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## Quinolizidines. XXX.<sup>1)</sup> A Ready Access to the Dibenzo[*a,f*]quinolizidine Ring System from 1,2,3,4-Tetrahydroquinoline

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An alternative synthesis of 9,10-dimethoxydibenzo[*a,f*]quinolizidine (**16**) has been accomplished through a route including mercuric acetate–edetic acid oxidation of a benzene-fused piperidine. The route started with an initial condensation of 1,2,3,4-tetrahydroquinoline (**5**) with 3,4-dimethoxyphenacyl bromide (**6**) and proceeded through the amino ketone (**7**), amino alcohol (**8**), lactam alcohol (**9**), *N*-substituted dihydrocarbostyryl (**10**), and quaternary iminium salt (**11** or **15**).

**Keywords** dibenzoquinolizidine synthesis; mercuric acetate–edetic acid oxidation tetrahydroquinoline; phenacylation; sodium borohydride reduction; catalytic hydrogenolysis; Bischler–Napieralski cyclization; catalytic reduction; disproportionation; <sup>1</sup>H-NMR

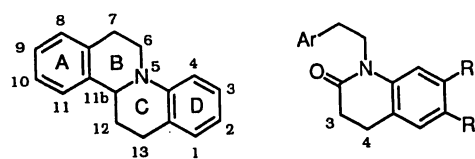
The dibenzo[*a,f*]quinolizidine ring system (**1**) is one of the seven theoretically possible dibenzoquinolizidines in which two benzene rings are fused to various sides of a quinolizidine ring.<sup>2)</sup> It has been synthesized in the form of the 2,3,9,10-tetramethoxy derivative,<sup>3)</sup> the 9,10-methylene-dioxy derivative,<sup>4)</sup> or the 9,10-dimethoxy derivative (**16**)<sup>5)</sup> via a route proceeding through Bischler–Napieralski cyclization of an *N*-arylethylated 3,4-dihydrocarbostyryl (type **2**) or carbostyryl (type **3**) intermediate. In the case of **16**, an alternative route following a low-yield intramolecular benzyne reaction of 1-(*m*-chlorophenethyl)-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline has also been reported.<sup>6)</sup> In addition, the parent skeleton (**1**) itself and its ring D-substituted derivatives have been prepared through a route including condensation of 2-aryl-3,4-dihydroisoquinolinium bromides with acetaldehyde.<sup>7)</sup>

The first of the above synthetic strategies to utilize the Bischler–Napieralski reaction, a useful vehicle for constructing a 3,4-dihydroisoquinoline skeleton from an amide or a lactam,<sup>8)</sup> would be most reasonable in view of the structural features of **1**, in which 1,2,3,4-tetrahydroisoquinoline is fused to 1,2,3,4-tetrahydroquinoline (**5**), and its value may be enhanced by a device for efficient preparation of the dihydrocarbostyryl intermediate (type **2**), a benzene-fused 2-piperidone. In the present study, therefore, we sought to synthesize such a dihydrocarbostyryl from **5** by application of the mercuric acetate–edetic

acid oxidation method. This method had been developed for generation of the lactam carbonyl function in a piperidine ring<sup>9–11)</sup> and had been utilized by us<sup>11i,12)</sup> for chiral syntheses of benzo[*a*]quinolizidine-type *Alangium* alkaloids (type **4**).

Condensation of **5** with 3,4-dimethoxyphenacyl bromide (**6**) was effected in boiling benzene in the presence of anhydrous K<sub>2</sub>CO<sub>3</sub> for 24 h, and the crude amino ketone **7** that formed in 85% yield was reduced with NaBH<sub>4</sub> in EtOH at room temperature for 24 h to give the amino alcohol **8** in 92% yield. Oxidation of **8** with mercuric acetate–edetic acid (in boiling 1% aqueous AcOH for 1.5 h) according to the previously reported procedure<sup>11b)</sup> produced the lactam alcohol **9** in 70% yield. Elongation of the reaction time from 1.5 h to 2.5 or 3 h did not improve the yield of **9**. The lactam alcohol **9** was then hydrogenolyzed in EtOH over 10% Pd–C catalyst using hydrogen (2–5 atm) in the presence of perchloric acid at 45 °C for 10 h, giving the desired dihydrocarbostyryl **10** as a crystalline solid in 81% yield.

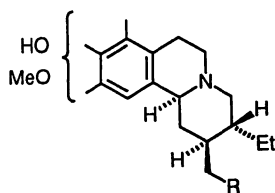
We next investigated the Bischler–Napieralski reaction of **10** to reach the title ring system (**1**), because Tourwé and Van Binst<sup>5)</sup> had followed a similar route only with the 3,4-didehydro derivative (type **3**) of **10**. On treatment with POCl<sub>3</sub> in boiling toluene for 3 h, **10** produced a cyclized product presumed to be the quaternary iminium chloride **11**. The crude chloride **11** was then hydrogenated in 50% aqueous EtOH over Adams catalyst for 2 h, giving the desired tetracyclic base **16**<sup>5,6)</sup> in 75% overall yield (from **10**). On the other hand, treatment of crude **11** with KI in H<sub>2</sub>O and repeated recrystallizations of the resulting iodide **12** from MeOH produced the 12,13-didehydro derivative **15** and the C(11b)–N(5) saturated derivative **16** in 38% and 18% yields, respectively. The formation of **15** and **16** is probably due to disproportionation of **11** or **12** during the cyclization or recrystallization process. Reduction of **15** with NaBH<sub>4</sub> in 80% aqueous EtOH or with hydrogen over Adams catalyst in 50% aqueous EtOH afforded **16** in 71% or 45% yield, respectively. The structure (**15**) with a fully aromatized quinoline moiety was assignable to the dehydrogenated product on the basis of its proton nuclear magnetic resonance (<sup>1</sup>H-NMR) spectrum in Me<sub>2</sub>SO-*d*<sub>6</sub>. It exhibited two two-proton triplets at δ 3.34 [C(7)–H's] and 5.10 [C(6)–H's] among other signals, including those assigned from nuclear Overhauser effect (NOE) data,



**1**

**2**: R = MeO or H

**3**: 3,4-didehydro



**4**: R = CH<sub>2</sub>OH, CO<sub>2</sub>H, or  
a heterocyclic ring

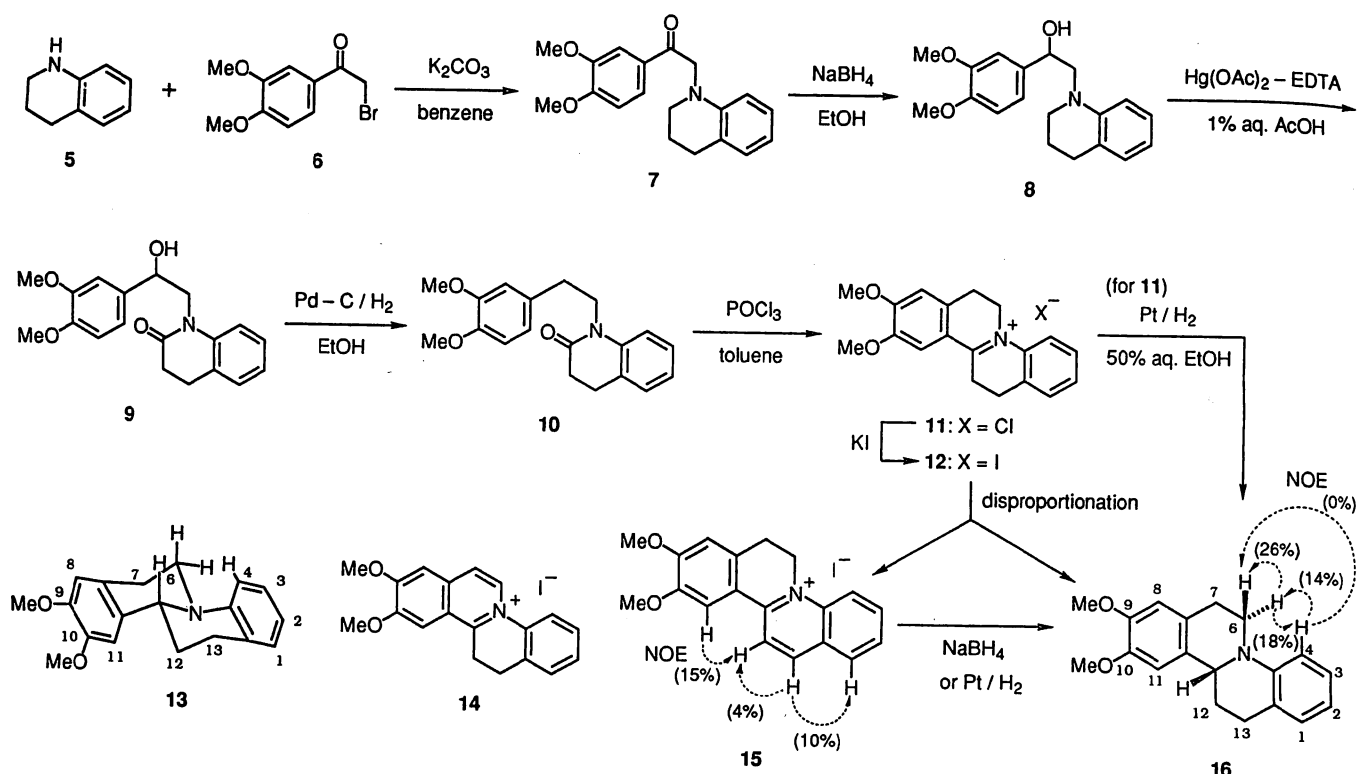


Chart 1

as shown in formula **15** (Chart 1). A large difference of 1.76 ppm in chemical shift between the above two methylene signals clearly eliminates the possibility of the alternative structure (**14**) (with a fully aromatized isoquinoline moiety) in which none of the two methylenes are directly connected to the positively charged heterocyclic nitrogen. The observed dehydrogenation of **11** or **12** in the quinoline moiety is in general agreement with that reported<sup>4</sup>) for the 9,10-methylenedioxy analogue.

As regards the problem of the conformation of the tetracyclic base **16**, Van Binst and Tourwé<sup>13</sup>) have determined the preferential *trans*-quinolizidine conformation (**13**) by measurement of the <sup>13</sup>C-H coupling constant for the angular C-H bond. In the present study, their conclusion was supported by the measurement of the <sup>1</sup>H-NMR spectrum of **16** in CDCl<sub>3</sub>. It may be seen from formula **16** (Chart 1) that the NOE observed for the C(6)-H (equatorial) signal on irradiation of the C(4)-H signal or *vice versa* revealed the proximity of the two protons in question. Inspection of molecular models indicates that such proximity is permissible only in the *trans*-quinolizidine conformer **13** and not in either of the two possible *cis*-quinolizidine conformers.

In conclusion, the above results represent an extension of the mercuric acetate-edetic acid oxidation method to a benzene-fused piperidine system and have revealed that the tetracycle **16** is accessible from 1,2,3,4-tetrahydroquinoline (**5**) in six steps in 33% overall yield. Further extension of this oxidation route to the synthesis of another dibenzoquinolizidine system is in progress in our laboratory.

#### Experimental

**General Notes** All melting points were determined by using a Yamato MP-1 capillary melting point apparatus and are corrected. Thin-layer chromatography (TLC) was developed on Merck silica gel 60 F<sub>254</sub> plates

(0.25-mm thickness), and spots were detected by means of ultraviolet (UV) absorbance measurement (at 254 nm) and/or by spraying with the standard I<sub>2</sub>-KI reagent. Flash chromatography<sup>14</sup>) was carried out by using Merck silica gel 60 (No. 9385). Spectra reported herein were recorded on a Hitachi model 320 UV spectrophotometer, a JASCO A-202 infrared (IR) spectrophotometer, a Hitachi M-80 mass spectrometer, or either a JEOL JNM-FX-100 (<sup>1</sup>H 100 MHz) or a JEOL JNM-GSX-500 (<sup>1</sup>H 500 MHz) nuclear magnetic resonance (NMR) spectrometer, and chemical shifts are reported in ppm downfield from internal Me<sub>4</sub>Si. Elemental analyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br=broad, d=doublet, dd=doublet-of-doubles, ddd=doublet-of-dd's, dddd=doublet-of-ddd's, H<sub>ax</sub>=axial H, H<sub>eq</sub>=equatorial H, m=multiplet, s=singlet, sh=shoulder, t=triplet.

**1-(3,4-Dimethoxyphenyl)-2-(1,2,3,4-tetrahydro-1-quinolinyl)ethanone (7)** A stirred mixture of 1,2,3,4-tetrahydroquinoline (**5**)<sup>15</sup>) (2.02 g, 15.2 mmol), anhydrous K<sub>2</sub>CO<sub>3</sub> (4.15 g, 30 mmol), 3,4-dimethoxyphenyl bromide (**6**)<sup>16</sup>) (3.89 g, 15 mmol), and dry benzene (40 ml) was heated under reflux in an atmosphere of N<sub>2</sub> for 24 h. After cooling, the reaction mixture was concentrated *in vacuo*, and the residue was partitioned by extraction with a mixture of H<sub>2</sub>O and CHCl<sub>3</sub>. The CHCl<sub>3</sub> extracts were washed with saturated aqueous NaCl, dried over anhydrous K<sub>2</sub>CO<sub>3</sub>, and concentrated *in vacuo* to leave a brown solid (4.62 g), mp 123–134.5°C. Recrystallization of the solid from MeOH gave a first crop (3.66 g) of **7** as brownish prisms, mp 136.5–138°C. Concentration of the mother liquor of this recrystallization yielded a second crop (256 mg) of **7**, mp 133–136.5°C, and concentration of the mother liquor from the second crystallization and purification of the residue by means of flash chromatography<sup>14</sup>) [hexane-AcOEt (3:1, v/v)] afforded a third crop (76 mg) of **7**. The total yield of **7** was 3.99 g (85% from **6**). For analysis, the crude **7** was recrystallized from MeOH to furnish faintly yellowish prisms, mp 137–138°C; MS *m/z*: 311 (M<sup>+</sup>); UV λ<sub>max</sub><sup>99% aq. EtOH</sup> 229 nm (ε 21400), 264 (18800), 303 (12100); IR ν<sub>max</sub><sup>Nujol</sup> 1678 cm<sup>-1</sup> (ArCO); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ<sup>17</sup>): 1.85–2.15 [2H, m, C(3)-H's], 2.83 [2H, t, *J*=6 Hz, C(4)-H's], 3.39 [2H, t, *J*=6 Hz, C(2)-H's], 3.90 and 3.96 (6H, s each, two MeO's), 4.66 [2H, s, N(1)-CH<sub>2</sub>CO], 6.2–6.65 and 6.8–7.0 [4H, m, C(5)-H, C(6)-H, C(7)-H, and C(8)-H], 6.91 [1H, d, *J*=8.5 Hz, C(5'-H)], 7.54 [1H, d, *J*=2 Hz, C(2'-H)], 7.66 [1H, dd, *J*=8.5 and 2 Hz, C(6'-H)]. *Anal.* Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub>: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.30; H, 6.88; N, 4.65.

**α-(3,4-Dimethoxyphenyl)-3,4-dihydro-1(2H)-quinolineethanol (8)** A stirred suspension of **7** (3.98 g, 12.8 mmol) in EtOH (80 ml) was heated at

80 °C to minimize the amount of **7** that remained insoluble. The resulting suspension was kept stirring under ice-cooling, and NaBH<sub>4</sub> (492 mg, 13 mmol) was added portionwise. After the mixture had been stirred at room temperature for 24 h, acetone (5 ml) was added and the reaction mixture was concentrated *in vacuo*. The residue was partitioned by extraction with a mixture of H<sub>2</sub>O and CHCl<sub>3</sub>. The CHCl<sub>3</sub> extracts were washed with saturated aqueous NaCl, dried over anhydrous K<sub>2</sub>CO<sub>3</sub>, and concentrated *in vacuo* to leave a brown, viscous oil (3.93 g). The oil crystallized from EtOH–H<sub>2</sub>O (2:1, v/v) (60 °C) to give a first crop (3.29 g, 82%) of **8** as slightly brownish prisms, mp 94–94.5 °C. Concentration of the mother liquor from this crystallization and recrystallization of the residue in a similar manner yielded a second crop (160 mg, 4%) of **8**. Concentration of the mother liquor of the last recrystallization and purification of the residue by means of flash chromatography<sup>14</sup> (CHCl<sub>3</sub>) furnished a third crop (241 mg, 6%) of **8**. The total yield of **8** was 3.69 g (92%). Recrystallizations of the crude **8** from EtOH–H<sub>2</sub>O (2:1, v/v) produced an analytical sample as colorless prisms, mp 96.5–97 °C; MS *m/z*: 313 (M<sup>+</sup>); UV λ<sub>max</sub><sup>99% aq. EtOH</sup> 230 nm (sh) (ε 11400), 266 (14700), 308 (2780); IR ν<sub>max</sub><sup>CHCl<sub>3</sub></sup> cm<sup>-1</sup>: 3620, 3540 (OH); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ<sup>17</sup>: 1.75–2.05 [2H, m, C(3)-H's], 2.44 (1H, br, s, OH), 2.77 [2H, t, *J* = 6.5 Hz, C(4)-H's], 3.1–3.35 [2H, m, C(2)-H's], 3.2–3.6 [2H, m, N(1)-CH<sub>2</sub>CH(OH)], 3.89 and 3.91 (6H, s each, two MeO's), 4.8–5.05 [1H, m, N(1)-CH<sub>2</sub>CH(OH)], 6.5–7.15 (7H, m, aromatic protons). *Anal.* Calcd for C<sub>19</sub>H<sub>23</sub>NO<sub>3</sub>: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.64; H, 7.58; N, 4.24.

**1-[2-(3,4-Dimethoxyphenyl)-2-hydroxyethyl]-3,4-dihydro-2(1H)-quinolinone (9)** A stirred mixture of **8** (627 mg, 2 mmol), (ethylenedinitrilo)tetraacetic acid disodium salt dihydrate (1.86 g, 5 mmol), and Hg(OAc)<sub>2</sub> (1.59 g, 5 mmol) in 1% aqueous AcOH (15 ml) was heated for 1.5 h in an oil bath kept at 110–120 °C. After cooling, the reaction mixture was extracted with three 15-ml portions of CHCl<sub>3</sub>. The CHCl<sub>3</sub> extracts were combined, washed successively with 10% aqueous HCl (2 × 15 ml), H<sub>2</sub>O (2 × 15 ml), 5% aqueous NaOH (2 × 15 ml), and saturated aqueous NaCl (2 × 15 ml), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo* to leave a brown oil. The residue was dissolved in CHCl<sub>3</sub> (4 ml), and the CHCl<sub>3</sub> solution was passed through a column packed with alumina (6 g), which was then eluted with CHCl<sub>3</sub> (66 ml). The eluate was concentrated *in vacuo*, and the residual light brown foam (584 mg) was dissolved in EtOH (10 ml). The resulting ethanolic solution was stirred, after addition of 50% aqueous NaOH (1.5 ml), at room temperature for 24 h. The reaction mixture was neutralized by addition of 10% aqueous HCl and then concentrated *in vacuo*. The resulting residue was partitioned by extraction with a mixture of H<sub>2</sub>O and CHCl<sub>3</sub>. The CHCl<sub>3</sub> extracts were washed successively with 10% aqueous HCl, H<sub>2</sub>O, 5% aqueous NaOH, and H<sub>2</sub>O, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo* to leave an orange oil. Purification of the oil by means of flash chromatography<sup>14</sup> [hexane–AcOEt (1:2, v/v)] gave **9** (457 mg, 70%) as a brownish solid. Recrystallization of the solid from hexane–AcOEt (1:1, v/v) yielded an analytical sample of **9** as faintly brownish prisms, mp 105.5–106 °C; MS *m/z*: 327 (M<sup>+</sup>); UV λ<sub>max</sub><sup>99% aq. EtOH</sup> 233 nm (ε 13200), 254 (10700); IR ν<sub>max</sub><sup>CHCl<sub>3</sub></sup> cm<sup>-1</sup>: 3420 (OH), 1650 (lactam CO); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ<sup>17</sup>: 2.55–3.0 [4H, m, C(3)-H's and C(4)-H's], 3.70 (1H, d, *J* = 4 Hz, OH), 3.88 and 3.90 (6H, s each, two MeO's), 3.97 (dd, *J* = 14.5 and 3 Hz) and 4.38 (dd, *J* = 14.5 and 8.5 Hz) [1H each, N(1)-CH<sub>2</sub>CH(OH)], 4.95–5.15 [1H, m, N(1)-CH<sub>2</sub>CH(OH)], 6.75–7.35 (7H, m, aromatic protons). *Anal.* Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>4</sub>: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.67; H, 6.56; N, 4.09.

**1-(3,4-Dimethoxyphenethyl)-3,4-dihydro-2(1H)-quinolinone (10)** A solution of **9** (917 mg, 2.8 mmol) in EtOH (50 ml) containing 70% aqueous HClO<sub>4</sub> (0.56 ml) was hydrogenated over 10% Pd–C catalyst (840 mg) at 2–5 atm and 45 °C for 10 h. The catalyst was removed by filtration and washed with EtOH. The filtrate and washings were combined and concentrated *in vacuo* to leave a brown oil, which was partitioned between H<sub>2</sub>O and CHCl<sub>3</sub>. The CHCl<sub>3</sub> layer was separated from the aqueous layer, washed successively with 10% aqueous HCl, H<sub>2</sub>O, saturated aqueous NaHCO<sub>3</sub>, and H<sub>2</sub>O, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo* to leave an orange oil. Purification of the oil by means of flash chromatography<sup>14</sup> [hexane–AcOEt (1:1, v/v)] afforded **10** (704 mg, 81%) as a faintly yellowish solid, mp 63–64 °C. Recrystallization of the solid from hexane–AcOEt (15:1, v/v) yielded an analytical sample as colorless needles, mp 64.5–65.5 °C; MS *m/z*: 311 (M<sup>+</sup>); UV λ<sub>max</sub><sup>99% aq. EtOH</sup> 233 nm (ε 13000), 254 (11000); IR ν<sub>max</sub><sup>CHCl<sub>3</sub></sup> cm<sup>-1</sup>: 1660 cm<sup>-1</sup> (lactam CO); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ<sup>17</sup>: 2.5–3.2 [6H, m, N(1)-CH<sub>2</sub>CH<sub>2</sub>Ar, C(3)-H's, and C(4)-H's], 3.86 (6H, s, two MeO's), 4.05–4.25 [2H, m, N(1)-CH<sub>2</sub>CH<sub>2</sub>Ar], 6.7–7.3 (7H, m, aromatic

protons). *Anal.* Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub>: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.02; H, 6.68; N, 4.39.

**7,11b,12,13-Tetrahydro-9,10-dimethoxy-6H-dibenzo[*a,f*]quinolizine (16)** i) From **10** via **11**: A stirred solution of **10** (226 mg, 0.73 mmol) and POCl<sub>3</sub> (1.12 g, 7.3 mmol) in dry toluene (5 ml) was heated under reflux for 3 h. The reaction mixture was concentrated *in vacuo* to leave an orange solid (presumed to be crude **11**), which was dissolved in 50% (v/v) aqueous EtOH (30 ml). The resulting solution was hydrogenated over Adams catalyst (50 mg) at 1 atm and room temperature for 2 h. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo*. The residual oil was partitioned by extraction with a mixture of aqueous K<sub>2</sub>CO<sub>3</sub> and CHCl<sub>3</sub>, and the CHCl<sub>3</sub> extracts were dried over anhydrous K<sub>2</sub>CO<sub>3</sub> and concentrated *in vacuo* to leave a brown oil. Purification of the oil by means of flash chromatography<sup>14</sup> (CH<sub>2</sub>Cl<sub>2</sub>) yielded **16** (160 mg, 75%) as a yellowish brown solid, mp 95–96 °C. Recrystallization of the solid from hexane furnished an analytical sample of **16** as slightly pinkish needles, mp 98–99 °C [lit. mp 113 °C (from EtOH)<sup>5</sup>]; 141–142 °C (from hexane)<sup>6</sup>]; MS *m/z*: 295 (M<sup>+</sup>); UV λ<sub>max</sub><sup>MeOH</sup> 232 nm (sh) (ε 12300), 252 (sh) (10100), 281 (7480); <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.08 [1H, dddd, *J* = 13, 10, 9.5, and 5.5 Hz, C(12)-H<sub>ax</sub>], 2.41 [1H, dddd, *J* = 13, 6, 5.5, and 3 Hz, C(12)-H<sub>eq</sub>], 2.70 [1H, ddd, *J* = 15.5, 4, and 3.5 Hz, C(7)-H<sub>ax</sub>], 2.81 [1H, ddd, *J* = 16, 5.5, and 5.5 Hz, C(13)-H<sub>ax</sub>], 2.93 [1H, ddd, *J* = 16, 10, and 6 Hz, C(13)-H<sub>ax</sub>], 3.00 [1H, ddd, *J* = 15.5, 10.5, and 4.5 Hz, C(7)-H<sub>ax</sub>], 3.22 [1H, ddd, *J* = 12.5, 10.5, and 3.5 Hz, C(6)-H<sub>ax</sub>], 3.86 and 3.88 (3H each, s, two MeO's), 3.98 [1H, ddd, *J* = 12.5, 4.5, and 4 Hz, C(6)-H<sub>eq</sub>], 4.39 [1H, dd, *J* = 9.5 and 3 Hz, C(11b)-H], 6.61 [1H, s, C(8)- or C(11)-H], 6.68 [1H, dd, *J* = 7.5 Hz each, C(2)-H], 6.75 [1H, s, C(11)- or C(8)-H], 6.87 [1H, d, *J* = 7.5 Hz, C(4)-H], 7.00 [1H, d, *J* = 7.5 Hz, C(1)-H], 7.10 [1H, dd, *J* = 7.5 Hz each, C(3)-H].<sup>18</sup> *Anal.* Calcd for C<sub>19</sub>H<sub>21</sub>NO<sub>2</sub>: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.27; H, 7.17; N, 4.81. The <sup>1</sup>H-NMR spectral data for the aliphatic protons are in agreement with those reported selectively in the literature.<sup>7b</sup>

ii) By NaBH<sub>4</sub> Reduction of **15**: A solution of **15**·H<sub>2</sub>O (150 mg, 0.34 mmol) in 80% (v/v) aqueous EtOH (15 ml) was stirred under ice-cooling, and NaBH<sub>4</sub> (26 mg, 0.69 mmol) was added portionwise. After the solution had been stirred at room temperature for 1 h, acetone (0.5 ml) was added. Concentration of the resulting mixture under vacuum left a yellow oil, which was partitioned by extraction with a mixture of 5% aqueous K<sub>2</sub>CO<sub>3</sub> and CH<sub>2</sub>Cl<sub>2</sub>. The CH<sub>2</sub>Cl<sub>2</sub> extracts were washed with saturated aqueous NaCl, dried over anhydrous K<sub>2</sub>CO<sub>3</sub>, and concentrated *in vacuo*. The residue was purified by flash chromatography<sup>14</sup> [CH<sub>2</sub>Cl<sub>2</sub>–hexane (3:1, v/v)] to yield **16** (72 mg, 71%) as an orange solid. Recrystallization of the solid from hexane gave a pure sample as slightly pinkish needles, mp 98–99 °C, shown to be identical (by comparison of the IR spectrum and TLC mobility) with the one prepared by method (i).

iii) By Catalytic Hydrogenation of **15**: A solution of **15**·H<sub>2</sub>O (336 mg, 0.77 mmol) in 50% (v/v) aqueous EtOH (40 ml) was hydrogenated over Adams catalyst (53 mg) at 1 atm and room temperature for 18 h. Work-up of the reaction mixture in a manner similar to that described above under method (i) afforded **16** (102 mg, 45%) as a brown oil. The IR spectrum and TLC behavior of this oil were identical with those of authentic **16**.

**Formation of 6,7-Dihydro-9,10-dimethoxydibenzo[*a,f*]quinolizinium Iodide (15) and 16 from 10** via **12** A solution of **10** (311 mg, 1 mmol) and POCl<sub>3</sub> (1.53 g, 10 mmol) in dry toluene (6 ml) was heated under reflux for 4.5 h. The reaction mixture was concentrated *in vacuo* to leave a yellow solid (presumed to be crude **11**), which was washed with hexane and then dissolved in hot H<sub>2</sub>O (15 ml). On addition of KI (1.00 g, 6 mmol), the hot aqueous solution deposited a yellowish brown precipitate, which was collected by filtration after the mixture had been cooled in an ice bath. Recrystallization of the precipitate from MeOH yielded **15**·H<sub>2</sub>O (168 mg, 38%). Further recrystallizations from MeOH and drying over P<sub>2</sub>O<sub>5</sub> at 2 mmHg and 50 °C for 10 h gave an analytical sample of **15**·H<sub>2</sub>O as yellow needles, mp 242–243 °C (dec.); UV λ<sub>max</sub><sup>99% aq. EtOH</sup> 249.5 nm (ε 15300), 293 (19800), 345.5 (8210), 412 (18400); <sup>1</sup>H-NMR (Me<sub>2</sub>SO-*d*<sub>6</sub>) δ: 3.34 [2H, t, *J* = 7 Hz, C(7)-H's], 3.95 and 3.96 (3H each, s, two MeO's), 5.10 [2H, t, *J* = 7 Hz, C(6)-H's], 7.27 [1H, s, C(8)-H], 7.83 [1H, s, C(11)-H], 7.95 [1H, dd, *J* = 8 and 7.5 Hz, C(2)-H], 8.20 [1H, ddd, *J* = 9, 7.5, and 1.5 Hz, C(3)-H], 8.39 [1H, dd, *J* = 8 and 1.5 Hz, C(1)-H], 8.65 [1H, d, *J* = 9 Hz, C(4)-H], 8.78 [1H, d, *J* = 9 Hz, C(12)-H],<sup>19</sup> 9.14 [1H, d, *J* = 9 Hz, C(13)-H].<sup>19–21</sup> *Anal.* Calcd for C<sub>19</sub>H<sub>18</sub>INO<sub>2</sub>·H<sub>2</sub>O: C, 52.19; H, 4.61; N, 3.20. Found: C, 52.19; H, 4.73; N, 3.13.

On the other hand, the mother liquor from the above first recrystallization was concentrated *in vacuo*, and the residue was purified by flash chromatography<sup>14</sup> (CHCl<sub>3</sub>) to give **16** (53 mg, 18%) as a reddish brown

oil. The IR spectrum and TLC mobility of the oil were identical with those of authentic **16**.

#### References and Notes

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- 17) For convenience, each skeletal atom in the quinoline moiety is indicated by a usual number and each aromatic carbon in the phenacyl moiety by a primed number.
- 18) See formula **16** for NOE's observed for selected protons.
- 19) In our opinion, the signal assignments reported by Brown *et al.*<sup>4)</sup> for C(12)-H and C(13)-H of the 9, 10-methylenedioxy analogue of **15** should be reversed.
- 20) See formula **15** for NOE's observed for selected protons.
- 21) See ref. 5 for spectral data for the corresponding chloride salt.