Deoxometaphanine-D (VIII) (From Metaphanine thiokeal (X))——A mixture of thiokeal (X) (80 mg.), MeOH (5 ml.), tetrahydrofuran (0.5 ml.) and Raney-W-2 nickel (1.2 g.) was refluxed for 7 hr. The catalyst was filtered off, washed with MeOH and the combined filtrate was evaporated to dryness in vacuo. The residue was chromatographed over silica-gel column from CHCl₃ and elution with the same solvent gave a crystalline solid. Recrystallization from a mixture of MeOH and CHCl₃ gave deoxometaphanine-D (VIII) as colorless needles, m.p. 249~250°. Yield, 30 mg. On admixture of this desulfurization product (VIII) with deoxometaphanine-D (derived from Huang-Minlon reduction of metaphanine) no depression of melting point was observed and the IR spectra (in Nujol) of these two compounds were quite identical. Anal. Calcd. for C₁₃H₁₈O₄N: C, 68.86; H, 7.60; N, 4.23. Found: C, 68.61; H, 7.61; N, 4.22.

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Summary

The structure of metaphanine was examined and the partial structure (Ic) was presented. (Received February 3, 1965)

93. Masao Tomita, Toshiro Ibuka,*¹ Yasuo Inubushi,*² and Kyoji Takeda*³: Studies on the Alkaloids of Menispermaceous Plants. CCXV. *⁴ Alkaloids of Stephania japonica Miers. (Suppl. 13). *⁴ Structure of Metaphanine. (2).*⁴

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In the preceding paper*⁴ of this series the authors reported that the partial structure of metaphanine should be represented by formula (Ia). In this paper, the complete structure of metaphanine is shown to be represented by formula (I) including the absolute stereostructure.

A degradative pathway of considerable importance was found in the benzilic acid type rearrangement of metaphanine (I) with aqueous methanolic potassium hydroxide or sodium hydroxide. From the evidence discussed below, this compound was established as VIII. The rearranged compound (VIII) showed a δ-lactone group at 1733 cm⁻¹ (CHCl₃), 1717 cm⁻¹ (KBr) and a hydroxyl group at 3475 cm⁻¹ (CHCl₃) in the infrared spectra. In the nuclear magnetic resonance spectrum*⁵ a proton geminal to the hydroxyl group forming the lactone group (\( \text{O}^\text{C} = \text{O} \)) revealed a signal at 4.60 \( \tau \) as a quartet \( (J_A = 4 \text{ c.p.s., } J_B = 2.5 \text{ c.p.s.}) \). The analytical value corresponded to a composition

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*⁵ All NMR spectra were taken on Varian Associates A–60 recording spectrometer.
Chart 1.
of C₁₅H₂₃O₄N·CH₃OH (methanol adduct). The molecular weight of this substance, C₁₅H₂₃O₂N, was confirmed by its mass spectrum*(parent peak at 345 (calcd. 345.38)).

This rearrangement of metaphanine (I) to δ-lactone (VII) may be considered to proceed through two possible pathways. By treatment of caustic alkali the α-diketone-monohemiketal system in the metaphamine molecule leads to a sodium α-hydroxy carboxylate (V) via α-diketone intermediate (III) which could not be trapped and then V is cyclized to the δ-lactone (VII) by acidification (route A). This process was partly supported by the following finding. Hydrolysis of the δ-lactone (VII) with potassium hydroxide in methanol gave a potassium α-hydroxy carboxylate (V) as an amorphous solid, whose infrared spectrum (in Nujol) revealed a carboxylate band at 1572 cm⁻¹. Treatment of V with dil. mineral acid gave the original δ-lactone (VII) in quantitative yield.

Alternatively, the δ-lactone (VII) is assumed to arise from Ib through the sequence cited in route B which may be analogue of known clevinic acid δ-lactone rearrangement. The two routes (route A and route B) were given somewhat arbitrarily and would require further experimental supports for verification.

Treatment of the δ-lactone (VII) with acetic anhydride and pyridine gave a δ-lactone acetate (VIII), m.p. 205°, C₂₉H₄₀O₄N. VIII showed a carbonyl band at 1730 cm⁻¹ (δ-lactone and acetyl groups) in the infrared spectrum (in CHCl₃). In the nuclear magnetic resonance spectrum (Fig. 1) VIII revealed an acetyl methyl at 7.83 r and a proton geminal to the hydroxyl group forming the δ-lactone (C=O) at 4.52 r as a quartet (J₆=4.5 c.p.s., J₅=2 c.p.s.) and none of the signal due to a proton geminal to an acetoxy group. This spectral evidence supported that the tertiary hydroxyl group is present in the δ-lactone molecule.

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* Mass spectrum was taken on Hitachi RMU 6C mass spectrometer.
three methoxyl groups at 6.07 \( \tau \), 6.17 \( \tau \) and 6.28 \( \tau \). Treatment of \( \text{X} \) with acetic anhydride and pyridine gave an acetyl methyl ester (\( \text{XI} \)), whose infrared spectrum (in CHCl\(_3\)) revealed an overlapped carbonyl band at 1733 cm\(^{-1}\) (COOH\(_3\) and COOCH\(_3\)). The nuclear magnetic resonance spectrum (Fig. 3) of this product showed a signal due to an acetyl methyl at 7.87 \( \tau \) and no signal of the proton geminal to an acetoxy group. Reduction of the amino acid methyl ester (\( \text{X} \)) or the acetyl methyl ester (\( \text{XI} \)) with lithium aluminum hydride gave a diol (\( \text{XI} \)), m.p. 174\( ^\circ \), C\(_{19}\)H\(_{16}\)O\(_2\)N. Tosylation of the diol (\( \text{XI} \)) with tosyl chloride and pyridine followed by reduction with lithium aluminum hydride afforded a tertiary C-methyl compound (\( \text{XII} \)), m.p. 122\( ^\circ \), C\(_{19}\)H\(_{22}\)O\(_{2}\)N. The nuclear magnetic resonance spectrum (Fig. 4) of \( \text{XII} \) showed a signal attributable to a tertiary C-methyl group at 8.81 \( \tau \) as a singlet. On the other hand, periodate oxidation of the diol (\( \text{X} \)) gave a five-membered ketone (\( \text{XIII} \)) whose infrared spectrum (in CHCl\(_3\)) showed a carbonyl band at 1730 cm\(^{-1}\). This result indicated that the diol (\( \text{X} \)) contains an \( \alpha \)-glycol system in the molecule and that rearranged product may have a five-membered ring which is formed as a result of the ring contraction occurring in the course of the rearrangement. All these facts are compatible with the proposed mechanism of the rearrangement.

It was reported that Veratr um alkaloids (cevine\(^{3}\), cevagenine\(^{3}\), zygadenine\(^{4}\))

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germine\(^5\) and protoverine\(^6\) etc.) and a terpenoid (cryptofauronol\(^9\)) containing a hemiketal grouping in the molecule are stable to acid treatment, and the hemiketal hydroxyl group resists to acetylation under usual condition. In the same manner, the \(\alpha\)-diketone monohemiketal group in metaphanamine was stable to acid and resisted to acetylation under usual condition. On the other hand dihydrometaphanamine (II) which showed two hydroxyl groups in the nuclear magnetic resonance spectrum (in dimethylsulfoxide) gave monoacetyldihydrometaphanamine (XIV) on treatment with acetic anhydride and pyridine.\(^*\)

Under forced conditions, metaphanamine (I) and dihydrometaphanamine (II) gave a brown resinous solid which resisted to purification. Dihydrometaphanamine (II) revealed no carbonyl band in its infrared spectrum. In connection with the results reported in the preceding paper\(^*\) all these facts established that the hemiketal linkage between the carbonyl group at C-8 and the hydroxyl group substituted on C-10 is present in metaphanamine (I) and dihydrometaphanamine (II). The stereochemistry of this hemiketal linkage will be discussed later.

Oxidation of monoacetyldihydrometaphanamine (XIV) with potassium permanganate in acetone under the presence of magnesium sulfate gave

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a γ-lactam (XV), m.p. 244~245°C, C_{21}H_{28}O_{2}N, as major product. The infrared spectrum of XV showed an acetyl carbonyl band at 1730 cm\(^{-1}\) and a γ-lactam band at 1683 cm\(^{-1}\). The latter frequency is in good agreement with those found in five-membered lactams. The nuclear magnetic resonance spectrum of XV revealed a signal due to N-methyl group at 6.91 \(\tau\). The displacement to lower side of the signal of the N-methyl group (metaphanamine, 7.43 \(\tau\)) explains adequately the structure (XV). This spectral evidence also supported that the ethanamine bridge consists of a five-membered ring. Reduction of II and XIV with lithium aluminum hydride caused the reductive fission of the hemiketal ether bridge to afford a triol (XVI), m.p. 161~162°C, C_{19}H_{25}O_{3}N, \([\alpha]^{25}_{D} +4^\circ\) (CHCl\(_3\)). This triol (XVI) was also obtainable by reduction of the γ-lactam (XV) with lithium aluminum hydride. These results supported that no transformation of the ring system was occurred during oxidation of monoacetylhidrometaphanamine (XIV) with permanganate.

The above reductive fission of the hemiketal ether linkage with lithium aluminum hydride is analogous to the reductive fission of hemiketal group of tazettine by the lithium aluminum hydride reduction\(^{7}\) and of cevine orthoacetate triacetate by reduction with lithium in liquid ammonia.\(^{60}\)

Treatment of the triol (XVI) with acetic anhydride and pyridine gave a triol triacetate (XVII), m.p. 100~104°C, C_{23}H_{26}O_{5}N. The infrared spectrum of XVII showed a carbonyl band at 1730 cm\(^{-1}\) and its nuclear magnetic resonance spectrum (Fig. 5) revealed signals due to three acetate methyls at 7.90 \(\tau\), 7.93 \(\tau\), and 8.12 \(\tau\). Reduction of XVII with lithium aluminum hydride regenerated the original triol (XVI). Treatment of XVI with dil. perchloric acid under mild condition caused dehydration producing an olefinic compound (XVII), m.p. 143°C, C_{19}H_{25}O_{3}N. The ultraviolet spectrum (Fig. 7) showed a characteristic absorption curve of the styrene type chromophore indicating that the hydroxyl group at C-10 in the triol molecule was dehydrated.

Catalytic hydrogenation of XVII over palladium-carbon afforded a diol (XIX), m.p. 161~162°C, C_{19}H_{26}O_{3}N, whose nuclear magnetic resonance spectrum (in dimethylsulfoxide) showed two secondary hydroxyl groups at 5.44 \(\tau\) (1H, doublet, \(J=4.5\) c.p.s.) and 5.72 \(\tau\) (1H, doublet, \(J=4.5\) c.p.s.). The diol (XIX) was also prepared from the triol (XVI) by catalytic hydrogenolysis over platinic oxide in acetic acid. Acetylation of the diol (XIX) with acetic anhydride and pyridine gave a diol diacetate (XX), m.p. 140°C, C_{23}H_{28}O_{4}N. The infrared spectrum of XX showed a carbonyl band at 1730 cm\(^{-1}\). The nuclear magnetic resonance spectrum (Fig. 6) revealed two acetate methyls at 7.90 \(\tau\) and 8.06 \(\tau\), and two protons geminal to the acetoxy groups at 4.72 \(\tau\) (2H) as unresolved multiplet.

From these degradative and spectroscopic evidence described above, it can be concluded that the structure (I) must be allocated to metaphanamine.

Information on the stereochemistry of metaphanamine was provided by the following observations. Since the \(\alpha\)-configuration of the ethanamine bridge has been established in the preceding paper,\(^{\dagger}\), the configuration of C-7~C-14 bond in the δ-lactone (\(\text{VI}\)) must

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be $\beta$-oriented. Consequently, the configuration of the $\delta$-lactone (VI) requires the $\beta$-configuration of the hydroxyl group at C-10. If the configuration of this hydroxyl group were $\alpha$-oriented, the cyclization to the lactone ring would not be achieved. In metaphanine (I), dihydrometaphanine (II) and monoacetyl/dihydrometaphanine (XIV) the existence of strong hydrogen bonding between the hemiketal hydroxyl group at C-8 and nitrogen atom was shown by their $\text{Phca}'$ values and their infrared spectra, and difficulty of methiodide formation of these compounds is also understandable by taking this interaction into consideration. Thus, the configuration of the hemiketal hydroxyl group should have the same configuration, $\alpha$-configuration, as that of ethanamine bridge. Consequently, the absolute stereostructure of metaphanine (I) must be represented by the perspective formula (XXI).*

**Experimental**

$\delta$-Lactone (VI) (Benzilic Acid Type Rearrangement of Metaphanine)—A mixture of metaphanine (I) (70 mg.), 20% sq. NaOH (0.5 ml.) and MeOH (20 ml.) was allowed to stand overnight at room temperature. After evaporation of the solvent in vacuo at room temperature 2 ml. of 10% HCl was added to the residue. The aqueous acidic solution was made alkaline with dil. NH$_4$OH and extracted with ether. The ether extract was washed, dried over MgSO$_4$, and evaporation to give a colorless oil. Trituration with a small amount of MeOH gave a crystalline solid. Recrystallization from MeOH gave a $\delta$-lactone (VI) as colorless prisms, m.p. 71–72°. Yield, 65 mg. IR $\nu_{C=O}$ cm$^{-1}$: 1730 (lactone), 3475 (OH). IR $\nu_{OH}$ cm$^{-1}$: 1717 ($\delta$-lactone). NMR (CDCl$_3$): benzene protons, 2.97 (1H, doublet, $J=8$ c.p.s.); 3.18 (1H, doublet, $J=8$ c.p.s.); $\gamma$-O-C=O, 4.60 (1H, quartet, $J_a=4$ c.p.s., $J_b=2.5$ c.p.s.); OCH$_3\times2$, 6.15 (6H); N-CH$_3$, 7.52 (3H). Anal. Calcd. for C$_{13}$H$_{20}$O$_5$-C$_6$H$_5$OH: C, 63.64; H, 7.21; N, 3.71. Found: C, 63.59; H, 7.01; N, 3.38. Hydroxide: m.p. 225° (from MeOH). Anal. Calcd. for C$_{13}$H$_{20}$O$_5$-C$_6$H$_5$: C, 48.21; H, 5.11; N, 2.96. Found: C, 48.41; H, 5.39; N, 3.19.

Potassium $\alpha$-Hydroxycarboxylate (V) (Hydrolysis of $\delta$-Lactone (VI))—A solution of $\delta$-lactone (VI) (37.7 mg.) in 1% MeOH-KOH (0.56 ml.) was refluxed for 1 hr. Evaporation of the solvent in vacuo gave a colorless amorphous solid (V). The product (V) resisted to crystallization. Yield, 39 mg. IR $\nu_{C=O}$ cm$^{-1}$: 1572 (carboxylate). A solution of potassium $\alpha$-hydroxy carboxylate (V) (8 mg.) in 3% HCl (1 ml.) was allowed to stand for 5 min. at room temperature and made alkaline with dil. NH$_4$OH and extracted with ether. The ether extract was washed, dried over Na$_2$SO$_4$. Evaporation of the solvent left a colorless oil. Trituration with MeOH gave a crystalline solid. Recrystallization from MeOH gave 6 mg. of $\delta$-lactone (VI) as colorless prisms, m.p. 71–72°. The compound was identified with the $\delta$-lactone (VI) (prepared from benzilic acid type rearrangement of metaphanine) by mixed melting point determination and comparison of their IR spectra (in CHCl$_3$).

$\delta$-Lactone Acetate (VII)—To a solution of $\delta$-lactone (VI) (40 mg.) in pyridine (1 ml.) was added 1 ml. of Ac$_2$O and the mixture was allowed to stand overnight at room temperature. After evaporation of the excess Ac$_2$O and pyridine in vacuo at room temperature 10 ml. of 3% NH$_4$OH was added to the residue and extracted with ether. The ether extract was washed, dried over Na$_2$SO$_4$ and evaporated to give a crystalline solid. Recrystallization from EtOH gave a $\delta$-lactone acetate (VII) as colorless prisms, m.p. 205°. Yield, 40 mg. IR $\nu_{C=O}$ cm$^{-1}$: 1730 ($\delta$-lactone and acetyl). NMR (CDCl$_3$): benzene protons, 3.0 (1H, doublet, $J=8$ c.p.s.); 3.21 (1H, doublet, $J=8$ c.p.s.); $\gamma$-O-C=O, 4.52 (1H, quartet, $J_a=4.5$ c.p.s., $J_b=2$ c.p.s.); OCH$_3\times2$, 6.12 (6H); N-CH$_3$, 7.64 (3H); OCCH$_3$, 7.83 (3H). Anal. Calcd. for C$_{13}$H$_{20}$O$_5$-C$_6$H$_5$OH: C, 65.10; H, 6.50; N, 3.62. Found: C, 65.16, 65.39; H, 6.67, 6.77; N, 3.54, 3.77.

Amino Acid Compound (VIII) (Hydrogenolysis of $\delta$-Lactone (VI))—A mixture of $\delta$-lactone (VI) (150 mg.), PtO$_2$(50 mg.) and AcOH (10 ml.) was hydrogenated at room temperature for 2 hr. The catalyst was filtered off, washed with AcOH and the combined filtrate was evaporated in vacuo. Recrystallization of the residue from H$_2$O gave an amino acid (VIII) (130 mg.) as colorless prisms, m.p. 176–177°. IR $\nu_{C=O}$ cm$^{-1}$: 1594 (carboxylate). NMR (D$_2$O+CD$_3$COOD): benzene protons, 2.65 (2H); OCH$_3\times2$, 5.68 (3H); 5.75 (3H); N-CH$_3$, 6.61 (3H). Anal. Calcd. for C$_{13}$H$_{20}$O$_5$-2H$_2$O: C, 59.51; H, 7.62; N, 3.65. Found: C, 60.07; H, 7.52; N, 3.82. Hydrochloride: m.p. 233–235° (from CHCl$_3$). IR $\nu_{C=O}$ cm$^{-1}$: 1700 (COOH), 2300–2750 (N-H). Anal. Calcd. for C$_{13}$H$_{20}$O$_5$-HCl·$\frac{1}{2}$H$_2$O: C, 58.08; H, 6.93; N, 3.56. Found: C, 58.22, 57.97; H, 6.98, 6.73; N, 3.45, 3.60.

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* Ring C may take either chair or boat form conformation, but we depicted only chair form herein.
** All melting points were uncorrected and determined by Yanagimoto Micro Melting Point Apparatus.
Amino Acid Methyl Ester (IX) (Methylation of the Amino Acid (VIII) Hydrochloride with Diazomethane)—A solution of NII hydrochloride (55 mg.) in MeOH (3 ml.) was treated with diazomethane in ether (10 ml.) (prepared from nitromethylenes (3 g.) and allowed to stand at room temperature for 3 hr. After evaporation of the solvent 5 ml. of 3% NH₂OH was added to the residue and the mixture was extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporation of the solvent gave crystals. Recrystallization from MeOH gave X (45 mg.) as colorless needles, m.p. 14³. IR νCH₂ cm⁻¹: 1728 (ester), 3300 (OH). NMR (CDCl₃): benzene protons, 3.27 (2H); OH, 4.18 (1H); OCH₂ × 3, 6.07 (3H), 6.17 (3H), 6.28 (3H); N-CH₃, 7.42 (3H). Anal. Calcd. for C₉H₁₇NO₃: C, 66.46; H, 7.53; N, 3.88. Found: C, 66.77, 66.50; H, 7.47, 7.34; N, 3.91, 3.88.

Acetyl Methyl Ester (X)—A mixture of methyl ester (X) (32 mg.), pyridine (0.5 ml.) and Ac₂O (2 ml.) was allowed to stand at room temperature for 2 day. After evaporation of the excess reagent in vacuo the residue was treated with dil. NH₂OH (5 ml.) and extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated to give an acetyl methyl ester (X) (31 mg.) as a colorless oil. IR νCH₂ cm⁻¹: 1733 (methyl ester and acetate). NMR (CDCl₃): benzene protons, 3.30 (2H); OCH₃ × 3, 6.11 (3H), 6.18 (3H), 6.30 (3H); N-CH₃, 7.41 (3H); OOCCH₃, 7.87 (3H).

Diol Compound (XI)—To a solution of the amino acid methyl ester (X) (or acetyl methyl ester (X)) (200 mg.) in ether (50 ml.) was added 100 mg. of LiAlH₄. The mixture was stirred at room temperature for 3 hr. and the excess reagent was decomposed by the addition of H₂O and the alkaline solution was extracted with ether. The extract was washed, dried over Na₂SO₄ and evaporated to give a crystalline solid. Recrystallization from MeOH–ether mixture gave XI as colorless prisms, m.p. 174°. Yield, 175 mg. Anal. Calcd. for C₁₀H₁₇NO: C, 68.44; H, 8.16. Found: C, 68.70; H, 8.22.

Tertiary C-Methyl Compound (XII)—A solution of diol (XI) (150 mg.) in pyridine (3 ml.) was treated with tosyl chloride (144 mg.) and allowed to stand at room temperature for 2 day. After evaporation of the excess pyridine in vacuo 10% Na₂CO₃ (10 ml.) was added to the residue and the alkaline solution was extracted with CHCl₃. The CHCl₃ solution was washed, dried over Na₂SO₄ and evaporated to give slightly yellow oil (130 mg.). To a solution of the tosylated product (130 mg.) in tetrahydrofuran (20 ml.) was added 100 mg. of LiAlH₄ in tetrahydrofuran (20 ml.). The mixture was heated under reflux for 6 hr. and after cooling the excess reagent was decomposed with H₂O and the mixture was extracted with ether. The ether extract was washed, dried over Na₂SO₄. Evaporation of the solvent left a crystalline solid which was chromatographed over alumina column from benzene and eluted with the same solvent. Recrystallization from hexane gave XII (50 mg.) as colorless prisms, m.p. 12². NMR (CDCl₃): benzene protons, 3.26 (2H); OCH₂ × 2, 6.03 (3H), 6.16 (3H); N-CH₃, 7.44 (3H); >OCH₃, 8.81 (3H, singlet). Anal. Calcd. for C₁₀H₁₇NO: C, 71.89; H, 8.57. Found: C, 71.62; H, 8.34.

Five Membered Ketone (XIII)—A solution of diol (X) (21 mg. in EtOH (3 ml.) was treated with HIO₂·2H₂O (10 mg. in H₂O (0.5 ml.) and allowed to stand at room temperature for 20 hr. The solvent was evaporated in vacuo and 10 ml. of 10% Na₂CO₃ was added to the residue and the alkaline solution was extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated to give slightly yellow oil which was chromatographed over alumina column from benzene and elution with the same solvent gave a five membered ketone (XII) (6 mg.) as colorless oil. The product revealed a single peak on the thin layer chromatography. IR νCH₂ cm⁻¹: 1730 (five membered ketone).

γ-Lactam (XV) (Oxidation of Monoacetylidyldihrometaphanetamine (XIV) with Permanganate)—A mixture of XIV (60 mg.), MgSO₄ (70 mg.), acetone (15 ml.) and H₂O (2 ml.) was treated with KMnO₄ (75 mg.) in acetone (5 ml.) and H₂O (8 ml.) at room temperature with stirring for 5 hr. The excess permanganate was decomposed with a solution of NaHSO₃ (150 mg.) in 5% H₂SO₄ (5 ml.). The solvent was evaporated in vacuo and the aconical solution was extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated to give a crystalline solid. Recrystallization from MeOH gave γ-lactam (XV) (41 mg.) as colorless needles, m.p. 244~245°. IR νC=O cm⁻¹: 3500~3350 (OH), 1730 (OAc). 1638 (~-lactam). NMR (CDCl₃): benzene protons, 3.19 (1H), 3.21 (1H); OH, 5.99 (1H); >OAc, 5.14 (1H); OCH₂ × 2, 6.13 (6H); N-CH₃, 6.91 (3H); OOCCH₃, 7.90 (3H). Anal. Calcd. for C₁₆H₁₈N₂O₄: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.68; H, 6.47; N, 3.68.

Triol Compound (XVI) (Reduction of Dihyrometaphanetamine (II) with Lithium Aluminum Hydride)—To a solution of II (97 mg.) in tetrahydrofuran (2 ml.) and ether (15 ml.) was added 100 mg. of LiAlH₄ and the reaction mixture was refluxed for 5 hr. and after cooling the excess reagent was decomposed with H₂O and the mixture was extracted with CHCl₃. The CHCl₃ extract was washed, dried over Na₂SO₄ and evaporated to give a crystalline solid. Recrystallization from MeOH–ether mixture gave a triol (XVI) (55 mg.), m.p. 161~162°, as colorless needles. [α]D + 4° (c=0.5, CHCl₃). NMR (pyridine): OCH₂ × 2, 6.11 (5H), 6.27 (3H); N-CH₃, 7.25 (3H). Anal. Calcd. for C₁₉H₂₁NO₉·HCl: C, 59.14; H, 7.32; N, 3.63. Found: C, 59.38; H, 7.47; N, 3.81.

Triol Compound (XVI) (Reduction of γ-Lactam (XV) with Lithium Aluminum Hydride)—To a solution of lactam (XV) (22 mg.) in tetrahydrofuran (3 ml.) and ether (15 ml.) was added 50 mg. of LiAlH₄. The
mixture was refluxed with stirring for 11 hr. and after cooling the excess reagent was decomposed with H₂O. Inorganic precipitate was filtered off, washed with CHCl₃ and the combined filtrate was evaporated to dryness in vacuo. The residue was dissolved in dil. HCl (15 ml.) and extracted with ether. The aqueous layer was made alkaline with dil. NH₄OH and extracted with CHCl₃. The CHCl₃ solution was washed, dried over Na₂SO₄ and evaporated to give a crystalline solid. Recrystallization from MeOH gave the triol (XVI) as colorless needles, m.p. 160~161°. Yield, 14 mg. On admixture of the product with the triol which was prepared from dihydroxymetaphenamine by the LiAIH₄ reduction no melting point depression was observed and the infrared spectra (in CHCl₃) of two compounds were identical.

**Triol Triacetate (XVII)**—A mixture of triol (XVI) (20 mg.), pyridine (2 ml.) and Ac₂O (1 ml.) was allowed to stand overnight at room temperature. The excess reagent was removed in vacuo and the residue was made alkaline with dil. NH₄OH and extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated. Recrystallization from ether gave a triol triacetate (XVII) as colorless needles, m.p. 100~104°. Yield, 15 mg. IR νₖₑ₅₄ cm⁻¹ : 1730 (OAc). NMR (CHCl₃) : benzene protons, 3.03 (1H), 3.15 (1H); >C=OAc x 3, 4.0 (1H, triplet), 4.83 (2H, broad multiplet); OCH₃ x 2, 6.14 (6H); N-CH₃, 7.55 (3H); OCOC₂H₅ x 3, 7.90 (3H), 7.93 (3H), 8.12 (3H). Anal. Calcd. for C₁₅H₂₃O₅N : C, 63.14; H, 7.00; N, 2.95. Found : C, 63.20; H, 7.24; N, 3.02.

**Reduction of Triol Triacetate with Lithium Aluminum Hydride**—A mixture of tritol triacetate (XVII) (12 mg.), tetrahydrofuran (20 ml.) and LiAIH₄ (50 mg.) was stirred at room temperature for 1 hr. The excess reagent was decomposed with H₂O. Treatment of the product as usual and recrystallization from MeOH—ether mixture gave the original triol (XVI), m.p. 158~159°, as colorless needles. On admixture of this product with the triol which was prepared from dihydroxymetaphenamine by the LiAIH₄ reduction no melting point depression was observed and the IR spectra (in CHCl₃) of two compounds were quite identical.

**Olefinic Compound (XVIII)**—A solution of triol (XVI) (110 mg.) in MeOH (10 ml.) and 60% HClO₄ (0.2 ml.) was refluxed for 20 min. and after cooling the solvent was removed in vacuo and the residue was made alkaline with dil. NH₄OH and extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated to give a crystalline solid. Recrystallization from MeOH gave an olefinic compound (XVIII) as colorless prisms, m.p. 143°. Yield, 91 mg. Anal. Calcd. for C₁₅H₂₁O₅N : C, 68.86; H, 7.86. Found : C, 68.95; H, 7.87.

**Diol Compound (XIX). a Catalytic Hydrogenolysis of Triol (XVI)**—A mixture of triol (19 mg.), AcOH (5 ml.) and Pd₃O₄ (5 mg.) was hydrogenated at room temperature for 5 hr. The catalyst was filtered off, washed with MeOH and the combined filtrate was evaporated to dryness in vacuo and the residue was made alkaline with dil. NH₄OH and extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated. Recrystallization from ether gave the diol (XIX) as colorless needles, m.p. 161~162°. Yield, 5 mg. On admixture of the product with the diol which was derived from the olefinic compound (XVIII) by catalytic hydrogenolysis no melting point depression was observed and the IR spectra (in CHCl₃) of two compounds were superimposable.

b) **Catalytic Hydrogenation of Olefinic Compound (XVIII)**—A mixture of olefinic compound (XVIII) (64 mg.), MeOH (3 ml.), Darco G-60 (30 mg.) and 5% PdCl₂ (1 ml.) was hydrogenated for 3 hr. at room temperature. The catalyst was filtered off, washed with MeOH and the combined filtrate was evaporated to dryness and the residue was made alkaline with 3% NH₄OH and extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated. Recrystallization from ether gave the diol (XIX) as colorless needles, m.p. 161~162°. Yield, 55 mg. NMR ν (dimethylsulfoxide) : OH, 5.44 (1H, doublet, J = 4.5 c.p.s.); OH, 5.72 (1H, doublet, J = 4.5 c.p.s.). Anal. Calcd. for C₁₅H₂₁O₅N : C, 68.44; H, 8.16. Found : C, 68.69; H, 8.14.

**Diol Diacetate (XX)**—A mixture of diol (XIX) (35 mg.), pyridine (0.5 ml.) and Ac₂O (1 ml.) was allowed to stand overnight at room temperature. The excess reagents were removed in vacuo. The residue was made alkaline with dil. NH₄OH and extracted with ether. The ether extract was washed, dried over Na₂SO₄ and evaporated. Recrystallization from MeOH gave a diol diacetate (XX) as colorless needles, m.p. 140°. Yield, 31 mg. IR νₖₑ₅₄ cm⁻¹ : 1730 (OAc). NMR (CDCl₃) : benzene protons, 3.22 (2H); >C=OAc x 2, 4.72 (2H, unresolved multiplet); OCH₃ x 2, 6.16 (3H), 6.20 (3H); N-CH₃, 7.52 (3H); OCOC₂H₅ x 2, 7.90 (3H), 8.06 (3H). Anal. Calcd. for C₁₅H₂₁O₅N : C, 66.16; H, 7.48. Found : C, 66.36; H, 7.56.

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**Summary**

Metaphenamine was shown to be an alkaloid derived from a new ring system "hasubanan." Degradative and spectroscopic evidence established metaphenamine as I. The absolute configuration of this alkaloid was established as shown by the perspective formula (XXI).

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