1, 152.1, 129.1, 127.7, 126.4, 126.0, 120.9, 110.7, 87.8, 55.1, 31.8, 28.8, 10.2; IR 2850, 1783 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_5$: C, 65.21; H, 5.84. Found: C, 65.46; H, 5.63.

2-Methyl-4-(2'-methoxy)phenyl-1-phenol (13): (0.152 g, 0.719 mmol, 8 %); pale white solid. ^1H NMR 9.31 (bs, exchangeable with D_2O , 1H), 7.26 (dt, *J* = 7.8 Hz, 1.9 Hz, 1H), 7.20

(dd, $J = 7.8$ Hz, 1.8 Hz, 1H), 7.16 (s, 1H), 7.10 (d, $J = 7.8$ Hz, 1H), 7.05 (d, $J = 7.8$ Hz, 1H), 6.97 (dt, $J = 7.8$ Hz, 1.9 Hz, 1H), 6.79 (d, $J = 7.8$ Hz, 1H), 3.73 (s, 3H), 2.14 (s, 3H); ^{13}C NMR 156.1, 154.5, 131.5, 130.1, 130.0, 128.7, 127.9, 127.6, 123.1, 120.6, 114.1, 111.6, 55.4, 16.1; IR 3305, 2952, 2834; MS (EI) 214 (M^+ , 100); HRMS (EI) calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2$ (M^+) 214.0994, found 214.0994. Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}_2$: C, 78.48; H, 6.59. Found: C, 77.89; H, 6.44. The foregoing combustion analysis of this sample indicates that the sample was probably wet. A sample of compound **13** sufficient for re-analysis is no longer available.

General Procedure for the Fragmentation of 1 with Lithium Methoxide to 20. Methyl (2E)-2-methyl-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (20). To a solution of MeOH (30 μL , 0.8 mmol) in THF (5 mL) was added *n*-BuLi (180 μL , 0.5 mmol, 2.5 M solution in hexanes) at -78 $^{\circ}\text{C}$. The resulting solution was stirred for 0.5 h. To this solution was added dropwise a solution of **1a** (106 mg, 0.4 mmol) in THF (5 mL) at -78 $^{\circ}\text{C}$. The resulting solution was stirred overnight at room temperature. The reaction mixture was diluted with water and extracted with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Flash column chromatography (hexanes/EtOAc, 3:1) of the crude residue gave the desired product **20** (61 mg, 87%) as a colorless oil: $[\alpha]_{\text{D}}^{27} -46.5$ (c 0.71); ^1H NMR 6.67 (dq, $J = 8.1$, 1.4 Hz, 1H), 5.25 (dd, $J = 15.1$, 8.1 Hz, 1H), 3.75 (s, 3H), 2.60-2.53 (m, 2H), 2.50-2.44 (m, 1H), 2.04-1.96 (m, 1H), 1.91 (d, $J = 1.4$ Hz, 3H); ^{13}C NMR 176.4, 167.4, 137.6, 131.2, 76.3, 52.1, 28.3, 28.2, 13.0; IR 1780, 1718 cm^{-1} ; MS (CI) 185 ($\text{M}^+ + 1$, 100), 153 (30). Anal. Calcd for $\text{C}_9\text{H}_{12}\text{O}_4$: C, 58.69; H, 6.57. Found: C, 58.59; H, 6.61.

Benzyl (2E)-2-methyl-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (21): colorless oil; $[\alpha]_{\text{D}}^{27} -48.4$ (c 0.31); ^1H NMR 7.37-7.32 (m, 5H), 6.76 (dq, $J = 8.1$, 1.4 Hz, 1H), 5.26 (dd, $J = 15.1$, 8.1 Hz, 1H), 5.19 (AB q, $J = 14.5$, 12.5 Hz, 2H), 2.59-2.55 (m, 2H), 2.49-2.43 (m, 1H), 2.04-1.96 (m, 1H), 1.94 (d, $J = 1.4$ Hz, 3H); ^{13}C NMR 176.4, 166.7, 137.9, 135.6, 131.1, 128.5,

128.1, 76.3, 66.8, 28.3, 28.1, 13.0; IR 1780, 1714 cm^{-1} ; MS (CI) 261 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$: C, 69.22; H, 6.22. Found: C, 69.11; H, 6.17.

(4-Methoxyphenyl)methyl (2E)-2-methyl-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (22): white solid; mp 75–76 °C; $[\alpha]_{\text{D}}^{23} -38.0$ (*c* 0.1); ^1H NMR 7.30 (d, $J = 11.7$ Hz, 2H), 6.89 (d, $J = 11.7$ Hz, 2H), 6.73 (d, $J = 8.1$ Hz, 1H), 5.24 (q, $J = 7.8$ Hz, 1H), 5.13 (s, 2H), 3.81 (s, 3H), 2.55 (m, 2H), 2.46 (m, 1H), 2.02 (m, 1H), 1.93 (s, 3H); ^{13}C NMR 176.6, 167.1, 159.9, 137.9, 137.8, 131.6, 130.3, 128.1, 114.2, 76.6, 66.9, 55.5, 28.6, 28.4; IR 3020, 1778, 1712 cm^{-1} ; MS (CI) 291 ($\text{M}^+ + 1$). Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_5$: C, 66.20; H, 6.25. Found: C, 66.30; H, 6.27.

(2E)-Methyl 2-(3-chloropropyl)-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (23): colorless oil; $[\alpha]_{\text{D}}^{23} -26.4$ (*c* 0.53); ^1H NMR 6.73 (d, $J = 8.6$ Hz, 1H), 5.30 (ddd, $J = 8.6, 6.9, 1.6$ Hz, 1H), 3.75 (s, 3H), 3.56–3.48 (m, 2H), 2.63–2.56 (m, 2H), 2.55–2.40 (m, 4H), 2.05–1.79 (m, 4H); ^{13}C NMR 176.4, 166.9, 138.9, 134.2, 75.9, 52.2, 44.3, 31.6, 28.6, 28.4, 24.5; IR 1780, 1717 cm^{-1} ; MS (CI) 249 ($\text{M}^+ + 1$, 34), 247 ($\text{M}^+ + 1$, 100); HRMS calcd for $\text{C}_{11}\text{H}_{15}\text{ClO}_4$ ($\text{M}^+ + 1$) 247.0737, found 247.0733.

Benzyl (2E)-2-(3-chloropropyl)-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (24): colorless oil; $[\alpha]_{\text{D}}^{26} -35.9$ (*c* 0.78); ^1H NMR 7.38–7.24 (m, 5H), 6.77 (d, $J = 8.8$ Hz, 1H), 5.30 (ddd, $J = 15.4, 8.3, 0.8$ Hz, 1H), 5.18 (AB q, $J = 15.1, 12.5$ Hz, 2H), 3.55–3.47 (m, 2H), 2.60–2.44 (m, 5H), 2.05–1.84 (m, 3H); ^{13}C NMR 176.3, 166.2, 139.2, 135.5, 134.2, 128.6, 128.4, 128.2, 75.9, 67.0, 44.3, 31.6, 28.5, 28.4, 24.5; IR 1780, 1714 cm^{-1} ; MS (CI) 325 ($\text{M}^+ + 1$, 33), 323 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{ClO}_4$: C, 63.26; H, 5.93. Found: C, 63.11; H, 5.87.

Benzyl (2E)-2-(4-chlorobutyl)-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (25): colorless oil; $[\alpha]_{\text{D}}^{26} -50.0$ (*c* 0.16); ^1H NMR 7.39–7.32 (m, 5H), 6.74 (d, $J = 8.5$ Hz, 1H), 5.25 (dd, $J = 15.4, 8.3$ Hz, 1H), 5.20 (AB q, $J = 15.4, 12.5$ Hz, 2H), 3.54–3.51 (m, 2H), 2.63–2.57 (m, 2H), 2.49–2.34 (m, 3H), 2.07–1.99 (m, 1H), 1.83–1.74 (m, 2H), 1.66–1.52 (m, 2H); ^{13}C NMR 176.3, 166.4, 138.0, 135.5, 135.4, 128.6, 128.3, 128.2, 75.9, 66.9, 44.5, 31.9, 28.5, 28.3, 26.6,

26.5; IR 1780, 1713 cm^{-1} ; MS (CI) 339 ($\text{M}^+ + 1$, 34), 337 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{ClO}_4$: C, 64.19; H, 6.28. Found: C, 64.05; H, 6.22.

Methyl (2E)-2-(2-[2-bromophenyl]ethyl)-3-[(2R)-3-tetrahydro-5-oxofuranyl]-2-propenoate (26): colorless oil; $[\alpha]_{\text{D}}^{22} -5.0$ (c 2.62); ^1H NMR 7.53 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.26-7.21 (m, 1H), 7.09-7.06 (m, 1H), 6.68 (d, $J = 8.8$ Hz, 1H), 5.07-5.02 (m, 1H), 3.80 (t, $J = 1.7$ Hz, 3H), 2.88-2.82 (m, 2H), 2.69-2.62 (m, 2H), 2.55-2.37 (m, 2H), 2.16-1.99 (m, 2H), 1.83-1.69 (m, 1H); ^{13}C NMR 176.4, 167.1, 140.0, 138.8, 134.1, 132.8, 131.2, 128.2, 127.6, 124.3, 76.4, 76.0, 52.2, 35.4, 28.1, 27.7; IR 2951, 1781, 1718 cm^{-1} ; MS (CI) 355 ($\text{M}^+ + 1$, 98), 353 ($\text{M}^+ + 1$, 100). Anal. Calcd for $\text{C}_{16}\text{H}_{17}\text{BrO}_4$: C, 54.41; H, 4.85. Found: C, 54.37; H, 4.88.

(5R)-[3-[2'-(2'Bromophenyl)ethyl]-5-(2'-methoxycarbonyl)ethyl]furan-2(5H)-one (30): colorless oil; $[\alpha]_{\text{D}}^{21} -16.7$ (c 0.84); ^1H NMR 7.52 (dd, $J = 8.0, 1.1$ Hz, 1H), 7.23 (dt, $J = 7.6, 1.1$ Hz, 1H), 7.18 (dd, $J = 7.6, 1.8$ Hz, 1H), 7.07 (dt, $J = 8.0, 1.8$ Hz, 1H), 6.91 (d, $J = 1.4$ Hz, 1H), 4.97-4.94 (m, 1H), 3.68 (s, 3H), 2.99 (t, $J = 7.7$ Hz, 2H), 2.65-2.61 (m, 2H), 2.49-2.38 (m, 2H), 2.16-2.09 (m, 1H); ^{13}C NMR 173.2, 172.9, 148.3, 139.6, 133.5, 132.9, 130.5, 128.1, 127.5, 124.4, 79.8, 51.8, 33.6, 28.9, 28.3, 25.2; IR 1794, 1739 cm^{-1} .

Methyl (2E)-2-ethyl-3-[(2R)-tetrahydro-2-methyl-5-oxofuranyl]-2-propenoate (27): ^1H NMR 6.74 (s, 1H), 3.73 (s, 3H), 2.56 (m, 2H), 2.40 (m, 2H), 1.56 (s, 3H), 1.03 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR 175.7, 167.8, 141.4, 135.9, 85.0, 51.9, 35.4, 28.5, 26.7, 20.8, 13.8; IR 1780, 1716 cm^{-1} .

(5R)-[3-Ethyl-5-(2'-methoxycarbonyl)ethyl]furan-2(5H)-one (31): ^1H NMR 6.85 (s, 1H), 3.62 (s, 3H), 2.60-2.05 (m, 6H), 1.42 (s, 3H), 1.11 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR 173.1, 164.6, 150.4, 135.5, 85.3, 51.6, 32.8, 28.1, 24.3, 18.3, 11.6; IR 1780, 1716 cm^{-1} .

Benzyl (2E)-2-ethyl-3-[(2R)-tetrahydro-2-methyl-5-oxofuranyl]-2-propenoate (28): colorless oil; $[\alpha]_{\text{D}}^{25} +21.5$ (c 2.0); ^1H NMR 7.38-7.35 (m, 5H), 6.82 (s, 1H), 5.20 (s, 2H), 2.60-2.30 (m, 6H), 1.58 (s, 3H), 1.07 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR 176.0, 167.6, 142.1, 136.3, 136.0,

128.8, 128.5, 128.4, 85.4, 67.0, 35.7, 28.8, 27.1, 21.2, 14.2, 1.8; IR 1779, 1713 cm^{-1} ; MS (CI) 289 ($M^+ + 1$, 100); HRMS calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4$ ($M^+ + 1$) 289.144, found 289.1438.

(4-Methoxyphenyl)methyl (2E)-2-ethyl-3-[(2R)-tetrahydro-2-methyl-5-oxofuranyl]-2-propenoate (29): yellow oil; $[\alpha]_D^{25} +16.1$ (*c* 2.6); ^1H NMR 7.31 (dd, $J = 6.5, 2.1$ Hz, 2H), 6.90 (dd, $J = 6.5, 1.9$ Hz, 2H), 6.77 (s, 1H), 5.12 (s, 2H), 3.80 (s, 3H), 2.58 (m, 2H), 2.45 (m, 2H), 2.25 (m, 1H), 1.56 (s, 3H), 1.04 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR 176.0, 167.6, 159.9, 141.9, 136.4, 130.3, 128.1, 114.2, 85.4, 66.8, 55.5, 35.7, 28.8, 27.1, 21.2, 14.2; IR 1779, 1711 cm^{-1} ; MS (CI) 318 ($M^+ + 1$, 1), 121 (100). Anal. Calcd for $\text{C}_{18}\text{H}_{22}\text{O}_5$: C, 67.91; H, 6.97. Found: C, 68.04; H, 6.99.

To determine the enantiomeric purity of the fragmentation products, **24** was chosen as a representative example and structurally modified to adapt to utilize Mosher method¹⁶ as shown in Scheme 1. Treatment of γ -butyrolactone **24** with benzylamine in *tert*-butanol cleanly gave the allylic alcohol **42** in a 76% yield. **42** was then converted into (*S*)-Mosher ester **43**. To prepare racemic analog of **43**, **42** was subjected to oxidation [tetrapropylammonium perruthenate (TPAP), 4-methylmorpholine *N*-oxide (NMO), CH_2Cl_2] and reduction (NaBH_4 , CeCl_3 , MeOH) sequence to give the racemic allylic alcohol **45** in a 69% yield for two steps. **45** was then reacted with (*S*)-Mosher acid to provide a diastereomeric mixture **46**. ^{19}F NMR analysis of **43** and diastereomeric **46** showed the enantiomeric purity of **24** to be 98% ee (major diastereomer, 4.33 ppm and minor diastereomer, 4.03 ppm).

SCHEME 1^a

^a Reagents and conditions: (a) BnNH₂, *t*-BuOH, rt; (b) (S)-MTPACl, 4-DMAP, Et₃N, CH₂Cl₂;

(c) TPAP, NMO, 4Å-MS, CH₂Cl₂; (d) NaBH₄, CeCl₃, MeOH.

(2*E*,4*R*)-2-(3-Chloropropyl)-4-hydroxy-7-oxo-7-[(phenylmethyl)amino]-2-heptenoic acid phenylmethyl ester (42). To a solution of lactone **24** (99 mg, 0.3 mmol) in *t*-BuOH (1 mL) was added benzylamine (122 μL, 1.1 mmol). The resulting solution was stirred at room temperature for 2 d. The reaction mixture was concentrated and directly purified by flash column chromatography (hexanes/EtOAc, 1:1) to give **42** (100 mg, 76%) as a colorless oil. $[\alpha]_D^{26} -22.2$ (*c* 0.36); ¹H NMR 7.37-7.22 (m, 10H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.32 (br t, *J* = 5.5 Hz, 1H), 5.17 and 5.14 (AB q, *J* = 12.7 Hz, 2H), 4.53 (br s, 1H), 4.38 (d, *J* = 5.8 Hz, 2H), 4.08 (br s, 1H), 3.49 (t, *J* = 6.4 Hz, 2H), 2.52-2.34 (m, 4H), 1.97-1.79 (m, 4H); ¹³C NMR 173.1, 167.1, 144.6, 137.9, 135.8, 131.1, 128.7, 128.5, 128.2, 128.1, 127.8, 127.5, 67.7, 66.6, 44.6, 43.7, 32.5, 32.1, 31.7, 24.4; IR 3305, 1710, 1646 cm⁻¹; CIMS 430 (*M*⁺+1, 1), 108 (100). Anal. Calcd for C₂₄H₂₈ClNO₄: C, 67.05; H, 6.56. Found C, 66.92; H, 6.60.

Mosher Ester of **42 (**43**).**¹ To a solution of allylic alcohol **42** (34 mg, 7.9 μ mol) and 4-*N,N*-dimethylaminopyridine (4-DMAP, 3 mg, 2.5 μ mol) in CH₂Cl₂ (5 mL) was added via cannula a solution of (*S*)-(+)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride ((*S*)-MTPACl, 98% ee, 30 mg, 12 μ mol) in CH₂Cl₂ (1 mL). The resulting solution was treated with triethylamine (Et₃N, 17 μ L, 12 μ mol) at 0 °C. The reaction mixture was stirred for 5 h at room temperature. The reaction mixture was diluted with additional CH₂Cl₂ (10 mL), washed with water and brine. The organic solution was dried over anhydrous Na₂SO₄ and concentrated to give the crude product which was purified by flash column chromatography (hexanes/EtOAc, 5:1) to give **43** (48 mg, 94%) as a colorless oil. Integration of vinyl protons of both ¹H and ¹⁹F NMR spectra showed that the ratio of major and minor diastereomers was 95:5. *R*_f 0.82 (hexanes/EtOAc, 1:1); [α]_D²³ +17.1 (*c* 0.76); ¹H NMR 7.47-7.17 (m, 15H), 6.63 (d, *J* = 9.3 Hz, 1H, major diastereomer), 6.51 (d, *J* = 9.3 Hz, 1H, minor diastereomer), 5.79-5.75 (m, 1H), 5.52 (br s, 1H), 5.23 and 5.18 (AB q, *J* = 24.9, 12.5 Hz, 2H), 4.42 and 4.35 (d of AB q, *J* = 32.7, 14.6, 5.8 Hz, 2H), 3.61-3.52 (m, 2H), 3.50 (s, 3H), 2.71-2.55 (m, 2H), 2.14-1.88 (m, 6H); ¹³C NMR 170.7, 166.4, 165.9, 137.9, 137.5, 135.6, 134.9, 132.2, 129.7, 128.8, 128.6, 128.4, 128.3, 128.1, 127.8, 127.7, 127.1, 105.3, 72.5, 66.9, 55.5, 44.6, 43.7, 31.6, 30.9, 29.4, 24.9; ¹⁹F NMR 4.88 (minor), 5.25 (major); IR 1750, 1718, 1654 cm⁻¹; CIMS 648 (M⁺+1, 0), 646 (M⁺+1, 0), 203 (100). Anal. Calcd for C₃₄H₃₅F₃ClNO₆: C, 63.21; H, 5.46. Found: C, 63.13; H, 5.46.

(2*E*)-2-(3-Chloropropyl)-4,7-dioxo-7-[(phenylmethyl)amino]-2-heptenoic acid phenylmethyl ester (44**).**² To a solution of alcohol **42** (134 mg, 31 mmol), 4-methylmorpholine *N*-oxide (NMO, 55 mg, 47 mmol), and 4Å-MS (200 mg) in CH₂Cl₂ (5 mL) was added tetrapropylammonium perruthenate (VII) (TPAP, 6 mg, 1.6 mmol) at room temperature. The resulting dark suspension was stirred overnight. The reaction mixture was directly purified by flash column chromatography (hexanes/EtOAc, 3:1) to give **44** (81 mg, 79% based on the 78% conversion of the starting material) as a white crystal and the unreacted starting material **42** (30 mg, 22%). mp 83–85 °C; ¹H NMR 7.39-7.26 (m, 10H), 7.16 (s, 1H), 5.96 (br s, 1H), 5.24 (s,

2H), 4.43 (d, $J = 5.7$ Hz, 2H), 3.53 (t, $J = 6.7$ Hz, 2H), 2.95 (t, $J = 6.2$ Hz, 2H), 2.81 (t, $J = 7.6$ Hz, 2H), 2.52 (t, $J = 6.2$ Hz, 2H), 1.94 (p, $J = 7.2$ Hz, 2H); ^{13}C NMR 200.0, 171.3, 166.8, 143.8, 138.1, 135.3, 132.9, 128.7, 128.5, 128.3, 127.7, 127.5, 67.4, 44.6, 43.7, 39.6, 31.9, 29.7, 25.9; IR 1716, 1694 cm^{-1} ; CIMS 430 ($\text{M}^+ + 1$, 18), 428 ($\text{M}^+ + 1$, 53), 320 (100). Anal. Calcd for $\text{C}_{24}\text{H}_{26}\text{ClNO}_4$: C, 67.36; H, 6.12. Found: C, 67.47; H, 6.13.

(2E)-2-(3-Chloropropyl)-4-hydroxy-7-oxo-7-[(phenylmethyl)amino]-2-heptenoic acid phenylmethyl ester (45).³ To a solution of ketone **44** (39 mg, 9.0 mmol) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (51 mg, 14 mmol) in MeOH (2 mL) was added NaBH_4 (3 mg, 9.0 mmol) at 0 °C. The resulting solution was stirred overnight. The reaction mixture was quenched with water and extracted with EtOAc (5×5 mL). The organic solution was dried over anhydrous Na_2SO_4 and concentrated to give the crude alcohol **45** (34 mg, 87%). ^1H and ^{13}C NMR spectra of the crude product were identical to those of **42**. The crude product was directly used for the next reaction without further purification.

Mosher Ester of 45 (46). This compound was prepared by the same procedure as of **43**. R_f 0.82 (hexanes/EtOAc, 1:1); ^1H NMR (diastomeric mixture) 7.47-7.17 (m, 30H), 6.63 (d, $J = 9.3$ Hz, 1H), 6.51 (d, $J = 9.3$ Hz, 1H), 5.80-5.74 (m, 4H), 5.68 (br s, 1H), 5.52 (br s, 1H), 5.24-5.21 (m, 4H), 4.45-4.33 (m, 4H), 3.65-3.52 (m, 4H), 3.50 (s, 6H), 2.70-2.53 (m, 4H), 2.29-1.87 (m, 12H); ^{13}C NMR 170.8, 168.9, 166.4, 165.9, 137.9, 137.5, 135.6, 134.9, 132.2, 131.8, 129.7, 129.6, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.8, 127.6, 127.5, 127.3, 127.1, 72.7, 72.5, 66.9, 66.8, 55.5, 55.4, 44.6, 44.5, 43.7, 43.6, 31.6, 31.5, 31.2, 30.9, 29.4, 24.9; ^{19}F NMR 4.88, 5.15; IR 1749, 1715, 1652 cm^{-1} ; CIMS 648 ($\text{M}^+ + 1$, 0), 646 ($\text{M}^+ + 1$, 0), 203 (100).

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Figure 1. ORTEP drawing of 22.

Table 1. Crystal data and structure refinement for 22.

Identification code	s070
Empirical formula	C ₁₆ H ₁₈ O ₅
Formula weight	290.30
Temperature	294(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁ (No. 19)
Unit cell dimensions	a = 5.1105(2) Å alpha = 90° b = 10.8349(3) Å beta = 90° c = 26.9620(10) Å gamma = 90°
Volume, Z	1492.93(9) Å ³ , 4
Density (calculated)	1.292 Mg/m ³
Absorption coefficient	0.796 mm ⁻¹
F(000)	616
Crystal size	0.12 x 0.16 x 0.24 mm
θ range for data collection	3.28 to 56.99°
Limiting indices	-5 ≤ h ≤ 1, -1 ≤ k ≤ 11, -29 ≤ l ≤ 1
Reflections collected	1718
Independent reflections	1538 (R _{int} = 0.0244)
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	1538 / 18 / 211
Goodness-of-fit on F ²	1.051
Final R indices [I > 2σ(I)]	R1 = 0.0417, wR2 = 0.1047
R indices (all data)	R1 = 0.0518, wR2 = 0.1144
Absolute structure parameter	0.1(4)
Extinction coefficient	0.0072(9)
Largest diff. peak and hole	0.150 and -0.139 eÅ ⁻³

Figure 2. ORTEP drawing of 35.

Table 2. Crystal data and structure refinement for 35.

Identification code	6-122P
Empirical formula	$C_{10}H_{12}O_4$
Formula weight	196.20
Temperature	198(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	$a = 6.6845(7)$ Å $\alpha = 90^\circ$ $b = 6.7458(11)$ Å $\beta = 90^\circ$ $c = 21.712(4)$ Å $\gamma = 90^\circ$
Volume, Z	979.0(3) Å ³ , 4
Density (calculated)	1.331 Mg/m ³
Absorption coefficient	0.103 mm ⁻¹
F(000)	416
Crystal size	.20 x .40 x .44 mm
θ range for data collection	1.88 to 30.57°
Limiting indices	$-9 \leq h \leq 9, -5 \leq k \leq 9, -31 \leq l \leq 27$
Reflections collected	9084
Independent reflections	3025 ($R_{int} = 0.0316$)
Completeness to $\theta = 30.57^\circ$	99.9 %
Absorption correction	SADABS
Max. and min. transmission	0.9808 and 0.7486
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3025 / 0 / 140
Goodness-of-fit on F^2	1.049
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0417, wR2 = 0.1042$
R indices (all data)	$R1 = 0.0535, wR2 = 0.1098$
Absolute structure parameter	-0.5(9)
Largest diff. peak and hole	0.289 and -0.189 eÅ ⁻³

9732352448;

[illegible]

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