Tandem Sakurai-Aldol Addition Reactions as a Route to Structurally Complex Carbocycles

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General Information: Unless otherwise stated all reactions were performed in dry glassware under an atmosphere of oxygen free nitrogen using standard inert atmosphere techniques for the manipulation of solvents and reagents. Anhydrous solvents were obtained by passing through successive alumina columns on a solvent purification system. $[\text{IrCl}(\text{C}_8\text{H}_{14})_2]_2^1$ and PCy_3 were stored and weighed out in a glove box. Chemical shifts are reported relative to residual CHCl_3 (7.27 ppm) for ^1H , and CDCl_3 (77.0 ppm) or CD_3CN (1.39 ppm) for ^{13}C NMR spectra. Internal temperature of microwave reactions was monitored by integrated infrared detector.

(E)-5-Methyl-1-(trimethylsilyl)hex-3-en-2-ol (4c): In a 250 mL flask equipped with a dry ice-cooled condenser was added 3.7 g of $\text{Mg}(0)$ (0.15 mol) (activated by mechanical agitation) and 75 mL of Et_2O . A solution of 10 mg of I_2 in 1 mL of $\text{BrCH}_2\text{CH}_2\text{Br}$ was added to the stirring suspension. Once the reaction had initiated (indicated by a brown-to-clear/white color change), a solution of 11 mL of chloromethyltrimethylsilane (9.4 g, 76 mmol) in 10 mL of Et_2O was added at a rate to maintain a gentle reflux. Once addition was complete, the reaction was stirred at ambient temperature for 1 h and the resulting solution of trimethylsilylmethylmagnesium chloride was added slowly via syringe to a -78°C solution of 5.0 g of 4-methyl-2-pentenal (5.9 mL, 51 mmol) in 150 mL of Et_2O . After stirring 30 min at -78°C , the reaction was quenched at -78°C with sat. aq. NH_4Cl and the resulting biphasic mixture was warmed to ambient temperature. The aqueous layer was extracted with Et_2O (3x), the combined organics were dried (MgSO_4) and concentrated. The resulting crude product mixture was purified by Kugelrohr distillation (43°C , 200 mtorr) to afford 7.7 g (81 %) of the title compound as a colorless oil. IR (thin film) 3358, 2957, 1670, 1248, 971, 839 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 5.59 (dd, $J = 15.4, 6.3$ Hz, 1H), 5.42 (dd, $J = 15.4, 7.4$ Hz, 1H), 4.28 – 4.20 (m, 1H), 2.36 – 2.23 (m, 1H), 1.35 (d, $J = 3.7$ Hz, 1H), 1.03 (dd, $J = 14.1, 6.2$ Hz, 1H), 1.00 (d, $J = 6.8$ Hz, 6H), 0.92 (dd, $J = 14.1, 8.5$ Hz, 1H), 0.03 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3): δ -1.0, 22.0, 22.1, 26.7, 30.3, 71.3, 132.2, 137.6; MS (EI) m/z 185 (M^+-H), 169, 143, 73; HRMS (EI) m/z calculated for $\text{C}_{10}\text{H}_{21}\text{OSi}$ (M^+-H): 185.1362, found 185.1363.

General Procedure A for Preparing Diallylethers 5: The diallyl ethers **5a-c** were prepared using a modification of the literature procedure.² To a solution of the allylic alcohol **7** (20 mmol) in 13 mL of THF was added 13 mL of a 1.0 M hexanes solution of Et_2Zn (13 mmol). The resulting solution was stirred at ambient temperature for 1 h. Into a separate flask were weighed 0.22 g (1.0 mmol) of $\text{Pd}(\text{OAc})_2$ and 1.3 g (5.0 mmol) of PPh_3 . The flask was purged with N_2 and 26 mL of THF was added and this mixture was stirred vigorously for 10 min whereupon 3.2 mL (3.0 g, 30 mmol) of allyl acetate was added in a single portion and this mixture was stirred an additional 10 min. The zinc alkoxide solution prepared above was added to this catalyst solution via cannula and the resulting reaction mixture was stirred for the indicated time. The reaction undergoes a color change from yellow to orange and returns to the original yellow color once the reaction is complete. The solvent was removed *in vacuo* and the salts were precipitated by adding Et_2O and removed by filtering through florisil. The crude product mixture was purified as indicated.

(E)-(2-Allyloxypent-3-enyl)trimethylsilane (5a):³ General Procedure A was followed employing 8.0 g (51 mmol) of (*E*)-1-trimethylsilylpent-3-en-2-ol⁴ and a final reaction time of 168 h. Purifying the crude product mixture by Kugelrohr distillation (35°C , 150 mtorr) and MPLC chromatography (39:1 hexanes/ Et_2O) yielded 8.0 g (79 %) of the title compound as a colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 5.96-5.84 (m, 1H), 5.55 (dq, $J = 15, 6.4$ Hz, 1H), 5.28 (ddq, $J = 15, 8.5, 1.6$ Hz, 1H), 5.23 (dq, $J = 17, 1.7$ Hz, 1H), 5.12 (dq, $J = 10, 1.3$ Hz, 1H), 3.97 (ddt, $J = 13, 5.3, 1.5$ Hz, 1H), 3.80-3.70 (m, 2H), 1.70 (dd, $J = 6.5, 1.5$ Hz, 1H), 1.06 (dd, $J = 14, 6.7$ Hz, 1H), 0.85 (dd, $J = 14, 8.0$ Hz, 1H), 0.01 (s, 9H).

¹ Onderdelinden, A. L.; van der Ent, A. *Inorg. Chim. Acta* **1972**, 6, 420.

² Kim, H.; Lee, C. *Org. Lett.* **2002**, 4, 4369.

³ Nelson, S. G.; Bungard, C. J.; Wang, K. *J. Am. Chem. Soc.* **2003**, 125, 13000.

⁴ Taylor, R. T.; Galloway, J. G. *J. Organomet. Chem.* **1981**, 220, 295.

(E)-(2-Allyloxy-4-phenylbut-3-enyl)trimethylsilane (5b):² General Procedure **A** was followed employing 5.0 g (23 mmol) of (*E*)-4-phenyl-1-trimethylsilylbut-3-en-2-ol⁵ and a final reaction time of 48 h. Purifying the crude product mixture by MPLC chromatography (39:1 hexanes/Et₂O) affording 3.1 g (52 %) of the title compound as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.61-7.24 (m, 5H), 6.04 (dd, *J* = 16, 8.3 Hz, 1H), 5.92 (m, 1H), 5.26 (ddd, *J* = 17, 3.5, 1.6 Hz, 1H), 5.15 (ddd, *J* = 10, 3.2, 1.3 Hz, 1H), 4.10-3.95 (m, 2H), 3.83 (ddt, *J* = 13, 5.9, 1.4 Hz, 1H), 1.17 (dd, *J* = 14, 7.2 Hz, 1H), 0.96 (dd, *J* = 14, 7.5 Hz, 1H), 0.28 (s, 9H).

(E)-2-(Allyloxy-5-methylhex-3-enyl)trimethylsilane (5c): The general Procedure **A** was followed employing 5.1 g (27 mmol) of alcohol **7b** and a final reaction time of 168 h. Purifying the crude product mixture by Kugelrohr distillation (35°C, 150 mtorr) followed by MPLC chromatography (39:1 hexanes/Et₂O) yielded 5.7 g (93 %) of the title compound as a colorless oil. IR (thin film) 2957, 1670, 1650, 1247, 1071, 972, 838 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.91, (dddd, *J* = 17.2, 10.4, 5.8, 5.3 Hz, 1H), 5.51 (dd, *J* = 15.5, 6.5 Hz, 1H), 5.28-5.17 (m, 2H), 5.14 (ddt, *J* = 9.1, 1.9, 1.3 Hz, 1H), 3.98 (ddt, *J* = 14.2, 5.3, 1.5 Hz, 1H), 3.80-3.72 (m, 2H), 2.39-2.23 (m, 1H), 1.08 (dd, *J* = 14.3, 6.5 Hz, 1H), 0.88 (dd, *J* = 14.3, 8.3 Hz, 1H), 1.01 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ -0.6, 22.1, 22.4, 25.1, 30.6, 68.4, 78.5, 116.2, 129.5, 135.5, 140.0; MS (EI) *m/z* 183 (*M*⁺-*i*Pr), 169, 139, 73; HRMS (EI) *m/z* calculated for C₁₀H₁₉OSi (*M*⁺-*i*Pr): 183.1205, found 183.1200.

General Procedure B for ICR Reactions: ICR reactions were performed using a modification of the literature procedure.³ Large-scale olefin isomerizations (≥ 2.0 g) proved to be moderately exothermic; performing the initial allyl ether isomerization at 0 °C generally afforded improved *E:Z* vinyl ether ratios. Also, using microwave irradiation for the thermal [3,3] sigmatropic rearrangements was found to require shorter reaction times relative to reactions performed using conventional heating.

A solution of 6.8 mg (0.020 mmol) of NaBPh₄ in 1.5 ml of CH₂Cl₂/acetone (25:1) was added to 9.0 mg (0.010 mmol) of [IrCl(C₈H₁₄)₂]₂ and 17 mg of (0.060 mmol) PCy₃ in 1.5 mL of anhydrous CH₂Cl₂ and the resulting yellow solution was stirred for 30 min at ambient temperature then cooled to 0 °C. The diallyl ether **5** (2.0 mmol) was added dropwise to the 0 °C catalyst solution and the reaction was stirred for 15-30 min while warming to ambient temperature. To the resulting reaction mixture was added 16 mg (0.060 mmol) of PPh₃ whereupon this solution was transferred to a microwave reaction tube and irradiated at 100°C, 150 W for the indicated time. Once the reaction was complete, the solvent was evaporated and the residual salts were removed by adding hexanes and filtering the resulting mixture through Celite. Evaporating the solvent afforded the crude aldehyde product that was used in subsequent transformations without purification. For characterization purposes, a small sample of each aldehyde was purified by flash chromatography (SiO₂) and the spectral data for these purified materials is provided. Diastereomer ratios were determined for the crude aldehydes **7** by integrating the aldehyde **CHO** resonances in the ¹H NMR (300 MHz); these resonances for the diastereomeric aldehydes were well resolved and readily integrated.

R*-(E,2S,3R)-2,3-Dimethyl-6-(trimethylsilyl)hex-4-enal (7a): General Procedure **B** was followed employing 2.00 g (10.1 mmol) of diallylether **5a** and a μW reaction time of 45 min to afford 1.96 g (98 %) of aldehyde **7a** as a yellow oil (*syn:anti* = 93:7). IR (thin film) 3018, 2958, 2700, 1727, 1673, 1248, 967, 854 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.67 (d, *J* = 2.2 Hz, 1H), 5.46 (dtd, *J* = 15.3, 8.0, 1.0 Hz, 1H), 5.21 (ddt, *J* = 15.2, 7.7, 1.1 Hz, 1H), 2.54 (m, 1H), 2.31 (pd, *J* = 7.0, 2.2 Hz, 1H), 1.44 (dd, *J* = 8.0, 0.9 Hz, 2H), 1.05 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.01 (s, 9H); ¹³C NMR (75

⁵ Wang, D.; Chen, D.; Haberman, J. X.; Li, C. *Tetrahedron* **1988**, *54*, 5129.

MHz, CDCl₃): δ -2.0, 10.3, 17.4, 22.7, 37.9, 51.4, 127.0, 131.0, 205.6; MS (EI) m/z 198 (M^+), 183, 130, 115, 73; HRMS (EI) m/z calculated for C₁₁H₂₂OSi: 198.1440, found 198.1431.

R*-(E,2S,3R)-2-Methyl-6-(trimethylsilyl)-3-phenylhex-4-enal (7b): General Procedure

B was followed employing 2.0 g (7.7 mmol) of diallylether **5b** and a μ W reaction time of 60 min to afford 2.0 g (quant) of aldehyde **7b** as a yellow oil (*syn:anti* = 92:8). IR (thin film) 3062, 3027, 2955, 2706, 1727, 1653, 1601, 1248, 966, 851 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.68 (d, J = 3.3 Hz, 1H), 7.39-7.16 (m, 5H), 5.54 (dt, J = 15.1, 6.9 Hz, 1H), 5.50 (dd, J = 15.2, 7.3 Hz, 1H), 3.46 (dd, J = 9.5, 7.5 Hz, 1H), 2.73 (dq, J = 9.6, 6.9, 3.2 Hz, 1H), 1.43 (d, J = 6.7 Hz, 2H) 0.91 (d, J = 6.9 Hz, 3H), -0.04 (s, 9H); ¹³C NMR (75 MHz, CD₃CN): δ -1.7, 13.1, 23.3, 51.7, 51.8, 127.5, 129.0, 129.6 (2C), 130.6, 143.8, 205.8; MS (EI) m/z 260 (M^+), 203, 130, 73; HRMS (EI) m/z calculated for C₁₆H₂₄OSi: 260.1596, found 260.1602.

R*-(E,2S,3R)-3-Isopropyl-2-methyl-6-(trimethylsilyl)hex-4-enal (7c): General Procedure **B**

was followed employing 2.0 g (8.8 mmol) of diallylether **5c** and a μ W reaction time of 75 min to afford 2.0 g (quant.) of aldehyde **7c** as a mixture of *E/Z* olefin isomers [*E:Z* = 88:12, *syn:anti* (*E*) = 91:9, *syn:anti* (*Z*) = 85:15] as determined by 500 ¹H MHz NMR [δ 9.61 (*E*, *syn*), 9.57 (*E*, *anti*), 9.64 (*Z*, *syn*), 9.59 (*Z*, *anti*)] and analytical GC (CP-Wax 52 CB (30 m x 0.25 mm), method: 60°C for 5.00 min, ramp @ 3°C/min to 250°C, hold for 20 min) [$T_{r(E, syn)} + T_{r(E, anti)} = 27.47$, $T_{r(Z, syn)} = 29.04$, $T_{r(Z, anti)} = 28.83$]. IR (thin film) 2958, 2701, 1727, 1655, 1248, 971, 853 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.61 (d, J = 3.1 Hz, 1H), 5.42 (dt, J = 15.1, 8.0 Hz, 1H), 5.07 (ddt, J = 15.1, 9.7, 1.1 Hz, 1H), 2.47 (pd, J = 6.9, 3.2 Hz, 1H), 1.97 (ddd, J = 9.7, 7.7, 5.8 Hz, 1H), 1.89-1.76 (m, 1H), 1.46 (dd, J = 7.9, 1.0 Hz, 2H), 1.05 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H), 0.00 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.8, 12.5, 18.3, 21.4, 23.0, 28.4, 48.1, 51.9, 126.4, 130.1, 205.8; MS (EI) m/z 183 ($M^+ - iPr$), 169, 139, 84, 73; HRMS (EI) m/z calculated for C₁₀H₁₉OSi ($M^+ - iPr$): 183.1205, found 183.1197.

General Procedure C for Preparing Allylic and Homoallylic

Alcohols C1-C5. To a -78 °C solution of aldehyde **7** (1.0 mmol) in 2.5 mL of CH₂Cl₂ was added a 1.5 mmol of either allylmagnesium bromide (1.0 M in Et₂O) or vinylmagnesium

bromide (1.0 M in THF). After stirring the reaction mixture for 15-60 min, the reaction was quenched by carefully adding sat. aq NH₄Cl at -78 °C then warming the mixture to ambient temperature. The layers were separated and the aqueous layer was extracted with Et₂O (3-5x) and the combined organic extracts were dried (MgSO₄) and concentrated. The resulting crude product mixture contained the desired allylic or homoallylic alcohols as diastereomeric mixtures (~1:1-3:1). In each case, the diastereomer with the higher *R_f* (TLC) was isolated by flash chromatography and fully characterized.

R*-(E,3R,4S,5R)-4,5-Dimethyl-8-(trimethylsilyl)octa-1,6-dien-3-ol + R*-(E,3S,4S,5R)-4,5-Dimethyl-8-(trimethylsilyl)octa-1,6-dien-3-ol (C1): General Procedure C was followed

using 1.38 g (6.96 mmol) of aldehyde **7a** (*syn:anti* = 93:7) and 10.4 mL (10.4 mmol) of vinylmagnesium bromide. Purifying the crude product mixture by flash chromatography on SiO₂ (25:1 hexanes/EtOAc) yielded 792 mg (50 %) of the title alcohol as a yellow oil. IR (thin film) 3373, 3078, 2958, 1650, 1644, 1248, 851 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.88 (ddd, J = 17.2, 10.5, 5.4 Hz, 1H), 5.43 (dt, J = 15.8, 8.0 Hz, 1H), 5.24 (dt, J = 17.2, 1.6 Hz, 1H), 5.14 (dt, J = 10.5, 1.6 Hz, 1H), 5.27-5.12 (m, 1H), 4.29-4.23 (m, 1H), 2.17 (sextet, J = 7.1 Hz, 1H), 1.48 (d, J = 5.3 Hz, 1H), 1.43 (dd, J = 7.8, 0.9 Hz, 2H), 1.47-1.33 (m, 1H), 0.97 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 0.00 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.9, 10.6, 18.1, 22.7, 39.5, 43.7, 74.4, 114.3, 125.8, 133.9, 140.9; MS (EI) m/z 226 (M^+), 211, 141, 73; HRMS (EI) m/z calculated for C₁₃H₂₆OSi: 226.1753, found 226.1756.

***R**-(*E*,3*R*,4*S*,5*R*)-4-Methyl-8-(trimethylsilyl)-5-phenylocta-1,6-dien-3-ol + *R**-(*E*,3*S*,4*S*,5*R*)-4-Methyl-8-(trimethylsilyl)-5-phenylocta-1,6-dien-3-ol (C2):**

General Procedure C was followed using 1.00 g (3.84 mmol) of aldehyde **7b** (*syn:anti* = 92:8) and 5.76 mL (5.76 mmol) of vinylmagnesium bromide. Purifying the crude product mixture by flash chromatography on SiO₂ (25:1→10:1 hexanes/EtOAc) yielded 802 mg (72 %) of the title alcohol as a yellow oil. IR (thin film) 3475, 3083, 3062, 3026, 2954, 1645, 1601, 1248, 966, 854 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.34-7.15 (m, 5H), 5.95 (ddd, *J* = 17.2, 10.6, 4.8 Hz, 1H), 5.55 (dt, *J* = 15.0, 7.4 Hz, 1H), 5.46 (dd, *J* = 15.1, 8.2 Hz, 1H), 5.28 (dt, *J* = 17.2, 1.6 Hz, 1H), 5.18 (dt, *J* = 10.6, 1.6 Hz, 1H), 4.55-4.50 (m, 1H), 3.24 (dd, *J* = 10.2, 8.7 Hz, 1H), 1.91 (dq, *J* = 10.3, 6.9, 2.3 Hz, 1H), 1.46 (d, *J* = 4.1 Hz, 1H), 1.43 (d, *J* = 6.2 Hz, 2H), 0.66 (d, *J* = 6.9 Hz, 3H), -0.05 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.8, 10.9, 22.9, 42.9, 53.1, 72.9, 114.1, 125.8, 127.7 (2C), 128.4, 131.6, 140.7, 144.7; MS (EI) *m/z* 288 (M⁺), 270, 203, 73; HRMS (EI) *m/z* calculated for C₁₈H₂₈OSi: 288.1909, found 288.1918.

***R**-(*E*,4*R*,5*S*,6*R*)-5,6-Dimethyl-9-(trimethylsilyl)nona-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-5,6-Dimethyl-9-(trimethylsilyl)nona-1,7-dien-4-ol (C3):** General Procedure C was followed using 1.9 g (9.4 mmol) of aldehyde **7a** (*syn:anti* = 93:7) and 11 mL (1.2 eq, 11 mmol) of allylmagnesium bromide. Purifying the crude product mixture by flash chromatography on

SiO₂ (25:1 hexanes/EtOAc) yielded 1.5 g (66 %) of the title alcohol as a yellow oil. IR (thin film) 3423, 3077, 2958, 1650, 1641, 1248, 853 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.82 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.42 (dt, *J* = 15.6, 8.0 Hz, 1H), 5.19 (dd, *J* = 15.2, 8.4 Hz, 1H), 5.15-5.08 (m, 2H), 3.79 (ddd, *J* = 8.2, 5.0, 3.2 Hz, 1H), 2.31-2.08 (m, 3H), 1.50 (s, 1H), 1.43 (dd, *J* = 7.9, 0.8 Hz, 2H), 1.33 (pd, *J* = 6.9, 3.1 Hz, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.9, 10.6, 18.5, 22.7, 39.9, 40.0, 42.9, 71.8, 117.2, 125.7, 133.8, 135.7; MS (EI) *m/z* 240 (M⁺), 225, 199, 141, 73; HRMS (EI) *m/z* calculated for C₁₄H₂₈OSi: 240.1909, found 240.1912.

***R**-(*E*,4*R*,5*S*,6*R*)-5-Methyl-9-(trimethylsilyl)-6-phenylnona-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-5-Methyl-9-(trimethylsilyl)-6-phenylnona-1,7-dien-4-ol (C4):**

General Procedure C was followed using 918 mg (3.52 mmol) of aldehyde **7b** (*syn:anti* = 92:8) and 5.29 mL (5.29 mmol) of allylmagnesium bromide. Purifying the crude product mixture by flash chromatography on SiO₂ (25:1→10:1 hexanes/EtOAc) yielded 0.660 g (62 %) of the title alcohol as a yellow oil. IR (thin film) 3475, 3081, 3026, 2953, 1650, 1641, 1601, 1248, 966, 851 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.31-7.14 (m, 5H), 5.85 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.52 (dt, *J* = 15.1, 7.6 Hz, 1H), 5.42 (dd, *J* = 15.1, 8.8 Hz, 1H), 5.15 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.12 (dm, *J* = 10.0 Hz, 1H), 4.02 (dtd, *J* = 9.2, 4.7, 2.0 Hz, 1H), 3.21 (dd, *J* = 10.3, 9.0 Hz, 1H), 2.38-2.16 (m, 2H), 1.82 (dq, *J* = 10.4, 6.8, 1.8 Hz, 1H), 1.42 (br. d, *J* = 7.2 Hz, 2H), 1.41 (d, *J* = 4.4 Hz, 1H), 0.69 (d, *J* = 6.9 Hz, 3H), -0.05 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.9, 10.5, 22.8, 40.1, 42.0, 53.6, 70.7, 117.5, 125.8, 127.5, 127.7, 128.4, 131.5, 135.6, 145.0; MS (EI) *m/z* 302 (M⁺), 261, 245, 203, 73; HRMS (EI) *m/z* calculated for C₁₉H₃₀OSi: 302.2066, found 302.2081.

***R**-(*E*,4*R*,5*S*,6*R*)-6-Isopropyl-5-methyl-9-(trimethylsilyl)nona-1,7-dien-4-ol + *R**-(*E*,4*S*,5*S*,6*R*)-6-Isopropyl-5-methyl-9-(trimethylsilyl)nona-1,7-dien-4-ol (C5):**

General Procedure C was followed using 1.07 g (4.70 mmol) of aldehyde **7c** (*syn:anti:Z_{syn}* = 81:7:12) and 7.06 mL (7.06 mmol) of allylmagnesium bromide. Purifying the crude product mixture by flash chromatography on SiO₂ (25:1 hexanes/EtOAc) yielded 853 mg (68 %) of the title alcohol as a yellow oil. IR (thin film) 3439, 3076, 2957, 1646, 1641, 1248, 974, 854 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.81 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.40 (dt, *J* = 15.5, 7.9 Hz, 1H), 5.13-5.01 (m, 3H), 3.83 (dtd, *J* = 9.3, 4.9, 1.7 Hz, 1H), 2.35-2.24 (m, 1H), 2.16-2.07 (m, 1H), 1.95-1.71 (m, 2H), 1.55-1.46 (m, 1H), 1.48 (br. d, *J* = 8.4 Hz, 2H), 1.45 (br. d, *J* = 4.4 Hz, 1H), 0.87 (d, *J* = 5.9 Hz, 3H), 0.85 (d, *J* = 5.7 Hz, 3H), 0.75 (d, *J* = 6.7 Hz, 3H), 0.01 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -2.1, 10.5, 16.5, 22.2, 23.1, 27.7, 38.5, 40.0, 52.2, 71.4, 116.9, 127.8,

129.3, 136.0; MS (EI) m/z 268 (M^+), 253, 225, 211, 167, 73; HRMS (EI) m/z calculated for $C_{16}H_{32}OSi$: 268.2222, found 268.2218.

***R**(2*E*,4*R*,5*S*,6*R*,7*E*)-5,6-Dimethyl-9-(trimethylsilyl)nona-2,7-dien-4-ol + *R**(2*E*,4*S*,5*S*,6*R*,7*E*)-5,6-Dimethyl-9-(trimethylsilyl)nona-2,7-dien-4-ol (10a):** The $Ir(PCy)_3^+$ isomerization catalyst was prepared according to General Procedure **B** using 25 mg (0.028 mmol) of $[IrCl(C_8H_{14})_2]_2$, 19 mg (0.056 mmol) of $NaBPh_4$ and 47 mg (0.17 mmol) of PCy_3 .

To this catalyst solution was added a solution of 1.34 g (5.57 mmol) of the homoallylic alcohol in 1.5 mL of CH_2Cl_2 via cannula. The flask was rinsed with an additional 1.5 mL of CH_2Cl_2 and this rinse was added to the catalyst solution. After 12 h, the reaction was diluted with hexanes and the heterogeneous mixture was filtered through florisil. The crude product mixture was purified by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) to afford 1.21 g (90 %) of the title compound mixture as a clear oil. The high R_f diastereomer was isolated by flash chromatography and fully characterized: IR (thin film) 3385, 2958, 1671, 1652, 1248, 967, 851 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 5.65 (dq, $J = 15.3, 7.5, 1.0$ Hz, 1H), 5.51 (ddq, $J = 15.3, 6.4, 1.4$ Hz, 1H), 5.41 (dtd, $J = 15.2, 7.7, 0.7$ Hz, 1H), 5.21 (ddt, $J = 15.2, 8.0, 1.0$ Hz, 1H), 4.15-4.10 (m, 1H), 2.16 (sextet, $J = 7.0$ Hz, 1H), 1.72 (dt, $J = 6.2, 1.1$ Hz, 3H), 1.43 (dd, $J = 7.9, 0.7$ Hz, 2H), 1.42-1.34 (m, 2H), 0.94 (d, $J = 6.8$ Hz, 3H), 0.88 (d, $J = 6.9$ Hz, 3H), 0.00 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ -1.9, 10.7, 17.4, 17.7, 22.7, 39.1, 44.1, 74.6, 125.5, 126.3, 133.6, 134.0; MS (EI) m/z 240 (M^+), 225, 197, 141, 73; HRMS (EI) m/z calculated for $C_{14}H_{28}OSi$: 240.1909, found 240.1913.

***R**(2*E*,4*R*,5*S*,6*R*,7*E*)-5-Methyl-9-(trimethylsilyl)-6-phenylnona-2,7-dien-4-ol + *R**(2*E*,4*S*,5*S*,6*R*,7*E*)-5-Methyl-9-(trimethylsilyl)-6-phenylnona-2,7-dien-4-ol (10b):** The $Ir(PCy)_3^+$ isomerization catalyst was prepared according to General Procedure **B** using 14.1 mg (0.0157 mmol) of $[IrCl(C_8H_{14})_2]_2$, 10.8 mg (0.0315 mmol) of $NaBPh_4$ and 26.5 mg (0.0944 mmol) of PCy_3 in 1.6 mL of 50:1 CH_2Cl_2 :acetone. This solution of the active catalyst was added to a solution of 476 mg (1.57 mmol) of the homoallylic alcohol in 1.6 mL of 50:1 CH_2Cl_2 :acetone. After 12 h, the reaction was

diluted with hexanes and the heterogeneous mixture was filtered through florisil. The crude product mixture was purified by flash chromatography on SiO_2 (15:1 hexanes/EtOAc) yielding 384 mg (81 %) of the product as an oil. The high R_f diastereomer was isolated *via* flash chromatography and fully characterized: IR (thin film) 3469, 3061, 3026, 2954, 1653, 1601, 1248, 964, 854 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 7.34-7.14 (m, 5H), 5.70 (dq, $J = 15.3, 6.2, 1.0$ Hz, 1H), 5.63-5.56 (m, 1H), 5.53 (dd, $J = 12.7, 5.4$ Hz, 1H), 5.44 (dd, $J = 15.1, 8.2$ Hz, 1H), 4.44-4.37 (m, 1H), 3.23 (dd, $J = 10.2, 8.5$ Hz, 1H), 1.87 (dq, $J = 10.3, 6.9, 2.5$ Hz, 1H), 1.74 (d, $J = 6.0$ Hz, 3H), 1.43 (br. d, $J = 7.5$ Hz, 2H), 1.39 (d, $J = 5.4$ Hz, 1H), 0.68 (d, $J = 6.9$ Hz, 3H), -0.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ -1.9, 11.1, 17.8, 22.8, 43.2, 53.1, 72.9, 125.8, 126.2, 127.6, 127.7, 128.4, 131.6, 133.2, 144.8; MS (EI) m/z 302 (M^+), 287, 203, 73; HRMS (EI) m/z calculated for $C_{19}H_{30}OSi$: 302.2066, found 302.2057.

***R**(2*E*,4*R*,5*S*,6*R*,7*E*)-6-Isopropyl-5-methyl-9-(trimethylsilyl)nona-2,7-dien-4-ol + *R**(2*E*,4*S*,5*S*,6*R*,7*E*)-6-Isopropyl-5-methyl-9-(trimethylsilyl)nona-2,7-dien-4-ol (10c):** The $Ir(PCy)_3^+$ isomerization catalyst was prepared according to General Procedure **B** using 4.1 mg (0.0046 mmol) of $[IrCl(C_8H_{14})_2]_2$, 3.1 mg (0.0091 mmol) of $NaBPh_4$ and 7.6 mg (0.027 mmol) of PCy_3 in 1.5 mL of 50:1 of CH_2Cl_2 :acetone. This catalyst solution was added to 123 mg (0.458 mmol) of the neat homoallylic alcohol. After 12 h, the reaction was diluted with hexanes and the resulting heterogeneous mixture was filtered through florisil. The crude product was purified by flash chromatography on SiO_2 (25:1 hexanes/EtOAc) yielding 0.100 g (81 %) of the product as an oil. The high R_f diastereomer was isolated *via* flash chromatography and fully characterized: IR (thin film) 3465, 2958, 1665, 1655, 1248, 969, 851 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 5.64 (dq, $J = 15.4, 6.2, 1.1$ Hz, 1H), 5.54 (ddq, $J = 15.4, 5.5, 1.2$ Hz, 1H), 5.41 (dt, $J = 15.2, 7.9$ Hz, 1H), 5.09 (ddt, $J = 15.2, 9.9, 1.0$ Hz, 1H), 4.29-4.26 (m, 1H), 1.93-1.77 (m, 2H), 1.71 (dt, $J = 6.0, 1.1$ Hz, 3H), 1.59-1.47 (m, 1H), 1.49 (dt, $J = 7.9, 1.2$ Hz, 2H), 1.43 (d, $J = 5.4$ Hz, 1H), 0.86 (d, $J =$

6.9 Hz, 3H), 0.85 (d, $J = 6.6$ Hz, 3H), 0.76 (d, $J = 6.7$ Hz, 3H), 0.02 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3): δ -1.8, 11.1, 16.3, 17.7, 22.2, 23.1, 27.6, 40.0, 51.7, 73.3, 125.4, 127.9, 129.4, 133.5; MS (EI) m/z 225 ($\text{M}^+ - \text{Pr}$), 169, 149, 73; HRMS (EI) m/z calculated for $\text{C}_{13}\text{H}_{25}\text{OSi}$ ($\text{M}^+ - \text{Pr}$): 225.1675, found 225.1669.

General Procedure D for Preparing Unsaturated Ketones 8 and 9: Ketones **8** and **9** were prepared using a modification of the literature procedure.⁶ To a solution of the diastereomeric mixture of alcohols obtained from General Procedure C (1.0 mmol) in 3.7 mL of CH_2Cl_2 and 2.9 mL of DMSO was added 0.70 mL (5.0 mmol) of triethylamine. The resulting solution was cooled to 0 °C and 0.48 g (3.0 mmol) of pyridine-sulfur trioxide was added in a single portion. The reaction was stirred for 1-4 h at 0 °C until complete as monitored by TLC. The reaction was quenched by adding pH 7 buffer and the layers were separated. The aqueous layer was extracted with Et_2O (3x), the combined organic extracts were dried (MgSO_4) and concentrated. The crude product mixture was purified as indicated. The purified ketone products contained the desired $\text{C}_{5,6}$ *syn* compound in addition to the corresponding ketones derived from the *anti* Claisen diastereomer and the *Z* allyl silane isomer. Purified product composition was established by means of GC-MS [HP-1 (12 m x 0.20 mm), pressure 21 kPa, method: 70°C for 2.00 min, ramp @ 10°C/min to 300°C, hold for 60 min] and/or ^1H -NMR.

***R**-(2*E*,5*S*,6*R*,7*E*)-5,6-Dimethyl-9-(trimethylsilyl)nona-2,7-dien-4-one (9a):** General Procedure **D** was followed using 1.38 g (5.74 mmol) of allylic alcohol **10a** (mixture of diastereomers). Purifying the crude product by flash chromatography on SiO_2 (25:1 hexanes/ EtOAc) afforded 1.18 g (86 %) of the product as a clear oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 7.9 % (*anti* diastereomer $T_r = 10.35$), 82.5 % (*syn* diastereomer $T_r = 10.49$), 9.7 % ($\text{C}_{7,8}$ *Z* $T_r = 11.69$). Product ratio by ^1H -NMR (300 MHz, $\text{Si}(\text{CH}_3)_3$): 8 % (*Z* allyl silane δ 0.011), 7 % (*anti* diastereomer δ -0.005), 85 % (*syn* diastereomer δ -0.029). IR (thin film) 2959, 1696, 1670, 1631, 1248, 969, 853 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 6.90 (dq, $J = 15.6$, 6.9 Hz, 1H), 6.18 (dq, $J = 15.5$, 1.6 Hz, 1H), 5.37 (dtd, $J = 15.2$, 8.0, 6.9 Hz, 1H), 5.16 (ddt, $J = 15.2$, 7.6, 1.0 Hz, 1H), 2.65 (p, $J = 6.9$ Hz, 1H), 2.56-2.36 (m, 1H), 1.89 (dd, $J = 6.9$, 1.6 Hz, 3H), 1.38 (br. dd, $J = 7.9$, 0.8 Hz, 2H), 1.02 (d, $J = 6.9$ Hz, 3H), 0.93 (d, $J = 6.8$ Hz, 3H), -0.03 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3): δ -2.1, 12.8, 17.2, 18.0, 22.6, 38.9, 49.0, 125.9, 131.1, 132.2, 141.5, 202.9; MS (EI) m/z 239 ($\text{M}^+ + \text{H}$), 170, 155, 141, 73, 69; HRMS (EI) m/z calculated for $\text{C}_{14}\text{H}_{26}\text{OSi}$: 238.1753, found 238.1758.

***R**-(2*E*,5*S*,6*R*,7*E*)-5-Methyl-9-(trimethylsilyl)-6-phenylnona-2,7-dien-4-one (9b):** General Procedure **D** was followed employing 272 mg (0.899 mmol) of allylic alcohol **10b** (mixture of diastereomers). Purifying the crude product by flash chromatography on SiO_2 (20:1 hexanes/ EtOAc) afforded 167 mg (62 %) of the product as a clear oil. Product ratio by ^1H -NMR (500 MHz, $\text{Si}(\text{CH}_3)_3$): 8 % (*Z* allyl silane δ -0.026), 86 % (*syn* diastereomer δ -0.085), 6 % (*anti* diastereomer δ -0.114). IR (thin film) 3027, 2954, 1694, 1668, 1629, 1247, 851 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.33-7.17 (m, 5H), 6.91 (dq, $J = 15.6$, 6.9 Hz, 1H), 6.21 (dq, $J = 15.5$, 1.4 Hz, 1H), 5.38-5.34 (m, 2H), 3.50 (dtd, $J = 10.4$, 6.4, 3.2 Hz, 1H), 3.14 (dq, $J = 10.4$, 6.9 Hz, 1H), 1.92 (dd, $J = 6.8$, 1.4 Hz, 3H), 1.35-1.33 (m, 2H), 0.92 (d, $J = 6.9$ Hz, 3H), -0.09 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3): δ -1.9, 16.2, 18.2, 22.8, 48.9, 52.1, 126.2, 127.9, 128.1, 128.4, 129.9, 131.3, 142.5, 143.2, 203.1; MS (EI) m/z 301 ($\text{M}^+ + \text{H}$), 286, 232, 203, 73; HRMS (EI) m/z calculated for $\text{C}_{19}\text{H}_{28}\text{OSi}$: 300.1909, found 300.1921.

***R**-(2*E*,5*S*,6*R*,7*E*)-6-Isopropyl-5-methyl-9-(trimethylsilyl)nona-2,7-dien-4-one (9c):** General Procedure **D** was followed employing 1.08 g (4.02 mmol) of epimeric allylic alcohol **10c** (mixture of diastereomers). Purifying the crude product mixture by flash chromatography on SiO_2 (40:1 hexanes/ EtOAc) afforded 893 mg (83 %) of the product as a

⁶ Parikh, J. R.; Doering, W. E. *J. Am. Chem. Soc.* **1967**, 89, 5505.

clear oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 81.6 % (*syn* diastereomer $T_r = 12.02$), 6.0 % (*anti* diastereomer $T_r = 12.10$), 10.6 % (*syn*_{C5-6} Z_{C7-8} $T_r = 12.23$), 2.0 % (*anti*_{C5-6} Z_{C7-8} $T_r = 12.34$). Product ratio by ¹H-NMR (500 MHz, Si(CH₃)₃): 2 % (*anti-Z*-diastereomer $\delta = 0.020$), 8 % (*Z*-allyl silane $\delta = 0.004$), 5 % (*anti*-diastereomer $\delta = -0.001$), 85 % (*syn*-diastereomer $\delta = -0.035$). IR (thin film) 2958, 1696, 1671, 1630, 1247, 969, 853 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.82 (dq, $J = 15.4, 6.9$ Hz, 1H), 6.15 (dq, $J = 15.5, 1.6$ Hz, 1H), 5.29 (dt, $J = 15.3, 7.9$ Hz, 1H), 5.00 (ddt, $J = 15.1, 9.6, 1.2$ Hz, 1H), 2.81 (dq, $J = 9.3, 6.9$ Hz, 1H), 2.05 (dt, $J = 9.4, 4.3$ Hz, 1H), 1.88 (dd, $J = 6.9, 1.6$ Hz, 3H), 1.90-1.80 (m, 1H), 1.38 (dd, $J = 7.9, 1.2$ Hz, 2H), 1.05 (d, $J = 6.9$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H), 0.79 (d, $J = 6.8$ Hz, 3H), -0.04 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -6.6, 11.6, 13.1, 14.7, 18.5, 19.7, 24.4, 44.3, 50.1, 129.0, 132.9, 134.2, 145.5, 211.1; MS (EI) m/z 266 (M⁺), 251, 223, 197, 73, 69; HRMS (EI) m/z calculated for C₁₆H₃₀OSi: 266.2066, found 266.2065.

R*-(E,4S,5R)-4,5-Dimethyl-8-(trimethylsilyl)octa-1,6-dien-3-one (8a): General Procedure **D** was followed employing 792 mg (3.50 mmol) of the allylic alcohol (mixture of diastereomers). Purifying the crude product mixture by flash chromatography on SiO₂ (25:1 hexanes/EtOAc) afforded 665 mg (85 %) of the product as a clear oil. Separation of the diastereomers by GC-

MS provided the diastereomer ratio: 10.2 % (*anti* diastereomer $T_r = 8.72$), 77.4 % (*syn* diastereomer $T_r = 8.90$), 12.3 % (*syn*_{C4-5} Z_{C6-7} $T_r = 8.98$). Product ratio by ¹H-NMR (300 MHz, Si(CH₃)₃): 9 % (*anti* diastereomer $\delta = 0.011$), 10 % (*Z* allyl silane $\delta = -0.005$), 81 % (*syn* diastereomer $\delta = -0.029$). IR (thin film) 2958, 1698, 1678, 1612, 1248, 966, 855 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.43 (dd, $J = 17.4, 10.4$ Hz, 1H), 6.23 (dd, $J = 17.4, 1.6$ Hz, 1H), 5.73 (dd, $J = 10.4, 1.6$ Hz, 1H), 5.38 (dtd, $J = 15.2, 8.0, 1.0$ Hz, 1H), 5.16 (ddt, $J = 15.2, 7.6, 1.1$ Hz, 1H), 2.74 (p, $J = 6.9$ Hz, 1H), 2.54-2.43 (m, 1H), 1.38 (br. dd, $J = 8.0, 0.9$ Hz, 2H), 1.05 (d, $J = 6.9$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H), -0.03 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -2.1, 12.7, 17.2, 22.5, 38.9, 49.1, 126.1, 127.5, 131.9, 135.6, 203.2; MS (EI) m/z 224 (M⁺), 209, 141, 73; HRMS (EI) m/z calculated for C₁₃H₂₄OSi: 224.1596, found 224.1599.

R*-(E,4S,5R)-4-Methyl-8-(trimethylsilyl)-5-phenylocta-1,6-dien-3-one (8b): Dess-Martin reagent was prepared and used according to literature precedent.^{7,8} To 0 °C a solution of 813 mg (2.82 mmol) of the allylic alcohol (mixture of diastereomers) in 30 mL of CH₂Cl₂ was added 1.80 g (4.23 mmol) of freshly-prepared Dess-Martin periodinane. The reaction was

stirred at 0°C for 1 h then warmed to ambient temperature over an additional 1.5 h. The reaction was diluted with hexanes, filtered through florisil (5:1 hexanes/EtOAc), and the crude product mixture was concentrated. Flash chromatography on SiO₂ (25:1 hexanes/EtOAc) yielded 513 mg (63 %) of the title compound as a clear oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 8.1 % (*anti* diastereomer $T_r = 14.15$), 83.8 % (*syn* diastereomer $T_r = 14.30$), 8.1 % (*syn*_{C4-5} Z_{C6-7} $T_r = 14.36$). Product ratio by ¹H-NMR (300 MHz, Si(CH₃)₃): 7 % (*Z* allyl silane $\delta = -0.035$), 87 % (*syn* diastereomer $\delta = -0.86$), 6 % (*anti* diastereomer $\delta = -0.112$). IR (thin film) 3061, 3026, 2954, 1698, 1678, 1611, 1248, 964, 854 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.34-7.18 (m, 5H), 6.46 (dd, $J = 17.5, 10.3$ Hz, 1H), 6.29 (dd, $J = 17.5, 1.4$ Hz, 1H), 5.80 (dd, $J = 10.3, 1.4$ Hz, 1H), 5.39-5.36 (m, 2H), 3.52 (ddd, $J = 10.4, 4.1, 2.7$ Hz, 1H), 3.21 (dq, $J = 10.4, 6.9$ Hz, 1H), 1.35-1.33 (m, 2H), 0.88 (d, $J = 6.9$ Hz, 3H), -0.09 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.9, 16.1, 22.8, 48.5, 52.0, 126.3, 127.9, 128.1 (2C), 128.5, 129.8, 135.9, 143.0, 203.4; MS (EI) m/z 286 (M⁺), 271, 257, 203, 73; HRMS (EI) m/z calculated for C₁₈H₂₆OSi: 286.1753, found 286.1755.

General Procedure E for Sakurai Annulation Reactions:⁹ To 1.2 mL (1.2 mmol) of a vigorously stirred solution of TiCl₄ in CH₂Cl₂ (1.0 M) at -78 °C was slowly added the unsaturated ketone **8** or **9** (1.0 mmol) in 10

⁷ Boeckman Jr., R. K.; Shao, P.; Mullins, J. *J. Org. Synth., Coll. Vol. X* **2000**, 2377.

⁸ Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.

⁹ Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, *17*, 1295.

mL of CH₂Cl₂ affording a deep red reaction mixture. The syringe and receptacle were washed with 1 mL of additional CH₂Cl₂ and this rinse was added to the reaction vessel. After stirring 15 min at -78 °C, the reaction was quenched with by carefully adding sat. aq NH₄Cl and the resulting mixture was slowly warmed to ambient temperature. The aqueous layer was extracted with CH₂Cl₂ (3x) and the combined organic extracts were dried (Na₂SO₄) and filtered through a fine glass frit with the filter cake being washed with Et₂O.¹⁰ Evaporating the solvents provided the crude product mixture that was purified using the indicated technique. Diastereomer ratios for the purified products were determined using GC-MS [HP-1 (12 m x 0.20 mm), pressure 21 kPa, method: 70 °C for 2.00 min, ramp @ 10 °C/min to 300 °C, hold for 60 min].

R*-(2S,3R,4S,5S)-2,3,5-Trimethyl-4-vinylcyclohexanone (11): General Procedure E was followed employing 0.10 g (0.42 mmol) of enone **9a** (82.5:7.9:9.7 *syn:anti:Z*). Purifying the crude product mixture by flash chromatography on SiO₂ (20:1 pentane/Et₂O) afforded 46 mg (67 %) of the product as a colorless volatile oil.¹¹ Separation of the diastereomers by GC-MS provided the diastereomer ratio: 91.7 % (*trans, trans, cis* T_r = 6.49), 8.3 % (T_r = 6.99). IR (thin film) 3076, 2969, 1713, 1638, 915 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.67 (dt, *J* = 18.0, 9.3 Hz, 1H), 5.11-5.06 (m, 2H), 2.63 (dd, *J* = 13.0, 5.0 Hz, 1H), 2.37-2.18 (m, 3H), 2.02 (dq, *J* = 12.9, 6.5, 0.7 Hz, 1H), 1.60-1.46 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 11.8, 13.9, 19.2, 36.9, 38.8, 48.6, 50.6, 52.2, 116.2, 140.6, 212.2; MS (EI) *m/z* 166 (M⁺), 138, 96, 68; HRMS (EI) *m/z* calculated for C₁₁H₁₈O: 166.1358, found 166.1357.

R*-(2S,3R,4S,5S)-2,5-Dimethyl-3-phenyl-4-vinylcyclohexanone (14b): General Procedure E was followed employing 0.050 g (0.17 mmol) of enone **9b** (86:6:8 *syn:anti:Z*). Purifying the crude product mixture by flash chromatography on SiO₂ (20:1 pentane/Et₂O) afforded 31 mg (82 %) of the product as a white solid; m.p. 86-88°C. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 94.6 % (*trans, trans, cis* T_r = 12.80), 3.8 % (T_r = 12.99), 1.7 % (T_r = 13.08). IR (thin film) 3064, 3027, 2969, 1712, 1639, 914 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.34-7.13 (m, 5H), 5.52 (ddd, *J* = 17.8, 9.8, 8.5 Hz, 1H), 4.82 (dm, *J* = 10.0 Hz, 1H), 4.81 (dm, *J* = 17.0 Hz, 1H), 2.97 (td, *J* = 9.8, 3.3 Hz, 1H), 2.86 (dd, *J* = 13.0, 5.4 Hz, 1H), 2.65 (t, *J* = 11.6 Hz, 1H), 2.65-2.55 (m, 1H), 2.50-2.45 (m, 1H), 2.38 (dd, *J* = 12.9, 2.9 Hz, 1H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.79 (d, *J* = 6.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 12.2, 13.7, 37.0, 48.8, 50.2, 50.8, 51.7, 116.3, 126.6, 128.0, 128.5, 139.3, 142.4, 211.6; MS (EI) *m/z* 228 (M⁺), 118, 68; HRMS (EI) *m/z* calculated for C₁₆H₂₀O: 228.1514, found 228.1512.

R*-(2S,3R,4S,5S)-3-Isopropyl-2,5-dimethyl-4-vinylcyclohexanone (14c): General Procedure E was followed employing 0.10 g (0.38 mmol) of enone **9c** (81.4:6.0:10.6:2.0 *syn : anti : syn*_{C5-6} *Z*_{C7-8} : *anti*_{C5-6} *Z*_{C7-8}). Purifying the crude product mixture by flash chromatography on SiO₂ (25:1 hexanes/EtOAc) afforded 65 mg (87 %) of the product as a clear oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 89.0 % (*trans, trans, cis* T_r = 8.83), 8.2 % (T_r = 8.99), 2.7 % (T_r = 9.07). IR (thin film) 3090, 2960, 1713, 1637, 913 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.65 (dt, *J* = 16.8, 10.0, 1H), 5.04 (dd, *J* = 10.3, 1.8 Hz, 1H), 5.00 (dd, *J* = 16.8, 1.8 Hz, 1H), 2.42 (dd, *J* = 16.2, 4.8 Hz, 1H), 2.47-2.36 (m, 2H), 2.34-2.23 (m, 1H), 2.11 (d, *J* = 16.0, 8.9 Hz, 1H), 2.04-1.94 (m, 1H), 1.39 (ddd, *J* = 8.3, 5.5, 2.8 Hz), 1.06 (d, *J* = 6.4 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 13.2, 16.9, 17.5, 20.3, 29.6, 32.7, 44.5, 45.0, 45.2, 50.4, 115.7, 140.1, 214.4; MS (EI) *m/z* 194 (M⁺), 179, 166, 151, 68; HRMS (EI) *m/z* calculated for C₁₃H₂₂O: 194.1671, found 194.1680.

¹⁰ Titanium salts were found to epimerize the α-chiral ketone products upon crude product concentration. Filtration through a fine glass frit effectively minimizes these deleterious byproducts.

¹¹ Due to the volatility of this product, isolated yields were found to improve for larger scale reactions.

R*-(2S,3R,4R)-2,3-Dimethyl-4-vinylcyclohexanone (13a): General Procedure **E** was followed employing 0.050 g (0.22 mmol) of acrylate **8a** (77.4:10.2:12.3 *syn:anti:Z*). Purifying the crude product mixture by flash chromatography on SiO₂ (20:1 pentane/Et₂O) afforded 0.020 g (59 %) of the product as a clear, highly volatile oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 89.8 % (*trans, trans* $T_r = 5.43$), 10.2 % ($T_r = 5.92$). IR (thin film) 3077, 2971, 1713, 1643, 914 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.57 (ddd, $J = 17.2, 10.1, 8.8$ Hz, 1H), 5.06 (dd, $J = 17.1, 2.0$ Hz, 1H), 5.03 (dd, $J = 10.2, 1.8$ Hz, 1H), 2.47-2.33 (m, 2H), 2.17-2.08 (m, 1H), 2.09 (dd, $J = 11.2, 6.7$ Hz, 1H), 2.06-1.95 (m, 1H), 1.67-1.50 (m, 1H), 1.34-1.20 (m, 1H), 1.04 (d, $J = 6.5$ Hz, 3H), 1.01 (d, $J = 6.5$ Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 11.8, 18.7, 33.2, 40.9, 44.6, 48.8, 50.4, 115.3, 141.6, 212.2; MS (EI) m/z 152 (M⁺), 126, 111; HRMS (EI) m/z calculated for C₁₀H₁₆O: 152.1201, found 152.1196.

R*-(2S,3R,4R)-2-Methyl-3-phenyl-4-vinylcyclohexanone (13b): General Procedure **E** was followed employing 0.050 g (0.17 mmol) of acrylate **8b** (83.8:8.1:8.1 *syn:anti:Z*). Purifying the crude product mixture by flash chromatography on SiO₂ (10:1 pentane/Et₂O) afforded 0.030 g (82 %) of the product as a clear, viscous oil. Separation of the diastereomers by GC-MS provided the diastereomer ratio: 92.6 % (*trans, trans* $T_r = 12.10$), 5.3 % ($T_r = 12.31$), 2.1 % ($T_r = 12.14$). IR (thin film) 3081, 3027, 2970, 1712, 913 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.34-7.12 (m, 5H), 5.44 (ddd, $J = 17.6, 10.4, 7.5$ Hz, 1H), 4.81 (dm, $J = 17.3$ Hz, 1H), 4.78 (dm, $J = 10.4$ Hz, 1H), 2.82-2.51 (m, 4H), 2.37 (t, $J = 11.5$ Hz, 1H), 2.20 (ddt, $J = 13.4, 6.1, 3.1$ Hz, 1H), 1.75 (qd, $J = 13.4, 5.1$ Hz, 1H), 0.78 (d, $J = 6.5$ Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 12.3, 32.5, 41.1, 47.2, 49.9, 57.9, 114.9, 126.6, 127.9, 128.5, 140.1, 142.2, 211.8; MS (EI) m/z 214 (M⁺), 147, 118, 68; HRMS (EI) m/z calculated for C₁₅H₁₈O: 214.1358, found 214.1353.

General Procedure F for Tandem Intermolecular Sakurai-Aldol Reactions: General Procedure **E** for the Sakurai annulation reactions was followed as described incorporating the following modifications. After reacting the enone with TiCl₄ for the indicated time, neat aldehyde (1.2 mmol) was added dropwise to the deep red solution of the titanium enolate intermediate. The reaction was stirred at -78 °C until complete as monitored by TLC (~1 h). Reaction work-up was performed as described in General Procedure **E**. Reaction products were purified using the indicated procedures. Diastereomer ratios of the purified products were determined by LC-MS [X-terra C-18, method: 35%:65% MeCN:H₂O for 24.00 min, ramp to 50:50 MeCN:H₂O] or 500 MHz ¹H NMR data.

R*-(2R,3R,4R,5R,6S)-2-((S)-1-Hydroxy-2-methylpropyl)-3,5,6-trimethyl-4-vinylcyclohexanone (18b): General Procedure **F** was followed employing 0.050 g (0.21 mmol) of enone **9a** (82.5:7.9:9.7 *syn : anti : Z*) and 23 μ L (18 mg, 0.25 mmol) of isobutyraldehyde. Flash chromatography on SiO₂ (5:1 hexanes/EtOAc) afforded 26 mg (52 %) of the product as a clear oil. Isolated diastereomer ratio determined by 500 MHz ¹H NMR (CH₂OH): 8 % (δ 3.98), 85 % (δ 3.88), 7 % (δ 3.32). IR (thin film) 3454, 3076, 2965, 1704, 1639, 999, 914 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.67 (ddd, $J = 16.8, 10.4, 9.0$ Hz, 1H), 5.10 (dm, $J = 10.3$ Hz, 1H), 5.07 (dm, $J = 16.8$ Hz, 1H), 3.92-3.86 (m, 1H), 2.38-2.28 (m, 3H), 2.12 (qdd, $J = 7.1, 4.3, 3.1$ Hz, 1H), 1.90 (pd, $J = 6.9, 3.5$ Hz, 1H), 1.63-1.52 (m, 1H), 1.51 (d, $J = 7.8$ Hz, 1H), 1.08 (d, $J = 6.5$ Hz, 3H), 1.04 (d, $J = 6.9$ Hz, 3H), 1.01 (d, $J = 6.4$ Hz, 3H), 0.89 (d, $J = 7.2$ Hz, 3H), 0.85 (d, $J = 6.8$ Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 12.4, 14.7, 15.1, 19.2, 20.1, 30.5, 37.9, 38.6, 48.1, 48.4, 61.2, 75.7, 116.4, 140.4, 214.7; MS (EI) m/z 220 (M⁺-H₂O), 205, 195, 166, 98, 68; HRMS (EI) m/z calculated for C₁₅H₂₄O (M⁺-H₂O): 220.1827, found 220.1835.

R*-(2R,3R,4R,5R,6S)-2-((R)-Hydroxy-(phenylmethyl))-3,5,6-trimethyl-4-vinylcyclohexanone (18a): General Procedure **F** was followed employing 0.050 g (0.21 mmol) of enone **9a** (82.5:7.9:9.7 *syn : anti : Z*) and 25 μ L (27 mg, 0.25 mmol) of benzaldehyde. Flash

chromatography on SiO₂ (5:1 hexanes/EtOAc) afforded 31 mg of the product (52 %) as a clear oil. Isolated diastereomer ratio determined by LC-MS [X-terra C-18, method: 35%:65% MeCN:H₂O for 24.00 min, ramp to 50:50 MeCN:H₂O]: 3.2 % (*T_r* = 34.68), 84.9 % (*T_r* = 37.49), 10.4 % (*T_r* = 39.56), 1.6 % (*T_r* = 42.32). IR (thin film) 3427, 3067, 3030, 2970, 1698, 1639, 915 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.39-7.24 (m, 5H), 5.67 (ddd, *J* = 17.6, 9.6, 8.7 Hz, 1H), 5.15-5.06 (m, 3H), 2.61 (dd, *J* = 7.9, 3.8 Hz, 1H), 2.60 (d, *J* = 3.8 Hz, 1H), 2.55-2.43 (m, 2H), 1.92 (dq, *J* = 10.6, 6.5 Hz, 1H), 1.53 (ddq, *J* = 10.6, 8.9, 6.5 Hz, 1H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 12.2, 15.3, 19.6, 35.6, 39.0, 48.3, 49.8, 64.0, 73.3, 116.4, 126.3, 128.2, 128.6, 139.9, 141.5, 213.9; MS (EI) *m/z* 272 (*M*⁺), 254, 166, 106, 69; HRMS (EI) *m/z* calculated for C₁₈H₂₄O₂: 272.1776, found 272.1784.

***R**-(*R*)-((1*R*,2*R*,3*R*,4*R*,5*S*)-2,4,5-Trimethyl-6-oxo-3-vinylcyclohexyl)(phenyl)-methyl-4-bromobenzoate (19):** To 54 mg (0.20 mmol) of cyclohexanone **18a** in 2 mL of CH₂Cl₂ at 0 °C was added 2.4 mg (0.020 mmol) of 4-(dimethylamino)pyridine, 52 mg (0.24 mmol) of 4-bromobenzoyl chloride, and 42 μL (31 mg, 0.24 mmol) of *N,N*-diisopropylethylamine in succession. The resulting solution was warmed to ambient temperature and stirred for 5 h. The reaction was quenched by adding aq. 1M HCl and the aqueous layer was extracted with EtOAc (4x). The combined organic extracts were

dried (MgSO₄), concentrated, and the resulting crude product mixture was purified by flash chromatography on SiO₂ (10:1 hexanes/EtOAc) to afford 71 mg (80 %) of the title compound as a colorless crystalline solid: mp 154-156 °C. Recrystallizing this solid from hexanes/EtOAc provided crystals suitable for X-ray diffraction analysis. IR (thin film) 3069, 2972, 1713, 1591, 1267, 914 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.92 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.37-7.31 (m, 5H), 6.56 (d, *J* = 10.5 Hz, 1H), 5.64 (dt, *J* = 17.1, 10.0 Hz, 1H), 5.09 (d, *J* = 17.2 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 2.99 (dd, *J* = 10.5, 2.3 Hz, 1H), 2.75 (td, *J* = 10.8, 4.1 Hz, 1H), 2.43-2.28 (m, 1H), 2.16 (dq, *J* = 12.7, 6.4 Hz, 1H), 1.63-1.53 (m, 1H), 1.05 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 7.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 11.8, 14.5, 19.2, 38.2, 39.5, 47.3, 49.7, 64.0, 74.6, 116.9, 127.1, 128.4, 128.7, 128.8, 129.0, 131.2, 131.8, 137.2, 139.8, 165.0, 210.4; MS (EI) *m/z* 456 (*M*⁺), 271, 254, 185, 183; HRMS (EI) *m/z* calculated for C₂₅H₂₇O₃Br: 454.1144, found 454.1139.

Pent-4-ynyl benzoate:¹² To 0 °C solution of 1.0 g (1.1 mL, 12 mmol) of 4-pentyn-1-ol in 40 mL of CH₂Cl₂ was successively added 2.0 g (14 mmol) of benzoyl chloride and 145 mg (1.19 mmol) of 4-(dimethylamino)pyridine, and 2.5 mL (1.8 g, 14 mmol) of *N,N*-diisopropylethylamine. The reaction solution was warmed to ambient temperature and stirred for 12 h. The reaction mixture was poured into aq. 1M HCl and the aqueous layer was extracted with EtOAc (4x). The combined organic extracts were washed with brine, dried (MgSO₄), and concentrated. The resulting crude product mixture was purified by flash chromatography on SiO₂ (20:1 hexanes/EtOAc) to afford 2.0 g (90 %) of the product as a clear oil. ¹H NMR (300 MHz, CDCl₃): δ 8.08-8.04 (m, 2H), 7.60-7.54 (m, 1H), 7.48-7.42 (m, 2H), 4.44 (t, *J* = 6.2 Hz, 2H), 2.40 (td, *J* = 7.1, 2.6 Hz, 2H), 2.02 (q, *J* = 6.5 Hz, 2H), 2.01-1.99 (m, 1H).

***R**-(4*E*,6*R*,7*S*,8*R*,9*E*)-6-Hydroxy-7,8-dimethyl-11-(trimethylsilyl)-undeca-4,9-dienyl-benzoate + *R**-(4*E*,6*S*,7*S*,8*R*,9*E*)-6-Hydroxy-7,8-dimethyl-11-(trimethylsilyl)-undeca-4,9-dienyl-benzoate (21):** Reactions were performed using a modification of the literature procedure.¹³ Schwartz's reagent was prepared according to literature methods.¹⁴ To 0 °C solution of 221 mg (0.861 mmol) of di(cyclopentadienyl)zirconium chloride hydride in 2.5 mL of CH₂Cl₂ added 171 mg (0.909 mmol) of pent-4-ynyl benzoate. The reaction mixture was warmed to ambient temperature and stirred until homogenous. To this stirring solution was added 0.100 g (0.504

¹² Sato, H.; Isono, N.; Miyoshi, I.; Mori, M. *Tetrahedron* **1996**, 52, 8143.

¹³ Suzuki, K.; Hasegawa, T.; Imai, T.; Maeta, H.; Ohba, S. *Tetrahedron* **1995**, 51, 4483.

¹⁴ Buchwald, S. L.; LaMaire, S. J.; Nielsen, R. B.; Watson, B. T.; King, S. M. *Org. Synth., Coll. Vol. IX* **1993**, 162.

mmol) of aldehyde **18** (93:7 *syn* : *anti*). A separate flask was charged with 15 mg (0.050 mmol) of AgAsF₆ and 2.5 mL of CH₂Cl₂ and the reaction solution prepared above was added carefully to this flask *via* syringe (colorless-to-brown color change). The resulting brown solution was stirred for 10 min then the reaction was quenched by adding sat. aq. NaHCO₃. The aqueous layer was extracted with EtOAc (4x) the combined organic extracts were dried (Na₂SO₄) and concentrated. The resulting crude product mixture was purified by flash chromatography on SiO₂ (5:1 hexanes/EtOAc) to afford 159 mg (81 %) of the title compound as a mixture of C-6 epimers. The higher R_f diastereomer was isolated *via* flash chromatography and fully characterized. IR (thin film) 3515, 2957, 1721, 1602, 1274, 1248, 970, 853, 675 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 8.05 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.57 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 5.68 (dt, *J* = 15.4, 6.5 Hz, 1H), 5.55 (dd, *J* = 15.4, 6.0 Hz, 1H), 5.41 (dt, *J* = 15.2, 7.9 Hz, 1H), 5.21 (dd, *J* = 15.2, 8.1 Hz, 1H), 4.35 (t, *J* = 6.6 Hz, 2H), 4.21-4.14 (m, 1H), 2.24 (q, *J* = 6.9 Hz, 2H), 2.22-2.09 (m, 1H), 1.88 (q, *J* = 6.6 Hz, 2H), 1.43-1.33 (m, 1H), 1.43 (br. d, *J* = 7.9 Hz, 2H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.9, 10.7, 17.7, 22.7, 28.4, 28.8, 39.3, 44.1, 64.3, 74.2, 125.6, 128.3, 129.6, 129.8, 130.5, 132.8, 133.4, 133.9, 166.6; MS (ESI) *m/z* 411 (M⁺+Na); HRMS (ESI) *m/z* calculated for NaC₂₃H₃₆O₃Si (M⁺+Na): 411.2331, found 411.2340.

R*-(4E,6R,7S,8R,9E)-7,8-Dimethyl-11-(trimethylsilyl)-undeca-4,9-diene-1,6-diol + R*-(4E,6S,7S,8R,9E)-7,8-Dimethyl-11-(trimethylsilyl)-undeca-4,9-diene-1,6-diol:

Reactions were performed using a modification of a literature procedure.¹⁵ To 524 mg (1.39 mmol) of C-6 epimeric alcohols **21** was added 13.9 mL of a 1% w/v solution of NaOH in MeOH at ambient temperature. The mixture was stirred for 1 h then diluted with brine and the layers were separated. The aqueous layer was extracted with Et₂O (3x) and the combined organic extracts were dried (Na₂SO₄) and concentrated. The resulting crude product mixture was purified by flash chromatography on SiO₂ (1:1 hexanes/EtOAc) to afford 373 mg (94 %) of the product as a clear oil. A sample of the diastereomerically pure benzoate **21** obtained above was subjected to identical reaction conditions to afford diastereomerically pure diol which was fully characterized. IR (thin film) 3353, 2957, 1656, 1247, 969, 852 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.66 (dt, *J* = 15.6, 6.5 Hz, 1H), 5.53 (dd, *J* = 15.5, 6.1 Hz, 1H), 5.42 (dt, *J* = 15.4, 7.8 Hz, 1H), 5.21 (dd, *J* = 15.2, 8.1 Hz, 1H), 4.17 (t, *J* = 4.9 Hz, 1H), 3.67 (t, *J* = 6.5 Hz, 2H), 2.19-2.12 (m, 1H), 2.16 (q, *J* = 6.8 Hz, 2H), 1.68 (q, *J* = 6.5 Hz, 2H), 1.44-1.34 (m, 1H), 1.43 (br d, *J* = 7.3 Hz, 2H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.00 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -1.7, 10.7, 17.8, 22.7, 28.6, 32.2, 39.2, 44.1, 62.4, 74.3, 125.6, 130.6, 133.0, 134.0; MS (EI) *m/z* 284 (M⁺), 269, 266, 169, 141, 73; HRMS (EI) *m/z* calculated for C₁₆H₃₂O₂Si: 284.2172, found 284.2170.

R*-(4E,7S,8R,9E)-7,8-dimethyl-11-(trimethylsilyl)-6-oxo-undeca-4,9-dienal (22):

To a 0 °C solution of 237 mg (0.833 mmol) of the C-6 epimeric alcohols in 8.3 mL of CH₂Cl₂ was added 883 mg (2.08 mmol) of Dess-Martin periodinane.¹⁹ The reaction was stirred at 0 °C for 1 h then slowly warmed to ambient temperature over an additional 3 h. The reaction mixture was diluted with hexanes, filtered through florisil (5:1 hexanes/EtOAc eluent), and concentrated. The resulting crude product mixture was purified by flash chromatography on SiO₂ (5:1 hexanes/EtOAc) to afford 0.160 g (68 %) of the title compound as a clear oil. Product ratio by GC-MS: 6.1 % (*anti*-diastereomer or *Z*-allyl silane T_r = 14.51), 87.8 % (*syn* T_r = 14.71), 6.1 % (*anti* or *Z*-allyl silane T_r = 14.90). Product ratio by ¹H-NMR (300 MHz, Si(CH₃)₃): 8 % (*Z*-allyl silane δ 0.013), 7 % (*anti* δ -0.007), 85 % (*syn* δ -0.029). IR (thin film) 2958, 1727, 1694, 1668, 1628, 1247, 971, 853 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.91 (s, 1H), 6.80 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.18 (dt, *J* = 15.6, 1.4 Hz, 1H), 5.37 (dt, *J* = 15.2, 7.9 Hz, 1H), 5.15 (dd, *J* = 15.2, 7.6 Hz, 1H), 2.69-2.42 (m, 6H), 1.38 (br. d, *J* = 7.8 Hz, 2H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), -0.02 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ -2.0, 12.8, 16.9, 22.6, 24.7, 39.0, 42.0, 49.9, 126.2, 130.1, 132.1, 143.6,

¹⁵ Mashimo, K.; Sato, Y. Tetrahedron, **1970**, 26, 803.

200.3, 202.9; MS (EI) m/z 280 (M^+), 265, 183, 73; HRMS (EI) m/z calculated for $C_{16}H_{28}O_2Si$: 280.1859, found 280.1857.

***R**(3*aS*,5*S*,6*R*,7*R*,7*aR*)-Octahydro-3-hydroxy-5,6-dimethyl-7-vinylinden-4-one (23):** To a -78°C solution of 65 mg (23 mmol) of ketoaldehyde **22** (87.8:6.1:6.1 *syn* : *anti* : *Z*) in 4.6 mL of CH_2Cl_2 was added 0.28 mL (0.28 mmol) of a 1.0 M CH_2Cl_2 solution of TiCl_4 . After stirring 20 min at -78°C , the reaction was quenched by careful addition of 5 mL of sat. aq. NH_4Cl and the biphasic mixture was warmed to ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic extracts were dried (Na_2SO_4) and filtered through a fine glass frit with the filter cake being washed with Et_2O . The solvent was evaporated and the resulting crude product mixture was purified by flash chromatography on SiO_2 (2:1 hexanes/ EtOAc) to give 25 mg (52 %) of the title compound as a clear, viscous oil. Isolated diastereomeric ratio by GC-MS: 5.78 % ($T_r = 10.15$), 6.10 % ($T_r = 10.42$), 5.33 % ($T_r = 11.63$), 82.8 % ($T_r = 11.95$). IR (thin film) 3400, 3075, 2969, 1706, 1639, 998, 913 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 5.59 (dt, $J = 17.1, 9.8$ Hz, 1H), 5.12 (dd, $J = 17.0, 1.9$ Hz, 1H), 5.09 (dd, $J = 9.9, 1.9$ Hz, 1H), 4.83 (dd, $J = 6.4, 2.3$ Hz, 1H), 2.85-2.73 (m, 2H), 2.48 (td, $J = 10.3, 4.7$ Hz, 1H), 2.20-2.09 (m, 2H), 1.81-1.71 (m, 1H), 1.58-1.40 (m, 3H), 1.26-1.09 (m, 1H), 1.03 (d, $J = 6.5$ Hz, 3H), 0.99 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 11.7, 18.7, 23.7, 33.1, 39.4, 46.6, 49.2, 50.1, 61.2, 72.3, 116.2, 140.5, 212.2; MS (EI) m/z 208 (M^+), 190, 140, 122, 68; HRMS (EI) m/z calculated for $C_{13}H_{20}O_2$: 208.1463, found 208.1468.

***R**(3*aS*,5*S*,6*R*,7*R*,7*aR*)-Octahydro-5,6-dimethyl-4-oxo-7-vinyl-1*H*-inden-3-yl 4-bromobenzoate (24):** To a 0°C solution of 25 mg (0.12 mmol) of hydrindanone **23** in 1.2 mL of CH_2Cl_2 was added 1.5 mg (0.012 mmol) of 4-(dimethylamino)pyridine, 31.4 mg (0.143 mmol) of 4-bromobenzoyl chloride and 25 μL (19 mg, 0.15 mmol) of *N,N*-diisopropylethylamine. The reaction was warmed ambient temperature and stirred 24 h. The reaction mixture was poured into aq. 1M HCl and extracted with EtOAc (4x). The combined organic extracts were dried (Na_2SO_4), concentrated and the crude product mixture was purified by flash chromatography on SiO_2 (2x) (2:1 hexanes/ EtOAc then 10:1 hexanes/ EtOAc) to afford 26 mg (55 %) of the title compound as a colorless crystalline solid: m.p. $98-100^\circ\text{C}$. Recrystallizing this solid from pentane/ Et_2O (slow evaporation) gave crystals suitable for X-ray diffraction analysis. IR (thin film) 3090, 2971, 1718, 1590, 1270 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.86 (d, $J = 8.5$ Hz, 2H), 7.57 (d, $J = 8.5$ Hz, 2H), 5.90 (dd, $J = 7.1, 1.9$ Hz, 1H), 5.61 (dt, $J = 17.1, 9.8$ Hz, 1H), 5.15 (dd, $J = 17.1, 1.8$ Hz, 1H), 5.12 (dd, $J = 10.0, 1.9$ Hz, 1H), 3.05 (d, $J = 7.3$ Hz, 1H), 2.82-2.72 (m, 1H), 2.52 (td, $J = 10.6, 5.1$ Hz, 1H), 2.41-2.27 (m, 1H), 2.23-2.13 (m, 1H), 1.86-1.66 (m, 2H), 1.62-1.48 (m, 1H), 1.33-1.18 (m, 1H), 1.05 (d, $J = 6.5$ Hz, 3H), 1.00 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (75 MHz, CD_3CN): δ 12.1, 19.0, 24.3, 31.0, 40.4, 48.5, 49.7, 50.6, 59.5, 77.4, 116.7, 128.4, 130.9, 132.1, 132.8, 142.0, 166.1, 211.6; MS (ESI) m/z 413 ($M^+ + \text{Na}$); HRMS (ESI) m/z calculated for $\text{NaC}_{20}\text{H}_{23}\text{O}_3\text{Br}$ ($M^+ + \text{Na}$): 413.0728, found 413.0749.

X-ray Structure Determinations for Compounds **19** and **24****I. Compound 19**

Figure S1. Crystal Structure of *R**,-(*R*)-((1*R*,2*R*,3*R*,4*R*,5*S*)-2,4,5-Trimethyl-6-oxo-3-vinylcyclohexyl)(phenyl)methyl 4-bromobenzoate (**19**)

Table 1. Crystal data and structure refinement for **19**

Identification code	bs0405t
Empirical formula	C ₂₅ H ₂₇ Br O ₃
Formula weight	455.38
Temperature	295(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	<i>a</i> = 22.148(3) Å $\alpha = 90^\circ$ <i>b</i> = 6.0518(8) Å $\beta = 93.333(3)^\circ$ <i>c</i> = 16.921(2) Å $\gamma = 90^\circ$
Volume	2264.1(5) Å ³
Z	4
Density (calculated)	1.336 Mg/m ³
Absorption coefficient	1.838 mm ⁻¹
F(000)	944
Crystal size	0.29 x 0.06 x 0.06 mm ³
Theta range for data collection	1.84 to 25.00°
Index ranges	-26 ≤ <i>h</i> ≤ 26, -7 ≤ <i>k</i> ≤ 7, -20 ≤ <i>l</i> ≤ 20
Reflections collected	17088
Independent reflections	3982 [R(int) = 0.1137]
Completeness to theta = 25.00°	100.0 %
Absorption correction	None
Max. and min. transmission	0.8977 and 0.6178
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3982 / 0 / 262
Goodness-of-fit on F ²	1.107
Final R indices [I > 2σ(I)]	R1 = 0.0841, wR2 = 0.1723
R indices (all data)	R1 = 0.1744, wR2 = 0.1974
Largest diff. peak and hole	0.424 and -0.428 e.Å ⁻³

II. Compound 24

Figure S2. Crystal Structure of *R**-(3*aS*,5*S*,6*R*,7*R*,7*aR*)-Octahydro-5,6-dimethyl-4-oxo-7-vinyl-1*H*-inden-3-yl 4-bromobenzoate (**24**)

Table 1. Crystal data and structure refinement for **24**

Identification code	bs03171s
Empirical formula	C ₂₀ H ₂₃ Br O ₃
Formula weight	391.29
Temperature	295(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	<i>a</i> = 8.0654(4) Å $\alpha = 90^\circ$ <i>b</i> = 22.8205(13) Å $\beta = 111.4580(10)^\circ$ <i>c</i> = 10.8106(6) Å $\gamma = 90^\circ$
Volume	1851.84(17) Å ³
<i>Z</i>	4
Density (calculated)	1.403 Mg/m ³
Absorption coefficient	2.234 mm ⁻¹
<i>F</i> (000)	808
Crystal size	0.33 x 0.14 x 0.03 mm ³
Theta range for data collection	1.78 to 32.50°.
Index ranges	-11 ≤ <i>h</i> ≤ 12, -34 ≤ <i>k</i> ≤ 34, -16 ≤ <i>l</i> ≤ 16
Reflections collected	24011
Independent reflections	6565 [R(int) = 0.0489]
Completeness to theta = 32.50°	98.0 %
Absorption correction	Sadabs
Max. and min. transmission	0.9401 and 0.5260
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data / restraints / parameters	6565 / 0 / 309

Goodness-of-fit on F^2

0.987

Final R indices [$I > 2\sigma(I)$]

R1 = 0.0523, wR2 = 0.1127

R indices (all data)

R1 = 0.1259, wR2 = 0.1394

Largest diff. peak and hole

0.447 and -0.179 e.Å⁻³

ppm

200

180

160

140

120

100

80

60

40

20

ppm

212.173

141.566

115.338

77.433

77.008

76.583

50.376

48.829

44.646

40.933

33.151

18.663

11.804

ppm

7.27133

5.69633
5.66699
5.63720
5.60700
5.11306
5.10407
5.09756
5.07127
5.06390

2.65473
2.63797
2.61152
2.60050
2.59672
2.32949
2.29702
2.28152
2.26513
2.25244
2.21383
2.20454
2.02632
2.02367
2.01160
2.00852
1.98710
1.51980
1.05364
1.03187
1.01184
0.99908
0.97752
0.94808
0.92423
0.89975
0.84491
0.82189

Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
6.487	1862761	91.697	100.000
6.994	168663	8.303	9.054

ppm

7.27016

5.67669
5.64349
5.62097
5.58765
5.05361
5.04752
5.03419
5.02820
5.01929
5.01308
4.97830
4.97216

2.45087
2.43480
2.42844
2.41400
2.40688
2.40005
2.39241
2.38093
2.14705
2.11738
2.09356
2.06406
1.58503
1.10140
1.07565
1.05416
1.00041
0.97629
0.97234
0.95293
0.94896
0.93301
0.92548
0.91482
0.90350
0.89228

Peak#	Ret Time	Type	Width	Area	%	Start Time	End Time
1	8.825	rbv	0.182	3893336	89.0%	8.682	8.864
2	8.994	rbv	0.091	360257	8.24%	8.955	9.046
3	9.072	rm	0.065	119444	2.73%	9.046	9.112
4373037

ppm
205.846

143.821
130.641
129.596
129.563
129.322
129.231
129.114
129.013
128.801
127.451
127.376
118.242

52.936
51.802
51.693

23.330
13.132
2.226
1.949
1.675
1.401
1.123
0.850
0.575
-1.487
-1.739