Diastereoselective Intermolecular Pauson Khand Reactions of Chiral Cyclopropenes

Mahesh K. Pallerla and Joseph M. Fox

*Brown Laboratories, Department of Chemistry and Biochemistry,
University of Delaware, Newark DE 19716*

Supporting Information

Starting Materials were prepared according to the Schemes below:

X-ray crystallography was used to characterize compound **24**, prepared as shown:

General Considerations : All reactions were carried out in glassware that was flame dried under vacuum, and cooled under nitrogen. Reactions were carried out in flasks with, septum fitted inlet adapters (similar to CHEMGLASS CG1062-14). So that flasks could be evacuated and refilled with N₂ prior to the addition of liquids through the septum. THF was distilled under nitrogen from Na/benzophenone. CH₂Cl₂ was dried with a column packed with activated neutral Alumina. Triethylamine was distilled under nitrogen from CaH₂. (S)-Phenyloxazolidione was purchased from Chemicrea Inc., Tokyo, JAPAN. Dicobalt octacarbonyl was purchased from Strem Chemicals Inc. Butyl methyl sulfide was purchased from Lancaster Synthesis. Hept-6-ynoic acid was purchased from GFS chemicals. Samarium was purchased from Acros Organics. Rh₂(OAc)₄ was purchased from Pressure Chemical Co. The other reagents were purchased from Aldrich and used without further purification. Chromatography was performed on silica gel (ICN SiliTech 32-62D, 60Å). For ¹³C NMR, multiplicities were distinguished using an APT pulse sequence: typical methylene and quaternary carbons appear ‘up’ (u); methine and methyl carbons ‘down’ (dn). Exceptions are methine carbons of cyclopropenes, and alkynes which usually have the same phase as ‘normal’ methylenes and quaternary carbons. Yields in Tables refer to isolated yields as the average of 2 or more runs, and the purity of the compounds was determined by ¹H NMR, and verified by GC where possible. All compounds were measured to be >95% pure unless noted otherwise.

The relative stereochemistry for compound **4** was verified by a series of HMBC, HSQC, and selective 1-D experiments using a double pulsed field gradient spin echo sequence.¹

Hept-6-ynoic acid ethyl ester (**16**)

A dry 250 mL round bottomed flask was outfitted with a stir bar, condenser, gas inlet adapter and a rubber septum. Before assembly, the apparatus was oven dried and cooled under N₂. Absolute ethanol (100 mL), hept-6-ynoic acid (**15**, 2.01 g, 15.80 mmol), and conc. H₂SO₄ (5 drops) were added sequentially and the mixture refluxed for 2.5 h, at which point TLC had indicated that the reaction was complete. The reaction mixture was cooled to rt, and the solvent removed under reduced pressure. The crude product was diluted with ethyl ether, and washed sequentially with saturated NaHCO₃ and water. The organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo to give 1.80 g (74%) of the title compound as a colorless liquid. A similar reaction starting with hept-6-ynoic acid (1.51 g, 11.9 mmol) gave 1.40 g (76%) of the title compound. The purity was found to be greater than 93% by ¹H NMR. ¹H NMR (CDCl₃, 400 MHz, d): 4.11-4.09 (m, 2H), 2.28 (t, J=7.2 Hz, 2H), 2.20-2.17 (m, 2H), 1.93 (t, J=2.8 Hz, 1H), 1.74-1.70 (m, 2H), 1.56-1.54 (m, 2H), 1.22 (t, J=7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz, d): 173.8 (u), 84.3 (u), 68.9 (u), 60.6 (u), 34.1 (u), 28.2 (u), 24.4 (u), 18.5 (u), 14.6 (dn); IR (neat, cm⁻¹): 1730, 1372, 1179, 1146, 1030, 633; HRMS-CI(NH₃) m/z: [M+H], calcd for C₉H₁₅O₂, 155.1072; found, 155.1070.

2-methyl-3-(trimethylsilyl)-cycloprop-2-ene-1-carboxylic ethyl ester (**1**)²

A dry 10 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was charged with rhodium tetraacetate (39 mg, 0.09 mmol), evacuated and filled with N₂. Trimethylsilyl acetylene (1.01g, 8.91 mmol) was added to the flask and the mixture was stirred. Ethyl diazoacetate (500 mg, 4.45 mmol) was then added via syringe pump at a rate of 1.85 mL/h, under nitrogen with stirring. After the addition was complete, the stirring was continued for 30 min. The mixture was concentrated and chromatographed over silica gel (gradient of 10-30% CH₂Cl₂ in hexanes) to give 360 mg (41%) of the title compound as a colorless oil. A similar experiment that started with 2.00 g of trimethylsilyl acetylene and an ethyl diazoacetate addition rate of 0.5 mL/h gave 760 mg (43%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 4.10-4.04 (m, 2H), 2.17 (s, 3H), 1.95 (s, 1H), 1.21 (t, J=6.8 Hz, 3H), 0.16 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 177.4 (u), 122.9 (u), 104.4 (u), 60.2 (u), 21.6 (dn), 14.8 (dn), 12.3 (dn), -1.1 (dn); IR (neat, cm⁻¹): 1730, 1694, 1247, 1181, 1150, 1055, 922, 845; HRMS-CI(NH₃) m/z: [M⁺], calcd for C₁₀H₁₈O₂Si, 198.1076; found, 198.1068.

2-(4-Ethoxycarbonyl-butyl)-cycloprop-2-ene-1-carboxylic acid ethyl ester (**17**)

A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was charged with rhodium tetraacetate (5 mg, 0.01 mmol), evacuated and filled with N₂. Hept-6-ynoic acid ethyl ester (**16**, 170 mg, 1.1 mmol) and CH₂Cl₂ (15 mL) were sequentially added to the flask, and the mixture was stirred. Ethyl diazoacetate (1 mL of a 0.99 M solution in CH₂Cl₂, 0.99 mmol) was then added dropwise via syringe pump at a rate of 0.30 mL/h. After the addition was complete, stirring was continued for 30 min. The mixture was concentrated and chromatographed over silica gel (5% ethyl acetate in hexanes) to give 125 mg (52%) of the title compound as a colorless liquid. A similar experiment starting with 1.20 g gave 950 mg (56%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 6.33 (m, 1H), 4.11-4.07 (m, 4H), 2.51-2.47 (m, 2H), 2.28 (t, J=6.8 Hz, 2H), 2.1 (d, J=1.6 Hz, 1H), 1.67-1.60 (m, 4H), 1.23-1.19 (m, 6H); ¹³C NMR (CDCl₃, 100 MHz, d): 176.9 (u), 173.7 (u), 115.4 (u), 94.9 (u), 60.7 (u), 60.5 (u), 34.3 (u), 26.5 (u), 25.0 (u), 24.7 (u), 20.0 (dn), 14.7(dn), 14.6 (dn); IR (neat, cm⁻¹): 1724, 1248, 1179, 1029, 726; HRMS-Cl(NH₃) m/z: [M+H], calcd for C₁₃H₂₁O₄, 241.1440; found, 241.1437.

2-(4-Ethoxycarbonyl-butyl)-3-trimethylsilyl-cycloprop-2-ene-1-carboxylic acid ethyl ester (18**)**

A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was rinsed with dry THF, which was added and withdrawn

through the septum using a syringe. THF (5 mL), **17** (60 mg, 0.25 mmol), and trimethylsilyl chloride (54 mg, 0.50 mmol) were sequentially added to the flask and the mixture was allowed to stir and cool in a bath of dry ice/acetone. A solution of LiHMDS (63 mg, 0.37 mmol) in THF (1 mL) was added via syringe pump at a rate of 0.25 mL/min. The reaction was then allowed to warm to rt, and the solvent was removed under reduced pressure. The residue was partitioned between CH₂Cl₂ and brine, and extracted three times with CH₂Cl₂. The organics were combined, dried over Na₂SO₄, concentrated, and the residue was chromatographed over silica gel (1% ethyl acetate in hexanes) to give 70 mg (90%) of the title compound as a colorless oil. An identical experiment gave 68 mg (87%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 4.15-4.07 (m, 4H) 2.53 (app dt, J=2.4, 7.2 Hz 2H), 2.30 (t, J=7.2 Hz, 2H), 1.98 (s, 1H), 1.70-1.63 (m, 4H), 1.26-1.99 (m, 6H), 0.18 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 177.2(u), 173.7(u), 126.4(u), 104.1(u), 60.5(u), 60.1(u), 34.3(u), 26.8(u), 26.4 (u), 24.7(u), 21.1(dn), 14.7 (dn), 14.5(dn), -1.1(dn); IR (neat, cm⁻¹): 1829, 1714, 1446, 1368, 1329, 1248, 1175, 1043, 840, 759; HRMS-EI m/z: [M+Na], calcd for C₁₆H₂₈NaO₄Si, 335.1655; found, 335.1647.

(4S)-3-[(1S)-2-hexyl-3-trimethylsilyl-cycloprop-2-ene-1-oyl]- 4-phenyloxazolidinone (20**)**

A dry 100 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was rinsed with dry THF, which was added and withdrawn

through the septum using a syringe. THF (12 mL), **19**³ (400 mg, 1.27 mmol), and trimethylsilyl chloride (277 mg, 2.55 mmol) were sequentially added to the flask and the mixture was allowed to stir and cool in a bath of dry ice/acetone. A solution of LiHMDS (267 mg, 1.59 mmol) in THF (2 mL) was added via syringe pump at a rate of 0.25 mL/min. The reaction was allowed to warm to rt, and the solvent was removed under reduced pressure. The residue was partitioned between CH₂Cl₂ and brine, and extracted three times with CH₂Cl₂. The organics were combined, dried over Na₂SO₄, concentrated, and the residue was chromatographed over silica gel (5% ethyl acetate in hexanes) to give 378 mg (76%) of the title compound as a colorless solid. mp 50 °C; [α]_D²³ +106.2° (*c* 1.00, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz, d): 7.33-7.26 (m, 5H), 5.44 (dd, *J*=4.0, 8.6 Hz, 1H), 4.68 (app t, *J*=8.7 Hz, 1H), 4.26 (dd, *J*=4.0, 8.6 Hz, 1H), 3.33 (s, 1H), 2.51-2.45 (m, 2H), 1.59-1.55 (m, 2H), 1.34-1.26 (m, 6H), 0.85 (t, *J*=7.2 Hz, 3H), 0.01 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 177.2(u), 154.8(u), 139.9(u), 129.3(dn), 128.7(dn), 126.4(dn), 124.5(u), 102.5(u), 70.2(u), 58.4(dn), 31.9(u), 29.3(u), 27.5(u), 26.7(u), 23.0(u), 21.9(dn), 14.5(dn), -1.17(dn); IR (neat, cm⁻¹): 2919, 1830, 1778, 1682, 1382, 1358, 1319, 1247, 1192, 1058, 840, 758, 698; HRMS-Cl(NH₃) *m/z*: [M+H], calcd for C₂₂H₃₂NO₃Si, 386.2151; found, 386.2161.

(4S)-3-[(1*R*)-2-hexyl-3-trimethylsilyl-cycloprop-2-ene-1-oyl]-4-phenyloxazolidinone (23**)**

A dry 100 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was rinsed with dry THF, which was added and withdrawn through the septum using a syringe. THF (9 mL), **22**³ (274 mg, 0.87 mmol), and trimethylsilyl chloride (190 mg, 1.75 mmol) were sequentially added to the flask and the mixture was allowed to stir and cool in a bath of dry ice/acetone. A solution of LiHMDS (183 mg, 1.09 mmol) in THF (1.1 mL) was added via syringe pump at a rate of 0.25 mL/min. The reaction was allowed to warm to rt, and the solvent was removed under reduced pressure. The residue was partitioned between CH₂Cl₂ and brine, and extracted three times with CH₂Cl₂. The organics were combined, dried over Na₂SO₄, concentrated, and the residue was chromatographed over silica gel (10% ethyl acetate in hexanes) to give 266 mg (79%) of the title compound as a colorless solid. Mp 55 °C; [α]_D²³ +200.7° (c 1.00, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz, d): 7.36-7.26 (m, 5H), 5.40 (dd, J=4.0, 8.6 Hz, 1H), 4.60 (app t, J=8.7 Hz, 1H), 4.20 (dd, J=4.0, 8.6 Hz, 1H), 3.30 (s, 1H), 2.38 (app t, J=7.3 Hz, 2H), 1.45-1.40 (m, 2H). 1.27-1.16 (m, 6H), 0.86 (t, J=6.7 Hz, 3H), 0.17 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 176.6(u), 154.4(u), 139.5(u), 128.9(dn), 128.3(dn), 125.8(dn), 124.7(u), 101.6(u), 69.9(u), 57.9(dn), 31.4(u), 28.7(u), 26.9(u), 26.1(u), 22.4(u), 21.5(dn), 14.0(dn), -1.3(dn); IR (neat, cm⁻¹): 2925, 1830, 1778, 1682, 1382, 1358, 1317, 1247, 1193, 1058, 840, 758, 698; HRMS-CI(NH₃) m/z: [M-Me], calcd for C₂₂H₂₈NO₃Si, 370.1838; found, 370.1853.

2-hexyl-3-(trimethylsilyl)-cycloprop-2-ene-(1S)-1-carboxylic methyl ester (21)

A dry 25 mL round bottomed flask was outfitted with a stir bar, a condenser, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was charged with **20** (70 mg, 0.18 mmol) and samarium(III) triflate (22 mg, 0.036 mmol), and the apparatus was then evacuated and filled with N₂. MeOH (2 mL) was added via syringe and then the mixture was heated at 50 °C for 6.5 h. The solvent was removed under reduced pressure and chromatographed over silica gel (2% ethyl acetate in hexanes) to give 35 mg (76%) of the title compound as a colorless oil. An identical experiment starting with **20** (83 mg, 0.21 mmol), gave 42 mg (79%) of the title compound. $[\alpha]_D^{23} +41.1^\circ$ (*c* 1.00, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz, d): 3.61 (s, 3H), 2.49-2.47 (m, 2H), 1.95 (s, 1H), 1.60- 1.55 (m, 2H), 1.30-1.26 (m, 6H), 0.87 (t, *J*=6.8 Hz, 3H), 0.15 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 177.0(u), 127.0(u), 103.5(u), 51.6(dn), 31.9(u), 29.2(u), 27.4(u), 26.8(u), 23.0(u), 21.0(dn), 14.4(dn), -1.1(dn); IR (neat, cm⁻¹): 1829, 1724,1248,1171,839; HRMS-Cl(NH₃) *m/z*: [M+], calcd for C₁₄H₂₆O₂Si, 254.1702; found, 254.1696.

General Procedure for the preparation of alkyne-dicobalt

hexacarbonyl complexes (**26a-e**)

Alkyne-cobalt complexes were prepared by the following modification of the literature protocol^{5a}: A dry 25 mL round bottomed flask was outfitted with a stir bar,

gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The alkyne and CH_2Cl_2 were sequentially added to the flask. Dicobalt octacarbonyl (1.1 equiv) was then added and the mixture was allowed to stir for 60 min. The solvent was then removed under reduced pressure and the residue was chromatographed over neutral alumina. Spectral data were in accord with those reported previously.⁵

General Procedures for Pauson-Khand reactions.

Procedure A: A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The alkyne-cobalt complex (2.0 equiv) and the cyclopropene (1.0 equiv) were then added, and the apparatus was evacuated and filled with N_2 . CH_2Cl_2 was added and the mixture was chilled in a cold bath ($-35\text{ }^\circ\text{C}$). NMO (6.0 equiv) was added and the reaction mixture was allowed to stir at $-35\text{ }^\circ\text{C}$ for 15 min, and then allowed to warm to rt. Solvent was removed under reduced pressure and the residue was chromatographed over silica gel.

Procedure B: The procedure is identical to Procedure A, except that the reaction was initially carried out using an ice bath ($0\text{ }^\circ\text{C}$) instead of a $-35\text{ }^\circ\text{C}$ bath.

Procedure C: A dry 25 mL round bottomed flask was outfitted with a stir bar, a condenser, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The alkyne-cobalt complex (2.0 equiv) and the cyclopropene (1.0 equiv) were then added, and the apparatus was evacuated and filled with N_2 . 1,4-Dioxane and n-butyl methyl sulfide were sequentially added via

syringe and the reaction mixture was heated to the indicated temperature. After the reaction was judged to be complete by TLC analysis, the reaction mixture was cooled and the solvent removed under reduced pressure. The residue was chromatographed over silica gel.

1,2-dimethyl-4-oxo-3,5-bis(trimethylsilyl)-bicyclo[3.1.0]-2-hexene-6-carboxylic acid ethyl ester (2)

General procedure B was followed using **1** (43 mg, 0.22 mmol), **26e** (173 mg, 0.43 mmol), NMO (762 mg, 6.51 mmol), and CH₂Cl₂ (4 mL). The reaction was carried out at 0 °C for 15 min and then allowed to warm to rt and stirred for 45 min. The volatile solvents were removed under reduced pressure. Diethyl ether was added and an insoluble material was removed by filtration through celite. The filtrate was concentrated and the residue was chromatographed over silica gel (1% ethyl acetate in hexanes) to provide 52 mg (71%) of the title compound as a colorless oil. A similar experiment with **1** (46 mg, 0.23 mmol), **26e** (185 mg, 0.46 mmol), NMO (815 mg, 6.97 mmol), and CH₂Cl₂ (4 mL), gave 58 mg (74%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 4.15-4.04 (m, 2H), 2.14 (s, 3H), 1.85 (s, 1H), 1.39 (s, 3H), 1.24 (t, J=7.2 Hz, 3H), 0.19 (s, 9H), 0.13 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 212.1(u), 186.9(u), 168.3(u), 133.1(u), 61.2(u), 52.5(dn), 43.4(u), 37.2(u), 17.0(dn), 14.6(dn), 10.2(dn), 0.4(dn), -0.1 (dn); IR (neat, cm⁻¹): 1730, 1679, 1588, 1375, 1244, 1178, 837; HRMS-CI(NH₃) m/z: [M⁺], calcd for C₁₇H₃₀O₃Si₂, 338.1733; found, 338.1749.

3-butyl-1-methyl-4-oxo-5-trimethylsilyl-bicyclo[3.1.0]-2-hexene-6-carboxylic acid ethyl ester (3)

General procedure C was followed using **1** (41 mg, 0.21 mmol), **26a** (152 mg, 0.41 mmol), n-butyl methyl sulfide (647 mg, 6.21 mmol), and 1,4-dioxane (4 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (gradient 20-40% CH₂Cl₂ in hexanes) to provide 41 mg (64%) of the title compound as a colorless oil. A similar experiment with **1** (204 mg, 1.03 mmol), **26a** (760 mg, 2.02 mmol), n-butyl methyl sulfide (3.27 g, 30.96 mmol), and 1,4-dioxane (20 mL), gave 195 mg (61%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 7.12 (m, 1H), 4.14-4.05 (m, 2H), 2.01 (m, 3H), 1.5 (s, 3H), 1.39-1.21 (m, 7H), 0.86 (t, J=7.2 Hz, 3H), 0.19 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 208.5(u), 167.1(u), 159.7(dn), 140.4(u), 60.7(u), 54.4(dn), 37.5(u), 35.1(u), 29.9(u), 23.9(u), 22.3(u), 14.2(dn), 13.8(dn), 11.8(dn), -0.07(dn); IR (neat, cm⁻¹): 1730, 1693, 1246, 1180, 1052, 842; HRMS-CI(NH₃) m/z: [M⁺], calcd for C₁₇H₂₈O₃Si, 308.1808; found, 308.1818.

Preparation of 3 with Et₂S as promoter: A similar protocol was followed using, **1** (50 mg, 0.25 mmol), **26a** (186 mg, 0.50 mmol), Et₂S (227 mg, 2.52 mmol), and 1,4-dioxane (2.5 mL). The reaction was carried out at 100 °C for 2 h, and purified over silica gel (gradient 20-40% CH₂Cl₂ in hexanes) to provide 48 mg (62 %) of the title compound as a colorless oil. A similar experiment with **1** (44 mg, 0.22 mmol), **26a**

(164 mg, 0.44 mmol), Et₂S (200 mg, 2.22 mmol), and 1,4-dioxane (2 mL), gave 44 mg (64 %) of the title compound.

1-methyl-4-oxo-3-phenyl-5-trimethylsilyl-bicyclo[3.1.0]-2-hexene-6-carboxylic acid ethyl ester (4)

General procedure C was followed using **1** (67 mg, 0.34 mmol), **26c** (262 mg, 0.67 mmol), n-butyl methyl sulfide (1.1 g, 10.15 mmol), and 1,4-dioxane (6 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (gradient 20-35% CH₂Cl₂ in hexanes) to provide 66 mg (59%) of the title compound as a colorless solid. A similar experiment with **1** (36 mg, 0.18 mmol), **26c** (141 mg, 0.36 mmol), n-butyl methyl sulfide (568 mg, 5.45 mmol), and 1,4-dioxane (3 mL), gave 33 mg (55%) of the title compound. mp 74-77 °C ¹H NMR (CDCl₃, 400 MHz, d): 7.75 (s, 1H), 7.61 (app dd, J=1.6, 6.4 Hz, 2H), 7.35-7.28 (m 3H), 4.17-4.13 (m, 2H), 2.23 (s, 1H), 1.67 (s, 3H), 1.27 (t, J=7.2 Hz, 3H), 0.29 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 206.6(u), 168.0(u), 161.4(dn), 137.4(u), 131.6(u), 128.8(dn), 128.7(dn), 127.5(dn), 61.4(u), 54.4(dn), 37.6(u), 37.0(u), 14.6(dn), 12.3(dn), 0.45(dn); IR (neat, cm⁻¹): 1730, 1693, 1247, 1180, 1062, 847; HRMS-CI(NH₃) m/z: [M+], calcd for C₁₉H₂₄O₃Si, 328.1495; found, 328.1502.

1-methyl-4-oxo-3,5-bis(trimethylsilyl) bicyclo[3.1.0]-2-hexene-6-carboxylic acid ethyl ester (5)

General procedure C was followed using **26d** (30 mg, 0.15 mmol), **1** (116 mg, 0.30 mmol), n-butyl methyl sulfide (474 mg, 4.54 mmol), and 1,4-dioxane (2 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (gradient 20-30% CH₂Cl₂ in hexanes) to provide 32 mg (65%) of the title compound as a colorless oil. A similar experiment with **26d** (37 mg, 0.18 mmol), **1** (144 mg, 0.37 mmol), n-butyl methyl sulfide (584 mg, 5.6 mmol), and 1,4-dioxane (2.5 mL), gave 38 mg (63%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 7.60 (s, 1H), 4.15-4.09 (m, 2H), 1.92 (s, 1H), 1.56 (s, 3H), 1.24 (t, J=7.2 Hz, 3H), 0.20 (s, 9H), 0.09 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 211.8(u), 175.0(dn), 167.6(u), 140.2(u), 60.7(u), 53.5(dn), 41.1(u), 36.8(u), 14.2(dn), 11.5(dn), -0.14(dn), -1.97(dn); IR (neat, cm⁻¹): 1730, 1682, 1574, 1247, 1179, 837; HRMS-CI(NH₃) m/z: [M⁺], calcd for C₁₆H₂₈O₃Si₂, 324.1577; found, 324.1573.

1-(4-Ethoxycarbonyl-butyl)-4-oxo-3-phenyl-5-trimethylsilyl-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (6)

General procedure C was followed using **18** (36 mg, 0.11 mmol), **26c** (90 mg, 0.23 mmol), n-butyl methyl sulfide (360 mg, 3.46 mmol), and 1,4-dioxane (2.5 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (gradient of 75-80% CH₂Cl₂ in hexanes) to provide 31 mg (61%) of the title compound as a colorless oil. A similar experiment with **18** (45 mg, 0.14 mmol), **26a** (112 mg, 0.26 mmol), n-butyl methyl sulfide (451 mg, 4.32 mmol), and 1,4-dioxane (3 mL), gave 41 mg (64%) of the title compound. The purity was measured to be 94% by ¹H NMR. ¹H NMR (CDCl₃, 400 MHz, d): 7.79 (s, 1H), 7.62-7.60 (m, 2H), 7.33-7.26 (m, 3H), 4.18-4.10 (m, 4H), 2.33 (t, J=7.2 Hz, 2H), 2.22 (s, 1H), 2.15-1.95 (m, 2H), 1.73-1.69 (m, 2H), 1.58-1.48 (m, 2H), 1.27-1.23 (m, 6H), 0.28 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 206.1(u), 173.3(u), 167.4(u), 159.1(dn), 137.4(u), 131.2(u), 128.3(dn, 2 carbons), 127.0(dn), 60.9(u), 60.2(u), 53.7(dn), 41.8(u), 36.4(u), 34.1(u), 27.9(u), 25.2(u), 24.9(u), 14.2(dn), 14.1(dn), -0.4(dn); IR (neat, cm⁻¹): 1730, 1692, 1372, 1246, 1177, 843; HRMS-EI m/z: [M+Na], calcd for C₂₅H₃₄NaO₅Si, 465.2073; found, 465.2080.

3-Butyl-1-(4-ethoxycarbonyl-butyl)-4-oxo-5-trimethylsilyl-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (7)

General procedure C was followed using **26a** (66 mg, 0.21 mmol), **18** (151 mg, 0.41 mmol), n-butyl methyl sulfide (661 mg, 6.35 mmol), and 1,4-dioxane (4 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel

(gradient of 75-85% CH₂Cl₂ in hexanes) to provide 76 mg (76%) of the title compound as a colorless oil. A similar experiment with **26a** (42 mg, 0.13 mmol), **18** (99 mg, 0.27 mmol), n-butyl methyl sulfide (421 mg, 4.04 mmol), and 1,4-dioxane (3 mL), gave 42 mg (74%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 7.26 (s, 1H), 4.13-4.07 (m, 4H), 2.28 (t, J=7.2 Hz, 2H), 2.01-1.97 (m, 4H), 1.67-1.64 (m, 2H), 1.40-1.21 (m, 13H), 0.86 (t, J=7.2 Hz, 3H), 0.20 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 208.4(u), 173.3(u), 167.6(u), 157.7(dn), 140.9(u), 60.7(u), 60.2(u), 54.1(dn), 42.2(u), 34.9(u), 34.1(u), 29.9(u), 27.7(u), 25.2(u), 24.9(u), 24.1(u), 22.3(u), 14.2(dn), 14.1(dn), 13.7(dn), -0.1(dn); IR (neat, cm⁻¹): 1730, 1692, 1375, 1246, 1179, 843; HRMS-EI m/z: [M+Na], calcd for C₂₃H₃₈NaO₅Si, 445.2386; found, 445.2392.

1-(4-Ethoxycarbonyl-butyl)-4-oxo-3,5-bis-trimethylsilyl-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (8)

General procedure C was followed using **18** (38 mg, 0.12 mmol), **26d** (95 mg, 0.25 mmol), n-butyl methyl sulfide (386 mg, 3.70 mmol), and 1,4-dioxane (2.5 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (gradient of 75-80% CH₂Cl₂ in hexanes) to provide 36 mg (66%) of the title compound as a colorless oil. A similar experiment with **18** (41 mg, 0.13 mmol), **26d** (111 mg, 0.26 mmol), n-butyl methyl sulfide (411 mg, 3.94 mmol), and 1,4-dioxane (3 mL), gave 38 mg (66%) of the title compound. The purity was measured to be 94% by ¹H NMR. ¹H NMR (CDCl₃, 400 MHz, d): 7.70 (s, 1H), 4.14-4.07 (m, 4H), 2.31 (t,

$J=7.2$ Hz, 2H), 1.93-1.90 (m, 3H), 1.69-1.65 (m, 2H), 1.52-1.40 (m, 2H), 1.27-1.23 (m, 6H), 0.26 (s, 9H), 0.11 (s, 9H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 211.8(u), 173.3(u), 172.9(dn), 167.5(u), 140.8(u), 60.8(u), 60.2(u), 53.2(dn), 45.8(u), 36.7(u), 34.1(u), 27.7(u), 24.9(u, 2 peaks), 14.1(dn, 2peaks), -0.17 (dn), -1.94 (dn); IR (neat, cm^{-1}): 1731, 1683, 1372, 1246, 1178, 839; HRMS-EI m/z : $[\text{M}+\text{Na}]$, calcd for $\text{C}_{22}\text{H}_{38}\text{NaO}_5\text{Si}_2$, 461.2155; found, 461.2156.

(4S)-3-[1-hexyl-4-oxo-3-phenyl-5-trimethylsilyl-bicyclo[3.1.0]-2-hexene-6(*R*)-oyl]-4-phenyloxazolidin-2-one (9**)**

General procedure C was followed using **23** (52 mg, 0.13 mmol), **26c** (105 mg, 0.27 mmol), *n*-butyl methyl sulfide (423 mg, 4.01 mmol), and 1,4-dioxane (3 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (10% ethyl acetate in hexanes) to provide 42 mg (60%) of the title compound as a colorless semi-solid. A similar experiment with **23** (79 mg, 0.21 mmol), **26c** (160 mg, 0.41 mmol), *n*-butyl methyl sulfide (644 mg, 6.18 mmol), and 1,4-dioxane (4 mL), gave 60 mg (61%) of the title compound. $[\alpha]_{\text{D}}^{23} +151.8^\circ$ (c 0.20, CH_2Cl_2); ^1H NMR (CDCl_3 , 400 MHz, d): 7.8 (s, 1H), 7.67-7.65 (m, 2H), 7.37-7.29 (m, 8H), 5.40 (dd, $J=2.8$, 8.8 Hz, 1H), 4.70 (app t, $J=8.8$ Hz, 1H), 4.35 (dd, $J=2.8$, 8.8 Hz, 1H), 3.20 (s, 1H), 1.82-1.74 (m, 1H), 1.33-1.11 (m, 9H), 0.89 (t, $J=7.2$ Hz, 3H), 0.16 (s, 9H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 207.0(u), 165.5(u), 160.4(dn), 153.8(u), 139.2(u), 138.2(u), 131.9(u), 129.4(dn), 129.2(dn), 128.75(dn), 128.71(dn), 127.6(dn), 126.7(dn), 70.4(u), 58.1(dn), 55.8(dn), 43.3(u), 36.2(u), 31.9(u), 29.8(u), 28.8(u), 27.0(u), 23.0(u),

14.5(dn), 0.6(dn); IR (neat, cm^{-1}): 1780, 1695, 1383, 1248, 1202, 846, 750; HRMS-EI m/z : $[\text{M}+\text{Na}]$, calcd for $\text{C}_{31}\text{H}_{37}\text{NNaO}_4\text{Si}$, 538.2390; found, 538.2411.

(4S)-3-[3-butyl-1-hexyl-4-oxo-5-trimethylsilyl-bicyclo[3.1.0]-2-hexene-6(S)-oyl]-4-phenyloxazolidin-2-one (10)

General procedure C was followed using **20** (50 mg, 0.13 mmol), **26a** (101 mg, 0.26 mmol), *n*-butyl methyl sulfide (405 mg, 3.9 mmol), and 1,4-dioxane (3 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (5% ethyl acetate in hexanes) to provide 34 mg (53%) of the title compound as a colorless semi-solid. A similar experiment with **20** (57 mg, 0.15 mmol), **26a** (110 mg, 0.29 mmol), *n*-butyl methyl sulfide (466 mg, 4.47 mmol), and 1,4-dioxane (3 mL), gave 45 mg (61%) of the title compound. $[\alpha]_{\text{D}}^{23} +12.6^\circ$ (c 0.30, CH_2Cl_2); ^1H NMR (CDCl_3 , 400 MHz, d): 7.41-7.25 (m, 6H), 5.43 (dd, $J=2.8, 8.8$ Hz 1H), 4.65 (app t, $J=8.8$ Hz, 1H), 4.35 (dd, $J=2.8, 8.8$ Hz 1H), 3.11 (s, 1H), 2.05-2.01 (m, 2H), 1.91-1.84 (m, 1H), 1.65-1.58 (m, 1H), 1.41-1.25 (m, 12H), 0.90-0.86 (m, 6H), 0.04 (s, 9H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 209.2(u), 166.2(u), 158.8(dn), 153.9(u), 141.6(u), 138.7(u), 129.5(dn), 129.2(dn), 126.5(dn), 70.1(u), 58.0(dn), 55.5(dn), 44.6(u), 36.0(u), 32.1(u), 30.3(u), 29.8(u), 28.7(u), 26.3(u), 24.6(u), 23.0(u), 22.7(u), 14.4(dn), 14.2(dn), 0.45(dn); IR (neat, cm^{-1}): 1780, 1692, 1458, 1382, 1324, 1245, 1196, 1048, 843; HRMS-EI m/z : $[\text{M}+\text{Na}]$, calcd for $\text{C}_{29}\text{H}_{41}\text{NNaO}_4\text{Si}$, 518.2703; found, 518.2698.

1-Hexyl-4-oxo-3-phenyl-5-trimethylsilyl-bicyclo[3.1.0] -2-hexene-6(S)-carboxylic methyl ester (11)

General procedure C, was followed using **21** (35 mg, 0.14 mmol), **26c** (107 mg, 0.27 mmol), n-butyl methyl sulfide (431 mg, 4.13 mmol), and 1,4-dioxane (2.5 mL). The reaction was carried out at 100 °C for 2 h, and chromatographed over silica gel (gradient of 20-25% CH₂Cl₂ in hexanes) to provide 42 mg (80%) of the title compound as a colorless oil. A similar experiment with **21** (40 mg, 0.16 mmol), **26c** (122 mg, 0.31 mmol), n-butyl methyl sulfide (492 mg, 4.72 mmol), and 1,4-dioxane (3 mL), gave 50 mg (83%) of the title compound. The purity of the title compound was measured to be 93% by ¹H NMR. [α]²³_D -254.2° (c 0.35, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz, d): 7.80 (s, 1H), 7.63-7.61 (m, 2H), 7.34-7.29 (m, 3H), 3.69 (s, 3H), 2.23 (s, 1H), 2.05-1.95 (m, 2H), 1.47-1.31 (m, 8H), 0.85 (t, J=7.2 Hz, 3H), 0.29 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz, d): 206.7(u), 168.4(u), 160.0(dn), 137.7(u), 131.7(u), 128.8(dn, 2 carbons), 127.5(dn), 53.9(dn), 52.4(dn), 42.6(u), 36.9(u), 32.1(u), 29.8(u), 28.9(u), 26.0(u), 23.0(u), 14.5(dn), 0.38(dn); IR (neat, cm⁻¹): 1732, 1694, 1437, 1247, 1194, 1172, 919, 841; HRMS-CI(NH₃) m/z: [M+], calcd for C₂₃H₃₂O₃Si, 384.2121; found 384.2123.

3, 5-Dihexyl -4-oxo-bicyclo[3.1.0]-2-hexene-6-carboxylic acid ethyl ester (12)

General procedure A was followed using **27**⁴ (57 mg, 0.29 mmol), **26b** (230 mg, 0.58 mmol), NMO (204 mg, 1.74 mmol), and CH₂Cl₂ (6 mL). The reaction was carried out at -35 °C for 15 min and then allowed to warm to rt. The solvent was removed under reduced pressure and the residue was chromatographed over silica gel (20-40% CH₂Cl₂ in hexanes) to provide 22 mg (22%) of the title compound as a colorless oil. A similar experiment with **27** (17 mg, 0.09 mmol), **26b** (70 mg, 0.17 mmol), NMO (61 mg, 0.52 mmol), and CH₂Cl₂ (2 mL), gave 7 mg (23%) of the title compound. ¹H NMR (CDCl₃, 400 MHz, d): 7.19 (app t, J=1.2 Hz 1H), 4.13 (q, J=7.2 Hz, 2H), 2.73 (app t, J=2.8, 1H), 2.13-2.01 (m, 3H), 1.70-1.64 (m, 1H), 1.47-1.22 (m, 20H), 0.87 (m, 6H); ¹³C NMR (CDCl₃, 100 MHz, d): 206.0(u), 169.35(u), 153.0(dn), 142.0(u), 61.3(u), 51.0(dn), 40.2(u), 32.0,(u), 31.9(u), 30.4(dn), 29.6(u), 29.3(u), 28.1(u), 27.8(u), 25.0(u), 23.5(u), 22.9(u, 2 peaks), 14.6(dn), 14.4(dn, 2peaks); IR (neat, cm⁻¹): 1729, 1705, 1464, 1173; HRMS-Cl(NH₃) m/z: [M+], calcd for C₂₁H₃₄O₃, 334.2508; found, 334.2507.

(4S)-3-[1-hexyl-4-oxo-3-phenyl-5-bicyclo[3.1.0]-2-hexene-6(R)-oyl]-4-phenyloxazolidin-2-one (24)

0 °C under nitrogen atmosphere for 60 min. The reaction was then allowed to warm to rt, quenched with NH₄Cl (aq), and the solvent removed under reduced pressure. The residue was partitioned between brine and CH₂Cl₂ and extracted three times with CH₂Cl₂. The organics were combined, dried over Na₂SO₄, concentrated, and the residue chromatographed over silica gel (gradient of 15-50% ethyl acetate in hexanes) to provide 19 mg (49%, unoptimized) of the title compound as a colorless solid that crystallized in ethyl acetate/hexanes. A similar experiment gave 16 mg (42%) of the title compound. mp 125 °C; [α]_D²⁵ -63.1° (c 0.45, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz, d): 7.74 (d, J=1.2 Hz, 1H), 7.65-7.63 (m, 2H), 7.42-7.26 (m, 8H), 5.44 (dd, J=4.8, 8.8 Hz, 1H), 4.71 (app t, J=8.8 Hz, 1H), 4.30 (dd, J=4.8, 8.8 Hz, 1H), 3.73 (d, J=3.2 Hz, 1H), 2.86 (dd, J=1.2, 3.2 Hz, 1H), 1.96-1.91 (m, 1H), 1.79-1.71 (m, 1H), 1.56 (s, 1H), 1.35-1.24 (m, 7H), 0.88 (t, J=6.8 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz, d): 201.9, 165.1, 156.5, 153.5, 138.8, 138.0, 130.9, 129.3, 129.0, 128.5, 128.4, 127.0, 126.0, 69.8, 57.8, 49.6, 40.5, 35.6, 31.5, 29.0, 27.7, 25.1, 22.4, 14.0; IR (neat, cm⁻¹): 1779, 1693, 1381, 1194, 1063, 697; HRMS-EI m/z: [M+Na], calcd for C₂₈H₂₉NNaO₄, 466.1994; found, 466.2003.

3-Butyl-1-methyl-4-oxo-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester

A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was charged with a solution of **3** (121 mg, 0.39 mmol) in THF (4 mL). TBAF (0.39 mL of 1.0 M solution in THF, 390 μmol) was added via syringe

and the mixture allowed to stir under nitrogen atmosphere for 30 min. The reaction was then quenched with NH_4Cl (aq), and the solvent removed under reduced pressure. The residue partitioned between brine and CH_2Cl_2 and extracted three times with CH_2Cl_2 . The organics were combined, dried over Na_2SO_4 , concentrated and the residue chromatographed over silica gel (5% ethyl acetate in hexanes) to provide 75 mg (81%) of the title compound as a colorless liquid. A similar experiment gave 80 mg (85%) of the title compound. ^1H NMR (CDCl_3 , 400 MHz, d): 7.26 (d, $J=1.2$ Hz, 1H), 4.15-4.12 (m, 2H), 2.55 (dd, $J=1.2, 3.2$ Hz, 1H), 2.24 (d, 3.2 Hz, 1H), 2.03 (dt, $J=1.2, J=8.0$ Hz, 2H), 1.53 (s, 3H), 1.37-1.24 (m, 7H), 0.83 (t, 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 204.0(u), 167.1(u), 156.9(dn), 141.4(u), 60.9(u), 50.1(dn), 35.4(dn), 34.1(u), 29.8(u), 23.9(u), 22.3(u), 14.1(dn), 13.7(dn), 10.8(dn); IR (neat, cm^{-1}): 1728, 1710, 1335, 1293, 1177, 1151, 1055; HRMS-EI m/z : $[\text{M}+\text{H}]^+$, calcd for $\text{C}_{14}\text{H}_{21}\text{O}_3$, 237.1491; found, 237.1486.

3-butyl -1-methyl-4-oxo-5-trimethylsilyl-bicyclo[3.1.0]hexane-6-carboxylic acid ethyl ester (b-isomer)

A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask charged with 10% Pd-C (23 mg, 0.02 mmol), evacuated and filled with nitrogen. A solution of **25** (52 mg, 0.22 mmol) in EtOH (2 mL) was added via syringe under nitrogen atmosphere. The mixture was then allowed to stir under an atmosphere of H_2 (balloon) for 60 min. The solvent removed under reduced pressure

and the residue chromatographed over silica gel (5% ethyl acetate in hexanes) to provide 51 mg (97%) of the title compound as a colorless oil. The ratio of α : β diastereomers was measured to be 4:96. A similar experiment with 202 mg (0.85 mmol) of **25** and 10%Pd-C (91 mg, 0.08 mmol) gave 195 mg (96%) of the title compound with a α : β ratio of 6:94. The purity of the combined diastereomers was measured to be greater than 97% by NMR. The relative stereochemistry was assigned by conversion to **14b**, which was assigned by NOE studies. ^1H NMR (CDCl_3 , 400 MHz, d): 4.17-4.11 (m, 2H), 2.34 (d, $J=3.6$ Hz, 1H), 2.29-2.25 (m, 2H), 1.96-1.93 (m, 2H), 1.66-1.65 (m, 1H), 1.41 (s, 3H), 1.29-1.21 (m, 8H), 0.83 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 215.2(u), 169.3(u), 61.5(u), 47.6(dn), 42.6(dn), 37.6(u), 35.5(u), 33.8(u), 32.1(dn), 30.9(u), 22.8(u), 15.7(dn), 14.7(dn), 14.3(dn); IR (neat, cm^{-1}): 1727, 1368, 1194, 1161, 1045; HRMS-EI m/z : $[\text{M}+\text{H}]^+$, calcd for $\text{C}_{14}\text{H}_{23}\text{O}_3$, 239.1647; found, 239.1645.

3-butyl -1-methyl-4-oxo-5-trimethylsilyl-bicyclo[3.1.0]hexane-6-carboxylic acid ethyl ester (α -isomer)

A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was charged with **13b** (59 mg, 0.25 mmol) in THF (2.5 mL). TBAF (0.247 mL of 1.0 M solution in THF, 247 mmol) was added via syringe and the mixture allowed to stir under nitrogen atmosphere for 30 min. The reaction was then

quenched with NH_4Cl (aq), and the solvent removed under reduced pressure. The residue was partitioned between brine and CH_2Cl_2 and extracted three times with CH_2Cl_2 . The organics were combined, dried over Na_2SO_4 , concentrated, and the residue chromatographed over silica gel (5% ethyl acetate in hexanes) to provide 44 mg (75%) of the title compound as a colorless liquid. The ratio of α : β diastereomers was measured to be 95:5. A similar experiment gave 46 mg (78%) of the title compound with a α : β ratio of 94:6. The purity of the combined diastereomers was found to be greater than 97% by NMR. The relative stereochemistry was assigned by conversion to **14a**, which was assigned by NOE studies. ^1H NMR(CDCl_3 , 400 MHz, d): 4.17-4.09 (m, 2H), 2.4 (dd, J =8.0, 13 Hz, 1H), 2.29 (d, J =2.8 Hz, 1H), 2.10 (d, J =2.8 Hz, 1H), 2.02-1.99 (m, 1H), 1.78-1.72 (m, 1H), 1.64-1.58 (dd, J =9.2, 13 Hz, 1H), 1.40 (s, 3H), 1.30-1.09 (m, 8H), 0.85 (t, J =6.8 Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 213.4(u), 169.5(u), 61.4(u), 43.2(dn), 41.8(dn), 38.6(u), 35.1(u), 33.2(dn), 29.8(u), 29.6(u), 22.9(u), 15.9(dn), 14.6(dn), 14.3(dn); IR (neat, cm^{-1}): 1730, 1370, 1229, 1644, 1134, 1031; HRMS-EI m/z : $[\text{M}^+]$, calcd for $\text{C}_{14}\text{H}_{22}\text{O}_3$, 238.1569; found, 238.1571.

(3-butyl-1-methyl-4-oxo-cyclopentyl)-acetic acid ethyl ester (β -isomer)

A dry 25 mL round bottomed flask was outfitted with a stir bar, gas inlet adapter and a rubber septum. The assembly was flame dried under vacuum and cooled under nitrogen. The flask was rinsed with dry THF, which was added and withdrawn

through the septum using a syringe. The flask was charged with **13b** (36 mg, 0.15 mmol) in THF:MeOH (7:2), (4 mL). A separate dry flask was charged with a freshly prepared solution of SmI₂ (14 mL of 0.08M in THF, 1.12 mmol). Both flasks were to stir and were cooled in a bath of dry ice/acetone (-78 °C). The SmI₂ solution was then transferred via cannula to the reaction flask in small portions, at -78 °C, until the purple color persisted in the reaction solution. The reaction was then allowed to warm to rt and was quenched with NaHCO₃ (aq). The solvents were removed under reduced pressure and the residue partitioned between NaHCO₃ (aq) and CH₂Cl₂, and extracted three times with CH₂Cl₂. The organics were combined, concentrated, dried over Na₂SO₄ and the residue chromatographed over silica gel (5% ethyl acetate in hexanes) to provide 30 mg (83%) of the title compound as a colorless oil. The ratio of diastereomers (α:β) was measured to be 4:96. A similar experiment with (37 mg, 0.15 mmol) gave 30 mg (80%) of the title compound with α:β ratio of 6:94. The relative stereochemistry was assigned through NOE studies. The purity of the combined diastereomers was measured to be 98% by ¹H NMR. ¹H NMR(CDCl₃, 400 MHz, d): 4.15-4.10 (m, 2H), 2.43 (s, 2H), 2.25-2.24 (m, 3H), 2.14-2.08 (m, 1H), 1.80-1.76 (m, 1H), 1.56 (app t, J=12 Hz, 1H), 1.28-1.23 (m, 8H), 1.12 (s, 3H), 0.8 (t, J=7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz, d): 220.7(u), 171.8(u), 60.7(u), 52.0(u), 47.6(dn), 47.2(u), 42.6(u), 36.4(u), 30.5(u), 30.0(u), 25.9(dn), 23.0(u), 14.7(dn), 14.3(dn); IR (neat, cm⁻¹): 1730, 1230, 1167, 1134, 1032; HRMS-EI m/z: [M⁺], calcd for C₁₄H₂₄O₃, 240.1725; found, 240.1730.

(3-butyl-1-methyl-4-oxo-cyclopentyl)-acetic acid ethyl ester (α-isomer)

The reaction was carried out by with a procedure identical to that used to prepare **14b** .

The following quantities were used: SmI_2 (11 mL of 0.08M in THF, 0.77 mmol), **X** (35 mg, 0.14 mmol) in THF:MeOH (7:2), (4 mL). Chromatography over silica gel (5% ethyl acetate in hexanes) provided 30 mg (85%) of the title compound as a colorless oil. The ratio of diastereomers (a:β) was measured to be 93:7. A similar experiment with (40 mg, 0.17 mmol) gave 33 mg (82%) of the title compound with an a:β ratio of 93:7. The purity of the combined diastereomers was measured to be greater than 99% by NMR. ^1H NMR (CDCl_3 , 400 MHz, d): 4.15-4.10 (m, 2H), 2.54-2.49 (app td, $J=1.2$, 18 Hz, 1H), 2.31 (s, 2H), 2.29-2.26 (m, 2H), 2.08-2.03 (d, $J=18$ Hz, 1H), 1.82-1.78 (m, 1H), 1.48-1.40 (m, 1H), 1.31-1.21 (m, 11H), 0.9-0.87 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz, d): 220.3(u), 171.5(u), 60.3(u), 51.7(u), 47.7(dn), 44.2(u), 42.1(u), 36.5(u), 30.3(u), 29.7(u), 27.4(dn), 22.5(u), 14.2(dn), 13.9(dn); IR (neat, cm^{-1}): 1730, 1200, 1094, 1031; HRMS-EI m/z : $[\text{M}+\text{H}]$, calcd for $\text{C}_{14}\text{H}_{25}\text{O}_3$, 241.1804; found, 241.1807.

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