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Studies on the Syntheses of Heterocyclic Compounds. DCLXXII.[1] A Synthesis of Coralydine and O-Methylcorytenchirine by Thermolysis of Benzocyclobutene

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A new synthetic method for the tetrahydro-8-methylprotoberberines, coralydine (VIb) and O-methylcorytenchirine (VIa), was described. 3,4-Dimethoxyacetophenone (IX) was converted into 4,5-dimethoxy-2-methylbenzocyclobutene-1-carboxylic acid (XVII) by our method, which was condensed with homoveratrylamine to give N-(3,4-dimethoxyphenethyl)-4,5-dimethoxy-2-methylbenzocyclobutene-1-carboxamide (XVIII). Thermolysis of the resulting 3,4-dihydroisoquinoline hydrochloride (XXIII), which was obtained by Bischler-Napieralski reaction of XVIII, in bromobenzene followed by sodium borohydride reduction gave VIa and VIb.

Corytenchirine (III),[3] a novel tetrahydroprotoberberine alkaloid having a methyl group at C-8 position, has been synthesized by an application of a photolytic cyclisation of the 2-acetyl-1-benzylidene-1,2,3,4-tetrahydroisoquinoline (I) or a Mannich reaction of laudanidine (II) with acetaldehyde by present authors.[4] Other methods for preparation of 8-methyl-

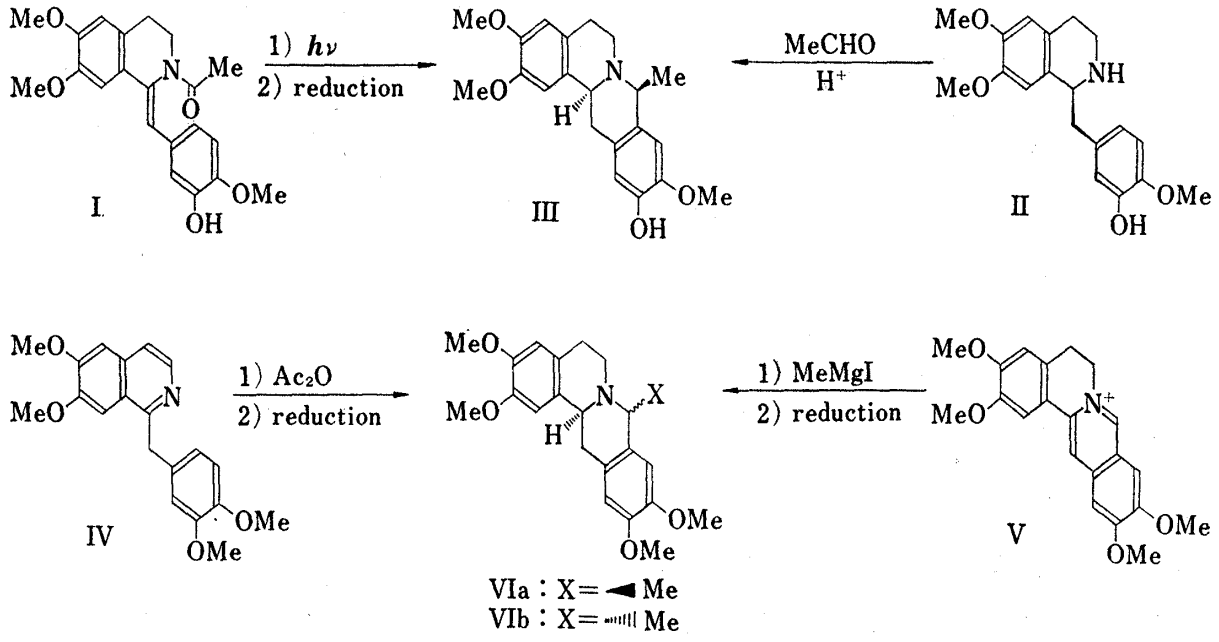

Chart 1

1) Part DCLXXI: T. Kametani, Y. Hirai, and K. Fukumoto, *Chem. Pharm. Bull.* (Tokyo), **24**, 2500 (1976).
2) Location: *Aobayama, Sendai.*
3) S-T. Lu, T.-L. Su, T. Kametani, A. Ujiie, M. Ihara, and K. Fukumoto, *Heterocycles*, **3**, 459 (1975).
4) T. Kametani, A. Ujiie, M. Ihara, K. Fukumoto, and S-T. Lu, *J. Chem. Soc. Perkin I*, **1976**, 1218.

protoberberines (VI) involve Friedel-Crafts type reaction of papaverine (IV) with acetic anhydride[5] or C-alkylation of berberine type compound (V) with methylmagnesium halide.[6]

The former three methods are the route that provides intermolecularly C–C unit in a formation of so-called berberine bridge, and the last one is an introduction of C-1 unit to berberine bridge carbon atom. Taking into consideration of the above fact, we have investigated a synthetic method which made C-methyl group and berberine bridge in one step, based on an intramolecular reaction of 1-benzylisoquinoline derivative. Here we wish to report a new synthetic method of the tetrahydro-8-methylprotoberberines (VI) by an application of an electrocyclic reaction[7] of *o*-quinodimethane derivative,[8,9] whose method forms a simple but interesting extension of the protoberberine (VIII) synthesis by a thermolysis of 1-benzocyclobutenyl-3,4-dihydroisoquinoline (VII) developed in our laboratory.[10–12]

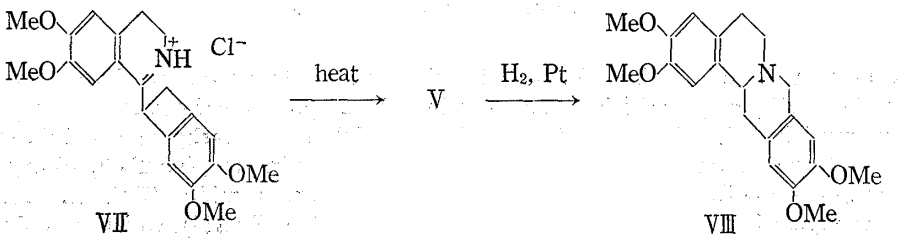

Chart 2

The key intermediate, 4,5-dimethoxy-2-methylbenzocyclobutene-1-carboxylic acid (XVII), was prepared by the standard method.[10–12] Knoevenagel condensation of 3,4-dimethoxyacetophenone (IX) with ethyl cyanoacetate in the presence of acetic acid and benzylamine in boiling benzene using a Dean-Stark apparatus[13] gave the α-cyanocinnamate (X), which on selective hydrolysis of an ester with 1N-ethanolic potassium hydroxide under reflux afforded the α-cyanocinnamic acid (XI). The geometry of substituents on a double bond of the compounds X and XI could not be determined. A direct preparation of this (XI) from the acetophenone and cyanoacetic acid under several conditions gave no good results. Reduction of the α-cyanocinnamic acid (XI) was carried out with sodium borohydride in the presence of saturated sodium bicarbonate to furnish the α-cyanophenylpropionic acid (XII), whose stereochemistry remained unclear. Decarboxylation of this product in dimethylacetamide[15] at 160—170° gave the phenylpropiononitrile (XIII), and the resulting nitrile was treated with bromine in the presence of sodium acetate in acetic acid to afford the 2-bromophenylpropiononitrile (XIV). Treatment of the bromo-nitrile (XIV) with an excess of sodium amide,[16] prepared freshly, in liquid ammonia gave the benzocyclobutene derivative (XVI) in 55% yield perhaps due to benzyne reaction *via* intermediate (XV).[12,17] This product consisted of a mixture of *cis*- and *trans*-compounds in a ratio of 1:1 by an NMR spectral

5) S.-T. Lu, T.-L. Su, T. Kametani, A. Ujiie, M. Ihara, and K. Fukumoto, *J. Chem. Soc. Perkin I*, **1967**, 63.
6) M. Freund and H. Beck, *Ber.*, **37**, 4673 (1904).
7) R.B. Woodward and R. Hoffmann, "The Conservation of Orbitary Symmetry," Academic Press, New York, 1970.
8) I.L. Klundt, *Chem. Revs.*, **70**, 471 (1970).
9) T. Kametani and K. Fukumoto, *Heterocycles*, **3**, 29 (1975).
10) T. Kametani, K. Ogasawara, and T. Takahashi, *Chem. Comm.*, **1972**, 675; *idem*, *Tetrahedron*, **29**, 73 (1973).
11) T. Kametani, Y. Hirai, F. Satoh, K. Ogasawara, and K. Fukumoto, *Chem. Pharm. Bull.* (Tokyo), **21**, 907 (1973).
12) T. Kametani, M. Takemura, K. Ogasawara, and K. Fukumoto, *J. Heterocyclic Chem.*, **11**, 179 (1974).
13) R.C. Paney and S. Dev, *Tetrahedron*, **24**, 3829 (1968).
14) F. Bohlmann, D. Schoumann, and O. Schmidt, *Ber.*, **99**, 2652 (1966).
15) G. Casini and L. Goodmann, *Can. J. Chem.*, **42** 1235 (1964).
16) J.A. Skorcz and F.E. Kaminski, "Organic Syntheses," Coll. Vol. V, ed. by H.E. Baumgarten, John Wiley and Sons, Inc., New York, 1973, p. 263.
17) T. Kametani, M. Kajiwara, and K. Fukumoto, *Tetrahedron*, **30**, 1053 (1974).

analysis, in which the resonance of C-methyl group in each compound appeared at δ 1.45 and 1.50 as a doublet having J=7 Hz. Hydrolysis of the nitrile (XVI) with ethanolic potassium hydroxide by Cava's method[18] yielded, in 92% yield, the corresponding carboxylic acid (XVII), whose stereochemistry was proven to be the thermodynamically more stable *trans* form by nuclear magnetic resonance (NMR) spectral analysis that showed a methine proton on C-1 position at 3.65 as doublet having J=1.6 Hz. It is well known that the coupling constant between C-1 and C-2 protons on a benzocyclobutene is 1—2 and 4—5 Hz in *trans* and *cis* configurations, respectively.[19] Finally, the carboxylic acid (XVII) was condensed with homoveratrylamine in the presence of dicyclohexylcarbodiimide in dichloromethane at room temperature to give the amide (XVIII), mp 108—109°, *m/e* 385 (M^+), which showed amide NH and CO groups at 3430 and 1650 cm^{-1}, respectively, in the infrared (IR) spectrum.

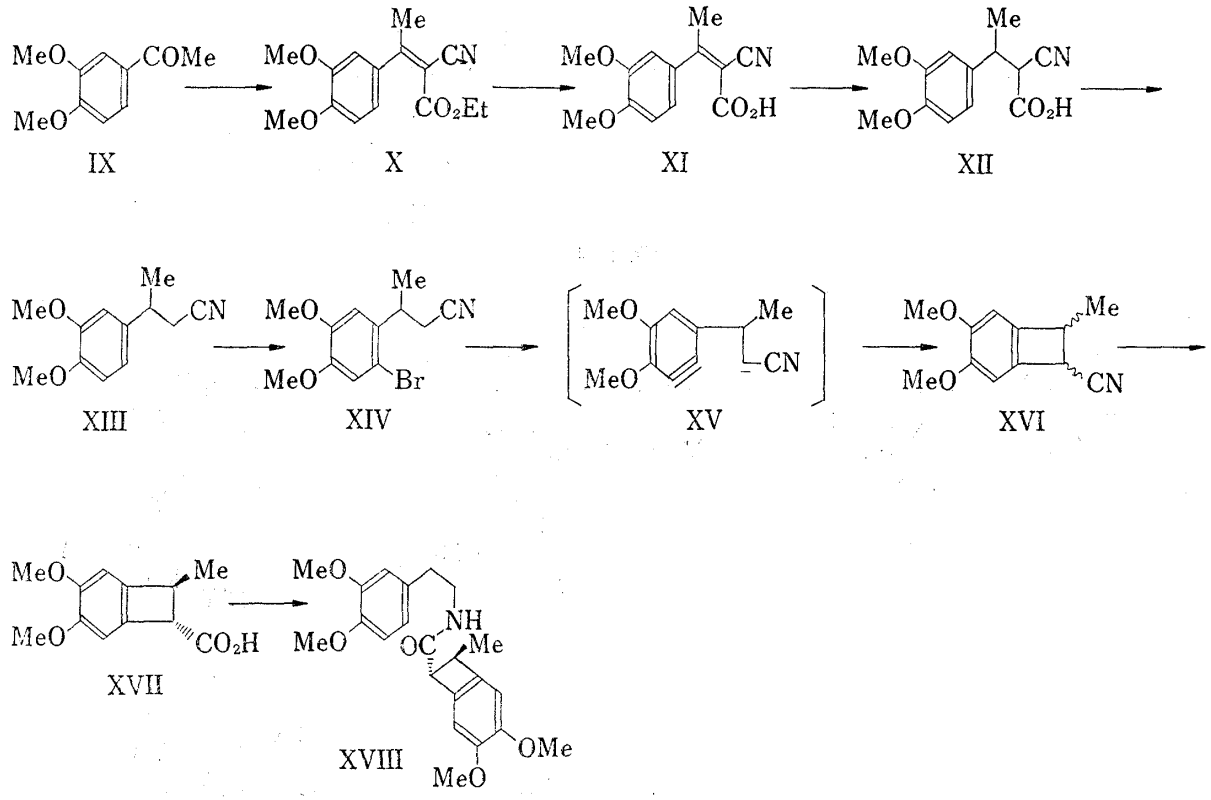

Chart 3

In case of Bischler-Napieralski reaction we had to take care of a decomposition of the benzocyclobutene ring because the amide (XIX) having no C-methyl group on the benzocyclobutene afforded a normal reaction product (XXI)[10-12] but the 1-methylbenzocyclobutene-1-carboxamide derivative (XX), an isomer of our amide (XVIII), gave the ochotensine-type isoquinoline (XXII) by this reaction.[20,21] Taking account of this fact, we examined Bischler-Napieralski reaction of our amide.

Treatment of the amide (XVIII) with phosphoryl chloride in boiling benzene for 2 hr gave the expected 1-benzocyclobutenyl-3,4-dihydroisoquinoline hydrochloride, which showed $>C=\overset{+}{N}H-$ absorption at 1620 cm^{-1} in IR spectrum and a 3,4-dihydroisoquinolinium system at 355, 305, 290 sh, 272 sh and 243 nm in ultraviolet (UV) spectrum. These data well supported

18) M.P. Cava and M.J. Mitchell, *J. Org. Chem.*, **27**, 631 (1962).
19) H.H. Wasserman, A.J. Solodar, and L.S. Keller, *Tetrahedron Letters*, **1968**, 5597.
20) T. Kametani, T. Takahashi, and K. Ogasawara, *J. Chem. Soc. Perkin I*, **1973**, 1464.
21) T. Kametani, Y. Hirai, H. Nemoto, and K. Fukumoto, *J. Heterocyclic Chem.*, **12**, 185 (1975).

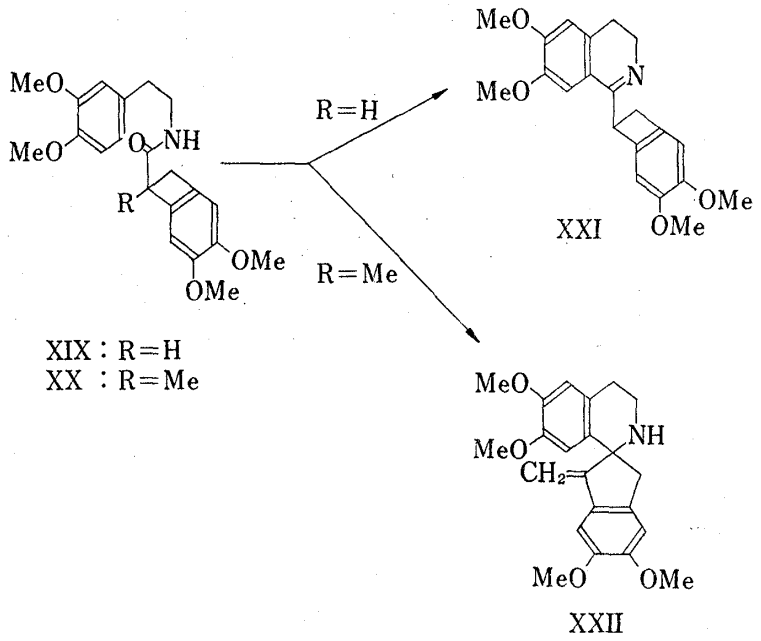

Chart 4

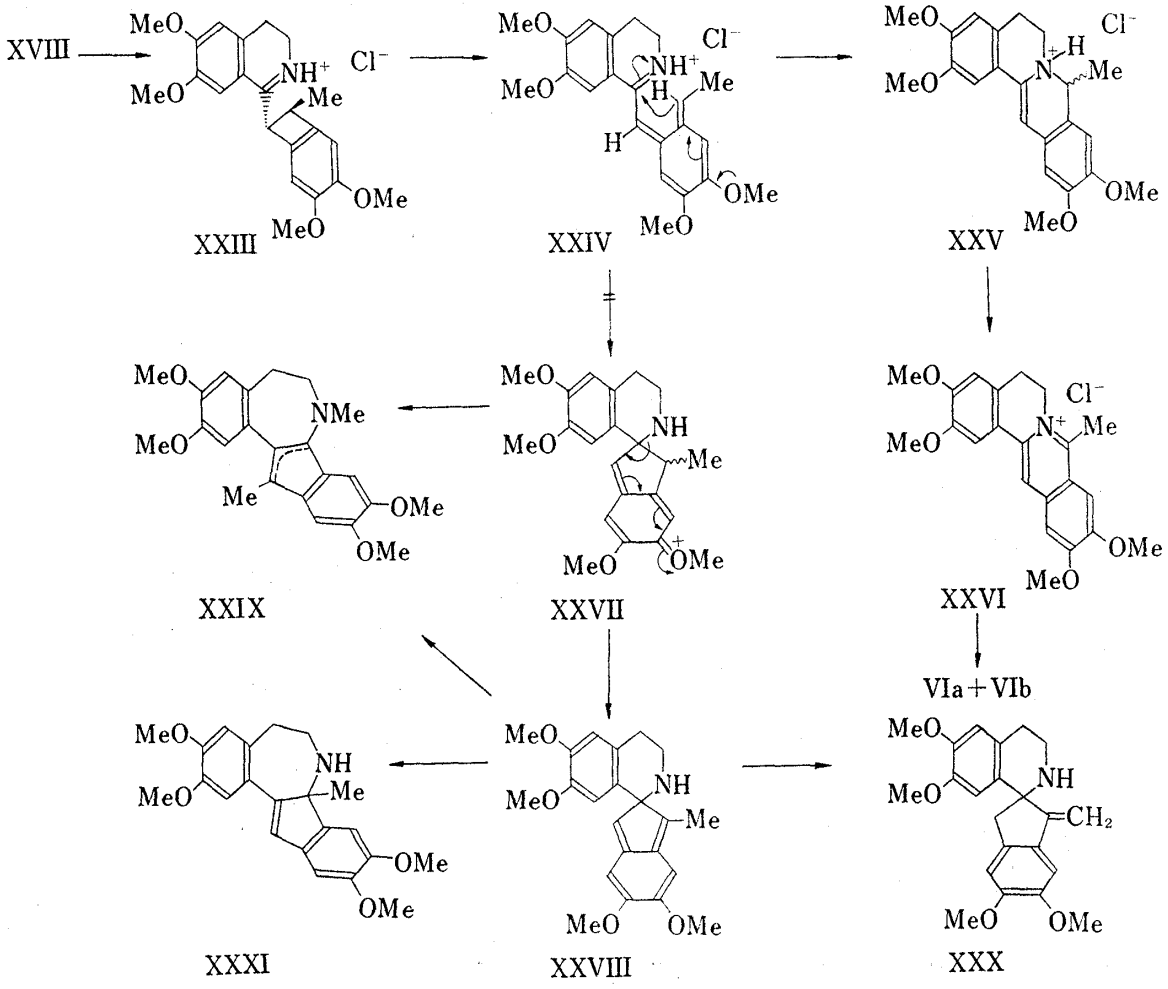

Chart 5

the product to be the 3,4-dihydroisoquinoline (XXIII) and ruled out the ochotensine-type structure.

In thermolysis of the 1-benzocyclobutenyl-3,4-dihydroisoquinoline hydrochloride (XXIII), four products XXVI, XXIX, XXX, and XXXI are possible as shown in Chart 5. Thus, conrotatory ring opening of the benzocyclobutene followed by an isomerization[11] would form the *o*-quinodimethane intermediate (XXIV), whose electrocyclic reaction and dehydrogenation of XXV would afford the 8-methylprotoberberinium chloride (XXVI).[10–12] On the other hand, the electrocyclic process indicated in XXIV would give the spirobenzylisoquinoline intermediate (XXVII),[20,21] which is converted into the stabilized products XXIX, XXX and XXXI.[22,23] Experimentally, we obtained only the protoberberinium chloride (XXVI) as an isolated product as follow. Thus, heating XXIII in purified bromobenzene at 150—160° for 19 min in a current of nitrogen afforded XXVI as a hygroscopic powder, *m/e* 366 (M^+—Cl), whose structure was proven by the UV spectrum [λ_{max}^{MeOH} nm: 345, 300 sh, 288, and 243].[24]

Reduction of this product with sodium borohydride in methanol gave a mixture of coralydine (VIb), mp 89—91° [lit.,[3] mp 94—95°] and O-methylcorytenchirine (VIa), which could be separated by recrystallization from methanol. Our synthetic coralydine (VIb) was identical with the authentic coralydine[3] in IR and NMR spectral comparisons, and O-methylcorytenchirine (VIa) was also identified by a comparison with the authentic sample[3] on thin-layer chromatography (TLC).

Thus, we have developed a new synthetic route for the tetrahydro-8-methylprotoberberine.

Experimental[25]

Ethyl α-Cyano-3,4-dimethoxy-β-methylcinnamate (X)——A mixture of 3,4-dimethoxyacetophenone (IX) (84.8 g), ethyl cyanoacetate (53.2 g), benzylamine (5.04 g), glacial AcOH (23.5 ml) and benzene (475 ml) was refluxed using a Dean and Stark apparatus. After a calculated amount of water had been separated, the mixture was cooled and washed with 10% HCl, 10% Na_2CO_3 and saturated NaCl aqueous solution, dried over Na_2SO_4, and evaporated *in vacuo* to give the cinnamate (X) (85.5 g, 66.2%) as yellow needles, mp 112—112.5° (from EtOH). IR ν_{max}^{KBr} cm^{-1}: 2210 (CN) and 1730 (CO). NMR ($CDCl_3$) ppm: 1.43 (3H, t, J=7 Hz, $CO_2CH_2CH_3$), 2.75 (3H, s, =C–CH_3), 3.97 (6H, s, 2×OCH_3), 4.37 (2H, q, J=7 Hz, $CO_2CH_2CH_3$), 7.03 (1H, s, ArH) and 7.10 (2H, s, ArH). *Anal.* Calcd. for $C_{15}H_{17}O_4N$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.30; H, 6.17; N, 5.02.

α-Cyano-3,4-dimethoxy-β-methylcinnamic Acid (XI)——A mixture of the ester (X) (67.8 g), 1 N ethanolic KOH (246.5 ml) and dioxane (246.5 ml) was refluxed with stirring for 15 hr and the solvent was then distilled off *in vacuo*. After dilution of the resulting residue with water and then washing with ether, the aqueous layer was acidified with 10% HCl and extracted with ether. The extract was washed with water, dried over Na_2SO_4, and evaporated *in vacuo* to afford the carboxylic acid (XI) (8.8 g, 14.5%) as pale orange plates, mp 185° (from ethanol). IR ν_{max}^{KBr} cm^{-1}: 2210 (CN) and 1725 (CO). NMR ($CDCl_3$+DMSO-d_6) ppm: 2.65 (3H, s, –C–CH_3), 3.90 (6H, s, 2×OCH_3), 6.94 (1H, s, ArH) and 7.03 (2H, s, ArH). *Anal.* Calcd. for $C_{13}H_{13}O_4N$: C, 63.15; H, 5.30; N, 5.67. Found: C, 62.98; H, 5.41; N, 5.61.

α-Cyano-3,4-dimethoxyphenyl-β-methylpropionic Acid (XII)——To a solution of the cinnamic acid (XI) (8.8 g) in MeOH (120 ml) and saturated $NaHCO_3$ aqueous solution (40 ml) was added $NaBH_4$ (15 g) in small portions with stirring at room temperature, and the mixture was stirred for 2 hr at room temperature. After evaporation of MeOH *in vacuo*, the residue was diluted with water and washed with ether. The aqueous layer was acidified with 10% HCl and extracted with ether. The extract was washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to give the phenylpropionic acid (XII) (8.37 g, 94.4%) as a pale brown oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250 (CN) and 1730 (CO). NMR ($CDCl_3$) ppm: 1.53 (3H, d, J=10 Hz, >$CHCH_3$), 3.45 (1H, m, >$CHCHCH_3$), 3.65 (1H, m, >$CHCHCH_3$), 3.85 (6H, s, 2×OCH_3) and 6.85 (3H, s, ArH). Mass Spectrum *m/e*: 249 (M^+). This product was used immediately for the next reaction because this was unstable on heating.

22) M. Shamma and C.D. Jones, *J. Am. Chem. Soc.*, **91**, 4009 (1969); *idem*, *ibid.*, **92**, 4943 (1970).
23) M. Shamma and J.F. Nugent, *Tetrahedron*, **29**, 1265 (1973).
24) V. Preininger, L. Hruban, V. Šimánek, and F. Šantavý, *Coll. Czech. Chem. Comm.*, **35**, 124 (1970).
25) All melting and boiling points are uncorrected. IR and UV spectra were taken with a Hitachi 215 grating spectrophotometer and a Hitachi 124 spectrophotometer, respectively, and NMR spectra with a JEOL PMX-60 spectrometer with Me_4Si as internal standard. Mass spectra were measured with a Hitachi RMU-7 spectrometer.

3,4-Dimethoxy-β-methylphenylpropiononitrile (XIII)——A solution of the phenylpropionic acid (XII) (8.37 g) in dimethylacetamide (50 ml) was heated at 160—170° for 1.5 hr and then cooled. The resulting solution was poured into water and the separated oil was extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4, and distilled to give the phenylpropiononitrile (XIII) (4.73 g, 68.7%) as a pale yellow oil, bp 120—121.5° (0.04 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2245 (CN). NMR ($CDCl_3$) ppm: 1.43 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.53 (2H, d, J=6 Hz, $CHC\underline{H}_2CN$), 3.31 (1H, m, $CH_3C\underline{H}CH_2$), 3.87 (6H, s, $2\times OCH_3$) and 6.80 (3H, s, ArH). Mass Spectrum *m/e*: 205 (M^+). *Anal.* Calcd. for $C_{12}H_{15}O_2N$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.40; H, 7.75; N, 6.83.

2-Bromo-4,5-dimethoxy-β-methylphenylpropiononitrile (XIV)——Br_2 (3.5 g) was added dropwise to a mixture of the nitrile (XIII) (4.5 g), NaOAc (3.5 g) and glacial AcOH (21 ml) with stirring at room temperature and then the mixture was further stirred for 1 hr at room temperature. The reaction mixture was poured into water and the separated oil was extracted with ether. The extract was washed with water and dried over Na_2SO_4. After evaporation of ether, the residue was distilled to give the bromo-nitrile (XIV) (5.36 g, 86.3%) as a yellow syrup, bp 151—153° (0.06 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250 (CN). NMR ($CDCl_3$) ppm: 1.45 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.51 (2H, d, J=6 Hz, $CHC\underline{H}_2CN$), 3.48 (1H, m, $CH_3C\underline{H}CH_2$), 3.80 (6H, s, $2\times OCH_3$), 6.79 (1H, s, ArH) and 6.93 (1H, s, ArH). Mass Spectrum *m/e*: 283 and 285 (M^+ and isotope peak of M^+). *Anal.* Calcd. for $C_{12}H_{14}O_2NBr$: C, 50.72; H, 4.97; N, 4.93; Br, 28.12. Found: C, 51.18; H, 5.20; N, 4.71; Br, 27.59.

1-Cyano-4,5-dimethoxy-2-methylbenzocyclobutene (XVI)——To a solution of $NaNH_2$ [prepared from metallic Na (3 g) and liq. NH_3 (300 ml)] in liq. NH_3 a solution of the nitrile (XIV) (4.66 g) in dry tetrahydrofuran (10 ml) was added slowly and the resulting mixture was stirred for 3.5 hr. After addition of crystalline NH_4Cl (8 g) an excess of NH_3 was evaporated with stirring. The residue was decomposed with water and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4 and evaporated to leave a brown syrup, which was chromatographed on silica gel (100 g) with benzene to give the benzocyclobutene (XVI) (1.84 g, 55%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2245 (CN). NMR ($CDCl_3$) ppm: 1.45 and 1.50 (3H, d, J=7 Hz, $CHC\underline{H}_3$, a mixture of *cis* and *trans* isomer), 3.55 (1H, m, $-C\underline{H}CH_3$), 3.75 (6H, s, $2\times OCH_3$), 4.20 (1H, d, J=4 Hz, CH–C$\underline{H}$CN), 6.60 (1H, s, ArH) and 6.71 (1H, s, ArH). Mass Spectrum *m/e*: 203 (M^+). *Anal.* Calcd. for $C_{12}H_{13}O_2N$: C, 70.91; H, 6.45; N, 6.89. Found: C, 71.06; H, 6.46; N, 6.52.

4,5-Dimethoxy-2-methylbenzocyclobutene-1-carboxylic Acid (XVII)——A solution of the nitrile (XVI) (1.63 g) in saturated ethanolic KOH solution (7 ml) was stirred at room temperature overnight and the mixture then refluxed with water (2 ml) for 3 hr. After evaporation of ethanol, the residue was poured into water (50 ml) and washed with ether. The aqueous layer was acidified with 10% HCl and extracted with ether. The extract was washed with water, dried over Na_2SO_4, and evaporated to leave a pale yellow syrup, which was subjected to silica gel (30 g) column chromatography by elution with benzene to give the carboxylic acid (XVII) (1.64 g; 92%) as colorless prisms, mp 146—148° (from benzene). IR $\nu_{max}^{CHCl_3}$: 1700 (CO). NMR (CCl_4) ppm: 1.47 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 3.65 (1H, d, J=1.6 Hz, –CH–C$\underline{H}CO_2H$), 3.75 (6H, s, $2\times OCH_3$), 6.57 (1H, s, ArH), 6.67 (1H, s, ArH) and 10.73 (1H, s, CO_2H). Mass Spectrum *m/e*: 222 (M^+). *Anal.* Calcd. for $C_{12}H_{14}O_4\cdot 0.2H_2O$: C, 63.82; H, 6.43. Found: C, 63.98; H, 6.16.

N-(3,4-Dimethoxyphenethyl)-4,5-dimethoxy-2-methylbenzocyclobutene-1-carboxamide (XVIII)——To a solution of homoveratrylamine (603 mg) and the carboxylic acid (XVII) (740 mg) in CH_2Cl_2 (13.3 ml) was added dicyclohexylcarbodiimide (756 mg) with stirring at room temperature in a current of N_2 and the mixture was stirred for 2 hr. After removal of an unsoluble material, the filtrate was diluted with CH_2Cl_2 (20 ml) and washed with 2% HCl, 5% $NaHCO_3$ and water, dried over Na_2SO_4, and evaporated to leave a brown syrup, which was chromatographed on silica gel (30 g) by elution with benzene–$CHCl_3$ (2: 3 v/v) to give the amide (XVIII) (452 mg; 35.3%) as colorless needles, mp 108—109° (from EtOAc). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430 (NH) and 1650 (CO). NMR ($CDCl_3$) ppm: 1.46 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.75 (2H, t, J=7 Hz, $ArC\underline{H}_2CH_2$), 3.44 (2H, t, J=7 Hz, $ArCH_2C\underline{H}_2N$), 3.65 (1H, m, CH), 3.77 (3H, s, OCH_3), 3.83 (9H, s, $3\times OCH_3$), 5.65 (1H, broad, NH), 6.56 (1H, s, ArH) and 6.67 (4H, ArH). Mass Spectrum *m/e*: 385 (M^+). *Anal.* Calcd. for $C_{22}H_{27}O_5N\cdot H_2O$: C, 65.49; H, 7.26. Found: C, 65.98; H, 6.96.

3,4-Dihydro-6,7-dimethoxy-1-(4,5-dimethoxy-2-methylbenzocyclobutenyl)isoquinoline Hydrochloride (XXIII)——A mixture of the amide (XVIII) (200 mg), $POCl_3$ (200 mg) and dry benzene (6.8 ml) was refluxed for 2 hr, and then the solvent and the excess of reagent were distilled off *in vacuo*. After addition of *n*-hexane to the residue, a yellow amorphous powder separated was collected by decantation to give the isoquinoline hydrochloride (XXIII) (200 mg) [IR ν_{max}^{KBr} cm^{-1}: 1620 ($C=\overset{+}{N}H$); UV λ_{max}^{MeOH} nm: 355, 305, 290_{sh}, 272_{sh}, and 243], which was hygroscopic strongly and used in the next reaction because its crystallization was very difficult.

2,3,10,11-Tetramethoxy-8-methylprotoberberinium Chloride (XXVI)——A suspension of the above chloride (XXIII) (70 mg) in distilled bromobenzene (1.5 ml) was heated at 150—160° for 19 min in a current of N_2. After addition of an excess of ether to the above cooled mixture, a yellow powder separated was collected by decantation to give the berberinium salt (XXVI) (65 mg) as a yellow amorphous powder, mp 183—185°, which showed a severe hygroscopic character. IR ν_{max}^{KBr} cm^{-1}: 1605 ($C=\overset{+}{N}\langle$). UV λ_{max}^{MeOH} nm: 345, 300_{sh}, 288, and 243. Mass Spectrum *m/e*: 366 (M^+-Cl).

Coralydine (VIb) and O-Methylcortenchirine (VIa)——To a solution of the above berberinium salt (XXVI)

(13 mg) in methanol (5 ml) was added in portions sodium borohydride (10 mg) with stirring below 5° and the mixture was stirred for 1 hr at room temperature. After evaporation of MeOH, the residue was decomposed with water and extracted with chloroform. The extract was washed with water, dried over K_2CO_3 and evaporated *in vacuo* to give coralydine (VIb) (6.6 mg) as colorless needles, mp 89—91°, after recrystallization from MeOH. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2900—2700 (weak Bohlmann bands). NMR ($CDCl_3$) ppm: 1.53 (3H, d, J=6.5 Hz, $CHC\underline{H}_3$), 3.83 (12H, s, $4\times OCH_3$), 3.0—3.8 (2H, m, $CH_3C\underline{H}$ and C_{13a}-$\underline{H}$), and 6.51, 6.53, 6.54, and 6.64 (each 1H, each s, $4\times$ArH). The IR and NMR spectra of VIb were superimposable upon those of the authentic sample.[3] The evaporation of the mother liquor on recrystallization gave O-methylcorytenchirine (VIa), whose thin layer chromatographic bahavior [*Rf* value 0.65, silica gel 0.8 mm, benzene: ethyl acetate: methanol 5: 4: 1] was identical with that of the authentic sample.[3]

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