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Studies on Tertiary Amine Oxides. LVIII.[1] Reactions of Substituted Dehydroquinolizidines with Pyridine N-Oxide. (2)[2]

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In order to introduce 2-pyridyl group into the 9 position of 1,1-disubstituted quinolizidine, N-benzoyloxypyridinium chloride (**1**) was treated with 9-dehydro-1-oxoquinolizidine (**3**), dehydro-1-ethoxycarbonyl-1-hydroxyquinolizidine (**13**) and 9-dehydro-1,1-ethylenedioxyquinolizidine (**16**) in dichloromethane, followed by reduction of the reactants with sodium borohydride in anhyd. ethanol. Although reactions with **3** and **13** gave no satisfactory result, that with **16** afforded the expected 1,1-ethylenedioxy-9-(2-pyridyl)-quinolizidine (**18**) in 17% yield together with dehydro-1,1-ethylenedioxy-x-(2-pyridyl)-quinolizidine (**19**).

Other observations encountered in reactions of **1** with **3** or **13** as well as in transformation of **2** into **13** and **16** were also described in some detail.

As a continuation of our study on the reaction of substituted dehydroquinolizidine and pyridine N-oxide[2] with an aim to open a new route to matrine type alkaloids, we chose 1-oxo-, 1-ethoxycarbonyl-1-hydroxy- and 1,1-ethylenedioxy-quinolizidines as 1,1-disubstituted quinolizidine, and examined reactions of their 9-dehydro derivatives with N-benzoyloxypyridinium chloride (**1**).

Freshly prepared 1-oxoquinolizidine (**2**)[4] was dehydrogenated by heating with 4 molar excess of mercuric acetate in 5% acetic acid at 70° for 1 hour. The reaction mixture was treated successively with hydrogen sulfide and 40% sodium hydroxide followed by distillation of the basic fraction under reduced pressure to give 9-dehydro-1-oxoquinolizidine (**3**), a colorless oil, bp 72° (4 mmHg), in 27.6% yield. Although the elemental analysis of **3** could not be done because of its high instability changing rapidly to black resin and crystallization of the corresponding immonium perchlorate also failed, the structure could be assigned from the infrared (IR) absorption at 1730 (C=O) and 1620 cm^{-1} (C=C) as well as a triplet at τ 4.22 (J= 4 Hz) due to a vinyl proton in the nuclear magnetic resonance (NMR) spectrum.

According to the usual procedure,[5] a dichloromethane solution of **3** and 1.5 equivalents of N-benzoyloxypyridinium chloride **1** was stirred at room temperature for 48 hours, and then the reactants were treated with sodium borohydride in anhydrous ethanol. Separation of the products by a preparative gas chromatography furnished four products (**4**, **5**, **6** and **7**) having retention times of 3.5, 7.7, 30.5 and 43 minutes, respectively.

The structure of **4** could not be elucidated because of the trace amount of sample. Product **5** with the empirical formula $C_9H_{17}ON$ was recrystallized from petroleum ether as colorless needles, mp 70°, and formed a picrate, yellow needles, mp 178°. The identity of **5** as 1(e)-hydroxyquinolizidine[6] was established by direct comparison with an authentic sample obtained

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1) Part LVII: K. Funakoshi, Y. Kuchino, H. Shigyo, H. Sonoda and M. Hamana, *Chem. Pharm. Bull.* (Tokyo), **24**, 2354 (1976).

2) Part (1): S. Saeki, A. Yamashita, Y. Morinaka and M. Hamana, *Yakugaku Zasshi*, **96** 456 (1976).

3) Location: *Maidashi, Higashi-ku, Fukuoka.*

4) T. Kunieda, K. Koga and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **15**, 337 (1967).

5) S. Saeki, A. Yamashita, Y. Matsukura, and M. Hamana, *Chem. Pharm. Bull.* (Tokyo), **22**, 2341 (1974).

6) H.S. Aaron, G.E. Wicks, Jr. and C.P. Rader, *J. Org. Chem.*, **29**, 2248 (1964).

by sodium borohydride reduction of **2** and also by admixture of their picrates. Product **6** was a yellow oil of bp 150—160° (0.01 mmHg) (bath temp.) and formed a dipicrate, yellow needles, mp 242—243° (decomp.). It was proved identical with an authentic sample of 1-(2-pyridyl)quinolizidine described in a previous paper.5) Product **7** was a yellow oil of bp 150—160° (0.01 mmHg) (bath temp.) and formed a dipicrate with the empirical formula $C_{14}H_{20}N_2\cdot 2C_6H_3O_7N_3$, yellow needles, mp 209—210°. The free base regenerated from the purified dipicrate displayed Bohlmann bands7) at 2830—2780 cm^{-1} and a band due to a double bond at 1590 cm^{-1} in the IR spectrum. Its NMR spectrum showed a pair of two-proton quartets at τ 2.52—2.30 and 1.00—1.44, which were reasonably assigned to two α-protons and two β-protons of a pyridine ring, respectively. From these observations, **7** was probably assigned 1-(4-pyridyl)quinolizidine (Chart 1). The yields of **5**, **6** and **7** were 6.2, 14.3 and 9.5%, respectively.

This unexpected result is remarkable from two points of view. At first, the formation of 4-pyridylquinolizidine **7** in a yield comparable with that of 2-pyridyl compound **6** is very interesting considering the fact that the reaction of **1** with enamines gave overwhelmingly 2-pyridyl derivatives, and the amounts of 4-substituted pyridines are very minute even when they form.8)

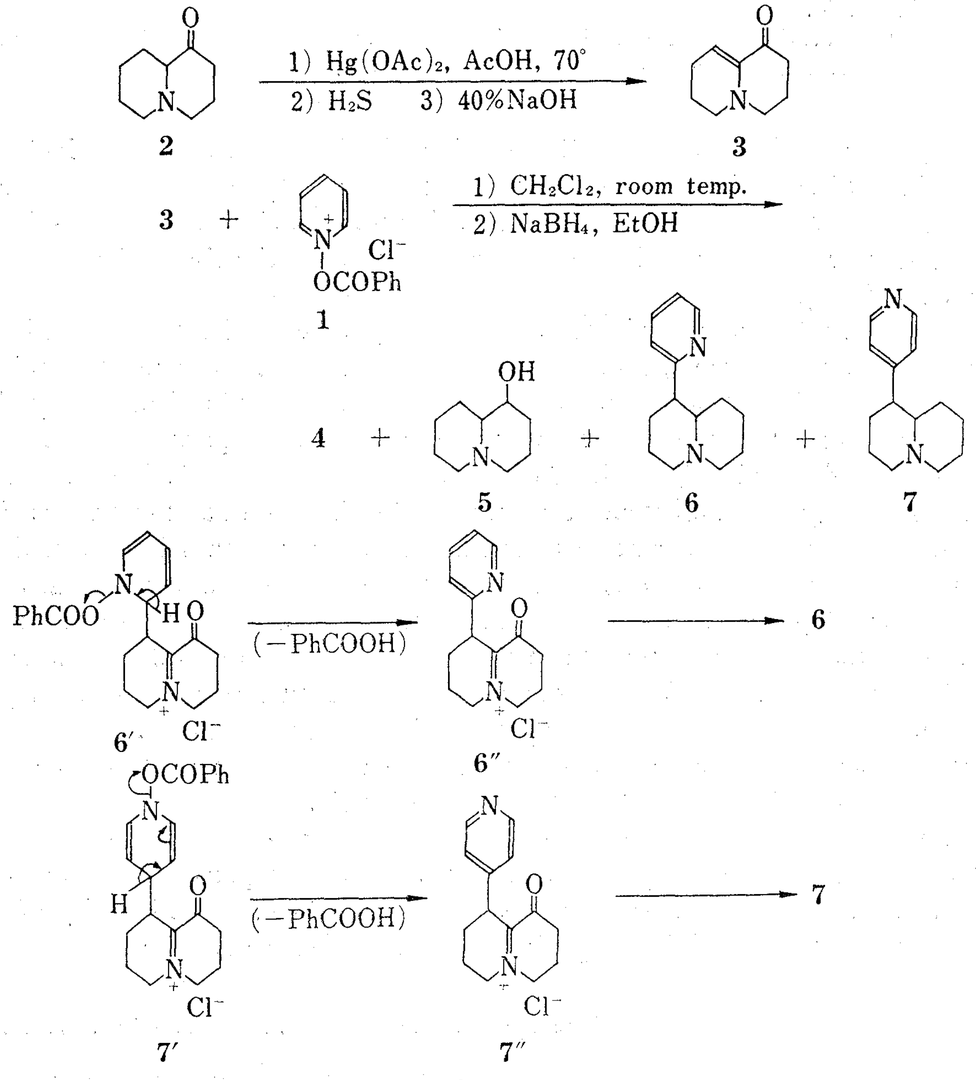

Chart 1

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7) *a*) F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958); *b*) J. Skolik and P.J. Krueger, *Tetrahedron*, **24**, 5439 (1968).

8) *a*) M. Hamana and H. Noda, *Chem. Pharm. Bull.* (Tokyo), **13** 912 (1965); *b*) M. Hamana and H. Noda, *Yakugaku Zasshi*, **89**, 641 (1969).

Secondary, the one-step reduction of the 1-keto group of 1-oxoquinolizidinium salts (**6″** and **7″**) conceivably formed from the corresponding dihydropyridines (**6′** and **7′**) to methylene group seems to be an unprecedented example in the reduction by means of sodium borohydride. The essential features of these rather unusual reactions are not clear at present (Chart 1).

Subsequently, 1-ethoxycarbonyl-1-hydroxyquinolizidines (**10a** and **10b**) were prepared by the reaction sequence shown in Chart 2. Although an attempt to derive **2** to its cyanohydrin (**8**) by treatment with potassium cyanide and hydrochloric acid was unsuccessful, it was found that a reaction apparently took place when a solution of **2** and 4 equivalents of acetone cyanohydrin was stirred at room temperature overnight, but the isolation of pure **8** failed, only black-brown resin being formed. However, the residue obtained on evaporation of the above mixture was refluxed successively with concentrated hydrochloric acid for 20 hours and with 40% sodium hydroxide for 6 hours to give the corresponding α-hydroxycarboxylic acid (**9**). Without further purification of **9**, a solution of **9** in anhydrous ethanol saturated with dried hydrogen chloride was refluxed for 6 hours to give a yellow oil, bp 120° (2 mmHg). Chromatography on a silica gel column with petroleum ether-ether (1: 1) afforded two products (**10a** and **10b**) in 56 and 4% yields, respectively. Table I shows some properties of **10a** and **10b**, which indicate that they are two stereoisomers of 1-ethoxycarbonyl-1-hydroxyquinolizidine.

Table I. Some Properties of **10a** and **10b**

	10a	**10b**
bp	115° (2 mmHg)	140—150° (2 mmHg) (bath temp.)
Picrate $C_{12}H_{18}O_3N \cdot C_6H_3O_7N_3$	mp 127—129° yellow column	mp 129—130° yellow column
IR (neat) cm^{-1}	2940—2760 (Bohlmann bands) 1715 (C=O, ester) 3480 (OH)	2950—2800 (Bohlmann bands) 1730 (C=O, ester) 3400 (OH)
NMR τ ($CDCl_3$)	8.69 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$) 5.66 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$) 6.18 (1H, b.s, OH)	8.70 (3H, t, J=7 Hz, $COOCH_2C\underline{H}_3$) 5.66 (2H, q, J=7 Hz, $COOC\underline{H}_2CH_3$) 6.69 (1H, b.s, OH)

In confirming the stereochemistry of **10a** and **10b**, the dehydration was tried. Heating **10a** with thionyl chloride in pyridine produced a colorless oil (**11**). The IR spectrum of **11** exhibited Bohlmann bands[7] at 2940—2800 cm^{-1} and bands due to an ester-carbonyl group and a double bond at 1715 and 1650 cm^{-1}, respectively, and its NMR spectrum showed a vinyl proton as a broad singlet centered at τ 3.20. These observations seemingly indicated that the hydroxy group of **10a** had the axial configuration[9] and a double bond was formed between the 1 and 2 positions of the quinolizidine ring. The reason why the normal 1(10)-dehydro derivative did not form is not yet clear. On the other hand, dehydration of **10b** under the same condition did not proceed, the starting material being recovered. Hence, *trans*-1(e)-ethoxycarbonyl-1(a)-hydroxyquinolizidine and *trans*-(1a)-ethoxycarbonyl-1(e)-hydroxyquinolizidine were likely assigned to **10a** and **10b**, respectively.

In order to convert **10a** into 1(a)-hydroxy-1(e)-methylquinolizidine, the stereochemistry of which had been established,[2,10] a series of reactions shown in Chart 2 was attempted.

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9) D.N. Kirk and M.P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier Publishing Co., Amsterdam, London and New York, 1968, p. 103.

10) D. Temple and I. Sam, *J. Heterocycl. Chem.*, 5, 441 (1968).

Reduction of **10a** with lithium aluminum hydride in ether gave a product (**12**), colorless pillars, mp 141—143°, conceivable to be an 1-hydroxy-1-hydroxymethylquinolizidine from its analytical values and IR spectrum, but any definite tosyl esters of **12** were not isolated on treatment with tosyl chloride in pyridine.

Dehydrogenation of **10a** was next carried out by heating with mercuric acetate in acetonitrile followed by treatment with 40% sodium hydroxide, and a dehydrogenated product (**13**) was obtained as a yellow oil, bp 170° (1.0 mmHg) (bath temp.). Whereas the elemental analysis of **13** could not be performed because of its high instability, and crystallization of its immonium perchlorate also failed, the presence of a double bond was demonstrated by an IR absorption at 1670 cm^{-1} and a signal due to a vinyl proton at τ 4.25 in its NMR spectrum. However, **13** seemed not a single 9-dehydroquinolizidine but a mixture with either or both of 3- and 6-dehydro derivatives in view of the fact that the vinyl proton signal was not a triplet but a multiplet.

Dehydro-1-ethoxycarbonyl-1-hydroxyquinolizidine **13** thus formed was treated with 1.5 equivalents of **1** in dichloromethane followed by reduction of the reactants with sodium borohydride in ethanol to yield a yellow oil (**14**), bp 250—270° (0.1 mmHg) (bath temp.). An attempt to crystallize its picrate was unsuccessful. The mass spectrum (M^+, *m/e* 452) and the IR spectrum which showed an ester-carbonyl band at 1740 cm^{-1} but no absorption at 1600—1700 cm^{-1} due to pyridine nucleus demonstrate that **14** is a dimer of **13**. Although its structure is not elucidated, such a dimerization of cyclic enamine is known to occur by

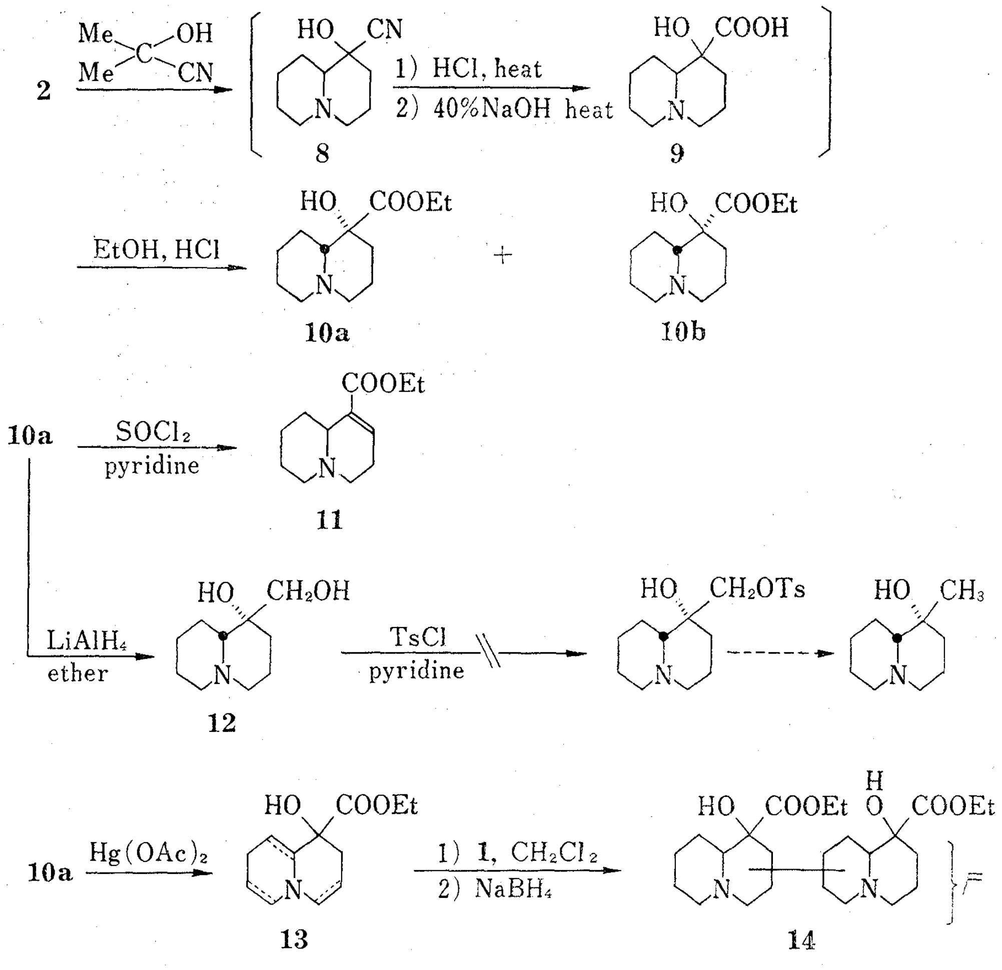

Chart 2

interaction between the enamine and the corresponding immonium species,[11] and dimerization of 3-dehydroquinolizidine has been described by Arata, *et al.* in quinolizidine series.[12]

Thus it was found that dimerization of the enamine **13** occurred much more readily than nucleophilic reaction of **1** with **13** under the above condition.

Finally, 9-dehydro-1,1-ethylenedioxyquinolizidine was applied to **1**. Heating a benzene solution of **2**, ethyleneglycol (1.5 eq.) and *p*-toluenesulfonic acid (1.1 eq.) for 5 hours gave readily 1,1-ethylenedioxyquinolizidine (**15**), a light yellow oil, bp 110° (4 mmHg), in a high yield of 91.1%. It gave a picrate with the empirical formula $C_{11}H_{19}O_2 \cdot C_6H_3O_7N_3$, mp 181 182°. Dehydrogenation of **15** by heating with mercuric acetate in acetonitrile for 5 hours followed by distillation under reduced pressure of the basic fraction resulted in the formation of 9-dehydro derivative (**16**), a light yellow oil, bp 120—130° (3 mmHg) and a brown oil (**17**), bp 191—200° (3 mmHg) in 37 and 31% yields, respectively. Compound **16** forms perchlorate with the empirical formula $C_{11}H_{17}ON_2 \cdot HClO_4$, colorless scales, mp 189—189.5°. The free base regenerated from perchlorate exhibited an IR absorption at 1675 cm^{-1} (C=C) and its NMR spectrum showed a triplet at τ 5.00 (J=4.0 Hz) due to a vinyl proton. Compound **17** is an fairly stable and highly viscous oil, and its elemental analysis and the mass spectrum (M^+, *m/e* 390) accorded with the molecular formula $C_{22}H_{34}O_4N_2$. Its IR spectrum exhibited a C=C band at 1675 cm^{-1}, and the NMR spectrum gave a one-proton broad singlet at τ 4.30—4.20 assignable to a vinyl proton and a broad singlet at τ 6.10—6.00 due to eight protons of two ethylenedioxy groups. Although attempts to obtain crystalline derivatives of **17** failed, the above observations indicate that **17** is a dimer or a mixture of dimers derived from dehydro-1,1-ethylenedioxyquinolizidines.

Compound **16** was allowed to react with **1** followed by treatment with sodium borohydride in the same way with the foregoing experiments. Chromatography on silica gel with dichloromethane-methanol afforded two products (**18** and **19**) in 17 and 7.3% yields, respectively.

Product **18** was recrystallized from petroleum ether as colorless needles, mp 82—83°, and gave analytical values in agreement with the empirical formula $C_{16}H_{22}O_2N \cdot 2H_2O$. The IR spectrum exhibited Bohlmann bands at 2830—2790 cm^{-1} as well as a C=N band at 1600 cm^{-1}. Its NMR spectrum showed a four-proton, a three-proton and a one-proton multiplets at τ 6.60—5.88, 3.10—2.40 and 1.58—1.40, which were reasonably assigned to four protons of ethylenedioxy group, two β- and one γ-protons of pyridine ring, and its one α-proton, respectively. From these observations, **18** was assigned 1,1-ethylenedioxy-9-(2-pyridyl)quinolizidine, and the presence of Bohlmann bands in the IR spectrum indicates that the quinolizidine ring is *trans*-fused and the 2-pyridyl group has the equatorial configuration; the exial 9-(2-pyridyl) group should be considered to deform the *trans*-quinolizidine ring into the *cis*-fused one and cause disappearance of Bohlmann bands.[7]

Product **19** is a yellow oil of bp 180—200° (3 mmHg) (bath temp.), and forms perchlorate, colorless needles, mp 195—196°. The mass spectrum (M^+, *m/e* 272) and the analytical values of its perchlorate ($C_{16}H_{20}O_2N_2 \cdot 2HClO_4$) indicate that the molecular formula of **19** is $C_{16}H_{20}O_2N_2$. The IR spectrum of **19** liberated from the perchlorate exhibited deformed Bohlmann bands at 2830—2800 cm^{-1} and absorption bands due to double bonds at 1625, 1595 and 1580 cm^{-1}. Its NMR spectrum showed a one-proton broad singlet, a three-proton and a one-proton multiplets at τ 5.54, 3.30—2.30 and 1.70—1.50, which are assignable to a vinyl proton, C_3-, C_4- and C_5-protons of pyridine ring, and its C_2-proton, respectively. These data demonstrate that **19** consists of one 2-pyridyl group and one dehydro-1,1-ethylenedioxyquinolizidine ring, although the positions of the 2-pyridyl group and the vinyl moiety are not elucidated at present. Curiously, the reduction of **19** with an excess of sodium borohydride in ethanol did not proceed.

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11) See for instance, N.J. Leonard and F.P. Hauck, Jr., *J. Am. Chem. Soc.*, **79**, 5279 (1957).

12) Y. Arata, H. Kato and T. Shioda, *Yakugaku Zasshi*, **88**, 614 (1968); see also, F. Bohlmann, H.J. Muller and D. Schumann, *Chem. Ber.*, **106**, 3026 (1973).

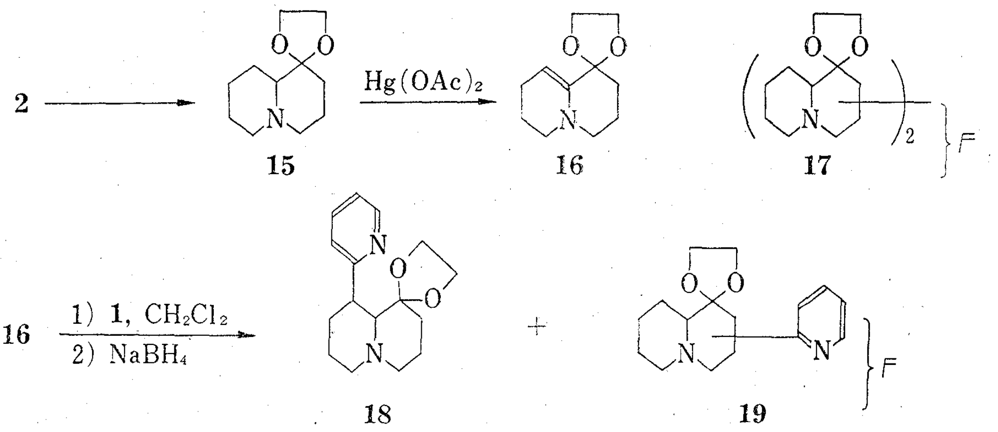

Chart 3

Thus it was found that the reaction of **1** with **2** or **13** gave no 9-(2-pyridyl)quinolizidine but that with 1,1-ethylenedioxyquinolizidine **16** afforded the expected 9-(2-pyridyl) derivative **18** though in rather low yield. Compound **18** is apparently a promising intermediate for the synthesis of matrine type alkaloids; our study on this object will be reported in the following paper.

Experimental[13]

9-Dehydro-1-oxoquinolizidine (3)——A solution of 1-oxo-quinolizidine (2) (7 g, 0.046 mole) and Hg $(OAc)_2$ (59 g, 0.184 mole) in 5% AcOH (300 ml) was heated at 70° for 1 hr. Precipitated $Hg_2(OAc)_2$ was filtered after cooling, H_2S was passed in the filtrate until the solution gave acidic reaction with Congo Red, and deposited HgS was filtered. The filtrate was concentrated *in vacuo*, made alkaline with 40% NaOH and extracted with ether to give 2 g (27.6%) of 3, colorless oil, bp 72° (4 mmHg). It was highly unstable and changed rapidly to black resin on standing. IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1730 (C=C), 1620 (C=C). NMR τ $(CDCl_3)$: 4.22 (1H, t, $J=4.5$ Hz, vinyl proton).

Reaction of Benzoyloxypyridinium Chloride (1) with 3——A CH_2Cl_2 (70 ml) solution of 3 (2 g, 0.0133 mole) and 1 preliminarily prepared from pyridine N-oxide (2.5 g, 0.0265 mole) and benzoyl chloride (3.7 g, 0.0266 mole) was stirred at room temperature for 48 hr. The solvent was evaporated *in vacuo*, and the residue was dissolved in anhyd. EtOH (500 ml) and treated with excess $NaBH_4$ overnight. The reaction mixture was evaporated *in vacuo*, treated with H_2O and extracted with ether. The extract was dried over $MgSO_4$ and evaporated to give an oil which was subjected to preparative gas chromatography[14] to give four products (**4**, **5**, **6**, and **7**).

Product **4**: a yellow oil, t_R 35 min. Because of the trace amount of sample, its structure could not be elucidated.

Product **5**: 1-(Hydroxy-*cis*-10-H)-quinolizidine,[6] colorless needles, mp 70° (petr. ether), t_R, 7.7 min, 0.13 g (6.2%). *Anal.* Calcd. for $C_9H_{17}ON$: C, 69.67; H, 10.97; N, 9.02. Found: C, 68.94; H, 10.66; N, 8.95. IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 3140 (OH), 2830—2780 (Bohlmann bands). NMR τ $(CDCl_3)$: 5.50 (1H, OH). It formed picrate, yellow needles, mp 178° (EtOH), undepressed on admixture with an authentic sample.[6]

Product **6**: 1-(2-Pyridyl)quinolizidine,[5] a yellow oil, bp 150—160° (0.01 mmHg) (bath temp.), t_R, 30.5 min, 0.3 g (14.3%). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 2830—2780 (Bohlmann bands), 1590 (C=N). NMR τ $(CDCl_3)$: 3.02—2.30 (3H, m, C_3-H, C_4-H and C_5-H of pyridine), 1.45—1.20 (1H, m, C_6-H of pyridine). It formed dipicrate, yellow needles, mp 242—243° (acetone), undepressed on admixture with an authentic sample.[5]

Product **7**: 1-(4-Pyridyl)quinolizidine, a yellow oil, bp 150—160° (0.01 mmHg) (bath temp.), t_R, 43.0 min, 0.2 g (9.5%). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 2830—2780 (Bohlmann bands), 1590 (C=N). NMR τ $(CDCl_3)$: 2.52—2.30 (2H, q, $J=4$ Hz, C_3-H and C_5-H of pyridine), 1.60—1.44 (2H, q, $J=4$ Hz, C_2-H and C_6-H of pyridine). Dipicrate: yellow needles, mp 209—210° (acetone). *Anal.* Calcd. for $C_{14}H_{20}N_2 \cdot 2C_6H_3O_7N_3$: C, 46.39; H, 3.85; N, 16.61. Found: C, 46.18; H, 3.92; N, 16.51.

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13) All melting and boiling points are uncorrected. IR spectra were recorded on JASCO DS-301, IR-S and IR-E spectrophotometers. NMR spectra were measured with JNM C-60H spectrometer at 60 MHz using tetramethylsilane (TMS) as internal reference.

14) Separation of products was performed using a Varian gaschromatograph Model 700 (TCD) under a flow rate of a carrier gas (He) controlled to 200 ml/min at 230°. The instrument was fitted with a 20'×3/8 aluminum spiral column packed with 30% SE-30.

Preparation of 1-Ethoxycarbonyl-1-hydroxyquinolizidines (10a and 10b)——A solution of **2** (1.53 g, 0.01 mole) and acetone cyanohydrin (3.4 g, 0.04 mole) in CH_2Cl_2 (50 ml) was stirred at room temperature for 12 hr. The solvent was evaporated *in vacuo* and the residue was dissolved in dil. HCl, washed with ether, made alkaline with K_2CO_3 and extracted with ether.

A solution of the extract residue (**8**) in conc. HCl (20 ml) was refluxed for 20 hr, and evaporated *in vacuo*. A mixture of the residue and 40% NaOH (30 ml) was refluxed for 5 hr, made acidic with conc. HCl, evaporated *in vacuo* and extracted with hot EtOH.

The EtOH extract residue (**9**) was heated with anhyd. EtOH (50 ml) saturated with HCl gas under reflux for 5 hr. After kept overnight, the EtOH solution was evaporated, made alkaline with K_2CO_3 and extracted with ether to give 1.45 g of a yellow oil, bp 120° (2 mmHg). Chromatography on a silica gel column with pert. ether–ether (1: 1) afforded successively **10a** and **10b**.

Product **10a**: 1-Ethoxycarbonyl-1-(hydroxy-*trans*-10-H)-quinolizidine, a yellow oil, bp 115° (2 mmHg), 1.26 g (56%). Picrate: yellow pillars, mp 127—129° (EtOH-isopropyl ether). *Anal.* Calcd. for $C_{12}H_{21}O_3N \cdot C_6H_3O_7N_2$: C, 47.37; H, 5.40; N, 12.28. Found: C, 47.28; H, 5.40; N, 12.15.

Product 10b: 1-Ethoxycarbonyl-1-(hydroxy-*cis*-10-H)-quinolizidine, a yellow oil, bp 140—150° (2 mmHg) (bath temp.), 0.1 g (4%). Picrate: yellow pillars, mp 129—130° (EtOH). *Anal.* Calcd. for $C_{12}H_{21}O_3N \cdot C_6H_3O_7N_3$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.45; H, 5.45; N, 12.18.

Dehydration of 10a——To an ice-cooled solution of **10a** (0.23 g, 0.001 mole) in pyridine (1 ml) was added $SOCl_2$ (0.12 g, 0.001 mole), and the whole was heated at 70° for 30 min. The reaction mixture was evaporated *in vacuo*, made alkaline with 20% K_2CO_3 and extracted with CH_2Cl_2 to give an oil, bp 150—170° (1 mmHg) (bath temp.). Chromatography on a silica gel column with ether–MeOH (50: 1) gave a small amount of a colorless oil (**11**), bp 150—170° (1 mmHg) (bath temp.). IR ν_{max}^{Film} cm^{-1}: 2940—2800 (Bohlmann bands), 1715 (C=O, ester), 1650 (C=C). NMR τ ($CDCl_3$): 8.72 (3H, t, J=7.0 Hz, $COOCH_2C\underline{H}_3$), 5.82 (2H, q, J=7.0 Hz, $COOC\underline{H}_2CH_3$), 3.20 (1H, b.s, vinyl proton).

Reduction of 10a with $LiAlH_4$——A mixture of **10a** (0.68 g, 0.003 mole), $LiAlH_4$ (0.06 g, 0.00157 mole) and anhyd. ether (30 ml) was stirred at room temperature for 24 hr and then refluxed for 5 hr. To the cooled reaction mixture was added moist ether to decompose excess $LiAlH_4$, and the ether solution was stirred with 40% NaOH. The ether layer was separated and the aqueous layer was washed several times with ether. The combined ether solution was dried over $MgSO_4$, and evaporated to give 0.06 g (10%) of colorless pillars (**12**), mp 142—143° (acetone). *Anal.* Calcd. for $C_{10}H_{19}O_2N$: C, 64.83; H, 10.34; N, 7.56. Found: C, 64.66; H, 10.17; N, 7.29. IR ν_{max}^{Nujol} cm^{-1}: 3380, 3180 (OH).

Dehydrogenation of 10a——A solution of **10a** (1.14 g, 0.01 mole) and Hg $(OAc)_2$ (12.8 g, 0.04 mole) in MeCN (10 ml) was refluxed for 5 hr. A similar processing with the case of dehydrogenation of **2** gave 0.32 g (35 %) of dehydro-1-ethoxycarbonyl-1-hydroxyquinolizidine (**13**), a yellow oil, bp 170° (1 mmHg) (bath temp.). Because it was highly unstable, the elemental analysis could not be done. IR ν_{max}^{Film} cm^{-1}: 1670 (C=C). NMR τ ($CDCl_3$): 4.25 (1H, m, vinyl proton).

Reaction of 13 with 1——A solution of **13** (0.315 g, 0.0014 mole) and **1** (prepared from 0.2 g of pyridine N-oxide and 0.3 g of benzoyl chloride) in CH_2Cl_2 (20 ml) was stirred at room temperature for 48 hr. The reactants were treated with $NaBH_4$ (0.5 g) in anhyd. EtOH in the same way with the case of **3** to give a minute amount of a dimer of **13** (**14**), a yellow oil, bp 250—270° (0.005 mmHg) (bath temp.). IR ν_{max}^{Film} cm^{-1}: 1740 (C=O, ester). Mass Spectrum *m/e*: 452 (M^+).

1,1-Ethylenedioxyquinolizidine (15)——A solution of **2** (5.2 g), ethylene glycol (6 g) and $TsOH \cdot 5H_2O$ (11 g) in benzene (200 ml) was refluxed with azeotropically removing the water formed for 5 hr. After cooling, 20% K_2CO_3 was added, the benzene layer was separated and the aqueous layer was washed several times with benzene. The combined benzene solution was washed with H_2O, dried and evaporated to give 6.1 g (91.1%) of **15**, a light yellow oil, bp 110° (4 mmHg). IR ν_{max}^{Film} cm^{-1}: 2800—2750 (Bohlmann bands). NMR τ ($CDCl_3$): 6.15 (4H, b.s, $-O-C\underline{H}_2-C\underline{H}_2-O-$). Picrate: yellow needles, mp 181—182° (EtOH). *Anal.* Calcd. for $C_{11}H_{19}O_2N \cdot C_6H_3O_7N_3$: C, 48.00; H, 4.94; N, 13.18. Found: C, 48.04; H, 5.07; N, 13.04.

Dehydrogenation of 15——A solution of **15** (8.5 g, 0.043 mole) and Hg (OAc), (75 g, 0.16 mole) in MeCN (1300 ml) was refluxed for 5 hr, and processed in the same way as the first-described reaction to give two products (**16** and **17**).

Product **16**: 9-Dehydro-1,1-ethylenedioxyquinolizidine, a colorless oil, bp 110—115° (3 mmHg), 3.4 g (37%). IR ν_{max}^{Film} cm^{-1}: 1650 (C=C). NMR τ ($CDCl_3$): 8.56—7.85 (8H, m, 4 $C\underline{H}_2$), 7.40—6.90 (4H, m, $-C\underline{H}_2-N-C\underline{H}_2-$), 6.05 (4H, b.s, $-O-C\underline{H}_2-C\underline{H}_2-O-$), 5.00 (1H, t, J=4 Hz, vinyl proton). Perchlorate: colorless needles, mp 189—189.5° (EtOH). *Anal.* Calcd. for $C_{11}H_{17}O_2N \cdot HClO_4$: C, 44.75; H, 6.10; N, 4.75. Found: C, 44.35; H, 5.88; N, 4.65.

Product **17**: A dimer of **15**, a brown oil, bp 200—240° (3 mmHg) (bath temp.), 2 g (31%). *Anal.* Calcd. for $C_{22}H_{34}O_4N_2$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.72; H, 8.81; N, 6.97. Mass Spectrum *m/e*: 390 (M^+). IR $\nu_{max}^{CH_2Cl_2}$ cm^{-1}: 1675 (C=C). NMR τ ($CDCl_3$): 8.70—6.70 (24H, m), 6.10—6.00 (8H, b.s, 2 $-O-C\underline{H}_2-C\underline{H}_2-O-$), 4.30—4.22 (1H, b.s, vinyl proton).

Reaction of 16 with 1——A solution of **16** (3.2 g, 0.016 mole) and **1** (0.033 mole, prepared from 3.2 g of pyridine N-oxide and 4.7 g of benzoyl chloride) in CH_2Cl_2 (120 ml) was stirred at room temperature for 48 hr, followed by reduction of the reactants with excess $NaBH_4$ in anhyd. EtOH. Oily products obtained by the similar processing as described earlier was chromatographed on a silica gel column with CH_2Cl_2 and MeOH. The first fraction eluted with CH_2Cl_2–MeOH (100: 0.5) gave product **19**, the second one with CH_2Cl_2–MeOH (100: 2) afforded a small amount of **15** and the last one with CH_2Cl_2–MeOH (100: 5) yielded product **18**.

Product **18**: 1,1-Ethylenedioxy-9-(2-pyridyl)quinolizidine, colorless needles, mp 82—83° (petr. ether), 0.7 g (17%). *Anal.* Calcd. for $C_{16}H_{22}O_2N_2 \cdot H_2O$: C, 65.75; H, 8.21; N, 9.92. Found: C, 65.93; H, 7.69; N, 9.65. IR $\nu_{max}^{CCl_4}$cm^{-1}: 2830—2790 (Bohlmann bands), 1600 (C=N). NMR τ ($CDCl_3$): 6.60—5.88 (4H, m, -O-C$\underline{H}_2$-C$\underline{H}_2$-O-), 3.10—2.40 (3H, m, C_3-H, C_4-H and C_5-H of pyridine), 1.58—1.40 (1H, m, C_6-H of pyridine). Dipicrate: yellow needles, mp 238—239° (EtOH—acetone). *Anal.* Calcd. for $C_{16}H_{22}O_2N_2 \cdot 2C_6H_3O_7N_3$: C, 45.90; H, 3.83; N, 15.30. Found: C, 46.08; H, 4.01; N, 15.22.

Product **19**: Dehydro-1,1-ethylenedioxy-x-(2-pyridyl)quinolizidine, a yellow oil, bp 180—200° (0.3 mmHg) (bath temp.), 0.4 g (7.3%). Mass Spectrum *m/e*: 272 (M^+). IR ν_{max}^{Film} cm^{-1}: 2830—2800 (deformed Bohlmann bands), 1625, 1595, 1580 (C=C, C=N). NMR τ ($CDCl_3$): 8.70—6.75 (10H, m), 6.70—6.50 (1H, m), 6.05—5.88 (4H, b.s, -O-C$\underline{H}_2$-C$\underline{H}_2$-O-), 5.54 (1H, b.s, vinyl proton), 3.30—2.30 (3H, m, C_3-H, C_4-H, and C_5-H of pyridine), 1.70—1.50 (1H, m, C_6-H of pyridine). Perchlorate, colorless needles, mp 195—196° (EtOH). *Anal.* Calcd. for $C_{16}H_{20}O_2N_2 \cdot 2HClO_4 \cdot 3C_2H_5OH$: C, 43.21; H, 4.58; N, 6.55. Found: C, 43.83; H, 4.82; N, 6.80.