umgefällt, wobei die erst abgefallene Fraktion (0.6 g) durch Absaugen gesammelt und mit V im IR sowie UV Spektrum ganz identisch bewiesen wurde.

Herrn Prof. Dr. Y. Kamura und seiner Assistanten danken wir für die Leitung der Dipolmoment-messungen und die Diskussion der Resultate. Herrn Dr. F. Yoneda haben wir für die Diskussion der Spektroskopie zu danken.

Zusammenfassung

Im Rahmen der Untersuchungen der Synthesemöglichkeit von *as*-Triazin-N-oxyden, oxydierten wir 3-Amino- bzw. 3-Amino-5,6-dimethyl-*as*-triazin durch Persäure, wobei sich die entsprechenden 5-Oxo-verbindungen und ein Mono-N-oxyd von 3-Amino-5,6-dimethyl-*as*-triazin erhalten ließen, deren Konstitutionen bzw. diejenigen der acetylierten Körpern durch Dipolmoment-Messungen sowie spektroskopisch diskutiert wurden.

(Eingegangen am 15. Juni 1964)

[Chem. Pharm. Bull. 12(11)1338~1343(1964)] UDC 547.834.2.07

186. Tetsuo Miyadera and Issei Iwai: The Studies on Quinolizinium Salts. I.*1 Syntheses of Quinolizinium and 1-, 2-, 3-, and 4-Methylquinolizinium Bromides.

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A number of quinolizinium salts have been synthesized, since a quinolizinium ion structure was found in the course of the structural investigation of the alkaloid Sempervirine by Woodward, *et al.* in 1949.[1] They first synthesized the parent quinolizinium salt in a rather low yield,[2] and since then other workers reported various synthetic methods for the parent compound and derivatives in moderate yields.[3~11] An excellent synthetic method for the preparation of the parent compound was devised by Glover, *et al.*[6] involving the aromatization of 1,2,3,4-tetrahydro-1-oxoquinolizinium salt (IIIa) with boiling acetic anhydride in quantitative yield. This synthetic route, however, is not

*1 When this and next part of the series were presented before the 84th Anual Meeting of Pharmaceutical Society of Japan, Tokyo, April 4~7, 1964, the name dehydroquinolizinium bromide was used for the parent compound (IVa). The nomenclature is very reasonable (see ref. 3), but we will employ the Chemical Abstracts name quinolizinium for the parent ion in this series.

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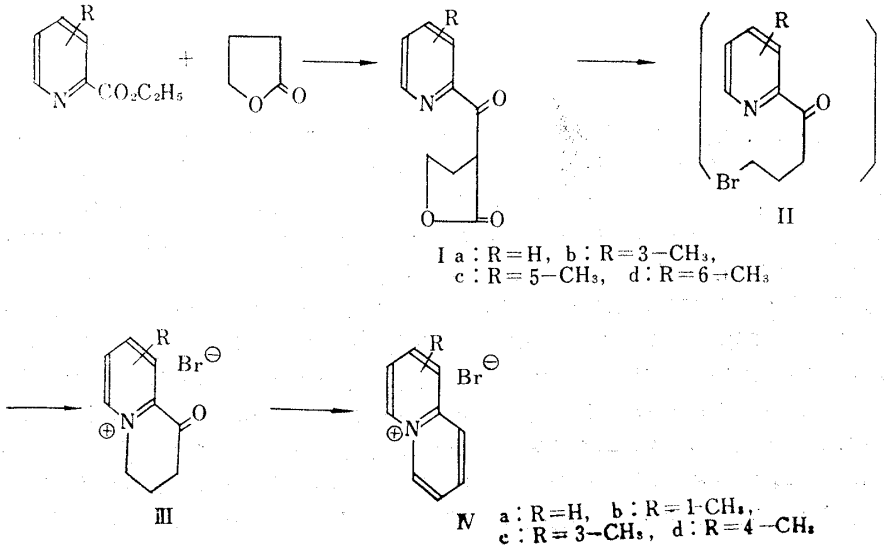
1) R. B. Woodward, B. Witkop: J. Am. Chem. Soc., **71**, 379 (1949); R. B. Woodward, W. M. McLamore: *Ibid.* **71**, 379 (1949).
2) R. B. Woodward, A. G. Beaman (Beaman, Ph. D. Thesis, Harvard University, 1951).
3) V. Boekelheide, W. G. Gall: J. Am. Chem. Soc., **76**, 1832 (1954); V. Boekelheide, J. M. Ross: *Ibid.*, **77**, 5691 (1955); V. Boekelheide, H. Fritz, J. M. Ross, H. X. Kaempfen: Tetrahedron, **20**, 33 (1964).
4) A. N. Nesmeyanov, I. Rybinskaya: Doklady Akad. Nauk S. S. S. R., **116**, 93 (1957).
5) A. Richards, T. S. Stevens: J. Chem. Soc., **1958**, 3067.
6) E. E. Glover, G. Jones: Chem. & Ind. (London), **1956**, 1456; *Idem*: J. Chem. Soc., **1958**, 3021.
7) *Idem*: *Ibid.*, **1959**, 1686.
8) O. Westphal, K. Jann, W. Heffe: Arch. Pharm., **294**, 37 (1961).
9) T. M. Moynehan, K. Schofield, R. A. Y. Jones, A. R. Katritzky: J. Chem. Soc., **1962**, 2637.
10) O. Westtphal, G. Feix: Angew. Chem., **75**, 206 (1963).
11) H. V. Hansen, E. D. Amstutz: J. Org. Chem., **28**, 393 (1963).

convenient for large scale preparation, since the starting materials picolinonitrile and γ-ethoxypropyl bromide are obtained from rather tedious procedures.

We wish to report a more convenient preparation of quinolizinium bromide (Ⅳa) in good overall yields, together with its extension to the preparation of 1-, 2-, 3-, and 4-methylquinolizinium bromides.

This synthetic method is essentially an adaptation of an ester condensation of ethyl picolinate with γ-butyrolactone derivative reported by Winterfeld, *et al.*[12] and the cyclic ketone (Ⅲa) could be synthesized in good yield from commercially available ethyl picolinate and γ-butyrolactone.

Ethyl picolinate was condensed with γ-butyrolactone in the presence of sodium hydride or potassium forming a keto-lactone (Ia), m.p. 53.5~54.5°, in 69.8% and 58.5% yields respectively. The infrared spectrum showed bands at 1710 (C=O) and 1770 cm^{-1} (lactone) and the ultraviolet spectrum exhibited absorptiom maxima at 233.5 and 270 mμ similar to those of 2-acetylpyridine and an absorption near 300 mμ indicative of the presence of enol form conjugated with pyridine and the carbonyl group of the γ-lactone.



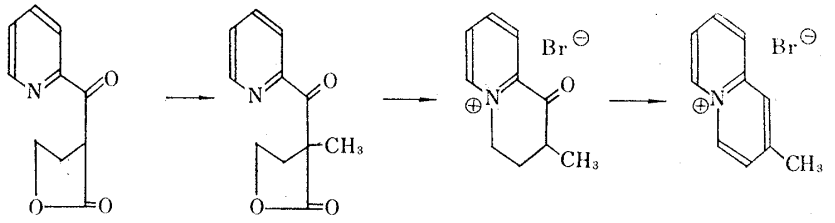
Cahrt 1.

Treatment of the keto-lactone (Ia) with 48% hydrobromic acid afforded the bromo-ketone (Ⅱa) with concurrent decarboxylation. The bromo-ketone was not isolated but immediately cyclized by either standing at room temperature or refluxing a chloroform solution giving 82.5% yield of the quaternary cyclic keto-bromide (Ⅲa), m.p. 210~211°. The melting point was somewhat higher than the reported ones,[6,13,14] but the analytical and spectral evidence of Ⅲa confirmed the structure. That the melting point was variable and there are rather difference among the reported values must result from the hygroscopic property of the substance. The cyclic keto-bromide (Ⅲa), thus obtainable in 57.6% yield from ethyl picolinate and γ-butyrolactone, gave quantitative yield of Ⅳa, m.p. 268~269°, on boiling with acetic anhydride according to the synthetic method by Glover, *et al.*[6] The ultraviolet spectrum and physical properties of Ⅳa and the picrate were almost identical with the reported ones.

While four monomethyl derivatives of Ⅳa have already been prepared by various methods,[3~9] they could also be prepared similarly except for the 2-methyl derivative.

12) K. Winterfeld, E. Müller : Ann., **581**, 77 (1953).
13) R. C. Elderfield, J. M. Lagowski, O. L. McCurdy, S. L. Wythe : J. Org. Chem., **23**, 435 (1958).
14) K. B. Prasad, G. A. Swan : J. Chem. Soc., **1958**, 2024.

In the preparation of 1- and 3-methylquinolizinium bromides (Ⅳb, Ⅳc), the quaternary keto-bromides (Ⅲb, Ⅲc) were aromatized without isolation in pure crystalline form. Owing to hygroscopic properties, some of the quaternary cyclic keto-bromides separated as oils on refluxing the chloroform solution, but the oils almost solidified by drying *in vacuo*. The yield of 1-metylquinolizinium bromide (Ⅳb) was lower than that of other methyl derivatives, because of tar formation, while no tar was formed in other syntheses. Although 2-methylquinolizinium bromide (Ⅶ) could be prepared from ethyl 4-methylpicolinate and γ-butyrolactone, it was more conveniently prepared by methylation of Ia.

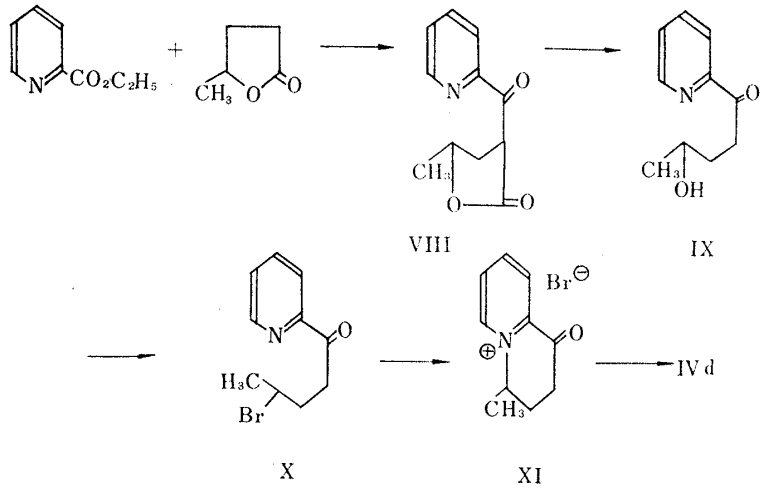


Ia V VI VII

Chart 2.

The sodium salt prepared from sodium and the keto-lactone (Ia) in benzene was treated with methyl iodide to afford a methyl keto-lactone (V), m.p. 65~66°, analytically corresponding to $C_{11}H_{11}O_3N$. The infrared spectrum showed bands at 1740 (lactone) and 1702 cm^{-1} (C=O) and the ultraviolet spectrum exhibited the absorption similar to those of the starting material (Ia), but no conjugated enol absorption. The methyl keto-lactone was treated with 48% hydrobromic acid affording quaternary cyclic keto-bromide (Ⅵ) *via* a bromo-ketone, followed by aromatization to 2-methylquinolizinium bromide (Ⅶ) with refluxing acetic anhydride. The melting point of Ⅶ was undepressed by admixture with the authentic sample prepared from 2-picolyllithum and 4,4-dimethoxybutan-2-one.[5]

Starting from ethyl picolinate and γ-valerolactone 4-methylquinolizinium bromide was also prepared as shown in chart 3. In this route, however, treatment of the keto-lactone (Ⅷ) with 48% hydrobromic acid resulted in the formation of mostly dark tar and



VIII IX X XI

Chart 3.

no pure cyclic keto-bromide (Ⅺ). However, the following alternative sequence yielded the desired compound in moderate yield. The keto-lactone (Ⅷ) was decarboxylated into the keto-alcohol (Ⅸ) in dilute sulfuric acid, followed by bromination of the alcohol with

phosphorus tribromide furnishing the bromo-ketone (X). Cyclization of X to the quaternary keto-bromide (XI) was affected by refluxing the chloroform solution and then XI was aromatized to 4-methylquinolizinium bromide (IVd) by refluxing in acetic anhydride.

Although some of the monomethylquinolizinium compounds have been reported only as the picrates or perchlorates, the authors could purify and characterize all of the methyl derivatives as the bromides as described below.

Quinolizinium bromide and all monomethyl derivatives formed picrates from which pure bromides were regenerated through anionic exchange resin and recrystallized for analytical sample.

Quinolizinium bromide and the methyl derivatives readily formed hydrates and some were difficult to dehydrate by drying at 100° *in vacuo*. For instance, the 4-methyl derivative remained as a monohydrate under such condition and the 1-methyl derivative, as a hemihydrate. On the other hand, the parent bromide, the 2- and 3-methyl derivatives were obtained as the anhydrous salts.

Experimental

α-(2-Hydroxyethyl)-β-oxo-2-pyridinepropionic Acid, γ-Lactone (Ia)——A) To a stirred and gently refluxed suspension of NaH (7.15 g.) in 500 ml. of dry toluene was added dropwise a mixture of ethyl picolinate (45.0 g.) and γ-butyrolactone (25.0 g.). The mixture was refluxed for 8 hr. with stirring. The resulting mixture was cooled and the Na salt of the lactone (Ia) was extracted with H_2O. Acidification of the aq. solution with AcOH gave a brown oil which was extracted with benzene. The benzene extract was washed with H_2O and dried over Na_2SO_4. Distillation *in high vacuo* gave 39.7 g. (69.5%) of a viscous oil, b.p. $130°/3\times10^{-5}$ mm., which crystallized on standing. It was recrystallized from ether-petr. ether giving colorless plates (Ia), m.p. 53.5~54.5°. *Anal.* Calcd. for $C_{10}H_9O_3N$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.75; H, 4.87; N, 7.35. UV λ_{max}^{EtOH} mμ (ε): 233.5 (8,450), 270 (4,850). IR ν_{max}^{Nujol} cm^{-1}: 1710 (C=O), 1770 (γ-lactone).

B) To a stirred suspension of finely grained K (11.5 g.) in 500 ml. of dry benzene was added a mixture of ethyl picolinate (45.0 g.) and γ-butyrolactone (25.0 g.). On warming to 75° an exothermic reaction ensued and the mixture was cooled to 40~45°. The reaction temperature was maintained at the same temperature by occasional cooling. After the reaction subsided, the mixture was refluxed for 4 hr. Work-up as described above gave 33.3 g. (58.5%) of the keto-lactone (Ia) which was identical with the compound prepared by method A.

1,2,3,4-Tetrahydro-1-oxoquinolizinium Bromide (IIIa)——A solution of the lactone (Ia) (80.6 g.) in 600 ml. of 48% HBr was heated at 110° until CO_2 evolution ceased. The solution was then refluxed for 1.5 hr. and the resulting solution was concentrated to about 150 ml.; cooled and diluted with H_2O, followed by neutralization with Na_2CO_3; and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 for a short period and after removal of Na_2SO_4 the filtrate was refluxed for 2.5 hr. Fine needles precipitated and were collected. Additional crystals were obtained from the concentrated filtrate. Total yield, 79.0 g. (82.5%). Recrystallization from EtOH after treatment with Norit gave needles, m.p. 210~211°. (lit. 197,[6] 204.5~206°,[23] 205°.[14]). *Anal.* Calcd. for $C_9H_{10}ONBr$: C, 47.39; H, 4.43; N, 6.14. Found: C, 47.16; H, 4.43; N, 6.09. UV λ_{max}^{EtOH} mμ (ε): 274.3 (6,000), 280~290 (sh). IR ν_{max}^{Nujol} cm^{-1}: 1727 (C=O), 1626, 1582 ($C=\overset{\oplus}{N}<$, arom, C=C).

Quinolizinium Bromide (IVa)——In the manner described by Glover, *et al.*,[6] the quaternary keto-bromide (IIIa) was treated with reflux Ac_2O giving a quantitative yield of IVa. The product was recrystallized from EtOH as plates which were dried at 100° *in vacuo*, m.p. 268~269° (lit.[6] 262~264°). *Anal.* Calcd. for C_9H_8NBr: C, 51.45; H, 3.84; N, 6.67. Found: C, 51.32; H, 3.95; N, 6.79. The picrate of IVa was prepared and recrystallized from EtOH, m.p. 180~181° (lit.[6] 179°). *Anal.* Calcd. for $C_{15}H_{10}O_7N_4$: C, 50.28; H, 2.81; N, 15.64. Found: C, 50.06; H, 2.92; N, 15.72.

α-(2-Hydroxyethyl)-β-oxo-6-methyl-2-pyridinepropionic Acid, γ-Lactone (Id)——A mixture of ethyl 6-methylpicolinate (14.9 g.) and γ-butyrolactone was reacted with finely grained K (3.6 g.) as described above for the preparation of Ia. From the resulting solution 11.3 g. of a viscous oil, b.p. 127~130°/3×10^{-5} mm., was obtained, which crystallized on standing. Recrystallization from ether-petr. ether gave colorless needles (Id), m.p. 91~93°. *Anal.* Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.22; H, 5.41; N, 6.64. UV λ_{max}^{EtOH} mμ (ε): 238 (8,100), 280 (6,800), 300~330 (sh). IR ν_{max}^{Nujol} cm^{-1}: 1680 (conj. lactone), 1642 (enol C=C).

1,2,3,4-Tetrahydro-6-methyl-1-oxoquinolizinium Bromide (IIId)——A solution of the lactone (Id, 49.3 g.) was treated as described for the preparation of IIIa. Refluxing a $CHCl_3$ solution of Ia afforded

the quaternary keto-bromide (IIId, 48.9 g.). Recrystallization from EtOH after treatment with Norit gave colorless needles, m.p. 260~261°. *Anal.* Calcd. for $C_{10}H_{12}ONBr$: C, 49.61; H, 5.00; N. 5.79. Found: C, 49.52; H, 5.12; N, 5.86. UV: λ_{max}^{EtOH} 282.5 mμ (ε 7,700). IR ν_{max}^{Nujol} cm^{-1}: 1722 (C=O), 1620, 1585 ($C=\overset{\oplus}{N}<$, arom. C=C)

4-Methylquinolizinium Bromide (IVd)——A) A suspension of the quaternary keto-bromide (IIId, 41.0 g.) in 600 ml. of Ac_2O was refluxed for 2 hr. The resulting solution was evaporated to dryness *in vacuo* and H_2O was added to the residue, followed by evaporation of the aq. solution. The solid residue was precipitated from an EtOH solution by AcOEt, giving IVd in a quantitative yield. Recrystallization from EtOH after treatment with Norit yielded pure IVd which was dried at 100° *in vacuo*. 4-Methyl derivative (IVd) did not show a sharp melting point. *Anal.* Calcd. for $C_{10}H_{10}NBr \cdot H_2O$: C, 49.61; H, 5.00; N, 5.79. Found: C, 49.76; H, 5.09; N, 5.82. UV λ_{max}^{EtOH} mμ (ε): 331 (19,500), 324.5 (11,500), 317.5 (12,000), 289 (4,900), 238 (4,900), 234 (25,000). IR ν_{max}^{Nujol} cm^{-1}: 3430 (H_2O), 1652, 1635 ($C=\overset{\oplus}{N}<$, arom. C=C).

The picrate of IVd was prepared and recrystallized from EtOH giving yellow needles, m.p. 137.5~138.5° (lit. 135°,[6] 135~135.5°[3]). *Anal.* Calcd. for $C_{16}H_{12}O_7N_4$: C, 51.62; H, 3.25; N, 15.05. Found: C, 51.57; H, 3.18; N, 14.94.

B) The ketoalcohol (IX, 3.0 g.) was heated with PBr_3 (30 ml.) on a steam-bath with stirring. The solution was cooled, poured onto ice, the aq. solution neutralized with Na_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 and after removal of Na_2SO_4 refluxed for 5 hr. Evaporation of the $CHCl_3$ solution gave 2.7 g. of X as an oil which was used in the next reaction without purification.

Crude X was treated with boiling Ac_2O giving IVd which was isolated as the picrate, 137.5~138.5°, which was confirmed by the mixed melting point and IR spectra.

α-(2-Hydroxyethyl)-β-oxo-5-methyl-2-pyridinepropionic Acid, γ-Lactone (Ic)——To a stirred suspension of NaH (4.65 g.) in 400 ml. of dry toluene was added dropwise under reflux a mixture of ethyl 5-methylpicolinate (30.0 g.) and γ-butyrolactone (15.7 g.). After addition the solution was refluxed for 10 hr. with stirring. Work-up of the resulting solution as described above afforded an oil (Ic) b.p. 136~137°/5×10^{-5} mm. (20.8 g.), which crystallized on standing. Recrystallization from ether-petr. ether gave colorless needles, m.p. 73~74°. *Anal.* Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.30; H, 5.28; N, 6.93. UV λ_{max}^{EtOH} mμ (ε): 246 (10,700), 273 (7,300), 295~330 (sh). IR ν_{max}^{Nujol} cm^{-1}: 1760 (γ-lactone), 1695 (C=C).

3-Methylquinolizinium Bromide (IVc)——A solution of Ic (19.0 g.) in 150 ml. of 48% HBr was decarboxylated at 110° and refluxed for 1 hr. The solution was concentrated to about 50 ml. and H_2O added, followed by neutralization of the aq. solution with Na_2CO_3 and extraction with $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4 for a short period and refluxed for 1 hr. depositing brown oil. Evaporation of the $CHCl_3$ solution gave an oil (IIIc) which crystallized by drying *in vacuo*, yield 20.8 g. The crude bromide (IIIc) was aromatized by reflux an Ac_2O solution for 2 hr. yielding IVc quantitatively. Recrystallization from EtOH-AcOEt furnished needles which were dried at 100° *in vacuo*. m.p. 189~190° (lit.[6] 189°). An analytical sample was prepared by recrystallizing the bromide which was regenerated from the pure picrate of IVc using ion-exchange resin (Dowex-1 Br^-). *Anal.* Calcd. for $C_{10}H_{10}NBr$: C, 53.59; H, 4.50; N, 6.25. Found: C, 53.65; H, 4.52; N, 6.58. IR ν_{max}^{Nujol} cm^{-1}: 1639, 1590 ($C=\overset{\oplus}{N}<$, arom. C=C). UV λ_{max}^{EtOH} mμ (ε): 329 (18,500), 322.5 (9,900), 316 (11,700), 305~311 (sh), 303 (4,800), 289 (2,800), 277.5 (2,500), 236 (20,400), 232 (21,000).

The picrate of IVc was prepared and recrystallized from EtOH giving yellow needles, m.p. 183~184° (lit.[6] 182°). *Anal.* Calcd. for $C_{16}H_{12}O_7N_4$: C, 51.62; H, 3.25; N, 15.05. Found: C, 51.61; H, 3.27; N, 14.87.

α-(2-Hydroxyethyl)-β-oxo-3-methyl-2-pyridinepropionic Acid, γ-Lactone (Ib)——A mixture of ethyl 3-methylpicolinate (12.8 g.) and γ-butyrolactone (6.65 g.) was reacted with NaH (1.9 g.) in dry toluene as described above. The resulting solution was refluxed for 10 hr. Acidification of the extracted aq. solution with AcOH gave a brown viscous oil which was distilled *in vacuo* giving 8.25 g. of Ib, b.p. 145°/5×10^{-4} mm. *Anal.* Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.11; H, 5.49; N, 6.47. UV λ_{max}^{EtOH} mμ (ε): 278 (5,100), 233.5 (7,100). IR $\nu_{max}^{liq.}$ cm^{-1}: 1770 (γ-lactone), 1690 (C=O).

1-Methylquinolizinium Bromide (IVb)——A solution of Ib (8.0 g.) in 80 ml. of 48% HBr was refluxed for 1 hr. after decarboxylation. The solution was concentrated to small volume *in vacuo*, diluted with H_2O and neutralized with Na_2CO_3. The precipitated bromide was extracted with $CHCl_3$ and the $CHCl_3$ solution refluxed for 3 hr. Removal of the solvent gave 6.8 g. of solid (IIIb) which was used without purification for subsequent aromatization. Crude IIIb was refluxed for 2 hr. in 100 ml. of Ac_2O and the resulting solution evaporated to dryness *in vacuo*. To the solid residue H_2O was added and an insoluble tar removed by filtration. The filtrate was evaporated to dryness and the residue recrystallized from EtOH-AcOEt giving 4.35 g. of plates (IVb), m.p. 159~160°, which was dried at 100° *in vacuo*. An analytical sample was prepared as described for the preparation of IVc. *Anal.* Calcd. for $C_{10}H_{10}NBr \cdot \frac{1}{2}H_2O$: C, 51.52; H, 4.76; N, 6.01. Found: C, 51.55; H, 4.64; N, 6.36. UV λ_{max}^{EtOH} mμ (ε): 332 (18,800),

325 (10,500), 317.5 (11,700), 289 (3,300), 229 (10,300). IR ν_{max}^{Nujol} cm^{-1} : 1640, 1594 (C=$\overset{\oplus}{N}$<, arom. C=C), 3430 (H_2O).

The picrate of Ⅳb was prepared and recrystallized from EtOH giving yellow needles, m.p. 152～153° (lit.[7] 149°). *Anal.* Calcd. for $C_{16}H_{12}O_7N_4$: C, 51.62; H, 3.25; N, 15.05. Found : C, 51.61, H, 3.36; N, 14.95.

α-(2-Hydroxyethyl)-α-methyl-β-oxo-2-pyridinepropionic Acid, γ-Lactone (V)——To a suspension of Na salt of Ia prepared from fine small pieces of Na (3.45 g.) and Ia (28.6 g.) in 200 ml. of benzene was added CH_3I (26.0 g.) and the mixture stirred at room temperature for 3 weeks. After removal of NaI formed and unchanged Na salt the filtrate was evaporated to leave 11.8 g. of an oil (V) which was distilled at 134°/5×10^{-4} mm. After solidification on standing, the solid was recrystallized from ether-petr. ether giving colorless needles, m.p. 65～66°. *Anal.* Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found : C, 64.22; H, 5.50; N, 6.86. UV λ_{max}^{EtOH} mμ (ε) : 233 (8,600), 269.3 (4,400). IR ν_{max}^{Nujol} cm^{-1} : 1702 (C=O), 1740 (γ-lactone).

2-Methylquinolizinium Bromide (Ⅶ)——The keto-lactone (V, 8.37 g.) was decarboxylated at 110° in 80 ml. of 48% HBr and the solution refluxed 2 hr. Work-up of the solution as described above yielded 5.2 g. of the crude Ⅵ as a brown oil subsequent aromatization in 100 ml. of boiling Ac_2O afforded 3.6 g. of solid Ⅶ. The product was recrystallized from EtOH-AcOEt forming plates, m.p. 194～195°, which was dried at 100° *in vacuo*. An analytical sample was prepared as described for the preparation of Ⅳc. *Anal.* Calcd. for $C_{10}H_{10}NBr$: C, 53.59; H, 4.50; N, 6.25. Found : C, 53.42; H, 4.62; N, 6.24. Drying *in vacuo* gave Ⅶ as a hemihydrate. *Anal.* Calcd. for $C_{10}H_{10}NBr\cdot\frac{1}{2}H_2O$: C, 51.52; H, 4.50; N, 6.01. Found : C, 51.66, H, 4.99; N, 6.32. UV λ_{max}^{EtOH} mμ (ε) : 327.5 (19,800), 320 (11,000), 313 (12,800), 285 (3,300), 274 (3,100), 227 (21,000). IR ν_{max}^{Nujol} cm^{-1} : 1649, 1640, 1585 (C=$\overset{\oplus}{N}$<, arom. C=C), 3420 (H_2O).

The picrate of Ⅶ was prepared and recrystallized from EtOH forming yellow needles, m.p. 163～164° (lit.[6] 162°). *Anal.* Calcd. for $C_{16}H_{12}O_7N_4$: C, 51.62; H, 3.25; N, 15.05. Found : C, 51.77; H, 3.62; N, 14.78.

α-(2-Hydroxypropyl)-β-oxo-2-pyridinepropionic Acid, γ-Lactone (Ⅷ)——A mixture of ethyl picolinate (30.6 g.) and γ-valerolactone (20.1 g.) was reacted with K (7.8 g.) in 300 ml. of dry benzene at 40～45° and the mixture refluxed for 5 hr. Treatment of the resulting solution as described above yielded 19.4 g. of Ⅷ as an oil, b.p. 122～124°/3×10^{-5} mm. *Anal.* Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found : C, 64.04; H, 5.45; N, 6.67. UV λ_{max}^{EtOH} mμ (ε) : 234 (8,500), 270 (5,000), 302 (2,600). IR $\nu_{max}^{liq.}$ cm^{-1} : 1770 (γ-lactone), 1698 (C=O), 1647 (enol C=C).

1-(2-Pyridyl)-4-hydroxy-1-pentanone (Ⅸ)——A solution of Ⅷ (10.3 g.) in 100 ml. of 6*N* H_2SO_4 was refluxed for 1 hr. after decarboxylation. The solution was cooled, made alkaline with Na_2CO_3 and extracted with Et_2O. The Et_2O extract was washed with H_2O, dried over Na_2SO_4 and after removal of the solvent, yielded 5.6 g. of Ⅸ as an oil which was distilled at 115～120°/3×10^{-3} mm. (bath temp.). *Anal.* Calcd. for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31; N, 7.82. Found : C, 66.86; H, 7.18; N, 7.69. UV λ_{max}^{EtOH} mμ (ε) : 229 (6,900), 266.5 (3,800). IR $\nu_{max}^{liq.}$ cm^{-1} : 3400 (OH), 1695 (C=O)

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Summary

Quinolizinium bromide (Ⅳa) was prepared in good yield from commercially available ethyl picolinate and γ-butyrolactone. This synthetic route is convenient for synthesis of the parent compound (Ⅵa) and was extended to preparations of the monomethyl derivatives (Ⅳb～d, Ⅶ).

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