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Total Synthesis of Decumbenine B

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Abstract: Decumbenine B, a 3-arylisoquinoline alkaloid isolated from *Corydalis decumbens*, has been first synthesized from piperonal via 18 steps. The key step was condensation of 5,6-(methylenedioxy)- homophthalic anhydride **5** with Schiff base **6**.

INTRODUCTION

The tubers of *Corydalis decumbens* (Thunb.) Pers. (Papaveraceae) have been used in Chinese folk medicine for treatment of hypertension, hemiplegia, rheumatoid arthritis and sciatic neuralgia.[1] Chemical investigation showed that it contains a large amount of various alkaloids, which may be divided into different structural types: protoberberines, protopines, phthalideisoquinolines, benzyl isoquinolines and aporphines.[2] Recently a new minor 3-arylisoquinoline alkaloid named decumbenine B (**1**) was isolated from the plant tubers.[3] Literature survey revealed that fewer 3-arylisoquinoline alkaloids were discovered from natural origin.[4] Besides, classical approaches to synthesis of isoquinolines are not very satisfactory to that with 3-aryl group, which resulted in failure or lower yield, especially for those with more substituents in 3-aryl group. The situation attracted our interest and encouraged us to undertake synthetic studies of this kind of alkaloid. In this paper we present the first total synthesis of decumbenine B and a preliminary study of its inhibition of spontaneous intestinal contraction.

RESULTS AND DISCUSSION

Several approaches to 3-arylisoquinolines have been reported, including the classical Bischler-Napieralski[5] and Pictet-Spengler reactions[6] and others[7] as key synthetic steps. However, their use in the synthesis of

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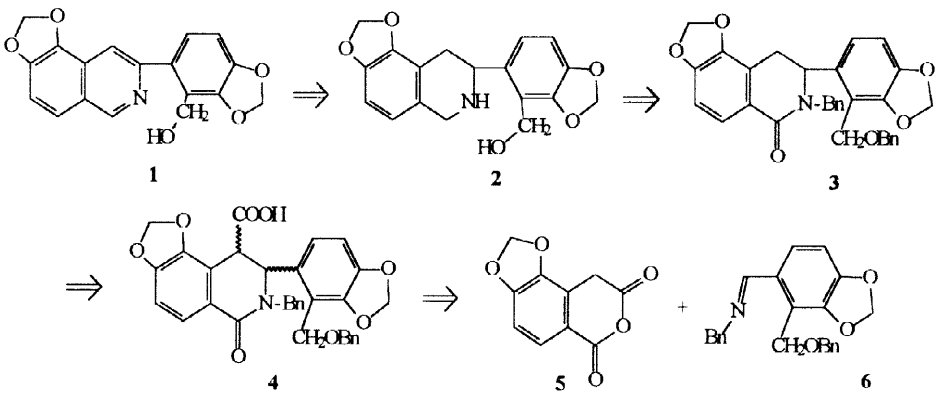
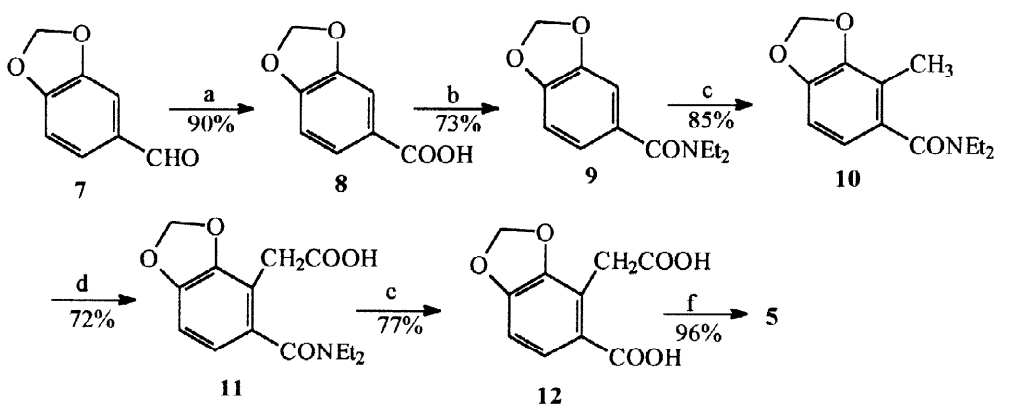
compounds with a polysubstituted 3-aryl group is likely to pose problems. Following successful procedure reported by M. Cushman *et al.*[8] our strategy for total synthesis of **1** is outlined in Scheme 1. Retrosynthetic analysis of **1** suggested that homophthalic anhydride **5** and Schiff base **6** are two key intermediates. Condensation of **5** and **6** to form **4**, followed by decarboxylation, deprotection and dehydrogenation would generate target molecule **1**.



Scheme 1. Synthetic strategy for 1

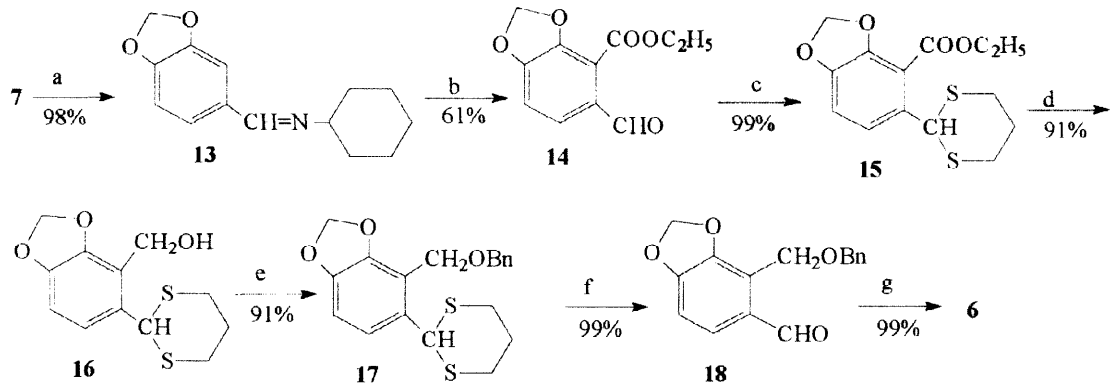
In the course of our study, piperonal **7**, which is commercially available, was used as a common starting material for the preparation of intermediates **5** and **6**. The intermediate **5** has not been prepared previously. The synthesis of **5** is outlined in Scheme 2, in which the known compounds **8-10** as reported compounds were prepared by general procedures and their structures were determined by comparision of physical data to literature values[9] and further spectral studies. Lithiation of **10** resulted in formation of a deep purple solution of diethyl *O*-toluamide anion, which was quenched with dry carbon dioxide to give homophthalic acid amide **11**. Hydrolysis of **11** with perchloric acid yielded homophthalic acid **12**, which was converted to the key intermediate **5** readily by treatment with acetyl chloride under reflux, in 30% overall yield from 7.



Reagents: a. Ag_2O, NaOH. b. i) $SOCl_2$, reflux ; ii) $HNEt_2$, C_6H_6, reflux. c. i) n-BuLi, THF, TMEDA, -78°C ; ii) CH_3I. d. i) n-BuLi, THF, TMEDA, -78°C ; ii) dry CO_2, H_3O^+. e. 10%$HClO_4$, reflux. f. CH_3COCl, reflux.

Scheme 2. Synthesis of the homophthalic anhydride **5**

The synthesis of the other key intermediate **6** is summarized in Scheme 3. Piperonal cyclohexylimine **13** reacted with n-butyllithium at -78°C to afford a metalated intermediate, which was carbethoxylated *in situ* by addition of excess of ethyl chloroformate to give aldehyde **14**.[10] The aldehyde group in **14** was protected with propane-1,3-dithiol to afford **15**, which was converted into **16** by reduction of the ethoxycarbonyl group with $LiAlH_4$. The alcohol **16** was transformed into benzyl ether **17**, and thioacetal was cleaved by bis-(trifluoro-

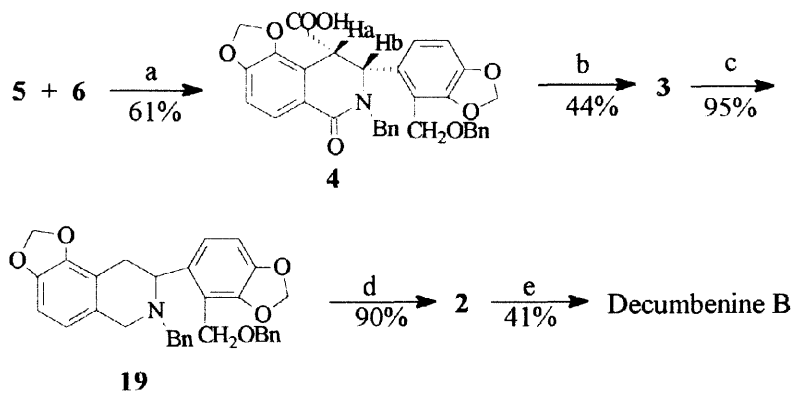


Reagents: a. $H_2NC_6H_{11}$, C_6H_6, 80°C, 8 h. b. i)n-BuLi, THF, -78° ii) $ClCOOC_2H_5$. c. $HS(CH_2)_3SH$, HOAc, BF_3OEt_2, $CHCl_3$, RT. d. $LiAlH_4$ THF, reflux, 8 h. e. BnBr, NaH THF, TBA. f. $(CF_3CO_2)_2IPh$, CH_3CN-H_2O RT. g. $BnNH_2$, C_6H_6, reflux, 10 h. [Bn=$PhCH_2$]

Scheme 3. Synthesis of Schiff base **6**

acetoxy)iodobenzene to give aldehyde **18**. The intermediate **6** was obtained by reaction of **18** with benzylamine. Except for **13** and **14**, found in the literature, other compounds (**15-18**) were first prepared in this study.

Finally, the target alkaloid decumbenine B ,**1** was synthesized successfully according to Scheme 4. Condensation of key intermediates **5** and **6** proceeded in acetonitrile at room temperature to the *cis*-isomer of



Reagents: a. CH_3CN, RT. b. DMSO, 160°C, 0.5 h. c. $LiAlH_4$, THF, RT,24 h. d. 10%Pd-C, H_2, HOAc, RT, 24 h. e. DDQ, C_6H_6, reflux, 24 h

Scheme 4. Synthesis of decumbenine B, **1**

isoquinolone **4** ($J_{Ha,Hb}$ =5.7 Hz).[7c] The thermal decarboxylation of **4** in DMSO afforded 3,4-dihydroisoquinolone **3** in 44% yield. $LiAlH_4$ reduction of **3** provided amine **19**, which then yielded **2** by debenzylation with hydrogen palladium on charcoal in acetic acid. The final step in the synthesis of **1** was dehydrogenation of the tetrahydroisoquinoline **2**. Although several reagents including Pd/C (in acetic acid) and DDQ/1,4-dioxan were tested, the best results were obtained by DDQ/benzene in 41% yield. The spectra (IR, ^1H NMR, ^{13}C NMR and HRMS) of the synthetic product **1** were identical with those of natural decumbenine B. In summary, a first total synthesis of decumbenine B has been achieved in 18 steps, starting from piperonal **7**. The overall yields of **5** and **6**, two key intermediates, from piperonal **7** were 30% and 48% respectively. In our preliminary study, the synthetic decumbenine B was found to induce a concentration-related inhibition on the spontaneous contraction of the intestine with a maximum effect at 2.8 μg/ml. Meantime, atropine (0.4 μg/ml), an antagonist of muscarinic agent, also induced an inhibitory effect on the intestine. Although the primary results suggest that **1** may block the spontaneous contraction by acting on muscarinic receptors, further studies are needed to determine the mechanism of this effect.

EXPERIMENTAL

General. All reactions were performed under nitrogen atmosphere. IR spectra were run on a PE-559B spectrometer. ^1H NMR and ^{13}C NMR spectra were measured on Brucker AM-400 and AC-100 instruments. Mass spectra were obtained on a MAT-711 spectrometer and HRMS on a Finnigan MAT 8430 spectrometer. Elemental analyses were performed by Carlo Erba 1106 autoanalytical meter. Melting points were determined on a Buchi 510 apparatus. Column chromatography was conducted on silica gel H (10-40 μ) from Qingdao Marine Chemical Factory. Tetrahydrofuran (THF) was distilled from sodium metal under nitrogen atmosphere.

6-(N,N-Diethylcarboxamido)-2,3-(methylenedioxy)phenylacetic acid **11**. To a solution of **10** (19 g, 0.081 mol, prepared by lit.[9] procedure) and tetramethylethylenediamine (12.2 ml, 0.081 mol) in THF (350 ml) was added a solution of n-butyllithium in hexane (35 ml of 2.5 M, 0.088 mol) dropwise at -78°C. The resulting purple solution was stirred for 0.5 h and then blanketed with a stream of dry carbon dioxide for 20 min. The solution was allowed to warm to room temperature and evaporated to yield a gum, which was suspended in water (700 ml) and washed with methylene chloride (100 ml × 2). The aqueous layer was acidified (10N HCl) and extracted with diethyl ether (4 × 400 ml). Standard work up yielded 20.1 g of a yellow semisolid, which was recrystallized from petroleum ether- ethyl acetate to afford **11** (16.2 g, 72.1%) as needles, mp 107-109°C. IR ν_{max} 3300-2500, 1730 (COOH),1640 ($CONEt_2$)cm^{-1} ; ^1H NMR ($CDCl_3$) δ 6.78 (1H, d, *J*=8.0 Hz), 6.73 (1H, d, *J*=8.0 Hz), 6.04(2H, s, OCH_2O), 3.56 (4H, q, *J*=7.0 Hz, NCH_2CH_3 + CH_2COOH), 3.36 (2H, q, *J*=7.0Hz, NCH_2CH_3),

1.26 (3H, t, *J*=7.0Hz, NCH_2CH_3), 1.15 (3H, t, *J*=7.0Hz, NCH_2CH_3); **Anal. Calcd. for $C_{14}H_{17}NO_5$** : C, 60.20 ; H, 6.14 ; N, 5.02. Found : C, 60.20 ; H, 5.91 ; N, 5.21.

6-Carboxy-2,3-(methylenedioxy)phenylacetic acid **12**. A solution of **11** (14.8 g, 0.053 mol) in 10% aqueous perchloric acid (500 ml) was refluxed for 18h, then cooled and extracted with diethyl ether. The ether layer was dried by azeotropic removal of water using benzene and evaporated to dryness yielding a gum which was recrystallized from benzene to give **12** (9.2g , 77%),needles, mp 221-223°C (dec). IR ν_{max} 3300-2500, 1715, 1670, 1625,1600, 1500cm^{-1} ; ^1H NMR (CD_3COCD_3) δ 7.73 (1H, d, *J*=8.2 Hz), 6.88 (1H, d, *J*=8.2 Hz), 6.14 (2H, s, OCH_2O), 4.02 (2H, s, CH_2COOH) ; EIMS (m/z) 224 (M^+).

5,6-(Methylenedioxy)-homophthalic anhydride **5**. A mixture of **12** (4.0 g, 0.018 mol) and acetyl chloride (30 ml) was refluxed for 6h, then cooled to -10°C and filtered. The obtained solid was recrystallised from ethanol to give **5** (3.52 g, 96%), needles, mp 216-217.5°C. IR ν_{max} 1790, 1740, 1637, 1600, 1500cm^{-1} ; ^1H NMR ($CDCl_3$) δ 7.85 (1H, d, *J*=8.2Hz), 6.94 (1H, d, *J*=8.2 Hz), 6.15 (2H, s, OCH_2O), 3.99 (2H,s,CH_2O) ; EIMS (m/z) 206 (M^+). Anal. Calcd for $C_{10}H_6O_5$: C, 58.26; H, 2.93. Found: C, 58.46; H, 2.89.

Ethyl-2-formyl-5,6-methylenedioxybenzoate **14**. To a stirred solution of **13** (46.6 g, 0.2 mol) in THF (600 ml) was added a solution of n-butyllithium in hexane (90 ml of 2.5 M, 0.23 mol) dropwise at -78°C. A yellow color appeared upon introduction of the n-Buli. After stirring for 15 min, to the lithiated imine at -78°C was added dropwise freshly distilled ethyl chloroformate (30 ml, 0.31 mol) dissolved in THF (90 ml). The yellow color of the solution was slowly discharged upon warming to room temperature. The reaction mixture was poured into water (200 ml), extracted with diethyl ether (200 ml × 6), dried over $MgSO_4$ and evaporated. The residual oil was purified by column chromatography (chloroform- petroleum ether) to give **14** (27 g, 61%) as crystals, mp 72-73.5°C (lit.[10] mp 71-73°C). IR ν_{max} 2980, 2935, 2855, 1715, 1680, 1615, 1590, 1500 cm^{-1} ; ^1H NMR ($CDCl_3$) δ 10.10 (1H, s, CHO), 7.50 (1H, d, *J*=8.1Hz, H-6), 6.96 (1H, d, *J*=8.1Hz, H-5), 6.14 (2H, s, OCH_2O), 4.44 (2H, q, *J*=7.2 Hz, OCH_2CH_3),1.39 (3H, t,J=7.2 Hz,CH_3);EIMS (m/z):222 (M^+)

2-[2-Ethoxycarbonyl-3,4-(methylenedioxy)phenyl]-1,3-dithiane **15**. To a solution of **14** (6.67 g, 0.03 mol) in $CHCl_3$ (60 ml) was added glacial acetic acid (8 ml), trifluoroborane etherate (4.5 ml, 0.037 mol) and propane-1,3-dithiol (4.5 ml, 0.045 mol). After stirring for 12 h at room temperature, the mixture solution was washed three times each with water (10 ml), 10% aqueous KOH (10 ml) and water (50 ml) and dried over K_2CO_3. Evaporation of solvent furnished crude products, which was recrystallized from diethyl ether to afford **15** (9.27 g, 99%) as neddles, mp 130-131°C. IR ν_{max} 2980, 2950, 2900, 2820, 1740, 1630, 1590, 1490, 1280, 1250cm^{-1} ; ^1H NMR ($CDCl_3$) δ 7.27 (1H, d, *J*=8.2 Hz), 6.86 (1H, d, *J*=8.2 Hz), 6.02 (2H, s, OCH_2O), 5.92 (1H,

s, CHS_2), 4.40 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 3.05 (2H, dt, *J*=2.2, 14.4 Hz, SCH_2), 2.87 (2H, dt, *J*=3.5, 14.4Hz, SCH_2), 2.15 (1H, m) , 1.86 (1H, m), 1.39 (3H, t, *J*=7.2 Hz, CH_3); EIMS (m/z) 312 (M^+).

2-[2-Hydroxymethyl-3,4-(methylenedioxy)phenyl]-1,3-dithiane **16**. To a solution of **15** (6.24 g, 0.02 mol) in THF (180 ml) was added $LiAlH_4$ (1.14 g, 0.03 mol). The mixture was stirred at room temperature for 8 h. The excess of reagent was destroyed by careful addition of THF-H_2O (1:1, 10 ml). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was recrystallized from dry diethyl ether to afford **16** (4.93 g, 91%) as needles, mp 120.5-121.0°C. IR ν_{max} 3405, 2950, 2895, 1600, 1500, 1450, 1250, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.11 (1H, d, *J*=8.1 Hz), 6.78 (1H, d, *J*=8.1 Hz), 5.97 (2H, s, OCH_2O), 5.43 (1H, s, CHS_2), 4.80 (2H, s, CH_2OH), 3.09 (2H, dt, *J*=2.1, 14.3Hz, SCH_2), 2.89 (2H, dt, *J*=3.5, 14.3Hz, SCH_2), 2.17(1H, m) ,1.87 (1H, m), 1.78 (1H, br, s, OH, D_2O exchangeable); EIMS (m/s) 270 (M^+).

2-[2-Benzyloxymethyl-3,4-(methylenedioxy)phenyl]-1,3-dithiane **17**. To a solution of **16** (3.0g, 0.011 mol) in THF (25 ml) was added 80% sodium hydride (0.39 g, 0.013 mol) under dry argon. After stirring the mixture for 30 min, tetrabutylammonium iodide (TBA, 60 mg) and benzyl bromide (1.35 ml, 0.012 mol) was added and then stirred for 25h at room temperature. The reaction mixture was added with water (10 ml), filtrated through kieselguhr filter agent layer, washed with brine (2 × 30 ml) and dried over Na_2SO_4. Filtration and concentration yielded a slightly yellow syrup, which was purified by flash chromatography (diethyl ether-petroleum ether) to afford **17** (3.62 g, 91%) as crystals, mp 83.7-84.2°C. IR ν_{max} 2960, 2920, 1600, 1500 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.37 (5H, m, 5Ar-H), 7.16 (1H, d, *J*=8.1 Hz), 6.76 (1H, d, *J*=8.1 Hz), 5.95 (2H, s, OCH_2O), 5.34 (1H, s, CHS_2), 4.65 (2H, s, CH_2O), 4.44 (2H, s, OCH_2), 2.92 (2H, dt, *J*=2.2, 14.6Hz, CH_2S) 2.81 (2H, dt, *J*=3.7, 14.6Hz, SCH_2), 2.07 (1H, m), 1.84 (1H, m); EIMS (m/s) 360 (M^+).

2-Benzyloxymethyl-3,4-(methylenedioxy)benzaldehyde **18**. Bis(trifluoroacetoxy)iodobenzene (3.58 g, 8.0 mmol) was added at room temperature to a stirred solution of **17** (2.0 g, 5.56 mmol) in acetonitrile-H_2O (9:1,10 ml). After reaction was completed, as judged by TLC, the solution was poured into saturated aqueous sodium bicarbonate (20 ml) and extracted with diethyl ether (30 ml × 3). Drying ($MgSO_4$) and removal of solvents gave a residue whch was purified by flash chromatography on silica gel (petroleum ether / EtOAc) to afford **18** (1.49 g, 99%) as an oil. IR ν_{max} 1680, 1620, 1600, 1500, 1450, 1355cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.10 (1H, s, CHO), 7.48 (1H, d, *J*=8.1 Hz), 7.39 (5H, m, 5Ar-H), 6.87 (1H, d, *J*=8.1 Hz), 6.08 (2H, s, OCH_2O), 4.88 (2H, s, CH_2O), 4.59 (2H, s, OCH_2) ; EIMS (m/s) 270 (M^+).

2-Benzyloxymethyl-3,4-(methylenedioxy)benzaldehyde benzylimine **6**. A solution of **18** (1.50 g, 5.56 mol) and benzylamine (0.61 ml, 5.56 mmol) in benzene (80 ml) was refluxed for 10 h. Evaporation of solvent gave **6** as an oil (1.99 g, 100%), which was used in the next step without further purification. ^1H NMR ($CDCl_3$)

δ 8.56 (1H, s, CH=N), 7.59 (1H, d, *J*=8.1 Hz), 7.20 (10H, m, 10 Ar-H), 6.79 (1H, d, *J*=8.1 Hz), 6.00 (2H, s, OCH_2O), 4.76 (2H, s, CH_2O), 4.72 (2H, s, CH_2O), 4.53 (2H, s, CH_2); EIMS (m/z) 359 (M^+). Anal. Calcd. for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: C, 76.91; H, 5.72; N, 3.98.

cis-N-Benzyl-3-[2-benzyloxymethyl-3,4-(methylenedioxy)phenyl-4-carboxy-5,6-(methylenedioxy)-3,4-dihydro-1(2H)-isoquinolinone **4**. The anhydride **5** (0.76 g, 3.7 mmol) was added to a stirred solution of **6** (1.33 g, 3.7 mmol) in CH_3CN (30 ml). The solution was stirred at room temperature for 12 h and then evaporated. The residure was purified by column chromatography ($CHCl_3$-EtOAc) to afford **4** (1.28 g, 61%), mp 201-202°C. IR ν_{max} 3450, 3200-2500, 1732, 1647, 1600, 1500, 1480, 1450, 1270, 1080, 1057, 1030 cm^{-1} ; ^1H NMR (CF_3CO_2D) δ 7.97 (1H, d, *J*=8.4 Hz), 7.30 (2H, d, *J*=5.4 Hz), 7.23 (6H, m), 7.12 (1H, d, *J*=8.4 Hz), 7.09 (1H, d, *J*=8.2 Hz), 6.96 (1H, d, *J*=8.2 Hz), 6.71 (2H, d, *J*=7.5 Hz), 6.15 (2H, d, *J*=3.5 Hz, OCH_2O), 6.06 (2H, d, *J*=15.8 Hz, OCH_2O), 5.78 (1H, d, *J*=15.3Hz, NCH_2Ph), 5.0 (1H, d, *J*=5.7 Hz, H-3), 4.78 (1H, d, *J*=11.5Hz, OCH_2Ph), 4.45 (1H, d, *J*=5.7 Hz, H-4), 4.41 (2H, dd, *J*=8.0, 11.5 Hz, CH_2O), 4.26 (1H, d, *J*=15.3 Hz, NCH_2Ph), 3.62 (1H, d, *J*=11.5 Hz, OCH_2Ph) ppm; $^{13}CNMR$ (CF_3COOD) δ 176.03 (COOH), 170.16 (CON), 154.83, 149.33, 149.23, 146.14, 135.58, 135.00, 130.28 (2CH), 130.03, 129.86 (2CH), 129.66 (2CH), 129.21, 128.37 (2CH), 128.06, 127.08, 123.77, 120.75, 117.80, 115.05, 110.27, 110.05, 104.31, 102.87, 74.38, 62.41, 57.42, 50.43, 45.76 ppm ; EIMS (m/z) 565 (M^+). HRMS (m/z), Found: 565.1759 (M^+); Calcd. for $C_{33}H_{27}NO_3$: 565.1728.

N-Benzyl-3-[2-benzyloxymethyl-3,4-(methylenedioxy)phenyl]-5,6-(methylenedioxy)-3,4-dihydro-1(2H)-isoquinolone **3**. **4** (0.57 g, 1.0 mmol) was dissolved in dry DMSO and heated at 160°C for 0.5 h. The solvent was removed under reduced pressure and the residue was extracted with $CHCl_3$. The $CHCl_3$ extract was evaporated to give a brown oil, which was subjected to column chromatography over silica gel, eluted with EtOAc and petroleum ether (1:1) to afford **3** (0.23 g, 44%) as crystals, mp 142-143°C. IR ν_{max} 1660, 1625, 1600, 1500, 1450, 1250cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80 (1H, d, *J*=8.2 Hz), 7.22 (10H, m, ArH), 6.78 (1H, d, *J*=8.2 Hz), 6.57 (1H, d, *J*=8.2 Hz), 6.49 (1H, d, *J*=8.2 Hz), 5.96 (1H, d, *J*=1.2 Hz, OCH_2O), 5.93 (2H, m, OCH_2O), 5.87 (1H, d, *J*=1.2 Hz, OCH_2O), 5.65 (1H, d, *J*=14.9 Hz, NCH_2Ph), 5.01 (1H, dd, *J*=2.4, 7.1 Hz, H-3), 4.45 (1H, d, *J*=10.5 Hz, CH_2O), 4.44 (2H, s, CH_2O), 4.28 (1H, d, *J*=10.5 Hz, CH_2O), 3.50 (1H, d, *J*=14.9 Hz, NCH_2Ph),3.08 (1H, dd, *J*=7.1, 16.3 Hz, H-4), 2.97 (1H, dd, *J*=2.4, 16.3 Hz, H-4) ppm ; EIMS (m/z) 521 (M^+); Anal. Calcd for $C_{32}H_{27}NO_6$: C, 73.69; H, 5.22; N, 2.69, Found : C, 73.78 ; H, 5.18 ; N, 2.73.

N-Benzyl-3-[2-benzyloxymethyl-3,4-(methylenedioxy)phenyl]-5,6-(methylenedioxy)-1,2,3,4-tetrahydro-isoquinoline **19**. To a solution of **3** (0.4 g, 0.77 mmol) in dried THF (200 ml) was added $LiAlH_4$ (90 mg, 2.34 mmol) and mixture was stirred for 24 h. The excess regent was destroyed by addition of water (2ml) and 15% sodium hydroxide (1ml). The reaction mixture was filtered and evaporated. The residue was chromatographed using diethyl ether-petroleum ether (1:1) as eluent to afford **19** (0.37 g, 95%), needles, mp

135-137°C. IR ν_{max} 1600, 1500, 1450, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.26 (10H, m, 10 Ar-H), 7.13 (1H, d, *J*=8.0 Hz), 6.79 (1H, d, *J*=8.0 Hz), 6.61 (1H, d, *J*=7.8 Hz), 6.40 (1H, d, *J*=7.8 Hz), 5.97 (2H, d, *J*=5.7Hz, OCH_2O), 5.90 (2H, d, *J*=6.1 Hz, OCH_2O), 4.71 (2H, s, CH_2O), 4.57 (1H, d, *J*=11.7 Hz, OCH_2Ph), 4.51 (1H, d, *J*=11.7 Hz, OCH_2Ph), 3.95 (1H, m, H-3), 3.83 (1H, d, *J*=13.3 Hz, H-1), 3.77 (1H, d, *J*=15.2 Hz, NCH_2Ph), 3.28 (1H, d, *J*=15.2 Hz, NCH_2Ph), 2.98 (1H, d, *J*=13.3 Hz, H-1), 2.96 (2H, m, H-4) ppm; EIMS (m/z) 506 (M^+-1), 416 (M^+-91); Anal. Calcd for $C_{32}H_{29}NO_5$: C, 75.72; H, 5.76; N, 2.76: Found : C, 75.93, H, 5.90; N, 2.46.

3-[2-Hydroxymethyl-3,4-(methylenedioxy)phenyl]-5,6-(methylenedioxy)-1,2,3,4-tetrahydroisoquinoline **2**. **19** (0.29 g, 0.58 mmol) was dissolved in glacial acetic acid (8 ml) and hydrogenolyzed at room temperature with 10% palladium on charcoal (60 mg) for 24 h. The reaction mixture was filtered through Celite and the filtrate was evaporated to dryness. The residue was dissolved in 5% aqueous NaOH (80 ml) and extracted with $CHCl_3$ (40 ml × 3). The combined extract was dried (Na_2SO_4) and evaporated to dryness to yield **2** (170 mg, 90%), needles, mp.207-208°C. IR ν_{max} 3280, 2960, 2860, 2820, 1600, 1500, 1480, 1450, 1350, 1250cm^{-1} ; ^1H NMR ($CDCl_3$) δ 6.82 (1H, d, *J*=8.0 Hz), 6.68 (2H, d, *J*=8.0 Hz), 6.55 (1H, d, *J*=8.0 Hz), 5.92 (4H, m, 2 × OCH_2O), 4.73 (1H, d, *J*=12.3 Hz, CH_2OH), 4.63 (1H, d, *J*=12.3 Hz, CH_2OH), 4.29 (1H, dd, *J*=5.8, 8.4 Hz, H-3), 4.13 (1H, d, *J*=16.8 Hz, H-1), 3.92 (1H, d, *J*=16.8 Hz, H-1), 3.07 (2H, m, H-4) ppm; EIMS (m/z) : 327 (M^+); Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.04; H, 5.23; N, 4.28. Found : C, 65.80; H, 5.18; N, 3.93.

3-[2-Hydroxymethyl-3,4-(methylenedioxy)phenyl]-5,6-(methylenedioxy)-isoquinoline ***1***. (Decumbenine B). A solution of **2** (50 mg, 0.15 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ,80 mg, 0.35 mmol) in dried benzene (25 ml)was refluxed under dry argon for 24h. The reaction mixture was filtered and the filtrate was washed with brine (15 ml × 4), dried with Na_2SO_4 and evaporated to dryness. The residue was purified by column chromatography (EtOAc -petroleum ether) and recrystallization from EtOAc-petroleum ether to yield **1** (20 mg, 41%) as needles, mp 222-224°C. IR ν_{max} 3254, 2972, 2918, 1648, 1599, 1501, 1462, 1348, 1306, 1279, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.14 (1H, s, H-1), 7.81 (1H, s, H-4), 7.63 (1H, d, *J*=8.6 Hz, H-7), 7.30 (1H, d, *J*=8.6 Hz, H-8), 7.12 (1H, d, J=8.0 Hz, H-5'), 6.83 (1H, d, *J*=8.0 Hz, H-6'), 6.25 (2H, s, OCH_2O), 4.53 (2H, s, CH_2OH) ppm ; ^{13}C NMR ($CDCl_3$) δ 152.34, 151.20, 148.02, 147.65, 146.98, 140.51, 134.78, 123.99, 123.70, 123.02, 122.98, 122.22, 119.92, 111.65, 107.57, 102.55, 101.45, 56.50 ppm ; EIMS (m/s) : 323 (M^+), 322, 306, 149, 97, 71, 57 ; HRMS : Found : 323.0808 (M^+), Calcd for $C_{18}H_{13}NO_5$: 323.0789. IR, ^1H and ^{13}C NMR spectra of the synthetic product **1** were identical with those of natural decumbenine B.[3]

Inhibition of the spontaneous contraction of intestine. Kunming strain mice, male, weighing 20 ± 2g, were decapitated. The intestine was dissected out and placed in Krebs solution of the following composition (mM): NaCl, 118; KCl, 4.75; $CaCl_2$, 2.54; KH_2PO_4, 1.19; $NaHCO_3$, 25; glucose, 11. After the intestine was cleaned, 1 cm of intestine was suspended under a tension of 300 mg in a organ bath with 25 ml Krebs solution at 37 ± 0.1°C

gassed with 95% O_2 + 5% CO_2. The test compounds were dissolved in H_2O and diluted with Krebs solution. The solution of each test compound was prewarmed to 37°C. Following an equilibration period of 45 min, the solution of test compound was added to the organ bath and contractions were recorded by means of a transducer connected to a polygraph recorder.

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