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Synthesis of a 3-Arylisoquinoline Alkaloid, Decumbenine B

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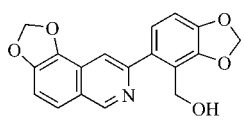
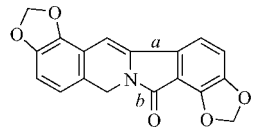
The synthesis of a 3-arylisoquinoline alkaloid, decumbenine B, was accomplished in a reaction sequence based on the formation of an indolizine ring {dibenz[*a*,*f*]indolizin-5(7*H*)-one} followed by its cleavage at the amide bond, starting with an interaction of 5,6-(methylenedioxy)isoquinoline with 2-bromo-5,6-(methylenedioxy)benzoyl chloride in the presence of Bu_3SnH.

Introduction

We have been interested in the construction of nitrogen-fused dibenzo 7/5-, 6/6-, or 6/5-membered bicyclic ring systems,[1] which are basic skeletons of indole and isoquinoline alkaloids. In this report, we describe a method for the preparation of one of the dibenzindolizine (6/5) ring systems and its use in the synthesis of a unique 3-arylisoquinoline alkaloid, decumbenine B (**1**). This alkaloid has been isolated from plant tubers of *Coridalis decumbens* Pers, which have been used in Chinese folk herbal medicine for the treatment of hypertension, hemiplegia, rheumatoid arthritis and sciatic neuralgia.[2] Only a few isoquinoline alkaloids with a 3-aryl group have been found in nature.[3,4] In contrast, a fair number of synthetic 3-arylisoquinolines with potent antitumor cytotoxicities and topoisomerase I inhibitory activities have been reported.[5,6] The synthesis of the alkaloid **1** was first accomplished by Xu et al. by the condensation of homophthalic anhydride and *N*-benzylbenzalimine in multiple steps.[7] The Larock group developed a method for a palladium-catalyzed coupling of terminal acetylenes and 2-iodobenzalimines to 3-arylisoquinolines which led to a short synthesis of the alkaloid.[8] We report the synthesis of **1** by a different route based on the construction of an indolizine ring by an intramolecular Heck cyclization at *a* followed by an oxidative amide-bond cleavage at *b*.



decumbenine B (**1**)



dibenz[*a*,*f*]indolizine (**2**)

Results and Discussion

Uchimoto et al. reported that a one-pot radical cyclization of isoquinoline (**3**) with an acid chloride **4** through the intermediate **5** produced an indolizidine **6**,[9] as shown in Scheme 1. It has been reported that an intramolecular Heck reaction[10,11] of the iodo derivative[11a–11c] of **5** and related iodides proceeded smoothly in DMF. When bromide **5** was treated with $Pd(OAc)_2$ (20 mol-%) and PPh_3 (40 mol-%) in the presence of K_2CO_3 (10 equiv.) in boiling toluene for 10 h, indolizine **8** was obtained in 70% yield.[12,13]

Attempts to hydrolyze the amide bond of **8** under both alkaline (NaOH, tBuOK,[14] or LiOH[15]) and acidic conditions (HCl,[16] H_2SO_4,[17] or *p*TsOH[12j]) failed to produce the acid. Indolizidine **6** also resisted being hydrolyzed under these conditions. Oxidative cleavage with MnO_2, CrO_3, or $FeCl_3$[18] gave a complex mixture or the unchanged starting lactam. An attempt to induce a reductive cleavage of **8** with $LiAlH_4$[19] resulted in the formation of a complex mixture, although **6** gave **7** in good yield. $NaAl(OEt)_2H_2$,[20] $LiAl(OEt)_3H$,[21] $LiB[CH(Me)Et]_3H$,[22] $LiR_2N{\cdot}BH_3$,[23] or Cp_2ZrHCl[24] failed to cleave the amide bond. In contrast, when **8** was treated with Br_2 in $CHCl_3$, followed by MeOH, on the basis of Dusemund's procedure,[12h] an oxidative cleavage of the amide bond occurred, being accompanied by the bromination of the isoquinoline ring to give 4-bromo

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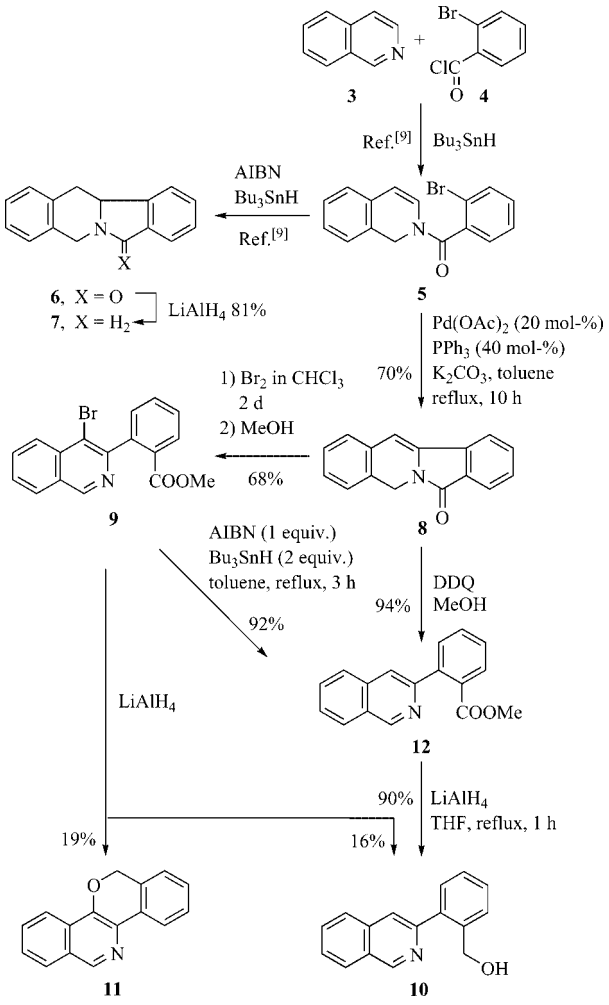
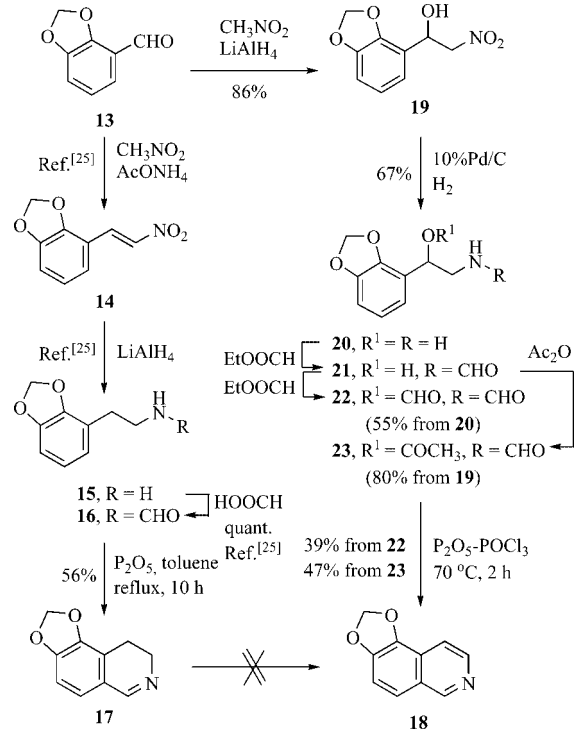


Scheme 1. Synthesis of model compound **10**.

ester **9** in 68% yield. The treatment of this compound with $LiAlH_4$ gave the desired benzyl alcohol **10** (16% yield) together with [2]benzopyrano[4,3-*c*]isoquinoline (**11**) (19% yield).[12j] Treatment of **9** with Bu_3SnH (2 equiv.) and AIBN (1 equiv.) in boiling toluene for 3 h gave ester **12** almost quantitatively (92% isolated yield) after 3 h. The $LiAlH_4$ reduction of this methyl ester **12** afforded **10** in 90% yield. The latter process by a radical reduction is promising compared with the former direct $LiAlH_4$ reduction. However, another oxidative cleavage involving no halogenation was found to be more efficient; the treatment of **8** with 1.2 equiv. of DDQ in boiling MeOH afforded methyl ester **12** almost quantitatively in 94% isolated yield after 2 h.

Next, the preparation of substrates more closely related to the alkaloid **1** was examined. We planned to obtain 5,6-(methylenedioxy)isoquinoline **18** through sequential methods by the Bischler–Napieralski cyclization of the corresponding phenethylformamide **16**, which was prepared from aldehyde **13** by the conventional procedure reported by Dallacker.[25] As shown in Scheme 2, the treatment of **16** with P_2O_5[26] in boiling toluene afforded dihydroisoquinoline **17** (56% yield), although cyclization with $POCl_3$[26] was unsuccessful. The successive dehydrogenation of **17** with Pd,[27] DDQ,[28] chloranil,[29] or *o*-iodoxybenzoic acid[30] could not produce isoquinoline **18** in more than a trace amount, and other efforts for the functionalization at its 4-position, such as halogenation and oxidation with Br_2, NBS, NCS or CrO_3, were also unsuccessful.[6x]



Scheme 2. Preparation of 5,6-(methylenedioxy)isoquinoline (**18**).

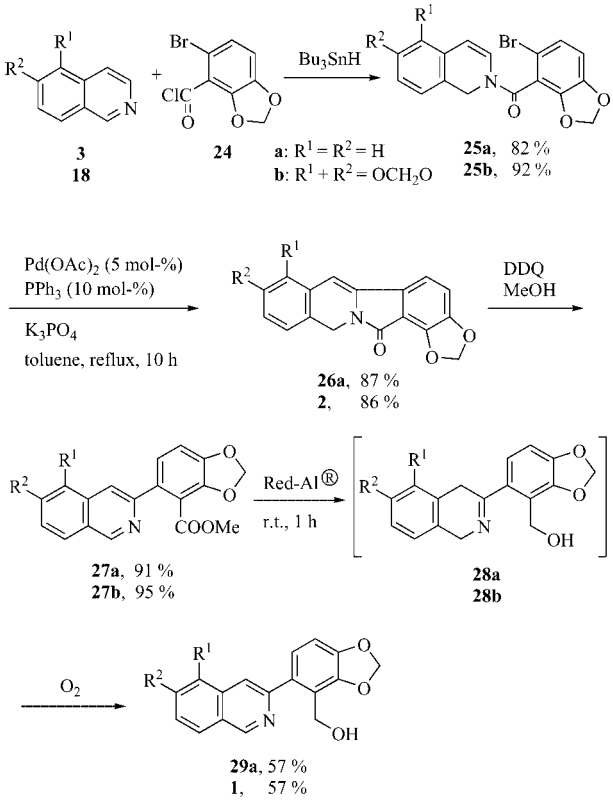
According to Kim's modification of the aldol reaction,[31] benzaldehyde **13** was treated with excess CH_3NO_2 in dry THF in the presence of a catalytic amount of $LiAlH_4$ (0.1 equiv.) at 0 °C for 4 h. The resultant nitroethanol **19** (86% yield) was reduced with hydrogen in the presence of 10% Pd/C to amino alcohol **20** (67% yield), which was quantitatively converted by heating in EtOOCH for 6 h to formamide **21**, and its acetate **23** was obtained by treating **21** with Ac_2O in the presence of Et_3N and 4-DMAP in 98% yield (80% overall yield from **19**). The *N*-formylformate **22** was prepared in 55% yield by heating aminoethanol **20** in EtOOCH in the presence of K_2CO_3 and molecular sieves (4 Å) for 48 h. The treatment of acetate **23** with P_2O_5 (2 equiv.) in $POCl_3$[32] at 70 °C for 2 h produced isoquinoline **18** in 47% yield (Entry 4 in Table 1). By using the same method, formate **22** gave isoquinoline **18** in lower yields, 39% at room temp. (Table 1, Entry 1) and 24% at 70 °C (Table 1, Entry 2). However, hydroxyformamide **21** did not give the isoquinoline but a complex mixture, probably because of a predominant dehydration leading to a *trans*-enamide.

Acid chloride **24** was obtained by the treatment of 6-bromo-2,3-methylenedioxybenzoic acid[33] with $SOCl_2$ (Scheme 3). As shown in Scheme 3, the aforementioned tin hydride induced *N*-benzoylation was carried out to couple benzoyl chloride **24** with either **3** or **18**, and **24** provided *N*-benzoyldihydroisoquinolines **25a**,**b** in 82% and 92% yields,

Table 1. Preparation of **18** by the Bischler–Napieralski reaction.

Entry	Substrate	Reagent	Solvent	Temp.	Time	Yield of **18**
1	**22**	P_2O_5 (2 equiv.)	$POCl_3$	reflux	2 h	14%
2	**22**	P_2O_5 (2 equiv.)	$POCl_3$	70 °C	2 h	24%
3	**22**	P_2O_5 (2 equiv.)	$POCl_3$	r.t.	2 h	39%
4	**23**	P_2O_5 (2 equiv.)	$POCl_3$	70 °C	2 h	47%
5	**23**	P_2O_5 (10 equiv.)	$POCl_3$	70 °C	2 h	29%

respectively. The Heck reaction of **25a**,**b** formed dibenz[*a*,*f*]-indolizines **26a** and **2** almost quantitatively (Entry 1 in Table 2) under the same conditions [$Pd(OAc)_2$ (20 mol-%), PPh_3 (40 mol-%), and K_2CO_3 (10 equiv.) in boiling toluene for 10 h] as those used for the preparation of **8**. However, **26a** and **2** were not easily separated from the by-product $OPPh_3$ by chromatography, as shown in the isolated yields being lower than 50%. The use of P(*o*-Tolyl)$_3$, which gives no oxide under the conditions, did not improve the cyclization (Table 2, Entry 2). A reduction in the amount of the catalyst and ligand by 4 [$Pd(OAc)_2$ (5 mol-%), PPh_3 (10 mol-%), and K_2CO_3 (10 equiv.)] resulted in an inefficient cyclization (Table 2, Entry 3), even in a more polar solvent such as DMA (Table 2, Entry 4). The addition of a quaternary ammonium salt, Bu_4NCl, was not effective (Table 2, Entry 5).[34] The use of a more basic alkali metal salt, wet K_3PO_4, which was added in order to induce a smoother *trans* elimination of HPdBr,[35] improved the cyclization dramatically to afford **26a** in 87% isolated yield by



Scheme 3. Synthesis of decumbenine B.

fractional crystallization. Likewise, indolizidine **2** was obtained from bromide **25b** in 87% yield after 10 h (Table 2, Entry 6).

Table 2. Preparation of dibenz[*a*,*f*]indolizine **26a**.

Entry	$Pd(OAc)_2$ (mol-%) / ligand (mol-%)	Additive (equiv.)	Base	Solvent	Time	**25a**/**26a**[a]	Yield of **26a**
1	20 / PPh_3 (40)		K_2CO_3	toluene	10 h	0:100	< 50%
2	20 / P(*o*-tol)$_3$ (40)		K_2CO_3	toluene	10 h	93: 7	
3	5 / PPh_3 (10)		K_2CO_3	toluene	24 h	67: 33	
4	5 / PPh_3 (10)		K_2CO_3	DMA	24 h	[b]	
5	5 / PPh_3 (10)	Bu_4NCl (2)	K_2CO_3	toluene	24 h	85: 15	
6	5 / PPh_3 (10)		wet K_3PO_4	toluene	10 h	0:100	87%

[a] Determined by ^1H NMR analysis. [b] A complex mixture was obtained.

The subsequent treatment of **26a** or **2** with DDQ in MeOH afforded ester **27a** or **27b** almost quantitatively. The crude products obtained by the $LiAlH_4$ reduction of esters **27a**,**b** were neither **29a** nor **1**. Their ^1H NMR spectra revealed three broad singlets due to 2 protons each at δ = 3.83, 4.49 and 4.90 ppm for **28a** or at δ = 3.78, 4.50 and 4.87 ppm for **28b**. Probably, 1,2- or 1,4-adducts with aluminum hydride were decomposed with water during the workup to give 1,4-dihydroisoquinolines, **28a** or **28b**.[36] These compounds on standing in air gradually changed to **29a** or **1**. The treatment of ester **27b** with $NaAl(OCH_2CH_2OCH_3)_2H_2$ followed by exposure of the crude product to oxygen in MeOH containing a few of drops of aq. 2 N NaOH for 7 h[37] produced decumbenine B (**1**) in 57% isolated yield, a yield higher than that obtained by other methods using $LiAlH_4$ and DIBAL as reagents.

Conclusion

The synthesis of a 3-arylisoquinoline alkaloid, decumbenine B, was accomplished in a reaction sequence based on the formation of an indolizine ring followed by its cleavage at the amide bond.

Experimental Section

General Remarks: Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra were recorded with a JASCO IR-810 infrared spectrophotometer. ^1H NMR spectra were obtained in $CDCl_3$ (99.8 atom% D, containing 0.03% TMS, Aldrich) with a JEOL EX-270 high-resolution spectrometer. Mass spectrometric data were recorded using a JEOL JMS-FABmate or JMS-700TZ spectrometer at 70 eV. Preparative TLC was performed with Merck silica gel 60 PF-254. Column chromatography was conducted using Cica-reagent silica gel 60 (100–210 μm, spherical, Kanto Chemical Co. Inc.).

Dibenz[*a*,*f*]indolizidine (7): To a stirred mixture of $LiAlH_4$ (16.3 mg, 0.43 mmol) in dry THF (1 mL) was added **6** [27.3 mg, 0.12 mmol, m.p. 120–121 °C (EtOAc/hexane; ref.[12g] m.p. 126–128 °C), as colorless crystals], prepared according to Uchimoto's procedure (72% yield).[9] After the mixture was refluxed for 3 h, water was added

to decompose the excess hydride. The precipitates were removed by suction filtration, and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2 (10 mL) and washed with water (2 × 10 mL) and brine (10 mL). The solution was dried (Na_2SO_4) and concentrated to give an oil (24.7 mg), which was purified by preparative TLC with silica gel (2% MeOH/CH_2Cl_2). A band with R_f = 0.3 gave **7** (20.7 mg, 81% yield) as colorless crystals, m.p. 109–110 °C (MeOH/Et_2O; ref.[12c] m.p. 105–106 °C; ref.[12a,12e] m.p. 109–110 °C). Compound **7** has been prepared by Stevens rearrangement of 2,2′-spirobi(2*H*-isoindolinium) bromide.[12a,12c,12e]

Dibenz[*a*,*f*]indolizin-5(7*H*)-one (8): To a stirred solution of isoquinoline (180.6 mg, 1.4 mmol) and Bu_3SnH (407.4 mg, 1.4 mmol) in CH_2Cl_2 (8 mL) at –78 °C was added 2-bromobenzoyl chloride (337.8 mg, 1.54 mmol), and the mixture was stirred at the same temperature for 2 h and then warmed to room temp. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2 (10 mL), extracted with CH_2Cl_2 (3 × 10 mL), washed with aq. NaOH (2 N, 2 × 10 mL) and brine (30 mL), and dried (Na_2SO_4). The solvent was evaporated to give an oily residue, which was dissolved in CH_3CN (10 mL) and washed with hexane (5 × 10 mL). The solution was concentrated to give enamide **5** as a colorless oil (348.3 mg). To this, $Pd(OAc)_2$ (62.8 mg, 0.28 mmol), PPh_3 (146.8 mg, 0.56 mmol), K_2CO_3 (1.935 g, 1.4 mmol), and toluene (40 mL) were added. The mixture was refluxed with stirring for 10 h, and cooled to room temperature. The precipitates were filtered off through a Celite pad. Toluene was evaporated, and a solid obtained (391.4 mg) was recrystallized from AcOEt/hexane to give **8** (229.6 mg, 70% yield) as yellow crystals, m.p. 147–148 °C (ref.[11c] m.p. 150–152 °C; ref.[12l] m.p. 157–158 °C), of which the spectroscopic data are identical with those previously reported.[11c,12l]

4-Bromo-3-[2-(methoxycarbonyl)phenyl]isoquinoline (9): To a solution of **8** (116.6 mg, 0.5 mmol) in $CHCl_3$ (25 mL) was added Br_2 (220 mg, 1.3 mmol), and the mixture was stirred at room temp. for 2 d. To the reaction mixture was added MeOH (5 mL), and the mixture was stirred at room temp. for 36 h. The solvent was evaporated. The residue was dissolved in CH_2Cl_2 (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL), washed with water (3 × 30 mL), dried (Na_2SO_4), and concentrated to give a colorless oil (194 mg). Purification by TLC with silica gel (R_f = 0.5, 2% MeOH/CH_2Cl_2) gave **9** (116 mg, 68% yield) as colorless crystals, m.p. 125–126 °C (EtOH/hexane). IR (neat): $\tilde{\nu}$ = 1619, 1571 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 3.62 (s, 3 H, Me), 7.48 (dd, J = 7.6, 1.3 Hz, 1 H, 5-H), 7.53 (dt, J = 1.3, 7.6, 7.6 Hz, 1 H, 5′-H), 7.65, 7.68 (each dt, J = 1.3, 7.6, 7.6 Hz, each 1 H, 7- and 6-H), 8.06 (d, J = 7.7 Hz, 3′-H), 8.11 (dd, J = 7.6, 1.3 Hz, 1 H, 6′-H), 8.27 (d, J = 8.5 Hz, 1 H, 8-H), 9.21 (s, 1 H, 1-H) ppm. EI-MS: *m*/*z* (%) = 342 (0.1) $[M]^+$, 340 (0.1) $[M]^+$, 262 (100) $[M – Br]^+$, 247 (49.7) $[M – Br – Me]^+$, 231 (5.4) $[M – Br – OMe]^+$. $C_{17}H_{12}BrNO_2$ (342.19): calcd. C 59.67, H 3.53, Br 23.35, N 4.09; found C 59.41, H 3.45, Br 23.21, N 3.98.

3-[2-(Hydroxymethyl)phenyl]isoquinoline (10) and 6*H*-[2]Benzopyrano[4,3-*c*]isoquinoline (11): To a stirred mixture of $LiAlH_4$ (17 mg, 0.45 mmol) in dry THF (1 mL) was added **9** (28 mg, 0.082 mmol). After the mixture was refluxed for 12 h, water was added to decompose the excess hydride. The precipitates were removed by suction filtration, and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2 (10 mL) and washed with water (2 × 10 mL) and brine (10 mL). The solvent was evaporated, and an oily residue was purified by preparative TLC with silica gel (2% MeOH/CH_2Cl_2). A band with R_f = 0.6 gave **10** (3.1 mg, 16.1% yield) as a colorless oil. IR (neat): $\tilde{\nu}$ = 3331, 1687, 1627, 1583 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 4.51 (s, 2 H, CH_2), 6.41 (br. s, 1 H, OH), 7.43–7.47 (m, 2 H), 7.51–7.69 (m, 3 H, Ar-H), 7.77 (dt, J = 1.0, 7.3, 7.3 Hz, 1 H, 6-H), 7.92 (d, J = 8.3 Hz, 1 H, 5-H), 7.97 (s, 1 H, 1-H), 8.04 (d, J = 8.3 Hz, 1 H, 8-H), 9.30 (s, 1 H, 1-H) ppm. EI-MS: *m*/*z* (%) = 235 (100) $[M]^+$, 218 (78.4) $[M – OH]^+$, 204 (30.9) $[M – CH_2OH]^+$, 128 (23.3) $[C_8H_6N]^+$. HRMS: calcd. for $C_{16}H_{13}ON$ 235.0997, found 235.0994. A band with R_f = 0.9 gave **11** (3.6 mg, 19% yield) as a colorless oil. IR (neat): $\tilde{\nu}$ = 1592 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 5.40 (s, 2 H, 6-H), 7.19 (d, J = 7.3 Hz, 1 H, 7-H), 7.35 (t, J = 7.3 Hz, 1 H, 8-H), 7.44–7.51, 7.54–7.61 (each m, each 1 H, 9- and 3-H), 7.69 (t, J = 7.6 Hz, 2-H), 7.95 (d, J = 8.3 Hz, 1 H, 10-H), 8.18 (d, J = 8.3 Hz, 1 H, 4-H), 8.24 (d, J = 7.6 Hz, 1 H, 1-H), 8.96 (s, 1 H, 12-H) ppm. EI-MS: *m*/*z* (%) = 233 (100) $[M]^+$, 219 (5.9) $[M – CH_2]^+$, 204 (23.0) $[M – CHO]^+$, 176 (16.7) $[C_{14}H_9]^+$. HRMS: calcd. for $C_{16}H_{11}ON$ 233.0841, found 233.0845.

Methyl 2-(3-Isoquinolinyl)benzoate (12): To a solution of **9** (40.8 mg, 0.12 mmol) in toluene (6 mL) was added Bu_3SnH (69.4 mg, 0.24 mmol) and AIBN (19.5 mg, 0.12 mmol), and the mixture was heated at reflux for 3 h. The solvent was evaporated, and the residue was dissolved in CH_3CN (10 mL), washed with hexane (5 × 10 mL), and dried ($MgSO_4$). The solvent was evaporated, and the oily residue (35.3 mg) was purified by preparative TLC with silica gel (3% MeOH/CH_2Cl_2) to give **12** (29.0 mg, 92% yield) as a colorless oil with R_f = 0.5. IR (neat): $\tilde{\nu}$ = 1720, 1627, 1594 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 3.67 (s, 3 H, Me), 7.48 (dt, J = 1.3, 7.6, 7.6 Hz, 1 H, 7-H), 7.55–7.75 (m, 4 H, 6-, 4′-, 5′- and 6′-H), 7.83 (dd, J = 7.6, 1.3 Hz, 2 H, 5-H and 6′-H), 7.88 (d, J = 7.6, 1.3 Hz, 1 H, 3′-H), 7.88 (s, 1 H, 4-H), 8.00 (d, J = 7.9 Hz, 1 H, 8-H), 9.27 (s, 1 H, 1-H) ppm. EI-MS: *m*/*z* (%) = 263 (20.7) $[M]^+$, 248 (13.6) $[M – Me]^+$, 232 (100) $[M – OMe]^+$, 204 (16.2) $[M – COOMe]^+$. HRMS: calcd. for $C_{17}H_{13}O_2N$ 263.0946; found 263.0937. These spectroscopic data are essentially identical with those reported by Desemund.[12h] A stirred mixture of **8** (47 mg, 0.2 mmol) and DDQ (58.2 mg, 0.24 mmol) in MeOH (2 mL) was refluxed for 5 h. To the cooled reaction mixture was added saturated aq. Na_2CO_3 (20 mL). The product was extracted with CH_2Cl_2 (3 × 10 mL), and the combined extracts were washed with saturated aq. Na_2CO_3 (2 × 10 mL) and water (10 mL), dried (Na_2SO_4), and concentrated to give a crude product (54.3 mg), which was purified by preparative TLC with silica gel (3% MeOH/CH_2Cl_2). A band with R_f = 0.5 gave **12** (50 mg, 94% yield) as a colorless oil.

$LiAlH_4$ Reduction of 12: To a stirred mixture of $LiAlH_4$ (8.4 mg, 0.22 mmol) in dry THF (1 mL) was added **12** (8.9 mg, 0.034 mmol). After the mixture was refluxed for 1 h, water was added to decompose the excess hydride. The precipitates were removed by suction filtration, and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2 (10 mL) and washed with water (2 × 10 mL) and brine (10 mL). The solution was concentrated to give an oil, which was purified by preparative TLC with silica gel (2% MeOH/CH_2Cl_2). A band with R_f = 0.3 gave **10** (7.3 mg, 90% yield) as a colorless oil.

5,6-(Methylenedioxy)-3,4-dihydroisoquinoline (17): To a solution of formamide **16** [193 mg, 1.0 mmol, b.p. 120 °C/1 Torr (ref.[25] b.p. 165 °C/2 Torr), prepared by a known method[25]] in toluene (10 mL) was added P_2O_5 (852 mg, 6.0 mmol) in portions. The mixture was refluxed for 4 h, then cooled to 0 °C, and treated with water (25 mL) and aq. NaOH (6 N, 20 mL). The alkaline mixture was extracted with CH_2Cl_2 (3 × 20 mL). The extracts were washed with water (2 × 25 mL), dried (Na_2SO_4), and concentrated. The residue (137 mg) was purified by preparative TLC with silica gel (5% MeOH/CH_2Cl_2). A main band with R_f = 0.2–0.4 gave **17** (97 mg,

56% yield) as colorless crystals, m.p. 73–74 °C (petroleum ether). IR (Nujol): $\tilde{\nu}$ = 1646, 1619, 1594, 1504 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 2.70 (t, J = 7.6 Hz, 2 H, 4-H), 3.74 (dt, J = 7.6, 7.6, 2.0 Hz, 2 H, 3-H), 6.02 (s, 2 H, OCH_2O), 6.73, 6.84 (AB type, J = 7.9 Hz, each 1 H, 7- and 8-H), 8.24 (s, 1 H, 1-H) ppm. EI-MS: m/z (%) = 175 (100) $[M]^+$, 174 (79.4) $[M - H]^+$, 148 (22.2) $[M - HCN]^+$, 116 (17.3) $[M - CH_2OH - HCN]^+$. $C_{10}H_9NO_2$ (175.18): calcd. C 68.56, H 5.18, N 8.00; found C 68.56, H 5.23, N 7.88. The reaction conditions of this cyclization have not been optimized yet.

1-[2,3-(Methylenedioxy)phenyl]-2-nitroethanol (19): To a slurry of $LiAlH_4$ (130 mg, 3.4 mmol) in dry THF (130 mL), which had been stirred at 0 °C for 30 min, was added CH_3NO_2 (8.95 mL, 167 mmol). After 30 min, 2,3-(methylenedioxy)benzaldehyde (**13**, 5.00 g, 33 mmol) was added in one portion. The mixture was stirred for 4 h and then quenched with a 1 N HCl solution. The reaction mixture was warmed to room temp., poured into water (200 mL), and extracted with CH_2Cl_2 (3 × 150 mL). The combined extracts were washed with water (3 × 100 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The residue was crystallized from Et_2O/hexane to give **19** (6.09 g, 86% yield) as yellow crystals, m.p.75–76 °C. IR (Nujol): $\tilde{\nu}$ = 3550, 1558 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 2.90 (d, J = 4.9 Hz, 1 H, OH), 4.64 (dd, J = 13.5, 3.6 Hz, 1 H, 1-H), 4.72 (dd, J = 13.5, 8.6 Hz, 1 H, 1-H), 5.56 (ddd, J = 8.6, 4.9, 3.6 Hz, 1 H, 2-H), 6.00, 6.02 (each d, J = 2.0 Hz, each 1 H, OCH_2O), 6.84 (dd, J = 7.6, 2.0 Hz, 1 H, 4′-H), 6.89 (t, J = 7.6 Hz, 5′-H), 6.95 (dd, J = 7.6, 2.0 Hz, 1 H, 6′-H) ppm. EI-MS: m/z (%) = 211 (38) $[M]^+$, 193 (13) $[M - H_2O]^+$, 164 (23) $[OCH_2OC_6H_3COCH_3]^+$, 150 (100) $[OCH_2OC_6H_3CHO]^+$, 121 (14) $[OCH_2OC_6H_3]^+$. $C_9H_9NO_5$ (211.17): calcd. C 51.19, H 4.30, N 6.63; found C 51.18, H 4.13, N 6.66.

***N*-{2-Acetoxy-2-[2,3-(methylenedioxy)phenyl]ethyl}formamide (23):** A solution of nitroethanol (**19**, 1.06 g, 5.0 mmol) in EtOH (30 mL) was stirred under H_2 in the presence of 10% Pd/C (304 mg) at room temp. for 15 h. The reaction mixture was filtered through a pad of $MgSO_4$ using EtOH (2 × mL) as a washing solvent. Evaporation of the solvent afforded 2-aminoethanol (**20**, 0.92 g) as colorless crystals, which were used in the following step without further purification. An analytical sample was prepared by recrystallization from benzene, m.p. 113–115 °C. IR (Nujol): $\tilde{\nu}$ = 3352, 3284, 1609 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 1.95 (br. s, 3 H, OH and NH_2), 2.90 (dd, J = 12.9, 7.6 Hz, 1 H, 1-H), 3.04 (dd, J = 12.9, 4.3 Hz, 1 H, 1-H), 4.76 (dd, J = 7.6, 4.3 Hz, 1 H, 2-H), 5.94, 5.98 (each s, each 1 H, OCH_2O), 6.77 (dd, J = 7.6, 1.3 Hz, 1 H, 4′-H), 6.84 (t, J = 7.6 Hz, 1 H, 5′-H), 6.91 (dd, J = 7.6, 1.3 Hz, 1 H, 6′-H) ppm. EI-MS: m/z (%) = 181 (33) $[M]^+$, 152 (85) $[M - CH_2{=}NH]^+$, 123 (30) $[HOCH_2C_6H_5O]^+$, 93 (100) $[C_6H_5O]^+$. $C_9H_{11}NO_3$ (181.19): calcd. C 59.66, H 6.12, N 7.73; found C 59.85, H 5.90, N 7.65. A stirred solution of **20** in EtOOCH (30 mL) was heated at reflux for 6 h. The evaporation of EtOOCH afforded formamide (**21**, 1.08 g) as a colorless oil, which was used in the following step without further purification. IR (Nujol): $\tilde{\nu}$ = 3288, 1662, 1654 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$, 5:1 rotamers): δ = 3.30 (br. s, 1 H, OH), 3.50 and 3.53 (1:5) (each dd, J = 5.3, 7.9 Hz, 1 H, 1′-H), 3.79 and 3.85 (5:1) (each dd, J = 3.3, 6.9 Hz, 1 H, 1′-H), 4.88 and 4.96 (1:5) (each dd, J = 3.3, 7.9 Hz, 1 H, 2′-H), 5.95, 5.99 (AB type, J = 1.3 Hz, each 1 H, OCH_2O), 6.07 (br. s, 1 H, NH), 6.77–6.93 (m, 3 H, 4′′-, 5′′- and 6′′-H), 7.99 (d, J = 12.2 Hz) and 8.20 (s) (1:5) (1 H, NCHO) ppm. EI-MS: m/z (%) = 209 (13) $[M]^+$, 191 (7) $[M - H_2O]^+$, 164 (48) $[M - NH_2CHO]^+$, 151 (100) $[M - CH_2NHCHO]^+$. HRMS: calcd. for $C_{10}H_{11}NO_4$ 209.0688, found 209.0687. To a solution of formamide **21**, Et_3N (0.73 mL, 5.3 mmol) and 4-(dimethylamino)pyridine (64 mg, 0.52 mmol) in CH_2Cl_2 (25 mL) was added dropwise Ac_2O (0.5 mL, 5.3 mmol). The mixture was stirred at room temp. for 1 h, washed with aq. HCl (1 N, 2 × 20 mL), saturated aq. $NaHCO_3$ (20 mL) and water (20 mL), and dried (Na_2SO_4). The solvent was evaporated, and the residue (1.24 g) was subjected to column chromatography with silica gel (7% MeOH/CH_2Cl_2) to give **23** (1.00 g, 3.98 mmol, 80% yield from **19**) as colorless crystals, m.p. 90.5–93 °C (Et_2O). IR (Nujol): $\tilde{\nu}$ = 1748, 1662 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$, 5:1 rotamers): δ = 2.13 and 2.14 (5:1) (2 s, 3 H, $COCH_3$), 3.60–3.67 and 3.67–3.85 (5:1) (each m, 2 H, 1′-H), 5.65 and 5.77 (5:1) (each br. s, 1 H, NH), 5.86–6.01 (m, 1 H, 2′-H), 5.99, 6.01 (AB type, J = 1.3 Hz, each 1 H, OCH_2O), 6.76–6.85 (m, 3 H, 4′′-, 5′′- and 6′′-H), 7.96 (d, J = 11.9 Hz) and 8.19 (s) (1:5) (1 H, NCHO) ppm. EI-MS: m/z (%) = 251 (14) $[M]^+$, 206 (28) $[M - NH_2CHO]^+$, 193 (11) $[M - CH_2NHCHO]^+$, 164 (16) $[OCH_2OC_6H_3COCH_3]^+$, 151 (100) $[OCH_2OC_6H_3CHOH]^+$. $C_{12}H_{13}NO_5$ (251.14): calcd. C 57.37, H 5.22, N 5.58; found C 57.23, H 5.12, N 5.57.

***N*-{2-(Formyloxy)-2-[2,3-(methylenedioxy)phenyl]ethyl}formamide (22):** A mixture of 2-aminoethanol **20** (181 mg, 1.0 mmol), K_2CO_3 (138 mg, 1.0 mmol) and molecular sieves (4 Å) in EtOOCH (10 mL) was heated at reflux for 48 h. The reaction mixture was filtered through a thin pad of $MgSO_4$ using CH_2Cl_2 (2 × 30 mL) as a washing solvent. The filtrate was then concentrated, and the residue (185 mg) was crystallized from EtOAc/Et_2O to give **22** (131 mg, 0.55 mmol, 55% yield) as colorless crystals, m.p. 114–115 °C (EtOAc/Et_2O). IR (Nujol): $\tilde{\nu}$ = 1720, 1664 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$, 5:1 rotamers): δ = 3.64–3.80 and 3.70–3.90 (1:5) (each m, 2 H, 1′-H), 5.70 and 5.78 (1:5) (each br. s, 1 H, NH), 5.96, 5.98 (each d, J = 1.3 Hz) and 6.00, 6.02 (each d, J = 1.3 Hz) (1:5) (2 H, OCH_2O), 6.09 (d, J = 11.9 Hz, 1 H, 2′-H), 6.78–6.88 (each m, 3 H, 4′-, 5′- and 6′-H), 7.97, 8.02 (each s) and 8.14, 8.20 (each s) (1:5) (2 H, NCHO and OCHO) ppm. EI-MS: m/z (%) = 237 (53) $[M]^+$, 192 (96) $[M - OCHO]^+$, 164 (32) $[OCH_2OC_6H_3COCH_3]^+$, 151 (100) $[OCH_2OC_6H_3CHOH]^+$. $C_{11}H_{11}NO_5$ (237.21): calcd. C 55.70, H 4.67, N 5.90; found C 55.78, H 4.70, N 5.82.

5,6-(Methylenedioxy)isoquinoline (18): A mixture of **23** (25 mg, 0.1 mmol) and P_2O_5 (28 mg, 0.2 mmol) in $POCl_3$ (2 mL) was stirred at 70 °C under nitrogen for 2 h. The reaction mixture was poured into cold aq. NaOH (6 N, 20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was washed with aq. NaOH (2 N, 30 mL) and water (30 mL), and dried (Na_2SO_4). The solvent was evaporated. The residue (15 mg) was purified by preparative TLC with silica gel. A main band with R_f = 0.4–5 (4% MeOH/CH_2Cl_2) gave **18** (8.1 mg, 0.47 mmol, 47% yield) as pale yellow crystals, m.p. 115–116 °C (petroleum ether). IR (Nujol): $\tilde{\nu}$ = 1652, 1595 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 6.23 (s, 2 H, OCH_2O), 7.29, 7.60 (AB type, J = 8.6 Hz, each 1 H, 4- and 3-H), 7.58, 8.42 (AB type, J = 5.9 Hz, each 1 H, 8- and 7-H), 9.15 (s, 1 H, 1-H) ppm. EI-MS: m/z (%) = 173 (100) $[M]^+$, 115 (28) $[M - CH_2O - HCN - H]^+$. $C_{10}H_7NO_2$ (173.17): calcd. C 69.36, H 4.07, N 8.09; found C 69.51, H 4.10, N 8.05.

2-[6-Bromo-2,3-(methylenedioxy)benzoyl]-5,6-methylenedioxy-1,2-dihydroisoquinoline (25b): To a solution of isoquinoline **18** (208 mg, 1.2 mmol) and Bu_3SnH (0.32 mL, 1.2 mmol) in CH_2Cl_2 (3 mL) was added 6-bromo-2,3-(methylenedioxy)benzoyl chloride {**24**, freshly prepared by refluxing 6-bromo-2,3-(methylenedioxy)benzoic acid,[33] [m.p. 174–176 °C (benzene; ref.[33c] m.p. 171–172 °C), 353 mg, 1.4 mmol] in $SOCl_2$ (1.4 mL) for 3 h} in CH_2Cl_2 (4 mL) at –78 °C and the mixture was stirred at that temperature for 2 h, then warmed to room temp. and washed with aq. NaOH (2 N, 2 × 20 mL) and water (20 mL), and dried (Na_2SO_4). The solvent was evaporated, and the residue was dissolved in CH_3CN (30 mL) and washed with hexane (5 × 30 mL). CH_3CN was evaporated, and

the crude product (477 mg) was chromatographed with silica gel (3% MeOH/CH_2Cl_2) to give **25b** (442 mg, 1.1 mmol, 92%) as colorless crystals, m.p. 183–185 °C (Et_2O/hexane). IR (Nujol): $\tilde{\nu}$ = 1668, 1644 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$, major isomer of 5:1 rotamers): δ = 4.99, 5.11 (AB type, J = 16.2 Hz, each 1 H, 1-H), 5.88, 6.40 (AB type, J = 7.9 Hz, each 1 H, 4-H and 3-H), 5.97 (s, 2 H, OCH_2O), 6.04, 6.10 (AB type, J = 1.3 Hz, each 1 H, OCH_2O), 6.65 (s, 2 H, 7-H and 8-H), 6.75, 7.08 (AB type, J = 8.2 Hz, each 1 H, 3′-H and 4′-H) ppm; ^1H NMR (270 MHz, $CDCl_3$, minor isomer of 5:1 rotamers): δ = 4.51, 4.63 (AB type, J = 14.5 Hz, each 1 H, 1-H), 5.98 (s, 2 H, OCH_2O), 6.04, 6.06 (AB type, J = 1.3 Hz, each 1 H, OCH_2O), 6.23, 6.43 (AB type, J = 7.9 Hz, each 1 H, 8- and 7-H), 6.59, 6.78 (AB type, J = 7.9 Hz, each 1 H, 4- and 3-H), 7.11, 7.42 (AB type, J = 7.9 Hz, each 1 H, 5′- and 4′-H) ppm. EI-MS: m/z (%) = 403 (61.1) $[M]^+$, 401 (61.0) $[M]^+$, 229 (99.2) $[COC_6H_2BrOCH_2O]^+$, 227 (100) $[COC_6H_2BrOCH_2O]^+$, 201 (9.0) $[C_6H_2BrOCH_2O]^+$, 199 (9.8) $[C_6H_2BrOCH_2O]^+$, 173 (81.5) $[OCH_2OC_9H_5N]^+$. $C_{18}H_{12}BrNO_5$ (402.20): calcd. C 53.75, H 3.01, Br 19.87, N 3.48; found C 53.89, Br 19.70, H 3.16, N 3.41.

2-[6-Bromo-2,3-(methylenedioxy)benzoyl]-1,2-dihydroisoquinoline (25a): A similar treatment of isoquinoline (**3**, 232 mg, 1.8 mmol), Bu_3SnH (0.48 mL, 1.8 mmol) and acid chloride **24** [prepared from 6-bromo-2,3-(methylenedioxy)benzoic acid[33] (491 mg, 2 mmol) and $SOCl_2$ (2 mL)] afforded **25a** (526 mg, 1.5 mmol, 82% yield), m.p. 165–167 °C (benzene), as colorless crystals. IR (Nujol): $\tilde{\nu}$ = 1668, 1627 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$, major rotamer of 5:1 rotamers): δ = 5.11, 5.22 (AB type, J = 16.5 Hz, each 1 H, 1-H), 5.78, 6.36 (AB type, J = 7.9 Hz, each 1 H, 4- and 3-H), 6.02, 6.05 (AB type, J = 1.3 Hz, each 1 H, OCH_2O), 6.76, 7.09 (AB type, J = 8.2 Hz, each 1 H, 5′- and 4′-H), 7.02–7.27 (m, 4 H, 5-, 6-, 7- and 8-H) ppm; ^1H NMR (270 MHz, $CDCl_3$, minor isomer of 5:1 rotamers): δ = 4.63, 4.76 (AB type, J = 14.8 Hz, each 1 H, 1-H), 6.03, 6.07 (AB type, J = 1.3 Hz, each 1 H, OCH_2O), 6.14, 6.79 (AB type, J = 8.2 Hz, each 1 H, 4- and 3-H), 6.97 (d, J = 7.3 Hz, 1 H, 8-H), 7.02–7.27 (m, 5 H, 5-, 6-, 7-, 8- and 5′-H), 7.39 (d, J = 8.2 Hz, 1 H, 4′-H) ppm. EI-MS: m/z (%) = 359 (43.6) $[M]^+$, 357 (44.0) $[M]^+$, 229 (98.6) $[COC_6H_2BrOCH_2O]^+$, 227 (100) $[COC_6H_2BrOCH_2O]^+$, 201 (9.8) $[C_6H_2BrOCH_2O]^+$, 199 (10.5) $[C_6H_2BrOCH_2O]^+$, 130 (28) $[C_9H_7]^+$. $C_{17}H_{12}BrNO_3$ (358.19): calcd. C 57.00, H 3.38, Br 22.31, N 3.91; found C 57.22, H 3.40, Br 22.08, N 3.84.

3,4,10,11-Bis(methylenedioxy)dibenz[*a*,*f*]indolizin-5(7*H*)-one (2): A mixture of **25b** (201 mg, 0.5 mmol), $Pd(OAc)_2$ (5.8 mg, 0.026 mmol), PPh_3 (13.4 mg, 0.051 mmol) and wet K_3PO (1.06 g, <5.0 mmol) in toluene (10 mL) was refluxed under argon for 10 h. The reaction mixture was diluted with CH_2Cl_2 (80 mL) and filtered through a pad of Celite using CH_2Cl_2 (2 × 20 mL) as a washing solvent. The solvent was then removed, and the residue (167 mg) was subjected to fractional crystallizations from CH_2Cl_2/EtOAc to give **2** (137.4 mg, 0.43 mmol, 86% yield) as yellow crystals, m.p. >238 °C (dec., CH_2Cl_2/EtOAc). IR (Nujol): $\tilde{\nu}$ = 1703 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 5.01 (s, 2 H, 7-H), 6.04 (s, 2 H, OCH_2O), 6.19 (s, 2 H, OCH_2O), 6.44 (s, 1 H, 4-H), 6.67 (s, 2 H, 8- and 9-H), 7.03, 7.28 (AB type, J = 8.2 Hz, each 1 H, 1- and 2-H) ppm. EI-MS: m/z (%) = 321 (72) $[M]^+$, 320 (100) $[M - H]^+$, 292 (9) $[M - CHO]^+$, 262 (7) $[M - CHO - HCHO]^+$. $C_{18}H_{11}NO_5$ (321.28): calcd. C 67.29, H 3.45, N 4.36; found C 67.14, H 3.48, N 4.35.

3,4-(Methylenedioxy)dibenz[*a*,*f*]indolizin-5(7*H*)-one (26a): A mixture of amide **25a** (1.40 g, 3.9 mmol), $Pd(OAc)_2$ (0.045 g, 0.2 mmol), PPh_3 (0.105 g, 0.4 mmol) and wet K_3PO_4 (8.29 g, 39 mmol) in toluene (39 mL) was treated in a similar manner to the above to afford **26a** (0.95 g, 3.4 mmol, 87% yield) as yellow crystals, m.p. >252 °C (dec., CH_2Cl_2/EtOAc). IR (Nujol): $\tilde{\nu}$ = 1702 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 5.11 (s, 2 H, 7-H), 6.19 (s, 2 H, OCH_2O), 6.35 (s, 1 H, 12-H), 7.04, 7.28 (AB type, J = 8.2 Hz, each 1 H, 1- and 2-H), 7.18–7.25 (m, 4 H, 8-, 9-, 10- and 11-H) ppm. EI-MS: m/z (%) = 277 (72) $[M]^+$, 276 (100) $[M - H]^+$, 248 (11) $[M - CHO]^+$. $C_{17}H_{11}NO_3$ (277.27): calcd. C 73.64, H 4.00, N 5.05; found C 73.58, H 4.05, N 4.96.

3-[2-(Methoxycarbonyl)-3,4-(methylenedioxy)phenyl]-5,6-(methylenedioxy)isoquinoline (27b): A stirred solution of **2** (96.6 mg, 0.3 mmol) and DDQ (81.4 mg, 0.36 mmol) in anhydrous MeOH (12 mL) was refluxed under nitrogen for 2 h. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2 (20 mL), washed with saturated aq. Na_2CO_3 (2 × 20 mL), water (20 mL), dried (Na_2SO_4) and the solvents were evaporated. The residue (113 mg) was purified by preparative TLC with silica gel developed with 2% MeOH/CH_2Cl_2. A main band with R_f = 0.35 gave **27b** (100 mg, 0.28 mmol, 95% yield) as pale yellow crystals, m.p. 184–186 °C (EtOAc/hexane). IR (Nujol): $\tilde{\nu}$ = 1723, 1645, 1600 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 3.72 (s, 3 H, OMe), 6.12, 6.23 (each s, each 2 H, OCH_2O), 6.95, 7.21 (AB type, J = 7.9 Hz, each 1 H, 6′- and 5′-H), 7.27, 7.57 (AB type, J = 8.2 Hz, each 1 H, 8- and 7-H), 7.78 (s, 1 H, 4-H), 9.10 (s, 1 H, 1-H) ppm. EI-MS: m/z (%) = 351 (84) $[M]^+$, 320 (100) $[M - OMe]^+$, 293 (18) $[M - COOMe]^+$. $C_{19}H_{13}NO_6$ (351.31): calcd. C 64.96, H 3.73, N 3.99; found C 64.90, H 3.83, N 3.96.

3-[2-(Methoxycarbonyl)-3,4-(methylenedioxy)phenyl]isoquinoline (27a): A similar treatment as that described above for **2** of **26a** (568 mg, 2.0 mmol) with DDQ (681 mg, 3.0 mmol) in anhydrous MeOH (100 mL) at reflux for 2 h afforded **27a** (558 mg, 1.8 mmol, 91% yield) as pale yellow crystals, m.p. 138–140 °C (EtOAc/hexane). IR (Nujol): $\tilde{\nu}$ = 1733, 1625, 1580 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ = 3.71 (s, 3 H, OMe), 6.13 (s, 2 H, OCH_2O), 6.97, 7.21 (AB type, J = 7.9 Hz, each 1 H, 5′-H, 6′-H), 7.60, 7.70 (each t, J = 7.9 Hz, each 1 H, 6-H and 7-H), 7.85 (d, J = 7.9 Hz, 1 H, 5-H), 7.86 (s, 1 H, 4-H), 7.97 (d, J = 7.9 Hz, 1 H, 8-H), 9.22 (s, 1 H, 1-H) ppm. EI-MS: m/z (%) = 307 (67) $[M]^+$, 292 (10) $[M - Me]^+$, 276 (100) $[M - OMe]^+$, 249 (11) $[MH - COOMe]^+$. $C_{18}H_{13}NO_4$ (307.30): calcd. C 70.35, H 4.26, N 4.56; found C 70.43, H 4.41, N 4.53.

Decumbenine B (1): To a stirred solution of $NaAl(OCH_2CH_2OCH_3)_2H_2$ (123 mg, 0.42 mmol, 70% toluene solution) in THF (2 mL) was added **27b** (34.7 mg, 0.1 mmol) in portions. After the mixture was stirred at room temp. for 1 h, water (1 mL) containing Rochelle's salt (0.5 g) and aq. NaOH (2 N, 1 mL) were added dropwise to quench the excess hydride reagent. The mixture was extracted with CH_2Cl_2 (3 × 15 mL), washed with water (20 mL), dried (Na_2SO_4) and concentrated. The residue [35 mg, **28b**, ^1H NMR (270 MHz, $CDCl_3$): δ = 3.78, 4.50, 4.87 (each br. s, each 2 H, 4-H, CH_2OH and 1-H), 5.98, 6.04 (each s, each 2 H, OCH_2O), 6.73, 6.76 (AB type, J = 7.9 Hz, each 1 H, 7- and 8-H), 6.68, 7.21 (AB type, J = 7.9 Hz, each 1 H) ppm] was stirred under oxygen in MeOH (2 mL) and aq. NaOH (2 N, 0.1 mL) at room temp. for 7 h. After the solvent was removed, the residue was dissolved in CH_2Cl_2 (10 mL), washed with water (2 × mL), and dried (Na_2SO_4). Evaporation of the solvent gave the crude product (24 mg), which was purified by preparative TLC with silica gel. A main band with R_f = 0.3–0.4 (3% MeOH/CH_2Cl_2) gave decumbenine B (**1**, 18.3 mg, 0.057 mmol, 57% yield) as colorless crystals, m.p. 226–227 °C (EtOAc/hexane; ref.[2] m.p. 222–224 °C, ref.[8a] m.p. 221–222 °C), of which the spectroscopic data are identical with those previously reported.[2,7]

3-[2-(Hydroxymethyl)-3,4-(methylenedioxy)phenyl]isoquinoline (29a): A similar treatment to that described above for **27b** of **27a** (31 mg, 0.1 mmol) with $Na(OCH_2CH_2OCH_3)_2H_2$ (123 mg, 0.42 mmol, 70% toluene solution) in THF (2 mL) afforded, by an autooxidation of **28a** [30 mg, ^{1}H NMR (270 MHz, $CDCl_3$): δ = 3.83, 4.49, 4.90 (each br. s, each 2 H, 4-H, benzylic H, 1-H), 6.03 (s, 2 H, OCH_2O), 6.81 (d, J = 7.9 Hz, 1 H, 5′-H), 7.16–7.33 (m, 5 H, 5-, 6-, 7-, 8- and 6′-H) ppm], **29a** [R_f = 0.35 (3% MeOH/CH_2Cl_2), 16 mg, 0.057 mmol, 57% yield] as colorless crystals, m.p. 180–182 °C (EtOAc/hexane). IR (Nujol): $\tilde{\nu}$ = 1627, 1583 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ = 4.54 (s, 2 H, benzylic CH_2), 6.09 (s, 2 H, OCH_2O), 6.35 (br. s, 1 H, OH), 6.86, 7.15 (AB type, J = 8.2 Hz, each 1 H, 5′- and 6′-H), 7.64, 7.75 (each t, J = 8.2 Hz, each 1 H, 6- and 7-H), 7.90 (d, J = 8.2 Hz, 1 H, 5-H), 7.91 (s, 1 H, 4-H), 8.03 (d, J = 8.2 Hz, 1 H, 8-H), 9.26 (s, 1 H, 1-H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 56.42 (t), 101.47 (t), 107.58 (d), 119.70 (d), 122.05 (s), 123.95 (d), 127.18 (d), 127.47 (d), 127.68 (d), 131.07 (d), 134.88 (s), 136.91 (s), 146.91 (s), 147.84 (s), 150.97 (d), 152.59 (s) ppm. EI-MS: m/z = 279 (100) $[M]^+$, 251 (33), 236 (26), 205 (34), 192 (18), 130 (21), 96 (20). $C_{17}H_{13}NO_3$ (279.29): calcd. C 73.11, H 4.69, N 5.02; found C 72.92, H 4.76, N 4.94.

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