Supporting Information for:

Asymmetric Synthesis of Bicyclic Ketones Having an Angular Substituent via Ti(II) Alkoxide-Mediated Tandem Cyclization of Tri-substituted Olefinic Substrates

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General. ^1H and ^{13}C NMR spectra were taken on a Varian Gemini-300 spectrometer at 300 and 75 MHz, respectively. $CDCl_3$ was used as the solvent. Chemical shifts are reported in parts per million shift (δ value) from Me_4Si (δ 0 ppm for ^1H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in hertz. Infrared (IR) spectra were recorded on a JASCO A-100 spectrometer and are reported in wave numbers (cm^{-1}). Optical rotation was measured on JASCO DIP-370 digital polarimeter. Enantiomeric excess was determined by chiral GC (Chirasil-DEX/Chrompack, 0.25 mm x 25 m, DF = 0.25). All reactions were performed under nitrogen or argon. Solvents and chemicals were purified or dried in a standard manner. (-)-8-Phenylmenthol and (-)-(1*R*,2*S*)-2-phenyl-1-cyclohexanol (99% ee) are commercially available from Aldrich Chemical Co. 8-(2-Naphthyl)menthol was prepared from (+)-pulegone (Tokyo Chemical Industry Co., Japan) according to the literature [d'Angelo, J.; Maddaluno, J. *J. Am. Chem. Soc.* **1986**, *108*, 8112-8114].

(±)-2,5-Dimethyl-1-bicyclo[3.3.0]octen-3-one (1). This racemic ketone is a known compound [Miyashita, M.; Yanami, T.; Kumazawa, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1984**, *106*, 2149-2156]. For characterization, see (-)-**1**.

(±)-5-Methyl-2-pentyl-1-bicyclo[3.3.0]octen-3-one (2). For characterization, see (-)-**2**.

(±)-5-Methyl-2-(trimethylsilyl)-1-bicyclo[3.3.0]octen-3-one (3). For characterization, see (-)-**3**.

(±)-5-Butyl-2-pentyl-1-bicyclo[3.3.0]octen-3-one (4). For characterization, see (-)-**4**.

Preparation of Enynoates 11-15 and 17. These were prepared from the corresponding methyl ketones or aldehyde and $(EtO)_2P(O)CH(R)CO_2Et$ (R = H or Me) (NaH, THF), which is illustrated in the preparation of **21**.

Ethyl (*E*)-3-Methyl-2-nonen-7-ynoate (11). ^{1}H NMR δ 1.27 (t, J = 7.2 Hz, 3 H), 1.65 (quintet, J = 7.2 Hz, 2 H), 1.78 (t, J = 2.4 Hz, 3 H), 2.13 (tt, J = 2.4, 7.2 Hz, 2 H), 2.15 (d, J = 1.2 Hz, 3 H), 2.23 (t, J = 7.2 Hz, 2 H), 4.14 (q, J = 7.2 Hz, 2 H), 5.68 (sextet, J = 1.2 Hz, 1 H); ^{13}C NMR δ 3.31, 14.21, 18.18, 18.62, 26.62, 39.78, 59.45, 76.20, 78.36, 115.97, 159.35, 168.55; IR (neat) 2979, 2937, 2862, 1714 (C=O), 1649, 1444, 1369, 1225, 1147, 1074, 1038, 874, 733 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.29; H, 9.43.

Ethyl (*E*)-3-Methyl-2-tridecen-7-ynoate (12). ^{1}H NMR δ 0.89 (t, J = 7.2 Hz, 3 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.24-1.40 (m, 4 H), 1.48 (quintet, J = 7.5 Hz, 2 H), 1.65 (quintet, J = 7.5 Hz, 2 H), 2.11-2.18 (m, 4 H), 2.15 (d, J = 1.5 Hz, 3 H), 2.23 (t, J = 7.5 Hz, 2 H), 4.14 (q, J = 7.2 Hz, 2 H), 5.68 (sextet, J = 1.5 Hz, 1 H); ^{13}C NMR δ 13.87, 14.20, 18.22, 18.58, 18.62, 22.11, 26.76, 28.70, 30.99, 39.76, 59.44, 79.17, 81.14, 116.00, 159.38, 166.96; IR (neat) 2933, 2860, 1716 (C=O), 1649, 1458, 1381, 1367, 1348, 1223, 1146, 1072, 1038, 874, 731 cm^{-1}. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.60; H, 10.25.

Ethyl (*E*)-3-Methyl-8-(trimethylsilyl)-2-octen-7-ynoate (13). ^{1}H NMR δ 0.15 (s, 9 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.69 (quintet, J = 7.2 Hz, 2 H), 2.15 (d, J = 1.2 Hz, 3 H), 2.23 (t, J = 7.2 Hz, 2 H), 2.25 (m, 2 H), 4.14 (q, J = 7.2 Hz, 2 H), 5.68 (sextet, J = 1.2 Hz, 1 H); ^{13}C NMR δ -0.03, 14.20, 18.59, 19.24, 26.16, 39.64, 59.48, 85.30, 106.51, 116.19, 159.02, 166.90; IR (neat) 2956, 2902, 2871, 2175, 1716 (C=O), 1651, 1446, 1367, 1250, 1223, 1146, 1072, 1036, 843, 760, 640 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_2Si$: C, 66.61; H, 9.58. Found: C, 66.80; H, 9.84.

Ethyl (*E*)-3-Butyl-2-tridecen-7-ynoate (14). ^{1}H NMR δ 0.89 (m, 6 H), 1.24 (t, J = 7.2 Hz, 3 H), 1.25-1.50 (m, 10 H), 1.62 (quintet, J = 6.9 Hz, 2 H), 2.12 (m, 4 H), 2.22 (t, J = 7.8 Hz, 2 H), 2.58 (t, J = 6.9 Hz, 2 H), 4.10 (q, J = 7.2 Hz, 2 H), 5.61 (s, 1 H); ^{13}C NMR δ 13.77, 13.81, 14.13, 18.27, 18.53, 22.08, 22.86, 26.98, 28.67, 30.66, 30.95, 31.75, 37.13, 59.33, 79.14, 81.05, 115.53, 163.95, 166.55; IR (neat) 2956, 2931, 2860, 1716 (C=O), 1643, 1458, 1377, 1234, 1192, 1146, 1041, 912, 735 cm^{-1}.

Ethyl (*E*)-2-Methyl-2-tridecen-7-ynoate (15). ^{1}H NMR δ 0.89 (t, J = 6.9 Hz, 3 H), 1.29 (t, J = 7.2 Hz, 3 H), 1.22-1.38 (m, 4 H), 1.48 (m, 2 H), 1.62 (quintet, J = 6.9 Hz, 2 H), 1.84 (d, J = 1.5 Hz, 3 H), 2.15 (m, 4 H), 2.28 (q, J = 7.5 Hz, 2 H), 4.18 (q, J = 7.2 Hz, 2 H), 6.74 (tq, J = 7.5, 1.5 Hz, 1 H); ^{13}C NMR δ 12.24, 13.86, 14.17, 18.33, 18.59, 22.11, 27.58, 27.89, 28.71, 30.99, 60.38, 79.27, 81.03, 128.53, 141.41, 168.38; IR (neat) 2960, 2931, 2860, 1712 (C=O), 1651, 1458, 1367, 1257, 1174, 1119, 1082, 744 cm^{-1}.

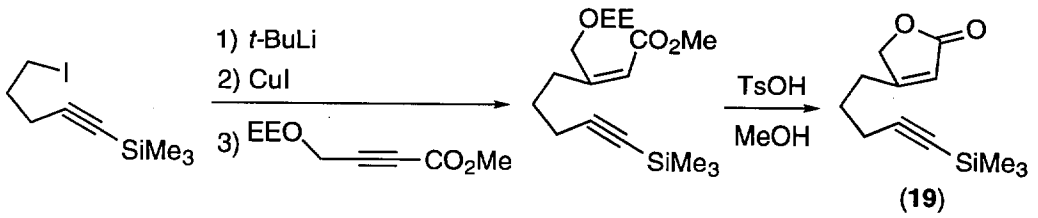
(4*RS*,5*SR*)-4-Methyl-2-pentyl-1-bicyclo[3.3.0]octen-3-one (16). ^{1}H NMR δ 0.86 (t, J = 6.9 Hz, 3 H), 0.99 (d, J = 7.8 Hz, 3 H), 1.20-1.38 (m, 4 H), 1.41 (m, 2 H), 1.80-2.23 (m, 6 H), 2.40-2.60 (m, 3 H), 2.86 (m, 1 H). The stereochemistry of this ketone was deduced based on NOE study of ^{1}H NMR spectroscopy. ^{13}C NMR δ 13.52, 13.90, 22.32,

23.65, 25.27, 25.35, 25.63, 27.54, 31.63, 42.92, 48.94, 134.22, 182.56, 214.37; IR (neat) 2956, 2871, 1705 (C=O), 1662, 1460, 1369, 1290, 1259, 1159, 1080, 1003, 727 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.42; H, 10.38.

Ethyl 2,3-Dimethyl-2-tridecen-7-ynoate (a 1:1 mixture of *E*- and *Z*-isomers) (17). ^1H NMR δ 0.86 (m, 3 H, both isomers), 1.25 (t, J = 7.2 Hz, 3 H, both isomers), 1.33 (m, 4 H, both isomers), 1.46 (m, 2 H, both isomers), 1.60 (m, 2 H, both isomers), 1.78 (s, 3 H, one isomer), 1.84 (s, 3 H, one isomer), 1.87 (d, J = 0.9 Hz, 3 H, one isomer), 1.97 (q, J = 1.5 Hz, 3 H, one isomer), 2.15 (m, 4 H, both isomers), 2.22 (m, 2 H, (*E*)-isomer), 2.39 (m, 2 H, (*Z*)-isomer), 4.17 (q, J = 7.2 Hz, 2 H, one isomer), 4.18 (q, J = 7.2 Hz, 2 H, one isomer); IR (neat) 2931, 2860, 1712 (C=O), 1635, 1458, 1377, 1331, 1300, 1271, 1211, 1163, 1095, 1055, 1034, 773, 733 cm^{-1} for a 1:1 mixture of the stereoisomers.

(±)-4,5-Dimethyl-2-pentyl-1-bicyclo[3.3.0]octen-3-one (18). ^1H NMR δ 0.86 (t, J = 6.6 Hz, 3 H), 0.99 (d, J = 7.5 Hz, 3 H), 1.10 (s, 3 H), 1.27 (m, 4 H), 1.41 (m, 2 H), 1.52 (m, 1 H), 1,95 (m, 2 H), 2.05 (m, 1 H), 2.14 (m, 2 H), 2.25 (q, J = 7.5 Hz, 1 H), 2.52 (m, 2 H); ^{13}C NMR δ 13.93, 14.07, 22.32, 22.92, 23.50, 23.81, 27.11, 27.65, 30.54, 31.55, 51.65, 51.92, 132.63, 185.84, 214.11; IR (neat) 2964, 2927, 2850, 1704 (C=O), 1662, 1458, 1375, 1261, 1097, 1032, 804 cm^{-1}.

3-(5-Trimethylsilyl-4-pentynyl)-2-buten-4-olide (19). This was prepared by the following reaction according to the literature [Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980; pp 58-62. Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851-1852. Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1853-1854. Corey, E. J.; Kim, C. U.; Chen, R. H. K.; Takeda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4395-4396].



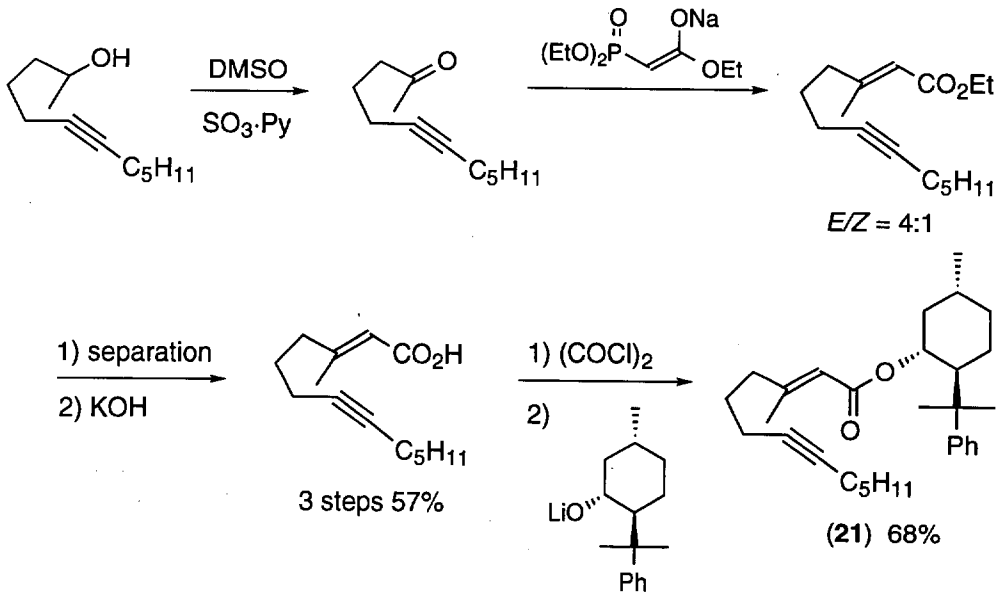
(19)

^1H NMR δ 0.12 (s, 9 H), 1.79 (quintet, J = 6.6 Hz, 2 H), 2.30 (t, J = 6.6 Hz, 2 H), 2.52 (br t, J = 6.6 Hz, 2 H), 4.74 (d, J = 1.8 Hz, 2 H), 5.84 (quintet, J = 1.8 Hz, 1 H); ^{13}C NMR δ 0.14, 19.18, 25.71, 27.24, 72.97, 86.21, 105.16, 115.79, 169.65, 174.03; IR (neat), 2985, 2173, 1751 (C=O), 1637, 1448, 1325, 1250, 1171, 1130, 1047, 1020, 841, 760, 698 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2Si$: C, 64.82; H, 8.16. Found: C, 64.95; H, 8.01.

6-[(*E*)-(Trimethylsilyl)methylene]-2-oxaspiro[4.4]nonan-3-one (20). ^1H NMR δ 0.09 (s, 9 H), 1.72 (t, J = 6.6 Hz, 2 H), 1.73 (m, 1 H), 1.84 (m, 1 H), 2.41 (d, J = 14.4 Hz, 1 H), 2.43 (tt, J = 2.4, 7.2 Hz, 2 H), 2.60 (d, J = 14.4 Hz, 1 H), 4.10 (s, 2 H), 5.49 (t, J = 2.4 Hz, 1 H); ^{13}C NMR δ -0.71, 23.08, 32.44, 38.22, 42.22, 51.97 (spiro-carbon), 79.14, 119.94, 162.86, 176.78; IR (neat) 2956, 2871, 1782 (C=O), 1620, 1466, 1415, 1248, 1165,

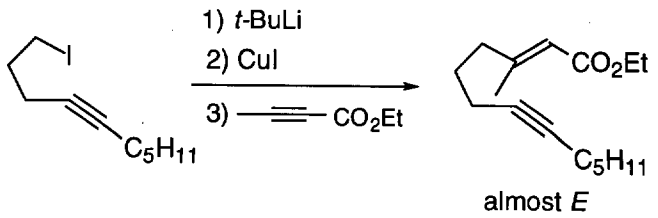
1016, 910, 870, 841, 733 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_2Si$: C, 64.24; H, 8.98. Found: C, 63.91; H, 8.76.

Typical Procedure for the Preparation of Optically Active Enynoates. (1*R*,2*S*,5*R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl (*E*)-3-Methyl-2-tridecen-7-ynoate (21). This was prepared according to the following scheme. The yields are not necessarily optimized.



To a mixture of 6-dodecyn-2-ol (2.30 g, 12.7 mmol), dimethylsulfoxide (17.9 mL, 253 mmol), and triethylamine (17.6 mL, 127 mmol) in 25 mL of CH_2Cl_2 was added sulfur trioxide-pyridine complex (12.1 g, 76 mmol) in portions at 0 °C. After stirring at room temperature for 30 min, the reaction was terminated by the addition of aqueous 1 N HCl. The organic layer was diluted with ether, separated, washed with aqueous $NaHCO_3$ solution, dried over Na_2SO_4, and finally concentrated to an oil of the methyl ketone.

To a suspension of NaH (718 mg of a 55% dispersion in oil, 16.5 mmol, the oil was washed off with hexane under nitrogen) in 23 mL of THF was added triethyl phosphonoacetate (3.55 mL, 17.9 mmol) at 0 °C. After stirring at room temperature for 10 min, the crude ketone obtained above in 1 mL of THF was added at 0 °C. After stirring at room temperature for 4 h, the reaction was terminated by the addition of water. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic parts were dried (Na_2SO_4) and concentrated to an oil of the ethyl ester as a mixture of olefinic stereoisomers (*E*/*Z* = 4:1). Separation on silica gel (hexane-ether) readily afforded a pure portion of the *E*-olefinic ester as an oil. (Alternatively, the isomerically pure *E*-olefinic ester was also obtained by the following reaction [Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980; pp 58-62. Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851-1852. Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1853-1854]).



almost *E*

To a solution of the *E*-olefinic ester in 15 mL of EtOH was added aqueous 2 N KOH (9.5 mL, 19 mmol). After stirring at reflux for 1.5 h, the bulk of the solvent was evaporated off and the residue was diluted with 1 N HCl and ether. The ether layer was separated and the aqueous layer was extracted with ether. The combined ethereal layers were dried and concentrated to an oil, which was chromatographed on silica gel (hexane-ether) to afford the carboxylic acid (1.62 g, 57% overall yield from the starting alkynol).

To a solution of the carboxylic acid (230 mg, 1.03 mmol) in 2 mL of benzene was added $(COCl)_2$ (0.18 mL, 2.06 mmol) at 0 °C. After stirring in an oil bath maintained at 70 °C for 2 h, the reaction mixture was cooled to room temperature and was concentrated to a crude oil of the acid chloride.

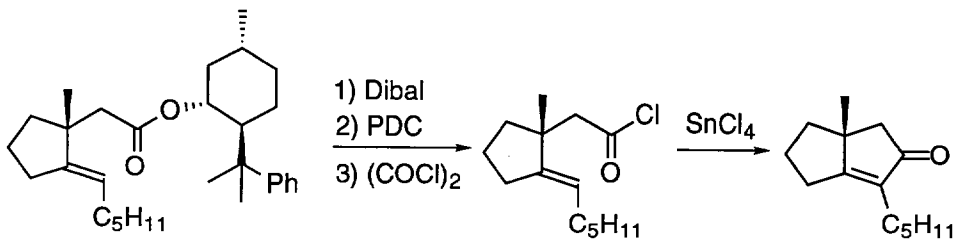
To a solution of (-)-8-phenylmenthol (217 mg, 0.94 mmol) in 1 mL of THF was added n-BuLi (1.54 M in hexane, 0.61 mL, 0.94 mmol) at 0 °C. After stirring at room temperature for 1.5 h, the crude acid chloride in 1 mL of THF was added at 0 °C. After stirring at room temperature for 2 h, the reaction was terminated by the addition of water. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried (Na_2SO_4) and concentrated to an oil, which was chromatographed on silica gel (hexane-ether) to afford the pure title compound (305 mg, 68%) as an oil. ^{1}H NMR δ 0.86 (d, J = 6.6 Hz, 3 H), 0.91 (t, J = 7.2 Hz, 3 H), 0.9-1.2 (m, 2 H), 1.22 (s, 3 H), 1.25-1.43 (m, 4 H), 1.31 (s, 3 H), 1.44-1.54 (m, 4 H), 1.55-1.64 (m, 4 H), 1.89 (m, 1 H), 2.00 (dt, J = 3.3, 9.0 Hz, 1 H), 2.07 (d, J = 1.2 Hz, 3 H), 2.14 (m, 6 H), 4.79 (dt, J = 4.5, 10.5 Hz, 1 H), 4.99 (sextet, J = 1.2 Hz, 1 H), 7.11 (m, 1 H), 7.25 (m, 4 H); ^{13}C NMR δ 13.91, 18.30, 18.56, 18.59, 21.70, 22.12, 25.43, 26.58, 26.70, 27.22, 28.72, 31.00, 31.23, 34.54, 39.65, 39.67, 41.86, 50.56, 73.30, 79.27, 81.02, 116.35, 124.94, 125.51, 127.94, 151.81, 158.58, 166.09; IR (neat) 3087, 3051, 3026, 2960, 2927, 2869, 1709 (C=O), 1647, 1458, 1389, 1223, 1146, 1093, 764, 700 cm^{-1}; $[\alpha]_D^{21}$ +15.3 (*c* 1.01, $CHCl_3$).

Typical Procedure of the Asymmetric Tandem Cyclization. (-)-5-Methyl-2-pentyl-1-bicyclo[3.3.0]octen-3-one (-)-(2) (93% ee) Prepared from 21. To a solution of the enynoate **21** (60 mg, 0.137 mmol) and Ti(O-*i*-Pr)3Cl (1 M solution in hexane, 0.179 mL, 0.179 mmol) in 1.4 mL of Et_2O was added *i*-PrMgCl (1.57 M in ether, 0.228 mL, 0.357 mmol) dropwise at -78 °C under nitrogen. After stirring for 30 min, the solution was warmed to -20 °C over 60 min and kept at this temperature for an additional 2 h. *s*-BuOH (1 M solution in ether, 0.179 mL, 0.179 mmol) was added at -20 °C and stirred at the same temperature for an additional 15 min. The reaction was terminated by the addition of aqueous 1 N HCl at -20 °C. The organic layer was separated, washed with aqueous $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated to an oil. Chromatography on silica gel (hexane-ether) afforded mono-cyclic

ester **24** (18 mg, 30%) as a colorless oil and, in this case, an inseparable mixture of (-)-**2** and 8-phenylmenthol. Thus, this portion was treated with acetic anhydride (0.040 mL, 0.411 mmol), dimethylaminopyridine (17 mg, 0.137 mmol), and triethylamine (0.12 mL, 0.822 mmol) in 0.5 mL of CH_2Cl_2 at 0 °C. Usual work-up and chromatography on silica gel (hexane-ether) afforded the unchanged title compound (17.5 mg, 62%, 93% ee) as a colorless oil and the acetate of 8-phenymenthol (24 mg, 64%), respectively. The enantiopurity was determined by chiral GC (retention times: 22.10 and 23.41 min, H_2: 0.5 kg/cm^2, air: 0.25 kg/cm^2, make up: [H_2] 0.5 kg/cm^2, carrier: [H_2] 1.5 kg/cm^2, column temp: 120 °C, injection temp: 250 °C, detection temp: 275 °C). ^{1}H NMR δ 0.86 (t, J = 6.6 Hz, 3 H), 1.08 (s, 3 H), 1.18-1.45 (m, 6 H), 1.86 (dd, J = 7.2, 12.0 Hz, 1 H), 2.00 (dd, J = 7.5, 13.5 Hz, 1 H), 1.94-2.20 (m, 4 H), 2.21 (d, J = 17.4 Hz, 1 H), 2.38 (d, J = 17.4 Hz, 1 H), 2.52 (t, J = 7.2 Hz, 2 H); ^{13}C NMR δ 13.89, 22.30, 23.45, 23.51, 23.58, 25.29, 27.70, 31.55, 36.69, 47.83, 50.65, 134.95, 187.18, 210.66; IR (neat) 2956, 2927, 2860, 1707 (C=O), 1662, 1458, 1375, 1288, 1072, 902 cm^{-1}; $[\alpha]_D^{22}$ -15.9 (*c* 0.65, $CHCl_3$) for a sample of 93% ee. Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.27; H, 10.38.

***(1R,2S,5R)*-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl [*(R)*-1-Methyl-2-(1-*(E)*-hexylidene)cyclopent-1-yl]acetate (24).** This was obtained as a 71:29 mixture of diastereoisomers. ^{1}H NMR major isomer δ 0.86 (d, J = 6.3 Hz, 3 H), 0.90 (t, J = 6.9 Hz, 3 H), 0.96 (s, 3 H), 0.92-1.18 (m, 2 H), 1.20 (s, 3 H), 1.28 (m, 6 H), 1.30 (s, 3 H), 1.42 (m, 2 H), 1.52-1.74 (m, 6 H), 1.80-2.08 (m, 6 H), 2.12-2.34 (m, 2 H), 4.76 (dt, J = 4.5, 10.5 Hz, 1 H), 4.93 (tt, J = 2.4, 7.2 Hz, 1 H), 7.13 (m, 1 H), 7.27 (m, 4 H); ^{1}H NMR minor isomer (only a characteristic peak is shown) δ 1.00 (s, 3 H); ^{13}C NMR major isomer δ 14.01, 21.72, 22.14, 22.52, 24.92, 26.38, 26.45, 27.22, 28.81, 29.16, 29.19, 31.20, 31.44, 34.52, 39.20, 39.57, 41.78, 43.47, 45.18, 50.28, 73.81, 119.90, 125.00, 125.46, 127.98, 149.76, 151.88, 171.75; IR (neat) 3087, 3057, 2956, 2925, 2871, 1726 (C=O), 1649, 1601, 1458, 1377, 1261, 1219, 1149, 1093, 1032, 806, 764, 700 cm^{-1} for a 71:29 mixture of the diastereoisomers. Anal. Calcd for $C_{30}H_{46}O_2$: C, 82.14; H, 10.57. Found: C, 82.10; H, 10.72.

The absolute structure of the cyclopentane ring was unambiguously determined by the correlation to (-)-**2** as shown in the following sequence.



(24) 42% de

(-)-**(2)** 48% ee
overall 41% yield

***(1R,2S,5R)*-2-(1-Methyl-1-phenylethyl)-5-methyl-cyclohexyl *(E)*-2-Tridecen-7-ynoate (22).** ^{1}H NMR δ 0.86 (d, J = 6.3 Hz, 3 H), 0.91 (t, J = 6.9 Hz, 3 H), 0.9-1.14 (m, 2 H), 1.21 (s, 3 H), 1.25-1.38 (m, 5 H), 1.30 (s, 3 H), 1.49 (m, 3 H), 1.56

(quintet, J = 7.5 Hz, 2 H), 1.66 (m, 2 H), 1.90 (m, 1 H), 2.04 (dt, J = 3.3, 9.0 Hz, 1 H), 2.15 (m, 6 H), 4.84 (dt, J = 4.5, 10.5 Hz, 1 H), 5.28 (dt, J = 15.6, 1.5 Hz, 1 H), 6.48 (dt, J = 15.6, 6.9 Hz, 1 H), 7.11 (m, 1 H), 7.24 (m, 4 H); ^{13}C NMR δ 13.86, 18.14, 18.56, 21.65, 22.08, 24.88, 26.47, 27.14, 27.72, 28.69, 30.85, 30.96, 31.15, 34.51, 39.55, 41.62, 50.46, 74.03, 79.09, 81.03, 122.10, 124.86, 125.44, 127.96, 147.69, 151.81, 165.85; IR (neat) 3087, 3057, 2827, 2870, 1711 (C=O), 1655, 1495, 1456, 1369, 1319, 1267, 1194, 1153, 1092, 1030, 978, 760, 700 cm^{-1}; $[\alpha]_D^{21}$ +0.22 (*c* 0.95, $CHCl_3$).

(*1R,2S,5R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl [(*RS*)-2-(1-(*E*)-Hexylidene)cyclopent-1-yl]acetate (23). This was obtained as an 85:15 mixture of diastereoisomers. ^{1}H NMR δ 0.86 (d, J = 6.6 Hz, 3 H), 0.90 (t, J = 6.6 Hz, 3 H), 0.94-1.18 (m, 2 H), 1.21 (s, 3 H), 1.27 (m, 6 H), 1.30 (s, 3 H), 1.49 (m, 3 H), 1.68 (m, 5 H), 1.80-2.05 (m, 6 H), 2.15 (m, 1 H), 2.17 (m, 1 H), 2.42 (m, 1 H), 4.81 (dt, J = 4.5, 10.5 Hz, 1 H), 5.00 (tt, J = 2.7, 6.9 Hz, 1 H), 7.13 (m, 1 H), 7.26 (m, 4 H); ^{13}C NMR major isomer δ 13.99, 21.70, 22.52, 23.81, 24.97, 26.48, 27.72, 28.74, 29.20, 29.23, 31.17, 31.44, 32.83, 34.51, 39.60, 39.62, 40.15, 41.62, 50.26, 73.92, 120.65, 125.08, 125.45, 127.99, 144.84, 151.78, 172.61; ^{13}C NMR minor isomer (only characteristic peaks are shown) δ 120.71, 151.82, 172.67; IR (neat) 3078, 3051, 3016, 2954, 2920, 2875, 1726 (C=O), 1601, 1458, 1369, 1269, 1169, 1093, 1032, 908, 764, 733, 700 cm^{-1} for an 85:15 mixture of the diastereoisomers.

(1*R*,2*S*,5*R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl (*E*)-3-Methyl-2-nonen-7-ynoate (25). ^{1}H NMR δ 0.86 (d, J = 6.6 Hz, 3 H), 1.00-1.20 (m, 2 H), 1.22 (s, 3 H), 1.31 (s, 3 H), 1.50 (m, 2 H), 1.60 (m, 4 H), 1.80 (t, J = 2.4 Hz, 3 H), 1.94 (m, 1 H), 2.00 (dt, J = 3.3, 9.0 Hz, 1 H), 2.07 (d, J = 1.2 Hz, 3 H), 2.12 (m, 4 H), 4.79 (dt, J = 4.5, 10.8 Hz, 1 H), 5.00 (sextet, J = 1.2 Hz, 1 H), 7.10 (m, 1 H), 7.25 (m, 4 H); ^{13}C NMR δ 3.31, 18.26, 18.52, 21.69, 22.54, 25.44, 26.58, 27.23, 31.24, 31.49, 34.57, 39.67, 41.87, 50.59, 73.32, 76.08, 78.46, 116.41, 124.94, 125.51, 127.94, 151.81, 158.47, 166.07; IR (neat) 3087, 3057, 3020, 2954, 2924, 2871, 1709 (C=O), 1649, 1458, 1365, 1223, 1147, 1093, 1003, 760, 700 cm^{-1}; $[\alpha]_D^{21}$ +16.6 (*c* 0.69, $CHCl_3$). Anal. Calcd for $C_{26}H_{36}O_2$: C, 82.06; H, 9.53. Found: C, 82.31; H, 9.61.

(-)-2,5-Dimethyl-1-bicyclo[3.3.0]octen-3-one (-)-(1) (93% ee) Prepared from 25. The *racemic* form of this ketone is a known compound [Miyashita, M.; Yanami, T.; Kumazawa, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1984**, *106*, 2149-2156]. ^{1}H NMR δ 1.10 (s, 3 H), 1.67 (t, J = 1.2 Hz, 3 H), 1.30 (m, 1 H), 1.87 (ddd, J = 1.2, 7.5, 12.0 Hz, 1 H), 1.98 (m, 1 H), 2.14 (m, 1 H), 2.24 (d, J = 17.7 Hz, 1 H), 2.39 (d, J = 17.7 Hz, 1 H), 2.51 (t, J = 7.5 Hz, 2 H); ^{13}C NMR δ 8.44, 23.30, 23.35, 25.13, 36.72, 47.83, 50.43, 130.58, 187.27, 210.92; IR (neat) 2958, 2912, 2858, 1707 (C=O), 1670, 1458, 1377, 1331, 1282, 1223, 1147, 1063, 1045, 922, 731 cm^{-1}; $[\alpha]_D^{27}$ -10.6 (*c* 0.35, $CHCl_3$) for a sample of 93% ee.

As this ketone did not show satisfactory peak separation on the chiral GC, its enantiopurity was determined by the analysis of the following alcohol **29** prepared by Dibal reduction of (-)-**1** (70% yield).

(+)-2,5-Dimethyl-1-bicyclo[3.3.0]octen-3-ol (93% ee) (29). This was produced as a single stereoisomer by the reduction of (-)-**1** and the NOE study (*vide infra*) revealed that the hydroxy group is *trans* to the angular methyl. The enantiopurity was determined by chiral GC (retention times: 4.98 and 5.63 min, H_2: 0.5 kg/cm^2, air: 0.25 kg/cm^2, make up: [H_2] 0.5 kg/cm^2, carrier: [H_2] 1.5 kg/cm^2, column temp: 120 °C, injection temp: 250 °C, detection temp: 275 °C). ^{1}H NMR δ 0.95 (s, 3 H), 1.23 (m, 2 H), 1.38 (dd, J = 7.8, 12.3 Hz, 1 H), 1.56 (s, 1 H, OH), 1.62 (s, 3 H), 1.85-2.20 (m, 4 H), 2.37 (dd, J = 6.3, 12.3 Hz, 1 H), 4.98 (br s, 1 H). Irradiation of the proton at δ 4.98 ppm (C<u>H</u>OH) showed a 0.9% enhancement to that at δ 0.95 ppm (angular Me), a 2.6% enhancement to that at δ 2.37 ppm (C<u>H</u>$_2$CHOH) and, a 0.9% enhancement to that at δ 1.62 ppm (allylic Me), respectively. ^{13}C NMR δ 10.68, 21.26, 24.21, 24.62, 39.01, 51.11, 51.74, 83.66, 127.41, 151.78; IR (neat) 3325 (br, OH), 2951, 2860, 1452, 1369, 1327, 1099, 1080, 1055, 1028, 964, 910, 735 cm^{-1}; [α]$_D^{26}$ +35.7 (*c* 0.14, $CHCl_3$) for a sample of 93% ee. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.44; H, 10.27.

(1*R*,2*S*,5*R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl (*E*)-3-Methyl-8-(trimethylsilyl)-2-octen-7-ynoate (26). ^{1}H NMR δ 0.17 (s, 9 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.9-1.2 (m, 2 H), 1.22 (s, 3 H), 1.31 (s, 3 H), 1.48 (m, 2 H), 1.62 (m, 4 H), 1.90 (m, 1 H), 2.02 (dt, J = 3.3, 9.0 Hz, 1 H), 2.07 (d, J = 1.2 Hz, 3 H), 2.11 (t, J = 6.9 Hz, 2 H), 2.21 (t, J = 7.2 Hz, 2 H), 4.79 (dt, J = 4.5, 10.5 Hz, 1 H), 4.96 (sextet, J = 1.2 Hz, 1 H), 7.13 (m, 1 H), 7.27 (m, 4 H); ^{13}C NMR δ -0.01, 18.54, 19.33, 21.70, 25.20, 26.15, 26.55, 27.42, 31.23, 34.55, 39.49, 39.64, 41.85, 50.54, 73.31, 85.14, 106.63, 116.50, 124.95, 125.49, 127.93, 151.84, 158.13, 166.02; IR (neat), 3020, 2956, 2925, 2871, 2173, 1701 (C=O), 1649, 1458, 1365, 1250, 1219, 1147, 843, 760, 700 cm^{-1}; [α]$_D^{21}$ +11.2 (*c* 0.724, $CHCl_3$).

(-)-(*R*)-5-Methyl-2-(trimethylsilyl)-1-bicyclo[3.3.0]octen-3-one (-)-(3) (91% ee) Prepared from 26. The enantiopurity was determined by chiral GC (retention times: 8.18 and 9.36 min, H_2: 0.5 kg/cm^2, air: 0.25 kg/cm^2, make up: [H_2] 0.5 kg/cm^2, carrier: [H_2] 1.5 kg/cm^2, column temp: 120 °C, injection temp: 250 °C, detection temp: 275 °C). The absolute configuration was correlated to (*R*)-(**5**). ^{1}H NMR δ 0.17 (s, 9 H), 1.08 (s, 3 H), 1.39 (m, 1 H), 1.86 (m, 1 H), 1.96 (m, 1 H), 2.10 (m, 1 H), 2.22 (d, J = 17.1 Hz, 1 H), 2.33 (d, J = 17.1 Hz, 1 H), 2.62 (m, 2 H); ^{13}C NMR δ -1.29, 23.31, 25.53, 25.78, 36.28, 51.64 (4° carbon), 52.16, 133.47, 202.55, 214.80; IR (neat) 2960, 2870, 1693 (C=O), 1603, 1456, 1414, 1246, 1227, 1161, 918, 841, 733, 646 cm^{-1}; [α]$_D^{21}$ -59.1 (*c* 0.20, $CHCl_3$) for a sample of 91% ee. Anal. Calcd for $C_{12}H_{20}OSi$: C, 69.17; H, 9.67. Found: C, 69.13; H, 9.98.

(1*R*,2*S*,5*R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl (*E*)-3-Butyl-2-tridecen-7-ynoate (27). ^{1}H NMR δ 0.87 (m, 9 H), 0.96-1.18 (m, 2 H), 1.22 (s, 3 H), 1.27 (m, 4 H), 1.31 (s, 3 H), 1.37 (m, 4 H), 1.50 (m, 4 H), 1.60 (m, 4 H), 1.92 (m, 1 H), 2.00 (m, 1 H), 2.16 (m, 6 H), 2.52 (m, 2 H), 4.78 (dt, J = 4.5, 10.5 Hz, 1 H), 4.94 (br s, 1 H), 7.14 (m, 1 H), 7.26 (m, 4 H); ^{13}C NMR δ 13.90, 14.00, 18.41, 18.61, 21.70, 22.13, 22.55, 22.91, 25.43, 26.59, 26.93, 28.75, 30.68, 31.01, 31.23, 31.50, 34.57, 37.07, 39.66, 41.83, 50.58, 73.24, 79.32, 81.02, 115.91, 124.94, 125.51, 127.96, 151.80, 163.14, 165.75; IR (neat) 3087,

3057, 3016, 2954, 2929, 2870, 1709 (C=O), 1643, 1456, 1389, 1232, 1194, 1147, 1093, 1049, 1032, 1007, 908, 874, 766, 733, 700 cm^{-1}; $[\alpha]_D^{23}$ +10.2 (*c* 0.51, $CHCl_3$).

(-)-5-Butyl-2-pentyl-1-bicyclo[3.3.0]octen-3-one (-)-(4) (94% ee) Prepared from 27. The enantiopurity was determined by chiral GC (retention times: 40.11 and 41.92 min, H_2: 0.5 kg/cm^2, air: 0.25 kg/cm^2, make up: [H_2] 0.5 kg/cm^2, carrier: [H_2] 2.5 kg/cm^2, column temp: 120 °C, injection temp: 250 °C, detection temp: 275 °C). ^1H NMR δ 0.86 (m, 6 H), 1.23 (m, 6 H), 1.40 (m, 4 H), 1.90-2.10 (m, 6 H), 2.20 (m, 2 H), 2.40 (s, 1 H), 2.46 (s, 1 H), 2.49 (m, 2 H); ^{13}C NMR δ 13.87, 13.92, 22.33, 23.02, 23.31, 23.62, 23.73, 27.27, 27.92, 31.58, 35.00, 36.34, 48.25, 51.42 (4° carbon), 136.05, 185.99, 210.78, IR (neat) 2956, 2929, 2858, 1705 (C=O), 1662, 1466, 1377, 1261, 1178, 1111, 1074, 1032, 918, 733 cm^{-1}; $[\alpha]_D^{22}$ -49.6 (*c* 0.26, $CHCl_3$) for a sample of 94% ee. Anal. Calcd for $C_{17}H_{28}O$: C, 82.20; H, 11.36. Found: C, 82.22; H, 11.37.

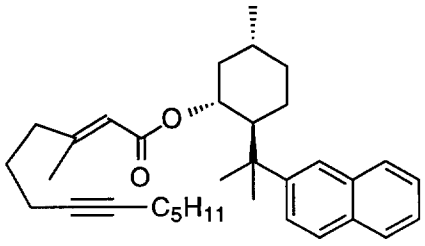
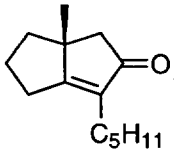
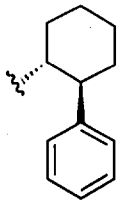
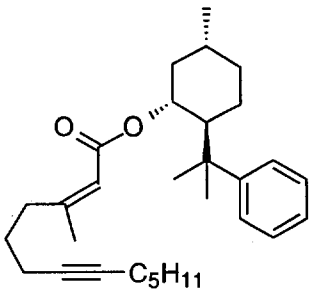
(*R*)-5-Methyl-1-bicyclo[3.3.0]octen-3-one (*R*)-(5) (91% ee). The *racemic* form of this ketone is a known compound [Miyashita, M.; Yanami, T.; Kumazawa, T.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1984**, *106*, 2149-2156]. To a solution of (-)-(**3**) (91% ee) (16 mg, 0.077 mmol) in 0.5 mL of THF was added TBAF (1 M in THF, 0.085 mL, 0.085 mmol) dropwise at 0 °C under nitrogen. After stirring for 30 min at room temperature, the reaction was terminated by the addition of aqueous NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic parts were dried (Na_2SO_4) and concentrated to an oil. Chromatography on silica gel (hexane-ether) afforded the title compound (8.4 mg, 80%, 91% ee) as a colorless oil. The enantiopurity was determined by chiral GC (retention times: 24.89 and 25.17 min, H_2: 0.5 kg/cm^2, air: 0.25 kg/cm^2, make up: [H_2] 0.5 kg/cm^2, carrier: [H_2] 0.5 kg/cm^2, column temp: 110 °C, injection temp: 250 °C, detection temp: 275 °C). The absolute configuration of this ketone was correlated to (-)-(1*R*,5*S*)-1-methylbicyclo[3.3.0]octan-3-one (**30**) shown below. ^1H NMR δ 1.10 (s, 3 H), 1.42 (m, 1 H), 1.82 (m, 1 H), 1.98 (m, 1 H), 2.13 (m, 1 H), 2.26 (d, J = 16.5 Hz, 1 H), 2.37 (d, J = 16.5 Hz, 1 H), 2.60 (m, 2 H), 5.78 (s, 1 H); ^{13}C NMR δ 23.02, 24.53, 24.91, 36.35, 50.15, 50.94, 123.35, 194.86, 210.82, IR (neat) 2960, 2868, 1711 (C=O), 1628, 1458, 1414, 1373, 1292, 1171, 901, 864, 845, 818, 746 cm^{-1}. Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.69; H, 8.98.

(-)-(1*R*,5*S*)-1-Methylbicyclo[3.3.0]octan-3-one (30). This is a known compound [Castro, J.; Sörensen, H.; Riera, A.; Morin, C.; Moyano, A.; Pericás, M. A.; Greene, A. E. *J. Am. Chem. Soc.* **1990**, *112*, 9388-9389. Greene, A. E.; Charbonnier, F. *Tetrahedron Lett.* **1985**, *26*, 5525-5528]. Its antipode is also known [Poch, M.; Valentí, E.; Moyano, A.; Pericás, M. A.; Castro, J.; DeNicola, A.; Greene, A. E. *Tetrahedron Lett.* **1990**, *31*, 7505-7508]. The above ketone (*R*)-(**5**) (91% ee) was hydrogenated with 10% Pd/C under 1 atm of hydrogen in EtOH and a trace amount of NEt_3 to give the title ketone in 80% yield. ^1H NMR δ 1.18 (s, 3 H), 1.63 (m, 2 H), 1.74 (m, 2 H), 1.86 (m, 1 H), 2.03 (m, 2 H), 2.14 (d, J = 18.6 Hz, 1 H), 2.22 (m, 1 H), 2.24 (d, J = 18.6 Hz, 1 H), 2.54 (ddd, J = 1.8, 9.6, 19.2 Hz, 1 H); ^{13}C NMR δ 24.15, 27.33, 32.75, 39.78, 44.86, 46.73, 46.88, 51.45, 220.69; IR (neat) 2952,

2868, 1739 (C=O), 1452, 1404, 1377, 1259, 1173, 916, 733, 648 cm^{-1}; $[\alpha]_D^{21}$ -28 (*c* 0.05, $CHCl_3$) for a sample of 91% ee. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.27; H, 10.23.

Addendum to Table 2 in the text. The following chiral enynoates were also subjected to the tandem cyclization to give optically active **2**. This table shows that the readily available 8-phenylmenthyl esters having *E*-olefinic configuration, such as **21**, proved to be superior to these starting materials.

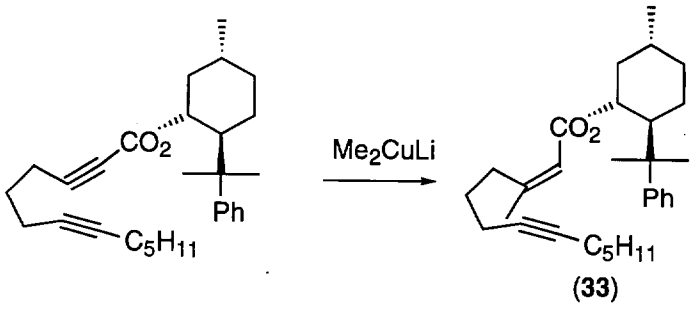
Table. The Cyclization of Enynoates Other Than 8-Phenylmenthyl Ester **21**.

Starting enynoates		Product	Yield (%)	Ee (%)
	**(31)**	 (-)-(**2**)	58	92
	**(32)**	〃	81	66
	**(33)**	〃	50	84

(1*R*,2*S*,5*R*)-2-[1-Methyl-1-(2-naphthyl)ethyl]-5-methylcyclohexyl (*E*)-3-Methyl-2-tridecen-7-ynoate (31). ^1H NMR δ 0.86 (d, J = 6.6 Hz, 3 H), 0.91 (t, J = 6.9 Hz, 3 H), 1.10-1.23 (m, 2 H), 1.29 (s, 3 H), 1.35 (m, 4 H), 1.42 (s, 3 H), 1.50 (m, 4 H), 1.60-1.82 (m, 5 H), 1.88 (m, 1 H), 1.94 (d, J = 1.2 Hz, 3 H), 1.96 (tt, J = 2.4, 7.2 Hz, 2 H), 2.14 (m, 4 H), 4.49 (br s, 1 H), 4.85 (dt, J = 4.5, 10.8 Hz, 1 H), 7.35 (m, 2 H), 7.50 (m, 1 H), 7.58 (s, 1 H), 7.75 (m, 3 H); ^{13}C NMR δ 13.91, 18.24, 18.52, 18.59, 21.71, 22.13, 24.06, 26.27, 26.42, 28.16, 28.74, 31.00, 31.24, 34.57, 39.38, 39.70, 41.88, 50.07, 72.90, 79.29, 80.83, 115.64, 122.68, 125.02, 125.22, 125.64, 127.24 (2 carbons), 127.95, 131.48, 133.64, 149.89, 158.74, 165.97; IR (neat) 3087, 3057, 3020, 2954, 2929, 2870, 1707 (C=O), 1649, 1456, 1389, 1365, 1223, 1147, 1093, 758, 700 cm^{-1}; $[\alpha]_D^{22}$ +15.4 (*c* 0.208, $CHCl_3$). Anal. Calcd for $C_{34}H_{46}O_2$: C, 83.90; H, 9.53. Found: C, 83.97; H, 9.70.

(1*R*,2*S*)-2-Phenylcyclohexyl (*E*)-3-Methyl-2-tridecen-7-ynoate (32). ^{1}H NMR δ 0.86 (t, J = 6.9 Hz, 3 H), 1.20-1.60 (m, 14 H), 1.70-1.98 (m, 2 H), 1.92 (s, 3 H), 2.05-2.20 (m, 6 H), 2.68 (dt, J = 4.2, 10.5 Hz, 1 H), 5.01 (dt, J = 4.2, 10.5 Hz, 1 H), 5.42 (sextet, J = 1.2 Hz, 1 H), 7.15-7.30 (m, 5 H); ^{13}C NMR δ 13.88, 18.17, 18.45, 18.55, 22.10, 24.68, 25.79, 26.64, 28.68, 30.96, 32.40, 34.05, 39.64, 49.65, 74.94, 79.19, 80.99, 116.14, 126.29, 127.56, 128.26, 143.45, 158.44, 166.20; IR (neat) 3070, 3028, 2931, 2858, 1712 (C=O), 1647, 1450, 1387, 1350, 1269, 1223, 1146, 1124, 1070, 1024, 912, 872, 756, 733, 700 cm^{-1}; $[\alpha]_D^{25}$ -33.4 (*c* 0.50, $CHCl_3$).

(1*R*,2*S*,5*R*)-2-(1-Methyl-1-phenylethyl)-5-methylcyclohexyl (*Z*)-3-Methyl-2-tridecen-7-ynoate (33). This was prepared as follows [Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; Wiley: New York, 1980; pp 58-62. Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851-1852. Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1853-1854].



(33)

^{1}H NMR δ 0.86 (d, J = 6.6 Hz, 3 H), 0.89 (t, J = 7.2 Hz, 3 H), 0.9-1.15 (m, 2 H), 1.23 (s, 3 H), 1.26-1.37 (m, 4 H), 1.31 (s, 3 H), 1.49 (m, 4 H), 1.61 (m, 4 H), 1.78 (d, J = 1.2 Hz, 3 H), 1.91 (m, 1 H), 2.00 (dt, J = 3.3, 9.0 Hz, 1 H), 2.17 (m, 4 H), 2.61 (m, 2 H), 4.77 (dt, J = 4.2, 10.5 Hz, 1 H), 5.02 (sextet, J = 1.2 Hz, 1 H), 7.14 (m, 1 H), 7.25 (m, 4 H); ^{13}C NMR δ 13.89, 18.62, 18.87, 21.68, 22.13, 24.91, 25.88, 26.64, 26.88, 27.80, 28.74, 30.98, 31.25, 32.52, 34.56, 39.73, 41.85, 50.62, 73.30, 79.76, 80.64, 117.11, 124.88, 125.56, 127.94, 151.69, 159.11, 165.50; IR (neat) 3087, 3060, 3016, 2954, 2927, 2870, 1707 (C=O), 1649, 1458, 1377, 1234, 1163, 1093, 1072, 1049, 1009, 858, 764, 700 cm^{-1}; $[\alpha]_D^{23}$ +10.6 (*c* 0.68, $CHCl_3$).