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Alkaloids of *Corydalis incisa* Pers. II.[1] The Structure of Corydalic Acid Methyl Ester[2]

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The structure (I) of a new alkaloid, corydalic acid methyl ester, mp 140—141°, $[\alpha]_D$ $+85.4°$, $C_{22}H_{23}O_6N$, isolated from *Corydalis incisa* Pers. (Papaveraceae) only in the vegetative stage, was established by the spectroscopic studies and chemical correlation with mesotetrahydrocorysamine. Furthermore, on the basis of the stereochemical investigation of mesotetrahydrocorysamine, the stereostructure of corydalic acid methyl ester was determined as XII.

Corydalic acid methyl ester is a noteworthy natural alkaloid in which aromatic ring is attached to the position-3 of the tetrahydroisoquinoline, and biogenetically it is supposed to be derived from protoberberine skeleton by a fission of B-ring, possibly through an aldehyde-type intermediate.

In a previous paper,[1] we described the isolation of eight new alkaloids, *l*-tetrahydrocorysamine, acetylcorynoline, acetylisocorynoline, TN-4 (I), -5, -12, -21 and -23 from the herb of *Corydalis incisa* Pers. in addition to four known alkaloids, isocorynoline, corynoline, corycavine and protopine, and we found the considerable variation in the alkaloidal pattern at the growing stages of the plant.

This paper deals with the strucutre elucidation of a new base (TN-4), named corydalic acid methyl ester (I), isolated only in the vegetative stage.

Corydalic acid methyl ester (I) was crystallized from acetone–petroleum ether to give colorless prisms, mp 140—141°, $[\alpha]_D$ $+85.4°$, $C_{22}H_{23}O_6N$. The nuclear magnetic resonance (NMR) spectrum of I showed signals for C-methyl protons (δ 1.05, 3H, d, $J=6.0$ Hz), N-methyl

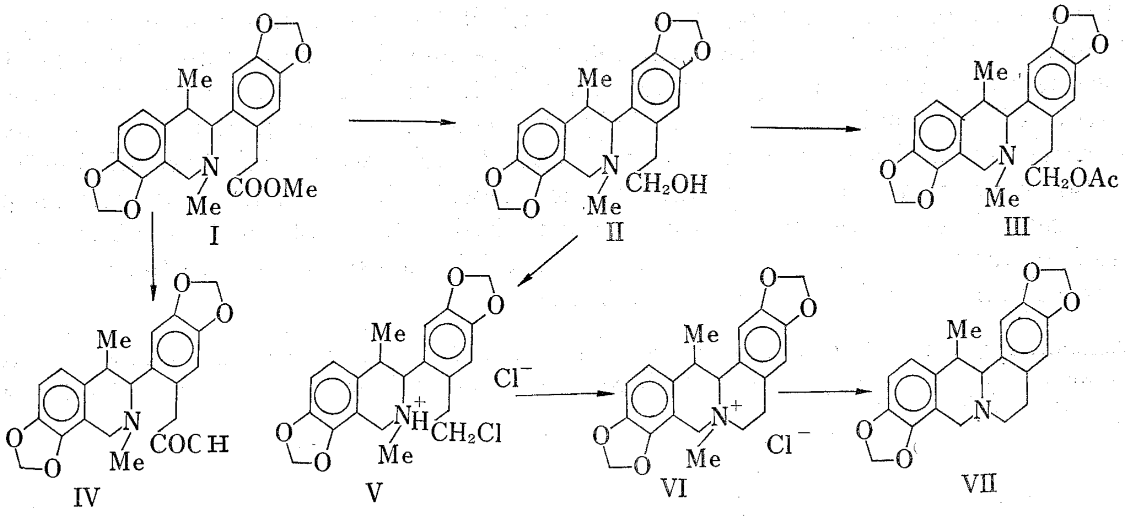

Chart 1

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[1] Part I: G. Nonaka, H. Okabe, I. Nishioka, and N. Takao, *Yakugaku Zasshi*, 93, 87 (1973).

[2] A part of this work was presented at the 90th Annual Meeting of the Pharmaceutical Society of Japan, Sapporo, July, 1970, Abst. II, p. 208.

[3] Location: *Katakasu, Higashi-ku, Fukuoka.*

protons (δ 2.10, 3H, s), O-methyl protons (δ 3.67, 3H, s), protons for two methylenedioxy groups (δ 5.95, 4H, s) and four aromatic protons (δ 6.72, 2H, d, J=1.0 Hz; δ 6.82, 2H, d, J=10.5 Hz), and the infrared (IR) spectrum exhibited the presence of carbonyl group at 1738, 1275 cm^{-1} and the absence of NH and OH groups.

On reduction with lithium aluminium hydride in tetrahydrofuran, I gave a base (II), colorless oil, $[\alpha]_D$ −18.0°, (methiodide: $C_{21}H_{23}O_5N \cdot CH_3I$). In the NMR spectrum, the signal (δ 3.67) of the O-methyl group in I disappeared and instead the increase in the integral curve accounting for additional two protons was observed in aliphatic proton region. II showed no IR absorption of the carbonyl group, and that of the expected hydroxyl group was not clear. However, on acetylation with acetic anhydride and pyridine, II afforded a mono-acetate (III), colorless oil, $[\alpha]_D$ +66.7°, $C_{23}H_{25}O_6N$, indicating that II possessed a hydroxyl group.

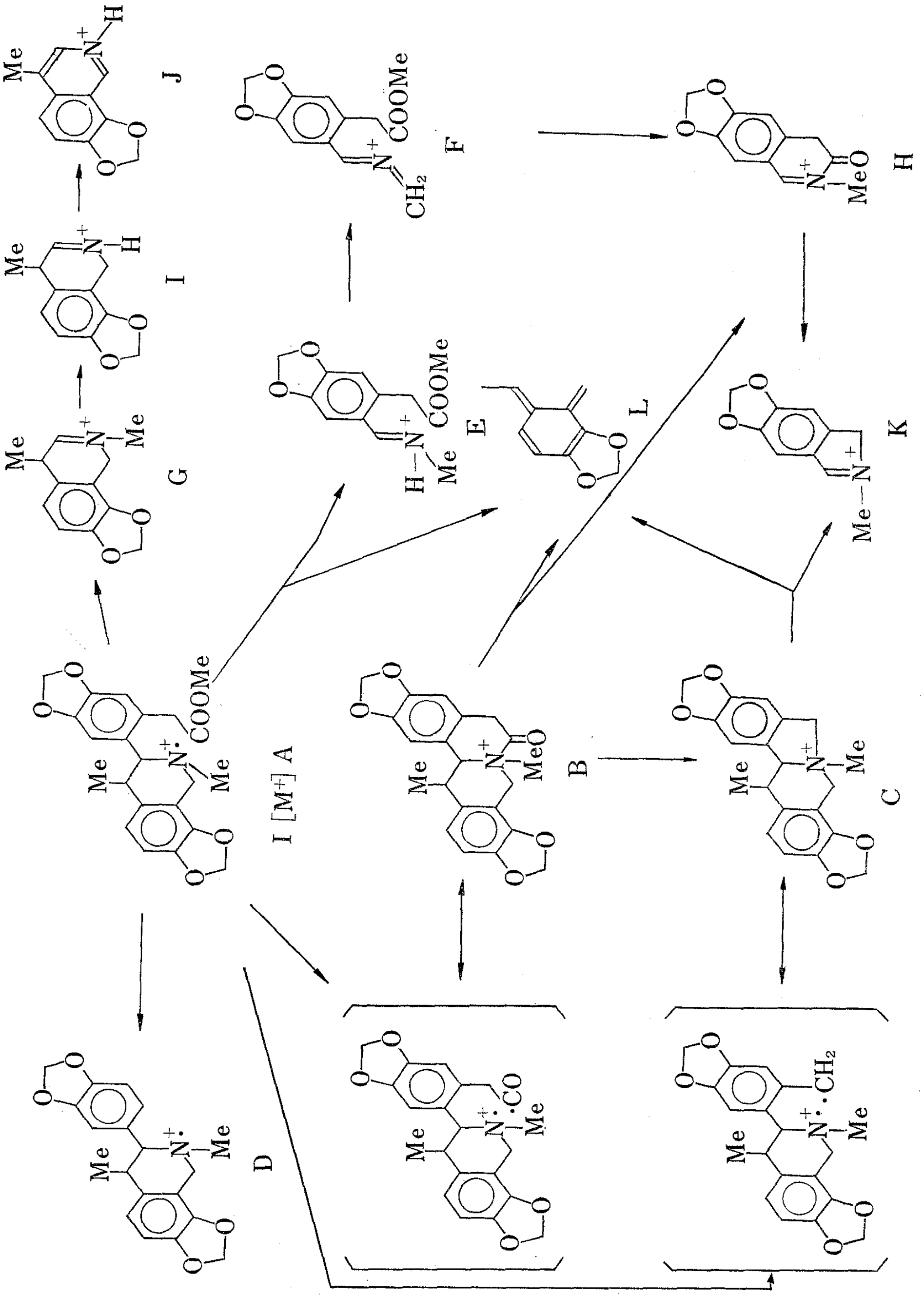

Chart 2. Fragmentation Pathway of Corydalic Acid Methyl Ester (I)

When saponified with methanolic sodium hydroxide, I gave an acid (IV), colorless oil, $[\alpha]_D$ +24.3°, $C_{21}H_{21}O_6N$, which depicted in the NMR spectrum the broad singlet at δ 10.65 due to the proton of carboxyl group.

These results indicated I to be a tertiary base having one N–CH_3, –$COOCH_3$ and two –O–CH_2–O– groups.

On treatment with thionyl chloride in benzene at 0°, II gave a chloride (V), mp 216—219°, $[\alpha]_D$ +50.0°, $C_{21}H_{23}O_4NCl_2$, which was neutralized with alkali to furnish a quaternary salt (VI). The mass spectrum of VI showed a base peak at *m/e* 162 and other major peaks at *m/e* 337, 322, 176, 174, 52, 50 and showed remarkably similar spectrum to those of *dl*-tetrahydrocorysamine and *dl*-mesotetrahydrocorysamine except the peaks of *m/e* 52 and 50 due to methyl chloride. VI was then treated with *ortho*-dichlorobenzene[4] at 200° to yield a tertiary base, *d*-mesotetrahydrocorysamine (VII), colorless oil, $[\alpha]_D$ +200.4°, $C_{20}H_{19}O_4N$, which was identified by the direct comparison of thin-layer chromatography (TLC), IR, NMR and mass spectra with those of the synthetic specimen of *dl*-mesotetrahydrocorysamine (VII').[5]

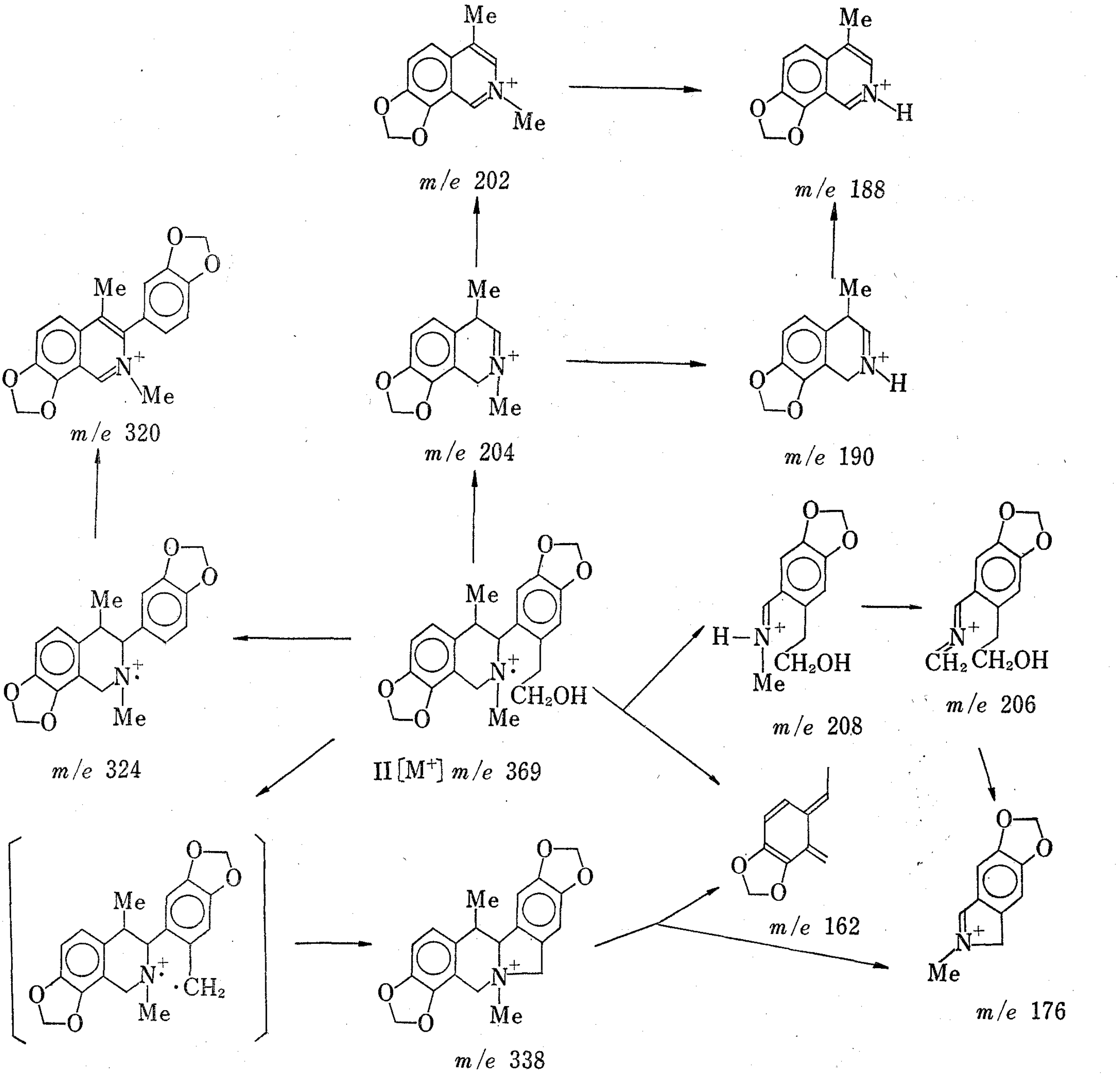

Chart 3. Fragmentation Pathway of II

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[4] M. Ohta, H. Tani, and S. Morozumi, *Chem. Pharm. Bull.* (Tokyo), **12**, 1072 (1964).

[5] *dl*-Tetrahydrocorysamine and *dl*-mesotetrahydrocorysamine were synthesized from coptisine chloride according to the procedure reported by C. Tani, *et al.* (*Yakugaku Zasshi*, **82**, 748 (1962)).

Furthermore, from the following mass spectral examination of corydalic acid methyl ester, structure I was supported. The mass spectrum of corydalic acid methyl ester disclosed a molecular peak at *m/e* 397 and a base peak at *m/e* 162. The fragmentation of these peaks were explained in Chart 2. The assignment of these structures was supported by high resolution measurement of the fragment ions and the mass spectrum of II which was characterized by displacement of the peaks at *m/e* 397, 236, 234 of I to lower mass number by 28 mass units at *m/e* 369, 208, 206, respectively (Chart 3). Structure II was established by the synthesis of II from *dl*-mesotetrahydrocorysamine (VII′). Treatment of VII′ with methyl iodide afforded a corresponding methiodide which was then submitted to Hofmann degradation to give a methine base (VIII) as a sole product. VIII showed a ABX–type splitting pattern, corresponding to one proton at δ 5.13 (q, J=1.5, 11.0 Hz), 5.43 (q, J=1.5, 17.0 Hz) and δ 7.20 (q, J=11.0, 17.0 Hz) in the NMR spectrum, and characteristic styrene–type absorption at 264 and 291 mμ in the ultraviolet (UV) spectrum. On treatment with diborane followed by oxidation with hydrogen peroxide in alkaline medium, VIII afforded an end alcohol, which was identified as II in terms of the direct comparison of TLC, IR, UV and mass spectra.

TABLE I. Mass Spectrum of Corydalic Acid Methyl Ester (I)

Assignment	*m/e*	Relative intensity	Formula	Calcd.	Found
A	397	98	$C_{22}H_{23}O_6N$	397.1548	397.1525
	382	89	$C_{21}H_{29}O_6N$	382.1291	382.1292
B	366	81	$C_{21}H_{20}O_5N$	366.1342	366.1292
C	338	9	$C_{20}H_{20}O_4N$	338.1392	338.1408
D	324	13	$C_{19}H_{18}O_4N$	324.1236	324.1244
E	236	27	$C_{12}H_{14}O_4N$	236.0923	236.0926
F	234	27	$C_{12}H_{12}O_4N$	234.0763	234.0809
G	204	50	$C_{12}H_{14}O_2N$	204.1025	204.1025
H			$C_{11}H_{10}O_3N$	204.0661	204.0704
I	190	20	$C_{11}H_{12}O_2N$	190.0868	190.0861
J	188	23	$C_{11}H_{10}O_2N$	188.0711	188.0715
K	176	20	$C_{10}H_{10}O_2N$	176.0712	176.0698
L	162	100	$C_{10}H_{10}O_2$	162.0681	162.0684

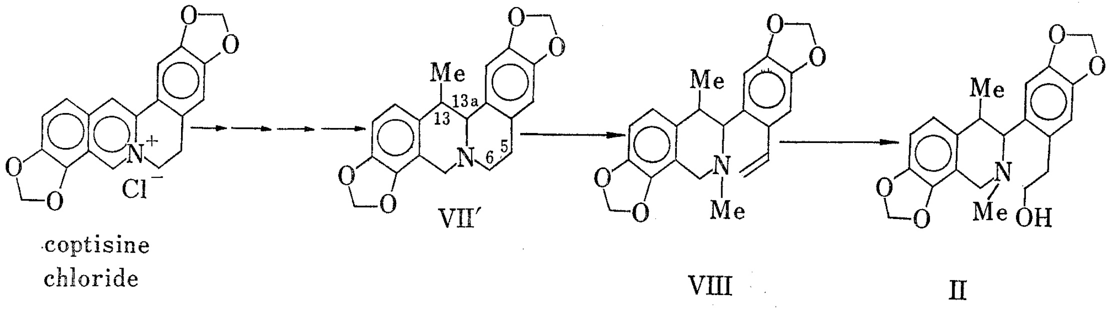

Chart 4

From the experimental results above-mentioned, corydalic acid methyl ester can now be depicted by the formula I. On the stereostructure of I, we first attempted the stereostructure elucidation of VII′ which was correlated with I without any configurational change at C_{13}, C_{13a} configuration. The IR spectrum of VII′ showed the absence of so-called Bohlmann bands[6] and in the NMR spectrum of VII′, the C_{13} methyl signal appeared at relatively downfield (δ 1.43) as compared to the chemical shift (δ 0.96) for the corresponding methyl signal

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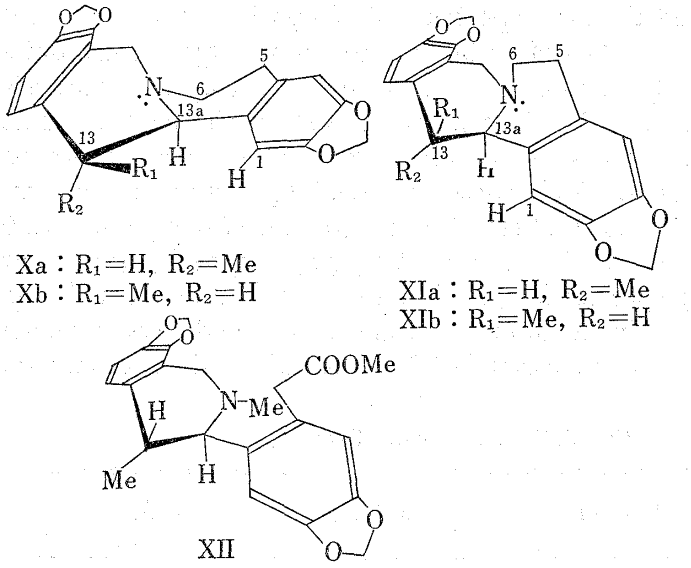
[6] F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958); *idem*, *ibid.*, **92**, 1798 (1959).

in tetrahydrocorysamine (*trans* quinolizidine ring system[7]; *cis* C_{13}, C_{13a} configuration). On methylation with methyl iodide, VII′ afforded a corresponding methiodide at very fast rates (in 10 min at room temperature[10]), suggesting the unhindered surroundings around the N-atom.[11] Dehydrogenation of VII′ with mercuric acetate[12] was unsuccessful to obtaine a quaternary base, corysamine (IX).



Xa : R_1=H, R_2=Me
Xb : R_1=Me, R_2=H

XIa : R_1=H, R_2=Me
XIb : R_1=Me, R_2=H

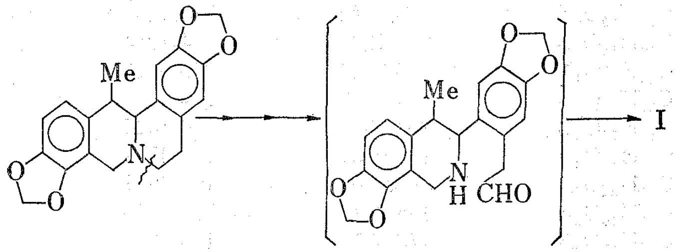
XII

Fig. 1

These results led us to conclude that the quinolizidine ring system of VII′ might be *cis* conformation.

Brossi, *et al.*[13] have demonstrated the existence of one *trans* and two possible *cis*-forms in the quinolizidine ring system. If VII′ has a *cis* quinolizidine ring system, two possible conformational forms which contained *cis* and *trans* configurational isomers at C_{13}, C_{13a}, can be illustrated in Fig. 1.

In order to clarify the C_{13}, C_{13a} configurations in VII′, we attempted Hofmann degradation on which VII′ afforded the styrene type methine (VIII) as a sole product due to the cleavage of C_6-nitrogen bond, whereas tetrahydrocorysamine gave a methine base of ten membered ring system, resulting from the cleavage of C_{13a}-nitrogen bond.[14] Since Hofmann degradation is known to be a kind of so-called *anti*-elimination reaction of *β*-hydrogen,[9,15] the fact that VII′ gave only the styrene-type methine (VIII) shows that the stereostructure of VII′ should be Xb[16] or XIa[17] (C_{13}H, C_{13a}–N bond: *cis*).



XIII XIV

Chart 5

On comparison of Dreiding models the close approach of C_{13} methyl hydrogens to aromatic hydrogen was revealed in Xb, however this steric compression is relieved in the case of XIa.

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[7] Tetrahydrocorysamine exhibited Bohlmann bands in the IR spectrum, and since it was converted to corydaline by cleavage of methylenedioxy followed by O-methylation,[8] it is supposed to have *trans* quinolizidine skeleton and *cis* C_{13}, C_{13a} configuration.[9]

[8] C. Tani, N. Takao, S. Takao, and K. Tagahara, *Yakugaku Zasshi*, **82**, 751 (1962).

[9] H.W. Bersh, *Arch. Pham.*, **291**, 595 (1958); P.W. Jeffs, *Experientia*, **21**, 690 (1965).

[10] *dl*-Tetrahydrocorysamine needed refluxing for 18 hr to form its methiodide.

[11] M. Shamma, C.D. Jones, and J.A. Weiss, *Tetrahedron*, **25**, 4348 (1969).

[12] T. Takemoto, Y. Kondo, and K. Kondo, *Yakugaku Zasshi*, **83**, 162 (1963); H. Taguchi and I. Imazeki, *ibid.*, **84**, 955 (1964).

[13] M. Uskoković, H. Bruderer, C. von Planta, T. Williams, and A. Brossi, *J. Am. Chem. Soc.*, **86**, 3364 (1964).

[14] C. Tani and N. Takao, *Yakugaku Zasshi*, **82**, 748 (1962).

[15] K. Sugimoto, K. Ohme, M. Akiba, and S. Ohki, *Chem. Pharm. Bull.* (Tokyo), **18**, 1276 (1970).

[16] C_{13}H, C_{13a}H: *cis*.

[17] C_{13}H, C_{13a}H: *trans*.

Consequently, the more preferable conformation is supposed to be XIa, and this assumption is quite consistent with Jeff's report that when the C_{13}, C_{13a} hydrogens are trans, the steric interference of a non–bonded interaction between the C_{13} methyl hydrogens and the aromatic C_1 hydrogen forces the quinolizidine ring system to be *cis*-fused.

Thus, the stereostructure of corydalic acid methyl ester is possibly represented as the formula XII.

Corydalic acid methyl ester (I) represents a new type of isoquinoline alkaloid in which aromatic ring is attached to position 3 of tetrahydroisoquinoline ring system. Biogenetically, I is presumably derived from *l*-tetrahydrocorysamine (XIII) by a cleavage of the B-ring in protoberberine skeleton, possibly through an aldehyde intermediate (XIV).

Experimental[18]

Corydalic Acid Methyl Ester (I)——Colorless prisms (acetone–petroleum ether), mp 140—141°, $[\alpha]_D$ $+85.4°$ ($c=0.68$, CH_2Cl_2). *Anal.* Calcd. for $C_{22}H_{23}O_6N$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.78; H, 5.89; N, 3.48. Mass Spectrum: Calcd. for [M+], $C_{22}H_{23}O_6N$: 397.153. Found: 397.155. UV λ_{max}^{MeOH} mμ (log ε): 240 (4.07), 289 (3.96). IR ν_{max}^{KBr} cm^{-1}: 1738, 1275, 920. NMR (δ): 1.05 (3H, d, $J=6.0$ Hz, $>CH-C\underline{H}_3$), 2.10 (3H, s, $>N-C\underline{H}_3$), 3.06—3.32 (2H, m, $Ar-\dot{C}\underline{H}-\dot{C}\underline{H}-Ar$), 3.67 (3H, s, $-OC\underline{H}_3$), 3.73 (2H, s, $Ar-C\underline{H}_2-CO$), 3.40, 4.09 (2H, ABq, $J=15.0$ Hz, $Ar-C\underline{H}_2-N$), 5.95 (4H, s, $-O-C\underline{H}_2-O-\times 2$), 6.72 (2H, d, $J=1.0$ Hz, aromatic proton), 6.82 (2H, d, $J=10.5$ Hz, aromatic proton).

Formation of II by Reduction of I——To a solution of I (100 mg) in dry tetrahydrofuran (THF) was added $LiAlH_4$ (120 mg in THF) and the solution was refluxed for 2 hr. After an excess of $LiAlH_4$ was decomposed with water, the reaction mixture was extracted with AcOEt. The AcOEt solution was washed with water, dried and then the solvent was evaporated to give an oil, which was chromatographed over alumina column. The benzene eluate gave a colorless oil (II) (60 mg): $[\alpha]_D^{28}$ $-18.0°$ ($c=2.69$, $CHCl_3$). UV λ_{max}^{MeOH}mμ: 237, 291. NMR (δ): 1.14 (3H, d, $J=6.0$ Hz, $>CH-C\underline{H}_3$), 2.13 (3H, s, $>N-C\underline{H}_3$), 2.70—4.16 (8H, aliphatic proton), 5.94 (4H, s, $-O-C\underline{H}_2-O-\times 2$), 6.75 (2H, s, aromatic proton), 6.78 (2H, d, $J=7.8$ Hz, aromatic proton). Mass Spectrum *m/e*: 369 (M+), 338, 324, 320, 208, 206, 204, 202, 190, 188, 176, 162 (base peak).

Methiodide: A solution of II (80 mg) in a mixture of acetone (2.5 ml) and CH_3I (1 ml) was refluxed for 30 min and the solvent was evaporated. The crystalline residue was recrystallized from MeOH–acteone to give colorless needles; mp 252—254°, $[\alpha]_D^{26}$ $-14.8°$ ($c=0.27$, MeOH). *Anal.* Calcd. for $C_{21}H_{23}O_5N\cdot CH_3I$: C, 51.67; H, 5.12; N, 2.74. Found: C, 51.54; H, 5.11; N, 2.74.

Acetate (III): II (100 mg) was acetylated with Ac_2O and pyridine in a usual manner and the product was chromatographed over silica gel (10 g). The benzene–$CHCl_3$ (1: 1) gave a colorless oil (III) (100 mg); Mass Spectrum: Calcd. for [M+], $C_{23}H_{25}O_6N$: 411.1682. Found: 411.1657. $[\alpha]_D^{28}$ $+66.7°$ ($c=2.07$, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (C=O). NMR (δ): 1.08 (3H, d, $J=7.0$ Hz, $>CH-C\underline{H}_3$), 2.02 (3H, s, $-OCOC\underline{H}_3$), 2.13 (3H, s, $>N-C\underline{H}_3$).

Corydalic Acid (IV)——I (50 mg) was suspended in 10% methanolic NaOH and refluxed for 20 min. The reaction mixture was adjusted to pH 6.0 with AcOH and the solvent was evaporated *in vacuo*. The residue was extracted with $CHCl_3$, and the solvent was evaporated to give a colorless oil, which was chromatographed on silica gel column. The $CHCl_3$–MeOH (9: 1) eluate gave a colorless oil (IV) (48 mg); $[\alpha]_D^{25}$ $+24.3°$ ($c=2.28$, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (C=O). NMR (δ): 1.25 (3H, d, $J=6.0$ Hz, $>CH-C\underline{H}_3$), 2.28 (3H, s, $>N-C\underline{H}_3$), 3.63 (2H, s, $Ar-C\underline{H}_2-N$), 4.09 (2H, s, $Ar-C\underline{H}_2-CO-$), 5.98 (4H, s, $-O-C\underline{H}_2-O-\times 2$), 6.86 (2H, d, $J=8.2$ Hz, aromatic proton), 6.82, 6.92 (1H, each s, aromatic proton), 10.65 (1H, broad s, $-COO\underline{H}$). Mass Spectrum: Calcd. for [M+], $C_{21}H_{21}O_6N$: 383.1369. Found: 383.1344.

Formation of V from II——To an ice-cooled solution of II (240 mg) in benzene (10 ml) was added $SOCl_2$ (0.5 ml in benzene) and the mixture was allowed to stand at 0° for 20 min. The solvent was evaporated *in vacuo* and the residue was washed with water. Recrystallization from MeOH gave pale yellow needles (V); mp 216—219°, $[\alpha]_D^{21}$ $+50.0°$ ($c=0.36$, MeOH). *Anal.* Calcd. for $C_{21}H_{23}O_4NCl_2$: C, 59.44; H, 5.46; N, 3.30. Found: C, 58.95; H, 5.52; N, 3.19. IR ν_{max}^{KBr} cm^{-1}: 2300—2800 ($>N^+<$).

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18) All melting points were determined on a Kopfler hot plate and are uncorrected. Optical rotations were measured with a JASCO DIP–SL automatic polarimeter. IR spectra were obtained with a Nippon Bunko DS-301 spectrometer, and UV spectra, with a Shimadzu SV-50A. Mass spectra were recorded on a JMS–OISG mass spectrometer with glass inlet system. NMR spectra were taken at 60 MHz on a JEOL–C–60H spectrometer in $CDCl_3$ solution and chemical shifts are given in δ-sacle with tetramethylsilane as internal standard (s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet). TLC was conducted on Kieselgel G nach Stahl. Column chromatography was performed with Kieselgel (E. Merck) and alumina (Brockmann).

Formation of *d*-Mesotetrahydrocorysamine (VII) from V——V (72 mg) was dissolved in hot water and neutralized with 10% ammonia and extracted with $CHCl_3$. $CHCl_3$ was evaporated to afford a crystalline residue (VI) (40 mg). Alkaline layer was acidified with HCl and $HgCl_2$ was added. Precipitates of the Hg-complex were filtered, washed with water and dissolved in MeOH, and decomposed by H_2S. HgS was filtered off and the filtrate was concentrated to dryness to give an additional amount of VI (22 mg); Mass Spectrum: *m/e* 337 ($[M^+]-CH_3Cl$), 322 (337-CH_3), 176, 174, 162 (base peak), 52 (CH_3Cl^{37}), 50 (CH_3Cl^{35}). VI (62 mg) was suspended in *ortho*-dichlorobenzene and heated at 200° for 2 hr. The solvent was evaporated *in vacuo* and the brown residue was extracted with benzene, the solvent was evaporated off to give an oily residue (51 mg). It was chromatographed over silica gel using benzene–$CHCl_3$ (1:1) as developer to give a colorless oil (VII) (18 mg); $[\alpha]_D^{26}$ +200.4° ($c=1.4$, $CHCl_3$), NMR (δ): 1.45 (3H, d, $J=6.5$ Hz, $>CH-C\underline{H}_3$), 5.88 (2H, s, $-O-C\underline{H}_2-O-$), 5.92 (2H, s, $-O-C\underline{H}_2-O-$), 6.58—6.68 (4H, aromatic proton), Mass Spectrum: Calcd. for $[M^+]$, $C_{20}H_{19}O_4N$: 337.131. Found: 337.133. VII gave the same *Rf* value on TLC and identical IR ($CHCl_3$), NMR and mass spectra with those of *dl*-mesotetrahydrocorysamine.

Formation of *dl*-Mesotetrahydrocorysamine (VII′) from Coptisine Chloride——Coptisine chloride was converted to *dl*-mesotetrahydrocorysamine according to the procedure reported by Takao[8]; Colorless needles, mp 137—138° (lit.[8] mp 138—139°). *Anal.* Calcd. for $C_{20}H_{19}O_4N$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.26; H, 5.82; N, 4.06.

Hofmann Degradation of *dl*-Mesotetrahydrocorysamine (VII′)——To a solution of VII′ (100 mg) in acetone (3 ml) was added CH_3I (0.4 ml). After standing at room temperature for 10 min, the solvent was evaporated *in vacuo*. The crystalline residue was recrystallized from MeOH to afford colorless needles (130 mg) of the methiodide, mp 290—291.5° (decomp.). The methiodide (50 mg) was dissolved in MeOH and passed through a column of Amberlite IRA-400 (OH^-), and the column was washed with MeOH. The eluate and washings were combined and the solvent was evaporated to give the corresponding methohydroxide. It was dissolved in 20% methanolic NaOH and heated for 4 hr, and then the reaction mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried and evaporated to give an oily compound, which was chromatographed on silica gel. The benzene eluate gave an oily methine base (VIII) (38 mg); UV λ_{max}^{MeOH} mμ: 264, 291. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 975 ($-CH=CH_2$). NMR (δ): 1.02 (3H, d, $J=6.0$ Hz, $>CH-C\underline{H}_3$), 2.10 (3H, s, $>N-C\underline{H}_3$), 5.13 (1H, q, $J=11.0$, 1.5 Hz, ${}^{H}{>}C{=}C{<}^{H}_{\underline{H}}$), 5.43 (1H, q, $J=1.5$, 17.0 Hz, ${}^{H}{>}C{=}C{<}^{\underline{H}}_{H}$), 7.20 (1H, q, $J=11.0$, 17.0 Hz, ${}^{\underline{H}}{>}C{=}C{<}^{H}_{H}$), 6.68—6.96 (4H, aromatic proton).

Formation of Racemic II from VIII——To a solution of VIII (95 mg) and $NaBH_4$ (100 mg) in dry THF (5 ml) was added BF_3-etherate (600 mg in THF) and the reaction mixture was left to stand at room temperature for 64 hr in an atmosphere of nitrogen. An excess of diboran was decomposed with water and the solution was made alkaline with aqueous NaOH. To the solution, 30% H_2O_2 (1 ml) was added and the mixture was stirred vigorously at room temperature for 15 min. The reaction mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, dried and evaporated to give a brown oily residue, which gave a colorless oily compound by silica gel column chromatographic purification (solvent: $CHCl_3$). The *Rf* value on TLC, IR ($CHCl_3$), UV and mass spectra of the product were identical with those of II.

Treatment of VII′ with $Hg(OAc)_2$ To a solution of VII′ (21 mg) in 5% acetic acid (6 ml) was added $Hg(OAc)_2$ (100 mg) and the mixture was warmed on a water bath for 3 hr. Precipitates were filtered after cooling and the filtrate was decomposed by H_2S. HgS was filtered and to the filtrate 25% aqueous KI was added. The black precipitates were filtered off, washed with water and extracted with MeOH. The MeOH solution was evaporated to give a resinous residue. The residue showed on TLC several spots, one of which showed the same *Rf* value with that of corysamine (IX), however, it could not be isolated because of its low content.[19]

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[19] Tetrahydrocorysamine gave corysamine quantitatively by the same treatment.