Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Continuous-flow synthesis of activated vitamin D_3 and its analogues

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1. General Techniques.

The microreactors were made of quartz and had a channel that is 200 μm deep, 1 mm wide, and 250 mm long with a volume of 50 μL. The microreactors were stored in the holders those were made of PEEK. Syringe pump (SSC-3710) and its regulating system (SSC-3792) was purchased from Senshu Scientific Co. Ltd. The microreactors and syringe pump were connected with PEEK tubing (Figure 1). 400W High-pressure mercury lamp, a Vycor filter and a glass UV filter (U-360) were purchased from Riko Kagaku Sangyo.

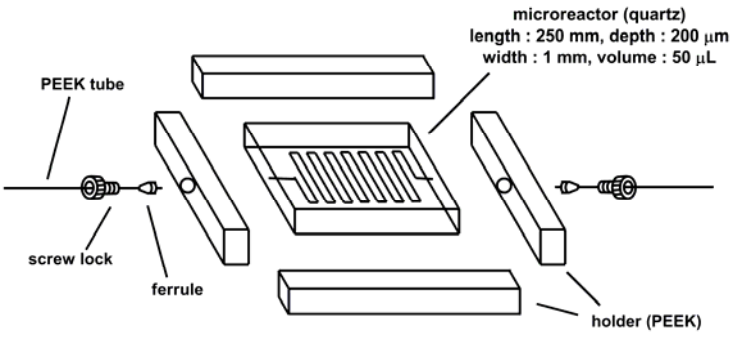

Figure1

2. Preparative HPLC conditions.

Preparative HPLC was carried on a Waters 515 HPLC pump using a Senshu Pak Silica-3301-N column (8ϕ x 300 mm) with a SHISEIDO SI-2/3002 and Shodex RI-71.

Vitamin D_2 (11)

10% EtOAc in hexane, flow rate 2 mL/min, retention time 44.3 min.

25-Hydroxyvitamin D_3 (12)

20% EtOAc in hexane, flow rate 2 mL/min, retention time 66.0 min.

1α-Hydroxyvitamin D_3 (13)

7% ^{i}PrOH in hexane, flow rate 2 mL/min, retention time 57.2 min.

1α, 25-Dihydroxyvitamin D_3 (2)

50% EtOAc in hexane, flow rate 3 mL/min, retention time 67.8 min.

Then, 7% ^{i}PrOH in hexane, flow rate 3 mL/min, retention time 96.5 min.

1α-Hydroxy-25-trimethylsilyloxyvitamin D_3 (25)

7% ^{i}PrOH in hexane, flow rate 2 mL/min, retention time 44.6 min.

3. NMR spectra.

3β-*tert*-Butyldimethylsilyloxy-5α,8α-(1,4-dioxo-1,2,3,4-tetrahydro-phthalazine-2,3-diyl)ergosta-6,22-diene (14)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (m, 2H), 7.68 (m, 2H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.25 (d, *J* = 8.3 Hz, 1H), 5.19 (m, 2H), 3.93 (dd, *J* = 12.7, 8.2, 1H), 3.88 (dd, *J* = 14.6, 4.9 Hz, 1H), 3.58 (m, 1H), 1.02 (s, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.80-0.84 (m, 9H), 0.09 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 159.6, 138.5, 135.3, 132.6, 132.5, 132.1, 130.6, 130.2, 128.7, 127.0, 126.5, 77.2, 68.5, 67.4, 67.1, 56.5, 50.6, 49.0, 44.2, 42.7, 40.4, 39.9, 39.3, 35.6, 34.7, 33.0, 30.5, 28.2, 25.9, 24.5, 21.9, 20.8, 19.9, 19.7, 18.5, 18.0, 17.4, 13.3, -4.4, -4.9; IR (neat): 2957, 2872, 1653, 1603, 1462, 1311, 1093, 837, 762 cm^{-1}.

3β-*tert*-Butyldimethylsilyloxy-22-hydroxy-23,24-bisnorchola-5,7-diene (16)

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55 (d, *J* = 5.4 Hz, 1H), 5.39 (m, 1H), 3.65 (dd, *J* = 10.5, 3.2, 1H), 3.58 (m, 1H), 3.40 (dd, *J* = 10.8, 6.8 Hz, 1H), 1.08 (d, *J* = 6.4 Hz, 3H), 0.94 (s, 3H), 0.89 (s, 9H), 0.64 (s, 3H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 119.1, 116.4, 71.2, 67.9, 54.2, 52.1, 46.3, 43.0, 41.3, 39.0, 38.5, 37.1, 32.4, 27.6, 25.9, 23.1, 21.1, 18.2, 16.9, 16.3, 11.9, -4.6; IR (neat): 3293, 2938, 2857, 1459, 1378, 1365, 1255, 1095, 878, 838, 774 cm^{-1}.

3β-*tert*-Butyldimethylsilyloxy-22-tosyloxy-23,24-bisnorchola-5,7-diene (17)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 5.54 (d, *J* = 4.9 Hz, 1H), 5.36 (m, 1H), 3.98 (dd, *J* = 9.6, 3.2, 1H), 3.81 (dd, *J* = 9.6, 6.1 Hz, 1H), 3.58 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 3H), 0.89 (s, 9H), 0.58 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 140.9, 140.3, 133.1, 129.7, 127.9, 119.1, 116.6, 75.5, 71.2, 54.0, 51.4, 46.1, 43.0, 41.3, 38.8, 38.5, 37.0, 36.4, 32.3, 27.3, 25.9, 22.9, 21.6, 21.0, 18.2, 16.9, 16.3, 11.7, -4.6; IR (neat): 2955, 2936, 2856, 1599, 1463, 1360, 1255, 1189, 1176, 1097, 965, 837, 669 cm^{-1}.