Synthetic studies towards garsubellin A: Synthesis of model systems and potential mimics by regioselective lithiation of bicyclo[3.3.1]nonane-2,4,9-trione derivatives from catechinic acid

Nadia M. Ahmad, Vincent Rodeschini, Nigel S. Simpkins, Simon E. Ward and Claire Wilson

a - School of Chemistry, The University of Nottingham, University Park, Nottingham NG7 2RD U.K

b - Psychiatry Medicinal Chemistry, GSK R & D Ltd, New Frontiers Science Park, Third Avenue, Harlow Essex CM19 5AW U.K.

nigel.simpkins@nottingham.ac.uk
Compounds prepared using procedure A (Table 1)

(1S, 5R, 7S, 8R)-(+)\textsuperscript{-}8-(3,4-Dimethoxyphenyl)-2,9,9-trimethoxy-7-triisopropylsilanyloxy-5-trimethylsilyl-bicyclo[3.3.1]non-2-en-4-one 19. Colorless oil (46%); \([\alpha]_D^{20} +173 (c 0.25 \text{ in CHCl}_3); \nu_{\text{max}} (\text{CHCl}_3) 2900, 1644, 1612, 1380, 1095 \text{ cm}^{-1}; ^1\text{H NMR} (400 \text{ MHz, CDCl}_3) \delta 0.00 (\text{s, 9H, Si(CH}_3)_3), 0.65 (\text{m, 21H, OSi(CH(CH}_3}_2)_3), 1.89 (\text{m, 2H, CH}_2), 2.73 (\text{dd, J 4.1, 1.6, 1H, 5-CH}), 2.98 (\text{s, 3H, OCH}_3), 3.05 (\text{dd, J 10.4, 4.1, 1H, ArCH}), 3.32 (\text{s, 3H, OCH}_3), 3.60 (\text{s, 3H, OCH}_3), 3.64 (\text{s, 3H, ArOCH}_3), 3.67 (\text{s, 3H, ArOCH}_3), 4.01 (\text{ddd, J 10.4, 10.4, 6.3, 1H, CHOSi(CH(CH}_3}_2)_3), 5.31 (\text{s, 1H, C=CH}), 6.43 (\text{m, 2H, 2 x ArH}), 6.58 (\text{d, J 8.7, 1H, ArH}); ^13\text{C NMR} (125 \text{ MHz, CDCl}_3) \delta 2.8 (\text{CH}_3), 12.6 (\text{CH}), 17.9 (\text{CH}_3), 43.4 (\text{CH}_2), 47.9 (\text{CH}), 49.6 (\text{CH}_3), 50.9 (\text{CH}_3), 51.5 (\text{CH}), 55.6 (\text{CH}_3), 55.8 (\text{CH}_3), 56.0 (\text{CH}_3), 68.5 (\text{CH}), 83.4 (\text{C}), 101.5 (\text{C}), 101.7 (\text{CH}), 110.8 (\text{CH}), 112.1 (\text{CH}), 120.7 (\text{CH}), 129.3 (\text{C}), 132.9 (\text{C}), 147.9 (\text{C}), 148.5 (\text{C}), 175.4 (\text{C}), 198.6 (\text{C}); \text{HRMS (ESI) m/z 607.3488 [M+H]^+}, [C_{32}H_{55}O_7Si_2]^+ \text{ requires 607.3486.}

(1S, 5S, 7S, 8R)-(+)\textsuperscript{-}5-Allyl-8-(3,4-dimethoxyphenyl)-2,9,9-trimethoxy-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 20. Clear oil (46%); \([\alpha]_D^{30} +160 (c 0.5 \text{ in CHCl}_3); \nu_{\text{max}} (\text{CHCl}_3) 2939, 2865, 1730, 1650, 1616, 1462, 1380, 1114, 1049 \text{ cm}^{-1}; ^1\text{H NMR} (500 \text{ MHz, CDCl}_3) \delta 0.74-0.90 (\text{m, 21H, OSi(CH(CH}_3}_2}_3), 1.79-2.10 (\text{m, 2H, 8-CH}_2), 2.54 (\text{dd, J 15.0, 7.2, 1H, C=HCH=CH}_2), 2.67 (\text{dd, J 15.0, 7.2, 1H, CHHCH=CH}_2), 2.92 (\text{d, J 4.0, 1H, 5-CH}), 3.11 (\text{dd, J 10.6, 4.0, 1H, ArCH}), 3.22 (\text{s, 3H, OCH}_3), 3.49 (\text{s, 3H, OCH}_3), 3.56 (\text{s, 3H, OCH}_3), 3.83 (\text{s, 3H, ArOCH}_3), 3.85 (\text{s, 3H, ArOCH}_3), 4.22 (\text{ddd, J 10.6, 10.6, 5.7, 1H, CHOSi(CH(CH}_3}_2}_3), 4.04 (\text{d, J 10.0, 1H, CHH=CH}), 5.01 (\text{d, J 17.1, 1H, CHH=CH}), 5.55 (\text{s, 1H, C=CH}), 6.10 (\text{ddt, J 17.1, 10.0, 7.2, 1H, CH}_2=CHCH}_2), 6.61 (\text{br s, 1H, ArH}), 6.65 (\text{d, J 8.2, 1H, ArH}), 6.78 (\text{d, J 8.2, 1H, ArH}); ^13\text{C NMR} (125 \text{ MHz, CDCl}_3) \delta 12.6 (\text{CH}), 17.6 (\text{CH}_3), 18.1 (\text{CH}_3), 37.1 (\text{CH}_2), 41.9 (\text{CH}_2), 48.2 (\text{CH}), 50.1 (\text{CH}_3), 50.7 (\text{CH}), 50.7 (\text{CH}_3), 55.5 (\text{CH}_3), 55.8 (\text{CH}_3), 56.0 (\text{CH}_3), 56.9 (\text{C}), 68.7 (\text{CH}), 103.5 (\text{CH}), 103.9 (\text{C}), 110.8 (\text{CH}), 111.9 (\text{CH}), 115.2
(1S, 5S, 7S, 8R)-(–)-5-Benzyl-8-(3,4-dimethoxyphenyl)-2,9,9-trimethoxy-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 21. Clear oil (56%); [α]D 22 = +115 (c 1.0 in CHCl3); \(\nu_{\text{max}}\) (CHCl3) 2940, 2865, 1730, 1650, 1616, 1462, 1379, 1100, 1050 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl3) \(\delta\) 0.58-0.88 (m, 21H, OSi(CH(CH\(_3\))\(_2\))\(_3\)), 1.48 (dd, \(J=12.0, 5.4, 1\)H, 8-CH\(_3\)H), 1.65-1.74 (m, 1H, 8-CHH), 3.00 (d, \(J=3.7, 1\)H, ArCH\(_3\)), 3.04 (d, \(J=3.7, 1\)H, 5-CH), 3.19 (d, \(J=13.7, 1\)H, PhCH\(_2\)H), 3.28 (d, \(J=13.7, 1\)H, PhCHH), 3.32 (s, 3H, OCH\(_3\)), 3.49 (s, 3H, OCH\(_3\)), 3.57 (s, 3H, OCH\(_3\)), 3.83 (s, 3H, ArOCH\(_3\)), 3.85 (s, 3H, ArOCH\(_3\)), 4.20 (ddd, \(J=10.4, 10.4, 5.4, 1\)H, CHOSi(CH(CH\(_3\))\(_2\))\(_3\)), 5.57 (s, 1H, C=CH), 6.58-6.60 (m, 1H, ArH), 6.64 (d, \(J=8.3, 1\)H, ArH), 6.75 (dd, \(J=8.3, 0.84, 1\)H, ArH), 7.14 (t, \(J=7.0, 1\)H, ArH), 7.22 (dd, \(J=8.0, 7.0, 2\)H, ArH, ArH), 7.45 (d, \(J=8.0, 2\)H, ArH, ArH); \(^{13}\)C NMR (125 MHz, CDCl3) \(\delta\) 14.2 (CH), 18.0 (CH\(_3\)), 35.4 (CH\(_2\)), 40.9 (CH\(_2\)), 48.0 (CH\(_3\)), 49.2 (CH\(_3\)), 49.5 (CH), 52.4 (CH\(_3\)), 55.6 (CH\(_3\)), 55.7 (CH\(_3\)), 55.9 (CH\(_3\)), 57.4 (c), 68.8 (CH), 103.5 (C), 103.7 (CH), 110.8 (CH), 111.8 (CH), 121.0 (CH), 125.6 (CH), 127.4 (CH), 131.8 (CH), 133.1 (C), 139.2 (C), 147.9 (C), 148.4 (C), 174.7 (C), 201.3 (C); HRMS (ES) m/z 625.3539 [M+H\(^+\)], [C\(_{36}\)H\(_{53}\)O\(_7\)Si]\(^+\) requires 625.3561.

(1S, 5S, 7S, 8R)-(–)-8-(3,4-Dimethoxyphenyl)-2,9,9-trimethoxy-5-methyl-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 22. Yellow oil (48%); [α]D 23 = +123 (c 1.0 in CHCl3); \(\nu_{\text{max}}\) (CHCl3) 2941, 2866, 1650, 1462, 1374, 1103, 1061, 882 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl3) \(\delta\) 0.78-0.90 (m, 21H, OSi(CH(CH\(_3\))\(_2\))\(_3\)), 1.44 (s, 3H, CH\(_3\)), 1.79-1.90 (m, 2H, CH\(_2\)), 2.92 (d, \(J=4.1, 1\)H, 5-CH), 3.17 (dd, \(J=10.5, 4.1, 1\)H, ArCH), 3.19 (s, 3H, OCH\(_3\)), 3.46 (s, 3H, OCH\(_3\)), 3.55 (s, 3H, OCH\(_3\)), 3.84 (s, 3H, ArOCH\(_3\)), 3.86 (s, 3H, ArOCH\(_3\)), 4.22 (dd, \(J=10.5, 10.5, 5.8, 1\)H, CHOSi(CH(CH\(_3\))\(_2\))\(_3\)), 5.52 (s, 1H, C=CH), 6.62 (d, \(J=1.8, 1\)H, ArH), 6.65 (dd, \(J=8.2, 1.8, 1\)H, ArH), 6.78 (d, \(J=8.2, 1\)H, ArH); \(^{13}\)C NMR (100 MHz, CDCl3) \(\delta\) 11.1 (CH), 16.7 (CH\(_3\)), 16.8 (CH\(_3\)), 42.1 (CH\(_2\)), 46.9 (CH), 47.8 (CH\(_3\)), 48.8
(CH₃)₅, 49.3 (CH), 52.6 (CH₃), 53.9 (CH₃), 54.2 (CH₃), 54.5 (CH₃), 67.0 (CH), 101.1 (C), 101.5 (CH), 109.4 (CH), 110.6 (CH), 119.4 (CH), 131.9 (C), 146.4 (C), 147.0 (C), 173.5 (C), 199.8 (C); HRMS (ES) m/z 549.3259 [M+H]+, [C₃₀H₄₉O₇Si]⁺ requires 549.3248.

(1S, 5R, 7S, 8R)-(+-8-(3,4-dimethoxyphenyl)-5-(hydroxyphenylmethyl)-2,9,9-trimethoxy-7-triisopropylsilyloxy-bicyclo[3.3.1]non-2-en-4-one 23. Less polar diastereoisomer; clear oil (26%): [α]D⁺22 +131 (c 1.0 in CHCl₃); v max (CHCl₃) 3494, 2942, 1614, 1462, 1382, 1109, 1053, 882 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 0.64-0.79 (m, 21H, OSi((CH(CH₃)₂)₃), 1.82-1.84 (m, 2H, C(H₂), 2.98 (dd, J 10.3, 3.9, 1H, ArCH), 3.11 (d, J 3.9, 1H, 5-CH), 3.32 (s, 3H, OCH₃), 3.46 (s, 3H, OCH₃), 3.59 (s, 3H, OCH₃), 3.85 (s, 3H, ArOCH₃), 4.14-4.19 (m, 1H, C(HOSi((CH(CH₃)₂)₃)), 4.67 (br s, 1H, OH), 5.39 (s, 1H, CHO), 5.62 (s, 1H, C=CH), 6.56 (d, J 1.9, 1H, ArH), 6.61 (dd, J 8.2, 1.9, 1H, ArH), 6.77 (d, J 8.2, 1H, ArH), 7.21 (t, J 7.4, 1H, ArH), 7.29 (dd, J 7.7, 7.4, 2H, 2 x ArH), 7.51 (d, J 7.7, 2H, 2 x ArH); ¹³C NMR (125 MHz, CDCl₃) δ 12.5 (CH), 17.8 (CH₃), 18.0 (CH₃), 37.9 (CH₂), 48.2 (CH), 49.3 (CH₃), 52.9 (CH₃), 55.8 (CH₃), 60.3 (C), 68.8 (CH), 73.9 (CH), 104.1 (C), 104.7 (CH), 110.8 (CH), 120.9 (CH), 126.8 (CH), 127.2 (CH), 128.7 (CH), 132.7 (C), 141.9 (C), 148.0 (C), 148.5 (C), 175.3 (C), 202.2 (C); HRMS (ES) m/z 663.3335 [M + Na]⁺, [C₃₆H₅₂NaO₈Si]⁺ requires 663.3324; more polar distereoisomer; clear oil (26%); [α]D⁻20 +155 (c 1.5 in CHCl₃); v max (CHCl₃) 2866, 1652, 1619, 1115, 1048, 1028, 882 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 0.79-0.87 (m, 21H, OSi(CH(CH₃)₂)₃), 1.87-1.94 (m, 1H, CHH), 2.21 (dd, J 12.0, 5.4, 1H, CHH), 2.95 (dd, J 10.3, 3.9, 1H, ArCH), 3.17 (d, J 3.9 1H, 5-CH), 3.27 (s, 3H, OCH₃), 3.32 (s, 3H, OCH₃), 3.59 (s, 3H, OCH₃), 3.82 (s, 3H, ArOCH₃), 3.85 (s, 3H, ArOCH₃), 4.23 (dd, J 10.3, 10.3, 5.4, 1H, CHOSi(CH(CH₃)₂)₃), 5.26 (s, 1H, CHO), 5.73 (s, 1H, C=CH), 6.57 (s, 1H, ArH), 6.61 (d, J 8.2, 1H, ArH), 6.78 (d, J 8.2, 1H, ArH), 7.17-7.20 (m, 1H, ArH), 7.24-7.27 (m, 2H, 2 x ArH), 7.33-7.35 (m, 2H,
2 x ArH); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 12.6 (CH), 17.9 (CH$_3$), 18.0 (CH$_3$), 40.3 (CH$_3$), 46.9 (CH), 48.5 (CH), 49.1 (CH$_3$), 53.4 (CH$_3$), 55.8 (CH$_3$), 55.8 (CH$_3$), 56.0 (CH$_3$), 59.8 (C), 68.7 (CH), 77.7 (CH), 104.8 (CH), 106.1 (CH), 111.9 (CH), 120.9 (CH), 126.5 (CH), 126.7 (CH), 128.4 (CH), 132.6 (C), 143.3 (C), 148.2 (C), 148.6 (C), 174.1 (C), 200.0 (C); HRMS (ES) $m/z$ 663.3324 [M + H]$^+$, [C$_{36}$H$_{52}$O$_8$Si]$^+$ requires 663.3329.

(1S, 5R, 7S, 8R)-(−)-8-(3,4-Dimethoxyphenyl)-5-(1R/S)-(1-hydroxy-2-methylpropyl)-2,9,9-trimethoxy-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 24. A Yellow oil (31%); $[\alpha]_D^{22}$ +151 (c 0.8 in CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$) 3414 (br), 2940, 1730, 1614, 1592, 1462, 1382, 1305, 1106, 1028, 883 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.76-0.90 (m, 21H, OSi(CH$_3$)$_2$), 1.01 (d, $J$ 7.0, 3H, CH(CH$_3$)$_2$), 1.02 (d, $J$ 7.0, CH(CH$_3$)$_2$), 1.92-1.96 (m, 1H, CHH), 2.56 (m, 1H, CH(CH$_3$)$_2$), 2.83 (dd, $J$ 12.4, 5.2, 1H, CHH), 3.00 (d, $J$ 4.4, 1H, 5-CH), 3.18 (s, 3H, OCH$_3$), 3.22 (dd, $J$ 10.8, 4.4, 1H, ArCH), 3.45 (s, 3H, OCH$_3$), 3.55 (s, 3H, OCH$_3$), 3.78 (dd, $J$ 10.4, 2.0, 1H, CH(OH)), 3.83 (s, 3H, ArOCH$_3$), 3.85 (s, 3H, ArOCH$_3$), 4.14 (ddd, $J$ 10.8, 10.8, 5.2, 1H, CHOSi(CH$_3$)$_2$), 5.09 (d, $J$ 10.4, 1H, CHO), 5.53 (s, 1H, C=CH), 6.61 (d, $J$ 1.8, ArH), 6.64 (dd, $J$ 8.2, 1.8, 1H, ArH), 6.78 (d, $J$ 8.2, 1H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 13.0 (CH), 18.0 (CH$_3$), 22.4 (CH$_3$), 29.5 (CH), 40.5 (CH$_2$), 48.6 (CH), 50.1 (CH$_3$), 50.7 (CH), 51.8 (CH$_3$), 55.6 (CH$_3$), 55.8 (CH$_3$), 56.0 (CH$_3$), 58.3 (C), 68.3 (CH), 81.3 (CH), 104.1 (CH), 110.9 (CH), 112.1 (CH), 120.8 (CH), 133.1 (C), 148.0 (C), 148.5 (C), 175.5 (C), 205.3 (C); HRMS (ES) $m/z$ 607.3698 [M + H]$^+$, [C$_{33}$H$_{55}$O$_8$Si]$^+$ requires 607.3666.

(1S, 5R, 7S, 8R)-(+)−8-(3,4-Dimethoxyphenyl)-2,9,9-trimethoxy-5-phenylsulfanyl-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 25. Pale oil (67%); $[\alpha]_D^{22}$ +126 (c 0.6 in CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$) 2941, 1731, 1617, 1462, 1374, 1128, 1046 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.50-0.75 (m, 21H, OSi(CH$_3$)$_2$), 1.75 (dd, $J$ 12.0, 6.0, 1H, CHH), 1.78-1.82 (m, 1H, CHH), 2.96 (dd, $J$ 4.4, 1H, 5-CH), 3.24 (s, 3H, OCH$_3$), 3.26 (dd, $J$ 10.4, 4.4, 1H, ArCH), 3.54 (s, 3H, OCH$_3$), 3.81 (s, 3H,
OCH₃), 3.83 (s, 3H, ArOC₃H₃), 3.84 (s, 3H, ArOC₃H₃), 4.13 (ddd, J 10.4, 10.4, 6.0, 1H, CHOSi(CH(CH₃)₂)₃), 5.61 (s, 1H, C=CH), 6.59 (d, J 2.0, 1H, ArH), 6.60 (dd, J 8.4, 2.0, 1H, ArH), 6.75 (d, J 8.4, 1H, ArH), 7.21-7.23 (m, 3H, 3 x SPhH), 7.76-7.78 (m, 2H, 2 x SPhH). \(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 12.4 (CH), 17.7 (CH₃), 41.0 (CH₂), 48.3 (CH), 50.3 (CH₃), 52.0 (CH), 52.2 (CH₃), 55.7 (CH₃), 55.8 (CH₃), 55.9 (CH₃), 66.1 (C), 69.2 (CH), 102.9 (C), 103.2 (CH), 110.9 (CH), 112.0 (CH), 120.7 (CH), 128.1 (CH), 128.4 (CH), 131.5 (C), 132.8 (C), 137.7 (CH), 148.0 (C), 148.5 (C), 174.5 (C), 198.0 (C); HRMS (ES) \(m/z\) 643.3098 [M + H]\(^+\), \([\text{C}_{35}\text{H}_{51}\text{O}_{7}\text{Si}]^+\) requires 643.3125.

\((1S, 5R, 7S, 8R)-(\pm)-8-(3,4-Dimethoxyphenyl)-2,9,9-trimethoxy-5-tributylstanny1-7-triisopropylsilyloxy-bicyclo[3.3.1]non-2-en-4-one 26. Clear oil (63%); \([\alpha]_D^{18} +96 (c 1.0 \text{ in CHCl}_3); v_{\text{max}} (\text{CHCl}_3) 2866, 1613, 1517, 1204, 1028, 830 \text{ cm}^{-1}; \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 0.70-0.99 (m, 27H, OSi(CH(CH₃)₂)₃), Sn(CH₂CH₂CH₂CH₃)₃), 1.24-1.69 (m, 21H, Sn(CH₂CH₂CH₂CH₃)₃), 2.21 (m, 2H, CH₂), 3.01 (dd, J 10.3, 3.9, 1H, ArCH), 3.18 (d, J 3.9, 1H, 5-CH), 3.29 (s, 3H, OCH₃), 3.42 (s, 3H, OCH₃), 3.56 (s, 3H, OCH₃), 3.83 (s, 3H, ArOCH₃), 3.86 (s, 3H, ArOCH₃), 4.19 (ddd, J 10.3, 10.3, 5.8, 1H, CHOSi(CH(CH₃)₂)₃), 5.52 (s, 1H, C=CH), 6.61 (d, J 1.6, 1H, ArH), 6.66 (dd, J 1.6, 8.0, 1H, ArH), 6.79 (d, J 8.0, 1H, ArH); \(^{13}\)C NMR (125 MHz, CDCl₃) \(\delta\) 12.0 (CH₂), 12.4 (CH), 13.8 (CH₃), 17.9 (CH₃), 18.0 (CH₃), 26.8 (CH₂), 29.1 (CH₂), 39.4 (CH₂), 47.0 (CH), 49.1 (CH), 53.1 (CH₃), 55.5 (CH₃), 55.8 (CH₃), 56.0 (CH₃), 58.6 (C), 69.2 (CH), 104.1 (C), 104.1 (CH), 111.0 (CH), 111.9 (CH), 121.0 (CH), 133.8 (C), 148.0 (C), 148.5 (C), 174.7 (C), 203.1 (C); HRMS (ESI) \(m/z\) 847.3972 [M+Na]\(^+\), \([\text{C}_{41}\text{H}_{72}\text{NaO}_{7}\text{SiSn}]^+\) requires 847.3962.

Compounds prepared using procedure B (Table 2)

\((1S, 5S, 7S, 8R)-(\pm)-8-(3,4-Dimethoxyphenyl)-2,9,9-trimethoxy-3-methyl-7-triisopropylsilyloxy-bicyclo[3.3.1]non-2-en-4-one 32. Clear viscous oil (36%); \([\alpha]_D^{20} +76 (c 0.5 \text{ in CHCl}_3); v_{\text{max}} (\text{CHCl}_3) 2961, 1713, 1356, 1090, 900 \text{ cm}^{-1}; \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 0.75-0.90 (m,
21H, OSi(CH(CH3)2)3), 1.78 (s, 3H, CH3), 1.83-1.91 (m, 1H, CHH), 2.15 (ddd, J 12.6, 9.2, 5.5, 1H, ArCH), 2.91 (s, 3H, OCH3), 2.91-2.94 (m, 1H, 1-C), 3.10 (s, 3H, OCH3), 3.17 (dd, J 10.5, 4.0, 1H, ArCH), 3.26-3.29 (m, 1H, 5-CH), 3.32 (s, 3H, OCH3), 3.84 (s, 3H, ArOCH3), 3.86 (s, 3H, ArOCH3), 4.19 (ddd, J 10.5, 10.5, 5.5, 1H, CHOSi(CH(CH3)2)3), 6.72 (d, J 1.8, 1H, ArH), 6.76 (dd, J 8.2, 1.8, 1H, ArH), 6.81 (d, J 8.2, 1H, ArH); 13C NMR (125 MHz, CDCl3) δ 7.3 (CH3), 12.6 (CH), 17.9 (CH3), 18.0 (CH3), 43.6 (CH3), 47.2 (CH3), 48.5 (CH3), 48.6 (CH), 49.2 (CH), 54.7 (CH3), 55.6 (CH3), 56.0 (CH3), 68.1 (CH), 101.1 (C), 111.1 (CH), 112.0 (CH), 116.1 (C), 121.0 (CH), 132.8 (C), 148.2 (C), 148.7 (C), 169.9 (C), 198.1 (C); HRMS (ES) m/z 549.3242 [M+H]+, [C30H48O7Si]+ requires 549.3247.

(1S, 5S, 7S, 8R)-(+)–3-Benzoyl-8-(3,4-dimethoxyphenyl)-2,9,9-trimethoxy-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 33. Pale yellow solid (60mg, 50%); [α]D20 +191 (c 0.5 in CHCl3); υmax (CHCl3) 2943, 1647, 1646, 1602, 1370, 1112, 1100, 1059, 1026, 882 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ 0.79-0.94 (m, 21H, OSi(CH(CH3)2)3), 1.89-1.98 (m, 1H, CHH), 2.22 (ddd, J 12.7, 9.2, 5.6, 1H, CHH), 2.99-3.03 (m, 1H, 1-C), 3.11 (s, 3H, OCH3), 3.19-3.26 (m, 2H, 5-CH, ArCH), 3.29 (s, 3H, OCH3), 3.38 (s, 3H, OCH3), 3.86 (s, 3H, ArOCH3), 3.92 (s, 3H, ArOCH3), 4.54 (ddd, J 10.6, 10.6, 5.6, 1H, CHOSi(CH(CH3)2)3), 6.80-6.91 (m, 3H, 3 x ArH), 7.46 (t, J 7.7, 2H, 2 x ArH), 7.54 (t, 7.0, 1H, ArH), 7.91 (d, J 7.3, 2H, 2 x ArH); 13C NMR (125 MHz, CDCl3) δ 12.6 (CH), 17.9 (CH3), 18.0 (CH3), 34.3 (CH2), 47.5 (CH3), 47.8 (CH), 48.6 (CH3), 49.0 (CH), 49.5 (CH), 55.9 (CH3), 56.0 (CH3), 57.3 (CH3), 67.9 (CH), 101.3 (C), 111.1 (CH), 111.1 (CH), 120.6 (CH), 121.4 (C), 128.6 (CH), 129.3 (CH), 132.7 (C), 133.3 (CH), 137.6 (C), 148.2 (C), 148.9 (C), 173.0 (C), 195.0 (C), 196.9 (C); HRMS (ES) m/z 639.3348 [M+H]+, [C36H51O8Si]+ requires 639.3353.

(1S, 5S, 7S, 8R)-(+)–8-(3,4-Dimethoxyphenyl)-2,9,9-trimethoxy-3-tri-tert-butylstannanyl-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 34. Clear oil (61%); [α]D24 +121 (c 1.5 in CHCl3); υmax (CHCl3) 2932, 2867, 1710, 1627, 1568, 1463, 1361, 1108, 882 cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 0.79-0.94 (m, 21H, OSi(CH(CH3)2)3), 1.89-1.98 (m, 1H, CHH), 2.22 (ddd, J 12.7, 9.2, 5.5, 1H, ArCH), 2.99-3.03 (m, 1H, 1-C), 3.11 (s, 3H, OCH3), 3.19-3.26 (m, 2H, 5-CH, ArCH), 3.29 (s, 3H, OCH3), 3.38 (s, 3H, OCH3), 3.86 (s, 3H, ArOCH3), 3.92 (s, 3H, ArOCH3), 4.54 (ddd, J 10.6, 10.6, 5.6, 1H, CHOSi(CH(CH3)2)3), 6.80-6.91 (m, 3H, 3 x ArH), 7.46 (t, J 7.7, 2H, 2 x ArH), 7.54 (t, 7.0, 1H, ArH), 7.91 (d, J 7.3, 2H, 2 x ArH); 13C NMR (125 MHz, CDCl3) δ 12.6 (CH), 17.9 (CH3), 18.0 (CH3), 34.3 (CH2), 47.5 (CH3), 47.8 (CH), 48.6 (CH3), 49.0 (CH), 49.5 (CH), 55.9 (CH3), 56.0 (CH3), 57.3 (CH3), 67.9 (CH), 101.3 (C), 111.1 (CH), 111.1 (CH), 120.6 (CH), 121.4 (C), 128.6 (CH), 129.3 (CH), 132.7 (C), 133.3 (CH), 137.6 (C), 148.2 (C), 148.9 (C), 173.0 (C), 195.0 (C), 196.9 (C); HRMS (ES) m/z 639.3348 [M+H]+, [C36H51O8Si]+ requires 639.3353.
CDCl$_3$ $\delta$ 0.75-1.01 (m, 33H, OSi(CH(CH$_3$)$_2$)$_3$), Sn(CH$_2$CH$_2$CH$_2$CH$_3$)$_3$, 1.25-1.36 (m, 9H, Sn(CH$_2$CH$_2$CH$_2$CH$_3$)$_3$), 1.45-1.54 (m, 6H, Sn(CH$_2$CH$_2$CH$_2$CH$_3$)$_3$), 1.81-1.86 (m, 1H, CH), 2.12 (ddd, $J$ 12.0, 9.0, 5.4, 1H, CHH), 2.83 (s, 3H, OCH$_3$), 2.84-2.89 (m, 1H, 1-CH), 3.04 (s, 3H, OCH$_3$), 3.14 (dd, $J$ 10.2, 3.8, 1H, ArCH), 3.23 (dd, $J$ 3.8, 2.4, 1H, 5-CH), 3.32 (s, 3H, OCH$_3$), 3.85 (s, 3H, ArOCH$_3$), 3.86 (s, 3H, ArOCH$_3$), 4.24 (ddd, $J$ 10.2, 10.2, 5.4, 1H, CHOSi(CH(CH$_3$)$_2$)$_3$), 6.76-6.83 (m, 3H, 3 x ArH); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 10.9 (CH), 12.3 (CH), 13.8 (CH$_3$), 17.9 (CH$_3$), 18.1 (CH$_3$), 27.4 (CH$_2$), 29.1 (CH$_2$), 34.1 (CH$_2$), 44.5 (CH), 47.3 (CH$_3$), 48.4 (CH), 48.5 (CH$_3$), 49.6 (CH), 54.3, 55.8 (CH$_3$), 56.0 (CH$_3$), 68.5 (CH), 102.0 (C), 111.2 (CH), 111.3 (CH), 119.0 (C), 133.1 (C), 148.2 (C), 148.8 (C), 180.0 (C), 202.0 (C); HRMS (ES) $m/z$ 847.3961 [M+Na]$^+$ [C$_{41}$H$_{72}$NaO$_7$SiSn]$^+$ requires 847.3967.

(1$S$, 5$R$, 7$S$, 8$R$)-(−)-5,3-Dibenzoyl-8-(3,4-dimethoxyphenyl)-2,9,9-trimethoxy-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-2-en-4-one 35. A solution of LTMP was prepared by adding $^n$BuLi (1.18 mL, 1.86 mmol, 1.6M solution in hexanes) to tetramethylpiperidine (0.38 mL, 1.86 mmol, 10 eq.) in THF (2 mL) at −78 °C. The solution was allowed to warm to RT and after 10 min re-cooled to −78 °C. This LTMP/THF solution was added dropwise via syringe to a solution of bridged ketone 16 (100 mg, 0.19 mmol) in THF (1 mL) at −78 °C resulting in a deep yellow-coloured solution. The solution was stirred at −78 °C for 3 h, followed by addition of benzoyl chloride (0.22 mL, 1.88 mmol, 10 eq.) and stirring for a further 3 h at −78 °C. The reaction mixture was quenched after this period with H$_2$O (5 mL) followed by extraction with EtOAc (3 x 5 mL). The organic layers were combined and washed with saturated aqueous NaCl (5 mL), dried (MgSO$_4$), and concentrated in vacuo. Purification by column chromatography (petroleum ether-EtOAc 4:1) gave the title compound 35 as a pale yellow solid (77 mg, 55%); [$\alpha$]$_D^{20}$ +161 (c 1.0 in CHCl$_3$); $\nu_{max}$ (CHCl$_3$) 2944, 2866, 1672, 1643, 1605, 1462, 1368, 1133, 1087, 1052, 882 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 0.82-0.98 (m, 21H, OSi(CH(CH$_3$)$_2$)$_3$), 2.39 (dd, $J$ 13.0, 5.6, 1H, CHH), 2.55-2.61 (m, 1H, CHH), 3.19 (s, 3H, OCH$_3$), 3.21 (s, 3H, OCH$_3$), 3.23
(s, 3H, OCH₃), 3.36 (d, J 4.5, 1H, 5-CH₃), 3.45 (dd, J 10.5, 4.5, 1H, ArCH), 3.86 (br s, 6H, ArOCH₃), 4.55 (td, J 10.5, 10.5, 5.6, 1H, CHOSi(CH(CH₃)₂)₃), 6.81 (d, J 8.2, 1H, ArH), 6.91-6.92 (m, 2H, ArH, ArH), 7.20-7.25 (m, 2H, ArH, ArH), 6.81 (d, J 8.2, 1H, ArH), 7.20-7.25 (m, 2H, ArH, ArH), 6.81-6.92 (m, 2H, ArH, ArH); 13C NMR (125 MHz, CDCl₃) δ 12.6 (CH), 17.9 (CH₃), 39.8 (CH₂), 49.0 (CH₃), 49.1 (CH), 49.7 (CH), 50.1 (CH₃), 55.9 (CH₃), 57.4 (CH₃), 67.6 (CH), 68.6 (C), 103.1 (C), 111.2 (CH), 120.1 (CH), 121.5 (C), 127.1 (CH), 128.6 (CH), 129.3 (CH), 130.7 (CH), 130.9 (CH), 131.8 (CH), 132.4 (C), 133.6 (CH), 137.7 (C), 137.7 (C), 148.2 (C), 149.0 (C), 172.8 (C), 194.5 (C), 196.1 (C), 199.3 (C); HRMS (ES) m/z 743.3610 [M+H]+, [C₄₃H₆₅O₉Si]+ requires 743.3615.

(1R, 5R, 7S, 8R)-(-)-8-(3,4-Dimethoxyphenyl)-4,9,9-trimethoxy-7-triisopropylsilanyloxy-3-trimethylsilylanyl-bicyclo[3.3.1]non-3-en-2-one 36. According to procedure A. Clear oil (31%); [α]D 30 −40 (c 0.4 in CHCl₃); υ max (CHCl₃) 2869, 1661, 1540, 1469, 1376, 1149, 1110, cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 0.22 (s, 9H, Si(CH₃)₃), 0.72-0.94 (m, 21H, OSi(CH(CH₃)₂)₃), 2.00-2.02 (m, 2H, CH₂), 2.86 (dd, J 3.9, 1H, 5-CH₃), 3.00 (dd, J 10.8, 3.9, 1H, ArCH), 3.12 (s, 3H, OCH₃), 3.17-3.20 (m, 1H, 1-C₃H), 3.32 (s, 3H, OCH₃), 3.83 (s, 9H, OCH₃), 4.32-4.38 (m, 1H, CHOSi(CH(CH₃)₂)₃), 6.55-6.57 (m, 2H, 2 x ArH), 6.73 (d, J 8.1, 1H, ArH); 13C NMR (125 MHz, CDCl₃) δ 0.78 (CH₃), 12.6 (CH), 17.9 (CH₃), 19.1 (CH₃), 32.3 (CH₂), 37.7 (CH), 47.1 (CH₃), 48.6 (CH₃), 50.2 (CH), 54.9 (CH₃), 55.9 (CH₃), 57.5 (CH), 68.7 (CH), 100.7 (C), 110.8 (CH), 112.8 (CH), 117.4 (C), 121.5 (CH), 132.6 (C), 147.8 (C), 148.4 (C), 179.9 (C), 200.3 (C); HRMS (ES) m/z 607.3479 [M+H]+, [C₃₂H₅₅O₇Si₂]+ requires 607.3486.

(1R, 5R, 7S, 8R)-(-)-8-(3,4-Dimethoxyphenyl)-4,9,9-trimethoxy-3-methyl-7-triisopropylsilanyloxy-bicyclo[3.3.1]none-3-en-2-one 37. According to procedure A. Clear viscous oil (60%); [α]D 22 −40 (c 1.0 in CHCl₃); υ max (CHCl₃) 2940, 1651, 1623, 1462, 1380, 1357, 1101, 1028, 882 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.70-0.90 (m, 21H, OSi(CH(CH₃)₂)₃), 1.79 (s, 3H, CH₃), 1.97-2.09
(m, 2H, CH$_2$), 2.96 (dd, J 4.2, 2.2, 1H, 5-CH), 3.02 (dd, J 10.5, 4.2, 1H, ArCH), 3.10 (s, 3H, CH$_3$), 3.18-3.22 (m, 1H, 1-CH), 3.32 (s, 3H, OCH$_3$), 3.81 (br s, 6H, ArOC$_3$H$_3$), 3.87 (s, 3H, OCH$_3$), 4.26 (ddd, J 10.5, 10.5, 5.2, 1H, CH/OSi(CH(CH$_3$)$_3$)$_3$), 6.51 (br s, 1H, ArH), 6.53 (d, J 1.9, 1H, ArH), 6.74 (d, J 7.9, 1H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 7.46 (CH$_3$), 12.6 (CH), 17.9 (CH$_3$), 18.0 (CH$_3$), 31.9 (CH$_2$), 37.4 (CH), 47.1 (CH$_3$), 48.6 (CH$_3$), 50.0 (CH), 55.4 (CH$_3$), 55.6 (CH$_3$), 55.8 (CH$_3$), 56.4 (CH), 68.7 (CH), 100.5 (C), 110.9 (CH), 112.7 (CH), 116.2 (CH), 121.2 (C), 132.4 (C), 147.8 (C), 148.2 (C), 168.8 (C), 197.0 (C); HRMS (ES) $m/z$ 549.3248 [M+H]$^+$, [C$_{30}$H$_{49}$O$_7$Si]$^+$ requires 549.3248.

(1$^R$, 5$^R$, 7$^S$, 8$^R$)-(−)-8-(3,4-Dimethoxyphenyl)-4,9,9-trimethoxy-3-(prenyl)-7-triisopropylsilanyloxy-bicyclo[3.3.1]non-3-en-2-one 38. According to procedure A. Yellow oil (25%); [$\alpha$]$_D^{30}$ +11 (c 0.9 in CHCl$_3$); $\nu_{\text{max}}$ (CHCl$_3$) 2940, 1670, 1630, 1469, 1349, 1111, 1035, 890 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 0.85 (m, 21H, OSi(CH(CH$_3$)$_3$)$_2$), 1.69 (s, 3H, CH$_3$), 1.75 (s, 3H, CH$_3$), 1.98-2.04 (m, 1H, 6-CH$_2$H), 2.05-2.10 (m, 1H, 6-CH$_2$H), 2.92-2.97 (m, 2H, CH$_2$CH=CH(CH$_3$)$_2$), 3.00 (dd, J 10.6, 4.1, 1H, ArCH), 3.11 (s, 3H, OCH$_3$), 3.15-3.22 (m, 2H, 1-CH, 5-CH), 3.3 (s, 3H, OCH$_3$), 3.80 (s, 3H, ArOCH$_3$), 3.82 (s, 3H, ArOCH$_3$), 3.88 (s, 3H, OCH$_3$), 4.33 (ddd, J 10.6, 10.6, 5.5, 1H, CHOSi(CH(CH$_3$)$_3$)$_3$), 5.17 (t, J 7.0, 1H, CH=CH(CH$_3$)$_2$), 6.53-6.57 (m, 2H, 2 x ArH), 6.70 (d, J 8.7, 1H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 12.6 (CH), 17.8 (CH$_3$), 18.0 (CH$_3$), 21.4 (CH$_2$), 25.7 (CH$_3$), 32.5 (CH$_2$), 37.1 (CH), 47.1 (CH$_3$), 48.5 (CH$_3$), 50.3, (CH), 55.2 (CH$_3$), 55.7 (CH$_3$), 55.9 (CH$_3$), 56.5 (CH), 68.5 (CH), 100.6 (C), 110.9 (CH), 113.0 (CH), 120.6 (C), 121.6 (CH), 122.2 (CH), 131.7 (C), 132.6 (C), 147.8 (C), 148.3 (C), 168.4 (C), 196.0 (C); HRMS (ES) $m/z$ 603.3711 [M+H]$^+$, [C$_{34}$H$_{55}$O$_7$Si]$^+$ requires 603.3717.

(1$^R$, 3$^S$, 8$^R$, 9$^R$, 10$^S$)-(−)-9-(3,4-Dimethoxy-phenyl)-3-(1-hydroxy-1-methyl-ethyl)-12,12-dimethoxy-10-triisopropylsilanyloxy-4-oxa-tricyclo[6.3.1.0$^{15}$]$^{15}$dodec-5-en-7-ones 39 and (1$^R$, 3$^R$, 8$^R$, 9$^R$, 10$^S$)-(−)-9-(3,4-Dimethoxy-phenyl)-3-(1-hydroxy-1-methyl-ethyl)-12,12-dimethoxy-10-
triisopropylsilanyloxy-4-oxa-tricyclo[6.3.1.01.5]dodec-5-en-7-ones 40. Dimethyldioxirane (15 mL, 0.05 M in acetone) was added to substrate 18 (180 mg, 0.29 mmol) in CH₂Cl₂ (4 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 3.5 h. MgSO₄ was then added to the solution which was filtered, then concentrated in vacuo. The crude orange oil was re-dissolved in CH₂Cl₂ (4 mL), cooled to 0 °C, then trimethylsilyl chloride (0.045 ml, 1.2 eq.) added and the reaction mixture was further stirred for 2 h. The reaction was quenched with saturated aqueous NH₄Cl (6 mL), the organic layer was separated and washed with saturated NaCl (8 mL), extracted with CH₂Cl₂ (2 x 10 mL), dried over MgSO₄, and concentrated in vacuo to give a 2:1 mixture of diastereoisomers. Purification by column chromatography (EtOAc-petroleum ether 1:9) gave firstly 40 as a white solid (115 mg, 66%); mp 82-85 °C; [α]D¹⁸ −0.6 (c 1.0 in CHCl₃); v max (CHCl₃) 2865, 1632, 1578, 1184, 1088, 836 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.84 (m, 21H, OSi(CH(CH₃)₂)₃), 1.25 (s, 3H, CH₃), 1.40 (s, 3H, CH₃), 1.80 (m, 2H, 11-CH₂H, 2-CHH), 2.49 (dd, J 13.1, 5.5, 1H, 11-CHH), 2.83 (dd, J 12.3, 10.5, 1H, 2-CHH), 2.97 (dd, J 4.3, 0.8, 1H, 8-CH), 3.17 (s, 3H, OCH₃), 3.28 (dd, J 10.8, 4.3, 1H, ArCH), 3.35 (s, 3H, OCH₃), 3.82 (s, 3H, ArOCH₃), 4.32 (m, 2H, CHOSi(CH(CH₃)₂)₃, CHC(CH₃)₂OH), 5.72 (s, 1H, C=CH), 6.63 (m, 2H, ArH, ArH), 6.76 (d, J 8.0, 1H, ArH); ¹³C NMR (100 MHz, CDCl₃) δ 12.6 (CH), 17.9 (CH₃), 18.1 (CH₃), 25.7 (CH₃), 27.2 (CH₃), 30.0 (CH₂), 40.2 (CH₂), 49.2 (CH₃), 49.4 (CH), 53.0 (C), 55.7 (CH₃), 56.0 (CH₃), 57.7 (CH), 69.7 (CH), 70.8 (C), 91.0 (CH), 101.6 (CH), 103.4 (CH), 110.9 (CH), 113.2 (CH), 121.3 (C), 132.2 (C), 147.9 (C), 148.4 (C), 181.5 (C), 197.1 (C); HRMS (ES) m/z 605.3504 [M+H]⁺, [C₃₃H₅₃O₈Si]⁺ requires 605.3509; and secondly 39 as a clear oil (47 mg, 27%); [α]D²² +27 (c 1.65 in CH₂Cl₂); v max (CHCl₃) 831, 968, 1028, 1053, 1088, 1518, 1632, 2865, 2921 3583 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.76-0.94 (m, 21H, OSi(CH(CH₃)₂)₃), 1.25 (s, 3H, CH₃), 1.38 (s, 3H, CH₃), 1.75 (dd, J 12.0, 5.6, 1H, 2-CHH), 1.95 (dd, J 12.8, 10.7, 1H, 11-CHH), 2.10 (dd, J 12.8, 5.6, 1H, 11-CHH), 2.74-2.82 (m, 1H, 2-CHH), 2.97 (d, J 4.4, 1H, 8-CH), 3.16 (s, 3H, OCH₃), 3.29 (dd, J 10.7, 4.4, 1H, ArCH), 3.35 (s, 3H, OCH₃), 3.82 (s, 3H, ArOCH₃), 3.85 (s, 3H, ArOCH₃), 4.39 (ddd, J 10.7, 10.7, 5.6, 1H, CHOSi(CH(CH₃)₂)₃), 4.49 (dd, J 10.7, 5.6, 1H, CH(CH₃)₂OH), 5.68 (s, 1H, C=CH),
6.62 (d, J 1.9, 1H, ArH), 6.65 (dd, J 8.2, 1.9, 1H, ArH), 6.78 (d, J 8.2, 1H, ArH); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 12.6 (CH), 17.9 (CH$_3$), 18.1 (CH$_3$), 24.1 (CH$_3$), 26.7 (CH$_3$), 31.4 (CH$_2$), 38.0 (CH$_2$), 49.1 (CH$_3$), 49.8 (CH), 53.9 (C), 55.7 (CH$_3$), 55.9 (CH$_3$), 57.5 (CH), 69.1 (CH), 71.2 (C), 90.2 (CH), 100.7 (C), 101.8 (CH), 110.8 (CH), 113.0 (CH), 121.1 (CH), 132.1 (C), 147.9 (C), 148.3 (C), 181.2 (C), 197.1 (C); HRMS (ES) m/z 604.3433 [M]$^+$, [C$_{33}$H$_{52}$O$_8$Si]$^+$ requires 604.3431.

(1$R$, 3$S$, 8$R$, 9$R$, 10$S$)-(-)-9-(3,4-Dimethoxyphenyl)-12,12-dimethoxy-3-(1-methyl-1-trimethylsilyloxyethyl)-10-triisopropylsilanyloxy-4-oxa-tricyclo[6.3.1.0$_{1.5}$]dodec-5-en-7-one 41 and (1$R$, 3$R$, 8$R$, 9$R$, 10$S$)-(+-)-9-(3,4-Dimethoxyphenyl)-12,12-dimethoxy-3-(1-methyl-1-trimethylsilyloxyethyl)-10-triisopropylsilanyloxy-4-oxa-tricyclo[6.3.1.0$_{1.5}$]dodec-5-en-7-one 42. Imidazole (110 mg, 10 eq.), DMAP (6 mg, 10 mol %), and trimethylsilyl chloride (0.10 mL, 0.81 mmol, 5 eq.) were added to a solution of tricyclic compounds 39 and 40 (98 mg, 0.16 mmol, 1:2 diastereoisomeric mixture) in DMF (0.5 mL) at 0 °C was added respectively. The reaction mixture was stirred for 2 h at 0 °C after which time the reaction was complete by TLC. Purification by column chromatography (10% EtOAc in petroleum ether) afforded firstly title compound 42 as a clear oil (70 mg, 65%); [α]$_{22}^D$ +57 (c 1.25 in CHCl$_3$); $\nu$_max (CHCl$_3$) 2927, 1736, 1628, 1604, 1369, 1112, 1057, 998, 883 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 0.00 (s, 9H, Si(CH$_3$)$_3$), 0.81 (m, 21H, OSi(CH$_3$)$_2$)$_3$, 1.32 (s, 3H, CH$_3$)$_3$, 1.33 (s, 3H, CH$_3$)$_3$, 1.74 (dd, J 12.8, 6.3, 1H, 2-CH$_2$), 1.87 (dd, J 12.9, 10.2, 1H, 11-CH$_2$), 2.16 (dd, J 12.9, 5.6, 1H, 11-CHH), 2.77 (dd, J 12.8, 10.1, 1H, 2-CHH), 2.96 (dd, J 4.3, 0.8, 1H, 8-CH), 3.16 (s, 3H, OCH$_3$), 3.29 (dd, J 10.8, 4.3, 1H, ArCH), 3.37 (s, 3H, OCH$_3$), 3.83 (s, 3H, ArOCH$_3$), 3.84 (s, 3H, ArOCH$_3$), 4.18 (dd, J 10.1, 6.3, 1H, CHC(CH$_3$)$_2$OSi), 4.35 (ddd, J 10.2, 10.2, 5.6, 1H, CHOSi(CH(CH$_3$)$_2$)$_3$), 5.70 (d, J 0.9, 1H, C=CH), 6.68 (m, 2H, 2 x ArH), 6.76 (d, J 8.0, 1H, ArH); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 2.5 (CH$_3$), 12.7 (CH), 18.0 (CH$_3$), 18.1 (CH$_3$), 25.4 (CH$_3$), 27.4 (CH$_3$), 30.1 (CH$_2$), 41.3 (CH$_2$), 49.2 (CH$_3$), 49.3 (CH$_3$), 49.5 (CH), 52.8 (C), 55.7 (CH$_3$), 55.9 (CH$_3$), 57.6 (CH), 69.7 (CH), 73.5 (C), 91.5 (CH), 101.7 (C), 101.7 (CH), 103.7 (CH), 110.9 (CH), 113.2 (CH), 132.2 (C),
147.9 (C), 148.4 (C), 181.6 (C), 197.0 (C); HRMS (ES) m/z 677.3905 [M+H]^+, \[C_{36}H_{60}O_8Si_2\]^+ requires 677.3905; and then title compound 41 as a clear oil (33 mg, 30%); [\(\alpha\)]_D^{22} −10 (c 1.75 in CHCl_3); \(\nu_{\text{max}}\) (CHCl_3) 2865, 1730, 1631, 1462, 1137, 1047, 883 cm\(^{-1}\); \(1H\) NMR (400 MHz, CDCl_3) \(\delta\) 0.16 (s, 9H, Si(CH_3)_3), 0.69-0.92 (m, 21H, OSi(CH(CH_3)_2)_3), 1.32 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.74 (dd, J 12.7, 6.3, 1H, 2-CH/H), 1.86 (dd, J 12.8, 10.8, 1H, 11-CH/H), 2.15 (dd, J 12.8, 5.6, 1H, 11-CH/H), 2.77 (dd, J 12.7, 10.2, 1H, 2-CH/H), 2.96 (d, J 4.3, 1H, 8-CH), 3.17 (s, 3H, OCH_3), 3.29 (dd, J 10.8, 4.3, 1H, ArCH), 3.37 (s, 3H, OCH_3), 3.82 (s, 3H, ArOCH_3), 3.83 (s, 3H, ArOCH_3), 4.18 (dd, J 10.2, 6.3, 1H, 3-CH), 4.35 (ddd, J 10.8, 10.8, 5.6, 1H, CHOSi(CH(CH_3)_2)_3), 5.70 (s, 1H, C=CH), 6.62-6.66 (m, 2H, 2 x ArH), 6.76 (d, J 8.0, 1H, ArH); \(^{13}C\) NMR (100 MHz, CDCl_3) \(\delta\) 2.5 (CH_3), 12.6 (CH), 18.0 (CH_3), 18.1 (CH_3), 25.3 (CH_3), 27.3 (CH_3), 30.1 (CH_2), 41.3 (CH_2), 49.2 (CH_3), 49.3 (CH_3), 49.5 (CH), 52.8 (C), 55.6 (CH_3), 55.9 (CH_3), 57.6 (CH), 69.7 (CH), 73.4 (C), 91.3 (CH), 101.6 (C), 103.6 (CH), 110.8 (CH), 113.1 (CH), 121.3 (CH), 132.2 (C), 147.8 (C), 148.3 (C), 181.6 (C), 197.0 (C); HRMS (ES) m/z 677.3905 [M+H]^+, \[C_{36}H_{60}O_8Si_2\]^+ requires 677.3905.

\((R, \, 3R, \, 8R, \, 9R, \, 10S)-(\cdot)-6\text{-Bromo-9-(3,4-dimethoxyphenyl)-12,12-dimethoxy-3-(1-methyl-1-trimethylsilanyloxy-ethyl)-10-triisopropylsilanyloxy-4-oxa-tricyclo[6.3.1.0^{1,5}]dodec-5-en-7-one 44.}\n
\(N\)-Bromosuccinimide (66 mg, 0.370 mmol, 10 eq.) was added to tricyclic compound 42 (25 mg, 0.037 mmol) in CCl_4 (2 mL) at 0 °C. The reaction mixture was stirred for 3 h at 0 °C, then at RT for 16 h. The solution was diluted with CH_2Cl_2 (5 mL), washed with saturated Na_2CO_3 (aq.), dried (MgSO_4), then concentrated in vacuo. Purification by column chromatography (petroleum ether-EtOAc 5:1) gave the title compound 44 as a yellow oil (20 mg, 65%); [\(\alpha\)]_D^{24} −11 (c 0.5 in CHCl_3); \(\nu_{\text{max}}\) (CHCl_3) 2866, 1668, 1619, 1463, 1379, 1064, 980, 882 cm\(^{-1}\); \(1H\) NMR (400 MHz, CDCl_3) \(\delta\) 0.00 (s, 9H, Si(CH_3)_3), 0.80-0.96 (m, 21H, OSi(CH(CH_3)_2)_3), 1.38 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.87 (dd, J 12.7, 6.3, 1H, 2-CH/H), 1.97 (dd, J 12.9, 10.1, 1H, 11-CH/H), 2.24 (dd, J 12.9, 5.6, 1H, 11-CH/H), 2.92 (dd, J 12.7, 10.1, 1H, 2-CH/H), 3.19-3.20 (m, 1H, CH), 3.21 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.83 (s, 3H, ArOCH_3),...
3.84 (s, 3H, ArOCH₃), 3.97 (dd, J 10.1, 4.4, 1H, ArCH), 4.27-4.37 (m, 2H, CHC(CH₃)₂OSi(CH₃)₃, CHOSi(CH(CH₃)₂)₃), 6.35 (s, 1H, ArH), 7.00 (s, 1H, ArH); ¹³C NMR (100 MHz, CDCl₃) δ 2.8 (CH₃), 13.0 (CH), 18.1 (CH₃), 18.3 (CH₃), 25.8 (CH₃), 27.4 (CH₃), 31.2 (CH₂), 41.4 (CH), 47.7 (CH), 49.7 (CH), 50.1 (CH₃), 55.5 (C), 56.0 (CH₃), 56.4 (CH₃), 56.6 (CH₃), 69.5 (CH), 73.7 (C), 92.9 (CH), 96.6 (C), 101.1 (C), 112.8 (CH), 115.8 (CH), 117.0 (C), 130.3 (C), 147.7 (C), 148.5 (C), 178.0 (C), 189.4 (C); HRMS (ESI) m/z 833.2121 [M+H]+, [C₃₆H₅₉Br₂O₈Si₂]⁺ requires 833.2037.

7-(tert-Butyl-dimethyl-silanyloxy)-8-(3,4-dihydroxy-phenyl)-2-methoxy-bicyclo[3.3.1]non-2-ene-4,9-dione 46 and 7-(tert-butyl-dimethyl-silyloxy)-8-(3,4-dihydroxy-phenyl)-4-methoxy-bicyclo[3.3.1]non-3-ene-2,9-dione 47. To a solution of crude catechinic acid (8) (4.30 g, 13.7 mmol) in DMF (100 mL) was added DMAP (15.0 g, 123 mmol, 9 eq.) followed by TBSCl (12.5 g, 82.0 mmol, 6 eq.). The resulting mixture was stirred at RT for 48 h. The reaction mixture was then filtered through a short pad of celite, rinsing with DMF (4 mL). To the resulting brown solution was added K₂CO₃ (18.0 g, 130 mmol, 9.5 eq.), then Me₂SO₄ (6.60 mL, 65.0 mmol, 5 eq.) and the reaction mixture was stirred 1 h at RT, then 2 h at 80 °C. The solid was filtered off and DMF was removed under high vacuum. The residue was diluted with AcOEt, and washed with a saturated aqueous NH₄Cl solution. The aqueous phase was then extracted twice with AcOEt. The combined organic phases were washed with brine, dried (MgSO₄) and concentrated in vacuo to give the crude product as a brown oil. Purification by flash column chromatography (petroleum ether-EtOAc 9:1 to 7:3) afforded a white foam (4.40 g). To this solid (550 mg, 852 µmol) in MeCN (20 mL) was added (HF)₃.Et₃N (300 µL, 1.88 mmol) and the resulting mixture was stirred at RT overnight. The reaction was quenched with saturated aqueous NaHCO₃ solution, and extracted with AcOEt. The combined organic layers were dried over MgSO₄ and concentrated in vacuo to give the crude product as a beige solid. Purification by flash column chromatography (petroleum ether-CH₂Cl₂-EtOAc 4:4:2 to 4:2:4) afford compound 46 (amorphous white solid, 170 mg, 24%); [α]D²⁰ +191.3 (c = 1.1, CHCl₃); νmax (CHCl₃) 3599, 2930, 1735, 1650, 1597, 1374,
1108 /cm\(^{-1}\); ¹H NMR (CDCl\(_3\), 400 MHz) \(\delta\) -0.35 (s, 3H, MeSi), -0.05 (s, 3H, MeSi), 0.62 (s, 9H, \(^1\)Bu), 1.95 (dd, \(J\) 13.2, 10.5, 4.4, 1H, CH\(Hax\)-CHOTBS), 2.49 (ddd, \(J\) 13.2, 5.5, 3.2, 1H, CH\(Heq\)-CHOTBS), 3.04 (dd, \(J\) 10.5, 4.5, 1H, CH-Ar), 3.30 (m, 2H, 2 C=O-CH), 3.66 (s, 3H, OMe), 4.30 (td, \(J\) 10.5, 5.5, 1H, CH-OTBS), 5.18 (br s, 1H, ArOH), 5.33 (br s, 1H, ArOH), 5.78 (s, 1H, CH=C(OMe)), 6.52 (dd, \(J\) 8.0, 2.0, 1H, ArH), 6.61 (d, \(J\) 2.0, 1H, ArH), 6.79 (d, \(J\) 8.0, 1H, ArH), 13C NMR (CDCl\(_3\), 125 MHz) \(\delta\) -5.3, -4.4, 17.7, 25.4, 38.9, 54.0, 56.6, 59.0, 59.5, 67.5, 105.0, 115.0, 115.3, 120.5, 131.5, 143.0, 143.9, 157.7, 195.9, 204.4; HRMS (EI) \(m/z\) 419.1894 [M+H\(^+\)] requires 419.1890; and then compound 47 (amorphous white solid, 121 mg, 17%); \(\alpha\)\(_D\)\(^{20}\) +66.3 (c = 0.7, CHCl\(_3\)); \(\nu\)\(_{\max}\) (CHCl\(_3\)) 3552, 2929, 1736, 1650, 1601, 1460, 1375, 1110 cm\(^{-1}\); ¹H NMR (CDCl\(_3\), 500 MHz) \(\delta\) -0.41 (s, 3H, MeSi), -0.08 (s, 3H, MeSi), 0.62 (s, 9H, \(^1\)Bu), 1.97 (dd, \(J\) 13.5, 10.5, 4.0, 1H, CH\(Hax\)-CHOTBS), 2.44 (ddd, \(J\) 13.5, 5.5, 3.0, 1H, CH\(Heq\)-CHOTBS), 3.04 (dd, \(J\) 10.5, 4.5, 1H, CH-Ar), 3.30 (br s, 1H, C=O-CH), 3.42 (br d, \(J\) 4.5, 1H, C=O-CH-C=O), 3.89 (s, 3H, OMe), 4.31 (td, \(J\) 10.5, 5.5, 1H, CH-OTBS), 5.84 (s, 1H, CH=C(OMe)), 6.15 (br s, 1H, ArOH), 6.38 (dd, \(J\) 8.0, 2.0, 1H, ArH), 6.53 (d, \(J\) 2.0, 1H, ArH), 6.59 (d, \(J\) 8.0, 1H, ArH), \(\alpha\)\(_D\)\(^{20}\) +164.7 (c = 0.95, CHCl\(_3\)); \(\nu\)\(_{\max}\) (CHCl\(_3\)) 3552, 2929, 1736, 1650, 1601, 1460, 1375, 1110 cm\(^{-1}\); ¹H NMR (CDCl\(_3\), 400 MHz) \(\delta\) -0.35 (s, 3H, MeSi), -0.05 (s, 3H, MeSi), 0.62 (s, 9H, \(^1\)Bu), 1.95 (dd, \(J\) 13.2, 10.5, 4.4, 1H, CH\(Hax\)-CHOTBS), 2.49 (ddd, \(J\) 13.2, 5.5, 3.2, 1H, CH\(Heq\)-CHOTBS), 3.04 (dd, \(J\) 10.5, 4.5, 1H, CH-Ar), 3.30 (m, 2H, 2 C=O-CH), 3.66 (s, 3H, OMe), 4.30 (td, \(J\) 10.5, 5.5, 1H, CH-OTBS), 5.18 (br s, 1H, ArOH), 5.33 (br s, 1H, ArOH), 5.78 (s, 1H, CH=C(OMe)), 6.52 (dd, \(J\) 8.0, 2.0, 1H, ArH), 6.61 (d, \(J\) 2.0, 1H, ArH), 6.79 (d, \(J\) 8.0, 1H, ArH), 13C NMR (CDCl\(_3\), 125 MHz) \(\delta\) -5.3, -4.4, 17.7, 25.4, 38.9, 54.0, 56.6, 59.0, 59.5, 67.5, 105.0, 115.0, 115.3, 120.5, 131.5, 143.0, 143.9, 157.7, 195.9, 204.4; HRMS (EI) \(m/z\) 419.1894 [M+H\(^+\)] requires 419.1890; and then compound 47 (amorphous white solid, 121 mg, 17%); \(\alpha\)\(_D\)\(^{20}\) +66.3 (c = 0.7, CHCl\(_3\)); \(\nu\)\(_{\max}\) (CHCl\(_3\)) 3552, 2929, 1736, 1650, 1601, 1460, 1375, 1110 cm\(^{-1}\); ¹H NMR (CDCl\(_3\), 500 MHz) \(\delta\) -0.41 (s, 3H, MeSi), -0.08 (s, 3H, MeSi), 0.62 (s, 9H, \(^1\)Bu), 1.97 (dd, \(J\) 13.5, 10.5, 4.0, 1H, CH\(Hax\)-CHOTBS), 2.44 (ddd, \(J\) 13.5, 5.5, 3.0, 1H, CH\(Heq\)-CHOTBS), 3.04 (dd, \(J\) 10.5, 4.5, 1H, CH-Ar), 3.30 (br s, 1H, C=O-CH), 3.42 (br d, \(J\) 4.5, 1H, C=O-CH-C=O), 3.89 (s, 3H, OMe), 4.31 (td, \(J\) 10.5, 5.5, 1H, CH-OTBS), 5.84 (s, 1H, CH=C(OMe)), 6.15 (br s, 1H, ArOH), 6.38 (dd, \(J\) 8.0, 2.0, 1H, ArH), 6.53 (d, \(J\) 2.0, 1H, ArH), 6.59 (d, \(J\) 8.0, 1H, ArH), \(\alpha\)\(_D\)\(^{20}\) +164.7 (c = 0.95, CHCl\(_3\)); \(\nu\)\(_{\max}\) (CHCl\(_3\))

\((-\))\(\text{-3-[(1S, 2R, 3S, 5R)-3-(tert-Butyl-dimethyl-silyloxy)-8-methoxy-6-oxo-bicyclo[3.3.1]non-7-en-2-yl]-hexa-2,4-dienedioic acid dimethyl ester 48.}\) To a solution of catechol 44 (100 mg, 239 µmol) in MeOH / toluene (800 µL, 1:1) was added a solution of freshly recrystallised Pb(OAc)\(_4\) (233 mg, 526 µmol, 2.2 eq.) in MeOH-toluene (1.4 mL, 1:1). The solution was stirred at RT for 36 h, then the solvents were evaporated. The residue was dissolved in AcOEt-H\(_2\)O, the phases separated, and the aqueous layer extracted with AcOEt. The organic phase was dried (MgSO\(_4\)) and concentrated in vacuo to give crude product as a yellow oil. Purification by flash column chromatography (petroleum ether-EtOAc 3:2 to 1:1) afforded diester 48 as a colorless oil (105 mg, 92%); \(\alpha\)\(_D\)\(^{30}\) +164.7 (c = 0.95, CHCl\(_3\)); \(\nu\)\(_{\max}\) (CHCl\(_3\))
2953, 2931, 2858, 2830, 1730, 1680, 1595, 1362, 1105 /cm -1; 1H NMR (CDCl3, 400 MHz) δ 0.00 (s, 3H, MeSi), 0.02 (s, 3H, MeSi), 0.81 (s, 9H, tBu), 1.87 (ddd, J 12.8, 10.5, 4.4, 1H, CHH-CHOTBS), 2.41 (ddd, J 12.8, 5.5, 3.6, 1H, CHH-CHOTBS), 2.96 (dd, J 10.5, 3.6, 1H, CH-CHOTBS), 3.22 (br s, 1H, CH2-CH-C=O), 3.65 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.73 (overlap, 1H, CH-C=O), 3.76 (s, 3H, OMe), 4.08 (td, J 10.5, 5.5, 1H, CHOTBS), 5.66 (d, J 2.0, 1H, C=CH-CO2Me), 5.75 (s, 1H, CH=C(OMe)), 5.91 (d, J 12.4, 1H, CH=CH-CO2Me), 7.02 (dd, 1H, J 12.4, 2.0, 1H, CH=CH-CO2Me); 13C NMR (CDCl3, 100 MHz) δ -5.1, -3.9, 17.8, 25.7, 38.4, 51.5, 51.6, 53.9, 55.6, 56.7, 59.3, 68.5, 105.7, 118.6, 120.4, 144.5, 153.1, 165.5, 165.7, 174.3, 194.5, 202.8; HRMS (ES) m/z found 497.2098 [M+H]+ [C24H35O8Si]+ requires 479.2101.

(1S, 5R, 7S, 8R)-(+-)7-(tert-Butyl-dimethyl-silanyloxy)-8-(3,4-dioxo-cyclohexa-1,5-dienyl)-4-methoxy-bicyclo[3.3.1]non-3-ene-2,9-dione 49. To a solution of catechol 47 (300 mg, 0.72 mmol) in THF (50 mL) was added Fetizon’s reagent (Ag2CO3 on celite, ~50% w/w, 1.6 g, 2.87 mmol, 4 eq.), and the resulting suspension was vigorously stirred at 60 °C for 3 h. The solid was filtered off, and the filtrate was evaporated under vacuo. The title compound 49 was obtained as an amorphous green solid (290 mg, 96%); [α]D 20 +132.0 (c = 0.3, CHCl3); νmax (CHCl3) 2955, 1711, 1666, 1599, 1361, 1111 cm-1; 1H NMR (CDCl3, 500 MHz) δ -0.04 (s, 3H, MeSi), 0.03 (s, 3H, MeSi), 0.74 (s, 9H, tBu), 1.96 (ddd, J 13.5, 10.5, 4.0, 1H, CHHax-CHOTBS), 2.45 (ddd, J 13.5, 5.5, 3.5, 1H, CHeqH-CHOTBS), 2.88 (dd, J 10.5, 5.5, 1H, CH-Ar), 3.31 (m, 1H, C=O-CH), 3.34 (m, 1H, C=O-CH), 3.87 (s, 3H, OMe), 4.27 (td, J 10.5, 5.5, 1H, CH-OTBS), 5.77 (s, 1H, CH=C(OMe)), 6.17 (br d, J 2.0, 1H, C=CH-C=O), 6.37 (d, J 10.0, 1H, CH-CH-C=O), 6.82 (dd, J 10.0, 2.0, 1H, CH-CH-C=O); 13C NMR (CDCl3, 100 MHz) δ -5.0, -4.0, 17.8, 25.5, 36.2, 51.4, 54.5, 57.5, 63.5, 66.1, 105.2, 129.2, 129.6, 140.7, 150.0, 175.9, 178.9, 179.7, 190.3, 201.7.
(−)-4-[(1S, 2R, 3S, 5R)-3-(tert-Butyl-dimethyl-silanyloxy)-6-methoxy-8,9-dioxo-bicyclo[3.3.1]non-6-en-2-yl]-furan-2-carboxylic acid methyl ester 50. To a solution of quinone 49 (100 mg, 240 µmol) in iPrOH (3.5 mL) and H2O (1.5 mL) was added NaIO4 (900 mg, 4. mmol, 18 eq) and OsO4 (240 µL, 10% in tBuOH, 24 µmol, 0.1 eq.). The resulting mixture was stirred at rt overnight, then the white precipitate was removed by filtration, and the filtrate diluted with AcOEt and NH4Cl aq. The phases were separated, and the aqueous layer extracted with AcOEt (4 × 10 mL). The organic phases were dried (MgSO4) and concentrated in vacuo to give crude acid as a yellow solid (106 mg). This crude acid was dissolved in acetone, and treated with K2CO3 (100 mg, 720 µmol, 3 eq) and Me2SO4 (46 µL, 480 µmol, 2 eq). The mixture was stirred at rt for 3 h, then the solid was removed by filtration and the solvent evaporated. The residue was purified by column chromatography (petroleum ether-EtOAc 7:3) to provide furan 50 (50 mg, 47%); mp 197-199 °C (petroleum ether-AcOEt); [α]D20 + 30.3 (c = 0.9, CHCl3); νmax (CHCl3) 2955, 2858, 1731, 1658, 1603, 1364, 1323, 1110 cm−1; 1H-NMR (CDCl3, 500 MHz) δ -0.31 (s, 3H, MeSi), -0.08 (s, 3H, MeSi), 0.70 (s, 9H, tBu), 1.94 (ddd, J 13.5, 11.0, 4.0, 1H, CHHax-CHOTBS), 2.40 (ddd, J 13.5, 5.0, 3.0, 1H, CHeqH-CHOTBS), 3.05 (ddd, J 10.5, 4.0, 1H, CH-furan), 3.26 (br s, 1H, C=O-CH), 3.36 (m, 1H, C=O-CH), 3.85 (s, 3H, OMe), 3.86 (s, 3H, OMe), 4.06 (td, J 10.5, 5.5, 1H, CH-OTBS), 5.78 (s, 1H, CH=C(OMe)), 7.01 (s, 1H, CH=C), 7.47 (s, 1H, CH=C); 13C-NMR (CDCl3, 125 MHz) δ -5.0, -4.5, 17.7, 25.4, 37.1, 46.4, 51.6, 51.9, 57.2, 65.2, 68.5, 105.2, 118.6, 124.8, 144.1, 144.5, 159.0, 175.7, 192.3, 203.1; HRMS (EI) m/z found 435.1828 [M+H]+ [C22H31O7Si]+ requires 435.1839.