

STRUCTURE OF PROMETAPHANINE

M. Tomita and T. Ibuka

Faculty of Pharmaceutical Sciences, Kyoto University  
Kyoto, Japan

Y. Inubushi

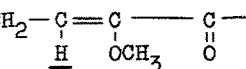
Faculty of Pharmaceutical Sciences, Osaka University  
Toyonaka, Osaka, Japan

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IN the preceding communication,<sup>1)</sup> the authors together with Takeda reported the structure of metaphanine which is one of the basic constituents of Stephania japonica Miers. We wish to report the structure of prometaphanine, which is seemed to be closely related to metaphanine and was isolated from the same plant.

Prometaphanine (I) was obtained as amorphous solid, which could not be induced to crystallize and its homogeneity was shown by thin layer chromatography<sup>\*1</sup> and paper partition chromatography<sup>\*2</sup> which gave a single spot. For characterization the base was derived to its methiodide, m.p. 207°, C<sub>20</sub>H<sub>25</sub>O<sub>5</sub>N·CH<sub>3</sub>I,<sup>\*3</sup>  $[\alpha]_D^{10}$ : -32° (MeOH).

Prometaphanine showed the absorption bands of a conjugated carbonyl group at 1670 and a enolic double bond at 1654 cm<sup>-1</sup> in the IR spectrum, and three OCH<sub>3</sub> groups at 6.01(3H), 6.22(3H), 6.50(3H); one N-CH<sub>3</sub> group at 7.30(3H);

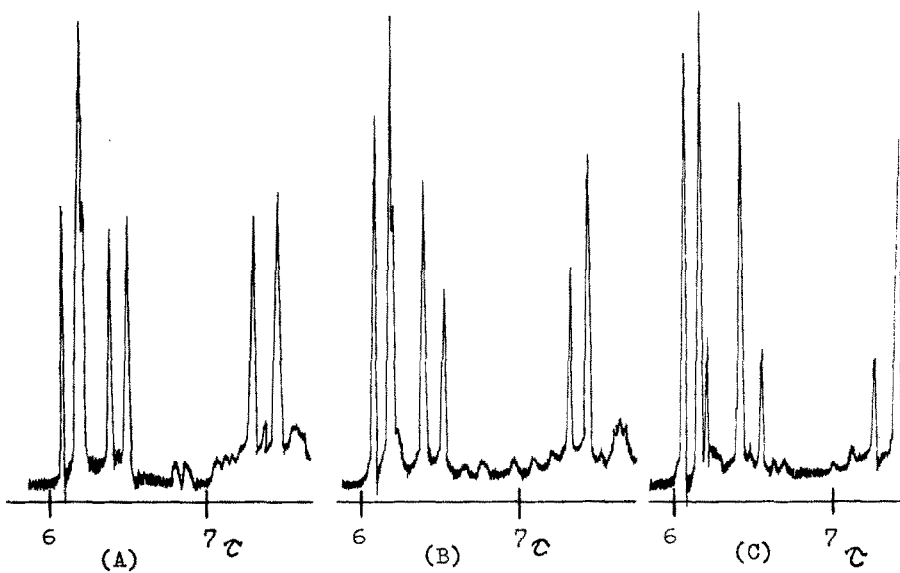


\*1 Kieselgel nach Stahl, solvent, methanol or Aluminiumoxyd nach Stahl, solvent, chloroform.

\*2 Toyo Filter Paper No. 50, solvent, AcOH: EtOH; H<sub>2</sub>O = 10; 63; 27.

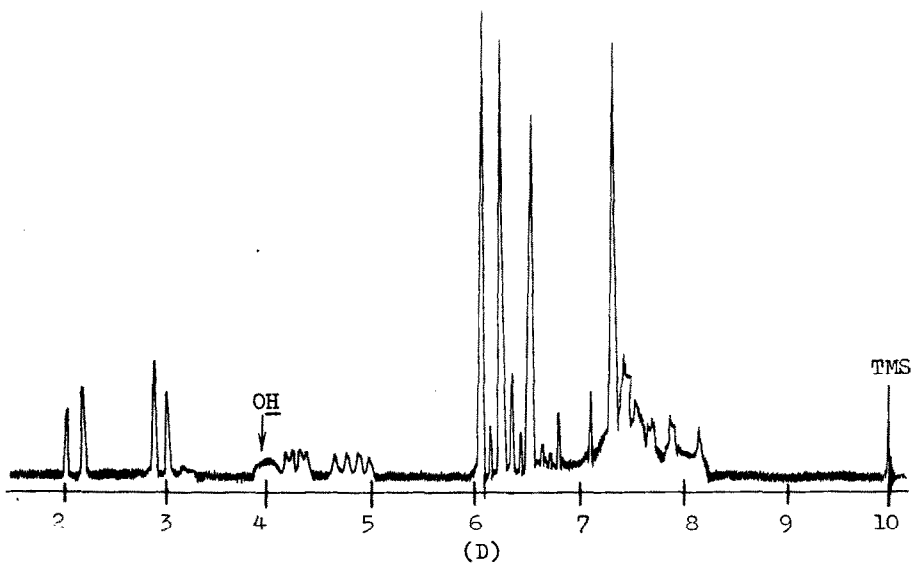
\*3 All compounds given by formulae in this communication gave correct elementary analysis.

CHART I



N. M. R. spectra of prometaphanine:

- (A)...in CCl<sub>4</sub>:CHCl<sub>3</sub> = 3:2,      (B)...in deuteriochloroform,  
(C)...in CDCl<sub>3</sub>:pyridine = 10:1,      (D)...in deuteriopyridine.



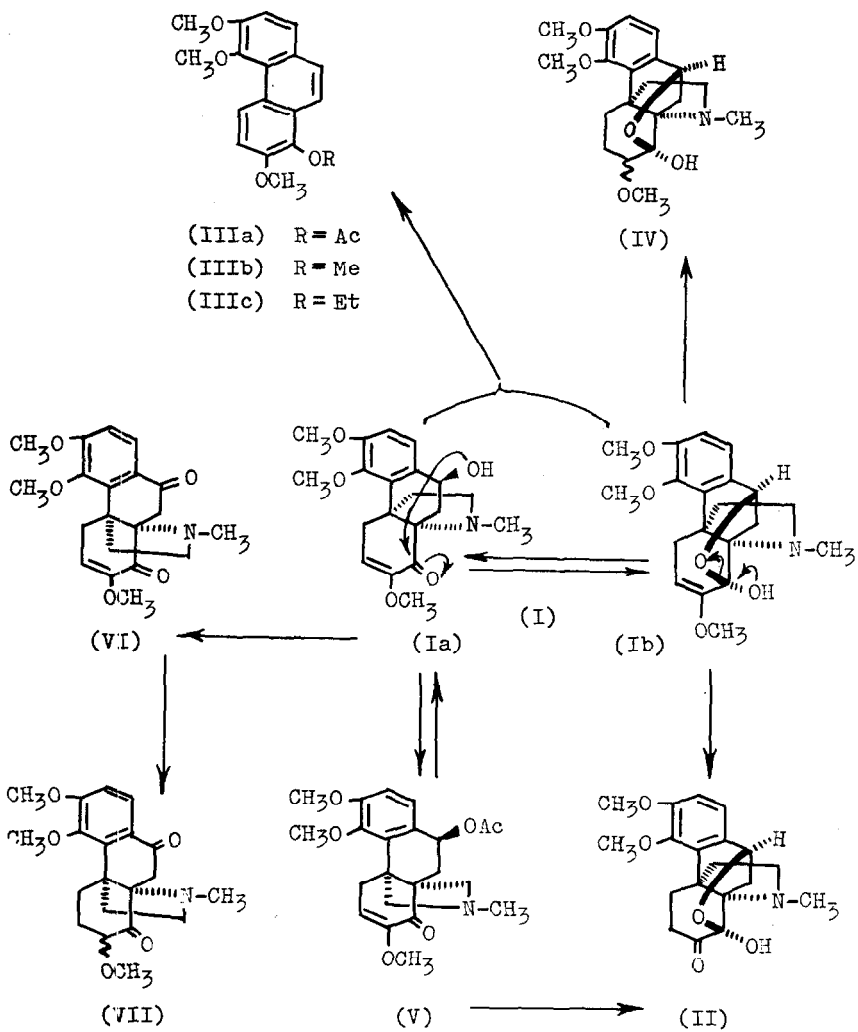
hydrogen at 4.30 (1H, quartet,  $J_A=2.5$  cps,  $J_B=7$  cps) and  $-\text{CH}_2-\overset{\text{OH}}{\underset{\text{H}}{\text{C}}}$  hydrogen at 4.83  $\tau$  (1H, quartet,  $J_A=12$  cps,  $J_B=6$  cps) were confirmed by its NMR<sup>\*4</sup> spectrum in deuteriopyridine.

As shown in CHART I, NMR spectra of prometaphanine taken in several different solvents showed the striking feature. This observation suggested that prometaphanine exists in an equilibrium mixture of the ketone (Ia) and the hemiketal (Ib) and the position of equilibrium is different in different solvents.

Treatment of (I) with dil. mineral acid under mild condition gave metaphanine<sup>1)</sup> (II), m.p. 232°,  $\text{C}_{19}\text{H}_{23}\text{O}_5\text{N}$ , in quantitative yield. This fact indicated that the enolic ether group (enolic methoxyl group) of prometaphanine was hydrolysed to the carbonyl group.

Heating of (I) with acetic anhydride in a sealed tube gave 3,4,7-trimethoxy-8-acetoxyphenanthrene (IIIa), m.p. 140°,  $\text{C}_{19}\text{H}_{18}\text{O}_5$ , IR  $\sqrt{\text{CHCl}_3}$  max.: 1763  $\text{cm}^{-1}$  (OAc), UV  $\lambda_{\text{max.}}^{\text{EtOH}}$  (log  $\epsilon$ ): 224(4.33), 268(4.67), 287(4.18), 305(4.01), 316(4.00), 345(3.19), 364(3.08), NMR.  $\tau$ :  $\text{OCH}_3 \times 3$ , 5.98(3H), 6.01(3H), 6.06(3H);  $\text{OCOCH}_3$ , 7.51(3H). Hydrolysis of (IIIa) with methanolic-KOH followed by methylation with methyl iodide gave 3,4,7,8-tetramethoxyphenanthrene (IIIb), which was characterized as its picrate, m.p. 146-148°,  $\text{C}_{24}\text{H}_{21}\text{O}_{11}\text{N}_3$  and was identified with an authentic sample<sup>2)</sup> by mixed melting point determination and comparison of their IR spectra. Hydrolysis of (IIIa) with ethanolic-KOH followed by ethylation with ethyl iodide

\*4 Unless otherwise stated, all NMR. spectra were taken on Varian Associates A-60 recording spectrometer at 60 Mc. in  $\text{CDCl}_3$  with  $\text{SiMe}_4$  as internal standard.



gave 3,4,7-trimethoxy-8-ethoxyphenanthrene (IIIc). (IIIc) was characterized as its picrate, m.p. 165°,  $C_{25}H_{23}O_{11}N_3$ , whose melting point did not depress by admixture with an authentic sample.<sup>3)</sup>

On catalytic hydrogenation over  $PtO_2$  (I) absorbed one mole of hydrogen to afford dihydroprometaphanine (IV), m.p. 205°,  $C_{20}H_{27}O_5N$ , NMR.  $\tau$ :  $OCH_3 \times 3$ , 6.17(6H), 6.61(3H), which was stable to acid treatment. Acetylation of (I) with  $Ac_2O$ -pyridine gave an acetylprometaphanine (V),  $IR \nu_{max}^{CHCl_3}$ : 1733(OAc), 1673(conj. C=O), 1646  $cm^{-1}$  (enolic C=C), NMR.  $\tau$ :  $OCH_3 \times 3$ , 6.07(3H), 6.14(3H), 6.40(3H); N- $CH_3$ , 7.40(3H);  $OCOCH_3$ , 7.90(3H);  $-CH_2-\overset{\overset{OAc}{\parallel}}{C}-\overset{\overset{H}{\parallel}}{C}$ , 4.07 (1H, quartet,  $J_A=8.5$  cps,  $J_B=5.5$  cps);  $-CH_2-\overset{\overset{H}{\parallel}}{C}=\overset{\overset{OCH_3}{\parallel}}{C}-\overset{\overset{O}{\parallel}}{C}$ , 4.32(1H, quartet,  $J_A=4$  cps,  $J_B=6$  cps), which on treatment with sodium bicarbonate gave the original prometaphanine (I). On the other hand, when treated with mineral acid, acetylprometaphanine gave metaphanine (II).

Oxidation of (I) with manganese dioxide in chloroform gave a diketone (VI), m.p. 201-202°,  $C_{20}H_{23}O_5N$ ,  $IR \nu_{max}^{CHCl_3}$ : 1680  $cm^{-1}$  (conj. C=O  $\times 2$ ),  $UV \lambda_{max}^{EtOH}$  ( $\log \epsilon$ ): 230(4.26), 272(4.13), 300 (3.87), NMR.  $\tau$ :  $OCH_3 \times 3$ , 6.04(3H), 6.07(3H), 6.38(3H);  $-CH_2-\overset{\overset{H}{\parallel}}{C}=\overset{\overset{OCH_3}{\parallel}}{C}-$ , 4.22(1H, quartet,  $J_A=6$  cps,  $J_B=3.5$  cps). On catalytic hydrogenation over  $PtO_2$  (VI) absorbed one mole of hydrogen to give a diketone (VII), m.p. 159°,  $C_{20}H_{25}O_5N$ ,  $IR \nu_{max}^{CHCl_3}$ : 1725(six membered ketone), 1680  $cm^{-1}$ (conj. carbonyl), NMR.  $\tau$ :  $OCH_3 \times 3$ , 6.07(3H), 6.17(3H), 6.64(3H);  $\overset{\overset{OCH_3}{\parallel}}{C}=\overset{\overset{H}{\parallel}}{C}$ , 5.62(1H, quartet,  $J_A=12$  cps,  $J_B=6$  cps).

All these results, in connection with the structure of metaphanine,<sup>1)</sup> interpret the behavior of prometaphanine as an equilibrium mixture consisting of (Ia) and (Ib) in solution and no alternative structure for prometaphanine could be devised.

## REFERENCES

- 1) M. Tomita, T. Ibuka, Y. Inubushi and K. Takeda, Tetrahedron Letters., in press.
- 2) H. Kondo, T. Nakamura, M. Fujii and T. Kato, Ann. Rept. ITSUU Lab. 1, 41 (1950).
- 3) M. Tomita, Y. Inubushi and T. Ibuka, unpublished results.