Supporting Information

Synthesis of Novel Vitamin K_2 Analogues with Modification at the ω-Terminal Position and their Biological Evaluation as Potent Steroid and Xenobiotic Receptor (SXR) Agonists

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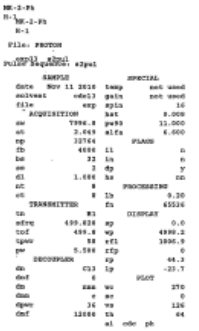
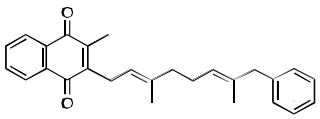
Contents:

I. ^{1}H and ^{13}C NMR chart of compound 10 and 11

^{1}H NMR chart of compound **10**





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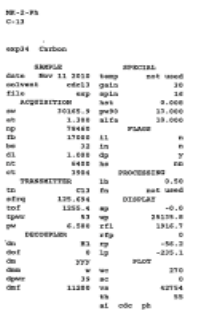
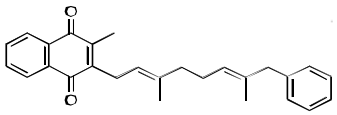
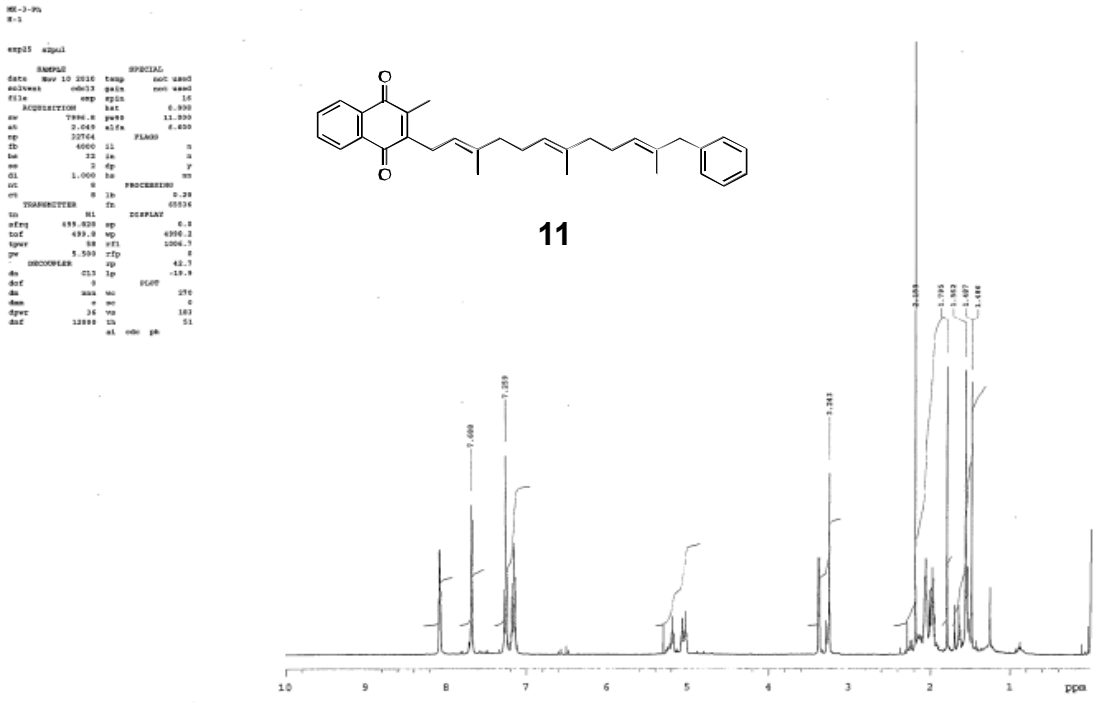
^{13}C NMR chart of compound **10**



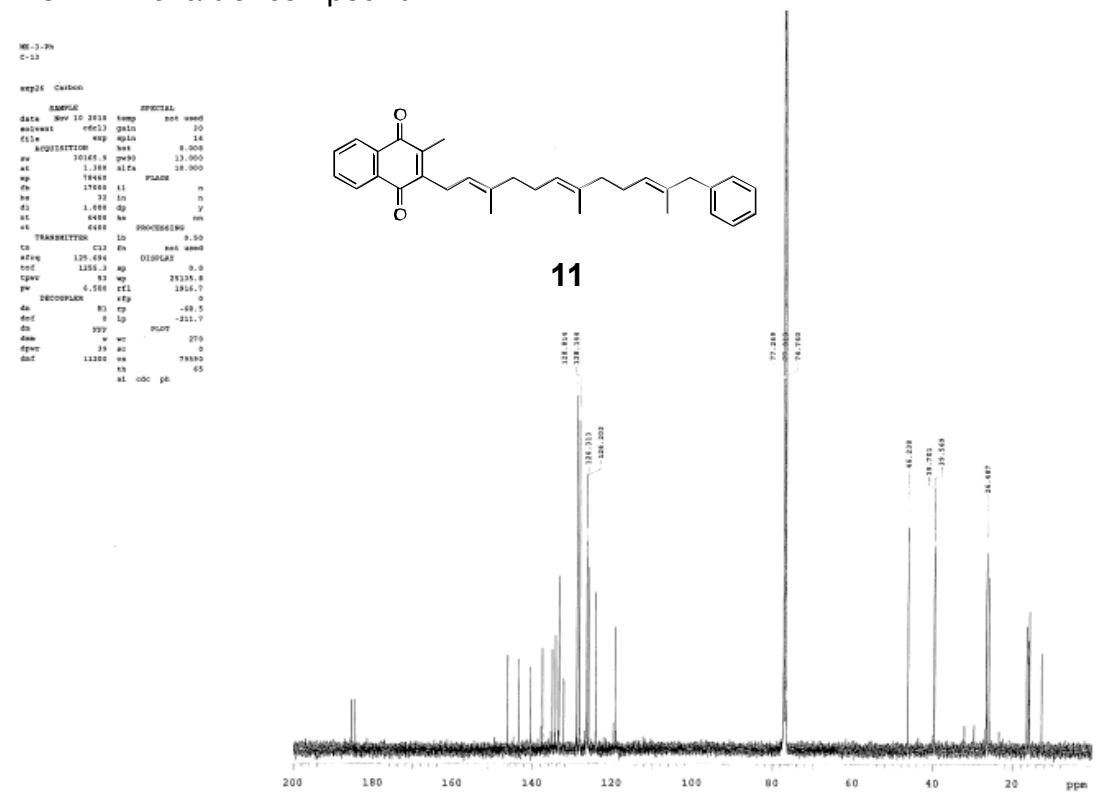


10

^{1}H NMR chart of compound **11**



^{13}C NMR chart of compound **11**



II. A comprehensive statement of confirming purity and the method

The purity of compound **3**-**11** was confirmed by following method. The HPLC analyses were conducted with a Shimadzu HPLC system (Simadzu, Kyoto, Japan) consisting of a binary pump (LC-20AD liquid chromatography), an automatic solvent degasser (DGU-20A_3 degasser), and a manualinjector. Separations were carried out using a reversed-phase C_{18} analytical column (COSMOSIL 5C_{18}-AR-II; 4.6 mm i.d. × 250 mm) (Nakalai tesque, Kyoto, Japan) with a solvent system consisting of an isocratic solvent. The solvent contained either methanol, ethanol, or water was delivered at 1.0 mL/min. This mobile phase was passed through the column at 1.0 mL/min. The column was maintained at 40 °C with a column oven (CTO-20A column oven). Vitamin K analogues were detected at 258 nm with an SPD-M20A diode array detector. The HPLC system was controlled by a CBM-20A System Controller (Shimadzu).

Table 1 overview the results of detection and the purity of the compound **3** – **11**. The purity of the each compound was calculated from a surface integral of detected peaks. Those purities were satisfied more than 95%.

Table 1. Results of HPLC detection and purity.

compound	isocratic solvent (v/v)	retention time (min)	purity (%)
3	MeOH / H_2O = 90 : 10	6.838	99
4	MeOH / H_2O = 95 : 5	7.568	98
5	MeOH / H_2O = 95 : 5	11.963	96
6	MeOH	9.115	99
7	MeOH / H_2O = 80 : 20	9.760	96
8	MeOH / H_2O = 90 : 10	8.273	97
9	MeOH / H_2O = 90 : 10	15.604	98
10	MeOH / H_2O = 95 : 5	9.334	98
11	MeOH / H_2O = 95 : 5	15.406	99

III. HPLC data of compound 3 - 11 used in biological assays

Sample: **3** (MK-1)

Sample Size: 20 μL (2.1 mg / 2 mL-EtOH)

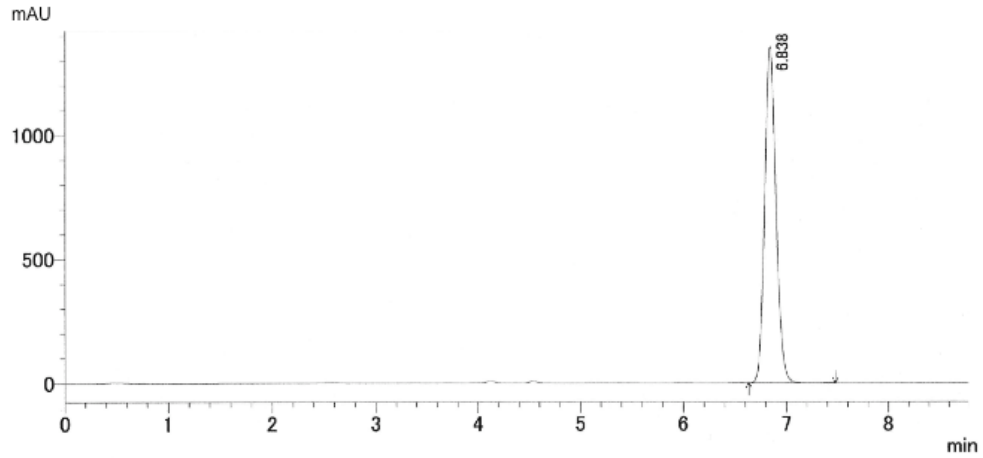
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 90 : 10, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.9 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 6.838 min

Purity: 99%



Sample: **4** (MK-2)

Sample Size: 20 μL (3.2 mg / 2 mL-EtOH)

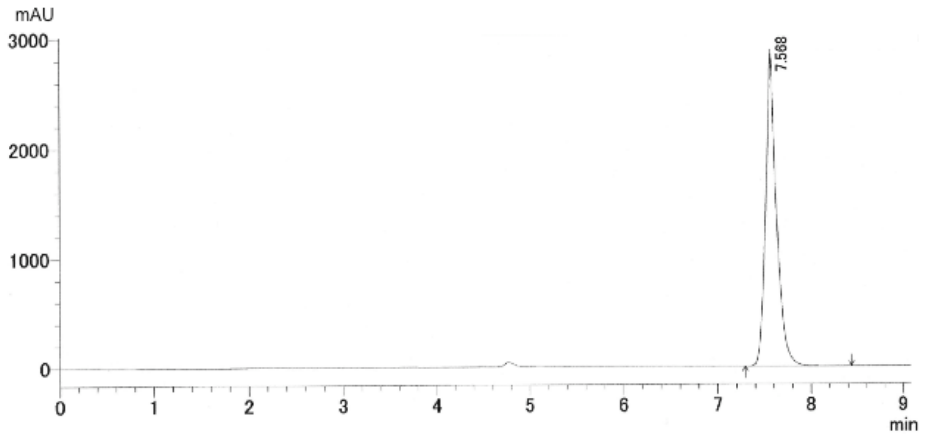
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 95 : 5, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.0 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 7.568 min

Purity: 98%



Sample: **5** (MK-3)

Sample Size: 20 μL (3.0 mg / 2 mL-EtOH)

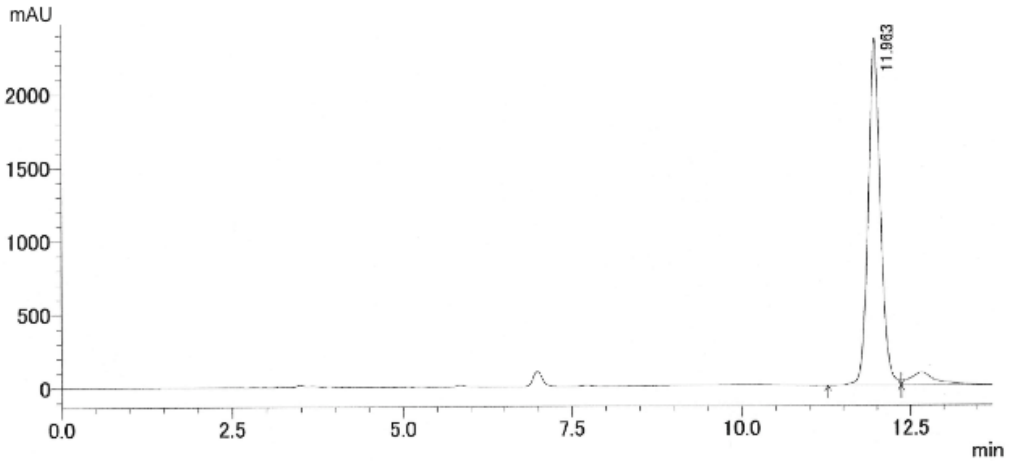
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 95 : 5, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.0 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 11.963 min

Purity: 96%



Sample: **6** (MK-4)

Sample Size: 20 μL (0.9 mg / 2 mL-EtOH)

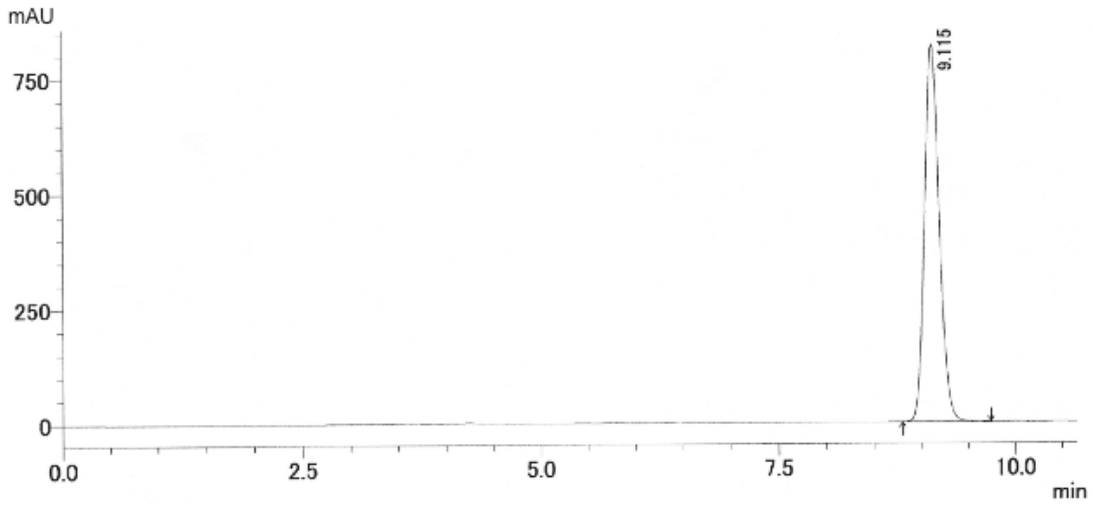
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.0 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 9.115 min

Purity: 99%



Sample: **7**

Sample Size: 20 μL (0.2 mg / 2 mL-EtOH)

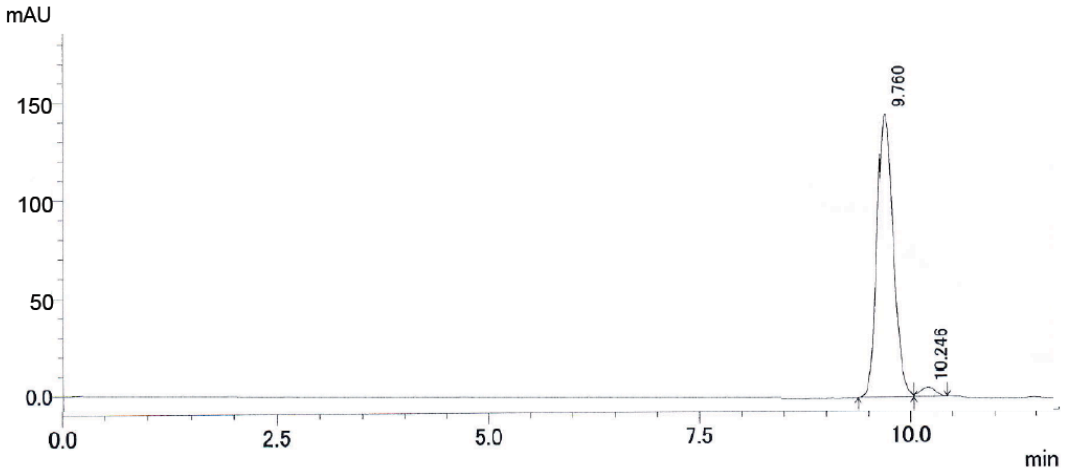
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 80:20, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 7.9 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 9.760 min

Purity: 96%



Sample: **8**

Sample Size: 20 μL (0.3 mg / 2 mL-EtOH)

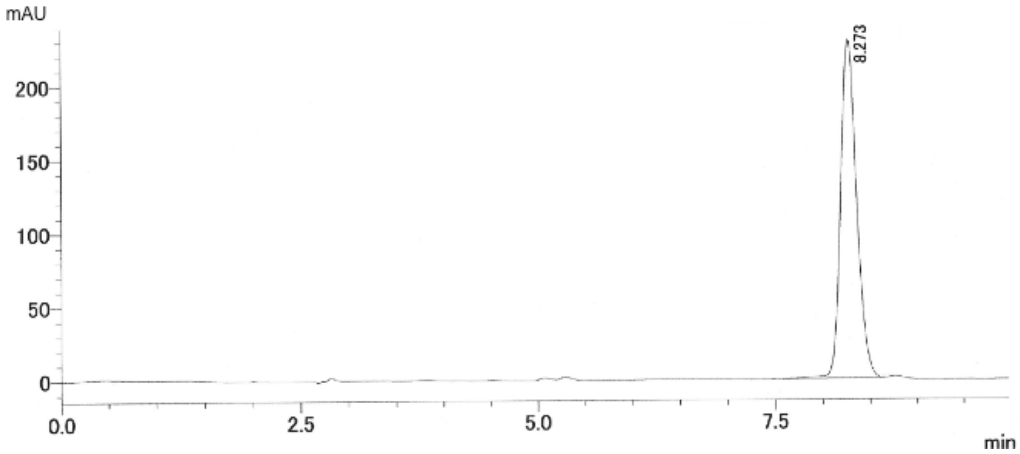
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 90 : 10, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.9 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 8.273 min

Purity: 97%



Sample: **9**

Sample Size: 20 μL (2.0 mg / 2 mL-EtOH)

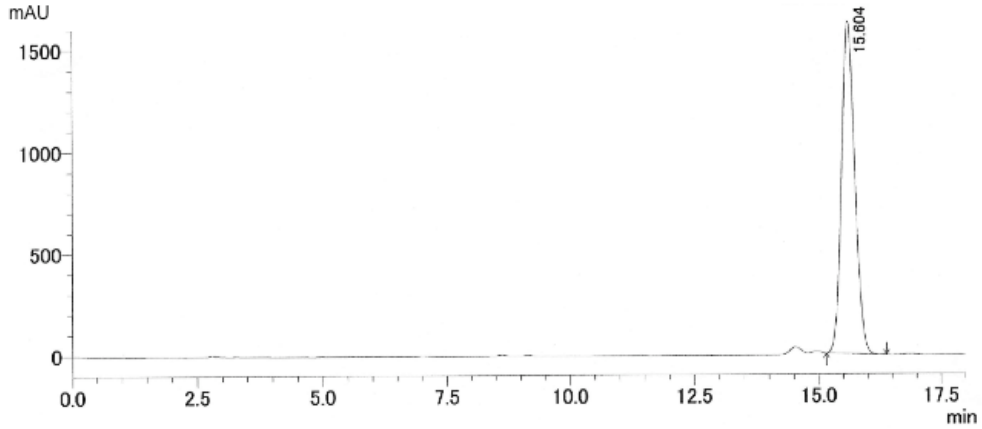
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 90 : 10, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.9 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 15.604 min

Purity: 98%



Sample: **10**

Sample Size: 20 μL (4.1 mg / 2 mL-EtOH)

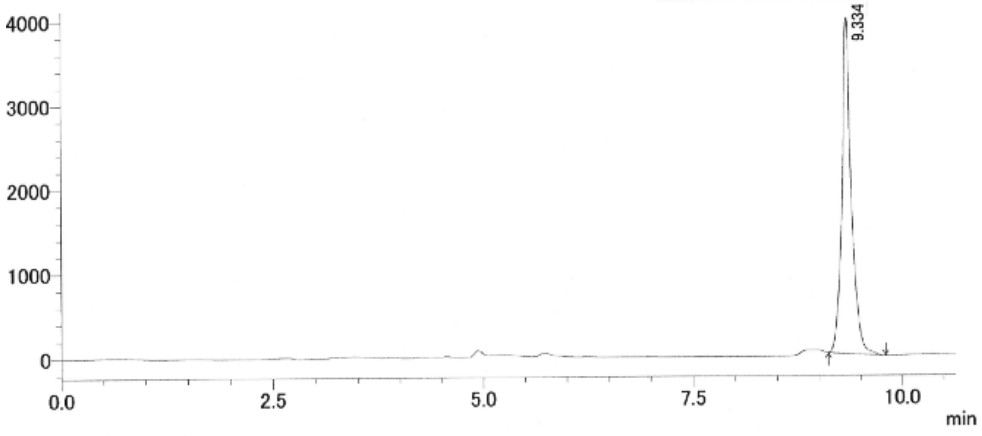
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 95 : 5, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.0 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, Retention Time: 9.334 min

Purity: 98%



Sample: **11**

Sample Size: 20 μL (3.8 mg / 2 mL-EtOH)

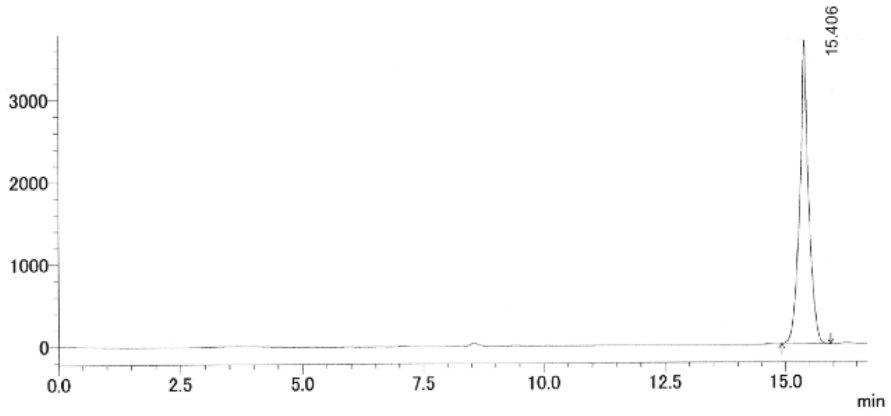
Column: 5C_{18}-AR-II (nacalai tesque), 4.6 × 250 mm

Eluant: MeOH / H_2O = 95 : 5, isocratic flow

Flow Rate: 1.0 mL / min, Press.: 5.0 MPa, Temp.: 40ºC

Detection: Ch.1 258 nm, , Retention Time: 15.406 min

Purity: 99%



IV. Experimental method and data of compound 15a and 15b

Synthesis of compounds 15a and 15b. Commercially available phenylmagnesium bromide (7.6 mL of a 3.0 M solution, 22.4 mmol) was added dropwise to a mixture of THP ether **14a** (538 mg, 2.12 mmol) or **14b** (684 mg, 2.12 mmol) and copper (I) iodide (1.98 g, 10.4 mmol) in THF (40 mL) with stirring at room temperature. The resulting mixture was heated to 50°C and allowed to stir for 4 h. The reaction was then quenched by addition of saturated NH_4Cl and extracted with ether. Concentration of the combined extracts *in vacuo* provided a yellow oil, which upon purification by flash column chromatography (60: 40 hexanes/ethyl acetate) afforded compound **15a** or **15b** as a colorless oil (**15a**: 368 mg, 76%, **15b**: 443 mg, 70%): The data of **15a** was reported in ref. 17. The data for **15b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.18 (m, 5H), 5.43 (t, 1H, *J*= 1.2 Hz), 5.24 (t, 1H, *J*= 1.2 Hz), 5.13 (t, 1H, *J*= 1.2 Hz), 4.17 (d, 2H, *J*= 6.9 Hz), 3.28 (s, 2H), 2.12-2.04 (m, 8H), 1.69 (s, 3H), 1.61 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 140.0, 135.2, 134.3, 129.5, 128.8 (2C), 128.1 (2C), 126.3, 125.8, 123.9, 123.1, 59.4, 46.2, 39.5, 26.8, 26.6, 16.2, 16.0, 15.8; ESI-HRMS ($M+H^+$) m/z calcd for $C_{21}H_{30}O$ 299.2375. Found 299.2377.