[CONTRIBUTION FROM THE INSTITUTE OF APPLIED MICROBIOLOGY, UNIVERSITY OF TOKYO]

Studies on the Synthesis of Matrine. II. The Synthesis of Octadehydromatrine and Allomatridine[1]

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Saponification of 11-ethoxycarbonyl-10-oxo-1,2,3,5,6,7-hexahydroquinolizo[1,8-*a*,*b*]quinolizine (Ia) yielded an acid Ib, m.p. 270–272°, which on heating with quinoline and copper sulfate formed octadehydromatrine (II). Catalytic hydrogenation of II over platinum oxide yielded didehydromatrine (III) which was converted to *rac*-allomatridine (IV) by high-pressure hydrogenation with copper chromite catalyst.

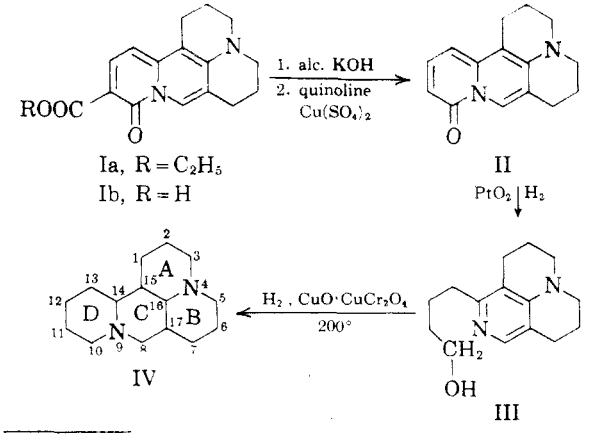
From the conformational analyses of the allomatrine series and its isomeric matrine series, the structure of allomatrine (Va), allomatridine (Vb), matrine (VIa), and matridine (VIb) were assigned.

Saponification of 11-ethoxycarbonyl-10-oxo-1,2,3,5,6,7-hexahydroquinolizo [1,8-*a*,*b*]quinolizine[3] afforded a carboxylic acid (Ib), m.p. 270–272°, and its decarboxylation by heating in quinoline with copper sulfate gave 10-oxo-1,2,3,5,6,7-hexahydroquinolizo[1,8-*a*,*b*]quinolizine (II), m.p. 174–176°; λ_{max}^{EtOH} mμ (log ε): 230 (4.36), 270 (4.05), 395 (4.22); ν quinolizone 1647 and 1518 cm.$^{-1}$ (KBr pellet). This was identified with octadehydromatrine,[4] obtained by the dehydrogenation of matrine with palladium, by mixed melting point and by comparison of their ultraviolet and infrared spectra.

Hydrogenation of II in acetic acid with platinum oxide catalyst afforded didehydromatrine,[4,5] whose ultraviolet spectrum exhibited absorption maxima at 226 mμ (log ε 4.32) and 274 mμ (log ε 4.18), and its hydrochloride showed maxima at 230 mμ (log ε 4.14) and 296 mμ (log ε 4.24). These absorption curves were similar to those[6] of dehydro-α-matrinidine (8-methyl-9-azajulolidine) and its hydrochloride, so that this hydrogenated product probably has a structure similar to those compounds, *i.e.* 8-alkyl-9-azajulolidine. The infrared spectrum of didehydromatrine had an absorption band at 3145 cm.$^{-1}$ besides those for the pyridine ring at 1592, 1558, and 1506 cm.$^{-1}$ (in Nujol). Since its benzoyl compound (as a hydrochloride) shows infrared absorption bands for ester C=O (1722 cm.$^{-1}$) and for C–O– (1281 and 1120 cm.$^{-1}$) (KBr pellet), the band at 3145 cm.$^{-1}$ is the absorption of OH. Therefore, it seems most appropriate to assume that didehydromatrine is 1-ω-hydroxybutyl-4,5,6,-8,9,10-hexahydropyrido [3,4,5-*i*,*j*]quinolizine (8-ω-hydroxybutyl-9-azajulolidine) (III) and this structure was conclusively determined by the formation of *rac*-allomatridine (IV) from III by the hydrogenation of the pyridine ring.

Therefore, this reaction effected reductive splitting of the =N–CO– bond in the quinolizone accompanied by aromatization to the pyridine ring, resulting in rearrangement to a 9-azajulolidine system. It is known that the 9-azajulolidine system is stable and is easily formed since it is obtained in good yield by the palladium dehydrogenation of 9-azahexahydrojulolidine;[3] furthermore the main reaction product from the palladium dehydrogenation of matrine is 8-propyl-9-azajulolidine,[5] and the soda-lime distillation of matrine affords a comparatively large amount of 9-azajulolidine, 8-methyl-9-azajulolidine, and 8-ethyl-9-azajulolidine.[4,7]

High-temperature and high-pressure hydrogenation of III with copper chromite catalyst resulted in the hydrogenation of the pyridine ring, with subsequent dehydration between the secondary amine in the piperidine ring and the primary alcohol group, affording perhydroquinolizo[1,8-*a*,*b*]quinolizine (IV) in a good yield. IV melts at 53–55° and agrees well with *rac*-allomatridine.[8] Through the hydrogenation of II with copper chromite catalyst below 170° gave III but IV was produced directly



(1) A brief report on this work appeared as a Communication to the Editor, *Pharm. Bull.* (*Tokyo*), **5**, 285 (1957).

(2) Present address: Takamine Research Laboratory, Sankyo Co., Ltd., Shinagawa, Tokyo.

(3) K. Tsuda, S. Saeki, S. Imura, S. Okuda, Y. Sato, and H. Mishima, *J. Org. Chem.*, **21**, 1481 (1956).

(4) R. H. F. Manske and H. L. Holmes, *The Alkaloids*, Vol. **III**, Academic Press Inc., New York, 1953, p. 178.

(5) H. Kondo and K. Tsuda, *Ber.*, **68**, 644 (1935).

(6) S. Okuda, *Pharm. Bull.* (*Tokyo*), **4**, 257 (1956).

(7) E. Ochiai and S. Okuda, *Pharm. Bull.* (*Tokyo*), **1**, 266 (1953); *Chem. Abstr.*, **49**, 8316 (1955).

(8) C. Schöpf, H. Arm, G. Benz, and H. Krim, *Naturwissenschaften*, **38**, 186 (1951); T. F. Platonov and A. D. Kuzovkov, *Zhur. Obshchei Khim.*, **26**, 283 (1956).

from II when the reaction temperature was above 200°.

In the ring system of matridine, there are eight geometrical isomers, two of which are matridine and allomatridine. There is some evidence useful in the conformational analysis of allomatrine and matrine. Matridine and allomatridine are respectively formed from matrine and allomatrine by reduction with lithium aluminum hydride[9] through the conversion of lactam carbonyl in the starting materials to methylene groups. It is clear that the allo series is more stable because matrine is isomerized to allomatrine on catalytic hydrogenation with platinum oxide[9] and forms allomatridine by high-temperature hydrogenation with copper chromite catalyst.[10]

In the present series of experiments, on the palladium dehydrogenation of matrine and matridine at 280°, we obtained allomatrine[11] and allomatridine. Isomerization of matridine with aluminum trichloride[12] at 220° afforded allomatridine. These reactions are analogous to those reported before in the conversion of sparteine[12] to α-isosparteine ($AlCl_3$) and in the conversion of sparteine[13] and anagyrine[14] respectively to α-isosparteine and thermopsine(Pd). Przbylska and Barnes[15] have definitely determined the conformation of α-isosparteine to have the all *trans* chair form by x-ray crystal analysis. Therefore, we can conceive that the allo series takes the most stable conformation *i.e.* all four ring-junctures with the chair form[16] are *trans*.

Measurement of palladium–dehydrogenation velocity[17] at 280° indicated that the evolution of hydrogenation in allomatrine was 27% of that of matrine 5 min. later, and that of allomatridine was 68% of that of matridine 5 min. later, showing that the dehydrogenation velocity of matridine series was always faster than that of allo series. This proves that the matridine series contains a larger number of *cis*-hydrogens and this agrees with the foregoing observation.

On the other hand, both matrine and allomatrine suffer cleavage of the lactam ring by the action of alcoholic potassium hydroxide to form the alkali salts of matrinic acid[4,18] and allomatrinic acid.[9] When the respective alkali solution is refluxed for a few hours, treated with ammonium chloride to form the original acid, and then heated, they respectively return to matrine and allomatrine without isomerization into the other series during this reaction. Soda-lime distillation of potassium matrinate affords matrine and its isomer is not obtained.

From the foregoing facts and the results of following experiments, it is concluded that the formula (V) should be assigned to the allomatridine series and formula (VI) for matridine series.

Matrine (VIa) remains inert to heating with cyanogen bromide in benzene, and the starting material is recovered,[5] while allomatrine (Va) forms bromoallomatrine-cyanamide (IX), m.p. 167–168.5°, in good yield under the same conditions.

Matridine (VIb),[19] when refluxed for 1 hr. in methanol with methyl iodide, forms N^9-methiodide[20] (XI), but allomatridine (Vb) forms N^4,N^9-dimethiodide (X), m.p. 296°, by the same reaction. Similar phenomena are observed in the reaction of potassium matrinate (XIII) and potassium allomatrinate (XII) with methyl iodide. While XIII forms N^9-methylmatrinate N^9-methiodide[21] (XV), XII forms N^9-methylallomatrinate N^4,N^9-dimethiodide (XIV).[9] These experimental facts indicate that the nitrogen atoms at 4 and 9 in allomatridine series are open to the attack of reagents while in matridine series, the nitrogen at 9 is open to the attack but that at 4 is shielded.

These properties can be explained by assuming all *trans* juncture for the ring system (V) in allomatridine series, and the formulas (VI and VI′) for matridine series. Of the six formulas (VI, VI′, VII, VII′, VIII, VIII′), the front side of nitrogen at 4 in VII, VII′, VIII, and VIII′ is shielded by the B- and C-rings, but the side of lone pair electrons of nitrogen is open to rear-side attack, while the lone-pair electron side of nitrogen in formulas VI and VI′ is shielded by the C-ring, so that the attack of chemical reagent on nitrogen at 4 is interfered with.

(9) E. Ochiai, S. Okuda, and H. Minato, *Yakugaku Zasshi*, **72**, 781 (1952); *Chem. Abstr.*, **48**, 2724 (1954).

(10) E. Ochiai, J. Haginiwa, and S. Okuda, *Yakugaku Zasshi*, **71**, 1279 (1951); *Chem. Abstr.*, **46**, 5604 (1952).

(11) The recovery of matrine reported by H. Kondo and K. Tsuda (footnote 5) was found to have been incorrect by later experiments.

(12) F. Galinovsky, P. Knoth, and W. Fischer, *Monatsh. Chem.*, **86**, 1014 (1955).

(13) N. J. Leonard, P. D. Thomas, and V. W. Gash, *J. Am. Chem. Soc.*, **77**, 1552 (1955).

(14) Unpublished data of Tsuda, *et al.*

(15) M. Przbylska and W. H. Barnes, *Acta Cryst.*, 6, 377 (1953).

(16) From this deduction, in this paper, we use chair form for all structures.

(17) Data regarding the difference in dehydrogenation velocity in *cis*- and *trans*-fused ring systems will be given in the following paper. *Cf.* M. Ehrenstein and W. Bunge, *Ber.*, **67**, 1715 (1935); B. Witkop, *J. Am. Chem. Soc.*, **70**, 2617 (1948); N. J. Leonard and B. L. Ryder, *J. Org. Chem.*, **18**, 598 (1953); E. Wenkert and L. H. Lin, *Experientia*, **11**, 302 (1955); E. Wenkert and D. K. Roychaudhuri, *J. Am. Chem. Soc.*, **79**, 1519 (1957).

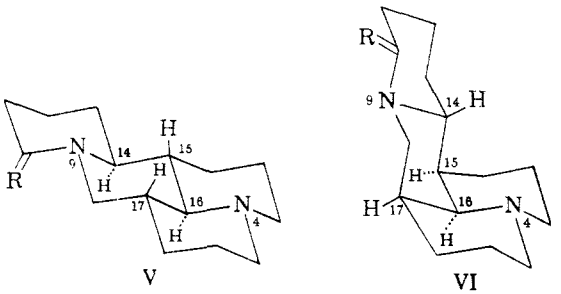
(18) H. Kondo and E. Ochiai, *Arch. Pharm.*, **266**, 4 (1928).

(19) Matrine is recovered when it is refluxed with methyl iodide for 5 hr. but matrine methiodide is obtained when a mixture of matrine and methyl iodide is heated in a glass tube at 100°.

(20) E. Ochiai and H. Minato, *Yakugaku Zasshi*, **73**, 914 (1953); *Chem. Abstr.*, **48**, 11438 (1954).

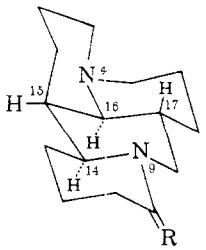
(21) Although reference to this salt was made earlier (see footnote 19), there was no proof whether the ammonium-type nitrogen was at 4 or 9. In the present case, it must be considered identical with that of matridine (see footnote 20).

Catalytic conversion of the matrine series to the allo series can well involve isomerization at both C-14 and C-16, so we could consider[22] the existence of an isomer of VI, VI′ with rings C/D *cis*-fused and the side chain axial (C-14). This would afford even greater hindrance to reactions involving *N*-4 than does structure VI.

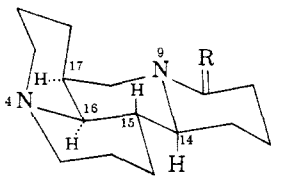


V

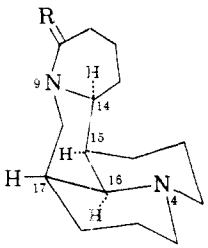
VI



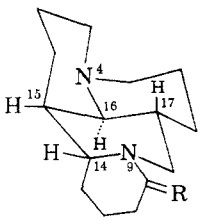
VII



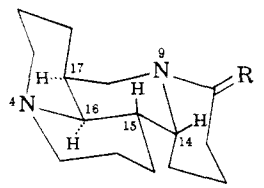
VIII



VI′



VII′



VIII′

a, R = O (matrine, allomatrine)
b, R = H_2 (matridine, allomatridine)

However, we can assume from the analogous result[23] in the reaction of methyl iodide toward a pair of isomers of hexahydrojulolidine (picrates, m.p. 187° and 226°) that the shielding effect would be afforded even by the C-ring of VI and that the greater hindrance due to C/D-*cis* isomer, VI′, would not be essential for the explanation of the hindrance. Moreover, the steric hindrance between the hydrogen atoms at C-2 and C-13 in VI′ would be inadequate to explain the stability of matrine (or matridine) during the drastic reactions of matrine series, such as soda-line distillation. Thus one can eliminate VI′ for matrine series leaving only VI for it.

Support[24] for formulas V and VI from dipole moment data will be reported in a separate paper.

EXPERIMENTAL[25]

11-Carboxy-10-oxo-1,2,3,5,6,7-hexahydroquinolizo[1,8-a,b]quinolizine (Ib). To a solution of 280 mg. of the ester (Ia) dissolved in 20 ml. of 95% ethanol, an aqueous solution of potassium hydroxide (130 mg. in 2 ml. of water) was added and the mixture was refluxed for 3 hr. Ethanol was distilled from the solution, 20 ml. of water was added to the residue, and the solution was neutralized with hydrochloric acid. A yellow substance was precipitated at *p*H 6 to give 200 mg. of crystals, m.p. 250° (with decomp.); yield, 77%. Several recrystallizations from pyridine raised the decomposition point to 272°.

Anal. 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.

λ_{max}^{EtOH} mμ (log ε): 230 (4.36), 270 (4.05), 395 (4.22). ν (COOH) 1712 cm^{-1}, ν (quinolizone) 1656, 1658, and 1661 $cm.^{-1}$ (KBr pellet).

10-Oxo-1,2,3,5,6,7-hexahydroquinolizo[1,8-a,b]quinolizine (II). A solution of 410 mg. of Ib dissolved in 5 ml. of quinoline, in which 40 mg. of crystalline copper sulfate was suspended, was heated for 2 hr. at 210–240° (bath temp.), quinoline was distilled off under reduced pressure, and the residue was dissolved in benzene. The benzene solution was washed with 10% sodium carbonate solution, dried over potassium carbonate, and passed through an alumina layer. Benzene was evaporated from the effluent and 50 mg. of yellow crystals, m.p. 167–170°, were obtained. Recrystallization from acetone raised the melting point to 174–176°, undepressed on admixture with the octadehydromatrine obtained by the palladium dehydrogenation of matrine.

Anal. Calcd. for $C_{15}H_{16}ON_2$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.02; H, 6.80; N, 11.68.

1-ω-Hydroxybutyl-4,5,6,8,9,10-hexahydropyrido[3,4,5-i,j]-quinolizine (didehydromatrine) (III). This was prepared from II by catalytic hydrogenation with platinum dioxide according to procedures described in the literature,[5] or by the following method.

A solution of 1 g. of II dissolved in 10 ml. of dioxane was mixed with 0.75 g. of copper chromite. The mixture was heated for 4 hr. at 160–170°, with initial hydrogen pressure of 100 atm. Recrystallization of the product from acetone gave colorless crystals of m.p. 105–106°.

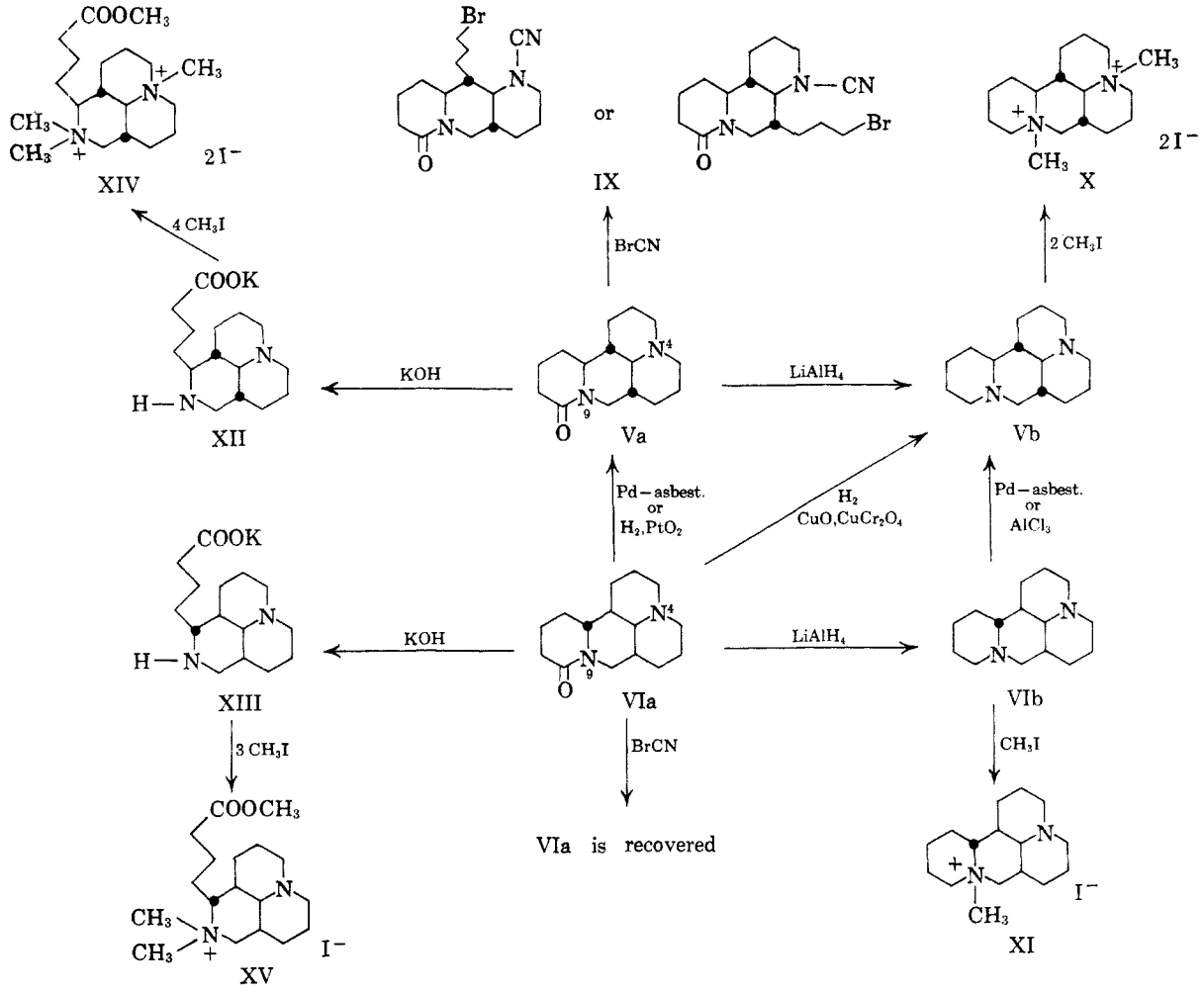
Anal. Calcd. for $C_{15}H_{22}ON_2$: C, 73.13; H, 9.00; N, 11.37. Found: C, 73.07; H, 8.87; N, 11.72.

(22) We are greatly indebted to the referees of this paper. They kindly pointed out that we overlooked this isomer at first.

(23) Unpublished work has revealed the following facts: hydrogenation of julolidine affords a pair of hexahydrojulolidines, one of which (picrate, m.p. 187°) reacts with methyl iodide while another (picrate m.p. 226°), which is convertible to the former with aluminum chloride, does not.

(24) After the appearance of our brief report (footnote 1), Bohlmann, *et al.* assigned the same structures for matrine and allomatrine by infrared spectra between 2700–2800 $cm.^{-1}$ and by some other chemical evidences which differ from ours. [F. Bohlmann, W. Weise, and D. Rahtz, *Angew. Chem.*, 69, 642 (1957); *cf.* F. Bohlmann, W. Weise, H. Sauder, *Ber.*, 90, 653 (1957)].

(25) All melting points and boiling points are uncorrected. Microanalyses were done by Mr. T. Onoe of the Takamine Research Laboratory, Sankyo Co., Ltd. Infrared spectra were measured on a Perkin-Elmer Model 21 double-beam recording spectrophotometer.



Perhydroquinolizo[1,8-a,b]quinolizine (IV) (*rac-allomatridine* IV). To a solution of 1.40 g. of III dissolved in 16 ml. of dioxane was added 0.60 g. of copper chromite and the mixture was heated for 3 hr. at 200–210° with an initial hydrogen pressure of 120 atm. The base obtained as a product was recrystallized from petroleum ether, m.p. 53–55°.

Anal. Calcd. for $C_{15}H_{26}N_2$: C, 76.86; H, 11.18; N, 11.95. Found: C, 76.92; H, 11.24; N, 12.12.

IV was also obtained from II under the same conditions. There was observed no depression of the melting point on admixture of IV with *d,l*-allomatridine,[8] m.p. 53–54°, by Schöpf.

Dehydrogenation of matridine with palladium-asbestos. A mixture of 5 g. of matridine[26] (VIb), m.p. 60°, and 2 g. of 40% palladium-asbestos was heated at 310–340° for 3 hr., during which 1200 ml. of hydrogen was generated. The base obtained was distilled to collect the fraction of b.p. 98–130°/1 mm., to which acetone and concd. hydriodic acid was added. The hydriodide (4.5 g.) so formed was recrystallized from acetone-methanol to give 3 g. of plates, m.p. over 220°. Further recrystallizations from the same solvent separated it into two kinds of crystals; the sparingly soluble needles, m.p. 305–310°, and somewhat soluble plates, m.p. 285–290°. Liberation of the base from the high-melting salt afforded allomatridine[27] (Vb), m.p. 76–78°, and the lower-melting salt regenerated the starting matridine.

The mother liquor left after separation of the hydriodides was concentrated and crystals that separated out were recrystallized from acetone to give 200 mg. of colorless plates, m.p. 194–195°.

(26) Optically active. α_D −11.6°.

Anal. Calcd. for $C_{15}H_{22}N_2 \cdot HI$: C, 50.20; H, 6.42; N, 7.82 Found: C, 50.44; H, 6.42; N, 8.58.

Ultraviolet absorption: λ_{max}^{EtOH} 296 mμ (log ε 4.22).

The structure of this substance has not been determined but it is assumed to be of 9-azajulolidine system because of its infrared absorptions at 1639, 1597, and 1548 cm.$^{-1}$ (KBr pellet) indicating the presence of a pyridine ring, the formation of a monohydriodide, and the character of its ultraviolet absorption curve.

Isomerization of matridine with aluminum chloride. A mixture of 2.6 g. of matridine[26] (VIb) and 2.6 g. of aluminum chloride was kept at 220° for 9 hr. in a nitrogen stream. This was dissolved in 5% hydrochloric acid, basified, and extracted with ether. The base obtained on evaporation of ether was distilled under reduced pressure. The distillate deposited 0.5 g. of crystals, m.p. 72–74° when petroleum ether was added. Recrystallization raised the melting point to 76–78°, identical with allomatridine[27] (Vb).

Dehydrogenation of matrine,[28] *allomatrine,*[29] *matridine,*[26] *and allomatridine.*[27] The apparatus and method followed those reported by Hyman.[30] Five hundred milligrams of the base and 200 mg. of 40% palladium-asbestos were used. The reaction vessel was immersed in a metal bath of 280° and the mixture was heated rapidly to 307° ± 3° in carbon

(27) Optically active. α_D +28.2°.

(28) Natural substance shows α_D +39.1°.

(29) Prepared by the isomerization of matrine. α_D +77.9°.

(30) L. F. Fieser, *Experiments in Organic Chemistry,* 2nd Ed., D. C. Heath and Co., New York, 1941, pp. 458–464.

	Hydrogen Gas Generated, Ml.								
Time (min.)	1	2	3	4	5	6	7	10	13
Sample									
Matrine	8.5	29.3	50.0	65.3	78.0	87.3	—	—	—
Allomatrine	1.1	5.1	10.2	15.2	21.1	26.2	31.0	43.9	54.1
Matridine	0.5	2.1	4.4	7.1	9.1	10.2	11.4	14.0	15.0
Allomatridine	0.4	2.0	4.1	5.2	6.2	7.0	7.2	8.2	—

dioxide stream and the hydrogen gas that generated was determined by azotometer.

Reaction of matrine and allomatrine with cyanogen bromide. A solution of 5 g. of allomatrine[29] dissolved in 30 ml. of dry benzene was warmed on a water bath to 60–70° and a solution of 2.3 g. of cyanogen bromide dissolved in 20 ml. of dry benzene was added dropwise. The mixture was heated for 30 min., the solvent was distilled off, and the residue was dissolved in chloroform. The chloroform solution was washed with 10% hydrochloric acid, dried over potassium carbonate, and the solvent distilled off. Addition of acetone to the residue separated some crystals which were washed with acetone and afforded 4.0 g. of bromoallomatrine cyanamide (IX), m.p. 153–157°. Further crystallization from acetone gave plates, m.p. 167–168°.

Anal. Calcd. for $C_{16}H_{24}ON_3Br$: C, 54.23; H, 6.80; N, 11.86. Found: C, 54.03; H, 6.85; N, 12.00.

The reaction of matrine with cyanogen bromide has already been described.[5]

Reaction of matridine[26] and allomatridine[27] with methyl iodide. A solution of 500 mg. of the base dissolved in 2 ml. of methanol and 1 g. of methyl iodide was refluxed for 1 hr., cooled, and crystals that separated out were recrystallized.

Allomatridine N^4,N^9-dimethiodide (X): plates (from methanol-water), m.p. 293–296° (decomp.).

Anal. Calcd. for $C_{15}H_{28}N_2 \cdot 2CH_3I$: C, 38.80; H, 6.58; N, 4.80. Found: C, 39.00; H, 6.41; N, 4.90.

Matridine N^9-methiodide (XI): white prisms (from acetone), m.p. 238–239°.

Anal. Calcd. for $C_{15}H_{26}N_2 \cdot CH_3I$: C, 50.10; H, 7.71; N, 7.44. Found: C, 50.75; H, 7.75; N, 7.29.

Acknowledgment. We thank Dr. C. Schöpf (Darmstadt) for kindly supplying a sample of *rac*-allomatridine. We are also very grateful to Dr. T. F. Platonov (Moscow), who had generously given us a sample of isoleontine.

Hongo, Tokyo, Japan

[Contribution from the Pharmaceutical Laboratory, Medical School Keio-Gijuku University]

Santonin and Related Compounds. XVII.[1] Reactions of the Bromo Derivatives of 4,9-Dimethyl-Δ^4-3-octalone-6-acetic Acid with Bases

SEIICHI INAYAMA

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The monobromides (IIa and IIb) of the *trans*- and *cis*-ketones (Ia and Ib) mentioned in the title were treated with a variety of bases. In most cases, the $\Delta^{4,5}$-dienones (IV and V) and the lactones (IIIa and IIIb) were obtained as the expected products. With aqueous alkali, each of the monobromides was converted in low yield to the corresponding α-ketol (VIIa or VIIb) under allylic rearrangement. As other anomalous products, a bromo lactone (VIa) and the $\Delta^{1,4}$-dienone acid (VIIIa) were obtained from the *trans*-monobromide (IIa) in a few instances. Reactions of the dibromides (IXa and IXb) with bases led predominantly to the bromo lactones (VIa and VIb), respectively. A probable mechanism for the unusual reactions of the monobromides with bases is discussed.

Miki has reported[2] that treatment of the 5-bromo compound (II) of the keto acid (I) with alkali led to a liquid lactone (III) in unspecified yield. Gunstone and Tulloch[3] have disclosed the isolation of a solid lactone (III) in low purity from the same monobromide (II) on reaction with sodium ethoxide. Ishikawa[4] has reported that the enol acetate of the malonate analog of the acetic acid compound (I), which was said to be a precursor for I, was treated with peracid followed by hydrolysis-decarboxylation of the resulting lactone ester to give two solid isomers of III. The melting points reported for these solid lactones were rather different. The starting keto acid (Ia), at that time regarded as *cis*, was recently revised to be *trans*, possessing the acetic acid side chain axial.[5] From steric considerations, it is obvious that the result of Ishikawa[4] is most unlikely. The purpose of this investigation was to reexamine the reaction of the *trans*-monobromide (Ia) with base and to study, for comparison purposes, the behavior of the *cis*-monoenone (Ib)[5] upon bromination and subsequent treatment with bases.

It has been reported[2,3] that monobromination of the *trans*-monoenone (Ia) with *N*-bromosuccinimide afforded a good yield of the 5-bromo compound (IIa). The simpler procedure using one equiv-

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