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8,13a-Propanoberbines. IV.[1] Potassium Permanganate Oxidation of Acetoneberberine Type Enamine

Shunsuke Naruto, Haruki Nishimura, and Hidehiko Kaneko

Research Laboratories, Dainippon Pharmaceutical Co., Ltd.[2]

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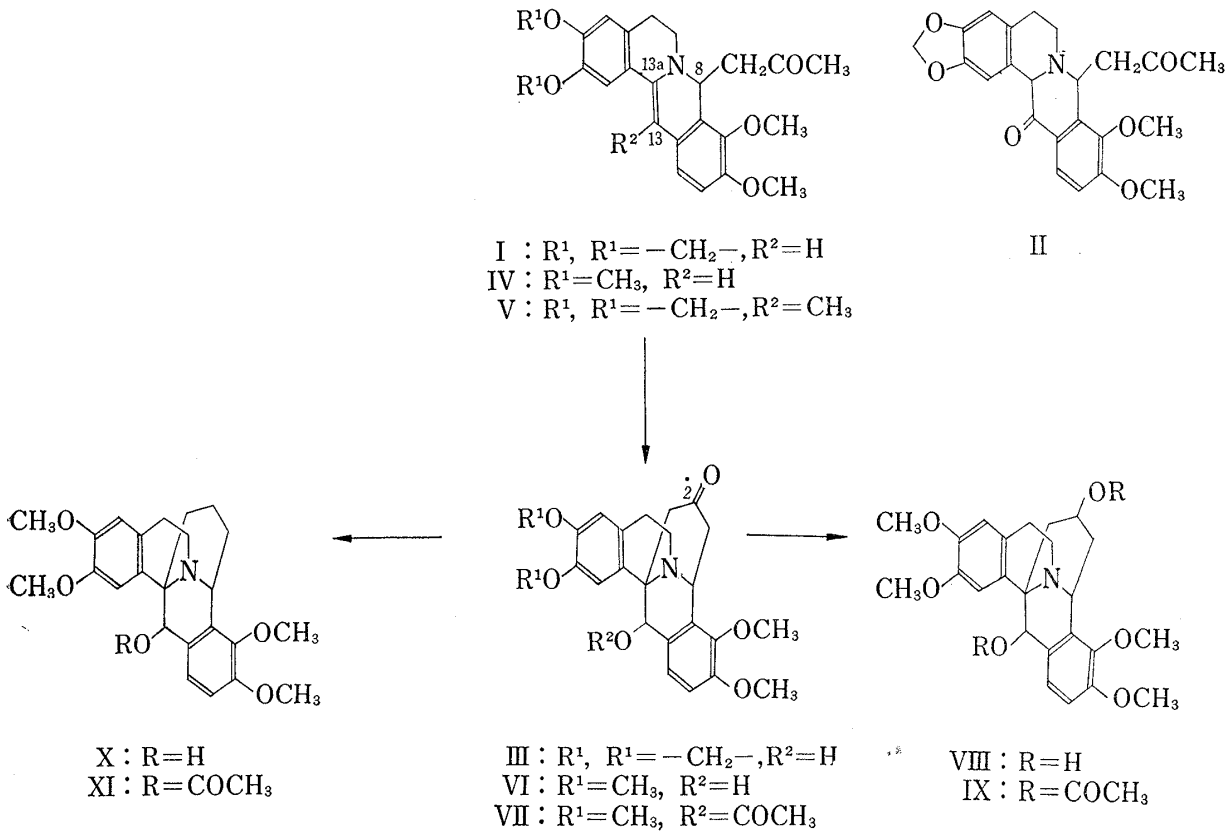
Oxidation of acetonepalmatine(IV) with potassium permanganate proceeded as well as acetoneberberine(I) to give 8, 13a-propanoberbine derivative(VI). On the other hand, 13-methylacetoneberberine(V) reacted with potassium permanganate to form mainly a lactam(XIV) as a result of the oxidative fission of C_{13}–C_{13a} double bond, together with minor 8, 13a-propanoberbine products, XV and XVI.

The oxidation product of acetoneberberine (I) with potassium permanganate was named as neoxyberberine acetone and assigned the structure II by Pyman.[3] In the previous paper[4] of this series, we presented a revised structure III having 8,13a-propanoberbine skeleton for neoxyberberine acetone on the basis of the nuclear magnetic resonance (NMR) spectral analysis and chemical reactions. The formation of 8,13a-propanoberbine derivative from I prompted us further to examine oxidations of other acetoneberberine type enamines, acetonepalmatine



I : R^1, R^1=$-CH_2-$, R^2=H
IV : R^1=CH_3, R^2=H
V : R^1, R^1=$-CH_2-$, R^2=CH_3

II

III : R^1, R^1=$-CH_2-$, R^2=H
VI : R^1=CH_3, R^2=H
VII : R^1=CH_3, R^2=$COCH_3$

X : R=H
XI : R=$COCH_3$

VIII : R=H
IX : R=$COCH_3$

Chart 1

1) Part III: S. Naruto, H. Nishimura, and H. Kaneko, *Chem. Pharm. Bull.* (Tokyo), **23**, 1271 (1975).
2) Location: *33-94, Enoki-cho, Suita, Osaka.*
3) L. Pyman, *J. Chem. Soc.*, **99**, 1690 (1911).
4) J. Iwasa and S. Naruto, *Yakugaku Zasshi*, **86**, 534 (1966).

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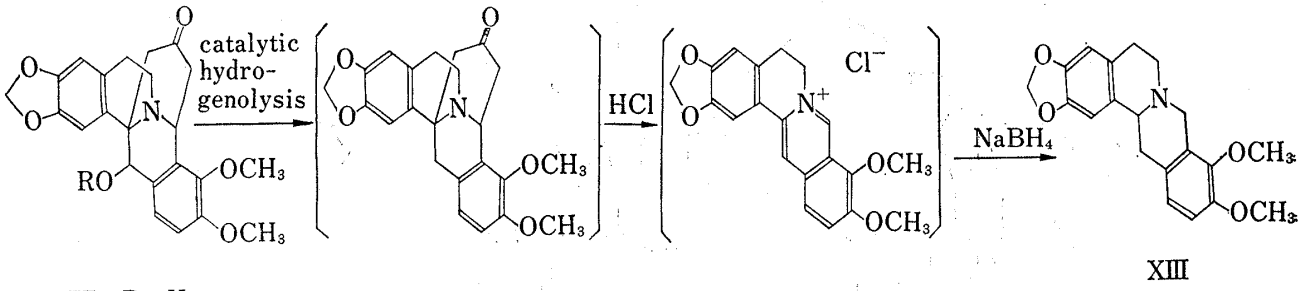
(IV) and 13-methylacetoneberberine (V). In the present paper, we wish to describe the details of the investigation.[5]

Firstly, the oxidation reaction of IV with potassium permanganate proceeded analogously to give so-called neoxypalmatine acetone, 8,13a-(2′-oxopropano)-13-hydroxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine (VI), in 40% yield. The structure of VI was deduced from the following evidences (Chart 1). Neoxypalmatine acetone (VI) was analyzed for $C_{24}H_{27}O_6N$, and its infrared (IR) spectrum exhibited the bands of carbonyl and hydroxyl group at 1700 and 3400 cm^{-1}, respectively. On usual acetylation, VI gave monoacetate (VII) whose acetyl signal appeared at δ 2.24 in the NMR spectrum. On reduction with sodium borohydride VI afforded a diol (VIII) which was acetylated to give a diacetate (IX). The NMR spectrum of IX showed two acetyl signals at δ 2.24 and 1.48. As was discussed in the previous papers,[1,4] the latter signal at higher field was assigned to 2′-acetyl group on 8,13a-propano bridge. Huang-Minlon reduction of VI gave a 2′-deoxy derivative (X) which afforded an acetate (XI). These chemical properties of VI were similar to those of III, and the physicochemical data of VI and its derivatives (VII to XI) resembled to those of III except the substituent groups at ring A. Furthermore, in order to confirm the 8,13a-propanoberbine skeleton of III, a catalytic hydrogenolysis of its acetate (XII) was attempted as an additional evidence. As shown in Chart 2, resulting products were treated with hydrochloric acid followed by sodium borohydride reduction to give the expected *dl*-canadine (XIII).



III : R=H
XII : R=$COCH_3$

Chart 2

Secondly, the oxidation of 13-methylacetoneberberine (V)[1] gave a complex mixture from which the following three compounds were isolated by means of column chromatography. A lactam (XIV) was obtained as a main product in 30% yield, and two 8,13a-propanoberbine derivatives, compound XV and XVI, were obtained in 1 and 4% yield, respectively. The structural elucidation of these compounds is discussed below.

The minor product, compound XV, was the expected 8,13a-propanoberbine derivative. This compound had a molecular formula $C_{24}H_{25}O_6N$ and its IR spectrum showed the carbonyl and hydroxyl bands at 1700 and 3470 cm^{-1}, respectively. Reduction of XV with sodium borohydride afforded a diol (XVII). The NMR spectrum of XVII taken in d_6-dimethylsulfoxide solution exhibited the signals of a secondary hydroxyl, a tertiary hydroxyl and a tertiary methyl protons. The latter two signals were also observed in XV. Treatment of XV with hydrochloric acid gave a dehydrated product (XVIII) whose IR and ultraviolet (UV) spectra had the absorption maxima at 1710 and 1620 cm^{-1} and 285 nm (log ε, 4.14), respectively. The NMR spectrum of XVIII showed two singlet vinyl protons at δ 5.65 and 4.74, and was lacking in methyl and hydroxyl protons at C_{13} of XV. From these data, an exomethylene function at C_{13} was suggested for XVIII. The dehydrated product (XVIII) was

5) Preliminary report: S. Naruto, H. Nishimura, and H. Kaneko, *Tetrahedron Letters*, **1972**, 2127.

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converted to the known 8,13a-(2′-oxopropano)-13-methylberbine derivative (XIX)[1] by catalytic reduction on platinic oxide. From these evidences the structure of XV became unequivocal.

Compound XVI was also analyzed for $C_{24}H_{25}O_6N$, and its IR spectrum exhibited hydroxyl bands at 3400 cm^{-1}. A hemiketal structure XVI for this compound was deduced from the following facts. It showed no carbonyl bands in its IR spectrum and a tertiary methyl signal at δ 1.51 in the NMR spectrum. Compound XVI was easily converted to XVIII by acidic treatment. Reduction of XVI with sodium borohydride afforded the diol (XVII). Furthermore, a treatment of the compound XV with ethanolic potassium hydroxide gave the hemiketal (XVI) (Chart 3).

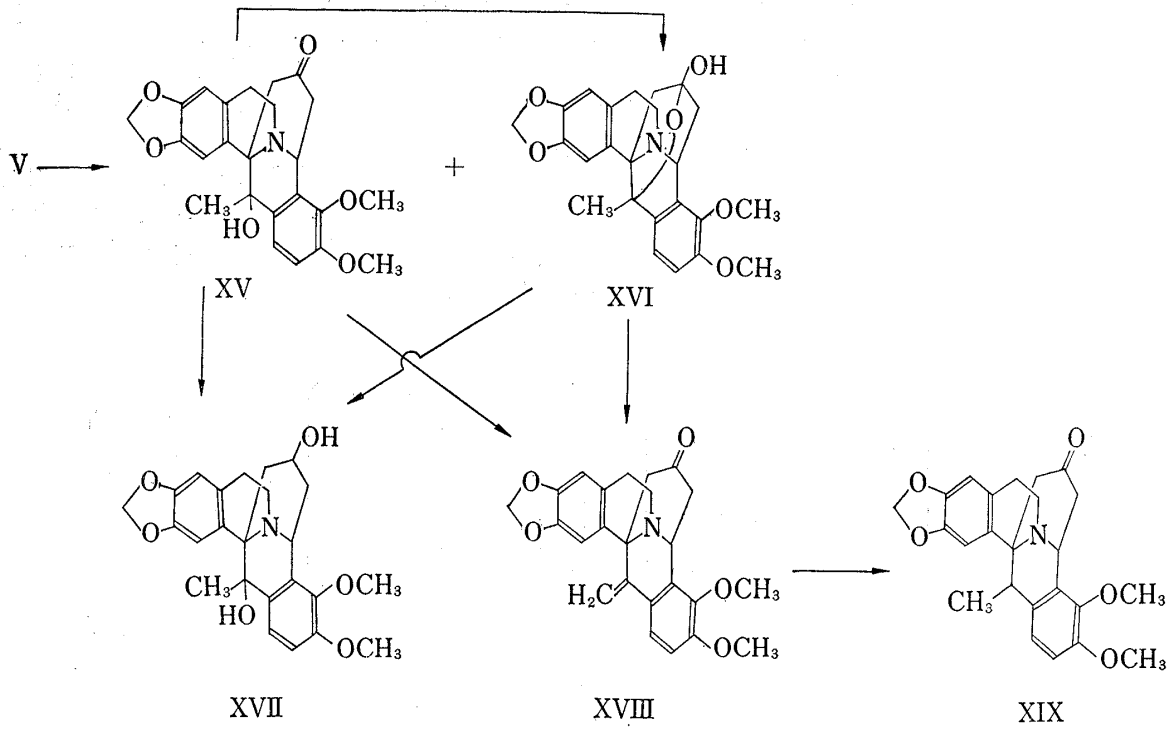

Chart 3

The major product, lactam XIV, was a neutral substance and analyzed for $C_{24}H_{23}O_6N$. Its IR spectrum exhibited the bands at 1645, 1610 and 1565 cm^{-1}, and its UV spectrum showed absorption maxima at 226 nm (log ε, 4.50), 264 (3.98), 274 (3.92), 314 (4.27) and 335 (4.22) indicating a conjugated system in XIV. The NMR spectral analysis of XIV was informative, showing one doublet vinyl methyl signal at δ 2.52 (J=2.2 Hz), one acetyl signal at δ 2.35, four methylene protons at about δ 2.78 as A_2B_2 type and one proton (C_1'-H) at δ 7.04 as broad doublet along with two methoxyl, one methylendioxy and four aromatic protons. The spin decoupling experiment confirmed that the doublet vinyl methyl protons were coupled with the low field proton at δ 7.04. In order to clearify a conjugated system of XIV, we attempted a reduction with sodium borohydride on which XIV afforded an amorphous alcohol (XX) showing hydroxyl bands at 3430 cm^{-1} and amide bands at 1640 cm^{-1} in its IR spectrum. It was found that XX was a mixture of epimeric alcohols on the basis of the NMR spectrum exhibiting two pair of doublet methyl signal (J=7 Hz) corresponding to $CH(OH)CH_3$ group from which the presence of $COCH_3$ group in XIV was presumable. On the other hand, catalytic reduction of XIV on platinic oxide yielded a dihydro derivative (XXI). Its UV spectrum showing absorption maxima at 222, 274 and 305 nm was similar to that of noroxyhydrastinine (XXII)[6]

6) W.H. Perkin, Jr. and R. Robinson, *J. Chem. Soc.*, **97**, 305 (1910).

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exhibiting maxima at 222, 261 and 305 nm. From this a partial structure XXIII for XXI was suggested. The IR spectrum of XXI exhibited amide bands at 1645 cm^{-1} and isolated carbonyl bands at 1710 cm^{-1}. The latter indicated that the parent acetyl group in XIV was conjugated with a double bond. The NMR spectrum of XXI was also informative, showing an acetyl signal at δ 2.30, a secondary methyl signal at δ 1.26 as doublet (J=6.5 Hz), a benzyl methine proton (C_3'-H) at 3.83 as quartet (J=6.5 Hz), a proton (C_2'-H) at δ 3.41 as doublet (J=8.5 Hz) and a proton (C_1'-H) at δ 6.92 as doublet (J=8.5 Hz). Comparison of the NMR spectrum of XXI with that of XIV indicated the increment of two methine protons at δ 3.83 and 3.41. Spin decoupling experiments confirmed that the former benzyl methine proton was coupled with secondary methyl protons and the latter with the low field proton at δ 6.92. These facts suggested that XIV had a double bond with a partial structure XXIV. Thus a

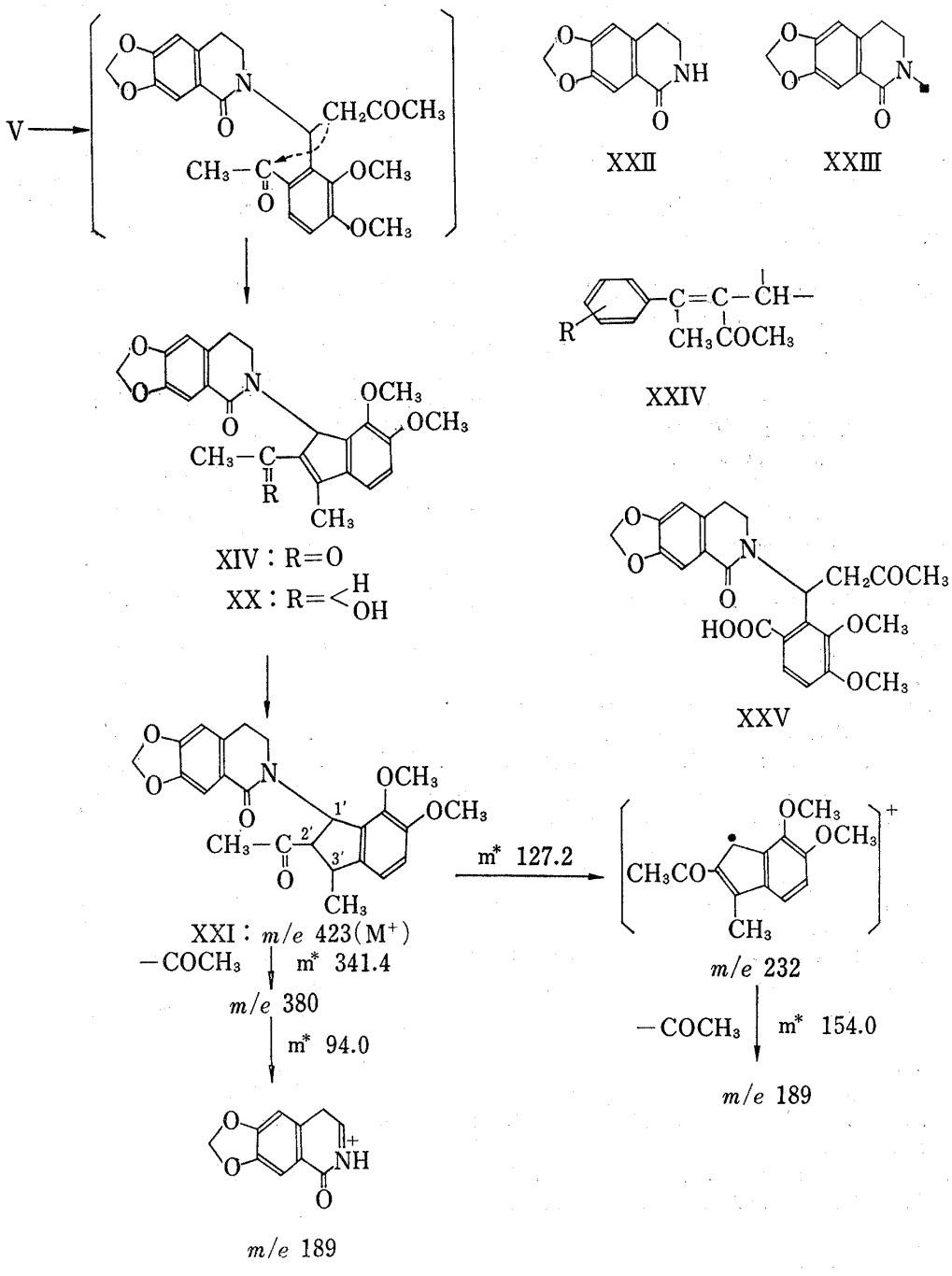

Chart 4

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tentative structure, 1-oxo-2-(2′-acetyl-3′-methyl-6′,7′-dimethoxy-1′-indenyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (XIV), for the lactam seems to be consistent with the above experimental results. A plausible mechanism including a cleavage of C_{13}-C_{13a} double bond with potassium permanganate followed by intramolecular aldol condensation may be considered. The intense peaks appeared at *m/e* 423 (M^+), 380, 232 and 189, and the corresponding metastable peaks in the mass spectrum of XXI was also explained reasonably as shown in Chart 4.

Recently, Kondo and Takemoto[7] proposed the structure XXV for a minor product of a potassium permanganate oxidation of acetoneberberine (I). The formation of lactam XIV is analogous to that of XXV. However, it is interesting to note that the oxidation of 13-methylacetoneberberine (V) proceeds mainly *via* oxidative fission of C_{13}-C_{13a} double bond whereas 13-unsubstituted acetoneberberine type enamines are oxidized to give 8,13a-propanoberbine derivatives as major product, although the effect of the methyl group at the 13 position cannot be fully explained with the data now available.

Experimental

All the melting points are uncorrected. NMR spectra were obtained in $CDCl_3$ or dmso-d_6 solution with tetramethylsilane as an internal standard on Varian A-60 spectrometer and IR spectra were taken in KBr disks with a Hitachi EPI-S2 spectrometer. All UV spectra were obtained in EtOH solution on Hitachi EPS-2U spectrometer. Mass spectra were taken with a Hitachi RMU-6 spectrometer with a heated direct inlet system.

8,13a-(2′-Oxopropano)-13-hydroxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine (Neoxypalmatine Acetone) (VI)——To a mixture of acetonepalmatine[8] (IV) (1 g) in acetone (50 ml) was added 1.1% $KMnO_4$ aq. solution(50 ml) with stirring at room temperature. After 15 min, MnO_2 was filtered off and the filtrate was evaporated to remove acetone. Resulting crystals were collected and recrystallized from $CHCl_3$–benzene to give VI(0.4 g), colorless prisms, mp 217—218° (decomp.). *Anal.* Calcd. for $C_{24}H_{27}O_6N$: C, 67.75; H, 6.40; N, 3.29. Found: C, 67.53; H, 6.37; N, 3.25. NMR(δ in $CDCl_3$): 3.86—3.93 (12H, OCH_3), 4.86 (m, 1H, C_8-H), 4.89 (d, 1H, J=8.5 Hz, C_{13}–H). IR: see text.

8,13a-(2′-Oxopropano)-13-acetoxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine (VII)——A mixture of VI (0.2 g). pyridine (10 ml) and acetic anhydride (5 ml) was heated on boiling water bath for 3 hr. The reaction mixture was evaporated to dryness. The residue was recrystallized from EtOH to give VII, colorless prisms, mp 198—200° (decomp.). *Anal.* Calcd. for $C_{26}H_{29}O_7N$: C, 66.79; H, 6.25; N, 3.00. Found: C, 66.45; H, 6.30; N, 3.03. NMR(δ in $CDCl_3$): 2.24 (s, 3H, $COCH_3$), 3.83—3.91 (12H, OCH_3), 6.27 (s, 1H, C_{13}–H).

8,13a-(2′-Hydroxypropano)-13-hydroxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine (VIII)——To a solution of VI (1 g) in MeOH (100 ml) was added portionwise $NaBH_4$ (0.4 g) at room temperature. After 4 hr, *ca.* 50 ml of MeOH was evaporated and resulting crystals were collected. Recrystallization from $CHCl_3$–MeOH afforded VIII(0.5 g), colorless prisms, mp 204—205°. *Anal.* Calcd. for $C_{24}H_{29}O_6N$: C, 67.43; H, 6.84; N, 3.28. Found: C, 67.15; H, 6.80; N, 3.50. HCl-salt. mp 217—218° (from H_2O), colorless prisms. *Anal.* Calcd. for $C_{24}H_{29}O_6N \cdot HCl$: C, 62.13; H, 6.52; N, 3.02; Cl, 7.64. Found: C, 61.95; H, 6.69; N, 3.12; Cl, 7.87. NMR (δ in $CDCl_3$): 3.85—3.92 (12H, OCH_3), 4.17 (m, 1H, C_8–H), 4.85 (d, J=13 Hz, 1H, C_{13}–H).

8,13a-(2′-Acetoxypropano)-13-acetoxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine (IX)——A mixture of VIII (0.2 g), pyridine (10 ml) and acetic anhydride (5 ml) was treated as in the case of VII to give IX, colorless columns, mp 104—105°. *Anal.* Calcd. for $C_{28}H_{33}O_8N$: C, 65.74; H, 6.50; N, 2.74. Found: C, 65.43; H, 6.51; N, 2.74. NMR (δ in $CDCl_3$): 1.48 (s, 3H, $COCH_3$), 2.24 (s, 3H, $COCH_3$), 3.82—3.90 (12H, OCH_3), 4.28 (m, 1H, C_8–H), 5.05 (m, 1H, C_2′–H), 6.35 (s, 1H, C_{13}–H).

8,13a-Propano-13-hydroxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine (X)——A mixture of VI (0.1 g), KOH (0.5 g), diethyleneglycol (2.5 ml) and 80% $NH_2NH_2 \cdot H_2O$ (2.4 ml) was heated on oil bath at 150—160° for 70 min. After cooling, the reaction mixture was poured into water (100 ml). Resulting precipitates were collected and recrystallized from $CHCl_3$–benzene to give X (60 mg), colorless needles, mp 230—231°. *Anal.* Calcd. for $C_{24}H_{29}O_5N$: C, 70.05; H, 7.10; N, 3.40. Found: C, 69.86; H, 6.84; N, 3.47. NMR (δ in $CDCl_3$): 3.86—3.88 (12H, OCH_3), 4.32 (m, 1H, C_8–H), 4.88 (d, J=7.5 Hz, C_{13}–H). HCl salt: colorless needles, mp 237—238° (decomp.) (H_2O). *Anal.* Calcd. for $C_{24}H_{29}O_5N \cdot HCl$: C, 64.35; H, 6.75; N, 3.13; Cl, 7.92. Found: C, 64.41; H, 6.71; N, 3.08; Cl, 8.04.

7) Y. Kondo and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **20**, 2134 (1972).
8) F. von Bruchhausen, *Arch. Pharm.*, **261**, 28 (1923).

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8,13a-Propano-13-acetoxy-2,3,9,10-tetramethoxydibenzo[*a*,*g*]quinolizidine(XI)——A mixture of X(210 mg), pyridine (12 ml) and acetic anhydride (6 ml) was treated as in the case of VII to give XI, colorless needles, mp 192—193° ($CHCl_3$–EtOH). *Anal.* Calcd. for $C_{26}H_{31}O_6N$: C, 68.85; H, 6.89; N, 3.09. Found: C, 68.49; H, 6.68; N, 3.25. NMR (δ in $CDCl_3$): 2.25 (s, 3H, $COCH_3$), 3.83—3.89 (12H, OCH_3), 4.32 (m, 1H, C_8–H), 6.22 (s, 1H, C_{13}–H).

***dl*-Canadine(XIII)**——A mixture of XII[4] (0.5 g), 10% Pd-C (1.2 g), AcOH (180 ml) and conc. $HClO_4$ (5 drops) was shaked at room temperature under atmospheric hydrogen pressure for 5.5 hr. The catalyst was filtered off and the filtrate was made alkaline by addition of KOH and of conc. NH_4OH. The alkaline solution was extracted with $CHCl_3$. The $CHCl_3$ layer was dried over K_2CO_3 and evaporated to give a residue which was recrystallized from $CHCl_3$–MeOH to give 270 mg of XII. The mother liquor was concentrated to dryness to afford a residue which was refluxed with 9% HCl–MeOH (60 ml) for 6 hr. The reaction mixture was evaporated to give a yellow crystalline residue which was dissolved in MeOH (30 ml). To the MeOH solution was added $NaBH_4$ (0.2 g) with stirring at room temperature. After refluxing for 30 min, the reaction mixture was evaporated. The residue was extracted with $CHCl_3$. The $CHCl_3$ extract was dried over K_2CO_3 and evaporated to give a residue which was chromatographed on Al_2O_3 column. From the first fraction eluted with CH_2Cl_2–ether (1:1), 12 mg of *dl*-canadine (XIII), mp 173—174°, was obtained and identified with an authentic sample[9] by the mixed melting point determination, IR and thin-layer chromatography (TLC) comparison. *dl*-Ophiocarpine[4] (119 mg) was obtained from the second CH_2Cl_2–ether (1:1) elute and identified with an authentic sample by IR and TLC comparison.

Potassium Permanganate Oxidation of 13-Methylacetoneberberine(V)——To a solution of V[1] (4 g) in acetone (200 ml) was added 1.1% $KMnO_4$ aq. solution (200 ml) with stirring at room temperature. After 15 min, resulting precipitates of MnO_2 were filtered off and the filtrate was evaporated to remove acetone. The residue was extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried over K_2CO_3. The solvent was removed to give a residue which was chromatographed on silica gel (40 g) column. The fraction eluted with $CHCl_3$ was combined and recrystallized from CH_2Cl_2–EtOH to give XIV (yield, 30%), colorless plates, mp 238—239°. *Anal.* Calcd. for $C_{24}H_{23}O_6N$: C, 68.40; H, 5.50; N, 3.33. Found: C, 68.27; H, 5.49; N, 3.28. NMR (δ in $CDCl_3$): 3.83 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 6.00 (s, 2H, OCH_2O) and also see text. IR and UV: see text. The mother liquor of XIV was concentrated to dryness. The residue was rechromatographed on silica gel (15 g) column. The first $CHCl_3$ fraction gave XVI (4%), colorless needles, mp 220—222° (decomp.), after recrystallization from CH_2Cl_2–EtOH. *Anal.* Calcd. for $C_{24}H_{25}O_6N$: C, 68.07; H, 5.95; N, 3.31. Found: C, 67.83; H, 6.20; N, 3.15. NMR (δ in $CDCl_3$): 1.51 (s, 3H, C_{13}–CH_3), 3.87 (s, 6H, OCH_3), 1.43 (s, 2H, C_3'–H), 4.68 (d—d, J=1.5 and 6 Hz, 1H, C_8–H), 5.95 (s, 2H, OCH_2O). UV: λ_{max} 287 nm (log ε, 3.75). The mother liquor of XVI was concentrated to dryness. The residue was recrystallized from CH_2Cl_2–EtOH to give XV (1%), colorless columns, mp 250—252° (decomp.). *Anal.* Calcd. for $C_{24}H_{25}O_6N$: C, 68.07; H, 5.95; N, 3.31. Found: C, 67.77; H, 6.16; N, 3.03. NMR (δ in $CDCl_3$): 1.17 (s, 3H, C_{13}–CH_3), 2.45 (s, 1H, OH), 3.92 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.73 (d—d, J=2 and 5 Hz, 1H, C_8–H), 5.93 (s, 2H, OCH_2O). UV: λ_{max} 287 nm (log ε, 3.79). IR: see text.

8,13a-(2′-Hydroxypropano)-13-methyl-13-hydroxy-2,3-methylenedioxy-9,10-dimethoxydibenzo[*a*,*g*]quinolizidine(XVII)——a) To a solution of XV (36 mg) in CH_2Cl_2–MeOH was added $NaBH_4$ (10 mg) at room temperature. After 30 min, the reaction mixture was concentrated to dryness. The residue was extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water, dried over K_2CO_3 and concentrated. The residue was recrystallized from $CHCl_3$–MeOH to give XVII, colorless needles, mp 255—260° (decomp.). *Anal.* Calcd. for $C_{24}H_{27}O_6N$: C, 67.75; H, 6.40; N, 3.29. Found: C, 67.75; H, 6.41; N, 3.13. NMR (δ in dmso-d_6): 1.00 (s, 3H, C_{13}–CH_3), 4.28 (d, J=4.5 Hz, 1H, C_2'–OH), 4.66 (s, 1H, C_{13}–OH), 3.78 (s, 6H, OCH_3), 4.13 (m, 1H, C_8–H), 5.96 (s, 2H, OCH_2O). IR: ν_{OH} 3490 cm^{-1}.

b) A mixture of XVI (20 mg), CH_2Cl_2–MeOH (1:1) (5 ml) and $NaBH_4$ (20 mg) was treated as a) described above to give a mixture from which 5 mg of colorless needles, mp 255—259° (decomp.), and 14 mg of the starting material were isolated by means of preparative TLC on Silica gel G (solvent: 3% MeOH–$CHCl_3$). The former was identified with XVII by IR and TLC comparisons.

8,13a-(2′-Oxopropano)-13-methylene-2,3-methylenedioxy-9,10-dimethoxydibenzo[*a*,*g*]quinolizidine(XVIII)——a) A mixture of XV (50 mg), CH_2Cl_2 (4 ml), MeOH (3 ml) and 20% HCl–MeOH (4 ml) was refluxed for 1.5 hr. After evaporation of the reaction mixture, the residue was treated with water, made alkaline with NH_4OH and extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over K_2CO_3 and evaporated to give a residue which was recrystallized from EtOH to yield XVIII, colorless plates, mp 228—230°. *Anal.* Calcd. for $C_{24}H_{23}O_5N$: C, 71.09; H, 5.72; N, 3.46. Found: C, 70.95; H, 5.60; N, 3.42. NMR (δ in $CDCl_3$): 3.86 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.61 (m, 1H, C_8–H), 4.74 (s, 1H, vinyl-H), 5.65 (s, 1H, vinyl-H), 5.95 (s, 2H, OCH_2O). UV: see text. IR: $\nu_{C=O}$ 1710 cm^{-1}, $\nu_{C=C}$ 1620 cm^{-1}.

b) A mixture of XVI (35 mg), CH_2Cl_2 (6 ml), EtOH (1 ml) and 20% HCl–EtOH (1 ml) was refluxed for 1.8 hr and the reaction mixture was treated as in the case of a) to give colorless needles, mp 225—228° (decomp.), which was identified with XVIII by IR, TLC and a mixed mp comparisons.

9) H. Kaneko, S. Naruto, and N. Ikeda, *Yakugaku Zasshi*, **88**, 235 (1968).

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8,13a-(2′-Oxopropano)-13-methyl-2,3-methylenedioxy-9,10-dimethoxydibenzo[*a*,*g*]quinolizidine (XIX)——A solution of XVIII (5 mg) in CH_2Cl_2–MeOH (1:1) (3 ml) was shaked at room temperature in the presence of PtO_2 (1 mg) under atmospheric hydrogen pressure for 1 hr. The catalyst was filtered off and the filtrate was evaporated to give a residue. The residue was recrystallized from CH_2Cl_2-MeOH to afford colorless plates, mp 227—229°, which was identified with an authentic sample of XIX[1] by IR, TLC and a mixed mp comparisons.

Isomerization of Compound XV——A mixture of XV (10 mg), MeOH (10 ml) and 5% KOH–EtOH (5 ml) was refluxed for 1 hr. After evaporation of solvents, the residue was treated with water and extracted with $CHCl_3$. The organic layer was dried over K_2CO_3 and evaporated to give a residue. The residue was found to be a mixture of XVI and XV by the analysis of TLC (*Rf* 0.45 for XVI and *Rf* 0.35 for XV, Silica gel G, solvent: 3% MeOH–$CHCl_3$). From this mixture, XVI (2 mg), mp 218—221° (decomp.), was obtained by means of preparative TLC on Silica gel G (solvent: 3% MeOH–$CHCl_3$) and identified with an authentic sample of XVI by IR and TLC comparisons.

Sodium Borohydride Reduction of Compound XIV——To a solution of XIV (0.2 g) in CH_2Cl_2–MeOH (1:2) (12 ml) was added $NaBH_4$ (0.2 g) at room temperature. After stirring for 30 min, the reaction mixture was treated as in the case of XVII-a) to give an amorphous powder which was found to be a mixture of epimeric alcohols (XX) by the analyses of the NMR spectrum and TLC. NMR (δ in $CDCl_3$): $C\underline{H}_3$-CH(OH)–; 1.33 (d, J=7 Hz) and 1.55 (d, J=7 Hz), and other signals corresponding to $C_{3'}$–$C\underline{H}_3$, $OC\underline{H}_3$ and $OC\underline{H}_2O$ appeared as a pair of a mixture of epimeric alcohols (XX, ratio=1:1). TLC: 2 spots (ratio=1:1) of *Rf* 0.5 and 0.4 on Silica gel G (solvent: 5% MeOH–$CHCl_3$).

1-Oxo-2-(2′-acetyl-3′-methyl-6′,7′-dimethoxy-1′-indanyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (XXI)——A solution of XIV (0.1 g) in CH_2Cl_2 (2 ml) and MeOH (3 ml) was shaked at room temperature in the presence of PtO_2 (50 mg) under atmospheric hydrogen pressure for 1 hr. The catalyst was filtered off and the filtrate was evaporated to give a residue which was recrystallized from EtOH to afford XXI, colorless prisms, mp 195—198°. *Anal.* Calcd. for $C_{24}H_{25}O_6N$: C, 68.07; H, 5.95; N, 3.31. Found: C, 67.97; H, 6.20; N, 3.19. NMR (δ in $CDCl_3$): 3.80 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.75 (m, A_2B_2 type, 4H, C_3–H_2 and C_4–H_2), 5.97 (s, 2H, OCH_2O), and see text. UV: see text. Mass: see text.

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