Article

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Asymmetric Synthesis of (+)-Aspicilin

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Aspicilin (**1**), an eighteen membered macrolide with four stereocenters, was synthesized using (3*R*,4*R*)-1,5-hexadiene-3,4-diol and (*S*)-propylene oxide as the starting materials. Sharpless epoxidation on the protected dienediol generated the required three consecutive stereocenters, and malonic ester synthesis added the acetyl unit. Yamaguchi protocol was applied to form the key ester with two terminal olefins ready for the ring-closing metathesis. RCM, hydrogenation, selenylation, oxidation and deprotections gave aspicilin with 4.7% total yield.

Keywords: Aspicilin; Ring-closing metathesis; Macrolide.

Aspicilin (**1**) is a polyhydroxylated, eighteen membered macrolide isolated from lichen of the *Lecanoraceae* family.[1] Although its biological function or application remains unknown, it is a popular target for many new synthetic methodologies probably due to its interesting but not too complicated structural features, which include four stereocenters and an α,β-unsaturated macro-lactone.[2]

(3*R*,4*R*)-1,5-Hexadiene-3,4-diol (**2**) is an interesting, useful synthetic building block.[3] Although this diene-diol is a chiral, multi-functional molecule, its C_2 symmetrical feature avoids the region-selectivity issues while performing chemical modifications. In addition, the thermally unfavored formation of cyclobutene by ring-closing metathesis (RCM) makes 1,5-dienes, such as **2**, an ideal substrate to lengthen the carbonic chains by cross metathesis (CM) or generate macrocyclic cimpounds by RCM.[4] These features, the entrance for stereochemistry and carbon-carbon bond formation, make **2** a valuable starting material for synthesis. As part of our current interest in applying **2** to natural product synthesis, we herein report a new approach to (+)-aspicilin.

Our design to assemble aspicilin using compound **2** is shown in Scheme I. This macrolide could be generated from the ring-closing metathesis of **3**, derived from the esterification of the lactone **4** with (*S*)-dodec-11-en-2-ol (**5**). The lactone could be prepared from the malonic ester synthesis with the epoxide **6**, which was prepared from the Sharpless epoxidation of the mono-protected **2**.

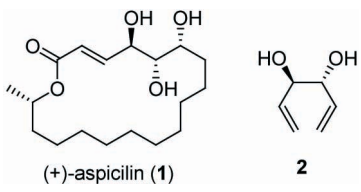
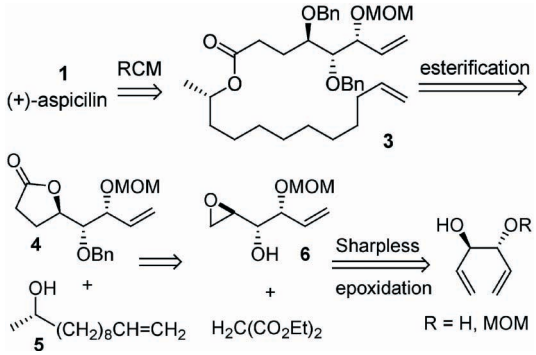


Fig. 1.

Scheme I Retrosynthetic analysis of aspicilin



The dienediol **2** was prepared in multi-gram quantity from D-mannitol according to the reported procedure,[3c] and our synthesis began with mono-protection of **2** with methoxymethyl (MOM) group (Scheme II). The allylic alcohol **7** underwent the Sharpless epoxidation to give the epoxide **6**, whose stereochemical outcome was concistent with Sharpless's model[5] and the reported spectroscopic data.[6] The remaining hydroxyl group was protected by a benzyl group to give **8**. The ring opening of the oxirane was achieved with the anion of diethyl malonate, and the following decarboxylation provided the lactone **4**.[7] Di-benzylations under an aqueous, basic condition gave the ester **10**,[8] which was hydrolyzed to the carboxylic acid **11** and

Dedicated to the memory of Professor Yung-Son Hon (1955–2011).

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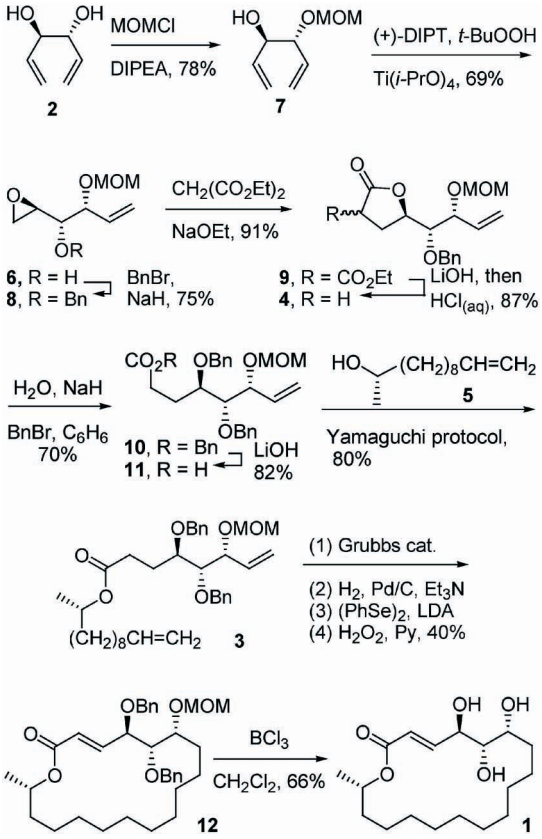
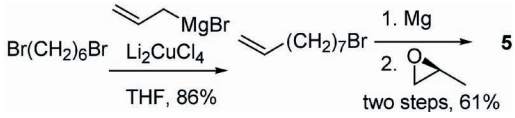
Scheme II Synthesis of aspicilin



converted to the desired ester **3** by the Yamaguchi protocol.[9] The corresponding chiral alcohol **5** was prepared according to the known procedure (Scheme III).[10] Thus, the ring-closing metathesis of diene **3** generated the macrolide, and the following hydrogenation, selenenylation, oxidation gave the α,β-unsaturated lactone **12**, whose *E*-configuration was supported with the large coupling constant (15.9 Hz) between the two olefinic hydrogens. Global deprotection with boron trichloride provided the target molecule, whose spectroscopic data were in agreement with those reported for aspicilin.[2e]

Scheme III Preparation of alcohol **5**



In conclusion, we have developed a convergent total synthesis of (+)-aspicilin. The three consecutive stereochenters were efficiently prepared from the Sharpless epoxidation of the mono-protected dienediol **7**, and the remaining chirality center was derived from the commercially available (*S*)-propylene oxide. The ester linkage was achieved with the Yamaguchi protocol to give the diene, and the macrocyclic structure was assembled with RCM. This new synthesis features simplicity and efficiency with 4.7% overall yield and thirteen steps.

EXPERIMENTAL

(3*R*,4*R*)-4-(methoxymethoxy)hexa-1,5-dien-3-ol (7)

Chlomethyl methyl ether (MOMCl, 0.6 g, 2.6 mmol) was added to the solution of dienediol **2** (0.5 g, 4.3 mmol), diisopropylethylamine (0.55 g, 4.3 mmol) and dichloromethane (10 mL) at 0 ºC. The reaction mixture was heated in a 40 ºC oil bath for 16 h, quenched with sat. $NaHCO_{3(aq)}$ (10 mL) and extracted with dichloromethane (10 mL × 3). The combined organic layers were dried over $Na_2SO_{4(s)}$, filtered and concentrated. The crude product was purified with column chromatography (SiO_2, ethyl acetate/hexanes, 1:5; R_f 0.40) to give pure compound **7** (0.32 g, 2 mmol, 78%). $[\alpha]_D^{20}$ -106.1 (*c* 1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.65 (d, *J* = 4.2 Hz, 1H), 3.38 (s, 3H), 3.90 (t, *J* = 7.2 Hz, 1H), 4.05-4.07 (m, 1H), 4.59 (d, *J* = 6.6 Hz, 1H), 4.71 (d, *J* = 6.6 Hz, 1H), 5.18-5.38 (m, 4H), 5.64-5.89 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.5, 74.3, 80.7, 93.9, 116.5, 119.5, 134.2, 136.4; HRMS (ESI) calcd for $[M+Na]^+$ ($C_8H_{14}O_3Na$) 181.0841, found 181.0843.

(1*S*,2*R*)-2-(methoxymethoxy)-1-((*R*)-oxiran-2-yl)but-3-en-1-ol (6)

Molecular sieves (4 Å, 1.25 g), titanium(IV) isopropoxide (935 μL, 3.16 mmol) and L-(+)-diisopropyl tartrate (L-(+)-DIPT, 790 μL, 3.79 mmol) were added to a solution of **7** (0.5 g, 3.16 mmol) in dichloromethane (3 mL) at -20 °C under nitrogen. The mixture was stirred at -20 °C for 15 min and added with *tert*-butylhydroperoxide (TBHP, 3.3 M in toluene, 1.8 mL, 5.3 mmol) dropwise. The reaction mixture was stirred at -10 °C for 72 h, quenched with an aqueous solution of ferrous sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$, 1.05 g, 3.79 mmol) and citric acid (364 mg, 1.9 mmol) in water (3 mL), warmed up to room temperature, and extracted with dichloromethane (20 × 3 mL). The organic layer was washed with sat. $NaCl_{(aq)}$ (20 mL), dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:3; R_f 0.15) to give **6** (380 mg, 2.18 mmol, 69%) as a colorless oil. $[\alpha]_D^{20}$ -96.6 (*c* 1.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.54 (d, *J* = 4.2 Hz, 1H), 2.76-2.78 (m, 2H), 3.02-3.06 (m, 1H), 3.37 (s, 3H), 3.55 (dd, *J* = 9.3Hz, 1H), 4.11 (dd, *J* = 7.5

Hz, 1H), 4.59 (d, *J* = 6.6Hz, 1H), 4.72 (d, *J* = 6.3Hz, 1H), 5.31-5.37 (m, 2H), 5.73-5.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.7, 51.7, 55.7, 72.6, 78.6, 94.0, 119.9, 133.8. HRMS (ESI) calcd for $[M+Na]^+$ ($C_8H_{14}O_4Na$) 197.0790, found 197.0794.

(*R*)-2-((1*S*,2*R*)-1-(benzyloxy)-2-(methoxymethoxy)but-3-enyl)oxirane (8)

Benzyl bromide (413 μL, 3.44 mmol) was added to the suspension of sodium hydride (60% in mineral oil, 138 mg, 3.44 mmol) and **6** (500 mg, 2.87 mmol) at 0 ºC. The reaction mixture was stirred at rt for 16 h, diluted with ethyl acetate (20 mL), washed with sat. $NaCl_{(aq)}$ (30 mL). The organic layer was dried over $Na_2SO_{4(s)}$, filtered and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:3; R_f 0.43) to give **8** (569 mg, 2.15 mmol, 75%) as a light yellow oil. $[\alpha]_D^{20}$ -61.40 (*c* 1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.67-2.70 (m, 1H), 2.77-2.80 (m, 1H), 3.16-3.20 (m, 1H), 3.35-3.41 (m, 1H), 3.39 (s, 1H), 4.28 (dd, *J* = 3.9 Hz, 7.5Hz, 1H), 4.60-4.77 (m, 4H), 5.30-5.38 (m, 2H), 5.85-5.97 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 45.6, 50.8, 55.5, 73.4, 77.4, 79.9, 93.9, 118.9, 127.7, 127.8, 128.2, 134.3, 138.0; HRMS (FAB) calcd for $[M+H]^+$ ($C_{15}H_{21}O_2$) 265.1433, found 265.1440.

(5*R*)-ethyl-5-((1*R*,2*R*)-1-(benzyloxy)-2-(methoxymethoxy)but-3-enyl)-2-oxotetrahydrofuran-3-carboxylate (9)

Diethyl malonate (2.98 g, 18.6 mmol) was added to a solution of sodium ethoxide, prepared with sodium metal (365 mg, 15.9 mmol) and anhydrous ethanol (30 mL). The solution was stirred for 10 min and then **8** in anhydrous ethanol (16 mL) was added. The reaction mixture was heated to reflux for 16 h, cooled, acidified with citric acid (10% wt) to pH 4, and concentrated. The residue was diluted with ethyl acetate (60 mL), washed with sat. $NaCl_{(aq)}$ (50 mL), dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:1; R_f 0.71) to give **9** (1.83 g, 4.83 mmol, 91%) as a light yellow oil. $[\alpha]_D^{20}$ -24.2 (*c* 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21-1.28 (m, 3H), 2.35-2.82 (m, 2H), 3.32 (s, 3H), 3.53-3.64 (m, 1H), 3.82-3.88 (m, 1H), 4.12-4.22 (m, 3H), 4.54-4.80 (m, 5H), 5.27-5.35 (m, 2H), 5.67-5.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 26.4, 27.0, 46.7, 46.8, 55.6, 61.9, 62.0, 75.1, 75.3, 76.6, 77.4, 78.3, 78.9, 80.6, 81.5, 93.9, 94.1, 119.3, 119.9, 127.7, 128.0, 128.2, 128.4, 133.7, 134.1, 137.5, 137.6, 167.5, 168.1, 171.3, 172.0; HRMS (FAB) calcd for $[M+H]^+$ ($C_{20}H_{27}O_7$) 379.1754, found 379.1757.

(*R*)-5-((1*R*,2*R*)-1-(benzyloxy)-2-(methoxymethoxy)but-3-enyl)dihydrofuran-2(3H)-one (4)

A solution of ester **9** (650 mg, 1.72 mmol), 1,2-dimethoxyethane (6 mL), lithium hydroxide (267 mg, 11.2 mmol) and water (6 mL) was heated to 50 °C for 6 h. The reaction mixture was cooled to rt, concentrated, acidified with $HCl_{(aq)}$ (1N) to pH 3 and extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residue was redissolved in toluene (6 mL), and the solution refluxed for 8 h in a Dean-Stark appratus, concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:1; R_f 0.65) to give **4** (460 mg, 1.5 mmol, 87%) as a light yellow oil. $[\alpha]_D^{20}$ -14.89 (*c* 1.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.05-2.57 (m, 4H), 3.32 (s, 3H), 3.82 (dd, *J* = 2.7 Hz, 6.3Hz, 1H), 4.13 (t, *J* = 7.2Hz, 1H), 4.55-4.76 (m, 5H), 5.27-5.33 (m, 2H), 5.68-5.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.9, 28.3, 55.5, 75.2, 77.2, 79.7, 81.7, 93.8, 119.5, 127.7, 128.0, 128.2, 133.9, 137.7, 177.2; HRMS (FAB) calcd for $[M+H]^+$ ($C_{17}H_{23}O_5$) 307.1545, found 307.1545.

(4*R*,5*R*,6*R*)-benzyl 4,5-bis(benzyloxy)-6-(methoxymethoxy)oct-7-enoate (10)

Sodium hydride (60% in mineral oil, 274 mg, 6.85 mmol) in a 25 mL flask was washed with pentane (10 mL × 3) and dried with nitrogen flow. A solution of **4** (300 mg, 0.98 mmol), 15-crown-5 (39 μL, 0.20 mmol) and toluene (12 mL) was added to the reaction flask. After adding water (35 μL, 1.96 mmol), the reaction mixture was stirred at rt for 2 h, added with benzyl bromide (605 μL, 4.90 mmol), stirred for another 2 h, and quenched with sat. $NH_4Cl_{(aq)}$ (3 mL) at 0 °C, extracted with ethyl acetate (5 mL × 3). The organic layers were combined, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:5; R_f 0.46) to give **10** (346 mg, 0.69 mmol, 70%) as a colorless oil. $[\alpha]_D^{20}$ +0.71 (*c* 1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.94-2.17 (m, 2H), 2.45-2.51 (m, 2H), 3.35 (s, 1H), 3.62-3.67 (m, 1H), 3.70 (dd, *J* = 3.6 Hz, 5.7 Hz, 1H), 4.20-4.24 (m, 1H), 4.41-4.77 (m, 6H), 5.06 (s, 2H), 5.25-5.36 (m, 2H), 5.74-5.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.9, 30.2, 55.6, 66.0, 71.4, 74.5, 77.9, 78.3, 81.6, 94.2, 118.7, 127.4, 127.6, 127.9, 128.1 128.3, 128.4, 135.1, 136.0, 138.2, 138.5, 173.5; HRMS (FAB) calcd for $[M+H]^+$ ($C_{31}H_{37}O_6$) 505.2593, found 505.2590.

(4*R*,5*R*,6*R*)-4,5-bis(benzyloxy)-6-(methoxymethoxy)oct-7-enoic acid (11)

A solution of **10** (270 mg, 0.535 mmol), lithium hydroxide (64 mg, 2.68 mmol) in acetonitrile (36 mL) and water (9 mL) was stirred for 16 h at rt. The reaction mixture was acidified with sat. $NH_4Cl_{(aq)}$, extracted with diethyl ether (5 mL × 3). The organic layers were combined, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:1; R_f 0.41) to give **11** (182 mg, 0.44 mmol, 82%) as a colorless oil. $[\alpha]_D^{20}$ +3.63 (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.95-2.16 (m, 2H), 2.44-2.50 (m, 2H), 3.38 (s, 3H), 3.64-3.69 (m, 1H), 3.73-3.76 (m, 1H), 4.24, (t, *J* = 7.5 Hz, 1H), 4.45-4.80 (m, 6H), 5.29-5.39 (m, 2H), 4.76-5.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.7, 30.0, 55.6, 71.5, 74.6, 78.0, 78.2, 81.5, 94.2, 118.9, 127.5, 127.6, 127.9, 128.2, 128.3, 135.0, 138.0, 138.5, 179.4; HRMS (FAB) calcd for $[M+H]^+$ ($C_{24}H_{31}O_6$) 415.2116, found 415.2121.

(4*R*,5*R*,6*R*)-((*S*)-pent-4-en-2-yl)-4,5-bis(benzyloxy)-6-(methoxymethoxy)oct-7-enoate (3)

A solution of **11** (300 mg, 0.724 mmol), in THF (5 mL) was added with triethylamine (121 μL, 0.87 mmol) and 2,4,6-trichlorobenzyl chloride (136 μL, 0.87 mmol), and stirred for 1 h at rt. This solution was added into a solution of alcohol **5** and 4-dimethylaminopyridine (442 mg, 3.62 mmol) in toluene (27 mL). The reaction mixture was heated to reflux for 2 h, cooled to rt, quenched with sat. $NaHCO_{3(aq)}$ (15 mL), extracted withethyl acetate (10 mL × 3). The organic layers were combined, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:9; R_f 0.42) to give **3** (404 mg, 0.70 mmol, 80%) as a light yellow oil. $[\alpha]_D^{20}$ +4.88 (*c* 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (d, *J* = 6.3Hz, 3H), 1.26-1.38 (m, 14H), 2.01-2.11 (m, 4H), 2.41-2.47 (m, 2H), 3.38 (s, 3H), 3.65-3.70 (m, 1H), 3.71-3.74 (m, 1H), 4.25 (t, *J* = 6.9 Hz, 1H), 4.47-4.80 (m, 6H), 4.84-5.05 (m, 3H), 5.29-5.40 (m, 2H), 5.78-5.90 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.9, 25.0, 25.4, 28.8, 29.0, 29.4, 29.6, 30.6, 33.7, 35.9, 55.6, 70.8, 71.6, 74.6, 77.9, 78.5, 81.8, 94.3, 114.1, 118.7, 127.4, 127.6, 127.8, 127.9, 128.2, 128.3, 135.1, 138.3, 138.6, 139.1, 170.3; HRMS (FAB) calcd for $[M+H]^+$ ($C_{36}H_{52}O_6$) 580.3764, found 580.3755.

(5*R*,6*S*,7*R*,18*S*,*E*)-5,6-bis(benzyloxy)-7-(methoxymethoxy)-18-methyloxacyclooctadec-3-en-2-one (12)

A solution of **3** (50 mg, 0.086 mmol) and Grubbs catalyst, 2nd generation (3.7 mg, 4.3 mmol) in dichloromethane (44 mL) was placed in a reaction tube, sealed and heated in a 60 ºC oil bath for 16 h. The crude lactone (48 mg) was harvested after concentrated. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.20-1.42 (m, 17H), 1.95-2.19 (m, 4H), 2.29-2.58 (m, 2H), 3.36 (s, 3H), 3.64-3.73 (m, 1H), 3.81-3.86 (m, 1H), 4.11-4.26 (m, 1H), 4.33-5.05 (m, 7H), 5.28-5.43 (m, 1H), 5.77-5.89 (m, 1H); HRMS (FAB) calcd for $[M+H]^+$ ($C_{34}H_{48}O_6$) 552.3451 found 552.3458. The crude lactone (117 mg, 0.212 mmol) was added to the suspension of palladium on charcoal (10% wt, 32 mg) and ethyl acetate/methanol/triethylamine (50:50:1, 16 mL). The reaction mixture was stirred for 1 h under hydrogen atmosphere, filtered and concentrated to give the saturated lactone (115 mg). $[\alpha]_D^{20}$ +56.9 (*c* 0.80, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85-1.68 (m, 23H), 1.81-2.05 (m, 2H), 2.40-2.46 (m, 2H), 3.34 (s, 3H), 3.49-3.80 (m, 3H), 4.39-4.96 (m, 7H), 7.22-7.34 (m, 10H); HRMS (ESI) calcd for $[M+Na]^+$ ($C_{34}H_{50}O_6Na$) 577.3505, found 577.3507. A solution of the saturated lactone (115 mg, 0.21 mmol) in THF (2.5 mL) was added to the solution of LDA (0.83 mmol) in THF (2.5 mL) at -78 ºC dropwise. The solution was stirred for 1 h and added with diphenyl diselenide (226 mg, 0.73 mmol) and HMPA (90 μl) at -78 ºC. The reaction mixture was stirred for another 1.5 h at -40 ºC, warmed to rt, quenched with sat. $NH_4Cl_{(aq)}$ (5 mL), diluted with water (5 mL), extracted with ether (5 mL × 3). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residue was redissolved in dichloromethane (2 mL). Pyridine (32 μL, 0.39 mmol) and hydrogen peroxide (35% in water, 48 μL, 1.58 mmol) was added to the solution at 0 ºC and stirred for 1 h. The reaction mixture was stirred for another 16 h at rt, quenched with water (2 mL). The organic layer was separated, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:9; R_f 0.36) to give **12** as a light yellow oil (46 mg, 0.083 mmol, 40%, three steps). $[\alpha]_D^{20}$ -3.92 (*c* 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24-1.57 (m, 23H), 3.29 (s, 3H), 3.44-3.49 (m, 1H), 3.80 (dd, *J* = 1.2 Hz, 6.9 Hz, 1H), 4.16 (d, *J* = 5.7 Hz, 1H), 4.32-4.93 (m, 6H), 5.01-5.07 (m, 1H), 6.01 (dd, *J* = 0.6 Hz, 15.9 Hz, 1H), 6.12 (dd, *J* = 8.7 Hz, 15.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.4, 23.4, 25.2, 26.1, 26.6, 26.9, 27.4, 28.0, 28.1, 31.0, 35.3, 55.9, 70.6, 71.0, 74.3, 79.2, 84.1, 97.7, 125.3, 127.5, 127.8, 128.2, 128.3, 138.1, 138.7, 144.0, 165.4; HRMS (ESI) calcd for $[M+Na]^+$ ($C_{34}H_{48}O_6Na$) 575.3349, found 575.3351.

Aspicilin (1)

Boron trichloride (1 M in hexanes , 828 μL, 0.83 mmol) was added to the solution of **12** (38 mg, 0.069 mmol) in dichloromethane (3.5 mL) at -78 ºC. The reaction mixture was stirrer for 11 h and warmed up to rt during this period. Methanol (1 mL) was added to the solution, stirred for 1 h, and concentrated. The crude product was purified by column chromatography (SiO_2, EtOAc/hexanes, 1:1; R_f 0.35) to give **1** as a colorless solid (15 mg, 0.046 mmol, 66%). m.p. 152.0~154.0 ºC; $[\alpha]_D^{20}$ +36.20 (*c* 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15-1.54 (m, 23H), 3.52-3.60 (m, 1H), 3.68-3.80 (m, 1H), 4.51-4.59 (m, 1H), 6.09 (dd, *J* = 1.2 Hz, 15.9 Hz, 1H), 6.88 (dd, *J* = 5.1 Hz, 15.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.5, 23.6, 24.3, 26.4, 27.1, 27.2, 27.5, 27.8, 28.3, 32.0, 35.7, 69.9, 71.2, 73.3, 74.8, 123.0, 144.7, 165.6; HRMS (ESI) calcd for $[M+Na]^+$ ($C_{18}H_{32}O_5Na$) 351.2147, found 351.2150.

Supplementary data

^{1}H and ^{13}C NMR spectra for all the synthesized compounds are available.

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