Synthesis of a Mimicking Hybrid of *Annonaceous* Acetogenin with Steroid for Antitumoral Activity Investigation†

JIANG, Sheng(蒋晟) **WU, Yu-Lin**(吴毓林) **YAO, Zhu-Jun***(姚祝军)

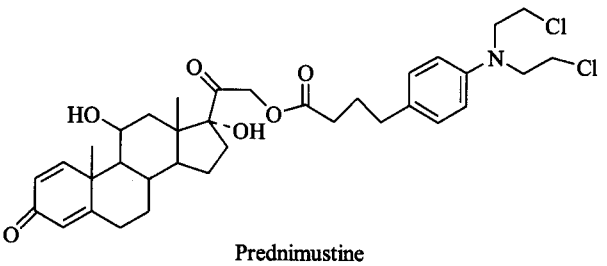
State Key Laboratory of Bioorganic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

The first example of *annonaceous* acetogenin-steroid hybrid was synthesized for the antitumoral study.

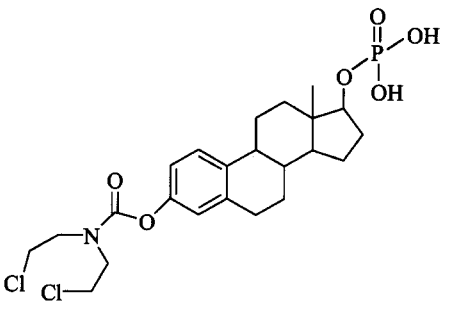
Keywords *annonaceous* acetogenin, steroid, mimicry, antitumor

Introduction

In the past two decades, a large family of natural products named *annonaceous* acetogenins were isolated and characterized by the global researchers from various species of the plant *annonaeae*.[1] Among over 400 members, most of them were found to show potent cytotoxic and antitumor activities. They have been shown to function by blocking complex I in mitochondria[2] as well as ubiquinone-linked NADPH oxidase in the cells of specific tumor cell lines, including some multidrug-resistant ones.[3] These features make these acetogenins excellent leads for the new antitumor agents. The latter is becoming more and more important in recent years based on the consideration of molecular diversity of these acetogenins, aiming to discover more active, more selective mimicking molecules with simpler structures for the future development of potential drug candidates.[4] The present work was initially based on the common existence of long hydrocarbon chain in acetogenins, which is considered to be one of the structural essentials for the antitumor activities. As part of our research interests on the investigation of polyether mimetics of *annonaceous* acetogenins and continuing our previous successful work, a steroid is designed to replace the straight hydrocarbon chain, mimicking the related lipophilic properties. The more important consideration of the hybrid design is that the steroid might play a better role in human cells to recognize certain target proteins, improve the membrane penetration and resultantly raise the cell selectivity. We know that steroids such as cholesterol, estrogen, not only have some activity but also are becoming medicinal study tools. Fig. 1 shows two



Prednimustine



Estramustine phosphate

Fig. 1 Two examples of steroid-based hybrids.

* E-mail: yaoz@pub.sioc.ac.cn; Fax: 86-21-64166128

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successful examples, prednimustine and estramustine phosphate (Fig. 1).[5] Herein we would like to report our synthesis of the first example of the hybrid of acetogenin with steroid (**1** in Fig. 2).

Chemical synthesis

As shown in Fig. 2, the hybrid **1** could be mainly disconnected into two parts: one is the steroid part **5**, and the other the diol-ester **7**. The desired oxygenated ether functional region was going to be pre-installed in the first part so that the protecting groups would be reduced to the minimal. The construction of butenolide segment was designed in the later steps so that the highest utilization would be achieved upon the chiral material *L*-lactal aldehyde **4**.

First of all, the synthesis of segment **7** was achieved by chiron approach utilizing (*R*)-glyceraldehyde acetonide, which is readily prepared from *D*-mannitol (Scheme 1). The commercially available *cis*-eruic acid **8** was cleaved by ozone oxidation and subsequent KBH_4 reduction afforded the ω-hydroxyl carboxylic acid **9**.[6] Then the hydroxyl group was brominated by hydrobromic acid to give ω-bromo acid **10**, which was further transformed to the corresponding methyl ester **11**. The Wittig reaction of (*R*)-glyceraldehyde acetonide with the triphenylphosphoronium salt prepared *in situ* from **11** and triphenylphosphite gave the olefin intermediate. A following hydrogenation and acidic deprotection of acetonide successively furnished the diol **7**.

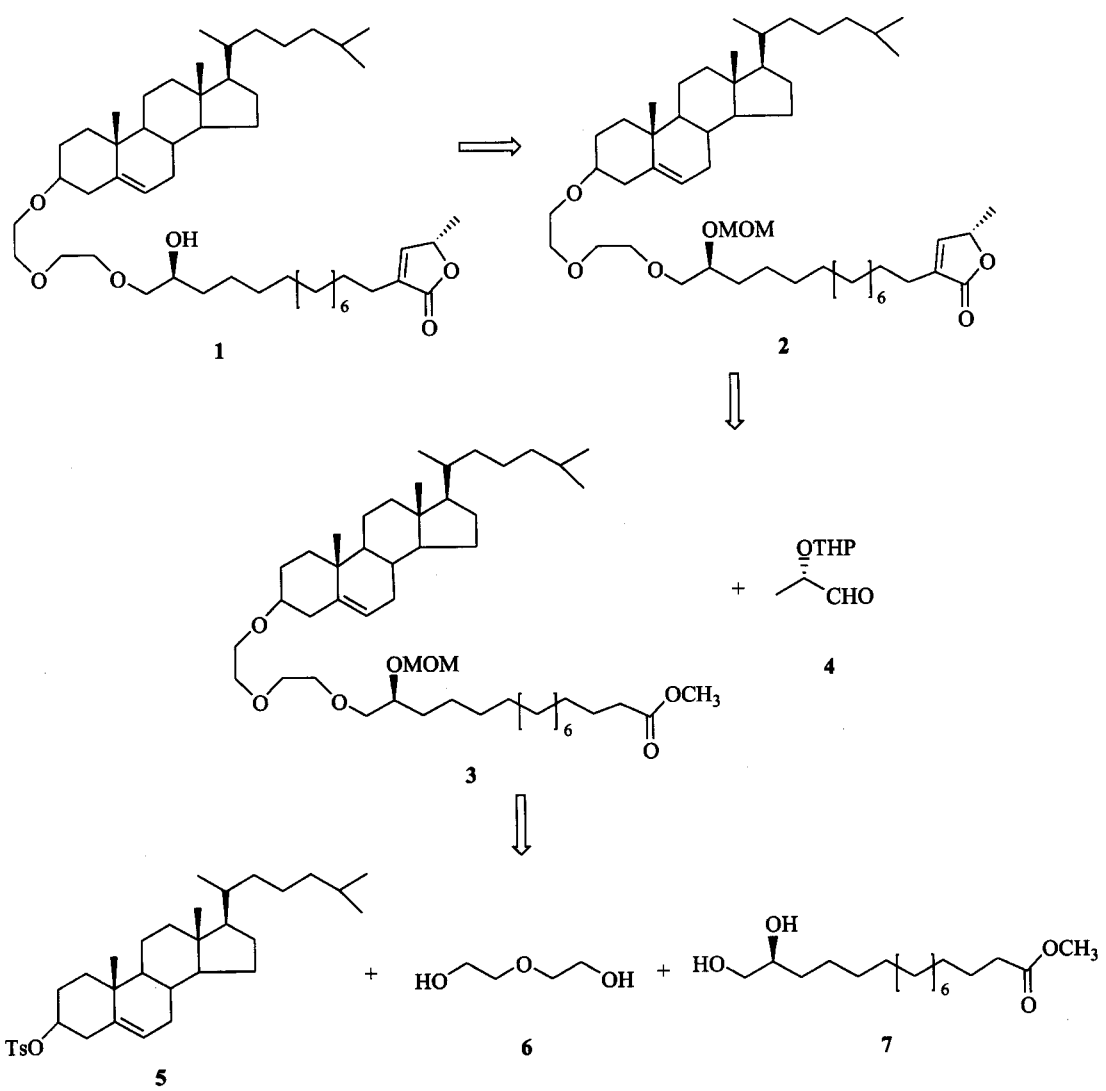
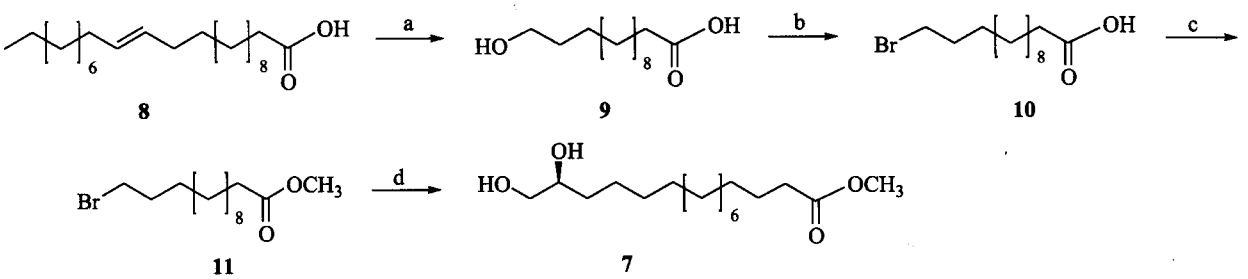


Fig. 2 Retrosynthetic analysis of mimicking hybrid **1**.

Scheme 1



Reagents and conditions: (a) 1) O_3, 0—5 ℃, EtOH:cyclohexane (1:5), 2) KBH_4, 87% from erucic acid; (b) HBr, HOAc, 75%; (c) MeOH, $SOCl_2$; (d) 1) PPh_3, 2) *t*-BuOK, then (*R*)-glyceraldehyde acetonide, 3) H_2, EtOH, Pd-C, 4) H^+, MeOH, 91% (61% over 4 steps).

The other segment started from commercially available cholesterol **12** (Scheme 2). It was treated with TsCl and pyridine to give high yield of tosylate **5**, which was further reacted with ethylene glycol to form the monoether **13**.[7] The free alcohol of **13** was then iodinated by I_2, imidazole and triphenylphosphite. With aid of Bu_2SnO, coupling of **7** and **14** was achieved by a regioselective way.[8] By this stage, the convergent synthesis of the linear skeleton finished at **15**. The following steps were set to install a butenolide sub-unit of the acetogenin, which applied a previously used sequence of aldol reaction, *in situ* lactonization and elimination.[9] Again, this approach was successfully utilized in this case upon the MOM protected compound **3**, giving **2** in higher overall yield. The final MOM deprotection of **2** using $BF_3 \cdot Et_2O$ in Me_2S afforded the designed hybrid **1**.

Biological evaluation

With the hybrid in hand, the activity study was set in Beijing Institute of Medical Materials. Unfortunately, the recent preliminary cytotoxic testing of **1** against several human tumor cell lines gave negative results (Table 1). This may lie in several reasons: one is that the steroid plate is not a proper mimetic of alphilic hydrocarbon chain; the second, a proper steroid molecule was not yet found to incorporate into the hybrid; the third may lie in the improper cell selection for activity testing. Further study of steroid hybrids is still going on in this laboratory.

Table 1

Sample	IC_{50} (μg/mL)			
	HT-29	HCT-8	KB	HELF
1	> 10	> 10	> 10	> 10
adrimycin	6.0×10^{-2} (37.5)	3.6×10^{-2}	7.6×10^{-2}	1.92

Conclusion

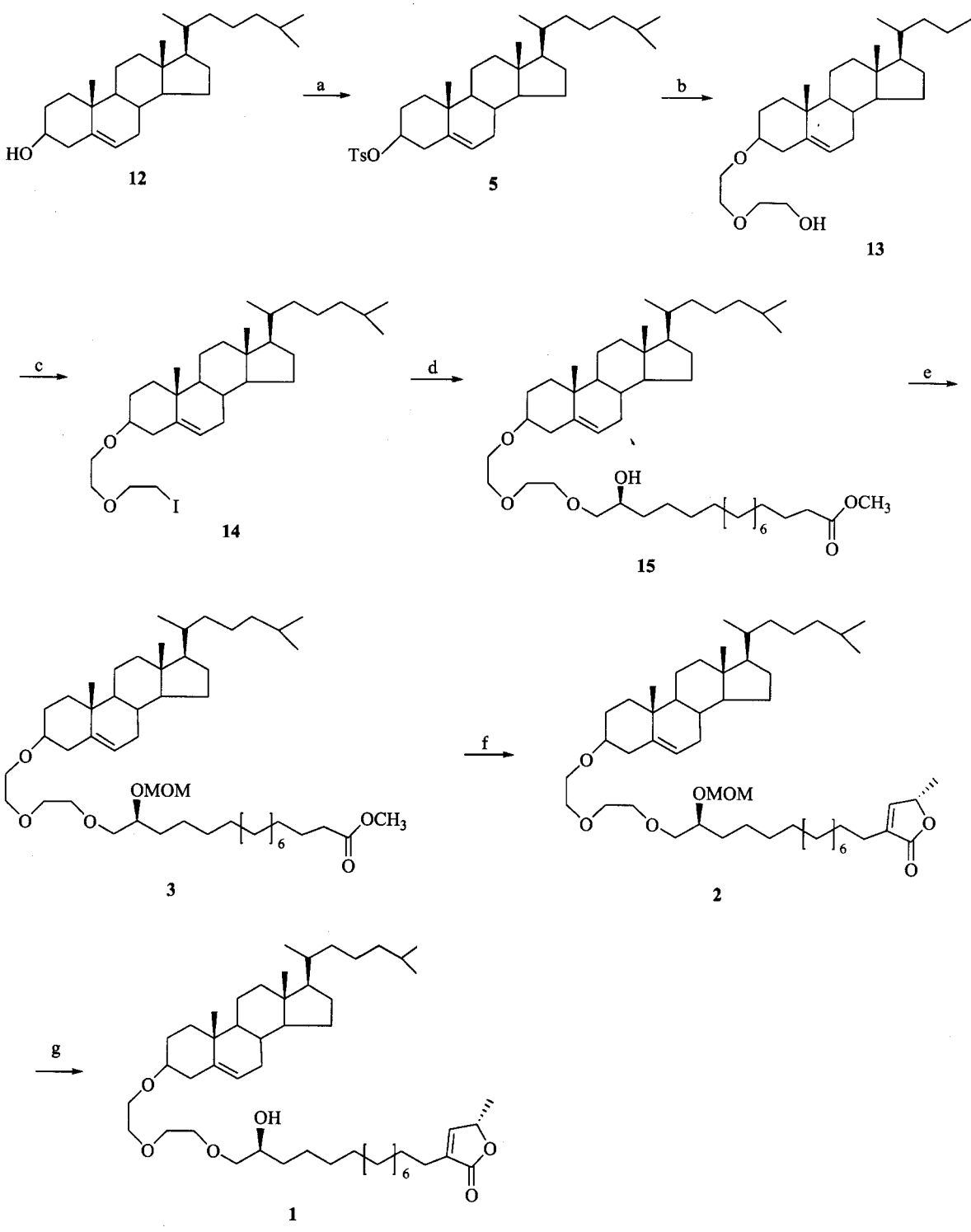
In summary, the first example of *annonaceous* acetogenin hybrid-mimetic with steroid was reported, for which the synthesis was achieved by a convergent approach. This opens a new acetogenin mimicking direction aiming to improve the cell-selectivity of these antitumoral agents by introduction of steroids in the chemical structures.

Experimental

General methods

All reactions were carried out under argon or nitrogen in oven-dried glassware using standard gastight syringes, cannulas and septa. Solvents and reagents were purified and dried by standard methods prior to use. Optical rotations were measured at room temperature. IR spectra were recorded on an FT-IR instrument. ^1H NMR spectra were recorded at 300 MHz and 600 MHz and are reported in ppm (δ) downfield relative to TMS as internal standard, and ^{13}C NMR spectra were recorded at 100 MHz and assigned in ppm (δ). Flash column chromatography was performed on silica gel (10—40 μm) using a mixture of petroleum ether (60—90 ℃) and ethyl acetate as the eluent.

Scheme 2



Reagents and conditions: (a) TsCl, anhydrous pyridine, 0 ℃, 79%; (b) diethyleneglycol, dioxane, reflux, 81%; (c) PPh_3, imidazle, I_2, dry benzene, 0 ℃, 81%; (d) 1) **7**, Bu_2SnO, $CHCl_3$-MeOH (10:1, *V*:*V*), reflux, 2) CsF, DMF, 75% over 2 steps; (e) MOMCl, *i*-Pr_2NH, CH_2Cl_2, 100%; (f) 1) LDA, THF-HMPA, −78 ℃, 2) (*S*)-*O*-tetrahydropyranyl lactal, −78 ℃, 3) 10% H_2SO_4, rt, 4) $(CF_3CO)_2O$, Et_3N, dry CH_2Cl_2, 0 ℃, 60% overall yield; (g) $BF_3 \cdot Et_2O$, Me_2S, 0 ℃, 60%.

Compound **5**

Compound **5** was prepared according to the method reported:[7] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.65—2.45 (m, 43H), 2.45 (s, 3H), 4.31—4.33 (m, 1H), 5.30 (bd, J = 5.2 Hz, 1H), 7.33 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.2 Hz, 2H).

Compound **13**

Compound **13** was prepared according to the method reported:[7] $[\alpha]_D^{25}$ − 29.2 (c 1.30, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.63—2.32 (m, 43H), 3.17—3.23 (m, 1H), 3.55—3.69 (m, 8H), 5.30 (brs, 1H).

Compound **14**

To a 100-mL flask was added **13** (2 g, 4.22 mmol), imidazole (1.95 g, 28.7 mmol), Ph_3P (3.77 g, 14.3 mmol), and anhydrous benzene (70 mL) under nitrogen atmosphere. Then iodine (3.64 g, 14.3 mmol) was added in portions at 0 ℃. The reaction mixture was stirred at room temperature for 5 h. Excess of iodine was removed by the addition of aqueous sodium thiosulfate. The mixture was transferred to a separating funnel. The organic layer was diluted with benzene, washed with water and dried ($MgSO_4$). The solid was filtered and the organic solution was concentrated. The residue was treated with diethyl ether and precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated and purified by column chromatography (petroleum-ether: ethyl acetate, 10:1) to yield the title compound (2.45 g, 99%). $[\alpha]_D^{25}$ − 24.4 (c 1.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.68 (s, 3H), 0.85—1.66 (m, 34H), 1.84—2.03 (m, 4H), 1.99—2.03 (m, 1H), 2.35—2.36 (m, 1H), 3.18—3.19 (m, 1H), 3.27 (t, J = 7.1 Hz, 2H), 3.65 (s, 4H), 3.77 (t, J = 6.6 Hz, 2H), 5.34 (bd, J = 5.4 Hz, 1H); IR (neat) ν: 2867, 1467, 1379, 1331, 1110, 629 cm^{-1}; MS (EI) m/z: 583 (M^+). Anal. calcd for $C_{31}H_{53}O_2I$: C 63.68, H 9.14; found C 63.69, H 8.91.

Compound **9**

Compound **9** was prepared according to the method reported in the literature:[5] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.27—1.30 (m, 16H), 1.54—1.66 (m, 4H), 2.35 (t, J = 7.2 Hz, 2H), 3.65 (t, J = 6.6 Hz, 2H); IR (neat) ν: 3284, 3147, 2916, 2850, 1694, 1471, 1441, 1411, 1311, 1285, 1261, 1235, 1211, 1189, 1057, 719 cm^{-1}.

Compound **10**

To a solution of compound **9** (11.5 g, 0.05 mol) in HOAc (25 mL) was added concentrated sulfuric acid slowly, followed by a slow addition of 48% hydrobromic acid (15.19 g, 0.075 mol). The mixture was then refluxed for 5 h. The solution was quenched with saturated $NaHCO_3$ (50 mL) and adjusted to pH 4—6. The aqueous phase was extracted with $CHCl_3$ (60 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated. Flash chromatography of the residue afforded **10** as yellow liquid (11 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.27—1.42 (m, 14H), 1.59—1.66 (m, 4H), 1.80—1.89 (m, 2H), 2.35 (t, J = 7.5 Hz, 2H), 3.41 (t, J = 6.7 Hz, 2H); IR (neat) ν: 2918, 2851, 1733, 1696, 1473, 1265, 1238, 1040, 718 cm^{-1}; MS (EI) m/z: 293 [MH^+].

Compound **11**

To a solution of **10** (8 g, 0.027 mol) in dry CH_3OH (100 mL) was added $SOCl_2$ (11.3 mL, 0.15 mol) slowly at 0 ℃. The mixture is then reacted at rt for 1 h. The solution was quenched with sat. $NaHCO_3$ (50 mL) and adjusted pH to 8. The aqueous phase was extracted with EtOAc (60 mL × 3). The combined organic layers were dried over sodium sulfate and concentrated. Flash chromatography of the residue afforded **11** as yellow liquid (7.83 g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.20—1.42 (m, 14H), 1.60—1.67 (m, 4H), 1.80—1.89 (m, 2H), 2.30 (t, J = 7.5 Hz, 2H), 3.41 (t, J = 3.6 Hz, 2H), 3.66 (s, 3H); IR (neat) ν: 2920, 2851, 1737, 1474, 1464, 1214, 1174 cm^{-1}; MS (EI) m/z: 307 [M^+].

Compound **7**

A stirred mixture of **11** (7.83 g, 25.5 mmol) and Ph_3P (6.71 g, 25.5 mmol) was heated at 140 ℃ under N_2. After 3 h, the reaction was cooled down and anhy-

drous THF (120 mL) was added to dissolve the syrup. To the cooled solution, was then added *t*-BuOK (3.15 g, 28.1 mmol) and THF (20 mL) under N_2 atmosphere at 0 ℃. The reaction was stirred for 15 min at 0 ℃, and then (*R*)-glyceraldehyde acetonide (4.97 g, 38.3 mmol) in dry THF (30 mL) was added. The reaction mixture was warmed to rt slowly and stirred overnight. Petroleum ether (60—90 ℃) (200 mL) and aqueous sat. NH_4Cl (20 mL) were added at rt, and the aqueous phase was extracted with petroleum ether. The combined organic layers were dried over sodium sulfate and concentrated. The residue was purified by flash chromatography to give the olefin intermediate (7 g, 90%). The mixture of resultant intermediate, CH_3OH (57 mL) and Pd-C (10%, 1.4 g) was stirred vigorously under H_2 atmosphere until hydrogen could not be absorbed. The catalyst was filtered and the methanol was evaporated. Flash chromatography of the crude product afforded the acetal-ester (7.1 g, 95%). $[\alpha]_D^{25}$ + 10.3 (*c* 3.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 1.25—1.64 (m, 24H), 1.36 (s, 3H), 1.41 (s, 3H), 2.30 (t, *J* = 7.6 Hz, 2H), 3.50 (t, *J* = 7.5 Hz, 1H), 3.67 (s, 3H), 4.03—4.05 (m, 2H); MS (EI) *m/z*: 342 (M^+). Anal. calcd for $C_{20}H_{28}O_4$: C 70.13, H 11.18; found C 70.14, H 11.26. A solution of the acetal compound (7.1 g) in 50% HOAc (30 mL) was stirred overnight at rt. The solvent was removed under reduced pressure and aqueous sat. $NaHCO_3$ was added to adjust pH to 7. The mixture was extracted with ethyl acetate (30 mL × 3), dried over sodium sulfate and concentrated. Recrytallization of crude product with ethyl acetate afforded **7** as a white solid (6.62 g, 90%). $[\alpha]_D^{25}$ + 10.6 (*c* 1.06, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.23—1.38 (m, 18H), 1.39 (bs, 2H), 1.57—1.61 (m, 2H), 1.92—1.93 (m, 1H), 2.04—2.06 (m, 1H), 2.32 (t, *J* = 7.2 Hz, 2H), 3.40—3.42 (m, 1H), 3.59—3.62 (m, 1H), 3.64 (s, 3H), 3.66—3.68 (m, 1H); IR (neat) ν: 3487, 2918, 2851, 1737, 1472 cm^{-1}.

Compound **15**

A mixture of compound **7** (0.3 g, 0.993 mmol), Bu_2SnO (0.273 g, 1.092 mmol) and $CHCl_3/CH_3OH$ (10:1, 8 mL) was refluxed until the solution turned clear. The solvent was removed under reduced pressure and the residue was dried in vaccum for 6 h. The residue was dissolved in DMF (9 mL) and treated with CsF (0.18 g, 1.191 mmol), followed by addition of **14** (0.579 g, 0.993 mmol) in DMF (15 mL). The reaction mixture was stirred for 18 h at 60 ℃. The solvent was removed under reduced pressure and the residue was treated with brine and stirred 0.5 h. The mixture was extracted with ethyl acetate (10 mL × 3). The organic phase was washed with saturated NH_4Cl and brine successively, dried over sodium sulfate and concentrated. Flash chromatography of the residue afforded **15** as an oil (0.356 g, 83%), along with **7** (0.13 g) and **14** (0.20 g) recovered. $[\alpha]_D^{25}$ − 15.87 (*c* 5.34, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.68 (s, 3H), 0.86—1.54 (m, 55H), 1.61—1.88 (m, 6H), 2.28—2.33 (m, 5H), 2.79 (brs, 1H), 3.15—3.23 (m, 1H), 3.30 (t, *J* = 8.8 Hz, 1H), 3.54 (dd, *J* = 2.8, 10.0 Hz, 1H), 3.65 (s, 3H), 3.64—3.71 (m, 8H), 3.79 (brs, 1H), 5.34 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.3, 140.0, 120.6, 78.6, 74.9, 69.9, 69.6, 69.2, 66.3, 55.8, 55.2, 50.4, 49.2, 41.3, 38.8, 38.6, 38.1, 36.3, 35.9, 35.2, 34.8, 33.1, 32.1, 31.0, 30.9, 28.8, 28.7, 28.6, 28.5, 28.3, 28.2, 27.4, 27.4, 27.3, 27.0, 24.6, 24.0, 23.3, 22.9, 21.8, 21.6, 20.1, 18.4, 17.8, 10.9; IR (neat) ν: 3454, 2916, 2851, 1739, 1472, 1114, 718 cm^{-1}; MS (ESI) *m/z*: 781 (M + Na) (HRMS (ESI) calcd for $C_{48}H_{86}O_6Na$ [M^+ + Na] 781.6314, found 781.6316).

Compound **3**

To a solution of compound **15** (0.24 g) in CH_2Cl_2 (2 mL) were added *i*-Pr_2NEt (0.34 mL, 0.19 mmol) and MOMCl (0.142 mL, 0.19 mmol) at 0 ℃. The reaction was stirred overnight at rt and quenched with aqueous NH_4Cl (5 mL). The mixture was extracted with ethyl acetate. The organic phase was washed with saturated brine, dried over sodium sulfate and concentrated. Flash chromatography of the crude product afforded **3** as a yellow liquid (0.226 g, yield 92%), along with **15** (0.08 g) recovered. $[\alpha]_D^{25}$ − 20.4 (*c* 3.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.68 (s, 3H), 0.85—1.64 (m, 60H), 1.79—2.03 (m, 4H), 2.28—2.35 (m, 2H), 3.16—3.19 (m, 1H), 3.38 (s, 3H), 3.50—3.55 (m, 3H), 3.62—3.71 (m, 8H), 3.68 (s, 3H), 4.64—4.68 (m, 1H), 4.77 (d, *J* = 6.9 Hz, 1H), 5.34 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR (100

MHz, $CDCl_3$) δ: 173.3, 140.0, 120.5, 95.7, 95.1, 78.5, 78.3, 75.3, 73.2, 69.9, 69.8, 69.7, 68.8, 68.2, 66.4, 55.8, 55.2, 54.5, 54.2, 50.4, 49.3, 41.4, 38.8, 38.6, 38.1, 36.3, 35.9, 35.2, 34.8, 33.2, 31.1, 31.0, 30.9, 28.8, 28.7, 28.6, 28.5, 28.3, 28.2, 27.4, 27.3, 27.0, 24.6, 24.5, 24.0, 23.3, 22.9, 21.8, 21.6, 20.1, 18.4, 17.8, 10.9; IR (neat) ν: 2930, 2854, 1743, 1467, 1145, 1109, 1041, 919 cm^{-1}; MS (ESI) m/z: 825 (M + Na); HRMS (ESI) calcd for $C_{50}H_{90}O_7Na$ $[M^+ + Na]$ 825.6575, found 825.6578.

Compound **2**

To a solution of diisopropylamine (0.277 mL, 1.97 mmol) in anhydrous THF (1 mL) was added *n*-BuLi (0.657 mL, 2.0 in hexane, 1.31 mmol) at 0 ℃, and the mixture was stirred for 30 min. After the mixture was stirred for additional 30 min at −78 ℃, anhydrous HMPA (0.44 mL, 2.52 mmol) was added and the mixture was stirred for 30 min. A solution of **3** (0.527 g, 0.657 mmol) in THF (6 mL) was injected into the above mixture. After 30 min, a solution of *O*-THP-(*S*)-lactal aldehyde (0.16 g, 0.99 mmol) in THF (2 mL) was introduced and the reaction mixture was stirred for 2 h at −78 ℃. The mixture was quenched with saturated aqueous NH_4Cl and extracted with ether. The organic layer was washed with brine and dried (Na_2SO_4). Removal of the solvents afforded a crude oil, which was treated with 10% H_2SO_4 (6.5 mL) in THF (12 mL) for 18 h at room temperature. The reaction mixture was diluted with ether, washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4) and evaporated to give a crude oil. To the mixture of the above oil and Et_3N (0.17 mL, 1.209 mmol) in CH_2Cl_2 (2 mL) at 0 ℃ was added $(CF_3CO)_2O$ (0.085 mL, 0.604 mmol). The reaction mixture was stirred at 0 ℃ for 12 h and at rt for 6 h, then quenched with saturated NH_4Cl and extracted with CH_2Cl_2. After being dried (Na_2SO_4), the extracts were filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford the pure **2** (0.327g, 60%). $[\alpha]_D^{25}$ − 11.1 (*c* 0.79, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.68 (s, 3H) 0.85—1.54 (m, 55H), 1.99—1.82 (m, 5H), 2.24—2.29 (m, 4H), 3.13—3.22 (m, 1H), 3.39 (s, 3H), 3.55 (d, J = 4.7 Hz, 2H), 3.63—3.74 (m, 9H), 4.66 (d, J = 6.9 Hz, 1H), 4.77 (d, J = 6.6 Hz, 1H), 4.96—5.03 (m, 1H), 5.35 (d, J = 5.0 Hz, 1H), 6.99 (d, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.9, 150.7, 141.0, 139.9, 134.4, 121.6, 96.1, 79.6, 79.3, 74.2, 71.0, 70.8, 70.7, 67.4, 65.0, 56.8, 56.2, 55.5, 50.3, 42.1, 39.9, 39.6, 39.1, 37.3, 36.9, 36.3, 35.8, 32.1, 32.0, 31.9, 31.4, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 28.4, 28.3, 28.1, 28.0, 27.5, 27.4, 25.5, 25.2, 24.3, 23.9, 22.9, 22.6, 21.5, 21.1, 19.4, 19.3, 18.8, 11.9; IR (neat) ν: 2958, 2931, 2870, 1769, 1467, 1378, 1365 cm^{-1}; MS (EI) m/z: 827 (M^+ + 1); HRMS (ESI) calcd for $C_{52}H_{90}O_7Na$ $[M^+ + Na]$ 849.6571, found 849.6578.

Compound **1**

To a solution of compound **2** (0.144 g, 0.174 mmol) in dimethyl sulfide (14.4 mL) was added $BF_3 \cdot Et_2O$ (2.2 mL, 17.1 mmol) at 0 ℃. The reaction mixture was stirred at rt for 40 min and quenched with aqueous $NaHCO_3$ (5.4 mL). The mixture was extracted with ethyl acetate (15 mL × 3) and the extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography to afford **1** (82 mg, 60%) as a waxy solid. $[\alpha]_D^{25}$ − 3.3 (*c* 1.23, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 0.68 (s, 3H), 0.85—1.54 (m, 55H), 2.03—1.82 (m, 5H), 2.21—2.36(m, 4H), 3.15—3.22 (m, 1H), 3.30 (dd, J = 8.5, 9.9 Hz, 1H), 3.54 (dd, J = 2.7, 9.9 Hz, 1H), 3.64—3.70 (m, 8H), 3.80 (m, 1H), 4.99 (dd, J = 1.7, 6.9 Hz, 1H), 5.34 (d, J = 4.9 Hz, 1H), 6.99 (d, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.2, 148.3, 141.0, 134.4, 121.6, 79.6, 75.9, 70.9, 70.6, 70.2, 67.3, 42.3, 39.8, 39.5, 39.0, 37.3, 36.9, 36.2, 35.8, 33.0, 32.0, 31.9, 29.7, 29.6, 29.5, 29.3, 29.2, 28.3, 28.2, 28.0, 27.4, 25.6, 25.2, 24.3, 23.8, 22.8, 22.6, 21.1, 19.4, 19.3, 18.7, 11.9; IR (neat) ν: 3500, 2927, 2851, 1755, 1744, 1469, 1320, 1114, 1026 cm^{-1}; MS (ESI) m/z: 805 (M^+ + Na); HRMS (ESI) calcd for $C_{50}H_{86}O_6Na$ $[M^+ + Na]$ 805.6326, found 805.6316.

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