Supporting information

Synthesis of the Southern Furan Segment of Furanocembranoids

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Experimental procedures

Compound 5 and 6 are prepared according to reported procedures.\textsuperscript{1,2}

2-((tert-Butyldiphenylysiloyloxy)methyl)-3-methylbutan-1-ol (8):

To argon flushed two-neck round-bottomed flask equipped with addition funnel, reflux condenser and drying tube, was added LiAlH\textsubscript{4} (1.9 g, 49.5 mmol) and dry THF (60 mL, drop wise addition). To this mixture, diethyl isopropylmalonate 7 (5 g, 24.7 mmol) in dry THF (50 mL) was added over 1 h at room temperature and the mixture was stirred for 3 days at reflux temperature. The mixture was cooled to 0 °C and quenched with saturated aq. sodium sulphate (30 mL), filtered, and concentrated under reduced pressure. The obtained crude diol was used for next step, without purification. Diol in CH\textsubscript{2}Cl\textsubscript{2} (60 mL) was added to the stirred solution of imidazole (2.02 g, 44.5 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (30 mL) and stirred at room temperature for 1 h. TBDPSCl (6.79 g, 24.7 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (30 mL) was added drop wise to the reaction mixture and stirring continued for 3 h at room temperature. The mixture was diluted with ether (20 mL), washed successively with aq. saturated K\textsubscript{2}CO\textsubscript{3} (2 x 20 mL) and brine (20 mL). The organic extract was concentrated and the residue was purified by column chromatography (EtOAc:hexanes = 1:3) to give the alcohol 8 (7.47 g, 85%) as colorless liquid. IR (neat): 2929, 2362, 1468, 1367, 1110, 1020 cm\textsuperscript{-1}. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz): δ 7.69 (ddd, J = 8.8, 7.0, 6.4 Hz, 4H), 7.48 – 7.35 (m, 6H), 3.87 – 3.71 (m, 4H), 2.72 (s, 1H), 1.71 (dd, J = 13.6, 6.8 Hz, 1H), 1.61 – 1.49 (m, 2H), 1.11 – 1.04 (m, 9H), 0.84 (dd, J = 17.1, 6.8 Hz, 6H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz): δ 135.6, 133.1, 133.0, 129.9, 127.8, 66.3, 64.7, 48.2, 26.9, 26.3, 20.3, 20.2, 19.1.

MS (ESI): \textit{m/z} 379 (M+Na)\textsuperscript{+}. HRMS (ESI): \textit{m/z} calcd for C\textsubscript{22}H\textsubscript{32}O\textsubscript{2}Si Na (M + Na)\textsuperscript{+}: 379.2064, found: 379.2049.
**(E)-9-Isopropyl-2,2,3,3,13,13-hexamethyl-12,12-diphenyl-4,11-dioxo-3,12-disilatetradec-7-en-6-one (9):**

To a stirred solution of alcohol 8 (6.25 g, 17.6 mmol) in CH₂Cl₂ (50 mL), Dess-Martin periodinane (8.93 g, 21.1 mmol) was added. Stirring continued for 1 h at 0 °C, and quenched with saturated aq Na₂S₂O₅ (5 mL). The aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The residue was used directly in next step. To a solution of ketophosphonate 6 (5.17 g, 17.6 mmol) in THF (50 mL) was treated with Ba(OH)₂·8H₂O (6.65 g, 21.1 mmol) and stirred for 30 min at room temperature. A solution of aldehyde in wet THF 20 mL (THF:H₂O = 40:1) was added and the reaction stirred for 12 h. The crude reaction mixture was diluted with CH₂Cl₂ (50 mL) and quenched with a saturated aq. NaHCO₃ (30 mL). The solution was stirred until two layers were clearly visible. The organic layer was collected and washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The product was purified using column chromatography (SiO₂, 95:5 = hexanes:EtOAc) to afford the enone 9 (6.9 g, 73%) in two steps as clear oil. IR (neat): 2930, 2334, 1701, 1630, 1430, 1259, 705 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz): δ 7.60–7.49 (m, 4H), 7.38–7.23 (m, 6H), 6.80 (dd, J = 15.9, 9.4 Hz, 1H), 6.27 (d, J = 15.9 Hz, 1H), 4.24 (d, J = 2.6 Hz, 2H), 3.67–3.53 (m, 2H), 2.09 (dt, J = 15.4, 5.9 Hz, 1H), 1.82 (dq, J = 13.5, 6.7 Hz, 1H), 0.94 (s, 9H), 0.71 (d, J = 6.8 Hz, 3H), 0.01–0.01 (m, 6H). ¹³C NMR (CDCl₃, 100 MHz): δ 197.1, 147.4, 134.6, 132.5, 128.8, 128.7, 0.83 (d, J = 2.8 Hz, 9H), 0.78 (d, J = 6.8 Hz, 3H) 126.7, 126.0, 67.6, 63.6, 51.0, 27.2, 25.8, 25.7, 24.8, 19.8, 18.3, 18.2, 17.4, -6.4. MS (ESI): m/z 547 (M+Na)+.

HRMS (ESI): m/z calcd for C₃₁H₄₈O₅Si₂Na (M + Na)+: 547.3034, found: 547.3028.
9-Isopropyl-2,2,3,3,13,13-hexamethyl-12,12-diphenyl-4,11-dioxo-3,12-disilatetradecan-6-one (4):

To a stirred solution of compound 9 (5.3 g, 10 mmol) in EtOAc (20 mL) was added Pd/C (10 mol%) and stirring continued for 40 min at room temperature, after completion of reaction (monitored by TLC) mixture was filter throw a small pad of celite and the residue was concentrated under reduced pressure. The crude residue was purified by column chromatography (1:9 = EtOAc:hexanes) provide the saturated ketone product 4 (5.15 g, 98%) as colorless oil. IR (neat): 2957, 2863, 1726, 1469, 1256, 1008, 841, 750 cm⁻¹.

¹H NMR (CDCl₃, 300 MHz): δ 7.58 (dd, J = 6.7, 1.2 Hz, 4H), 7.41 – 7.26 (m, 6H), 4.03 (d, J = 17.4 Hz, 2H), 3.51 (d, J = 5.6 Hz, 2H), 2.42 – 2.25 (m, 2H), 1.77 (td, J = 12.9, 6.6 Hz, 1H), 1.61 (dd, J = 14.2, 10.2, 5.5 Hz, 1H), 1.45 (dd, J = 14.1, 8.4 Hz, 1H), 1.30 – 1.20 (m, 2H), 0.98 (s, 9H), 0.86 – 0.82 (m, 9H), 0.78 (dd, J = 13.8, 6.9 Hz, 6H), -0.01 (d, J = 14.4 Hz, 6H). ¹³C NMR (CDCl₃, 100 MHz): δ 210.9, 135.7, 135.7, 133.9, 133.8, 129.6, 127.6, 69.3, 64.5, 46.1, 36.8, 28.3, 26.9, 25.8, 21.7, 20.0, 19.3, 18.4, -5.4. MS (ESI): m/z 549 (M+Na)⁺. HRMS (ESI): m/z calcld for C₃₁H₅₀O₃₀Si₂Na (M + Na)⁺: 549.3196, found: 549.3196.

9-Isopropyl-6-(4-(4-methoxybenzyloxy)pent-1-ynyl)-2,2,3,3,13,13-hexamethyl-12,12-diphenyl-4,11-dioxo-3,12-disilatetradecan-6-ol (10):

To a solution of terminal alkyne 5 (2.2 g, 9.0 mmol) in dry THF (15 mL), was added n-butyl lithium (2.5 M solution, 4.36 mL, 10.9 mmol) at -78 °C, stirring for 30 min and solution of saturated ketone 9 (4.8 g, 1.0 mmol) in dry THF (20 mL) and stirring continued for 1 h, after completion of reaction (monitored by TLC), the reaction mixture was diluted with a saturated aqueous NH₄Cl solution (30 mL) and extracted with ethyl acetate (2 x 20 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and
concentrated under reduced pressure. The crude residue was purified by column chromatography (1:9 = EtOAc:hexanes) afforded product 10 (5.65 g, 86%) as colorless oil. IR (neat): 2930, 2334, 1615, 1466, 1252, 1107, 705 cm⁻¹. ¹H NMR (CDCl₃, 500 MHz): δ 7.66 (d, J = 6.6 Hz, 4H), 7.44 – 7.34 (m, 6H), 7.29 – 7.21 (m, 2H), 6.86 (d, J = 8.5 Hz, 2H), 4.48 – 4.41 (m, 2H), 3.79 (d, J = 4.1 Hz, 3H), 3.66 – 3.55 (m, 4H), 3.47 (ddd, J = 19.1, 9.5, 2.0 Hz, 1H), 2.73 (d, J = 23.3 Hz, 1H), 2.53 (dd, J = 16.4, 4.6 Hz, 1H), 2.27 (ddd, J = 16.4, 8.1, 4.7 Hz, 1H), 1.87 (dd, J = 12.7, 5.9 Hz, 1H), 1.66 – 1.58 (m, 1H), 1.54 – 1.44 (m, 3H), 1.37 – 1.22 (m, 5H), 1.04 (s, 9H), 0.89 (d, J = 1.6 Hz, 9H), 0.87 – 0.79 (m, 6H), 0.16 – 0.01 (m, 6H). ¹³C NMR (CDCl₃, 100 MHz): δ 159.1, 135.6, 133.9, 130.7, 129.5, 129.2, 127.6, 113.8, 82.9, 81.7, 73.4, 71.4, 70.3, 70.1, 69.9, 64.6, 64.5, 55.3, 46.8, 46.7, 36.5, 28.1, 27.9, 26.9, 26.3, 25.9, 22.4, 22.2, 20.1, 20.0, 19.7, 19.3, 19.2, 18.4, -5.3, -5.4. MS (ESI): m/z 753 (M+Na)⁺. HRMS (ESI): m/z calcd for C₄₄H₆₆O₅Si₂Na (M + Na)⁺: 753.4341, found: 753.4339.

2-(3-((tert-Butyldiphenylsilyloxy)methyl)-4-methylpentyl)-6-(4-methoxybenzyloxy)hept-3-yn-1,2-diol (11): To a solution of 10 (5.3 g, 7.3 mmol) in CH₂Cl₂:MeOH (1:1, 50 mL) was added PPTS (546 mg, 2.17 mmol) and stirred for 15 h, reaction mixture quenched with water (30 mL) extracted with CH₂Cl₂ (3x10 mL). Solvent was evaporated under reduced pressure and purified by SiO₂ column (EtOAc:hexane = 2:8) to give 11 (2.94 g, 90%) colorless oil. IR (neat): 2930, 2863, 2362, 1888, 1614, 1250, 1038, 705 cm⁻¹. ¹H NMR (CDCl₃, 500 MHz): δ 7.71 – 7.61 (m, 4H), 7.46 – 7.33 (m, 5H), 7.29 – 7.20 (m, 2H), 6.87 (t, J = 5.7 Hz, 2H), 4.52 – 4.40 (m, 2H), 3.84 – 3.76 (m, 3H), 3.70 – 3.54 (m, 4H), 3.49 – 3.36 (m, 1H), 2.54 – 2.30 (m, 2H), 1.84 (ddd, J = 11.5, 8.1, 5.7 Hz, 2H), 1.64 – 1.47 (m, 4H), 1.34 (d, J = 3.2 Hz, 1H), 1.30 – 1.20 (m, 4H), 1.05 (s, 9H), 0.90 – 0.78 (m, 6H). ¹³C NMR (CDCl₃, 75 MHz): δ 159.2, 135.7, 133.9, 130.5, 129.6, 129.2, 127.6, 113.8, 83.1, 82.5, 77.4, 77.2, 77.0, 76.6, 72.9, 72.2, 70.3, 70.1, 64.6, 64.5,
55.3, 46.7, 46.7, 36.0, 28.3, 28.2, 26.9, 26.2, 22.4, 22.3, 20.0, 19.6, 19.5, 19.4, 19.3, 0.0. MS (ESI): \textit{m/z} 639 \ (M+Na)^{\dagger}. HRMS (ESI): \textit{m/z} \text{ calcd for } C_{38}H_{52}O_5SiNa \ (M + Na)^{\dagger}: 639.3476, \text{ found: } 639.3471.

References

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[2] Miyatake-Ondozabal, H.; Barrett, A. G. M. \textit{Org. Lett.} 2010, \textit{12}, 5573.
$^1$H NMR Spectrum compound 8 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum of compound 8 (125 MHz, CDCl$_3$)
$^1$H NMR Spectrum compound 9 (400 MHz, CDCl$_3$)
\(^{13}\text{C}\) NMR Spectrum of compound 9 (125 MHz, CDCl\(_3\))
$^1$H NMR Spectrum compound 4 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum of compound 4 (125 MHz, CDCl$_3$)
$^1$H NMR Spectrum compound 10 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum of compound 10 (125 MHz, CDCl$_3$)
$^1$H NMR Spectrum compound 11(400 MHz, CDCl$_3$)
$^1$H NMR Spectrum compound 11(125 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum compound 12 (125 MHz, CDCl$_3$)
$^1$H NMR Spectrum compound 2 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum compound 2 (125 MHz, CDCl$_3$)