Synthetic Studies Toward FR182877. Remarkable Solvent Effect in the Vinylogous Morita-Baylis-Hillman Cyclization

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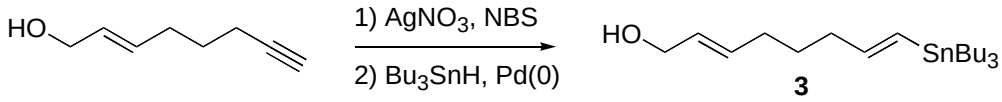
SUPPORTING INFORMATION

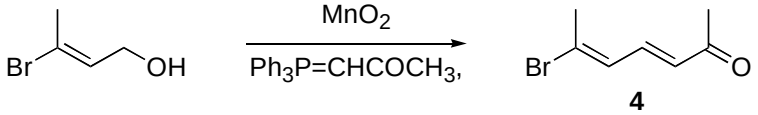
General Methods. Reactions were performed in dry glassware under an atmosphere of nitrogen. Tetrahydrofuran, dichloromethane and diethyl ether were purified by passage over activated A-1 alumina.[1] All other reagents and solvents were used as received from commercial sources. Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with ceric ammonium molybdate or potassium permanganate. Flash column chromatography was performed according to the method of Still[2] using Kieselgel 60 (230-400 mesh) silica gel or pH=7.7 neutral silica gel. Proton and carbon-13 nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded in $CDCl_3$ on a Varian VXR-400 spectrometer or on a Varian Inova-500 spectrometer. The proton signal of residual, non-deuterated $CHCl_3$ (d 7.27 ppm) and the carbon-13 signal of $CDCl_3$ (d 77.2 ppm) were used as internal references. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as thin films on a Perkin-Elmer Spectrum 1000 FTIR. Optical rotations were measured on a Rudolph Autopol III polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Mass spectra were recorded on a VG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester UK). HPLC purifications were performed using a HPLC system composed of two Rainin HPXL pumps connected to either various Dynamax® axial compression columns packed with Rainin 60 Å irregular silica gel. Samples were loaded into the system with a 2 mL Rheodyne 7125 injector and were detected using a either Rainin Dynamax® UV-C detector or a Rainin Dynamax® RI-1 detector. Integration of the various signals was performed using the reprocessing program within the Dynamax® HPLC Method Manager.

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
[2] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.



3

(*E*,*E*)-8-(Tributylstannanyl)-octa-2,7-dien-1-ol (3). A suspension of (*E*)-2-octen-7-yn-1-ol[3] (400 mg, 3.22 mmol) and *N*-bromosuccinimide (600 mg, 3.37 mmol) in acetone (10 mL) was treated with $AgNO_3$ (50 mg, 0.29 mmol) and stirred for 1 h.[4] The mixture was diluted with ether and washed with 10% HCl, 10% KOH, dried (Na_2SO_4), filtered and concentrated. The oily residue was dissolved in THF (10 mL) and treated with $Pd(PPh_3)_4$ (40 mg, 0.035 mmol) and cooled to 0 °C. Bu_3SnH (1.90 mL, 7.06 mmol) was added dropwise over 15 min, the mixture was stirred for 1 h and finally concentrated to an oil. Purification of the crude product by chromatography on neutral SiO_2 (ether/hexanes, 0:1 to 1:1) gave 1.03 g (77%) of the desired vinyl stannane **3**: R_f 0.28 (ether/hexanes, 1:1); ^{1}H NMR (500 MHz) d 6.00-5.80 (m, 2 H), 5.74-5.62 (m, 2 H), 4.11 (t, 2 H, *J* = 5.6 Hz), 2.16 (dt, 2 H, *J* = 7.3, 5.6 Hz), 2.07 (q, 2 H, *J* = 7.6 Hz), 1.53-1.47 (m, 8 H), 1.35-1.28 (m, 6 H), 1.22 (t, 1 H, *J* = 5.9 Hz), 0.94-0.86 (m, 6 H), 0.90 (t, 9 H, *J* = 7.3 Hz); ^{13}C NMR (100 MHz) d 149.3, 133.3, 129.3, 127.8, 63.9, 37.4, 31.8, 29.3, 28.5, 27.4, 13.9, 9.6; IR (neat) 3326, 2956, 2926, 2872, 2854, 1599, 1464 cm^{-1}; HRMS (EI), calcd for $C_{20}H_{40}OSnNa$ 439.1999 $[M+Na]^+$, found 439.2003 *m/z*.



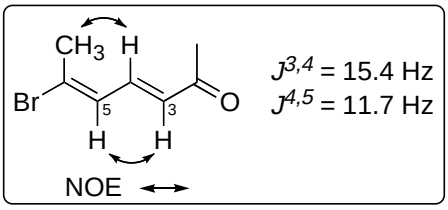
4

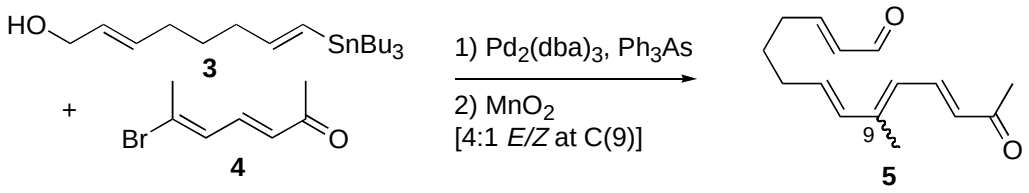
(*E*,*E*)-6-Bromohepta-3,5-dien-2-one (4). A suspension of (*E*)-3-bromo-2-buten-1-ol[5] (245 mg, 1.62 mmol), MnO_2 (1.41 g, 16.2 mmol) and 1-triphenylphosporanylidene-2-propanone (1.00 g, 3.14 mmol) in CH_2Cl_2 (5 mL) was stirred vigorously for 15 h.[6] The mixture was filtered through Celite, concentrated and chromatographed on SiO_2 (CH_2Cl_2) giving 207 mg (68%) of the dienyl ketone **4**: R_f 0.50 (ether/hexanes, 1:1); ^{1}H NMR (500 MHz) d 7.20 (dd, 1 H, *J* = 15.4, 11.7 Hz), 6.62 (dq, 1 H, *J* = 11.5, 1.2, 1.2, 1.2 Hz), 6.17 (d, 1 H, *J* = 15.1 Hz), 2.50 (d, 3 H, *J* = 1.0 Hz), 2.29 (s, 3 H); ^{13}C NMR (100 MHz) d 197.9, 136.1, 133.0, 130.6, 129.8, 28.0, 24.4; IR

[3] Harvey, D. F.; Lund, K. P.; Neil, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 8424.
[4] Boden, C. D. J., Pattenden, G.; Ye, T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2417.
[5] Roush, W. R.; Brown, B. B. *J. Am. Chem. Soc.* **1993**, *115*, 2268.

(neat) 1661, 1640, 1620 cm^{-1}; HRMS (EI), calcd for C_7H_9OBr 187.9837 $[M]^+$, found 187.9840 *m/z*.

Stereochemical assignment for **4** is based on ^1H NMR coupling contants and NOE data:





[2(*E*),7(*E*),9(*E*),11(*E*)]-9-Methyl-13-oxo-tetradeca-2,7,9,11-tetraenal (5). A solution of the vinyl stannane **3** (1.03 g, 2.48 mmol) and the vinyl bromide **4** (300 mg, 1.59 mmol) in THF (10 mL) was treated with $Pd_2(dba)_3$•$CHCl_3$ (80 mg, 0.077 mmol) and Ph_3As (95 mg, 0.31 mmol). The mixture was stirred for 13 h and concentrated. Separation of the mixture by chromatography on neutral SiO_2 (ether/hexanes, 1:4 to 3:2) gave 305 mg (82%) of the tetraenyl ketone as an inseparable 4:1 *E/Z* olefin mixture at C(9).[7] The oil was dissolved in CH_2Cl_2 (20 mL), treated with MnO_2 (1.00 g, 11.5 mmol), stirred for 3 h and treated with additional MnO_2 (300 mg, 3.45 mmol). The suspension was stirred another 2 h, filtered through a pad of Celite and then through a pad of neutral SiO_2 (washing with ether). Concentration of the filtrate provided 278 mg (92%) of the desired aldehyde **5** as an inseparable 4:1 *E/Z* olefin mixture at C(9): ^1H NMR (500 MHz) d 9.53 (d, 1 H, *J* = 7.8 Hz), 7.54 (dd, 1 H, *J* = 15.1, 11.7 Hz), 6.86 (dt, 1 H, *J* = 15.6, 6.8, 6.8 Hz), 6.12-6.22 (m, 4 H), 5.94 (dt, 1 H, *J* = 15.6, 7.1, 7.1 Hz), 2.39 (q, 2 H, *J* = 7.4 Hz), 2.31 (s, 3 H), 2.25 (q, 2 H, *J* = 7.1 Hz), 2.01 (d, 3 H, *J* = 1.0 Hz), 1.68 (dq, 2 H, *J* = 7.6, 7.6, 7.6, 7.6 Hz); ^{13}C NMR (125 MHz) d 199.0, 198.8, 145.4, 139.6, 134.7, 134.6, 132.7, 129.7, 129.6, 127.4, 32.8,

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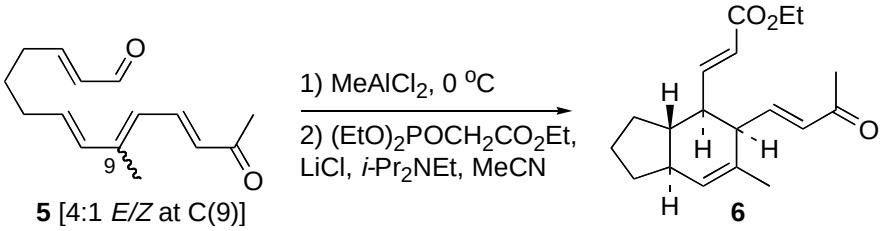
[6] Wei, X.; Taylor, R. J. K. *J. Org. Chem.* **2000**, *65*, 616.

[7] The *E/Z* mixture is at the trisubstituted olefin. Isomerization was also observed in the presence of LiCl, PPTs and SiO_2. For related examples see (a) Laurent, A.; Prat, V.; Valla, A.; Andriamialisoa, Z.; Giraud, M.; Labia, R.; Potier, P. *Tetrahedron Lett.* **2000**, *41*, 7221; (b) Andriamialisoa, Z.; Valla, A.; Zennache, S.; Giraud, M.; Potier, P. *Tetrahedron Lett.* **1993**, *34*, 8091; (c) Lugtenburg, J. *Pure & Appl. Chem.* **1985**, *57*, 753; (d) Liu, R. S. H.; Asato, A. E.; Denny, M. *J. Am. Chem. Soc.* **1977**, *99*, 8095; (e) Stork, G.; Kraus, G. A. *J. Am. Chem. Soc.* **1976**, *98*, 2351.

31.9, 31.8, 28.8, 27.9; IR (neat) 2927, 1688, 1652, 1590, 1572 cm^{-1}; HRMS (EI), calcd for $C_{15}H_{20}O_2$ 232.1463 $[M]^+$, found 232.1458 *m/z*.



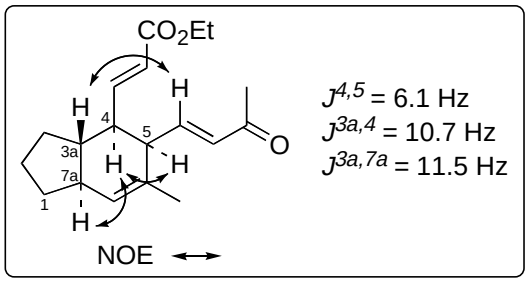
5 [4:1 *E/Z* at C(9)] **6**

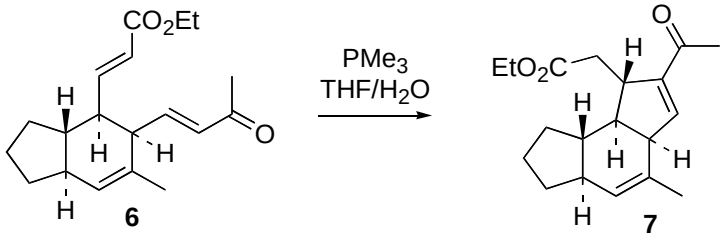
***rac*-[3a(*S*),4(*S*),5(*S*),7a(*S*)]-3-[6-Methyl-5-(3-oxo-but-1(*E*)-enyl)-2,3,3a,4,5,7a-hexahydro-1*H*-inden-4-yl]-(*E*)-acrylic Acid Ethyl Ester (6).** A solution of aldehyde **5** as a 4:1 *E/Z* olefin mixture at C(9) (70 mg, 0.30 mmol) in CH_2Cl_2 (3 mL) was treated at -78 °C with a 1 M solution of $MeAlCl_2$ in hexane (0.25 mL, 0.25 mmol) and warmed to 0 °C. The mixture was stirred for 1 h, quenched with pH = 7 buffer solution and partitioned between CH_2Cl_2 and water. The organic phase was dried (Na_2SO_4), filtered and concentrated. Purification of the crude product by chromatography on neutral SiO_2 (ether/hexanes, 1:9 to 3:7) gave 14 mg (20%) of recovered unsaturated aldehyde **5** (1:4 *E/Z* from crude ^1H NMR analysis) and 36 mg (52%) of the Diels-Alder product (>15:1 diastereomeric purity): R_f 0.38 (ether/hexanes, 1:1); ^1H NMR (500 MHz) d 9.68 (d, 1 H, *J* = 2.4 Hz), 6.66 (dd, 1 H, *J* = 16.1, 9.5 Hz), 6.09 (d, 1 H, *J* = 16.1 Hz), 5.79 (br s, 1 H), 3.30 (dd, 1 H, *J* = 8.8, 5.9 Hz), 2.68 (ddd, 1 H, *J* = 11.5, 5.6, 2.2 Hz), 2.25 (s, 3 H), 2.03 (dq, 1 H, *J* = 11.7, 6.1, 6.1, 6.1 Hz), 1.95-1.85 (m, 2 H), 1.82-1.76 (m, 2 H), 1.69 (dtd, 1 H, *J* = 11.5, 11.5, 11.5, 6.3 Hz), 1.62 (s, 3 H), 1.25-1.17 (m, 2 H); ^{13}C NMR (125 MHz) d 203.2, 198.1, 145.5, 133.4, 131.9, 127.9, 56.3, 46.1, 45.2, 39.4, 28.5, 27.2, 27.1, 22.3, 21.6; IR (neat) 2953, 2871, 1721, 1673, 1619 cm^{-1}; HRMS (EI), calcd for $C_{15}H_{20}O_2$ 232.1463 $[M]^+$, found 232.1465 *m/z*.

A suspension of the cycloadduct (65 mg, 0.28 mmol), LiCl (20 mg, 0.48 mmol) and $(EtO)_2P(O)CH_2CO_2Et$ (0.10 mL, 0.50 mmol) in MeCN (3 mL) was treated at -20 °C with *i*-Pr_2NEt (0.080 mL, 0.45 mmol) and stirred for 1 h.[8] The mixture was slowly warmed to 23 °C over 5 h, stirred another 10 h, poured into ether, washed with water, dried (Na_2SO_4), filtered and concentrated. Chromatography of the crude product on SiO_2 (ether/hexanes, 1:9 to 2:3) gave 61

mg (72%) of the ethyl ester **6**: R_f 0.32 (ether/hexanes, 1:2); ^{1}H NMR (500 MHz) d 6.78 (dd, C*H*=CHCO$_2$Et, *J* = 15.4, 9.8 Hz), 6.66 (dd, C*H*=CHCOMe, *J* = 15.9, 9.3 Hz), 6.04 (d, CH=C*H*COMe, *J* = 15.9 Hz), 5.85 (d, CH=C*H*CO$_2$Et, *J* = 15.6 Hz), 5.77 (s, H-7), 4.19 (q, CO$_2$C*H*$_2$CH$_3$, *J* = 7.1 Hz), 2.96 (t, H-5, *J* = 6.1 Hz), 2.60 (ddd, H-4, *J* = 10.7, 10.7, 5.9 Hz), 2.28 (s, CH=CHCOC*H*$_3$), 1.94-1.88 (m, 1 H), 1.88 (m, H-7a), 1.75-1.68 (m, 3 H), 1.60 (s, Me-6), 1.54 (dtd, H-3a, *J* = 11.5, 11.5, 11.5, 5.4 Hz), 1.29 (t, CO$_2$CH$_2$C*H*$_3$, *J* = 7.1 Hz), 1.25-1.20 (m, 1 H), 1.11-1.05 (m, 1 H); ^{13}C NMR (125 MHz) d 198.2, 166.2, 149.2, 146.4, 133.5, 132.6, 127.7, 122.1, 60.3, 49.7, 47.1, 46.1, 42.6, 29.2, 27.7, 27.1, 21.9, 21.8, 14.2; IR (neat) 2959, 2871, 1719, 1675, 1652, 1621 cm^{-1}; HRMS (EI), calcd for $C_{19}H_{26}O_3Na$ 325.1780 [M+Na]$^+$, found 325.1787 *m/z*.

Stereochemical assignment for **6** is based on ^{1}H NMR coupling contants and NOE data:



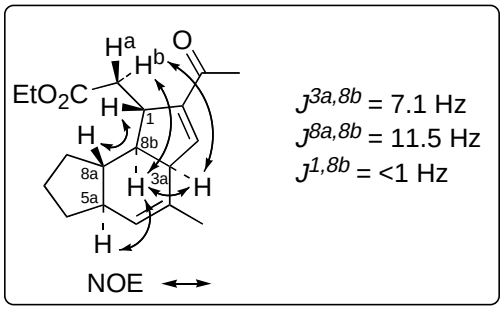


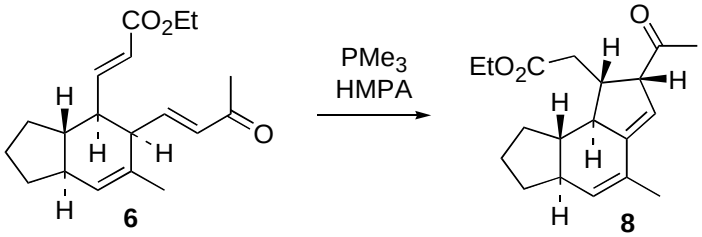
***rac*-[1(*S*),3a(*S*),5a(*S*),8a(*S*),8b(*S*)]-(2-Acetyl-4-methyl-1,3a,5a,6,7,8,8a,8b-octahydro-*as*-indacen-1-yl)-acetic Acid Ethyl Ester (7).** A solution of the enone **6** (10.3 mg, 0.034 mmol) in THF (0.60 mL) was degassed by the freeze-pump-thaw method and treated with H_2O (0.20 mL; also degassed) followed by PMe_3 (7 mL, 0.065 mmol). The reaction mixture was stirred for 8 h until TLC analysis indicated complete substrate consumption. It was then poured into ether, washed with brine, dried (Na_2SO_4), filtered and concentrated. ^{1}H NMR analysis of the crude

[8] Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183.

product indicated no significant byproduct formation. Purification of this material by chromatography on SiO_2 (ether/hexanes, 1:9 to 3:7) gave 7.4 mg (74%) of cycloadduct **7**: R_f 0.46 (ether/hexanes, 1:1); ^{1}H NMR (500 MHz) d 6.75 (d, H-3, *J* = 2.2 Hz), 5.69 (br s, H-5), 4.14 and 4.13 (2q, $CO_2CH_2CH_3$, *J* = 7.1 Hz), 3.49 (dd, H-3a, *J* = 4.9, 1.5 Hz), 3.27 (ddd, H-1, *J* = 10.5, 3.7, 3.7 Hz), 2.67 (dd, H-a, *J* = 15.1, 3.9 Hz), 2.33 (s, $COCH_3$), 2.24 (dd, H-b, *J* = 14.9, 10.5 Hz), 2.12 (dd, H-8b, *J* = 11.5, 7.1 Hz), 1.93-1.86 (m, 1 H), 1.87-1.76 (m, 1 H), 1.84 (d, Me-4, *J* = 0.7 Hz), 1.82 (m, H-5a), 1.70-1.62 (m, 2 H), 1.27 (t, $CO_2CH_2CH_3$, *J* = 7.1 Hz), 1.24-1.06 (m, 2 H), 1.10 (m, H-8a); ^{13}C NMR (125 MHz) d 197.1, 172.8, 146.0, 145.1, 132.3, 128.2, 60.6, 52.1, 49.0, 45.9, 44.9, 43.5, 37.6, 30.1, 28.5, 27.0, 22.3, 22.2, 14.6; IR (neat) 2928, 2867, 1734, 1667 cm^{-1}; HRMS (EI), calcd for $C_{19}H_{26}O_3Na$ 325.1780 $[M+Na]^+$, found 325.1779 *m/z*.

Stereochemical assignment for **7** is based on ^{1}H NMR coupling contants and NOE data:

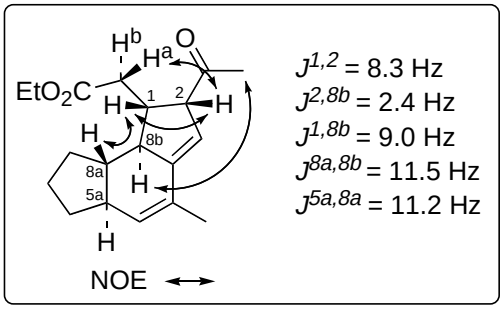


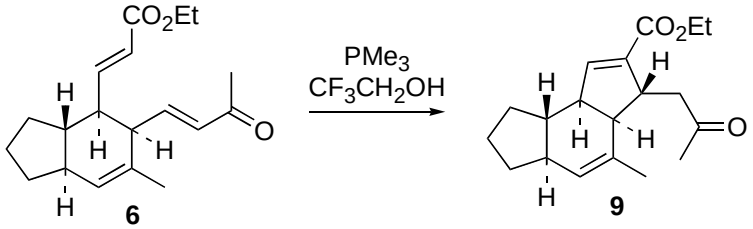


***rac*-[1(*S*),2(*S*),5a(*S*),8a(*S*),8b(*S*)]-(2-Acetyl-4-methyl-1,2,5a,6,7,8,8a,8b-octahydro-*as*-indacen-1-yl)-acetic Acid Ethyl Ester (8).** A solution of the enone **6** (14.4 mg, 0.048 mmol) in HMPA (1 mL) was degassed by the freeze-pump-thaw method and treated with PMe_3 (50 mL, 0.46 mmol). The reaction mixture was stirred for 18 h, poured into ether, washed with excess water, brine, dried (Na_2SO_4), filtered and concentrated. ^{1}H NMR analysis of the crude product indicated a 9:1 mixture of the olefin migration product **8** to the undesired regioisomer **9**. Purification of this material by chromatography on SiO_2 (ether/hexanes, 1:9 to 3:7) followed by

HPLC (EtOAc/hexane, 1:4) gave 9.4 mg (65%) of the olefin migration product **8**: R_f 0.45 (ether/hexanes, 1:1); ^{1}H NMR (500 MHz) d 5.77 (br s, H-5), 5.42 (br s, H-3), 4.10 (q, $CO_2CH_2CH_3$, J = 7.1 Hz), 3.65 (br d, H-2, J = 8.5 Hz), 2.68 (dd, H-b, J = 15.6, 3.9 Hz), 2.67 (dtd, H-1, J = 8.3, 8.3, 8.3, 3.9 Hz), 2.43 (dd, H-a, J = 15.6, 9.8 Hz), 2.36 (ddt, H-8b, J = 11.5, 9.0, 2.4, 2.4 Hz), 2.24 (s, COC*H*3), 2.09-2.02 (m, 1 H), 1.93 (m, H-5a), 1.85 (dtd, 1 H, J = 12.0, 7.3, 7.3, 3.7 Hz), 1.80 (t, Me-4, J = 1.7 Hz), 1.78-1.71 (m, 2 H), 1.33 (dtd, H-8a, J = 11.2, 11.2, 11.2, 6.1 Hz), 1.26 (t, $CO_2CH_2CH_3$, J = 7.1 Hz), 1.30-1.14 (m, 2 H); ^{13}C NMR (100 MHz) d 209.6, 172.8, 148.1, 131.8, 130.1, 119.2, 64.5, 60.6, 55.0, 50.5, 46.7, 44.0, 37.8, 28.7, 28.6, 28.3, 22.6, 18.8, 14.4; IR (neat) 2924, 2854, 1734, 1717 cm^{-1}; HRMS (EI), calcd for $C_{19}H_{26}O_3Na$ 325.1780 $[M+Na]^+$, found 325.1791 *m/z*.

Stereochemical assignment for **8** is based on ^{1}H NMR coupling contants and NOE data:

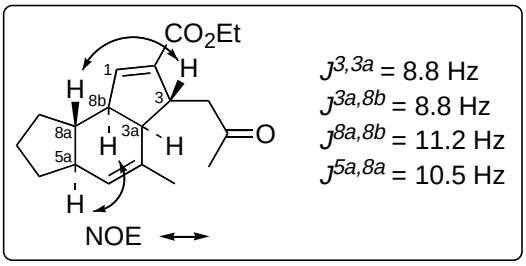


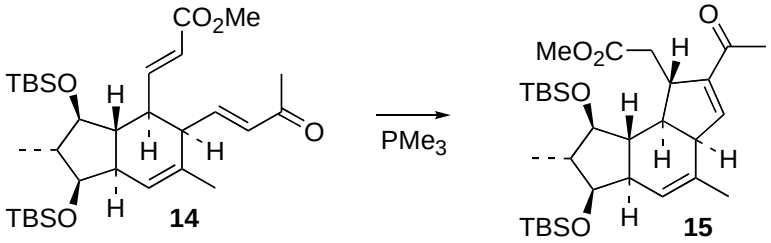


***rac*-[3(*R*),3a(*S*),5a(*S*),8a(*S*),8b(*R*)]-4-Methyl-3-(2-oxo-propyl)-3,3a,5a,6,7,8,8a,8b-octa-hydro-*as*-indacene-2-carboxylic Acid Ethyl Ester (9).** A solution of the enone **6** (4.0 mg, 0.013 mmol) in CF_3CH_2OH (0.40 mL) was degassed by the freeze-pump-thaw method and treated with PMe_3 (15 mL, 0.14 mmol). The reaction mixture was stirred for 1 h and concentrated. ^{1}H NMR analysis of the crude product indicated no significant byproduct formation. Purification of this material by chromatography on SiO_2 (ether/hexanes, 1:9 to 3:7) gave 3.1 mg (78%) of the undesired product **9**: R_f 0.45 (ether/hexanes, 1:1); ^{1}H NMR (500 MHz)

d 6.85 (t, H-1, J = 2.4 Hz), 5.63 (br s, H-4), 4.17 and 4.15 (2q, $CO_2CH_2CH_3$, J = 7.1 Hz), 3.35 (m, H-3), 2.85 (d, CH_2COCH_3, J = 4.9 Hz), 2.65 (ddt, H-8b, J = 11.2, 5.4, 2.7, 2.7 Hz), 2.57 (t, H-3a, J = 8.8 Hz), 2.18 (s, CH_2COCH_3), 1.88-1.80 (m, 2 H), 1.78 (m, H-5a), 1.77 (br s, Me-4), 1.74-1.67 (m, 2 H), 1.28 (t, $CO_2CH_2CH_3$, J = 7.1 Hz), 1.24-1.08 (m, 2 H), 0.97 (dtd, H-8a, J = 10.5, 10.5, 10.5, 6.3 Hz); ^{13}C NMR (125 MHz) 207.7, 165.6, 146.8, 136.5, 135.6, 128.7, 127.2, 60.4, 50.2, 50.0, 49.0, 48.0, 44.3, 30.9, 29.6, 28.6, 23.1, 22.8, 14.5; IR (neat) 2962, 2929, 2881, 1706 cm^{-1}; HRMS (EI), calcd for $C_{19}H_{27}O_3$ 303.1960 $[M+H]^+$, found 303.1968 *m/z*.

Stereochemical assignment for **9** is based on ^{1}H NMR coupling contants and NOE data:



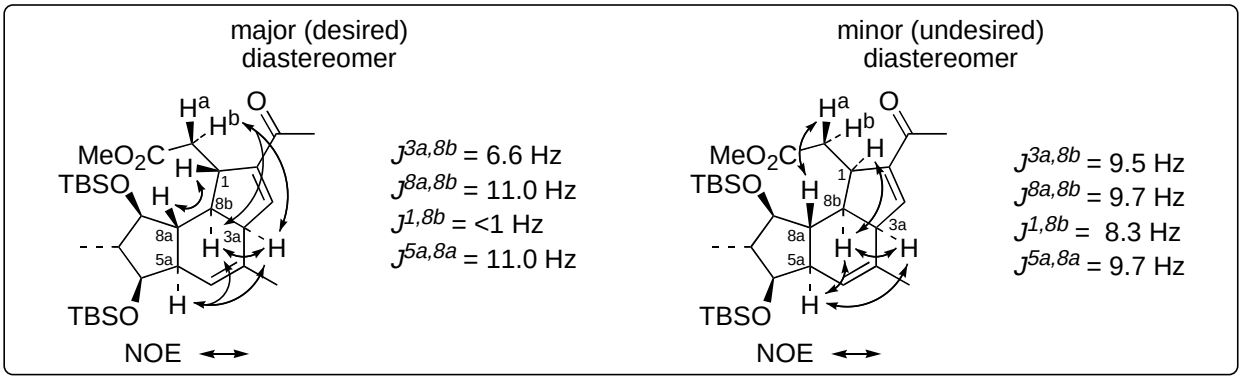


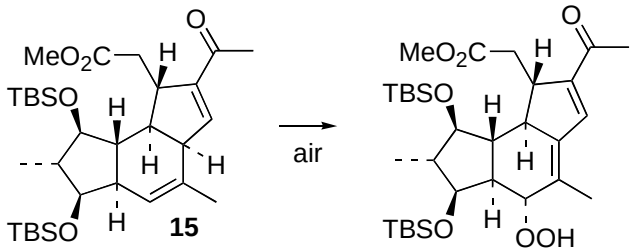
[1(*S*),3a(*S*),5a(*R*),6(*R*),7(*S*),8(*S*),8a(*R*),8b(*S*)]-[2-Acetyl-6,8-bis-(*tert*-butyldimethylsilanyl-oxy)-4,7-dimethyl-1,3a,5a,6,7,8,8a,8b-octahydro-*as*-indacen-1-yl]-Acetic Acid Methyl Ester. A solution of the enone **14** (50 mg, 0.089 mmol) in THF (3 mL) was degassed by the freeze-pump-thaw method. To this solution, deionized water (1 mL, degassed by freeze-pump-thaw method) was then added followed by trimethylphosphine (35 mL, 0.34 mmol). The reaction mixture was stirred for 12 h., partitioned between EtOAc and brine, the organic layer was dried (Na_2SO_4), filtered and concentrated. Chromatography of the crude product on SiO_2 (1:4 to 1:2 ether/hexanes) gave 42 mg (84%) of a 6:1 diastereomeric mixture of air-sensitive cycloadducts **15**:**16**, which was then separated by HPLC (21 mm column using 15% EtOAc/hexanes with a flow rate of 10 mL/min, t_R (major) = 17 min; t_R (minor) = 21 min).

Data for major diastereomer **15**: R_f 0.48 (EtOAc/hexanes, 1:4); $[\alpha]^{23}_D$ -100° (*c* 1.18, CH_2Cl_2); ^{1}H NMR (500 MHz) δ 6.71 (d, H-3, *J* = 2.0 Hz), 5.53 (br s, H-5), 3.76 (ddd, H-1, *J* = 9.3, 5.1, 2.2 Hz), 3.66 (s, CO_2*Me*), 3.62 (d, H-6, *J* = 3.4 Hz), 3.55 (dd, H-8, *J* = 7.6, 3.4 Hz), 3.44 (br d, H-3a, *J* = 6.1 Hz), 2.59 (dd, H-a, *J* = 14.6, 4.6 Hz), 2.39 (dd, H-b, *J* = 14.6, 9.0 Hz), 2.32 (s, CO*Me*), 2.29 (dd, H-8b, *J* = 11.0, 6.6 Hz), 1.94 (dt, H-8a, *J* = 11.0, 11.0, 7.5 Hz), 1.91 (m, H-5a), 1.81 (dtd, H-7, *J* = 7.6, 7.6, 7.6, 3.4 Hz), 1.81 (br s, Me-4), 1.03 (d, Me-7, *J* = 7.8 Hz), 0.87 (s, 9 H), 0.85 (s, 9 H), 0.14 (s, 3 H), 0.08 (s, 3 H), 0.03 (2s, 6 H); ^{13}C NMR (100 MHz) δ 196.4, 173.3, 145.2, 145.0, 133.1, 125.5, 84.7, 79.1, 53.2, 52.3, 51.5, 49.3, 47.6, 44.2, 42.5, 36.9, 26.9, 26.1, 25.9, 22.0, 19.3, 18.3, 18.0, -3.3, -4.2, -4.5, -4.6; IR (neat) 2956, 2928, 2856, 1740, 1670, 1462, 1434 cm^{-1}; HRMS (EI), calcd for $C_{31}H_{54}O_5Si_2Na$ 585.3408 $[M+Na]^+$, found 585.3411 *m/z*.

Data for minor diastereomer **16**: R_f 0.35 (EtOAc/hexanes, 1:4); $[\alpha]^{23}_D$ +22° (*c* 0.16, CH_2Cl_2); ^{1}H NMR (500 MHz) δ 6.82 (d, H-3, *J* = 2.9 Hz), 5.68 (br s, H-5), 3.73 (d, H-6, *J* = 4.2 Hz), 3.55 (s, CO_2*Me*), 3.51 (dt, H-1, *J* = 8.3, 8.3, 4.9 Hz), 3.42 (dd, H-8, *J* = 8.5, 4.4 Hz), 3.28 (br d, H-3a, *J* = 10.5 Hz), 2.79 (dd, H-a, *J* = 13.2, 5.1 Hz), 2.68 (q, H-8b, *J* = 9.5 Hz), 2.35 (s, CO*Me*), 2.17 (dd, H-b, *J* = 13.3, 8.6 Hz), 2.17 (dt, H-8a, *J* = 9.7, 9.7, 5.8 Hz), 1.92 (m, H-5a), 1.86 (dtd, H-7, *J* = 7.3, 7.3, 7.3, 4.6 Hz), 1.76 (br d, Me-4, *J* = 1.7 Hz), 1.07 (d, Me-7, *J* = 7.6 Hz), 0.92 (s, 9 H), 0.90 (s, 9 H), 0.12 (s, 3 H), 0.08 (3s, 9 H); ^{13}C NMR (125 MHz) δ 196.9, 173.6, 149.0, 143.7, 135.9, 124.2, 86.8, 78.5, 53.4, 51.5, 50.7, 47.0, 45.8, 44.3, 42.4, 37.5, 27.1, 26.2, 26.1, 26.0, 20.8, 18.9, 18.3, 18.1, -3.6, -4.0; IR 2955, 2930, 2886, 2857, 1738, 1674, 1472, 1463, 1434 cm^{-1}; HRMS (EI), calcd for $C_{31}H_{54}O_5Si_2Na$ 585.3408 $[M+Na]^+$, found 585.3399 *m/z*.

Stereochemical assignments for **15** and **16** are based on ^{1}H NMR coupling contants and NOE data:





[1(*S*),5(*R*),5a(*S*),6(*S*),7(*R*),8(*S*),8a(*R*),8b(*R*)]-[2-Acetyl-6,8-bis-(*tert*-butyldimethyl-silanyloxy)-5-hydroperoxy-4,7-dimethyl-1,5,5a,6,7,8,8a,8b-octahydro-*as*-indacen-1-yl]-acetic Acid Methyl Ester. The Morita-Baylis-Hillman product **15** (5 mg) was allowed to stand neat exposed to the atmosphere for three days before being chromatographed on SiO_2 (EtOAc/hexanes, 1:4 to 1:1). This gave 3.8 mg (72%) of the oxidation product as a single diastereomer: R_f 0.15 (EtOAc/hexanes, 1:4); ^{1}H NMR (500 MHz) d 7.31 (br, OOH), 7.12 (d, H-3, *J* = 2.0 Hz), 4.71 (d, H-5, *J* = 8.3 Hz), 3.86 (d, H-6, *J* = 3.4 Hz), 3.67 (dd, H-8, *J* = 7.3, 3.4 Hz), 3.60 (s, CO_2*Me*), 3.30 (dd, C*H*CO_2Me, *J* = 15.6, 4.6 Hz), 3.19 (br d, H-1, *J* = 3.4 Hz), 2.63 (dd, C*H*CO_2Me, *J* = 15.6, 3.7 Hz), 2.49 (m, H-8b), 2.39 (s, CO*Me*), 2.17 (ddd, H-8a, *J* = 13.4, 10.5, 7.3 Hz), 2.11 (ddd, H-5a, *J* = 13.4, 8.3, 3.4 Hz), 1.97 (dq, H-7, *J* = 7.8, 7.8, 7.8, 3.4 Hz), 1.92 (br d, Me-4, *J* = 1.0 Hz), 1.11 (d, Me-7, *J* = 7.6 Hz), 0.88 (2s, 18 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.08 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (100 MHz) d 197.6, 173.1, 149.4, 145.3, 138.2, 130.1, 84.9, 84.7, 52.4, 51.6, 51.4, 50.5, 45.9, 44.5, 35.0, 27.4, 26.0, 19.3, 18.2, 18.1, 16.0, -2.7, -4.2, -4.7, -4.8; IR (neat) 3392, 2955, 2930, 2897, 2857, 1736, 1666, 1638, 1571 cm^{-1}; HRMS (EI), calcd for $C_{31}H_{54}O_7Si_2Na$ 617.3306 $[M+Na]^+$, found 617.3311.

The ^{1}H NMR resonance at 7.31 ppm disappears in $D_2O/CDCl_3$.

Stereochemical assignments for this oxidation product are based on ^{1}H NMR coupling contants and NOE data: