

# **CHEMISTRY**

---

## **A EUROPEAN JOURNAL**

### Supporting Information

© Copyright Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2011

#### **Gram-Scale Synthesis of Iejimalide B**

**Julien Gagnepain, Emilie Moulin, and Alois Fürstner\*<sup>[a]</sup>**

chem\_201100178\_sm\_miscellaneous\_information.pdf

**General:** All reactions were carried out in flame-dried glassware under Ar. The solvents were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et<sub>2</sub>O, 1,4-dioxane (Mg-anthracene), CH<sub>2</sub>Cl<sub>2</sub> (P<sub>4</sub>O<sub>10</sub>), MeCN, Et<sub>3</sub>N, pyridine, DMSO, EtOAc (CaH<sub>2</sub>), MeOH (Mg), DMF (Desmodur<sup>®</sup>, dibutyltin dilaurate), hexane, toluene (Na/K). Flash chromatography: Merck silica gel 60 (230-400 mesh) or CombiFlash (Teledyne Isco). NMR: Spectra were recorded on a Bruker DPX 300, AV 400, or DMX 600 spectrometer in the solvents indicated; chemical shifts ( $\delta$ ) are given in ppm relative to TMS, coupling constants ( $J$ ) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl<sub>3</sub>:  $\delta_C \equiv 77.0$  ppm; residual CHCl<sub>3</sub> in CDCl<sub>3</sub>:  $\delta_H \equiv 7.24$  ppm; CD<sub>2</sub>Cl<sub>2</sub>:  $\delta_C \equiv 53.8$  ppm; residual CH<sub>2</sub>Cl<sub>2</sub> in CD<sub>2</sub>Cl<sub>2</sub>:  $\delta_H \equiv 5.32$  ppm). IR: Magna IR750 (Nicolet) or spectrum One (Perkin Elmer) spectrometer, wavenumbers ( $\tilde{\nu}$ ) in cm<sup>-1</sup>. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan). Melting points: Büchi melting point apparatus B-540 (corrected). Elemental analyses: H. Kolbe, Mülheim/Ruhr. Unless stated otherwise, commercially available compounds (Fluka, Lancaster, Aldrich) were used as received.

***O*-tert-Butyldimethylsilyl-L-serine benzyl ester (6):** DBU (6.46 mL, 43.2 mmol) was added to a suspension of L-serine benzyl ester hydrochloride **5** (5.0 g, 21.6 mmol) and TBSCl (3.42 g, 22.68 mmol) in MeCN (650 mL) at 0 °C and the resulting homogeneous mixture stirred overnight at ambient temperature. After evaporation of the solvent, the residue was suspended in H<sub>2</sub>O (50 mL) and the aqueous phase extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over MgSO<sub>4</sub> and evaporated to give product **6**, which was pure enough for use in the next step (6.7 g, quant., *ee* ≥ 99 %, HPLC). For analytical purposes, a sample was purified by flash chromatography (hexanes/EtOAc, 5:1→1:5).  $[\alpha]_D^{20} = -11.6$  ( $c = 1.4$ , CH<sub>2</sub>Cl<sub>2</sub>),  $[\alpha]_D^{20} = -7.8$  ( $c = 1.0$ , CH<sub>2</sub>Cl<sub>2</sub>),  $[\alpha]_D^{20} = -3.4$  ( $c = 0.8$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 7.33$ – $7.36$  (m, 5H), 5.17 (virt. d,  $J = 1.8$  Hz, 2H), 3.96 (dd,  $J = 4.2, 9.7$  Hz, 1H), 3.83 (dd,  $J = 3.7, 9.7$  Hz, 1H), 3.57 (t,  $J = 3.7$  Hz, 1H), 1.83 (brs), 0.86 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 173.8, 135.7, 128.6, 128.3, 128.3, 66.8, 65.2, 56.61, 25.8, 18.2, -5.5, -5.6$ ; IR (film):  $\tilde{\nu} = 3387, 3319, 3091, 3066, 3034, 2954, 2929, 2884, 2857, 1743, 1687, 1589, 1545, 1498, 1471, 1463, 1389, 1371, 1362, 1310, 1257, 1216, 1169, 1140, 1103, 1042, 1006, 959, 939, 837, 810, 778, 750, 734, 697, 666, 604, 576$  cm<sup>-1</sup>; HRMS (ESI):  $m/z$ : calcd for

$C_{16}H_{28}NO_3Si$  [ $M^+ + H$ ]: 310.18372; found: 310.18385; elemental analysis calcd (%) for  $C_{16}H_{27}NO_3Si$ : C 62.10, H 8.79; found: C 62.22, H 8.71.

***O*-tert-Butyldimethylsilyl-*N*-formyl-*L*-serine benzyl ester (7)**: A solution of amine **6** (6.68 g, 21.6 mmol) and DMAP (270 mg, 2.16 mmol) in  $CH_2Cl_2$  (540 mL) was cooled to 0 °C before formic acid (860  $\mu$ L, 22.68 mmol) and EDC-HCl (4.55 g, 23.76 mmol) were introduced. The mixture was stirred for 2 h at ambient temperature and evaporated, and the residue purified by flash chromatography (hexanes/EtOAc 4:1 $\rightarrow$ 1:1) to give product **7** as a colorless oil (6.87 g, 94 %, *ee* = 98.3 %, HPLC).  $[\alpha]_D^{20} = +10.1$  (*c* = 0.89,  $CH_2Cl_2$ );  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 8.26 (s, 1H), 7.26–7.36 (m, 5H), 6.42 (brs, 1H), 5.19 (s, 2H), 4.80 (d, *J* = 8.4 Hz, 1H), 4.11 (dd, *J* = 10.1, 2.4 Hz, 1H), 3.86 (dd, *J* = 10.1, 3.0 Hz, 1H), 0.84 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 169.8, 160.6, 135.2, 128.7, 128.5, 128.4, 67.4, 63.4, 53.0, 25.7, 18.2, –5.6, –5.6; IR (film):  $\tilde{\nu}$  = 3309, 3066, 3035, 2954, 2929, 2884, 2857, 1748, 1689, 1588, 1499, 1471, 1464, 1387, 1362, 1337, 1257, 1213, 1188, 1118, 1045, 1006, 958, 836, 814, 779, 750, 735, 697, 665  $cm^{-1}$ ; MS (EI): *m/z* (%): 280 (10), 202 (2), 91 (100), 75 (8), 73 (14); HRMS (ESI): *m/z*: calcd for  $C_{17}H_{27}NO_4SiNa$  [ $M^+ + Na$ ]: 360.16065; found: 360.16071; elemental analysis calcd (%) for  $C_{17}H_{27}NO_4Si$ : C 60.50, H 8.06; found: C 60.33, H 7.94.

***O*-tert-Butyldimethylsilyl-*N*-formyl-*L*-serine (8)**: Palladium on charcoal (10 % *w/w*, 347 mg) was added to a solution of compound **7** (1.53 g, 4.51 mmol) in EtOAc (10 mL). After three vacuum/ $H_2$ -refill cycles, the suspension was vigorously stirred for 30 min under  $H_2$  (1 atm) before MeOH (3 mL) was added to dissolve the precipitated product. Stirring was continued for 2 h before the catalyst was filtered off through Celite, which was carefully rinsed with EtOAc and MeOH. Evaporation of the combined filtrates gave acid **8** as a white solid (1.10 g, 98 %).  $[\alpha]_D^{20} = +47.6$  (*c* = 0.85, MeOH);  $^1H$  NMR (400 MHz,  $CD_3OD$ ):  $\delta$  = 8.14 (s, 1H), 4.59 (t, *J* = 3.3 Hz, 1H), 4.08 (dd, *J* = 10.2, 3.7 Hz, 1H), 3.89 (dd, *J* = 10.2, 3.5 Hz, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CD_3OD$ ):  $\delta$  = 173.1, 164.0, 64.9, 55.0, 26.7, 19.5, –5.0, –5.1; IR (film):  $\tilde{\nu}$  = 3349, 2955, 2928, 2884, 2857, 2741, 2450, 1923, 1714, 1619, 1521, 1471, 1444, 1370, 1345, 1289, 1252, 1233, 1125, 1104, 1051, 1006, 987, 948, 908, 835, 779, 716, 698, 665, 628, 581, 551, 494  $cm^{-1}$ ; MS (EI): *m/z* (%): 190 (34), 172 (15), 162 (38), 144 (62), 134 (22), 116 (63), 89 (25), 75 (100), 73 (59), 59 (18), 45 (15), 28 (15); HRMS (ESI): *m/z*: calcd for

$C_{10}H_{21}NO_4SiNa [M^+ +Na]$ : 270.11333; found: 270.11321; elemental analysis calcd (%) for  $C_{10}H_{21}NO_4Si$ : C 48.55, H 8.56, N 5.66; found: C 48.58, H 8.44, N, 5.60.

**(E)-Methyl 3-bromo-2-methylacrylate (9)**: A 2 L two-necked round bottom flask fitted with a dropping funnel and an Ar inlet was charged with methyl 2-methylacrylate (**13**) (59.9 g, 0.598 mol) and  $CH_2Cl_2$  (600 mL). The solution was cooled to 0 °C before  $Br_2$  (95 g, 0.598 mol) was slowly added via the funnel over 45 min. The resulting orange mixture was stirred for 2 h at ambient temperature before  $Et_3N$  (15 mL) was added to quench unreacted  $Br_2$ . The resulting colorless solution was cooled to 0 °C and DBU (100 g, 0.658 mol) was slowly introduced. The cooling bath was removed and the resulting brown mixture stirred for 16 h at ambient temperature. For work up, the mixture was washed with aq. HCl (2 M, 2 × 200 mL), the aqueous phase was extracted with  $CH_2Cl_2$  (3 × 50 mL), the combined organic layers were washed with brine (200 mL), dried over  $Na_2SO_4$ , filtered and evaporated to give a crude pale brown oil. Purification by filtration through a short pad of silica, which was eluted with pentanes/ $Et_2O$  (95:5), afforded bromide **9** as a colorless oil (98.9 g, 92 %).  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  = 7.49 (q,  $J$  = 1.4 Hz, 1H), 3.73 (s, 3H), 1.97 (d,  $J$  = 1.4 Hz, 3H);  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz):  $\delta$  = 165.5, 133.8, 122.9, 52.2, 15.6; IR (film):  $\tilde{\nu}$  = 1717, 1614, 1435, 1307, 1229, 1108, 729  $cm^{-1}$ ; MS (EI):  $m/z$  (%): 178 (66,  $M^+$ ), 147 (100), 119 (57), 99 (94).

**Phthalimide 14**: To a solution of phthalimide (70.5 g, 0.48 mol) in DMF (500 mL) were added  $K_2CO_3$  (132.6 g, 0.96 mol) and 3-chloro-2-methylpropene (45.4 mL, 0.72 mol). The resulting suspension was stirred at 80 °C for 12 h before it was cooled at 0 °C and diluted with  $H_2O$  (750 mL). The aqueous phase was extracted with  $EtOAc$  (3 × 300 mL), the combined organic layers were successively washed with  $H_2O$  (3 × 300 mL) and brine (300 mL), dried over  $MgSO_4$ , filtered and evaporated to give product **14** as a white solid (91.4 g, 91 %).  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  = 7.87–7.80 (m, 2H), 7.74–7.66 (m, 2H), 4.88–4.84 (m, 1H), 4.79 (s, 1H), 4.19 (s, 2H), 1.75 (s, 3H);  $^{13}C$  NMR ( $CDCl_3$ , 75.5 MHz):  $\delta$  = 168.0, 139.3, 134.0, 133.2, 123.3, 111.9, 43.2, 20.4; IR (film):  $\tilde{\nu}$  = 2921, 1768, 1707, 1659, 1611, 1465, 1443, 1426, 1414, 1390, 1326, 1242, 1189, 1121, 1087, 1042, 947, 897, 884, 846, 726, 712  $cm^{-1}$ ; MS (EI):  $m/z$  (%): 201 (100,  $M^+$ ), 186 (35), 182 (44), 160 (33), 144 (6), 130 (10), 104 (22), 76 (25).

**Methyl (2E,4E)-N-(phthalimido)-6-amino-2,5-dimethylhex-2,4-dienoate (15)**: A 0.5 L two-necked round bottom flask fitted with a condenser connected to the Ar inlet and a mechanical stirring was

charged with **14** (50.0 g, 0.248 mol), bromide **9** (53.4 g, 0.298 mol), Pd(OAc)<sub>2</sub> (1.67 g, 7.46 mmol), P(*o*-tol)<sub>3</sub> (4.58 g, 14.92 mmol) and Et<sub>3</sub>N (70 mL, 0.5 mol). The resulting yellow suspension was stirred at 100 °C for 48 h, during which time it first slowly became homogeneous before the desired product started to precipitate. After reaching ambient temperature, the suspension was filtered and the collected yellow solid carefully washed with *tert*-butyl methyl ether until the eluent was colorless. The remaining grey solid was dissolved in CHCl<sub>3</sub> (200 mL) and the solution was successively washed with aq. HCl (1 M, 50 mL) and brine (50 mL). The organic phase was dried over MgSO<sub>4</sub>, filtered, and evaporated to give diene **15** as a white solid (50.6 g, 68 %). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 7.90–7.81 (m, 2H), 7.77–7.68 (m, 2H), 7.38 (d, *J* = 12.0 Hz, 1H), 6.29 (d, *J* = 11.3 Hz, 1H), 4.33 (s, 2H), 3.72 (s, 3H), 1.89 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz): δ = 168.9, 168.0, 139.8, 134.1, 133.1, 131.9, 127.2, 123.4, 122.5, 51.8, 45.1, 15.6, 12.6; IR (film):  $\tilde{\nu}$  = 2950, 2864, 1772, 1706, 1642, 1609, 1467, 1422, 1386, 1331, 1253, 1118, 1010, 940, 751, 726, 712 cm<sup>-1</sup>; MS (EI): *m/z* (%): 299 (9, *M*<sup>+</sup>), 267 (45), 252 (13), 249 (15), 223 (18), 208 (3), 196 (4), 160 (23), 139 (100), 130 (8), 120 (10), 92 (14), 77 (18); HRMS (ESI): *m/z*: calcd for C<sub>17</sub>H<sub>17</sub>NO<sub>4</sub>+Na [*M*<sup>+</sup> +Na]: 322.10497, found 322.10498; elemental analysis calcd (%) for C<sub>17</sub>H<sub>17</sub>NO<sub>4</sub>: C 68.21, H 5.72; found: C 68.18, H 5.69.

**Methyl (2*E*,4*E*)-*N*-(trimethylsilylethoxycarbonyl)-6-amino-2,5-dimethylhex-2,4-dienoate (16):** A solution of MeNH<sub>2</sub> in EtOH (33 % *w/w*, 100 mL) was added to diene **15** (20 g, 66.9 mmol). The resulting mixture was stirred at room temperature for 16 h before the yellow-orange precipitate was filtered off and dried in vacuo to give an orange solid. This material was triturated with *tert*-butyl methyl ether (200 mL) and the resulting suspension rapidly filtered. The orange filtrate was evaporated and dried under high vacuum for 1 h to give the corresponding crude amine as an orange solid (11 g).

Et<sub>3</sub>N (9 mL, 62.9 mmol) and 4-nitrophenyl-2-trimethylsilylethyl-carbonate (10 g, 41.95 mmol) were introduced to a solution of the crude amine in CH<sub>2</sub>Cl<sub>2</sub> (80 mL). The resulting yellow solution was stirred for 24 h before it was successively washed with aq. sat. Na<sub>2</sub>CO<sub>3</sub> (200 mL) and H<sub>2</sub>O (100 mL). The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2× 50 mL), the combined organic layers were washed with brine (100 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated, and the residue purified by flash chromatography (hexanes/EtOAc, 15:1→6:1, containing 1 % Et<sub>3</sub>N) to give product **16** as a colorless oil

(11.1 g, 85 % over both steps).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.38 (d,  $J$  = 11.7 Hz, 1H), 6.19 (d,  $J$  = 11.7 Hz, 1H), 4.90 (bs, 1H), 4.13 (t,  $J$  = 8.5 Hz, 2H), 3.79 (d,  $J$  = 4.9 Hz, 2H), 3.70 (s, 3H), 1.87 (s, 3H), 1.82 (s, 3H), 0.93 (t,  $J$  = 8.5 Hz, 2H), -0.02 (s, 9H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 169.0, 156.7, 143.2, 133.4, 126.4, 120.2, 63.2, 51.7, 48.3, 17.7, 15.4, 12.5, -1.6; IR (film):  $\tilde{\nu}$  = 3348, 2952, 1695, 1523, 1434, 1244, 1110, 1059, 941, 834, 751  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{15}\text{H}_{27}\text{NO}_4\text{Si}+\text{Na}$  [ $M^+$  +Na]: 336.16016; found: 336.16042; elemental analysis calcd (%) for  $\text{C}_{15}\text{H}_{27}\text{NO}_4\text{Si}$ : C 57.47, H 8.68; found: C 57.40, H 8.72.

**(2E,4E)-N-(Trimethylsilylethoxycarbonyl)-6-amino-2,5-dimethylhex-2,4-dien-1-ol**: Dibal-H (1 M in hexane, 78 mL) was added dropwise at  $-78$  °C to a solution of ester **16** (11.1 g, 35.44 mmol) in  $\text{CH}_2\text{Cl}_2$  (250 mL). After stirring for 15 min at that temperature, the cooling bath was removed and the reaction carefully quenched with an aq. solution of Rochelle salt (1 M, 200 mL). After stirring at room temperature for 2 h, the aqueous phase was extracted with EtOAc (2 $\times$  20 mL), the combined organic layers were dried over  $\text{MgSO}_4$ , filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 2:1) to give the title alcohol as a white solid (8.68 g, 86 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 6.25 (d,  $J$  = 11.2 Hz, 1H), 6.15 (d,  $J$  = 11.2 Hz, 1H), 4.80 (bs, 1H), 4.14 (t,  $J$  = 8.4 Hz, 2H), 4.04 (s, 2H), 3.76 (d,  $J$  = 6.1 Hz, 2H), 1.76 (s, 3H), 1.75 (s, 3H), 1.63 (s, 1H), 0.98 (t,  $J$  = 8.4 Hz, 2H), 0.04 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 157.0, 137.7, 135.2, 121.1, 120.3, 68.8, 63.3, 48.8, 18.0, 14.9, 14.2, -1.5; IR (film):  $\tilde{\nu}$  = 3331, 2954, 2914, 1689, 1531, 1346, 1246, 1130, 1063, 1001, 832, 690, 664  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{14}\text{H}_{27}\text{NO}_3\text{Si}+\text{Na}$  [ $M^+$  +Na]: 308.16525; found: 308.16515; elemental analysis calcd (%) for  $\text{C}_{14}\text{H}_{27}\text{NO}_3\text{Si}$ : C 58.91, H 9.53; found: C 58.84, H 9.57.

**(2E,4E)-N-(Trimethylsilylethoxycarbonyl)-6-amino-2,5-dimethylhex-2,4-dien-1-al (17)**:  $\text{MnO}_2$  (120 g, 1.35 mol) was added to a solution of (2E,4E)-N-(trimethylsilylethoxycarbonyl)-6-amino-2,5-dimethylhex-2,4-dien-1-ol (8.68 g, 33.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (340 mL) and the resulting mixture stirred for 2 h. Filtration through a pad of Celite and evaporation of the filtrate gave aldehyde **17** which was directly used in the next step. Characteristic data:  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  = 9.45 (s, 1 H), 7.13 (d,  $J$  = 11.6 Hz, 1H), 6.44 (d,  $J$  = 11.6 Hz, 1H), 4.98 (bs, 1H), 4.16 (t,  $J$  = 8.6 Hz, 2H), 3.87 (d,  $J$  = 5.9 Hz, 2H), 1.97 (s, 3H), 1.82 (s, 3H), 0.99 (t,  $J$  = 8.6 Hz, 2H), 0.1 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  =

196.7, 158.4, 148.4, 145.4, 139.1, 121.4, 65.0, 50.0, 19.5, 17.3, 10.9, 0.0; HRMS (ESI):  $m/z$ : calcd for  $C_{14}H_{25}NO_3Si+H [M^+ +H]$ : 284.16820; found: 284.16823.

**(2E,4E,6S,7S)-N-(Trimethylsilylethoxycarbonyl)-1-amino-9-triisopropylsilyl-2,5,7-trimethylnona-**

**2,4-dien-8-yn-6-ol (19)**:  $PPh_3$  (398 mg, 1.52 mmol) was added to a solution of  $Pd(OAc)_2$  (341 mg, 1.52 mmol) in THF (250 mL) at  $-78\text{ }^\circ\text{C}$ . Once a homogenous solution had formed, a solution of mesylate **18** (12.15 g, 39.6 mmol) and aldehyde **17** (8.92 g, 30.44 mmol) in THF (50 mL) were added. Next,  $ZnEt_2$  (1.0 M in hexanes, 91.3 mL, 91.3 mmol) was slowly introduced and the resulting mixture stirred at  $-78\text{ }^\circ\text{C}$  for 30 min before it was warmed to  $-20\text{ }^\circ\text{C}$  over a period of 1 h. Stirring was continued overnight at that temperature before the reaction was carefully quenched with aq. sat.  $NH_4Cl$  (100 mL) and  $H_2O$  (100 mL). The resulting suspension was filtered, the organic layer decanted and the aqueous phase extracted with EtOAc (2 $\times$  40 mL). The combined organic layers were dried over  $MgSO_4$ , filtered and evaporated, and the residue purified by flash chromatography (hexanes/EtOAc, 20:1 $\rightarrow$ 9:1) to give product **19** as a colorless oil (10.54 g, 70 %).  $[\alpha]_D^{20} = +47.5$  ( $c = 0.9$ ,  $CH_2Cl_2$ );  $^1H$  NMR (400 MHz,  $CD_2Cl_2$ ):  $\delta = 6.26$  (d,  $J = 11.2$  Hz, 1H), 6.16 (d,  $J = 11.2$  Hz, 1H), 4.78 (bs, 1H), 4.15 (t,  $J = 8.4$  Hz, 2H), 3.85 (dd,  $J = 7.0, 4.3$  Hz, 1H), 3.76 (d,  $J = 6.1$  Hz, 2H), 2.75 (m, 1H), 2.29 (d,  $J = 4.3$  Hz, 1H), 1.75 (s, 3H), 1.72 (s, 3H), 1.13 (d,  $J = 6.9$  Hz, 3H), 1.05 (m, 21H), 0.98 (t,  $J = 8.4$  Hz, 2H), 0.04 (s, 9H);  $^{13}C$  NMR (100 MHz,  $CD_2Cl_2$ ):  $\delta = 157.0, 136.9, 135.8, 123.1, 121.0, 110.3, 83.7, 81.0, 63.3, 48.8, 33.2, 18.8, 18.2, 18.1, 15.0, 12.2, 11.5, -1.4$ ; IR (film):  $\tilde{\nu} = 3344, 2943, 2865, 2160, 1701, 1515, 1462, 1382, 1249, 1124, 1060, 1016, 858, 835, 675\text{ cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $C_{27}H_{51}NO_3Si_2+Na [M^+ +Na]$ : 516.32997; found: 516.33032; elemental analysis calcd (%) for  $C_{27}H_{51}NO_3Si_2$ : C 65.66, H 10.41; found: C 65.76, H 10.34.

**(2E,4E,6S,7S)-N-(Trimethylsilylethoxycarbonyl)-1-amino-2,5,7-trimethylnona-2,4-dien-8-yn-6-ol**

**(20)**: TBAF (1 M in THF, 7.4 mL) was added in portions over 1 h to a solution of compound **19** (10.5 g, 21.37 mmol) in THF (210 mL) at  $0\text{ }^\circ\text{C}$  and the resulting mixture was stirred at that temperature for 30 min. The reaction was quenched with  $H_2O$  (100 mL) and the aqueous phase extracted with *tert*-butyl methyl ether (3  $\times$  30 mL). The combined organic layers were washed with brine (100 mL), dried over  $MgSO_4$ , filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 6:1 $\rightarrow$ 3:1) to give product **20** as a colorless oil (6.24 g, 87 %).  $[\alpha]_D^{20} = +49.3$  ( $c = 1.55$ ,

CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ = 6.25 (d, *J* = 11.2 Hz, 1H), 6.14 (qd, *J* = 11.2, 1.3 Hz, 1H), 4.87 (bs, 1H), 4.14 (t, *J* = 8.4 Hz, 2H), 3.89 (d, *J* = 7.4 Hz, 1H), 3.76 (d, *J* = 6.1 Hz, 2H), 2.67 (m, 1H), 2.34 (bs, 1H), 2.18 (d, *J* = 2.4 Hz, 1H), 1.75 (s, 3H), 1.71 (s, 3H), 1.10 (d, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 8.4 Hz, 2H), 0.04 (s, 9H); <sup>13</sup>C NMR (75.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ = 157.0, 136.8, 136.1, 123.4, 120.7, 86.3, 81.0, 70.8, 63.3, 48.7, 31.7, 18.0, 17.8, 15.0, 12.0, -1.4; IR (film):  $\tilde{\nu}$  = 3310, 2970, 2953, 1737, 1721, 1520, 1372, 1248, 1230, 1217, 1058, 858, 836, 694 cm<sup>-1</sup>; HRMS (ESI): *m/z*: calcd for C<sub>18</sub>H<sub>31</sub>NO<sub>3</sub>Si+Na [*M*<sup>+</sup> +Na]: 360.19654; found: 360.19610; elemental analysis calcd (%) for C<sub>18</sub>H<sub>31</sub>NO<sub>3</sub>Si: C 64.05, H 9.26; found: C 64.11, H 9.30.

**(2*E*,4*E*,6*S*,7*S*,8*E*)-*N*-(Trimethylsilylethoxycarbonyl)-1-amino-9-(tributylstannyl)-2,5,7-trimethylnona-2,4,8-trien-6-ol (21)**: *n*BuLi (1.6 M in hexanes, 13.25 mL, 21.2 mmol) was added to a solution of (Bu<sub>3</sub>Sn)<sub>2</sub> (12.31 g, 21.2 mmol) in THF (21 mL) at -78 °C and the mixture was stirred at -40 °C for 20 min. The resulting bright yellow solution was cooled to -78 °C before CuCN (1.84 g, 20.72 mmol) was added as a solid. The cooling bath was removed and stirring was continued until all CuCN had dissolved to give a bright yellow solution. After stirring for 1 h at ambient temperature, the mixture was again cooled to -78 °C before a solution of alkyne **20** (1.74 g, 5.18 mmol) in THF (5 mL) was introduced. After 10 min, the reaction was quenched with MeOH (5 mL) and diluted with aq. sat. NH<sub>4</sub>Cl (20 mL). Stirring was continued at room temperature until all copper salts had dissolved in the aqueous phase. The blue colored aqueous layer was extracted with *tert*-butyl methyl ether (3 × 10 mL), the combined organic phases were dried over MgSO<sub>4</sub>, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 1:0→6:1, containing 1 % Et<sub>3</sub>N) to give vinyl stannane **21** as a colorless oil (3.11 g, 95 %, *E/Z* ≈ 30:1). [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +24.4 (*c* = 1.10, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 6.14 (s, 2H), 6.08 (d, *J* = 19.0 Hz, 1H), 5.80 (dd, *J* = 19.0, 7.8 Hz, 1H), 4.65 (bs, 1H), 4.15 (t, *J* = 8.4 Hz, 2H), 3.77 (d, *J* = 5.7 Hz, 2H), 3.68 (dd, *J* = 8.5, 1.5 Hz, 1H), 2.32 (m, 1H), 1.92 (s, 1H), 1.73 (s, 3H), 1.71 (s, 3H), 1.40–1.50 (m, 6H), 1.28 (sext., *J* = 7.3 Hz, 6H), 0.83–1.00 (m, 20H), 0.01 (s, 9H); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ = 156.8, 151.1, 137.2, 134.6, 131.3, 123.2, 121.2, 80.9, 63.1, 48.6, 46.6, 29.1, 27.2, 17.7, 16.7, 14.8, 13.7, 11.7, 9.5, -1.5; IR (film):  $\tilde{\nu}$  = 3338, 2955, 2924, 1699, 1513, 1456, 1249, 1061, 999, 858, 835, 692 cm<sup>-1</sup>; HRMS (ESI): *m/z*: calcd for C<sub>30</sub>H<sub>59</sub>NO<sub>3</sub>Si+Na [*M*<sup>+</sup> +Na]: 652.31783; found: 652.31777.

**(2E,4E,6S,7S,8E)-N-(Trimethylsilylethoxycarbonyl)-1-amino-9-iodo-2,5,7-trimethylnona-2,4,8-trien-6-ol (12)**: A solution of I<sub>2</sub> (1.31 g, 5.18 mmol) in Et<sub>2</sub>O (20 mL) was added to a solution of vinyl stannane **21** (3.11 g, 4.94 mmol) in Et<sub>2</sub>O (50 mL) at 0 °C. The resulting brown mixture was stirred at ambient temperature for 15 min before the reaction was quenched with aq. sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (50 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 30 mL), the combined organic layers were dried over MgSO<sub>4</sub>, filtered and evaporated. The crude product was purified by flash chromatography (hexanes/EtOAc, 10:1→7:1, containing 1 % Et<sub>3</sub>N), affording iodide **12** as a colorless oil (2.0 g, 90 %).  $[\alpha]_D^{20} = +28.1$  (*c* = 1.05, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ = 6.55 (dd, *J* = 14.5, 8.3 Hz, 1H), 6.15 (m, 3H), 4.76 (bs, 1H), 4.15 (t, *J* = 8.4 Hz, 2H), 3.78 (m, 3H), 2.40 (m, 1H), 1.94 (bs, 1H), 1.76 (s, 3H), 1.71 (s, 3H), 0.98 (t, *J* = 8.4 Hz, 2H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.05 (s, 9H); <sup>13</sup>C NMR (75 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ = 157.0, 149.2, 137.7, 135.9, 123.2, 120.8, 81.4, 75.9, 63.3, 48.7, 44.8, 18.0, 16.5, 15.0, 12.0, -1.4; IR (film):  $\tilde{\nu} = 3337, 2966, 2887, 1694, 1519, 1466, 1394, 1248, 1171, 1060, 945, 856, 835, 776, 693$  cm<sup>-1</sup>; HRMS (ESI): *m/z*: calcd for C<sub>18</sub>H<sub>32</sub>NO<sub>3</sub>Si+Na [*M*<sup>+</sup> +Na]: 488.10884; found: 488.10826; elemental analysis calcd (%) for C<sub>18</sub>H<sub>32</sub>NO<sub>3</sub>Si: C 46.45, H 6.93; found: C 46.53, H 7.06.

**(S)-3-(tert-Butyldimethylsilyloxy)-2-formamido-N-((2E,4E,6S,7S,8E)-6-hydroxy-9-iodo-2,5,7-trimethylnona-2,4,8-trienyl)propanamide (22)**: A solution of anhydrous Et<sub>4</sub>NF (2.4 g, 16 mmol) and compound **12** (1.25 g, 2.68 mmol) in MeCN (7 mL) was stirred for 16 h at 40 °C. For work up, the solvent was evaporated, the residue was dissolved in EtOAc (5 mL) and the organic phase was washed with aq. sat. Na<sub>2</sub>CO<sub>3</sub> (10 mL). The aqueous phase was re-extracted with EtOAc (6 × 5 mL), the combined extracts were washed with brine (5 mL), dried over MgSO<sub>4</sub>, filtered and evaporated to give the somewhat unstable free amine as a pale yellow oil, which was immediately used without further characterization.

Acid **8** (692 mg, 2.8 mmol), HOBt (409 mg, 3 mmol), and N-methylmorpholine (NMM, 0.64 mL, 5.82 mmol) were successively added to a solution of this material (750 mg, 2.33 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (23 mL) at 0 °C. EDC-HCl (670 mg, 3.5 mmol) was then introduced and the mixture stirred at ambient temperature for 16 h. For work up, all volatile materials were evaporated and the pale brown residue was purified by flash chromatography (hexanes/EtOAc, 4:1→1:2) to give product **22** as a white solid (1.15 g, 90 %).  $[\alpha]_D^{20} = +29.3$  (*c* = 1.0, CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 8.21 (s, 1H), 6.69 (d, *J* =

6.2 Hz, 1H), 6.63 (bs, 1H), 6.50 (dd,  $J = 14.4, 8.2$  Hz, 1H), 6.14–6.08 (m, 3H), 4.48–4.41 (m, 1H), 4.03 (dd,  $J = 9.7, 4.1$  Hz, 1H), 3.87 (d,  $J = 5.6$  Hz, 2H), 3.76 (d,  $J = 8.0$  Hz, 1H), 3.57 (dd,  $J = 9.6, 8.2$  Hz, 1H), 2.37 (m, 1H), 1.90 (bs, 1H), 1.71 (s, 3H), 1.68 (s, 3H), 0.88 (d,  $J = 6.9$  Hz, 3H), 0.85 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 169.6, 161.1, 148.4, 137.6, 134.1, 122.9, 121.9, 81.0, 76.0, 62.6, 52.9, 47.3, 44.5, 25.7, 18.0, 16.2, 15.0, 11.8, -5.5, -5.6$ ; IR (film):  $\tilde{\nu} = 3302, 2928, 2857, 1650, 1530, 1385, 1255, 1107, 953, 834, 710$   $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{22}\text{H}_{39}\text{N}_2\text{O}_4\text{Si}+\text{Na}$  [ $M^+ + \text{Na}$ ]: 573.16161; found: 573.16167.

**1-(Trimethylsilyl)hept-6-en-1-yn-3-one (24)**:  $\text{AlCl}_3$  (14.9 g, 0.111 mol) was added in small portions over 5 min to a solution of bis(trimethylsilyl)acetylene (25.3 mL, 0.111 mol) and acid chloride **23** (12.3 mL, 0.111 mol) in  $\text{CH}_2\text{Cl}_2$  (140 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 10 min and at 20 °C for 1 h before it was carefully poured onto aq. HCl (1 M) at 0 °C. The aqueous phase was extracted with  $\text{Et}_2\text{O}$  (3 x 100 mL), the combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , filtered and evaporated (because of the volatility of the product, the heating bath was set to 20 °C and the applied vacuum was kept at  $\geq 30$  mbar). The residue was purified by Kugelrohr distillation to yield **24** as a colorless oil (16.64 g, 83 %).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 5.81$  (tdd,  $J = 16.8, 10.2, 6.4$  Hz, 1H), 5.04 (m, 2H), 2.66 (t,  $J = 7.4$  Hz, 2H), 2.42 (m, 2H), 0.25 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 186.9, 136.3, 115.7, 101.9, 98.0, 44.3, 27.8, 0.8$ ; IR (film):  $\tilde{\nu} 3081, 2963, 2902, 2152, 1680, 1643, 1439, 1409, 1356, 1253, 1227, 1115, 1094, 1031, 998, 968, 915, 865, 847, 762, 704, 626, 589$   $\text{cm}^{-1}$ ; MS (EI):  $m/z$  (%): 165 (46), 137 (10), 126 (12), 125 (100), 123 (24), 97 (41), 91 (16), 83 (21), 75 (45), 73 (64), 67 (12), 59 (19), 55 (15), 53 (10), 43 (17); HRMS (EI):  $m/z$ : calcd for  $\text{C}_{10}\text{H}_{16}\text{OSi}$  [ $M^+$ ] 180.09704; found 180.09723; elemental analysis calcd (%) for  $\text{C}_{10}\text{H}_{16}\text{OSi}$ : C 66.61; H 8.94; found: C 66.46, H 8.98.

**(3S)-1-(Trimethylsilyl)-6-hepten-1-yn-3-ol (26)**: A flame-dried Schlenk flask was charged with ketone **24** (8.368 g, 46.41 mmol) and degassed *iso*-propanol (350 mL, 3 freeze-thaw cycles). The resulting solution was purged with Ar for 1.5 h before the ruthenium complex **25** was added as a solid (175 mg, 0.292 mmol). The resulting solution was stirred for 19 h at 20 °C before the mixture was evaporated and the residue purified by flash chromatography (hexanes/ $\text{EtOAc}$ , 50:1→30:1) to give alcohol **26** as a colorless oil (8.31 g, 98 %, 98.8 % *ee*).  $[\alpha]_D^{20} = +6$  ( $c = 0.43, \text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,

CDCl<sub>3</sub>):  $\delta$  = 5.84 (tdd,  $J$  = 6.7, 10.2, 16.9 Hz, 1H), 5.03 (m, 2H), 4.38 (t,  $J$  = 6.5 Hz, 1H), 2.23 (m, 2H), 1.77–1.83 (m, 2H), 0.18 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 137.7, 115.3, 106.5, 89.7, 62.4, 36.8, 29.4, -0.1; IR (film):  $\tilde{\nu}$  = 3336, 3079, 2959, 2900, 2863, 2173, 1642, 1440, 1415, 1332, 1251, 1121, 1068, 1046, 1016, 955, 913, 895, 844, 761, 700, 648, 612, 555, 489 cm<sup>-1</sup>; MS (EI):  $m/z$  (%): 167 (9), 149 (8), 140 (17), 127 (15), 125 (12), 99 (45), 92 (10), 91 (32), 75 (100), 73 (73), 61 (12), 45 (21), 43 (13), 41 (13); elemental analysis calcd (%) for C<sub>10</sub>H<sub>18</sub>OSi: C 65.87, H 9.95; found: C 65.72, H 9.84.

**(3S)-3-Methoxy-1-(trimethylsilyl)hept-6-en-1-yne (27)**: *n*BuLi (1.6 M in hexanes, 10.6 mL, 16.96 mmol) was added dropwise to a solution of alcohol **26** (3.1 g, 17 mmol) in THF (60 mL) at -78 °C. After stirring for 10 minutes, MeI (8.5 mL, 136.54 mmol) was slowly introduced before the temperature was raised to -25 °C. DMSO (2.5 mL) was added dropwise, causing the formation of a white precipitate. After stirring for 1 h at that temperature, the cooling bath was removed and stirring continued for 21 h. For work up, the mixture was poured onto a mixture of ice and sat. aq. NH<sub>4</sub>Cl (1:1), the aqueous phase was extracted with Et<sub>2</sub>O (3 × 50 mL), the combined organic layers were washed with H<sub>2</sub>O and brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated (due to high volatility of the product, the heating bath was set to 20 °C and pressure kept at ≥ 35 mbar) to give product **27** as a pale yellow oil (3.30 g, 99 %, *ee* = 98.8 %, GC). The crude product was pure enough for use in the next step without further purification.  $[\alpha]_D^{20}$  = -37.9 ( $c$  = 0.61 in CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 5.83 (tdd,  $J$  = 6.7, 10.2, 16.9 Hz, 1H), 5.00 (m, 2H), 3.93 (t,  $J$  = 6.6 Hz, 1H), 3.36 (s, 3H), 2.19 (m, 2H), 1.67–1.82 (m, 2H), 0.18 (s, 9H); <sup>13</sup>C NMR (MHz, CDCl<sub>3</sub>):  $\delta$  = 138.4, 115.1, 105.0, 90.9, 71.3, 56.4, 35.1, 29.8, 0.0; IR (film):  $\tilde{\nu}$  = 3079, 2958, 2927, 2854, 2822, 2170, 1642, 1465, 1450, 1415, 1335, 1251, 1160, 1107, 1011, 994, 922, 844, 761, 700, 652, 612 cm<sup>-1</sup>; MS (EI):  $m/z$  (%): 181 (5), 154 (21), 142 (13), 141 (92), 123 (15), 114 (10), 113 (94), 109 (18), 97 (15), 91 (18), 89 (65), 83 (56), 79 (5), 75 (23), 73 (100), 67 (10), 59 (44), 58 (10), 55 (13), 45 (20), 43 (24), 41 (14); HRMS (CI):  $m/z$ : calcd for C<sub>11</sub>H<sub>21</sub>OSi [ $M^+$  +H]: 197.13598, found 197.13607.

**(3S)-3-Methoxy-1-(trimethylsilyl)hex-1-yn-6-al (28)**: O<sub>3</sub> was bubbled through a solution of compound **27** (6.65 g, 33.9 mmol) and Sudan Red 7B (38.5 mg, 0.1 mmol) in MeOH (240 mL). Once the red color disappeared (ca. 6.5 h), the solution was purged with Ar for 1 h before PPh<sub>3</sub> (9.6 g, 37.3 mmol) was introduced. The resulting mixture was stirred overnight before all volatile materials were evaporated.

The residue was purified by flash chromatography (hexanes/EtOAc, 100:1→30:1) to give aldehyde **28** as a pale yellow oil (6.2 g, 92 %).  $[\alpha]_D^{20} = -82.1$  ( $c = 0.51$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 9.79$  (t,  $J = 1.5$  Hz, 1H), 4.01 (t,  $J = 6.1$  Hz, 1H), 3.38 (s, 3H), 2.61 (m, 2H), 2.04 (dt,  $J = 7.2, 6.2$  Hz, 2H), 0.18 (s, 9H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 201.8, 103.5, 91.7, 70.5, 56.6, 39.7, 28.2, 0.1$ ; IR (film):  $\tilde{\nu} = 2960, 2941, 2900, 2824, 2724, 2170, 1727, 1466, 1440, 1412, 1390, 1334, 1251, 1201, 1178, 1114, 1091, 1017, 989, 958, 919, 844, 761, 700, 668, 612$   $\text{cm}^{-1}$ ; HRMS (CI):  $m/z$ : calcd for  $\text{C}_{10}\text{H}_{18}\text{O}_2\text{Si}+\text{H}$  [ $M^+ + \text{H}$ ]: 199.11543; found: 199.11528; elemental analysis calcd (%) for  $\text{C}_{10}\text{H}_{18}\text{O}_2\text{Si}$ : C 60.56, H 9.15; found: C 60.43, H 9.08.

**Methyl (2Z,6S)-6-methoxy-2-methyl-8-(trimethylsilyl)oct-2-en-8-ynoate (30)**: KHMDS (0.5 M in toluene, 62.5 mL) was slowly added to a solution of  $(\text{CF}_3\text{CH}_2\text{O})_2\text{P}(\text{O})\text{CH}(\text{Me})\text{COOMe}$  (6.2 g, 31.3 mmol) and 18-crown-6 (6.6 g, 25.0 mmol) in THF (170 mL) at  $-40$  °C. After 15 min, the mixture was cooled to  $-78$  °C and stirred for 30 min before a solution of aldehyde **28** (6.2 g, 31.3 mmol) in THF (91 mL) was added dropwise. Stirring was continued for 1 h before the reaction was carefully quenched with sat. aq.  $\text{NaHCO}_3$  and allowed to stir at ambient temperature. The mixture was extracted with EtOAc (3 x 100 mL) and the combined organic phases were washed with aq. sat.  $\text{NH}_4\text{Cl}$  and brine, before being dried over  $\text{MgSO}_4$  and evaporated. Purification of the residue by flash chromatography (hexanes/EtOAc, 100:1→50:1) afforded ester **30** as a colorless oil (7.12 g, 85 %).  $[\alpha]_D^{20} = -18.1$  ( $c = 0.44$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 5.95$  (qt,  $J = 7.5, 1.5$  Hz, 1H), 3.94 (t,  $J = 6.5$  Hz, 1H), 3.74 (s, 3H), 3.39 (s, 3H), 2.59 (m, 2H), 1.90 (dd,  $J = 2.7, 1.3$  Hz, 3H), 1.80 (m, 2H), 0.18 (s, 9H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 168.5, 141.9, 127.7, 104.3, 90.7, 71.1, 56.4, 51.3, 35.2, 25.7, 20.7, 0.0$ ; IR (film):  $\tilde{\nu} = 2955, 2901, 2843, 2822, 2169, 1720, 1648, 1456, 1435, 1367, 1334, 1251, 1227, 1198, 1175, 1134, 1108, 1074, 1009, 950, 844, 761, 700, 672, 616$   $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{14}\text{H}_{24}\text{O}_3\text{Si}+\text{Na}$  [ $M^+ + \text{Na}$ ]: 291.13916; found: 291.13924; elemental analysis calcd (%) for  $\text{C}_{14}\text{H}_{24}\text{O}_3\text{Si}$ : C 62.64, H 9.01; found: C 62.76, H 8.89.

**(2Z,6S)-6-Methoxy-2-methyl-8-(trimethylsilyl)oct-2-en-7-yn-1-ol (31)**: Dibal-H (1 M in hexane, 29.5 mL) was slowly added to a solution of compound **30** (3.05 g, 11.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (111 mL) at  $-78$  °C. After 1 h, the reaction was quenched with EtOAc (100 mL), warmed to ambient temperature and treated with aq. Rochelle's salt solution (1 M, 80 mL). The resulting mixture was stirred at  $40$  °C for 1

h to ensure a clean phase separation. The aqueous layer was extracted with EtOAc (3 x 100 mL) and the combined organic phases were dried over MgSO<sub>4</sub>, filtered and evaporated to give the crude title alcohol as a colorless oil (2.7 g, quant.) which was pure enough for use in the next step without further purification.  $[\alpha]_D^{20} = -17.8$  ( $c = 1.7$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 5.25$  (t,  $J = 7.6$  Hz, 1H), 4.10 (s, 2H), 3.93 (t,  $J = 6.6$  Hz, 1H), 3.37 (s, 3H), 2.20 (q,  $J = 7.2$  Hz, 2H), 1.79 (d,  $J = 1.2$  Hz, 3H), 1.80–1.67 (m, 2H), 0.00 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 135.8, 127.0, 104.3, 91.2, 70.6, 61.5, 56.1, 35.2, 23.4, 22.0, 0.0$ ; IR (film):  $\tilde{\nu} = 2360, 2358, 2550, 2341, 667$  cm<sup>-1</sup>; HRMS (ESI):  $m/z$ : calcd for C<sub>13</sub>H<sub>24</sub>O<sub>2</sub>Si+Na [ $M^+$  +Na]: 241.16214, found: 241.16239; elemental analysis calcd (%) for C<sub>13</sub>H<sub>24</sub>O<sub>2</sub>Si: C 64.95, H 10.06; found: C 64.91, H 10.25.

**(6Z,3S)-6-Methoxy-7-methylnona-2,8-dien-1-yne (33)**: A solution of **31** (4.3 g, 17.9 mmol) in a mixture of CH<sub>2</sub>Cl<sub>2</sub>/phosphate buffer (1:1, pH 8.6, 180 mL) was sequentially treated with tetra-*n*-butylammonium chloride (995 mg, 3.58 mmol), TEMPO (560 mg, 3.58 mmol) and NCS (5.02 g, 37.6 mmol). After stirring for 1.5 h at ambient temperature, the organic phase was washed with brine (30 mL), dried over MgSO<sub>4</sub> and concentrated to afford crude aldehyde **32** which was immediately used in the next step.

A solution of **32** in THF (130 mL) was added dropwise to a solution of preformed CH<sub>2</sub>=PPh<sub>3</sub> (5.44 g, 19.7 mmol) in THF (51.6 mL) at -78 °C. The mixture was then allowed to reach ambient temperature and stirred for 1.5 h before it was quenched with sat. aq. NH<sub>4</sub>Cl. The aqueous phase was extracted with EtOAc (3 x 50 mL), the combined organic extracts were dried over MgSO<sub>4</sub>, filtered and evaporated to give the corresponding diene, which was directly used in the next step.

K<sub>2</sub>CO<sub>3</sub> (7.4 g, 53.7 mmol) was added to a solution of the crude diene in MeOH (300 mL) and the resulting mixture stirred for 30 min. For work up, the mixture was filtered through a pad of Celite, which was carefully rinsed with Et<sub>2</sub>O. The combined filtrates were evaporated and the residue was purified by flash chromatography (pentane/Et<sub>2</sub>O, 1:0→100:1), affording alkyne **33** as a colorless oil (2.08 g, 71 % over 3 steps).  $[\alpha]_D^{20} = -17$  ( $c = 0.75$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 6.79$  (ddd,  $J = 17.3, 10.8, 0.8$  Hz, 1H), 5.37 (t,  $J = 7.6$  Hz, 1H), 5.20 (dd,  $J = 17.3, 0.7$  Hz, 1H), 5.09 (dt,  $J = 10.8, 1.6$  Hz, 1H), 3.91 (td,  $J = 6.6, 2.0$  Hz, 1H), 3.40 (s, 3H), 2.45 (d,  $J = 2.0$  Hz, 1H), 2.40–2.28 (m, 2H), 1.82 (d,  $J = 1.1$  Hz, 3H), 1.87–1.71 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 133.5, 133.3, 129.5, 113.7, 82.6, 73.8,$

70.2, 56.5, 35.5, 23.0, 19.8; IR (film):  $\tilde{\nu}$  = 3297, 2939, 2856, 2824, 1644, 1597, 1462, 1441, 1382, 1355, 1260, 1107, 920, 905, 638  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{11}\text{H}_{16}\text{O}+\text{Na}$  [ $M^+$  +Na]: 164.11995; found: 164.12001.

**(1E,6Z,3S)-6-Methoxy-7-methyl-1-(tributylstannyl)nona-1,2,8-triene (35)**: *n*BuLi (1.6 M in hexanes, 7.75 mL, 12.4 mmol) was added to a solution of  $(\text{Bu}_3\text{Sn})_2$  (7.19 g, 12.4 mmol) in THF (12 mL) at  $-78^\circ\text{C}$  and the resulting bright yellow mixture was stirred at  $-40^\circ\text{C}$  for 20 min. After cooling to  $-78^\circ\text{C}$ , solid CuCN (1.06 g, 12 mmol) was introduced, the cooling bath was removed and stirring continued until all CuCN had dissolved and a bright yellow solution had formed (5–10 min). After cooling to  $-78^\circ\text{C}$ , a solution of alkyne **33** (0.656 g, 4 mmol) in THF (4 mL) was added and stirring continued for 10 min before the reaction was quenched with MeOH (2 mL) and diluted with aq. sat.  $\text{NH}_4\text{Cl}$  (20 mL). The resulting mixture was stirred at ambient temperature until all copper salts had dissolved in the aqueous phase. The blue colored aqueous layer was extracted with *tert*-butyl methyl ether (3  $\times$  2 mL), the combined organic phases were dried over  $\text{MgSO}_4$ , filtered and evaporated, and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0 $\rightarrow$ 20:1, containing 1%  $\text{Et}_3\text{N}$ ) to give vinyl stannane **35** as a colorless oil (1.47 g, 81%).  $[\alpha]_D^{20} = +11.3$  ( $c = 1$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.74$  (dd,  $J = 17.4, 10.9$  Hz, 1H), 6.08 (d,  $J = 19.1$  Hz, 1H), 5.74 (dd,  $J = 19.1, 7.2$  Hz, 1H), 5.36 (t,  $J = 7.6$  Hz, 1H), 5.16 (d,  $J = 17.4$  Hz, 1H), 5.04 (d,  $J = 10.9$  Hz, 1H), 3.43 (q,  $J = 6.7$  Hz, 1H), 3.24 (s, 3H), 2.28–2.10 (m, 2H), 1.79 (s, 3H), 1.70–1.58 (m, 1H), 1.54–1.42 (m, 7H), 1.34–1.22 (m, 6H), 0.98–0.78 (m, 15H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta = 148.6, 133.7, 132.6, 131.5, 130.7, 113.3, 85.1, 56.1, 35.3, 29.1, 27.2, 23.2, 19.8, 13.7, 9.5$ ; IR (film):  $\tilde{\nu}$  = 2955, 2924, 2871, 2853, 1644, 1599, 1463, 1376, 1337, 1101, 989, 899, 689, 666  $\text{cm}^{-1}$ ; MS (EI):  $m/z$  (%): 399 (100,  $M^+ - \text{Bu}$ ), 367 (7), 343 (8), 265 (31), 235 (67), 179 (79), 151 (38), 133 (56); HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{23}\text{H}_{44}\text{OSn}+\text{Na}$  [ $M^+$  +Na]: 479.23072; found: 479.23056.

**Compound 36**: A 25 mL Schlenk tube was charged with vinyl stannane **35** (1.22 g, 2.67 mmol), vinyl iodide **22** (1.4 g, 2.545 mmol),  $[\text{Ph}_2\text{PO}_2][\text{NBu}_4]$  (1.4 g, 3.05 mmol)<sup>1</sup> and DMF (5 mL).  $\text{Pd}(\text{PPh}_3)_4$  (117.5 mg, 0.1 mmol) followed by CuTC (579 mg, 3.05 mmol)<sup>2</sup> were added to the vigorously stirred mixture, causing an instantaneous color change to brown-black. After stirring for 10 min, the reaction was

<sup>1</sup> J. Srogl, G. D. Allred, L. S. Liebeskind, *J. Am. Chem. Soc.* **1997**, *119*, 12376-12377.

<sup>2</sup> G. D. Allred, L. S. Liebeskind, *J. Am. Chem. Soc.* **1996**, *118*, 2748-2749.

quenched with H<sub>2</sub>O (15 mL) at 0 °C. The resulting suspension was passed through a pad of Celite which was carefully rinsed with EtOAc (150 mL). The aqueous phase was extracted with EtOAc (2 × 5 mL), the combined organic layers were successively washed with H<sub>2</sub>O (3 × 30 mL) and brine (30 mL), dried over MgSO<sub>4</sub>, filtered and evaporated. The remaining yellow solid was purified by flash chromatography (hexanes/EtOAc, 4:1→1:1) to give compound **36** as a colorless oil (1.3 g, 87 %).  $[\alpha]_D^{20} = +6.3$  ( $c = 0.5$ , CH<sub>2</sub>Cl<sub>2</sub>); <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>): 8.26 (s, 1H), 6.76 (ddd,  $J = 17.3, 10.8, 0.6$  Hz, 1H), 6.61–6.59 (br. m, 2H), 6.20–6.13 (m, 4H), 5.63 (dd,  $J = 12.1, 3.9$  Hz, 1H), 5.46 (dd,  $J = 14.4, 8.1$  Hz, 1H), 5.36 (t,  $J = 7.2$  Hz, 1H), 5.18 (d,  $J = 17.3$  Hz, 1H), 5.07 (d,  $J = 10.8$  Hz, 1H), 4.49–4.44 (m, 1H), 4.09 (dd,  $J = 9.6, 4.0$  Hz, 1H), 3.96–3.86 (m, 2H), 3.75 (d,  $J = 8.5$  Hz, 1H), 3.58 (dd,  $J = 9.6, 8.4$  Hz, 1H), 3.56–3.50 (m, 1H), 3.24 (s, 3H), 2.38 (m, 1H), 2.21–2.18 (m, 2H), 1.81 (s, 3H), 1.75 (s, 3H), 1.74 (s, 9H), 1.68–1.50 (m, 2H), 0.90 (d,  $J = 8.1$  Hz, 3H), 0.88 (s, 9H), 0.12 (s, 6H); <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta = 169.2, 160.6, 137.5, 135.9, 133.5, 133.4, 132.6, 32.4, 132.0, 131.0, 130.1, 122.8, 121.8, 113.0, 81.5, 80.9, 75.9, 62.2, 55.9, 52.5, 47.0, 40.9, 35.2, 25.5, 22.9, 19.5, 17.7, 16.7, 14.6, 11.4, -5.8, -5.9$ ; IR (film):  $\tilde{\nu} = 3286, 2929, 2859, 1652, 1548, 1462, 1386, 1257, 1106, 990, 837, 778$  cm<sup>-1</sup>; HRMS (ESI):  $m/z$ : calcd for C<sub>33</sub>H<sub>56</sub>N<sub>2</sub>O<sub>5</sub>Si+Na [ $M^+ + Na$ ]: 611.38535; found: 611.38507.

**(E)-3-(Tributylstannyl)but-2-en-1-ol (38)**:<sup>3</sup> *n*BuLi (1.6 M in hexanes, 35.1 mL, 56.2 mmol) was added to a solution of (Bu<sub>3</sub>Sn)<sub>2</sub> (34.16 g, 58.9 mmol) in THF (60 mL) at –78 °C and the resulting bright yellow mixture was stirred at –40 °C for 20 min. After cooling to –78 °C, solid CuCN (4.76 g, 53.5 mmol) was introduced, the cooling bath was removed and stirring continued until all CuCN had dissolved and a bright yellow homogeneous solution was formed. This solution was cooled to –78 °C before a solution of butyn-1-ol (**37**) (1.87 g, 26.77 mmol) in THF (27 mL) was added. After 30 min at this temperature, the cooling bath was removed and the mixture stirred at ambient temperature for 3 h. The reaction was quenched with MeOH (5 mL) and diluted with aq. sat. NH<sub>4</sub>Cl (60 mL). Stirring was continued until all copper salts had dissolved in the aqueous phase, which was extracted with *tert*-butyl methyl ether (3 × 10 mL), the combined organic layers were dried over MgSO<sub>4</sub>, filtered and evaporated, and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0→7:1) to yield vinyl stannane **38** as a colorless oil (8.38 g, 86 %). <sup>1</sup>H NMR (CD<sub>2</sub>Cl<sub>2</sub>, 300 MHz):  $\delta = 5.76$  (tq,  $J = 6.1, 1.9$  Hz, 1H), 4.21 (t,  $J = 5.4$  Hz, 2H), 1.88 (d,  $J = 0.9$  Hz, 3H), 1.58–1.44 (m, 6H),

<sup>3</sup> B. H. Lipshutz, G. C. Clososki, W. Christmann, D. W. Chung, D. B. Ball, J. Howell, *Org. Lett.* **2005**, *7*, 4561-4564.

1.40–1.26 (m, 6H), 0.96–0.85 (m, 15H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  = 142.3, 140.1, 59.1, 29.5, 27.8, 19.5, 13.9, 9.4; IR (film):  $\tilde{\nu}$  = 3301, 2955, 2923, 2871, 2851, 1463, 1417, 1376, 1339, 1291, 1058, 1002, 960, 873, 687, 661  $\text{cm}^{-1}$ ; MS (EI):  $m/z$  (%): 305 (100,  $M^+$  –Bu), 249 (51), 193 (42), 177 (17), 137 (25), 121 (16).

**(E)-3-(Tributylstannyl)but-2-en-1-al (39)**:<sup>3</sup>  $\text{MnO}_2$  (76 g, 880 mmol) was added to a solution of alcohol **38** (6.3 g, 17.6 mmol) in  $\text{CH}_2\text{Cl}_2$  (400 mL). The resulting suspension was stirred for 4 h before being filtered through a pad of Celite. The filtrate was evaporated and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 20:1) to give aldehyde **39** as a pale yellow oil (5.58 g, 88 %).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  = 10.03 (d,  $J$  = 7.9 Hz, 1H), 6.19 (dq,  $J$  = 7.9, 1.9 Hz, 1H), 2.42 (d,  $J$  = 1.9 Hz, 3H), 1.60–1.41 (m, 6H), 1.35–1.22 (m, 6H), 1.00–0.83 (m, 15H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 187.5, 174.5, 139.9, 28.9, 27.3, 20.8, 13.6, 9.4; IR (film):  $\tilde{\nu}$  = 2956, 2923, 2871, 2851, 1673, 1463, 1143, 1072, 934, 875, 674  $\text{cm}^{-1}$ ; MS (EI):  $m/z$  (%): 303 (100,  $M^+$  –Bu), 247 (68), 191 (32), 177 (25), 159 (11), 137 (12), 121 (21).

**(2E,4S)-2-(Tributylstannyl)hept-2,6-dien-4-ol (40)**: A solution of allylmagnesium bromide (1 M in  $\text{Et}_2\text{O}$ , 22 mL) was added dropwise over 30 min to a solution of freshly prepared (–)-Ipc<sub>2</sub>BOMe (7.35 g, 23.26 mmol)<sup>4</sup> in  $\text{Et}_2\text{O}$  (46 mL) at 0 °C. The resulting mixture was stirred for 30 min at 0 °C before it was allowed to reach ambient temperature over the course of 1 h. The precipitated salts were filtered off under Ar and the filtrate was cooled to –100 °C. A solution of freshly prepared aldehyde **39** (5.58 g, 15.5 mmol) in  $\text{Et}_2\text{O}$  (10 mL) was added dropwise along the cold glass wall of the flask over a period of 30 min, and the resulting mixture was stirred at that temperature for 30 min. The mixture was quenched with MeOH (300  $\mu\text{L}$ ) at –100 °C and then allowed to stir at ambient temperature.  $\text{H}_2\text{O}_2$  (8 mL, 30 % w/w) and aq. NaOH (3 M, 4 mL) were carefully added, the resulting mixture was stirred for 1 h at ambient temperature and decanted. The aqueous phase was extracted with *tert*-butyl methyl ether (3  $\times$  2 mL), the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and evaporated, and the residue was purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0  $\rightarrow$  20:1) to yield product **40** as a colorless oil (6.2 g, 99 %,  $ee$  = 95 %, HPLC).  $[\alpha]_D^{20}$  = –12 ( $c$  = 0.23,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 5.80 (m, 1H), 5.54 (m, 1H), 5.10 (m, 2H), 4.59 (m, 1H), 2.28 (m,

<sup>4</sup> a) U. S. Racherla, H. C. Brown, *J. Org. Chem.* **1991**, *56*, 401-404; b) U. S. Racherla, Y. Liao, H. C. Brown, *J. Org. Chem.* **1992**, *57*, 6614-6617.

2H), 1.89 (s, 3H), 1.47 (m, 6H), 1.31 (m, 6H), 0.89 (m, 15H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 142.5, 141.6, 134.4, 117.8, 66.5, 41.9, 29.1, 27.3, 19.6, 13.6, 9.1; IR (film):  $\tilde{\nu}$  = 3321, 2956, 2923, 2871, 2853, 1641, 1463, 1376, 1339, 1292, 1070, 1018, 998, 911, 864, 663  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{19}\text{H}_{38}\text{OSn}+\text{Na}$  [ $M^+$  +Na]: 425.18362; found: 425.18330; elemental analysis calcd (%) for  $\text{C}_{19}\text{H}_{38}\text{OSn}$ : C 56.88, H 9.55; found: C 56.68, H 9.56.

**(2E,4S)-4-Methoxy-2-(tributylstannyl)hept-2,6-diene (41)**: A solution of compound **40** (6.20 g, 15.42 mmol) in  $\text{CH}_2\text{Cl}_2$  (25 mL) was added dropwise over 15 min to a mixture of Meerwein salt (3.26 g, 22.2 mmol) and proton sponge (5.28 g, 24.67 mmol) in  $\text{CH}_2\text{Cl}_2$  (125 mL) at 0 °C. After slowly warming to ambient temperature, the suspension was stirred for 3 h before it was diluted with hexanes (50 mL) and filtered through a pad of Celite. The filtrate was evaporated and the residue purified by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0→20:1) to give product **41** as a colorless oil (6.08 g, 95 %).  $[\alpha]_D^{20} = -23.6$  ( $c = 1.5$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 5.80 (m, 1H), 5.37 (dd,  $J = 8.6$ , 1.8 Hz, 1H), 5.05 (m, 2H), 4.14 (m, 1H), 3.27 (s, 3H), 2.35 (m, 1H), 2.22 (m, 1H), 1.88 (d,  $J = 1.8$  Hz, 3H), 1.49 (m, 6H), 1.30 (m, 6H), 0.88 (m, 15H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 142.5, 140.5, 134.4, 116.3, 75.1, 55.5, 28.8, 26.9, 19.4, 13.3, 13.3, 7.2; IR (film):  $\tilde{\nu}$  = 2956, 2924, 1641, 1463, 1098  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{20}\text{H}_{40}\text{OSn}+\text{Na}$  [ $M^+$  +Na]: 439.19926; found: 439.19912.

**Ethyl (2E,4S)-5-((*tert*-butyl(diphenyl)silyl)oxy)-2,5-dimethylpent-2-enoate (49)**: Dibal-H (1 M in hexanes, 101.6 mL, 101.6 mmol) was added dropwise over 15 min to a solution of **48** (34.5 g, 96.8 mmol)<sup>5</sup> in hexanes (605 mL) at -78 °C. After stirring for 1 h at this temperature, the cold mixture was slowly poured into an aq. solution of Rochelle's salt (1 M, 600 mL). The resulting mixture was vigorously stirred at ambient temperature for 1 h until a clean separation of the phases was reached. The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 100 mL), the combined organic layers were washed with brine (100 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated to give a colorless oil. This crude aldehyde was dissolved in  $\text{CH}_2\text{Cl}_2$  (50 mL) and added to a solution of freshly prepared  $\text{Ph}_3\text{PC}(\text{Me})\text{CO}_2\text{Et}$  (70 g, 194 mmol)<sup>6</sup> in  $\text{CH}_2\text{Cl}_2$  (170 mL). The resulting bright yellow mixture was stirred at ambient temperature for 4 h before all volatile materials were evaporated. The residue was purified by flash chromatography (hexanes/ $\text{EtOAc}$ , 1:0→95:5) to give ester **49** as a colorless oil

<sup>5</sup> A. Fürstner, E. Kattinig, O. Lepage, *J. Am. Chem. Soc.* **2006**, *128*, 9194-9204.

<sup>6</sup> O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, P. Zeller, *Helv. Chim. Acta* **1957**, *40*, 1242-1249.

(32.5 g, 82 %).  $[\alpha]_D^{20} = -2.5$  ( $c = 1.1$ ,  $\text{CHCl}_3$ ) (ref.<sup>7</sup>  $[\alpha]_D^{20} = -2.3$  ( $c = 1.58$ ,  $\text{CHCl}_3$ ));  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta = 7.67\text{--}7.61$  (m, 4H), 7.44–7.32 (m, 6H), 6.58 (dd,  $J = 9.9$ , 1.3 Hz, 1H), 4.18 (dq,  $J = 7.1$ , 1.3 Hz, 2H), 3.54 (d,  $J = 6.5$  Hz, 2H), 2.81–2.65 (m, 1H), 1.79 (d,  $J = 1.3$  Hz, 3H), 1.28 (t,  $J = 7.1$  Hz, 3H), 1.04 (s, 9H), 1.03 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75.5 MHz):  $\delta = 168.2$ , 144.4, 135.6, 135.6, 133.6, 129.6, 128.0, 127.6, 67.7, 60.4, 36.1, 26.8, 19.2, 16.3, 14.3, 12.6; IR (film):  $\tilde{\nu} = 2956$ , 2931, 2858, 1716, 1428, 1267, 1236, 1111, 1083, 823, 740, 701  $\text{cm}^{-1}$ ; MS (EI):  $m/z$  (%): 353 (5,  $M^+ - t\text{Bu}$ ), 277 (100), 227 (2), 199 (14), 183 (16), 152 (9).

**Ethyl (2E,4S)-5-hydroxy-2,4-dimethylpent-2-enoate (50)**: TBAF (1 M in THF, 237 mL, 237 mmol) was slowly added to a solution of ester **49** (32.5 g, 79.22 mmol) in THF (500 mL) at 0 °C. After stirring at room temperature for 1 h, the reaction was quenched with  $\text{H}_2\text{O}$  (200 mL), the THF was evaporated, and the remaining aqueous layer extracted with  $\text{Et}_2\text{O}$  (6 × 50 mL). The combined extracts were dried over  $\text{MgSO}_4$ , filtrated and evaporated. Purification of the crude product by flash chromatography (hexanes/*tert*-butyl methyl ether, 4:1→1:1) afforded alcohol **50** as a colorless oil (11.64 g, 86 %,  $ee \geq 99.9$  % by GC).  $[\alpha]_D^{20} = -20.3$  ( $c = 0.3$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.52$  (dd,  $J = 9.9$ , 1.4 Hz, 1H), 4.15 (q,  $J = 7.1$  Hz, 2H), 3.58–3.42 (m, 2H), 2.80–2.63 (m, 1H), 1.86 (bs, 1H), 1.84 (d,  $J = 1.4$  Hz, 3H), 1.26 (t,  $J = 7.1$  Hz, 3H), 0.98 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta = 168.1$ , 143.8, 129.0, 67.0, 60.6, 36.2, 16.0, 14.2, 12.7; IR (film):  $\tilde{\nu} = 3440$ , 2962, 2932, 2874, 1707, 1649, 1448, 1368, 1259, 1128, 1032, 748  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_9\text{H}_{16}\text{O}_3 + \text{H} [M^+ + \text{H}]$ : 173.1178; found: 173.1176.

**Ethyl (2E,4S)-6-iodo-2,4-dimethylpent-2,5-dienoate (53)**: TEMPO (9 mg, 0.058 mmol) and an aqueous solution of KBr (1 M, 0.58 mL, 0.58 mmol) were added to a solution of alcohol **50** (1.0 g, 5.8 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL). A mixture of aqueous NaOCl (12 %, 9 mL, 6.96 mmol) diluted with a sodium phosphate buffer (18 mL, 0.68 M, pH = 7.4) was then slowly introduced. After 15 min, the reaction was quenched with aq. sat.  $\text{Na}_2\text{S}_2\text{O}_3$  (10 mL), decanted, and the aqueous phase extracted with  $\text{CH}_2\text{Cl}_2$  (2 × 5 mL). The combined organic layers were washed with  $\text{H}_2\text{O}$  (10 mL) and brine (10 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated to give crude aldehyde **51** as a colorless oil (0.98 g) which was immediately used in the next step.

<sup>7</sup> D. Díez-Martin, N. R. Kotecha, S. V. Ley, S. Mantegani, J. C. Menéndez, H. H. Organ, A. D. White, B. J. Banks, *Tetrahedron* **1992**, *48*, 7899-7938.

A 250 mL Schlenk flask was charged with  $\text{CrCl}_2 \cdot (\text{THF})_{1.8}$  (7.34 g, 29 mmol), THF (10 mL), 1,4-dioxane (55 mL) and  $\text{CHI}_3$  (4.57 g, 11.6 mmol) and the initially blue suspension was stirred at ambient temperature for 2 h until it had turned brown. A solution of aldehyde **51** in dioxane (5 mL) was added and stirring continued for 30 min. The reaction was quenched with  $\text{H}_2\text{O}$  (60 mL) and the aqueous phase extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with aq. sat.  $\text{Na}_2\text{S}_2\text{O}_3$  (10 mL) and brine (20 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated. Purification of the yellow solid residue by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0→25:1) afforded iodide **53** as a colorless oil (1.0 g, 59 %, *E:Z* ≥ 20:1).  $[\alpha]_D^{20} = +60$  ( $c = 1.38$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.50$  (qd,  $J = 9.6, 1.4$  Hz, 1H), 6.44 (dd,  $J = 14.5, 6.7$  Hz, 1H), 6.06 (dd,  $J = 14.5, 1.3$  Hz, 1H), 4.17 (q,  $J = 7.1$  Hz, 2H), 3.27–3.13 (m, 1H), 1.81 (d,  $J = 1.5$  Hz, 3H), 1.28 (t,  $J = 7.1$  Hz, 3H), 1.12 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta = 168.0, 147.6, 142.2, 128.0, 75.3, 60.7, 39.7, 19.3, 14.2, 12.5$ ; IR (film):  $\tilde{\nu} = 2973, 1711, 1447, 1367, 1248, 1179, 1117, 947, 748, 720, 682$   $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{10}\text{H}_{15}\text{O}_2\text{I} + \text{Na}$  [ $M^+ + \text{Na}$ ]: 317.00109; found: 317.00090.

**Ethyl (2*E*,4*R*,5*E*,7*E*,9*S*)-9-methoxy-2,4,7-trimethyldodeca-2,5,7,10-tetraenoate (55)**: A 25 mL Schlenk flask was charged with stannane **41** (1.55 g, 3.74 mmol), iodide **53** (1.0 g, 3.4 mmol),  $[\text{Ph}_2\text{PO}_2][\text{NBu}_4]$  (1.87 g, 4.08 mmol) and DMF (6.8 mL).  $\text{Pd}(\text{PPh}_3)_4$  (157 mg, 0.136 mmol) followed by CuTC (775 mg, 4.08 mmol) were then added to the vigorously stirred mixture, causing an immediate color change to black. After 10 minutes, the reaction was quenched at 0 °C with  $\text{H}_2\text{O}$  (20 mL), the resulting suspension was filtered through a short pad of Celite, which was carefully washed with EtOAc (100 mL). The aqueous phase was extracted with EtOAc (2 × 5 mL), the combined organic layers were washed with  $\text{H}_2\text{O}$  (3 × 30 mL) and brine (30 mL), dried over  $\text{MgSO}_4$ , filtered and evaporated to leave a pale brown residue. Purification by flash chromatography (hexanes/*tert*-butyl methyl ether, 1:0→20:1) furnished ester **55** as a colorless oil (0.83 g, 84 %).  $[\alpha]_D^{20} = -10.3$  ( $c = 1.48$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.60$  (d,  $J = 9.7$  Hz, 1H), 6.08 (d,  $J = 15.7$  Hz, 1H), 5.77 (m, 1H), 5.57 (dd,  $J = 15.7, 6.8$  Hz, 1H), 5.28 (d,  $J = 9.0$  Hz, 1H), 5.05 (m, 2H), 4.19 (q,  $J = 7.1$  Hz, 2H), 4.04 (m, 1H), 3.28 (m, 1H), 3.24 (s, 3H), 2.37 (m, 1H), 2.23 (m, 1H), 1.87 (s, 3H), 1.77 (s, 3H), 1.29 (t,  $J = 7.1$  Hz, 3H), 1.16 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 168.4, 144.8, 136.5, 134.6, 133.5, 131.5, 131.5, 126.8, 117.0, 76.9, 60.6, 56.1, 40.1, 36.4, 20.4, 14.4, 13.1, 12.6$ ; IR (film):  $\tilde{\nu} = 2977, 2929, 2873, 1711, 1643$ ,

1448, 1367, 1263, 1240, 1098, 966, 750  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{18}\text{H}_{28}\text{O}_3+\text{Na}$  [ $M^+ +\text{Na}$ ]: 315.19307; found: 315.19283.

**(2E,4R,5E,7E,9S)-9-Methoxy-2,4,7-trimethyldodeca-2,5,7,10-tetraenoic acid (56)**: A solution of LiOH (6 M in  $\text{H}_2\text{O}$ , 4 mL) was added to a solution of ester **55** (1.15 g, 3.93 mmol) in MeOH/THF (1:1, 4 mL) and the resulting mixture was stirred for 24 h. HCl (1 M) was slowly added until a  $\text{pH} \approx 3$  was reached and the aqueous phase was extracted with EtOAc (3  $\times$  5 mL). The combined organic phases were dried over  $\text{MgSO}_4$ , filtered and evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 10:1 $\rightarrow$ 5:1) to give acid **56** as a colorless oil (828 mg, 80 %).  $[\alpha]_D^{20} = -36.8$  ( $c = 1.2$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 6.75$  (dd,  $J = 9.8, 1.2$  Hz, 1H), 6.11 (d,  $J = 15.7$  Hz, 1H), 5.82-5.70 (m, 1H), 5.61 (dd,  $J = 15.7, 6.9$  Hz, 1H), 5.27 (d,  $J = 9.0$  Hz, 1H), 5.08–4.99 (m, 2H), 4.10–4.00 (m, 1H), 3.38–3.23 (m, 1H), 3.21 (s, 3H), 2.40–2.30 (m, 1H), 2.27–2.18 (m, 1H), 1.87 (d,  $J = 1.2$  Hz, 3H), 1.78 (d,  $J = 1.2$  Hz, 3H), 1.17 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 174.3, 148.3, 137.2, 135.5, 134.4, 132.5, 131.8, 126.6, 117.2, 77.5, 56.4, 40.7, 37.3, 20.7, 13.6, 12.7$ ; IR (film):  $\tilde{\nu} = 2964, 2927, 1683, 1640, 1418, 1274, 1094, 963$   $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{16}\text{H}_{23}\text{O}_3$  : [ $M^+ -\text{H}$ ] 263.16527; found: 263.16549.

**Ester 57**: EDC·HCl (489 mg, 2.55 mmol) was added to a solution of acid **56** (539 mg, 2.04 mmol) and 4-pyrrolidinyl-pyridine (25 mg, 0.17 mmol) in  $\text{CH}_2\text{Cl}_2$  (4 mL) at 0 °C. The cooling bath was removed and the solution stirred at ambient temperature for 10 minutes. At this time, TLC [hexanes/EtOAc, (4:1)] indicated full consumption of **56** and the formation of a less polar spot (if necessary, more EDC·HCl was added to ensure full conversion).<sup>8</sup> A solution of alcohol **36** (1.0 g, 1.7 mmol) in  $\text{CH}_2\text{Cl}_2$  (2 mL) was added and the solvent removed using a stream of Ar. The resulting viscous residue was slowly stirred for 18 h before it was taken up in the minimum amount of  $\text{CHCl}_3$  and transferred on top of a silica gel column. Purification by flash chromatography (hexanes/EtOAc, 4:1 $\rightarrow$ 1:1) provided ester **57** as a white solid (1.17 g, 82 %).  $[\alpha]_D^{20} = +10$  ( $c = 1.1$ ,  $\text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 8.22$  (s, 1H), 6.76 (ddd,  $J = 16.2, 11.1, 0.6$  Hz, 1H), 6.56 (dd,  $J = 9.6, 1.2$  Hz, 1H), 6.51–6.48 (brm, 2H),

<sup>8</sup> This activated acid derivative is soluble in the medium, whereas the corresponding derivative formed from DCC may precipitate from the mixture and therefore slow down the esterification. If the conversion of **56** is not quantitative at this stage, further EDC·HCl has to be added. Moreover, it was found that the use of HOBT forms an activated acid derivative which does not react with alcohol **36** in the absence of base. Excess base, however, should be avoided due to the sensitivity of the compounds.

6.23 (d,  $J = 10.2$  Hz, 1H), 6.15–6.06 (m, 4H), 5.77 (ddt,  $J = 17.4, 10.2, 7.2$  Hz, 1H), 5.61–5.57 (m, 2H), 5.41–5.33 (m, 2H), 5.24 (d,  $J = 9.0$  Hz, 1H), 5.19 (d,  $J = 17.4$  Hz, 1H), 5.07–5.05 (m, 4H), 4.42 (td,  $J = 6.6, 4.2$  Hz, 1H), 4.07–4.00 (m, 2H), 3.62 (dd,  $J = 9.6, 7.8$  Hz, 1H), 3.50 (dd,  $J = 12.6, 7.8$  Hz, 1H), 3.29–3.20 (m, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 2.55 (m, 1H), 2.25–2.18 (m, 2H), 1.85 (d,  $J = 1.2$  Hz, 3H), 1.82 (d,  $J = 1.2$  Hz, 3H), 1.79 (d,  $J = 1.2$  Hz, 3H), 1.76 (bs, 6H), 1.65–1.60 (m, 1H), 1.52–1.46 (m, 1H), 1.15 (d,  $J = 6.6$  Hz, 3H), 0.98 (d,  $J = 6.6$  Hz, 3H), 0.90 (s, 9H), 0.13 (s, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 169.8, 167.4, 161.1, 145.1, 136.8, 136.2, 135.3, 135.2, 134.9, 134.1, 133.7, 133.1, 132.9, 132.7, 131.9, 131.9, 131.0, 130.7, 127.1, 124.3, 121.8, 116.8, 113.4, 83.0, 81.6, 77.1, 63.1, 56.1, 56.0, 53.5, 47.4, 40.4, 39.9, 36.7, 36.0, 25.9, 23.6, 20.5, 19.8, 18.4, 17.0, 15.2, 13.2, 12.8, 12.6, -5.4, -5.5$ ; IR (film):  $\tilde{\nu} = 3294, 2926, 2855, 1733, 1653, 1547, 1462, 1378, 1259$   $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{49}\text{H}_{78}\text{N}_2\text{O}_7\text{Si}+\text{Na}$  [ $M^+ + \text{Na}$ ]: 857.54774; found: 857.54705.

**Macrocycle 59:** Complex **58** (30.5 mg, 0.0359 mmol, 10 mol %) was added to a solution of ester **57** (300 mg, 0.359 mmol) in toluene (359 mL) and the resulting mixture was stirred at 50 °C for 4 h. Ethyl vinyl ether (3.4 mL, 35.9 mmol) was then introduced and stirring continued for 30 min at ambient temperature before the mixture was concentrated to a volume of ca. 3 mL. Purification of this solution by flash chromatography (hexanes/EtOAc, 4:1→1:1, containing 1 %  $\text{Et}_3\text{N}$ ) gave macrocycle **59** as a white solid (207 mg, 72 %).  $[\alpha]_D^{20} = +4$  ( $c = 0.54, \text{CH}_2\text{Cl}_2$ );  $^1\text{H}$  NMR (600 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 8.22$  (s, 1H), 6.57 (dd,  $J = 10.3, 1.3$  Hz, 1H), 6.56–6.48 (m, 2H), 6.46 (d,  $J = 15.5$  Hz, 1H), 6.28 (d,  $J = 11.6$  Hz, 1H), 6.15 (d,  $J = 11.6$  Hz, 1H), 6.04 (dd,  $J = 14.6, 10.2$  Hz, 1H), 5.97 (dd,  $J = 15.2, 10.2$  Hz, 1H), 5.89 (d,  $J = 15.4$  Hz, 1H), 5.52 (ddd,  $J = 15.5, 10.2, 4.8$  Hz, 1H), 5.48 (dd,  $J = 15.4, 8.9$  Hz, 1H), 5.40–5.35 (m, 2H), 5.19–5.17 (m, 1H), 5.09 (d,  $J = 10.1$  Hz, 1H), 5.08 (d,  $J = 8.8$  Hz, 1H), 4.44–4.41 (m, 1H), 4.12 (ddd,  $J = 9.8, 9.6, 2.8$  Hz, 1H), 4.06 (dd,  $J = 9.7, 3.9$  Hz, 1H), 3.95–3.83 (m, 2H), 3.62 (dd,  $J = 9.7, 7.7$  Hz, 1H), 3.29–3.24 (m, 1H), 3.22 (s, 3H), 3.19–3.14 (m, 1H), 2.96 (s, 3H), 2.64 (brd,  $J = 12.8$  Hz, 1H), 2.58–2.52 (m, 2H), 2.31 (dt,  $J = 12.8, 9.8$  Hz, 1H), 1.91–1.86 (m, 1H), 1.79 (s, 3H), 1.78 (brs, 6H), 1.77 (s, 3H), 1.76 (s, 3H), 1.63–1.59 (m, 1H), 1.30–1.28 (m, 1H), 1.06 (d,  $J = 6.7$  Hz, 3H), 0.93 (d,  $J = 6.8$  Hz, 3H), 0.90 (s, 9H), 0.13 (s, 6H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 169.8, 167.5, 161.1, 145.6, 137.1, 136.2, 135.8, 134.3, 133.8, 133.8, 133.3, 132.4, 132.3, 132.0, 131.2, 129.8, 128.8, 125.9, 125.5, 125.4, 121.8, 83.2, 79.8, 77.0, 63.0, 56.5, 55.9, 53.8, 47.4, 41.0, 40.9, 38.3, 35.3, 25.9, 23.2, 21.5, 20.8, 18.4, 16.8, 15.2, 13.2, 12.1, 12.1, -5.4, -5.5$ ; IR (film):  $\tilde{\nu} = 3300, 2926, 2856, 1651$  (br), 1533, 1462, 1385, 1257, 1216,

1105, 989, 964, 837, 778, 744  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{47}\text{H}_{74}\text{N}_2\text{O}_7\text{Si}+\text{Na}$  [ $M^+$  +Na]: 829.51592; found: 829.51575.

**Iejimalide B (2)**: TBAF (1 M in THF, 0.4 mL) was added dropwise to a solution of macrocycle **59** (291 mg, 0.36 mmol) in THF (3.6 mL) at 0 °C. After stirring at that temperature for 15 min, the mixture was directly added on top of a silica gel column and purified by eluting with EtOAc/MeOH, (1:0→50:1→20:1) to give Iejimalide B (**1**) as a white solid (247 mg, 99 %).  $[\alpha]_D^{20} = -16$  ( $c = 0.2$ ,  $\text{CH}_2\text{Cl}_2$ ), ref.<sup>9</sup>:  $[\alpha] = -17.6$ ,  $\text{CHCl}_3$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 8.26$  (s, 1H), 6.70 (d,  $J = 6.5$  Hz, 1H), 6.63 (t,  $J = 5.8$  Hz, 1H), 6.58 (dq,  $J = 10.4, 1.4$  Hz, 1H), 6.45 (d,  $J = 16.1$  Hz, 1H), 6.28 (dd,  $J = 11.2, 1.5$  Hz, 1H), 6.14 (dq,  $J = 11.2, 1.4$  Hz, 1H), 6.05 (dd,  $J = 14.5, 10.5$  Hz, 1H), 5.99 (dd,  $J = 15.2, 10.5$  Hz, 1H), 5.89 (d,  $J = 15.5$  Hz, 1H), 5.52 (ddd,  $J = 15.1, 10.1, 4.8$  Hz, 1H), 5.49 (dd,  $J = 15.5, 8.9$  Hz, 1H), 5.39 (dd,  $J = 14.0, 9.1$  Hz, 1H), 5.38 (dd,  $J = 14.5, 8.4$  Hz, 1H), 5.20–5.17 (m, 1H), 5.09 (d,  $J = 9.8$  Hz, 1H), 5.07 (d,  $J = 9.7$  Hz, 1H), 4.48–4.46 (m, 1H), 4.15–4.09 (m, 2H), 3.92–3.85 (m, 2H), 3.64 (ddd,  $J = 11.3, 8.6, 4.9$  Hz, 1H), 3.30–3.25 (m, 1H), 3.21 (s, 3H), 3.19–3.14 (m, 1H), 3.01 (dd,  $J = 8.6, 3.9$  Hz, 1H), 2.96 (s, 3H), 2.65–2.61 (m, 1H), 2.58–2.47 (m, 2H), 2.29 (dt,  $J = 13.8, 10.2$  Hz, 1H), 1.91–1.86 (m, 1H), 1.78 (d,  $J = 0.9$  Hz, 3H), 1.77 (s, 6H), 1.75 (d,  $J = 0.7$  Hz, 3H), 1.73 (d,  $J = 1.2$  Hz, 3H), 1.61–1.58 (m, 1H), 1.33–1.30 (m, 1H), 1.05 (d,  $J = 6.7$  Hz, 3H), 0.93 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta = 170.7, 167.5, 161.8, 145.6, 137.2, 136.1, 135.5, 134.4, 133.7, 133.7, 133.3, 132.4, 132.3, 132.1, 131.2, 129.8, 128.8, 126.0, 125.3, 125.1, 121.2, 83.1, 80.0, 77.1, 62.8, 56.5, 55.9, 52.9, 47.1, 41.0, 40.8, 38.2, 35.3, 23.3, 21.5, 20.8, 16.8, 15.2, 13.2, 12.3, 12.1$ ; IR (film):  $\tilde{\nu} = 3329, 2925, 2856, 1654$  (br), 1541, 1453, 1383, 1260, 1096, 965, 800, 698  $\text{cm}^{-1}$ ; HRMS (ESI):  $m/z$ : calcd for  $\text{C}_{41}\text{H}_{60}\text{N}_2\text{O}_7+\text{Na}$  [ $M^+$  +Na]: 715.42934; found: 715.42927.

<sup>9</sup> a) J. Kobayashi, J. Cheng, T. Ohta, H. Nakamura, S. Nozoe, Y. Hirata, Y. Ohizumi, T. Sasaki, *J. Org. Chem.* **1988**, *53*, 6147-6150; b) Y. Kikuchi, M. Ishibashi, T. Sasaki, J. Kobayashi, *Tetrahedron Lett.* **1991**, *32*, 797-798; c) M. Tsuda, K. Nozawa, K. Shimbo, H. Ishiyama, E. Fukushi, J. Kawabata, J. Kobayashi, *Tetrahedron Lett.* **2003**, *44*, 1395-1399; d) K. Nozawa, M. Tsuda, H. Ishiyama, T. Sasaki, T. Tsuruo, J. Kobayashi, *Bioorg. Med. Chem.* **2006**, *14*, 1063-1067.