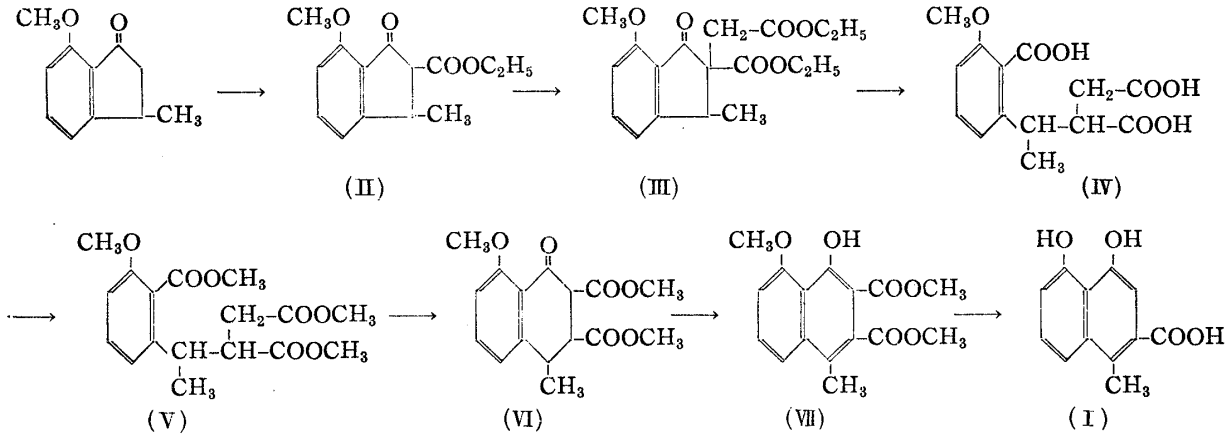

(II) (III) (IV) (V) (VI) (VII) (I)

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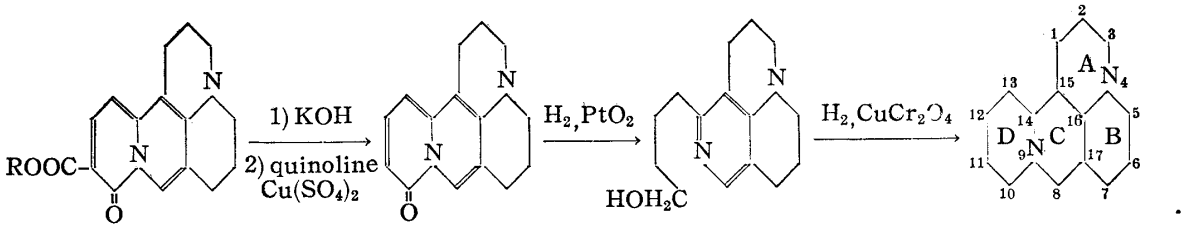
Synthesis of Octadehydromatrine and Allomatridine

In 1935, Kondo and Tsuda[1] obtained octadehydromatrine, $C_{15}H_{16}ON_2$, by dehydrogenation of matrine over palladium-asbestos.

While the saponification of 11-ethoxycarbonyl-10-oxo-1,2,3,5,6,7-hexahydroquinolizino[1,8-*ab*]quinolizine (Ia),[2] synthetically prepared, afforded an acid (Ib), m.p. 270~272° (Calcd. for $C_{16}H_{16}O_3N_2$: C, 67.59; H, 5.67; N, 9.85. Found : C, 67.72; H, 5.85; N, 10.07), and subsequent decarboxylation gave 10-oxo-1,2,3,5,6,7-hexahydroquinolizino[1,8-*ab*]quinolizine (II), m.p. 174~176°; λ_{max}^{EtOH} mμ (log ε) : 230(4.39), 270(4.05), 395(4.22); ν_{max} 1647 cm^{-1}(C=O) and 1518 cm^{-1}(C=C) (in KBr pellet). All physical properties of (II) agreed with those of octadehydromatrine. (II) was converted by hydrogenation over platinum oxide to a compound, $C_{15}H_{22}ON_2$,[1] m.p. 105°; λ_{max}^{EtOH} 226 and 274 mμ (log ε 4.32 and 4.18); ν_{max} 1592, 1558, 1506 cm^{-1}(C=C), and 3145 cm^{-1}(OH), indicating the presence of a pyridine ring and OH group. The data of the ultraviolet absorption spectrum are analogous to those of dehydro-α-matrinidine.[3] The benzoate[1] shows the stretching vibration band for an ester group at 1722 cm^{-1}(-O-CO-) and copper chromite catalyzed its high-pressure hydrogenation to give *dl*-allomatridine (IV),[4] m.p. 53~55°. Though the high-pressure hydrogenation of (II) with copper chromite catalyst at high temperature afforded (IV), the same reaction at lower temperature gave the foregoing substance. Therefore, we assigned the structure of (III) to $C_{15}H_{22}ON_2$.

On the conformationl analyses of matrine and its isomeric allomatrine, some observations have been reported. (A) When matrine was submitted to hydrogenation over

1) H. Kondo, K. Tsuda : Ber., **68**, 644(1935).
2) K. Tsuda, S. Saeki, S. Imura, S. Okuda, Y. Sato, H. Mishima : J. Org. Chem., **21**, 1481(1956).
3) S. Okuda : This Bulletin, **4**, 257(1956).
4) C. Schöpf, H. Arm, G. Benz, H. Krim : Naturwiss., **38**, 186(1951); Platanov, Kuzovkov: J. Gen. Chem. (U.S.S.R.), **26**, 283(1956). The writers are indebted to Dr. Schöpf for the kind donation of a sample of *dl*-allomatridine.

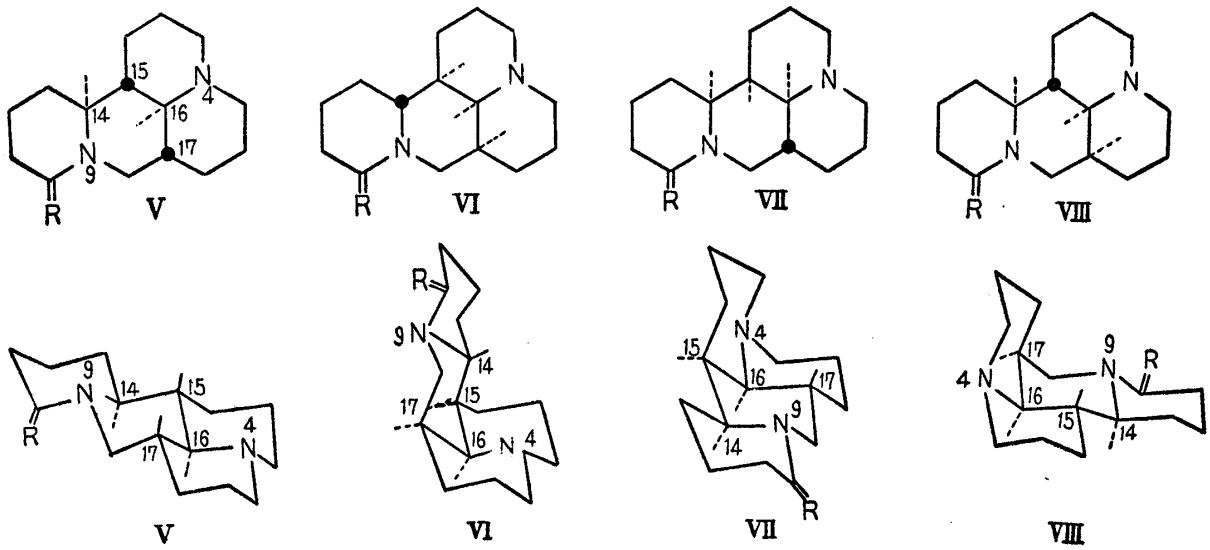


(Ia) R=Et
(Ib) R=H
(II) (III) (IV)

platinum oxide in acetic acid[5] or dehydrogenation over palladium catalyst,[6] allomatrine was produced. (B) Matrinic or allomatrinic acid was not changed to the corresponding isomer in either case by boiling them in alcoholic potassium hydroxide for 3 hours. In addition, soda lime distillation[7] of potassium matrinate always afforded matrine besides other products and the isomers of matrine were not found. (C) Cyanogen bromide did not attack the nitrogen atom at 4-position of matrine and matrine was recovered from reaction mixture,[1] but the reaction of the same reagent towards allomatrine under the same conditions afforded two kinds of bromoallomatrine cyanamide,[8] m.p. 126°(Calcd. for $C_{16}H_{24}ON_3Br$: C, 50.80; H, 6.80. Found. C, 51.00; H, 7.25), and m.p. 166°, which were separated from the non-basic fraction. (D) When matridine was heated with methyl iodide in methanol for 1 hour, N^9-methiodide[9] of m.p. 238~239° was produced, but the same treatment of allomatridine afforded N^4,N^9-dimethiodide, m.p. 296°(Calcd. for $C_{15}H_{26}N_2 \cdot 2CH_3I$: C, 38.80; H, 6.58; N, 4.80. Found : C, 39.00; H, 6.31; N, 4.90). (E) Treatment of potassium matrinate with methyl iodide in methanol under heating for 3 hours yielded methyl N^9-methyl matrinate N^9-methiodide,[5] while the reaction of potassium allomatrinate gave methyl N^9-methyl allomatrinate N^4,N^9-dimethiodide.[5] (F) The velocity[10] of hydrogen liberation of allomatrine during dehydrogenation over palladium asbestos was 1/4 of that of matrine and the velocity of allomatridine was 1/2 of matridine.

From the observations cited above, we assume that methylene linkages at 13—14 position in matrine and allomatrine are in stable, equatorial bond, indicating that the C and D rings are *trans*-fused. If so, the conformations that would be permitted for matrine and allomatrine to take are limited to the structures (V to VIII). Moreover, allomatrine would be the most stable (A) and nitrogen in its 4-position is not protected from attacks of reagents (C, D, E), while matrine is less stable than allomatrine (A) and its nitrogen at 4 is shielded by the C-D ring group from attacks of reagents (C, D, E). As for the configurations of hydrogen atoms attached to the carbon at 14-, 15-, 16-, 17-positions, we can assume[11] that matrine series possess more *cis*-H bonds than allomatrine series (F). These qualitative conformational analyses would be most logically understood by giving the structure (V) to allomatrine series and (VI) to matrine series.

5) E. Ochiai, S. Okuda, H. Minato : J. Pharm. Soc. Japan, **72**, 781(1952).
6) H. Kondo and Tsuda reported (cf. Footnote 1) that the recovered substance in this reaction was matrine, but from our recent reëxperiment it was found to be allomatrine.
7) H. Kondo : Arch. Pharm. u. Ber. Dtsch. Pharmaz. Ges., **266**, 4(1928).
8) Experimental data of S. Okuda (Unpublished).
9) E. Ochiai, H. Minato : J. Pharm. Soc. Japan, **73**, 914(1953).
10) Details will be published shortly.
11) Studies on the difference of the velocity of dehydrogenation reaction between *cis*- and *trans*-fused ring systems were made by many workers, e.g. M. Ehrenstein, W. Bunge : Ber. **67**, 1715(1935); B. Witkop : J. Am. Chem. Soc., **70**, 2617(1948); N. J. Leonard, B. L. Ryder : J. Org. Chem., **18**, 598(1953); E. Wenkert, L. H. Liu : Experientia, **11**, 302(1955); E. Wenkert, D. K. Roychaudhuri: J. Am. Chem. Soc., **79**, 1519(1957).



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