SUPPORTING INFORMATION

Total synthesis of (±)-Simonsol C using acid-induced dearomatization as key reaction

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# Ⅰ. Comparison of the Spectra of Natural and Synthetic

**Table S1**. Comparison of the 1H NMR Data Recorded for simonsol C Obtained by the Present Route with those Reported by Dong.



|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No. | **Synthetic product (**δH**)** a | No. | **Isolated product (**δH**)** b | **Δδ** |
| OH-1’’ | 7.89 (1H, s) | OH-1’’ | 7.77 (1H, s) | +0.11 |
| 3’ | 7.22 (1H, d, 1.9) | 3’ | 7.23 (1H, d, 1.2) | -0.01 |
| 5’ | 7.12 (1H, d, 1.9) | 5’ | 7.12 (1H, d, 1.2) | 0 |
| 3’’ | 7.07 (1H, d, 2.3) | 3’’ | 7.07 (1H, d, 2.1) | 0 |
| 5’’ | 7.00 (1H, dd, 8.2, 2.1) | 5’’ | 7.01 (1H, dd, 8.2, 2.1) | -0.01 |
| 6’’ | 6.86 (1H, d, 8.2) | 6’’ | 6.86 (1H, d, 8.2) | 0 |
| 3 | 6.71 (1H, dd, 10.2, 1.9) | 3 | 6.71 (1H, dd, 10.2, 1.8) | 0 |
| 8’’ | 6.11-5.81  (4H, m) | 8’’ | 6.01(1H, ddt, 18.0, 12.4, 6.6)  5.96 (1H, ddt, 13.6, 11.7, 6.8)  5.93 (1H, d, 10.2)  5.91 (1H, dddd, 16.9, 10.1, 7.8, 6.8) | -- |
| 8’ | 8’ |
| 2 | 2 |
| 8 | 8 |
| 9 | 5.34 (1H, m)  5.17 (1H, dd, 10.1, 2.0) | 9 | 5.29 (1H, dd, 16.9, 2.0)  5.18 (1H, dd, 10.1, 2.0) | +0.05  -0.01 |
| 9’ | 5.14-4.95  (5H, m) | 9’ | 5.11 (1H, dd, 13.6, 3.6)  5.08 (1H, dd, 11.7, 3.6)  5.03 (1H, ddt, 18.0, 3.6, 1.7)  5.02 (1H, ddt, 12.4, 3.6, 1.7)  4.99 (1H, ddd, 3.4, 1.8, 1.5) | -- |
| 9’’ | 9’’ |
| 5 | 5 |
| 7’ | 3.39 (2H, d, 6.8) | 7’ | 3.40 (2H, d, 6.8) | -0.01 |
| 7’’ | 3.30 (2H, dt, 6.6, 1.7) | 7’’ | 3.30 (2H, dt, 6.6, 1.7) | 0 |
| 7 | 2.97 (1H, dd, 14.0, 6.8) | 7 | 2.97 (1H, dd, 14.0, 6.8) | 0 |
| 2.84(2H,dd,8.3, 3.4) | 2.79 (1H, dd, 14.0, 7.8)  2.89 (1H,dd, 16.0, 3.4) | -- |
| 6α | 6α |
| 6β | 2.81（m, 1H） | 6β | 2.83 (1H, dd, 16.0, 1.5) | -0.02 |

a spectrum recorded in (CD3)2CO at 400 MHz; b data obtained from Dong, spectrum recorded in (CD3)2CO at 600 MHz.

**Table S2**. Comparison of the 13C NMR Data Recorded for simonsol C Obtained by the Present Route with Those Reported by Dong.



|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No. | **Synthetic product** (δC) a | No. | **Isolated product** (δC) b | Δδ |
| 1 | 195.2 | 1 | 195.1 | +0.1 |
| 1’ | 155.4 | 1’ | 155.2 | +0.2 |
| 1’’ | 153.7 | 1’’ | 153.5 | +0.2 |
| 3 | 149.7 | 3 | 149.5 | +0.2 |
| 8’’ | 139.2 | 8’’ | 139.0 | +0.2 |
| 8’ | 139.1 | 8’ | 138.9 | +0.2 |
| 4’ | 134.4 | 4’ | 134.2 | +0.2 |
| 8 | 134.0 | 8 | 133.8 | +0.2 |
| 4’’ | 132.9 | 4’’ | 132.7 | +0.2 |
| 3’’ | 132.1 | 3’’ | 131.9 | +0.2 |
| 2’ | 132.0 | 2’ | 131.8 | +0.2 |
| 5’ | 131.8 | 5’ | 131.6 | +0.2 |
| 5’’ | 129.8 | 5’’ | 129.7 | +0.1 |
| 2 | 127.7 | 2 | 127.5 | +0.2 |
| 2’’ | 125.1 | 2’’ | 124.9 | +0.2 |
| 3’ | 123.5 | 3’ | 123.3 | +0.2 |
| 6’ | 122.4 | 6’ | 122.2 | +0.2 |
| 9 | 119.8 | 9 | 119.6 | +0.2 |
| 6’’ | 117.4 | 6’’ | 117.2 | +0.2 |
| 9’ | 115.9 | 9’ | 115.7 | +0.2 |
| 9’’ | 115.6 | 9’’ | 115.5 | +0.1 |
| 5 | 85.9 | 5 | 85.7 | +0.2 |
| 4 | 49.7 | 4 | 49.5 | +0.2 |
| 7 | 40.9 | 7 | 40.7 | +0.2 |
| 7’ | 40.5 | 7’ | 40.3 | +0.2 |
| 7’’ | 40.0 | 7’’ | 39.9 | +0.1 |
| 6 | 39.5 | 6 | 39.3 | +0.2 |

a spectrum recorded in (CD3)2CO at 100 MHz; b data obtained from Dong, spectrum recorded in (CD3)2CO at 150 MHz.

**Ⅱ.** **Experimental Procedures**

**General Experimental Procedures:** All reactions were performed with dry solvents under anhydrous conditions unless otherwise noted. Heating reactions involved in the experiment were performed using an oil bath unless specified otherwise. Dry tetrahydrofuran (THF) was distilled over sodium. Dichloromethane (DCM) was distilled over calcium hydride. N,N-Dimethylformamide (DMF) was dried over calcium hydride. Dichloromethane were distilled over calcium hydride. Reagents were used as received without further purification unless otherwise stated. Silica gel (200-300 mesh, Qingdao Marine Chemical Ltd., China), light petroleum ether (bp 60–90 ºC), and ethyl acetate were used for product purification by flash column chromatography. Proton nuclear magnetic resonance (1H-NMR) spectra were recorded on Bruker Avance 400 spectrometer at 400 MHz. Carbon-13 nuclear magnetic resonance (13 C NMR) was recorded on Bruker Avance 400 at 100 MHz. Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad, coupling constant (*J*) in Hertz (Hz), and integration. Mass spectra were recorded on a VG-AutoSpec-3000 spectrometer. High-resolution mass spectral analysis (HRMS) data were recorded via electron impact mass spectrometry using a time-of-flight analyzer.



**Synthesis of compound 17：**To a solution of **11** (3.0 g, 11 mmol, 1.0 equiv.) in DCM (37.5 mL) was added DIPEA (6.2 mL, 33 mmol, 3 equiv.) stirring for 5 minutes at 0 ℃, after add MOMCl (1.0 mL, 14 mmol, 1.2 equid.) stirring for 5 h at 0 ℃, the reaction mixture was quenched with NH4Cl aqueous solution. The mixture was concentrated in vacuo and diluted with EtOAc (50 mL), and washed with brine (3×10 mL). The organic phase was dried over Na2SO4 and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **17** (3.1 g, 89%) as colorless liquid.**1H NMR** (400 MHz, CDCl3) δ 7.21 – 7.04 (m, 5H), 6.96 (d, J = 8.2 Hz, 1H), 6.09 (s, 1H), 5.98 (m, 2H), 5.17 – 5.03 (m, 6H), 3.38 (q, J = 5.3, 3.6 Hz, 7H). **13C NMR** (100 MHz, CDCl3) δ 152.0, 151.9, 137.9, 137.4, 135.4, 132.6, 132.5, 131.3, 129.5, 129.5, 128.4, 126.2, 117.4, 116.7, 116.2, 115.7, 96.2, 77.5, 77.2, 76.8, 56.6, 39.6.



**Synthesis of compound 18：**To a solution of **17** (2.6 g, 8.4 mmol, 1.0 equiv.) of in 9 mL of THF was cooled to 0 ℃ to a suspension of 60% NaH (0.67 g, 17 mmol, 2 equiv.) in 19 mL of THF, Stirring for 30 minutes at 0 ℃. After add Tert-butyl bromoacetate (1.5 mL, 10 mmol, 1.2 equiv.) stirring for 2 h at RT, the reaction mixture was quenched with H2O aqueous solution. The mixture was concentrated in vacuo and diluted with EtOAc (50 mL), and washed with brine (3×10 mL). The organic phase was dried over Na2SO4 and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **18** (3.4 g, 95%) as colorless liquid.**1H NMR** (400 MHz, CDCl3) δ 7.22 – 7.10 (m, 5H), 6.84 – 6.77 (m, 1H), 6.02 (m, 2H), 5.19 – 5.05 (m, 6H), 4.45 (s, 2H), 3.44 – 3.34 (m, 7H), 1.48 (s, 9H). **13C NMR** (100 MHz, CDCl3) δ 168.3, 154.1, 153.5, 137.8, 137.7, 133.3, 132.8, 132.0, 131.7, 128.8, 128.7, 128.4, 128.4, 115.8, 115.7, 115.7, 112.5, 95.6, 81.9, 77.5, 77.2, 76.8, 66.7, 55.8, 39.5, 39.4, 28.1. HRMS (ESI+): C26H36O5 [M+NH4]+ calcd.442.2588, found 442.2579.



**Synthesis of compound 16：**To a solution of **18** (3.0 g, 7.1 mmol, 1.0 equiv.) of in 14mL of THF was cooled to-78 ℃ to a suspension of 1M LDA (11 ml, 11 mmol, 1.5 equiv.) stirring for 1 h. Dissolve 4-Bromobenzyl bromide (2.1 g, 8.5 mmol, 1.2 equiv.) in THF and added to the flask stirring for 2 h at -78 ℃, the reaction mixture was quenched with H2O aqueous solution. The mixture was concentrated in vacuo and diluted with EtOAc (50 mL), and washed with brine (3×10 mL). The organic phase was dried over Na2SO4 and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **16** (2.9 g, 69%) as colorless liquid.**1H NMR** (400 MHz, CDCl3) δ 7.24 – 7.11 (m, 4H), 7.08 – 6.98 (m, 3H), 6.72 – 6.60 (m, 3H), 6.08 – 5.83 (m, 2H), 5.20 – 4.95 (m, 6H), 4.47 (m, 1H), 3.43 – 3.26 (m, 7H), 2.91 (dd, *J* = 6.0, 3.6 Hz, 2H), 1.36 (s, 9H).**13C NMR** (100 MHz, CDCl3) δ 170.0, 153.6, 153.5, 137.8, 137.7, 135.3, 133.2, 132.5, 131.9, 131.8, 131.5, 131.0, 128.5, 128.4, 128.2, 115.9, 115.7, 115.6, 112.4, 95.6, 82.0, 77.8, 55.9, 39.6, 39.4, 38.4, 28.0. HRMS (ESI+): C33H41BrNO5 [M+NH4]+ calcd. 610.2163, found 610.2147;



**Synthesis of compound 19：**To a solution of **16** (1.2 g, 2.0 mmol, 1.0 equiv.) of in 7mL of THF was cooled to 0 ℃. After add LAH (0.15 g, 4.1 mmol, 2 equiv.) stirring for 10 minutes at 0 ℃, the reaction mixture was quenched with H2O aqueous solution. The mixture was concentrated in vacuo and diluted with EtOAc (50 mL), and washed with brine (3×10 mL). The organic phase was dried over Na2SO4 and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **19** (0.93g, 89%) as colorless liquid.**1H NMR** (400 MHz, CDCl3) δ 7.35 – 7.25 (m, 2H), 7.16 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.13 – 7.04 (m, 4H), 6.94 – 6.89 (m, 2H), 6.81 (d, *J* = 9.1 Hz, 1H), 5.97 (m, 2H), 5.14 – 5.02 (m, 4H), 4.99 (d, *J* = 6.5 Hz, 1H), 4.90 (d, *J* = 6.5 Hz, 1H), 4.38 (s, 1H), 3.69 (d, *J* = 12.0 Hz, 1H), 3.45 – 3.30 (m, 5H), 3.20 (s, 3H), 2.91 (dd, *J* = 13.8, 6.2 Hz, 1H), 2.74 (dd, *J* = 13.8, 7.1 Hz, 1H).**13C NMR** (100 MHz, CDCl3) δ 153.1, 153.0, 137.6, 137.6, 136.6, 134.7, 132.7, 131.8, 131.5, 131.4, 131.28, 128.9, 128.7, 115.9, 115.7, 96.8, 77.4, 77.1, 76.8, 62.4, 56.2, 39.5, 39.4, 36.3. HRMS (ESI+): C29H35BrNO4 [M+NH4]+ calcd.540.1744 found 540.1732.



**Synthesis of compound 20：**The **19** (0.58 mg, 1.1 mmol, 1 equiv.), LiOH·H2O (0.10 g, 2.4 mmol, 2.2 equiv.), Cu(acac)2 (29 mg, 0.1 mmol, 0.1 equiv.) and ligand L5 (36 mg, 0.1 mmol, 0.1 equiv.) were placed into a Schlenk tube (10 mL) with a magnetic stir bar. The reaction vessel was evacuated and backfilled with argon three times, and DMSO:H2O = 4:1 (3.7 mL) was added afterwards. The reaction mixture was heated at 80 °C for 24 h under vigorous stirring. The mixture was concentrated in vacuo and diluted with EtOAc (50 mL), and washed with brine (3×10 mL). The organic phase was dried over Na2SO4 and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **20** (431 mg, 85%) as yellow liquid.**1H NMR** (400 MHz, CDCl3) δ 7.21 – 7.08 (m, 5H), 6.97 – 6.86 (m, 3H), 6.74 – 6.62 (m, 3H), 6.00 (m, 2H), 5.18 – 5.05 (m, 4H), 5.00 (d, *J* = 6.5 Hz, 1H), 4.90 (d, *J* = 6.6 Hz, 1H), 4.43 (s, 1H), 3.71 (d, *J* = 11.6 Hz, 1H), 3.49 (dd, *J* = 11.3, 5.6 Hz, 1H), 3.43 – 3.37 (m, 4H), 3.19 (s, 3H), 2.95 (dd, *J* = 13.9, 5.0 Hz, 1H), 2.69 (dd, *J* = 13.9, 8.6 Hz, 1H). **13C NMR** (100 MHz, CDCl3) δ154.8, 153.3, 152.7, 137.7, 137.5, 135.1, 132.6, 131.8, 131.5, 130.8, 130.4, 129.0, 128.9, 128.8, 128.8, 118.2, 115.9, 115.7, 115.4, 97.0, 80.1, 77.4, 77.3, 77.1, 76.8, 62.6, 56.2, 39.5, 39.4, 35.9. HRMS (ESI+): C29H31O5 [M-H]- calcd. 459.2177, found 459.2170.



**Synthesis of compound 14：**To a solution of **16** (430 mg, 0.935 mmol, 1.0 equiv.) of in 14mL of TFE was cooled to -30 ℃ stirring for 5 minutes. Dissolve PIDA (278 mg, 1.12 mmol, 1.2 equiv.) in TFE and added to the flask stirring for 0.5 h at -30 ℃, the reaction mixture was quenched with H2O aqueous solution. The mixture was concentrated in vacuo and diluted with EtOAc (50 mL), and washed with brine (3×10 mL). The organic phase was dried over Na2SO4 and concentrated in vacuo. The crude product was purified by column chromatography to provide compound **14** (248 mg, 58%) as colorless liquid[1].**1H NMR** (400 MHz, CDCl3) δ 7.23 – 7.00 (m, 5H), 6.88 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.73 (d, *J* = 2.2 Hz, 1H), 6.46 (dd, *J* = 10.0, 1.9 Hz, 1H), 6.26 (dd, *J* = 10.1, 1.9 Hz, 1H), 6.06 – 5.81 (m, 2H), 5.19 – 4.88 (m, 6H), 4.46 – 4.27 (m, 1H), 3.84 (dd, *J* = 12.1, 2.9 Hz, 1H), 3.58 (dd, *J* = 12.0, 4.4 Hz, 1H), 3.39 (d, *J* = 6.9 Hz, 2H), 3.27 (d, *J* = 6.9 Hz, 5H), 2.37 (t, *J* = 12.9 Hz, 1H), 1.83 (dd, *J* = 13.7, 2.4 Hz, 1H).**13C NMR** (100 MHz, CDCl3) δ 185.9, 153.9, 153.4, 150.2, 137.6, 137.3, 133.5, 132.1, 131.6, 131.5, 129.0, 128.9, 128.5, 128.2, 127.6, 119.2, 116.0, 115.8, 115.6, 95.4, 62.2, 55.9, 41.4, 39.5, 39.3, 32.8.



**Synthesis of compound 15：**After stirring a solution of imidazole (30 mg, 0.44 mmol, 2.0 equiv.) and PPh3 (115 mg, 0.44 mmol, 2.0 equiv.) in DCM (1 mL) at room temperature for 0.5 h, iodine (112 mg, 0.44 mmol, 2 equiv.) was added and the resulted solution was stirred at room temperature for 0.5 h. Then, **compound 14** (100 mg, 0.22 mmol, 1.0 equiv.) in 1 mL DCM was added dropwise and stirring was continued overnight until the starting material was consumed (judged by TLC). The reaction mixture was quenched with saturated Na2S2O3 solution (3 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic phases were washed with brine (3 × 10 mL), dried over Na2SO4 and concentrated under vacuum. The crude product was purified by column chromatography to obtain white solid **compound 15** (86 mg, 75%). **1H NMR** (400 MHz, CDCl3) δ 7.20 – 6.99 (m, 5H), 6.87 (dd, J = 9.9, 3.0 Hz, 1H), 6.70 (d, J = 2.3 Hz, 1H), 6.45 (dd, J = 10.0, 1.9 Hz, 1H), 6.26 (dd, J = 10.0, 1.9 Hz, 1H), 6.07 – 5.82 (m, 2H), 5.12 – 5.07 (m, 3H), 5.06 – 5.00 (m, 2H), 4.14 (dq, J = 9.6, 5.8 Hz, 1H), 3.38 (s, 3H), 3.31 – 3.24 (m, 3H), 2.21 – 2.07 (m, 2H).**13C NMR** (100 MHz, CDCl3) δ 185.7, 154.1, 153.2, 152.5, 137.8, 137.1, 133.1, 132.4, 132.0, 129.0, 128.8, 127.6, 126.5, 119.0, 116.0, 115.6, 115.3, 95.4, 71.1, 56.0, 42.1, 39.47, 39.2, 38.1, 29.7, 7.4.



**Synthesis of compound (±)-simonsol C：** Zinc powder (53 mg, 0.82 mmol, 10.0 equiv.) and acetic acid (1 drop) was added to a solution of **compound 15** (43 mg, 0.08 mmol, 1.0 equiv.) in methanol (1 mL). After stirring at room temperature for 0.5 h, the reaction mixture was refluxed for 1 h until the starting material was consumed. The reaction mixture was subsequently concentrated under reduced pressure and purified by column chromatography, yielding **(±)-Simonsol C** (22 mg, 70% yield) as white amorphous. **1H NMR** (400 MHz, Acetone-d6) δ 7.89 (s, 1H), 7.22 (d, *J* = 1.9 Hz, 1H), 7.12 (d, *J* = 1.9 Hz, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 7.00 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.71 (dd, *J* = 10.2, 1.9 Hz, 1H), 6.11 – 5.81 (m, 4H), 5.34 – 5.24 (m, 1H), 5.17 (dd, *J* = 10.2, 2.1 Hz, 1H), 5.14 – 4.95 (m, 5H), 3.39 (d, *J* = 6.8 Hz, 2H), 3.29 (d, *J* = 6.8 Hz, 2H), 2.90 (d, *J* = 3.9 Hz, 1H), 2.84 (dd, *J* = 8.3, 3.4 Hz, 2H), 2.81 – 2.74 (m, 1H). **13C NMR** (100 MHz, Acetone-d6) δ 195.2, 149.7, 139.2, 139.1, 134.0, 132.1, 131.8, 129.8, 127.7, 123.5, 119.8, 117.4, 115.9, 115.6, 85.9, 49.7, 40.9, 40.5, 40.1, 39.5.

# Ⅲ. NMR Spectra for the Synthesized Compounds

**1H NMR (400 MHz, CDCl3) of Compound 17**



**13C NMR (100 MHz, CDCl3) of compound 17**



**1H NMR (400 MHz, CDCl3) of compound 18**



**13C NMR (100 MHz, CDCl3) of compound 18**



**1H NMR (400 MHz, CDCl3) of compound 16**



**13C NMR (100 MHz, CDCl3) of compound 16**



**1H NMR (400 MHz, CDCl3) of compound 19**



**13C NMR (100 MHz, CDCl3) of compound 19**



**1H NMR (400 MHz, CDCl3) of compound 20**



**13C NMR (100 MHz, CDCl3) of compound 20**



**1H NMR (400 MHz, CDCl3) of compound 14**



**13C NMR (100 MHz, CDCl3) of compound 14**



**1H NMR (400 MHz, CDCl3) of compound 15**



**13C NMR (100 MHz, CDCl3) of compound 15**



**1H NMR (400 MHz, (CD3)2CO) of (±)-simonsol C**



**13C NMR (100 MHz, (CD3)2CO) of (±)-simonsol C**



[1] J.-J. Sui, K. Wang, S.-J. Luo, K. Guo, M.-W. Yuan, H.-B. Qin, *J. Org. Chem.* **2024**, *89*, 7821-7827.