Supporting Information

Continuous-Flow Synthesis of Vitamin D_3

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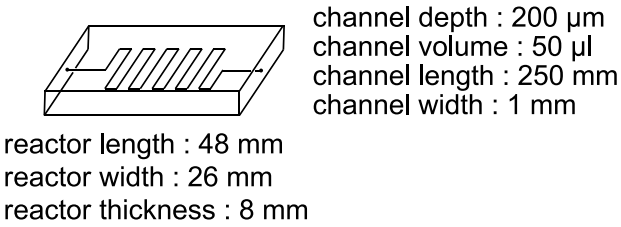
1. General Techniques.

Provitamin D_3 (7-dehydrocholesterol) was purchased from Aldrich. Vitamin D_3, 1,4-dioxane, toluene and butanol were purchased from TCI. All chemical reagents were used as received. Analytical high-performance liquid chromatography (HPLC) was carried on a Waters 2695 Separation Module using a Senshu Pak PEGASIL Silica-3301-N (8Φ × 300 mm) or Daicel Chiralpak AD-H (4.6Φ × 250 mm) with a Waters 2996 Photodiode Array Detector. Preparative HPLC was carried on a Waters 515 HPLC Pump using a Senshu Pak PEGASIL Silica 60-5 (20Φ ×

250 mm) with a SSC-5200 and Shodex RI-71. UV absorption was measured with a Perkin-Elmer Lambda 40 UV/VIS spectrometer. The custom-made microreactors, a syringe pump (SSC-3710) and its regulating system (SSC-3792) were purchased from Senshu Scientific Co. Ltd.

Microreactor is made of quartz and has a channel that is 200 μm deep, 1 mm wide, and 250 mm long with a volume of 50 μL (Figure 1).



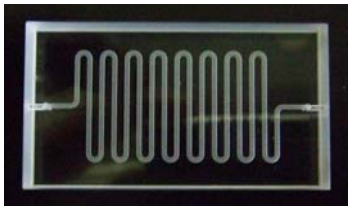
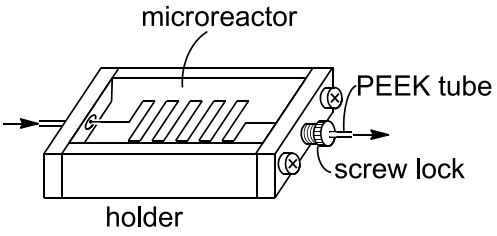


Figure 1.

The microreactors and syringe pump (Senshu Scientific Co. Ltd. SSC-3710) were connected with PEEK tubing. The microreactors were stored in the holders those were made of PEEK (Figure 2).



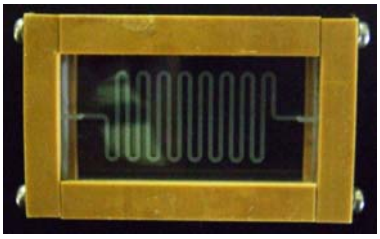


Figure 2.

400 W high-pressure mercury lamp, a Vycor filter and a glass UV filter (U-360) were purchased

from Riko Kagaku Sangyo. The irradiation at 360 nm was generated by using a 400 W high-pressure mercury lamp with a Vycor filter and a glass UV filter.

2. Experimental Detail

Photolysis of provitamin D_3 (3) (batch reactor, HPLC-UV yield). A solution of provitamin D_3 (**3**) (77 mg, 0.20 mmol, 20 mM) in 10 mL of THF was added into a quartz test tube (13Φ). The solution was irradiated with 400 W high-pressure mercury lamp with a Vycor filter at －10 °C for 150 min. Then 5μL of the mixture was collected and analyzed by HPLC. The composition of products was calculated based on the relative UV absorption after allowance was made for the extinction coefficient (Table 2) at 282 nm.

vitamin D_3 (**1**): 2%, provitamin D_3 (**3**): 50%, previtamin D_3 (**4**): 20%, lumisterol (**5**): 25%, tachysterol (**6**): 3%

High-performance liquid chromatography. Reaction products were analyzed by HPLC eluted with 20% ethyl acetate in hexane at a constant flow rate of 3 mL/min and the column was kept at 30 °C. The composition of products was calculated based on the relative UV absorption after allowance was made for the extinction coefficient at 282 nm (Table 2). Retention time of reaction products was shown in Table 1.

compound	vitamin D_3 (**1**)	provitamin D_3 (**3**)	previtamin D_3 (**4**)
Retention time (min)	13.4	15.9	8.4
compound	lumisterol (**5**)	tachysterol (**6**)	*trans*-vitamin D_3 (**7**)
Retention time (min)	10.7	12.7	8.6

Table 1.

3. Physical Data

Molar extinction coefficient. Molar extinction coefficient of reaction products was measured in 20% ethyl acetate in hexane. Provitamin D_3 (**3**) and vitamin D_3 (**1**) were used as received. Previtamin D_3 (**4**), lumisterol (**5**), tachysterol (**6**) and *trans*-vitamin D_3 (**7**) were prepared in our laboratory by the photo-isomerization of provitamin D_3 (**3**) or vitamin D_3 (**1**).

Preparation of previtamin D_3 (4), lumisterol (5) and tachysterol (6). Provitamin D_3 (**1**) (76.9 mg, 0.200 mmol) in THF (10.0 ml) was irradiated with 400 W high-pressure mercury lamp with a Vycor filter at －10 °C for 150 min. The reaction mixture was concentrated in vacuo and the crude residue was subjected to preparative HPLC (10% ethyl acetate in hexane, flow rate; 6 mL/min) yielding previtamin D_3 (**4**) (16.8 mg, 0.0436 mmol, 21%), lumisterol (**5**) (11.7 mg, 0.0304 mmol, 15%) and tachysterol (**6**) (6.5 mg, 0.017 mmol, 9%).

Preparation of *trans*-vitamin D_3 (7). Vitamin D_3 (**1**) (76.9 mg, 0.200 mmol) in THF (10.0 ml)

was irradiated with 400 W high-pressure mercury lamp with a Vycor filter at －10 °C for 180 min. The reaction mixture was concentrated in vacuo and the crude residue was subjected to preparative HPLC (10% ethyl acetate in hexane, flow rate; 6 mL/min) yielding *trans*-vitamin D_3 (7.2 mg, 0.019 mmol, 9%). The determined molar extinction coefficient of reaction products at 282 nm was shown in the Table 2.

compound	vitamin D_3 (**1**)	provitamin D_3 (**3**)	previtamin D_3 (**4**)
ε [l/mol·cm]	8900	9400	4900
compound	lumisterol (**5**)	tachysterol (**6**)	*trans*-vitamin D_3 (**7**)
ε [l/mol·cm]	5000	20000	22000

Table 2.