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17. Hitoshi Minato and Ken'ichi Takeda : Synthesis of Matrine Derivatives. III.[1] Studies on the von Braun Degradation of Matridine.

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In the preceding paper of this series,[2] it was reported that matridine (I) gave a monomethiodide quaternarized at 9-N, whereas allomatridine[3] (II) gave a dimethiodide. Since matridine (I) and allomatridine (II) are shown by the steric formulae (I') and (II'),[4,5] respectively, the lone-pair electrons of 4-N of matridine (I') are sterically hindered by the rings C and D, and the lone-pair electrons of 4-N of allomatridine (II') are not sterically hindered. Accordingly, (I') gave only the monomethiodide and (II'), the dimethiodide.

In this paper will be described the steric effect on von Braun degradation of matridine (I) and the structural elucidation of the degradation product.

In the beginning, *l*-sparteine (III), an isomer of matridine (I), was chosen as a reference compound and its degradation was examined in order to compare the behavior of these compounds in this reaction. When *l*-sparteine (III) was treated with 2 equivalents of cyanogen bromide at refluxing temperature of benzene, monobromosparteine-monocyanamide was obtained as colorless needles, m.p. 86°, whereas on treatment of (III) with cyanogen bromide at refluxing temperature of toluene, monobromosparteine-monocyanamide and dibromosparteine-dicyanamide, colorless prisms, m.p. 136~138°, were obtained.

However, when matridine (I) was treated with 2.2 equivalents of cyanogen bromide at refluxing temperature of benzene or toluene, only monobromomatridine-monocyanamide (IV), colorless prisms, m.p. 49°, was obtained in 84% and 14% yield, respectively. It was just as expected that dibromomatridine-dicyanamide was not obtained at all in the case of the degradation of (I) with cyanogen bromide. Added with the results obtained in the quaternarization of (I), the structure of monobromomatridine-monocyanamide should be either (IVa), (IVb), or (IVc), cleaved around 9-N.

Subsequently, (IV) was hydrogenated with 38% palladized charcoal in methanol containing potassium hydroxide and then heated with conc. hydrochloric acid in a sealed tube at 100~110° to yield the corresponding secondary amine (V) as colorless needles, m.p. 67~68°, in a good yield. This secondary amine is positive to Liebermann's color-test for a secondary amine and should be either (Va), (Vb), or (Vc); but when its acylation was attempted by the application of *p*-nitrobenzoyl chloride, only the starting material was recovered.

On treatment with methyl iodide, the amine (V) gave a monomethiodide (XIV), m.p. 220~221°, which possessed an absorption band at 3497 cm^{-1} related to N-H stretching frequency, and this was converted to the original amine (V) by Hofmann degradation, no N-methylated compound being obtained. Therefore, it seemed somewhat doubtful that the compound (V) was the anticipated secondary amine. However, the structure of the secondary amine (V) was supported by its infrared absorption band at 3247 cm^{-1} (N-H) and by the degradation reaction described below. Although alkaline air-oxidation of (V) or oxidation of (V) with copper chromite in decalin resulted in the recovery of the starting material, matridine (I) was obtained from (V) in 25~30% yield on allowing to stand at room temperature for

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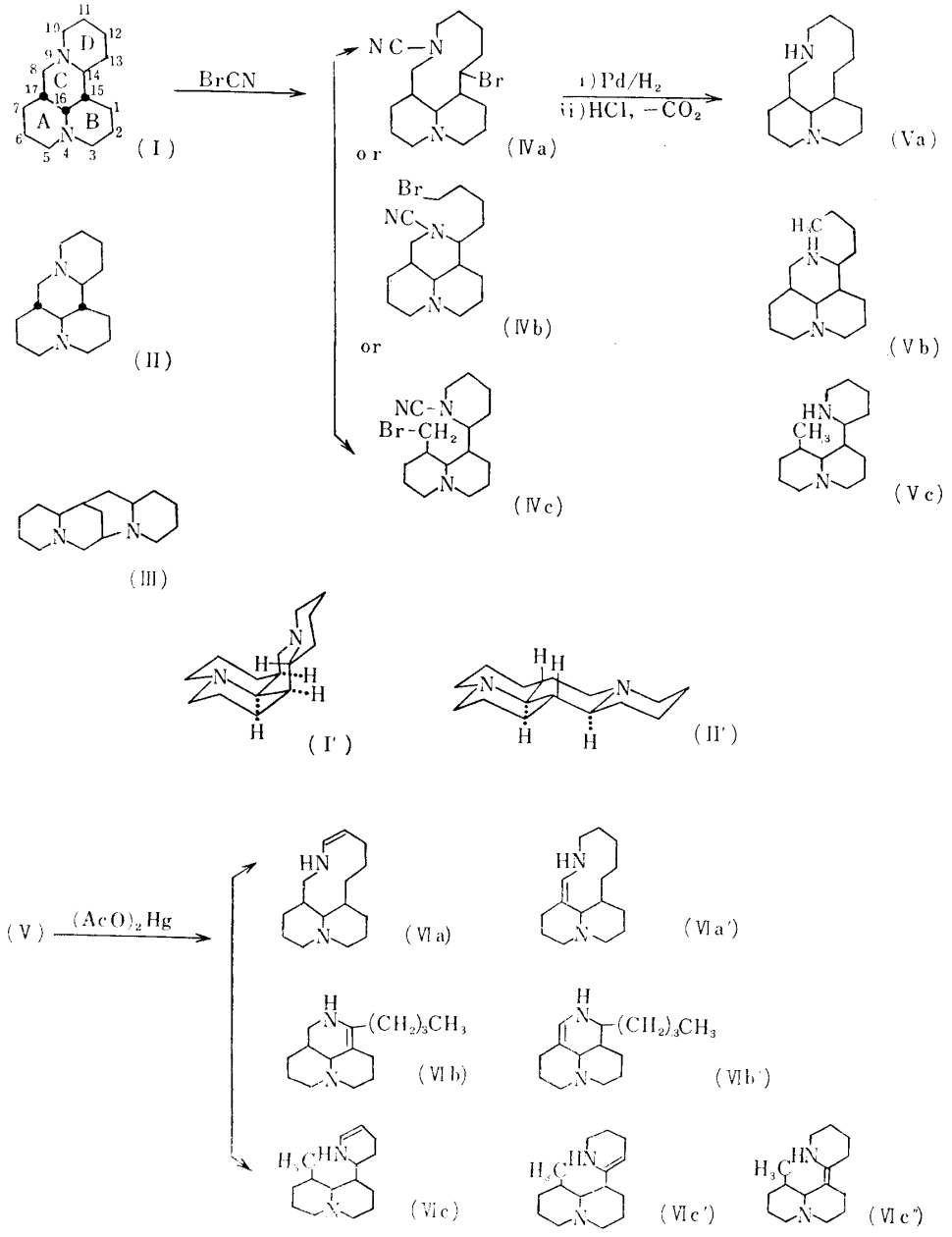
1) Part II : This Bulletin, **9**, 92 (1961).
2) E. Ochiai, H. Minato : Yakugaku Zasshi, **73**, 914 (1953).
3) E. Ochiai, S. Okuda, H. Minato : *Ibid.*, **72**, 781 (1952).
4) F. Bohlmann, W. Weise, D. Rahtz : Angew. Chem., **69**, 642 (1957).
5) K. Tsuda, H. Mishima : This Bulletin, **5**, 285 (1957).

eight months. This fact and the following dehydrogenation with mercuric acetate are powerful keys to reveal the structure of (V).

(V) was dehydrogenated with 8 equivalents of mercuric acetate in dilute acetic acid at 40° for 50 days or at refluxing temperature for 9 hours to furnish colorless needles, m.p. 84°. This crystalline substance, the enamine (VI), was weakly positive to Liebermann's color-test for a secondary amine and possessed one double bond which absorbed one molar hydrogen to yield (V) by catalytic hydrogenation. It did not indicate any maximum of absorption beyond 220 mμ in the ultraviolet spectrum, and possessed absorption bands at 3247 (ν_{N-H}), 3030 (ν^{II}_{C-H}), 2750~2800, 1650 ($\nu_{C=C}$), and 705 cm^{-1} in its infrared spectrum. The strong absorption band at 1650 cm^{-1} is probably related to the double bond with a negative atom, i.e. O or N,[6] and the absorption band at 3030 cm^{-1} and the strong band at 705 cm^{-1}, which disappeared by catalytic hydrogenation, indicate that this double bond is *cis*-disubstituted.



6) H. Rosenkrantz, M. Gut : Helv. Chim. Acta, **36**, 1000 (1953).

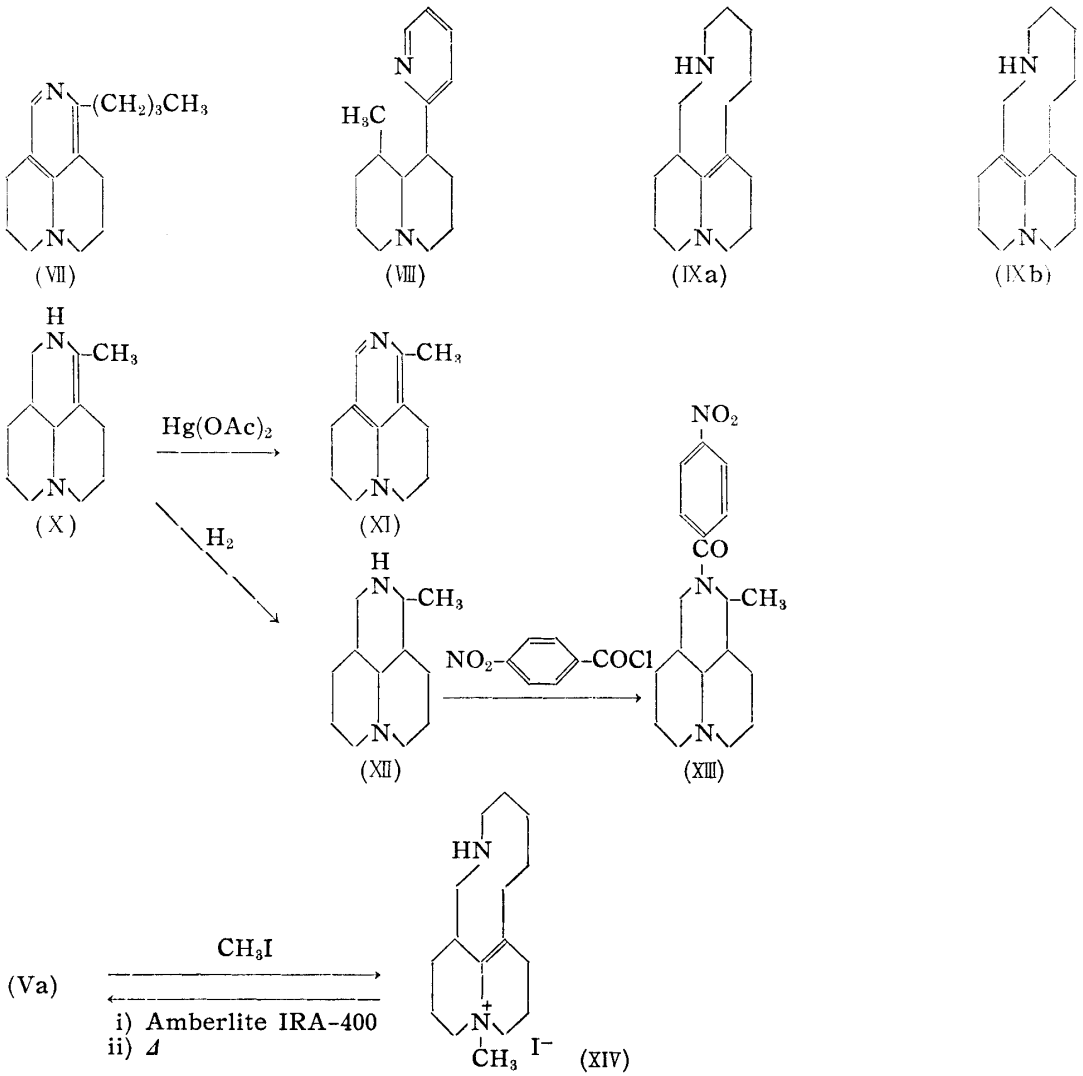


Chart 1.

The strong absorption band*[2] at 2750~2800 cm^{-1} was proposed by Bohlmann[7] as being related to *trans*-quinolizidine and this band was also found in matrine, matridine,[7] and (V). These facts show that *trans*-quinolizidine ring (A and B rings) of (V) was not affected by treatment with mercuric acetate; there was no double bond at 16–17 (IXa) or 16–15 (IXb). Leonard[8] studied the dehydrogenation of tertiary amine with mercuric acetate and reported that the normal order of removal of hydrogen from the α-N-carbon was *tert*-C-H, *sec*-C-H, *prim.*-C-H, and that *trans*-quinolizidine reacted more rapidly than *cis*-quinolizidine. On the other hand, Bohlmann[7] reported that a ring system with distortion reacted more rapidly with mercuric acetate than a compound of stable conformation. From these investigations on dehydrogenation with mercuric acetate by Leonard and Bohlmann, it is unlikely that ring A or B is dehydrogenated with mercuric acetate. Consequently, the enamine obtained by dehydrogenation of (V) with mercuric acetate should be either one of (VIa), (VIa'), (VIb), (VIb'), (VIc), (VIc'), and (VIc'').

*[2] Since (XIV), the methiodide of (V), no longer showed this absorption band in its infrared spectrum, it was concluded that the absorption band at 2750~2800 cm^{-1} is related to *trans*-quinolizidine ring (A and B rings) of (V).

7) F. Bohlmann : Angew. Chem., **69**, 641 (1957); Chem. Ber., **91**, 2157 (1958).
8) N. J. Leonard, A. S. Hay, R. W. Fulmer, V. W. Gash : J. Am. Chem. Soc., **77**, 439 (1955); N. J. Leonard, D. F. Morrow : *Ibid.*, **80**, 371 (1958).

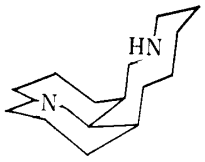
In order to determine the correct formula, the following considerations were made : (1) (VIa'), (VIb), (VIb'), (VIc'), and (VIc'') are unlikely, because the infrared spectrum of enamine possesses an absorption for *cis*-disubstituted double bond.

(2) α-Matrinidine (X) was easily dehydrogenated to dehydro-α-matrinidine (XI) under rather milder conditions than in the reaction of (V),[9] while (VII) was not obtained in the present series of work. From this fact, (VIb) and (VIb') are unlikely.

(3) If the enamine is represented by (VIc), (VIc'), or (VIc''), (VIII) should reasonably be formed in the present conditions of dehydrogenation; but (VIII) was not obtained at all. Therefore (VIc), (VIc'), and (VIc'') should be omitted.

(4) Ochiai and Tsuda[10] obtained (XIII) by the acylation of dihydro-α-matrinidine (XII), formed by hydrogenation of α-matrinidine (X) with *p*-nitrobenzoyl chloride. Application of *p*-nitrobenzoyl chloride or methyl iodide to (V) resulted in recovery of the starting material, as stated above, and the secondary amine (Vb), as well as (VIb) and (VIb'), are also unlikely. It was therefore concluded that the constitution of the secondary amine (V) is represented by formula (Va), and its dehydrogenated product, the enamine (VI), by formula (VIa).

This ten-membered ring system containing nitrogen, in the left figure, shows that the NH group resists acylation or methylation because it is sterically much hindered by the quinolizidine ring in addition to its position in the ten-membered ring, if the formula (Va) can explain the fact that the secondary amine (V) is oxidized to matridine (I) on being allowed to stand in the air for a long time.



Finally, examination was made to see whether perhydroazecine (XXI), a ten-membered ring compound, resists acylation or not. This amine was prepared by Ruzicka's method[11] (see Chart 2) and the perhydroazecine (XXI) obtained in this way gave

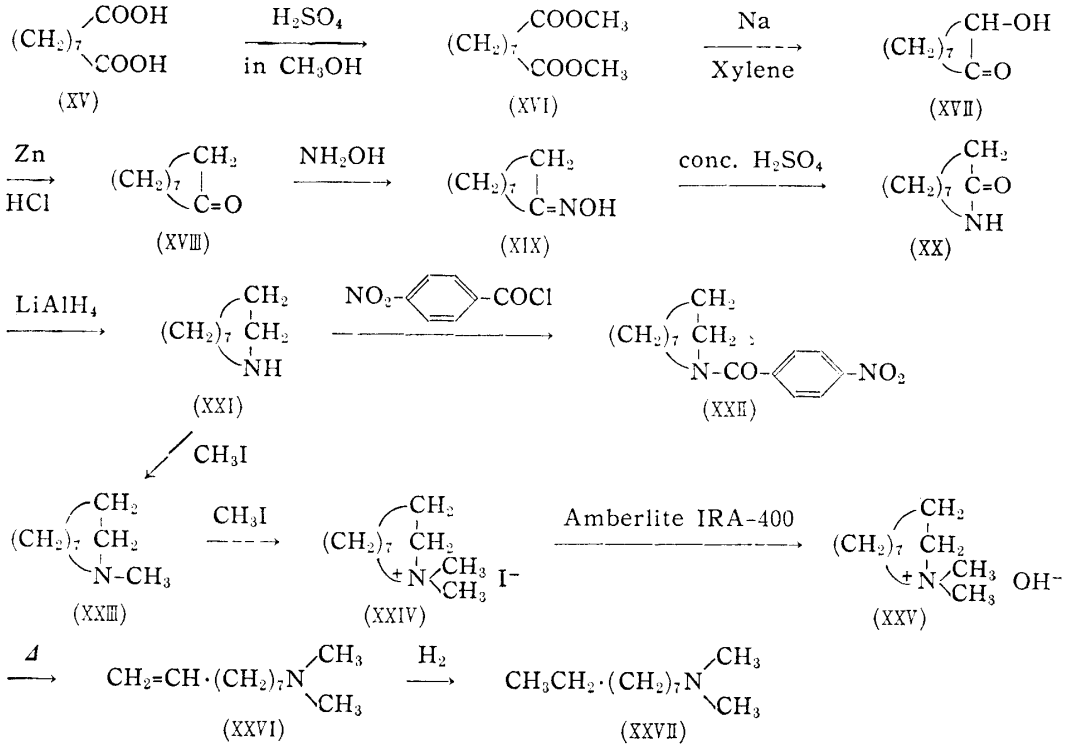


Chart 2.

9) H. Kondo, K. Tsuda : Yakugaku Zasshi, **51**, 533 (1931).
10) H. Kondo, E. Ochiai, K. Tsuda, S. Yoshida : Chem. Ber., **68**, 570 (1953); Yakugaku Zasshi, **55**, 483 (1935).
11) L. Ruzicka, M. Kobelt, O. Häfliger, V. Prelog : Helv. Chim. Acta, **32**, 544 (1949).

a picrate, m.p. 182~183°, and a chloroaurate, m.p. 123~125°(decomp.), and acylation of (XXI) with *p*-nitrobenzoyl chloride yielded an acylated derivative (XXII) of colorless needles, m.p. 71~73°. Application of methyl iodide to (XXI) gave a quaternary salt (XXIV) which was decomposed by Hofmann degradation to N,N-dimethyl-8-nonenylamine (XXVI).

The fact that (XXI) does react ordinarily on acylation or methylation indicates that the cause of abnormal reactivity of the NH group in (Va) is not merely its position in the ten-membered ring system but the severe steric hinderance it receives by the quinolizidine and ten-membered ring, as stated above.

Experimental

All paper partition chromatography was carried out with the solvent system of BuOH-EtOH-0.5*N* AcOH (6:2:3) by the ascending method; detection reagent, 10% H_2PtCl_6-4% KI-H_2O (1:25:24).

von Braun Degradation of *l*-Sparteine (III)—A solution of 3.0 g. (2.2 equiv.) of BrCN in 30 cc. of dehyd. toluene was added dropwise into a solution of 3.0 g. of *l*-sparteine in 30 cc. of dehyd. toluene, with stirring at 85~90° for 50 min. This mixture was refluxed with stirring for 2.5 hr., during which time some crystalline substance separated from the solution, and the mixture was allowed to stand overnight at room temperature.

After filtration, collected crystals, m.p. 234° (decomp.) (from MeOH-Et_2O), were dissolved in water, made alkaline with conc. NH_4OH, and extracted with Et_2O. The residue obtained upon removal of the solvent was recrystallized from petr. ether-Et_2O to yield 1.55 g. of monobromosparteine-monocyanamide as colorless needles, m.p. 84~86°. *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot BrCN$: C, 56.47; H, 7.65. Found: C, 56.65; H, 7.38.

The toluene solution was evaporated *in vacuo* to leave 4.0 g. of a dark red oil which was dissolved in 3% HCl, extracted with Et_2O and then with $CHCl_3$, and 2.3 g. of an orange oil was obtained from the Et_2O extract and was crystallized with the addition of Me_2CO and Et_2O. Recrystallization from Me_2CO-Et_2O gave dibromosparteine-dicyanamide as colorless prisms, m.p. 136~138°; yield, 400 mg. *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot 2BrCN$: C, 45.74; H, 5.83. Found : C, 45.94; H, 5.23.

From the $CHCl_3$ extract, 150 mg. of a dark red oil was obtained. The oil was dissolved in 3% HCl, made alkaline with K_2CO_3, and extracted with Et_2O. The residue obtained upon removal of the solvent was crystallized with the addition of Et_2O to yield 1.0 g. of monobromosparteine-monocyanamide as colorless needles, m.p. 82~83°, undepressed on admixture with the crystals, m.p. 84~86°, described above.

von Braun Degradation of Matridine (I)—A solution of 4.0 g. (2.2 equiv.) of BrCN in 40 cc. of dehyd. benzene was added dropwise to a solution of 4.0 g. of matridine (I) in 40 cc. of dehyd. benzene with stirring at 79~80° for 1 hr. This mixture was refluxed for 3.5 hr. and allowed to stand at room temperature overnight. The mixture was extracted with 10% NaH_2PO_4, the benzene layer was washed with water, and dried over Na_2SO_4. Evaporation of benzene gave 4.23 g. of a dark red oil, which was digested with Et_2O to give 3.8 g. of an orange red oil. The oil was dissolved in 100 cc. of Et_2O and filtered through a column of 40 g. of alumina. The residue of the filtrate gave after recrystallization from petr. ether, 3.2 g. of monobromomatridine-monocyanamide (IVa) as colorless needles, m.p. 45~48°, which was positive to Beilstein's test for halogen atom.

The above 10% NaH_2PO_4 extract was made alkaline with 10% NaOH, extracted with Et_2O, the extract was washed with water, and dried over Na_2SO_4. The residue obtained upon removal of the solvent was crystallized with the addition of petr. ether to yield 1.43 g. of colorless needles, m.p. 43~46°, undepressed on admixture with (IVa), m.p. 45~48°. Recrystallization from petr. ether gave monobromomatridine-monocyanamide (IVa) as colorless needles, m.p. 49~49.5°; yield, 4.6 g. (79.1%). *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot BrCN$: C, 56.47; H, 7.56; N, 12.34. Found : C, 56.63; H, 7.53; N, 12.42. Chloroaurate : Orange prisms (from MeOH), m.p. 190~191° (decomp.). *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot BrCN \cdot HAuCl_4$: C, 28.22; H, 3.98; N, 6.18; Au, 28.97. Found : C, 28.58; H, 4.22; N, 5.98; Au, 28.38.

Reduction of Monobromomatridine-Monocyanamide (IVa) and Hydrolysis of Matridine-Monocyanamide—A solution of 3.0 g. of (IVa) and 1.8 g. of KOH in 25 cc. of MeOH was catalytically reduced at room temperature by the dropwise addition of a suspension of 500 mg. of 38% Pd-C catalyst in 10 cc. of MeOH. After 8 hr., 109 cc. (0.55 mole) of H_2 was absorbed and the reaction stopped. Then, additional 500 mg. of 38% Pd-C was added to this mixture and the reduction was continued until 52 cc. (0.26 mole) of H_2 was absorbed, and the reaction stopped. This procedure was repeated with another addition of 150 mg. of the catalyst, and a total of 173 cc. (0.87 mole) of H_2 was absorbed during 18 hr. After removal of the catalyst, CO_2 was passed through the solution and the separated K_2CO_3 was filtered off. The filtrate was evaporated *in vacuo* and the residue was extracted with Et_2O, which was wahsed with water and dried over Na_2SO_4. The residue obtained upon evaporation of the

solvent was a pale yellow oil, which was negative to Beilstein's test; yield, 2.35 g. The oil was dissolved in 70 cc. of petr. ether and filtered through a column of 20 g. of alumina. From the petr. ether eluate, 2.0 g. of matridine-monocyanamide was obtained as a colorless oil. The chloroaurate was obtained as yellow prisms (from MeOH), m.p. 199~200° (decomp.), undepressed on admixture with the same salt of matridine, m.p. 197~199° (decomp.).

From the Et_2O eluate, 300 mg. of a secondary amine (Va) was obtained as colorless needles, m.p. 63~65°, which was obtained also by heating matridine monocyanamide with conc. HCl.

The colorless oil of matridine monocyanamide was dissolved in 25 cc. of conc. HCl and heated in a sealed tube at 100~110° for 14 hr. The solution was made alkaline with K_2CO_3, extracted with Et_2O, the extract was washed with water, and dried over anhyd. K_2CO_3. The solvent was evaporated and the residue was crystallized from petr. ether to 1.68 g. (92.5%) of (Va) as colorless needles, m.p. 67~68°, which was positive to Liebermann's test for secondary amine. *Anal.* Calcd. for $C_{15}H_{28}N_2$: C, 76.21; H, 11.94; N, 11.85. Found: C, 76.03; H, 11.67; N, 11.76. IR ν_{max}^{Nujol} cm^{-1}: 3247 (ν_{N-H}), 2750~2800 (*trans*-quinolizidine). Rf value in paper partition chromatography: 0.60.

Acylation of (Va) with *p*-Nitrobenzoyl Chloride—A mixture of 100 mg. of (Va) and 100 mg. (1.2 equiv.) of *p*-nitrobenzoyl chloride in 2 cc. of pyridine was heated at 60~80° for 5 hr. with protection from moisture. After evaporation *in vacuo*, the residue was dissolved in water, acidified with 10% H_2SO_4, and extracted with Et_2O. The aqueous layer was made alkaline with K_2CO_3, extracted with Et_2O, the extract was washed with water, and dried over anhyd. K_2CO_3. Removal of the solvent left 100 mg. of yellow needles as the residue. This was dissolved in 10 cc. of petr. ether and filtered thorough a column of 3 g. of alumina to give 80 mg. of colorless needles, m.p. 63~64°, undepressed on admixture with (Va). Rf, 0.60. Each fraction of the above chromatography was examined by paper partition chromatography, but there were no spots other than that of (Va).

Methylation of (Va) with Methyl Iodide—A solution of 100 mg. of (Va) and 500 mg. of MeI in 3 cc. of MeOH was refluxed for 4 hr. After evaporation *in vacuo*, the residue was dissolved in water, made alkaline with K_2CO_3, and extracted with Et_2O and $CHCl_3$. The Et_2O extract was evaporated to leave 70 mg. of an orange oil which was refluxed again with an excess of MeI in MeOH for 3 hr. The solvent was evaporated, the residue was dissolved in water, made alkaline with K_2CO_3, and extracted with $CHCl_3$. After removal of the solvent, the orange crystalline residue was recrystallized from Me_2CO-AcOEt to colorless needles (XIV), m.p. 219~220°. The foregoing $CHCl_3$ extract was evaporated to leave 100 mg. of yellow crystals, which was recrystallized from Me_2CO-AcOEt to colorless needles, m.p. 220~221°, undepressed on admixture with (XIV). *Anal.* Calcd. for $C_{15}H_{28}N_2 \cdot CH_3I$: C, 50.79; H, 8.20; N, 7.41. Found: C, 51.02; H, 8.09; N, 6.98. IR ν_{max}^{Nujol} 3497 cm^{-1} (ν_{N-H}).

A solution of 40 mg. of (XIV) in 5 cc. of water was filtered through a column of 1 cc. of Amberlite IRA-400 (treated preliminarily with 2*N* NaOH) and eluted with 10 cc. of water. The filtrate was evaporated *in vacuo* and the residue was distilled in a reduced pressure (3 mm. Hg) to yield a yellow oil, which was chromatographed on alumina. Each fraction of chromatography was examined by paper partition chromatography, but there was only one spot of (Va) with Rf 0.60. This base gave a methiodide of colorless needles, m.p. 216~217°, undepressed on admixture with (XIV).

Alkaline Air-oxidation of (Va)—Dry air was passed through a boiling solution of 40 mg. of (Va) in 10 cc. of MeOH containing 1 g. of KOH for 20.5 hr. The mixture was evaporated and extracted with Et_2O. Evaporation of the Et_2O extract gave 40 mg. of a pale yellow oil, which showed only one spot of (Va) at Rf 0.60 on paper partition chromatography.

Oxidation of (Va) with Copper Chromite—50 mg. of copper chromite was added to a solution of 50 mg. of (Va) in 3 cc. of decalin and the mixture was refluxed for 9.5 hr. After filtration, the solution was evaporated *in vacuo*, dissolved in Et_2O, and extracted with 10% HCl. The acid solution was made alkaline with K_2CO_3 and extracted with Et_2O. Evaporation of the solution left 40 mg. of brown needles, which showed only one spot of (Va) at Rf 0.60 on paper partition chromatography.

Air-oxidation of (Va)—600 mg. of pure (Va) in a flask stoppered with cork was allowed to stand at room temperature for 8 months. The orange residue was dissolved in 60 cc. of petr. ether and filtered through a column of 12 g. of alumina. Petr. ether eluate gave 125 mg. of colorless needles, m.p. 54~57°, undepressed on admixture with matridine (I) and showed a spot of (I) at Rf 0.46. From petr. ether eluate and petr. ether-Et_2O (9:1) eluate, 305 mg. of (Va) was obtained.

Dehydrogenation of (Va) with $(AcO)_2Hg$—A solution of 340 mg. of (Va) in 3 cc. of 10% AcOH and 5 cc. of water was added to a solution of 4 g. (8 equiv.) of $(AcO)_2Hg$ in 3 cc. of glacial AcOH and 1.5 cc. of H_2O, and this mixture was refluxed for 9 hr., during which time 2.18 g. of AcOHg separated from the solution (this amount of AcOHg corresponded to dehydrogenation of ca. 3 moles of H_2). After filtration, H_2S was passed through the filtrate and a small amount of 10% HCl was added to this filtrate. This mixture was centrifuged to remove HgS. This solution was refluxed with charcoal, filtered, and evaporated *in vacuo*. The residue was dissolved in water, made alkaline with K_2CO_3, and extracted with Et_2O and then with $CHCl_3$. From the $CHCl_3$ extract, 90 mg. of a dark red resin was obtained. From the Et_2O extract, 280 mg. of an orange oil was obtained, which

was digested with petr. ether to give 230 mg. of an orange oil. The oil was dissolved in 30 cc. of petr. ether and filtered through a column of 8 g. of alumina to give 160 mg. of (VIa) as pale yellow needles, m.p. 74~82°. Recrystallization from petr. ether gave (VIa) as colorless needles, m.p. 84~85°; yield, 120 mg. Each fraction of chromatography was examined by paper partition chromatography, but there was only one spot of (VIa) at Rf 0.76. *Anal.* Calcd. for $C_{15}H_{26}N_2$: C, 76.86; H, 11.18; N, 11.95; mol. wt., 234.37. Found : C, 76.86; H, 10.92; N, 11.67; mol. wt. (micro-Rast), 257.3, 265.5. IR ν_{max}^{Nujol} cm^{-1} : 3247 (ν_{N-H}), 3030 (ν_{C-H}), 2750~2800 (*trans*-quinolizidine), 1650 ($\nu_{C=C}$), 705 (*cis*-disubstituted double bond).

Microdetermination of double bond : Sample, 3.770 mg.; solvent, glacial AcOH; catalyst, PtO_2. $\delta=0.99$. After determination of the double bond, this solution was evaporated *in vacuo*, the residue was dissolved in water, made alkaline with K_2CO_3, and extracted with Et_2O. Removal of the solvent left a pale yellow oil which was chromatographed on alumina. Each fraction of chromatography was examined by paper partition chromatography, but there was only one spot of (Va) at Rf 0.60.

Perhydroazecine (XXI)—As shown in Chart 2, perhydroazecine (XXI) was obtained from azelaic acid (XV) via (XVI), (XVII), (XVIII), (XIX), and (XX) by Ruzicka's method.[11]

Picrate of (XXI) : Yellow needles, m.p. 182~183° (from Me_2CO-Et_2O). *Anal.* Calcd. for $C_9H_{19}N\cdot C_6H_3O_7N_3$: C, 48.64; H, 5.99; N, 15.13. Found : C, 48.19; H, 5.62; N, 15.51.

Chloroaurate of (XXI) : Orange prisms, m.p. 123~125° (decomp.).

Acylation of (XXI) with *p*-Nitrobenzoyl Chloride—A mixture of 100 mg. of (XXI) and 220 mg. (1.2 equiv.) of *p*-nitrobenzoyl chloride in 2 cc. of pyridine was heated at 70~80° for 5 hr. with protection from moisture. This mixture was evaporated *in vacuo*, dissolved in water, acidified with 10% H_2SO_4, and extracted with Et_2O. The Et_2O extract was washed with water and 10% Na_2CO_3, and dried over Na_2SO_4. Removal of the solvent left 150 mg. of an orange oil. This oil was dissolved in 30 cc. of Et_2O and filtered through a column of 5 g. of alumina to give 145 mg. of colorless needles, m.p. 67~70°. Recrystallization from petr. ether-Et_2O gave (XXII) as colorless needles, m.p. 71~73°; yield, 135 mg. (63.6%). *Anal.* Calcd. for $C_{16}H_{22}O_3N_2$: C, 66.18; H, 7.64; N, 9.65. Found : C, 66.08; H, 7.37; N, 9.80.

Methylation of (XXI) with Methyl Iodide and Hofmann Degradation of the Quaternary Salt—A solution of 60 mg. of (XXI) and 300 mg. of MeI in 3 cc. of MeOH was refluxed for 4 hr. The mixture was evaporated *in vacuo*, the residue was dissolved in water, made alkaline with K_2CO_3, and extracted with Et_2O and $CHCl_3$. The $CHCl_3$ extract gave 20 mg. of colorless amorphous powder, which was recrystallized from MeOH-Me_2CO to yield colorless prisms (XXIV), m.p. 246° (deomp.); Beilstein's test, positive.

The Et_2O extract was evaporated to leave 30 mg. of a yellow oil (XXIII), which was refluxed again with an excess of MeI in MeOH for 3.5 hr. This mixture was worked up as described above, and 25 mg. of colorless prisms (from MeOH-Me_2CO), m.p. 244~245° (decomp.), was obtained, which was identical with (XXIV). *Anal.* Calcd. for $C_{10}H_{21}N\cdot CH_3I$: C, 44.44; H, 8.08; N, 4.72. Found : C, 44.53; H, 7.81; N, 5.00.

A solution of 70 mg. of (XXIV) in 5 cc. of water was filtered through a column of 1 cc. of Amberlite IRA-400 (treated preliminarily with 2*N* NaOH) and eluted with 10 cc. of water. The filtrate was negative to I_2 color-test with fuming HNO_3-CCl_4 and evaporated *in vacuo* to leave 40 mg. of colorless needles (XXV). The residue was distilled in atmospheric pressure to give a colorless oil of the methine base. This methin base was dissolved in Et_2O and extracted with 10% HCl. The acid layer was made alkaline with $NaHCO_3$, extracted with Et_2O, and 30 mg. of the methine base (XXVI) was obtained as a pale yellow oil.

Methiodide : Colorless needles (from Me_2CO-AcOEt), m.p. 136~143°.

Micro-determination of double bond of the methine base : Sample, 0.852 mg.; solvent, 0.2 cc. of *N* HCl; catalyst, PtO_2, $\delta=0.70$.

Hydrogenation of (XXVI)—A mixture of 50 mg. of Adams PtO_2 added to a solution of 50 mg. of N,N-dimethyl-8-nonenylamine (XXVI) in 5 cc. of glacial AcOH was subjected to hydrogenation at room temperature and atmospheric pressure. After removal of the catalyst and the solvent, the residue was dissolved in water, made alkaline with K_2CO_3, and extracted with Et_2O. Removal of the solvent gave 20 mg. of N,N-dimethylnonenylamine (XXVII) as a yellow oil.

Methiodide : Colorless needles (from Me_2CO-AcOEt), m.p. 143~146°. *Anal.* Calcd. for $C_{11}H_{25}N\cdot CH_3I$: N, 4.48. Found : N, 4.37.

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Summary

The steric effect of matridine (I) on von Braun degradation was investigated. It was concluded that the structure of the degradation product, monobromomatridine monocyanamide (IV), was represented by formula (IVa) and its dehydrogenated product with mercuric acetate, enamine (VI) by formula (VIa).

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18. Yoji Arata*1 and Shigehiko Sugasawa*2 : A New Cyclization Reaction of Cyclic Ketoxime.

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As the hitherto unknown prototype of benzoquinolizine derivatives, synthesis of 2,6-methano-9,10-dimethoxy-1,2,3,4,6,7-hexahydro-11b*H*-benzo[*a*]quinolizine (I) was attempted. For this purpose, end cyclization of lactam (II) appears attractive, because the cyclization product (III) should give (I) on hydrogenation.

At first sight, however, the formation of (III) appears quite problematic, because this compound has an N-C double bond at a bridge head of the bicyclic ring system violating the Bredt's rule. In order to examine the possibility of the formation of such a ring system, cyclization of a simpler lactam (IV) was preliminarily investigated, which may be advantageously prepared by the Beckmann rearrangement of readily accesible 2-veratryl-cyclopentanone oxime (V).

It is known in the literature that oximes of suitably substituted carbonyl compounds give rise to isoquinoline derivatives in one step in Beckmann rearrangement conditions, sometimes in an excellent yield. Thus, Sugasawa and Yoshikawa[1] prepared 1-(3,4-dimethoxyphenethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (VIII) in 85% yield by treating Bis-(3,4-dimethoxyphenethyl) ketone oxime (VII) with phosphoryl chloride in boiling toluene. Several other similar examples are also recorded.[2]

2-Veratrylidenecyclopentanone was prepared after Walton's method.[3] This was reduced catalytically to afford 2-veratrylcyclopentanone whose oxime (V) was treated with phosphoryl chloride in boiling toluene, when intermediary formation of 6-veratryl-2-piperidone (IV) was to be expected as one of the rearrangement products. By the agency of boiling phosphoryl chloride, the latter may suffer further change, in which case formation of isoquinolinium derivative (VI) might not be excluded.

From the reaction mixture there was obtained a crystalline base of m.p. 120~121°, the ethanol solution of which exhibited ultraviolet maxima at 335 (4.15) and 325 mμ (log ε

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