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ARTICLE

Synthesis and anti-inflammatory effect of morachalcone B, morachalcone C, and analogs

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An efficient method to synthesize morachalcones B and C (**1** and **2**) is described. Rap−Stoermer condensation and 1,3-prenyl rearrangement were used as two key synthetic methods. Morachalcone C was obtained by photo-oxygenation of morachalcone B. Morachalcones B and C showed moderate anti-inflammatory activity.

KEYWORDS

anti-inflammatory activity, morachalcone B, morachalcone C, Rap−Stoermer condensation

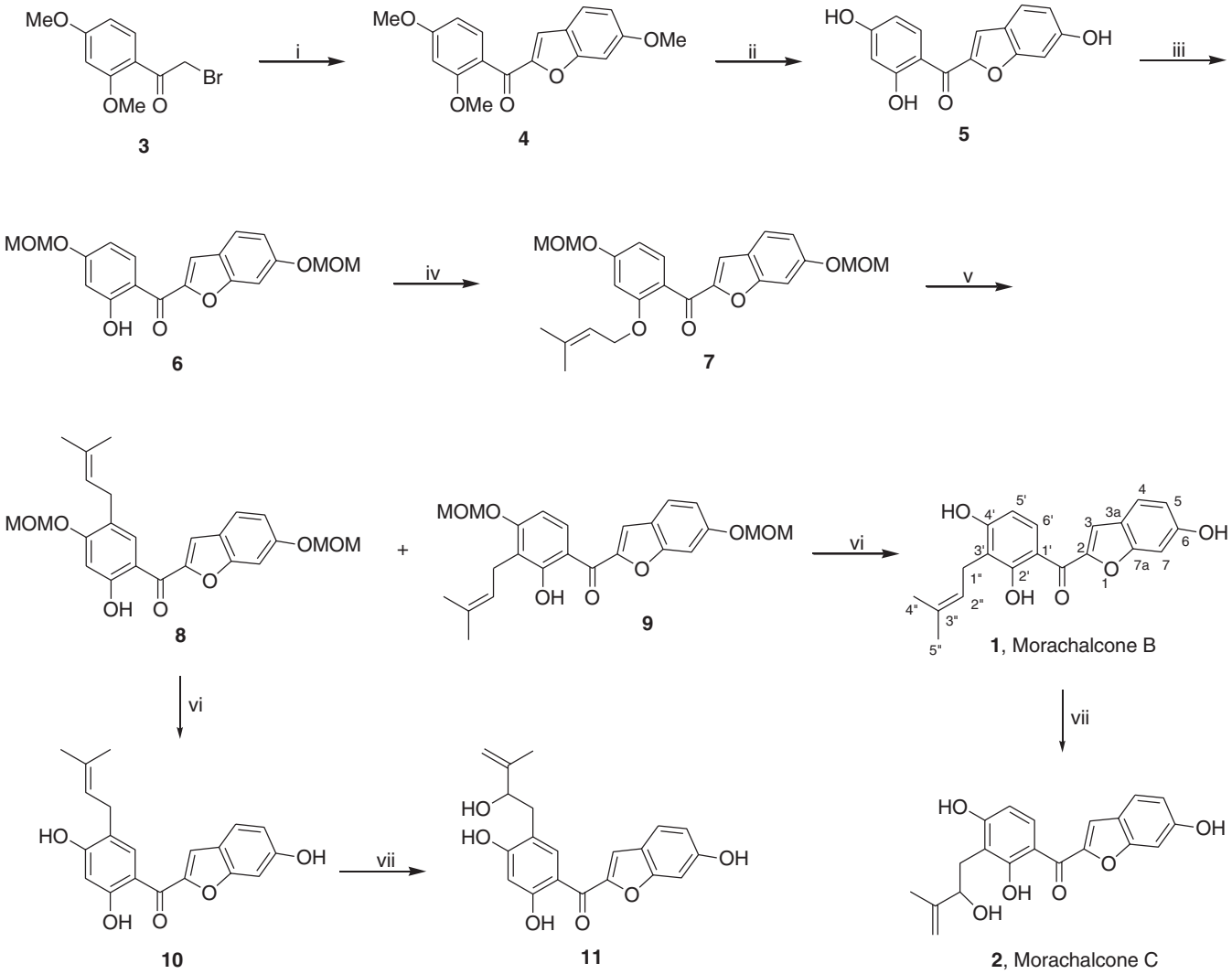
1 | INTRODUCTION

Morachalcones B and C (**1** and **2**), two novel chalcone derivatives, were isolated and characterized from the leaves of *Mora alba* L., and showed moderate cytotoxic activity against HCT-8 and BGC823 human cancer cell lines.[1] Leaves of *M. alba* L. is used in traditional Chinese medicine for the treatment of cold, headache, diabetes, keratitis, and otitis media.[2] Naturally occurring chalcones and synthesized analogs have been reported to have various bioactivities such as antioxidant, antimicrobial, antimalarial, anticancer, and vasorelaxant.[3–7] Because of their various beneficial effects, compounds related to chalcones have attracted attention as synthetic targets. Previously, morachalcone A, a naturally occurring chalcone, was synthesized and exhibited aromatase inhibitory activity.[8,9] To our knowledge, no work has been done on total synthesis of **1** and **2**. It seems important to develop synthetic routes of **1** and **2** for further studies on their biological activity. Here we report a facile synthesis of **1** and **2** and evaluation of their anti-inflammatory activity.

2 | RESULTS AND DISCUSSION

The synthetic strategy shown in Scheme 1 was employed for the synthesis of morachalcones B and C (**1** and **2**). The starting 2-bromo-1-(2,4-dimethoxyphenyl)ethanone (**3**) was prepared from 2',4'-dimethoxyacetophenone by a known procedure.[10] Rap−Stoermer condensation of **3** and 2-hydroxy-4-methoxybenzaldehyde in the presence of K_2CO_3 under reflux gave **4** in moderate yield.[11] Demethylation of **4** with excess BBr_3 in CH_2Cl_2 provided **5**. Two hydroxyl groups of **5** were protected with chloromethyl methyl ether (MOMCl) in the presence of *N*, *N*-diisopropylethylamine (DIPEA) in CH_2Cl_2 to yield **6**, which was then treated with prenyl bromide to afford **7**. 1,3-Prenyl rearrangement of **7** using montmorillonite K10 as a catalyst in CH_2Cl_2 gave a mixture of **8** and **9**.[12,13] Deprotection of the MOM group in **8** and **9** was achieved by reaction with H_2SO_4 to afford **10** and **1**, respectively.[14] Finally, compounds **11** and **2** were obtained from **10** and **1**, respectively, by photo-oxygenation reaction at 15°C using tetraphenylporphin (TPP) as the photosensitizer.[15] The ^1H and ^{13}C NMR data of **1**, **2**, **10**, and **11** are summarized in Table 1. The spectroscopic data of the synthesized **1** and **2** were identical to those of naturally occurring morachalcones B and C, respectively. The corresponding ^1H and ^{13}C NMR spectra of **1**, **2**, and **4**-**11** are shown in Supporting Information Figures S1 to S20.

Inhibitory effect of selected compounds **1**, **2**, **4**, **5**, **10**, and **11** in nitric oxide (NO) production in the microglia cell line (BV2)[16] was evaluated, and results are shown in Table 2. Ammonium pyrrolidinedithiocarbamate (PDTC), a selective NF-κB inhibitor, was used as the positive control.



SCHEME 1 *Reagents and conditions*: (i) 2-hydroxy-4-methoxybenzaldehyde, K_2CO_3, reflux; (ii) excess BBr_3, CH_2Cl_2; (iii) MOMCl, DIPEA, CH_2Cl_2; (iv) prenyl bromide, K_2CO_3, acetone, reflux; (v) montmorillonite K10, CH_2Cl_2; (vi) H_2SO_4, THF/i-PrOH; (vii) TPP, acetone, O_2, hν

The 50% effective concentration (EC_{50}) for inhibiting the production of NO was calculated on the basis of nitrite released into the culture media. Cell viability under this condition was still >95% as measured by MTT assay, indicating that the inhibition of nitrite production by these compounds was not due to cell death. As shown in Table 2, compounds **1** and **2** displayed moderate effect for inhibiting NO production. Compounds **10** and **11** strongly inhibited NO production with EC_{50} values of 14.1 and 11.2 μM, respectively.

Compounds **1**, **2**, **4**, **5**, **10**, and **11** were also evaluated for antioxidant effect by a DPPH radical scavenging assay. The results showed no free-radical scavenging activities.

3 | EXPERIMENTAL

3.1 | General experimental procedures

Melting points were determined on a Yanaco MP-13 micro-melting point apparatus and are uncorrected. Infrared spectra were obtained on a Thermo Scientific Nicolet is5 FTIR spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian Unity Inova 500 MHz and VNMRS 600 FT-NMR spectrometers. Chemical shifts are reported in parts per million (δ) units relative to the internal standard tetramethylsilane. The electron ionization mass (EI-MS) spectra were measured with a direct insertion probe on a Finnigan DSQ II mass spectrometer at 70 eV. High resolution mass spectra were recorded on Thermo Scientific Q Exactive Focus Orbitrap instrument. Column chromatography was performed with E. Merck 230–400 mesh silica gel.

3.2 | (6-Methoxybenzofuran-2-yl) (2,4-dimethoxyphenyl)-methanone (4)

To a stirred solution of **3** (1.55 g, 6.0 mmol) in acetone (60 mL) was added K_2CO_3 (2.76 g, 20.0 mmol) and 2-hydroxy-4-methoxybenzaldehyde (0.76 g, 5.0 mmol), and the mixture was refluxed for 20 hr. After cooling, acetone was removed using a rotavaporator, and water was added. The mixture was extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4, filtered, and

TABLE 1 NMR spectral data for **1**, **2**, **10**, and **11** in acetone-d_6

	1		**10**		**2**		**11**	
Position	δ_H[a]	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2	—	152.7	—	152.9	—	152.6	—	152.4
3	7.71 (d, 1.0)	117.2	7.69 (s)	116.9	7.73 (s)	117.3	7.70 (s)	117.1
3a	—	120.5	—	120.5	—	120.5	—	120.5
4	7.66 (d, 8.5)	124.7	7.66 (d, 8.5)	124.7	7.66 (d, 8.5)	124.7	7.65 (d, 8.5)	124.7
5	6.96 (dd, 8.5, 2.5)	115.3	6.97 (dd, 8.5, 2.0)	115.3	6.97 (dd, 8.5, 2.0)	115.3	6.96 (dd, 8.5, 2.0)	115.3
6	—	159.8		159.8	—	159.8	—	159.8
7	7.09 (m)	98.5	7.08 (m)	98.4	7.10 (m)	98.5	7.08 (m)	98.5
7a	—	158.4	—	158.3	—	158.4	—	158.3
1'	—	113.0	—	112.9	—	112.8	—	113.0
2'	—	165.1	—	166.0	—	165.5	—	166.1
3'	—	116.2	6.45 (s)	103.4	—	114.1	6.40 (s)	104.3
4'	—	163.0		163.7	—	164.8	—	164.7
5'	6.60 (d, 9.0)	108.5		121.4	6.55 (d, 8.5)	109.7	—	119.4
6'	8.26 (d, 9.0)	132.1	8.29 (s)	133.6	8.31 (d, 8.5)	132.8	8.26 (s)	136.0
1″	3.39 (d, 7.5)	22.3	3.31 (d, 7.0)	28.0	2.93 (dd, 14.0, 8.0)	30.0	2.88 (dd, 14.5, 7.5)	37.7
					3.12 (dd, 14.0, 3.5)		2.96 (dd, 14.5, 4.0)	
2″	5.27–5.30 (m)	123.1	5.40–5.43 (m)	123.1	4.43 (dd, 8.0, 3.5)	76.5	4.43 (dd, 7.5, 4.0)	76.2
3″	—	131.7	—	133.5	—	148.3	—	148.2
4″	1.78 (s)[b]	17.9[b]	1.76 (s)[b]	17.8[b]	1.84 (s)	18.3	1.83 (s)	18.4
5″	1.64 (d, 0.5)[b]	25.8[b]	1.79 (d, 1.0)[b]	26.0[b]	4.76–4.77 (m)	110.4	4.79–4.80 (m)	110.9
					4.94–4.95 (m)		4.94–4.95 (m)	
2'-OH	13.2 (s)	—	12.8 (s)	—	13.4 (s)	—	12.6 (s)	—
C=O	—	185.4	—	184.9	—	185.3	—	185.1

[a] (Multiplicity, J in Hz) in ppm.
[b] Interchangeable.

TABLE 2 Inhibitory effects of compounds **1**, **2**, **4**, **5**, **10**, and **11** in nitric oxide production in cell line (BV2)[a]

Compound	**EC_{50} (μM)**
1	29.2 ± 0.8
2	33.2 ± 3.2
4	29.5 ± 4.1
5	>50
10	14.1 ± 1.6
11	11.2 ± 0.7
PDTC	10.7 ± 0.3

[a] Results are expressed as the mean ± SE of triplicate tests. EC_{50} represented the 50% effective concentration to inhibit NO production.

concentrated. The residue was purified by silica gel column chromatography eluting with 15% EtOAc in hexane to give **4** (800 mg, 51%) as a white solid. M.p. 88–89°C (EtOAc/hexane); Infrared (IR) (ν_{max}, KBr) 3,017, 2,991, 2,946, 1,643, 1,608, 1,550, 1,492, 1,339, 1,307, 1,267, 1,209, 1,154, 1,112, 976, 842, 819, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 3.78 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 6.52–6.54 (m, 2H), 6.90 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 (d, J = 2.4 Hz, 1H), 7.23 (d, J = 0.6 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 55.5, 55.7, 55.8, 95.6, 99.0, 104.3, 114.1, 116.4, 120.5, 121.0, 123.5, 131.7, 153.0, 157.5, 159.6, 161.0, 163.4, 183.2; HRMS (ESI-Orbitrap) m/z 313.1069 $[M + H]^+$ (calcd for $C_{18}H_{17}O_5$, 313.1071).

3.3 | (6-Hydroxybenzofuran-2-yl) (2,4-dihydroxyphenyl)-methanone (5)

To a stirred solution of **4** (1.25 g, 4.0 mmol) in dry CH_2Cl_2 (20 mL) under N_2 was added 1.0 M BBr_3 in CH_2Cl_2 (24 mL, 24.0 mmol) at 0°C, and the mixture was stirred at room temperature for 40 hr. The reaction mixture was added to 1:1 MeOH/H_2O (20 mL) cautiously and stirred for further 2 hr. The reaction mixture was concentrated and water was added. The mixture was extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with 20% EtOAc in hexane to give **5** (670 mg, 62%) as a yellow solid. M.p. > 300°C (EtOAc/hexane); IR (ν_{max}, KBr) 3,320, 3,246, 3,116, 1,623, 1,595, 1,539, 1,491, 1,446, 1,337, 1,293, 1,242, 1,152, 1,117, 892, 850, 824, 772 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 6.42 (dd, J = 2.5 Hz, 1H), 6.54 (dd, J = 9.0, 2.5 Hz, 1H), 6.96 (dd, J = 8.5, 2.0 Hz, 1H), 7.10 (m, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.73 (d, J = 1.0 Hz, 1H), 8.41 (d, J = 9.0 Hz, 1H), 12.9 (br s, OH); ^{13}C NMR (acetone-d_6, 125 MHz) δ 98.5, 103.7, 109.2, 113.1, 115.3, 117.2, 120.4, 124.7, 135.0, 152.6, 158.4, 159.9, 165.8, 167.3, 185.0;

HRMS (ESI-Orbitrap) *m/z* 269.0449 $[M-H]^-$ (calcd for $C_{15}H_9O_5$, 269.0444).

3.4 | (2-Hydroxy-4-[methoxymethoxy]phenyl) (6-[methoxy-methoxy]benzofuran-2-yl)methanone (6)

To a stirred solution of **5** (310 mg, 1.14 mmol) in dry CH_2Cl_2 (40 mL) under N_2 was added DIPEA (1 mL, 5.48 mmol) and MOMCl (0.48 mL, 2.85 mmol) at 0°C, and the mixture was stirred at 0°C for 1 hr. To the reaction mixture was added water and extracted with CH_2Cl_2 three times. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with 10% EtOAc in hexane to give 6 (320 mg, 78%) as a yellow oil. IR (ν_{max}, KBr) 3,078, 2,959, 2,910, 2,831, 1,620, 1,582, 1,536, 1,489, 1,370, 1,309, 1,253, 1,230, 1,150, 1,109, 1,008, 989, 952, 829 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 3.47 (s, 3H), 3.48 (s, 3H), 5.32 (s, 2H), 5.33 (s, 2H), 6.63 (d, J = 3.0 Hz, 1H), 6.70 (dd, J = 9.0, 3.0 Hz, 1H), 7.11 (dd, J = 9.0, 2.0 Hz, 1H), 7.38 (m, 1H), 7.75 (d, J = 9.0 Hz, 1H), 7.80 (d, J = 1.0 Hz, 1H), 8.51 (d, J = 9.0 Hz, 1H), 12.7 (s, OH); ^{13}C NMR (acetone-d_6, 125 MHz) δ 56.3, 56.5, 94.9, 95.5, 99.5, 104.3, 109.5, 114.3, 116.3, 117.3, 122.0, 124.7, 134.6, 153.1, 157.9, 159.5, 164.8, 167.1, 185.3; HRMS (ESI-Orbitrap) *m/z* 359.1121 $[M + H]^+$ (calcd for $C_{19}H_{19}O_7$, 359.1125).

3.5 | (2-(3-Methylbut-2-enyloxy)-4-[methoxymethoxy] phenyl) (6-[methoxymethoxy]benzofuran-2-yl) methanone (7)

To a stirred solution of **6** (608 mg, 1.91 mmol) in acetone (35 mL) was added K_2CO_3 (790 mg, 5.73 mmol) and prenyl bromide (0.4 mL, 2.87 mmol), and the reaction mixture was refluxed overnight. After cooling, acetone was removed using a rotavaporator, and water was added. The mixture was extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with 15% EtOAc in hexane to give 7 (600 mg, 74%) as a yellow oil. IR (ν_{max}, KBr) 2,954, 2,924, 2,854, 1,624, 1,579, 1,542, 1,492, 1,376, 1,338, 1,243, 1,152, 1,070, 1,059, 991, 921, 831 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.61 (s, 3H), 1.63 (d, J = 0.5 Hz, 3H), 3.48 (s, 3H), 3.50 (s, 3H), 4.50 (d, J = 7.0 Hz, 2H), 5.21 (s, 4H), 5.22–5.25 (m, 1H), 6.66 (d, J = 2.0 Hz, 1H), 6.68 (dd, J = 8.5, 2.0 Hz, 1H), 7.00 (dd, J = 8.5, 2.0 Hz, 1H), 7.24 (m, 1H), 7.27 (d, J = 1.0 Hz, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.51 (d, J = 8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.2, 25.6, 56.1, 56.2, 65.8, 94.3, 94.8, 99.3, 101.8, 107.3, 114.7, 115.7, 119.2, 121.7, 122.3, 123.4, 131.5, 137.8, 153.5, 157.0, 158.1, 158.8, 160.9, 183.6; HRMS (ESI-Orbitrap) *m/z* 427.1750 $[M + H]^+$ (calcd for $C_{24}H_{27}O_7$, 427.1751).

3.6 | (2-Hydroxy-4-(methoxymethoxy)-5-[3-methylbut-2-enyl]phenyl)(6-[methoxy-methoxy]benzofuran-2-yl) methanone (8) and (2-hydroxy-4-(methoxymethoxy)-3-[3-methylbut-2-enyl]phenyl)(6-(methoxymethoxy)-benzofuran-2-yl)methanone (9)

To a stirred solution of **7** (550 mg, 1.29 mmol) in dry CH_2Cl_2 (25 mL) was added montmorillonite K10 (550 mg) at 0°C, and the reaction mixture was stirred at 0°C for 2 hr. After completion of the reaction, the reaction mixture was filtrated and concentrated under vacuum. The residue was purified by silica gel column chromatography eluting with 15% EtOAc in hexane to give **8** (83 mg, 15%) and **9** (91 mg, 17%).

Compound 8: A yellow solid: M.p. 70°C; IR (ν_{max}, KBr) 3,330, 2,966, 1,623, 1,533, 1,506, 1,362, 1,274, 1,170, 1,120, 975, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.74 (s, 3H), 1.79 (d, J = 1.0 Hz, 3H), 3.29 (d, J = 7.5 Hz, 2H), 3.48 (s, 3H), 3.50 (s, 3H), 5.24 (s, 2H), 5.26 (s, 2H), 5.32–5.35 (m, 1H), 6.67 (s, 1H)), 7.05 (dd, J = 8.5, 2.0 Hz, 1H), 7.30 (d, J = 2.0 Hz, 1H), 7.55 (d, J = 1.0 Hz, 1H), 7.59 (d, J = 8.5 Hz, 1H), 8.20 (s, 1H), 12.6 (s, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.8, 25.8, 27.8, 56.1, 56.4, 94.0, 94.9, 99.0, 102.0, 113.0, 115.2, 115.8, 121.3, 122.0, 122.2, 123.3, 132.1, 133.3, 152.6, 157.0, 158.3, 161.6, 165.0, 184.5; HRMS (ESI-Orbitrap) *m/z* 427.1753 $[M + H]^+$ (calcd for $C_{24}H_{27}O_7$, 427.1751).

*Compound **9***: A yellow solid. M.p. 67–68°C; IR (ν_{max}, KBr) 2,971, 2,938, 1,612, 1,581, 1,509, 1,450, 1,403, 1,342, 1,252, 1,188, 1,120, 1,024, 1,005, 845, 769 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.67 (d, J = 1.0 Hz, 3H), 1.80 (d, J = 0.5 Hz, 3H), 3.42 (d, J = 7.0 Hz, 2H), 3.48 (s, 3H), 3.50 (s, 3H), 5.23–5.25 (m, 1H), 5.24 (s, 2H), 5.29 (s, 2H), 6.72 (d, J = 9.0 Hz, 1H), 7.04 (dd, J = 8.5, 2.0 Hz, 1H), 7.30 (m, 1H), 7.56 (d, J = 1.0 Hz, 1H), 7.59 (d, J = 8.5 Hz, 1H), 8.23 (d, J = 9.0 Hz, 1H), 12.7 (s, OH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.8, 22.0, 25.8, 56.2, 56.3, 93.8, 94.8, 99.1, 105.2, 113.9, 115.2, 116.0, 118.4, 121.3, 121.9, 123.4, 131.1, 131.9, 152.4, 157.0, 158.3, 160.9, 163.2, 185.1; HRMS (ESI-Orbitrap) *m/z* 427.1750 $[M + H]^+$ (calcd for $C_{24}H_{27}O_7$, 427.1751).

3.7 | (2,4-Dihydroxy-5-(3-methylbut-2-enyl)phenyl) (6-hydroxybenzofuran-2-yl)methanone (10)

To a stirred solution of **8** (50 mg, 0.12 mmol) in tetrahydrofuran (THF) (6 mL) and isopropanol (1 mL) was added 98% H_2SO_4 (0.5 mL) at 0°C, and the reaction mixture was stirred at room temperature for 3 hr. After completion of the reaction, the reaction mixture was concentrated under vacuum. The residue was purified by silica gel column chromatography eluting with 15% EtOAc in hexane to give 10 (34 mg, 67%) as a yellow solid. mp 199–200°C; IR (ν_{max}, KBr) 2,971, 2,938, 1,612, 1,581, 1,509, 1,450, 1,403, 1,342, 1,252, 1,188, 1,120, 1,024, 1,005, 845, 769 cm^{-1}; ^1H and

^{13}C NMR, see Table 1; HRMS (ESI-Orbitrap) *m/z* 339.1239 $[M + H]^+$ (calcd for $C_{20}H_{19}O_5$, 339.1227).

3.8 | (2,4-Ddihydroxy-3-(3-methylbut-2-enyl)phenyl) (6-hydroxybenzofuran-2-yl)methanone (1, morachalcone B)

To a stirred solution of **9** (70 mg, 0.16 mmol) in THF (6 mL) and isopropanol (1 mL) was added 98% H_2SO_4 (0.5 mL) at 0°C, and the reaction mixture was stirred at room temperature for 3 hr. After completion of the reaction, the reaction mixture was concentrated under vacuum. The residue was purified by silica gel column chromatography eluting with 15% EtOAc in hexane to give **1** (51 mg, 75%) as a yellow solid. M.p. 191–192°C; IR (ν_{max}, KBr) 3,361, 2,913, 1,617, 1,538, 1,484, 1,293, 1,249, 1,162, 1,137, 1,116, 1,065, 1,022, 993, 837, 793 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; HRMS (ESI-Orbitrap) *m/z* 339.1241 $[M + H]^+$ (calcd for $C_{20}H_{19}O_5$, 339.1227).

3.9 | (2,4-Dihydroxy-5-[2-hydroxy-3-methylbut-3-enyl]- phenyl)(6-hydroxybenzofuran-2-yl) methanone (11)

To a stirred mixture of 10 (75 mg, 0.22 mmol) in acetone (60 mL) was added tetraphenylporphine (6 mg) as the photosensitizer. The reaction mixture was water-cooled at 15°C, and dried oxygen gas was bubbled through the mixture. After the mixture was irradiated with a halogen lamp (500 W) for 1.5 hr at 15°C, triphenylphosphine (314 mg, 1.20 mmol) was added and stirred overnight at room temperature. After completion of the reaction, the reaction mixture was concentrated under vacuum. Then the residue was dissolved in EtOAc and washed three times with 2N NaOH. The combined aqueous layers were acidified with 2N HCl to pH 3 and extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with 20% EtOAc in hexane to give 11 (30 mg, 39%) as a yellow solid. M.p. 188–189°C; IR (ν_{max}, KBr) 3,361, 2,913, 1,617, 1,538, 1,484, 1,293, 1,249, 1,162, 1,137, 1,116, 1,065, 1,022, 993, 837, 793 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; HRMS (ESI-Orbitrap) *m/z* 355.1175 $[M + H]^+$ (calcd for $C_{20}H_{19}O_6$, 355.1176).

3.10 | (2,4-Dihydroxy-3-[2-hydroxy-3-methylbut-3-enyl]- phenyl)(6-hydroxybenzofuran-2-yl)methanone (2, morachalcone C)

To a stirred mixture of **1** (86 mg, 0.25 mmol) in acetone (60 mL) was added tetraphenylporphine (6 mg) as the photosensitizer. The reaction mixture was water-cooled at 15°C, and dried oxygen gas was bubbled through the mixture. After the mixture was irradiated with a halogen lamp (500 W) for 2 hr at 15°C, triphenylphosphine (72 mg, 0.27 mmol) was added and stirred overnight at room temperature. After completion of the reaction, the reaction mixture was concentrated under vacuum. The residue was dissolved in EtOAc and washed three times with 2N NaOH. The combined aqueous layers were acidified with 2N HCl to pH 3 and extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography eluting with 20% EtOAc in hexane to give **2** (61 mg, 69%) as a yellow solid. M.p. 185–187°C; IR (ν_{max}, KBr) 3,361, 2,913, 1,617, 1,538, 1,484, 1,293, 1,249, 1,162, 1,137, 1,116, 1,065, 1,022, 993, 837, 793 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; HRMS (ESI-Orbitrap) *m/z* 355.1177 $[M + H]^+$ (calcd for $C_{20}H_{19}O_6$, 355.1176).

3.11 | Determination of anti-inflammatory activity

A microglial cell line BV2 was cultured in Dulbecco's Modified Eagle Medium (DMEM, Gibco Laboratories, and Grand Island, NY, USA). Production of NO was measured after 24 hr of lipopolysaccharide (LPS, 0.5 μg/mL) activation. The accumulation of nitrite in the culture medium was measured by the Griess reagent for NO production.[16]

4 | CONCLUSIONS

In conclusion, the total synthesis of morachalcones B and C (**1** and **2**) was accomplished in seven steps from **3**. Rap −Stoermer condensation was used for constructing the core skeleton of **1** and **2**. Insertion of a prenyl group onto the aryl ring was achieved by a 1,3-prenyl rearrangement after using a prenylation reaction to establish the prenyl ether precursor. Photo-oxidation was used for the transformation of the prenyl group into the 2-hydroxy-3-methylbut-3-enyl group. Te synthetic compounds **10** and **11** displayed similar activity as PDTC, a NO production inhibitor, in microglial cells. It is suggested that these compounds have strong potential in the treatment of inflammation-associated brain disorders such as ischemic stroke, Alzheimer's disease, etc.[16]

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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