Provided that this oxidation products were C–O dehydro compounds, VI or VII would be identical with a metho–salt of V. Comparisons of their NMR spectra (1 N NaOD–$D_2O$), however, revealed that they were all different.

Thus, the foregoing fact and investigation of NMR spectra of VI and VII were probably indicative of the structure of VI as 1,1′,2,2′-tetramethyl–6,6′-dimethoxy–7,7′-dihydroxy–1,1′,2,2′-tetrahydro–8,8′-bisisoquinolinium dimethiodide, though contrary to the common belief that such an oxidation gave C–O dehydro compounds, and VII was assumed to be a trimer, whose structure was still obscure.

From the above–mentioned results, although ferricyanide oxidation products were susceptible to a kind of substituents at 1–position, they were largely dependent on both oxidants and solvents, which would have controlling effect upon the product ratio, namely C–C dehydro and C–O dehydro compounds.

Further research on this problem and the syntheses of bis–coclaurine alkaloids having bis–diphenyl ether linkage from corresponding tertiary amines as an extention of the oxidation are currently undertaken.

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## Syntheses of Ten-membered Ring Amines from Quinolizidine[1,2]

The structural relation of the ten–membered ring alkaloids to the corresponding quinolizidine alkaloids has led us to develope syntheses of medium–sized ring amines from 1–azabicycloalkanes. This paper deals with the syntheses of ten–membered ring amines from quinolizidine.

The iminium salt[3] (II) (perchlorate: mp 233—234° (decomp.), picrate: mp 105.5—106°) obtained by mercuric acetate oxidation of quinolizidine (I) was treated with potassium cyanide to give cyanoquinolizidine (III),[4] which was neutralized with perchloric acid or picric acid to give back the iminium salt (II). Methiodide (IV), mp 242—243° (decomp.) (*Anal.* Calcd. for $C_{11}H_{19}N_2I$: C, 43.14; H, 6.26; N, 9.15. Found: C, 43.16; H, 6.27; N, 9.33) of III, when treated with silver oxide, gave an amide (V), which was neutralized with hydrobromic acid into a methobromide (VI), mp 286—289° (decomp.) (IR $cm^{-1}$: 3200, 3350 ($NH_2$),

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[1] Presented at the Hokuriku branch meeting of the Pharmaceutical Society of Japan, November, 1967.
[2] All melting points were measured with a micro–melting point apparatus, the Yanagimoto Mfc. Co.
[3] N.J. Leonald, A.S. Hay, R.W. Fulmer, and V.W. Gash, *J. Am. Chem. Soc.*, **77**, 439 (1955).
[4] N.J. Leonald and A.S. Hay, *J. Am. Chem. Soc.*, **78**, 1984 (1956).

1605, 1670 ($CONH_2$); *Anal.* Calcd. for $C_{11}H_{21}ON_2Br$: C, 47.66; H, 7.63; N, 10.11. Found: C, 47.34; H, 7.43; N, 10.33).

Now, attempts to produce the respective medium-sized ring amines from the compounds IV, V and VI were successfully carried out, as shown in Chart 1.

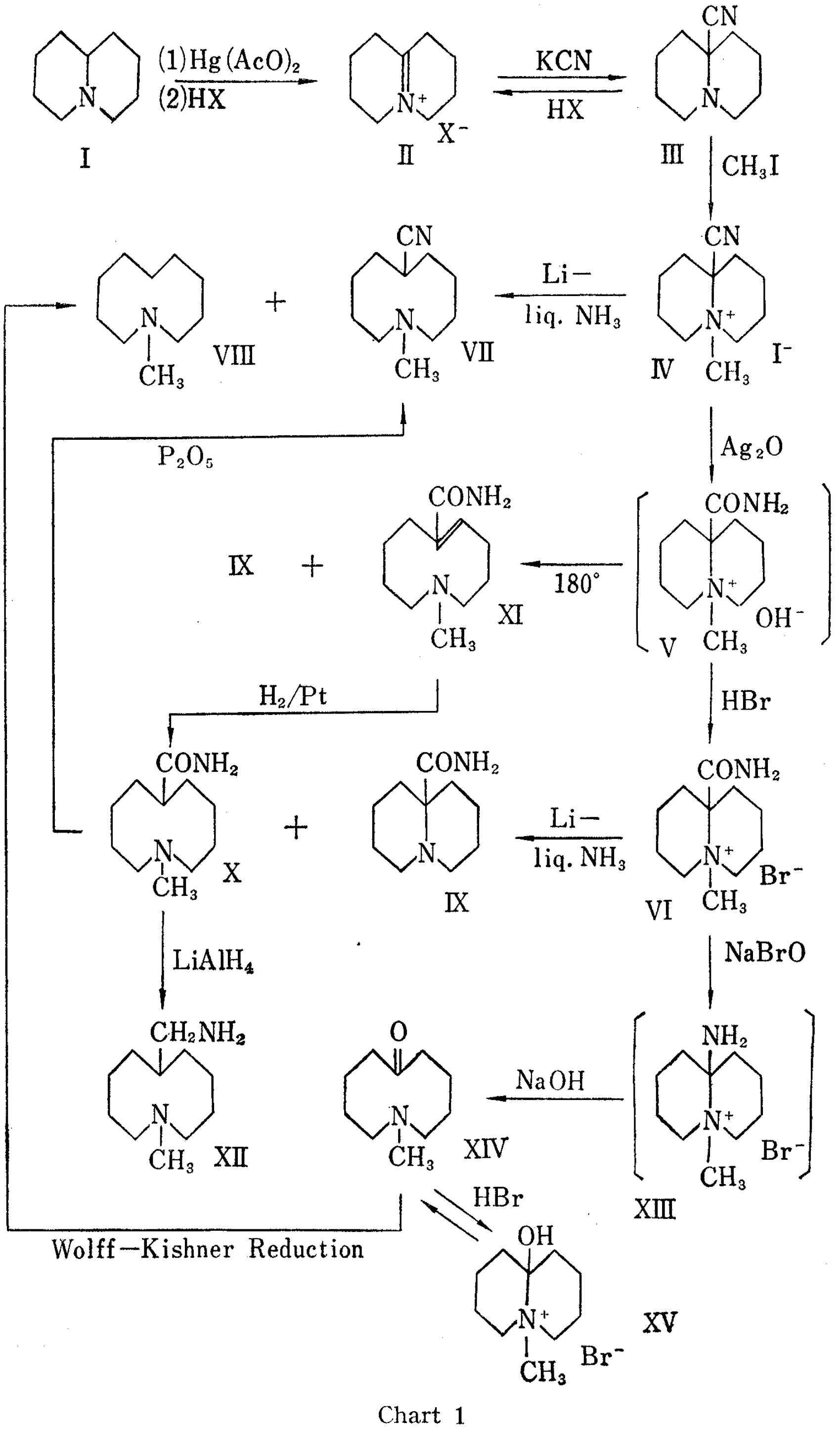

Chart 1

Reaction of the methiodide (IV) with lithium in liquid ammonia gave the expected compounds VII, bp 170° (18 mmHg) (bath temp.) (IR $cm^{-1}$: 2800 ($N-CH_3$), 2210 (CN); picrate: mp 181—182°, *Anal.* Calcd. for $C_{17}H_{23}O_7N_5$: C, 49.87; H, 5.66; N, 17.11. Found: C, 50.00; H, 5.52; N, 17.38), and VIII, bp 92—95° (18 mmHg) (bath temp.) (IR $cm^{-1}$: 2800

(N-$CH_3$); picrate: mp 189—191°. *Anal.* Calcd. for $C_{16}H_{23}O_7N_4$: C, 49.99; H, 6.29; N, 14.58. Found: C, 49.91; H, 6.29; N, 14.36) in 7% and 70% yields, respectively.

Reaction of the methobromide (VI) with lithium in liquid ammonia gave the compounds IX, mp 116—117° (IR $cm^{-1}$: 3200, 3420 ($NH_2$), 1560, 1680 ($CONH_2$); *Anal.* Calcd. for $C_{10}H_{18}ON_2$: C, 65.89; H, 9.96; N, 15.37. Found: C, 65.20; H, 9.91; N, 15.14; perchlorate: mp 255—257° (decomp.). *Anal.* Calcd. for $C_{10}H_{19}O_5N_2Cl$: C, 42.49; H, 6.77; N, 9.91. Found: C, 42.54; H, 6.51; N, 9.96) in 18% yield, and X, mp 177—178° (IR $cm^{-1}$: 3180, 3400 ($NH_2$), 1640 ($CONH_2$), 2800 (N-$CH_3$), *Anal.* Calcd. for $C_{11}H_{22}ON_2$: C, 66.62; H, 11.18; N, 14.13. Found: C, 67.05; H, 11.30; N, 13.79. NMR $\tau$: 7.91 (3H, singlet, N-$CH_3$).

Hofmann degradation of the methyl hydroxide (V) by heating gave the demethylated compound (IX) in 25% yield, and the methine base (XI), mp 154—155° (IR $cm^{-1}$: 3180, 3400 ($NH_2$), 1600, 1650 ($CONH_2$), 2800 (N-$CH_3$), *Anal.* Calcd. for $C_{11}H_{20}ON_2$: C, 67.30; H, 10.27; N, 14.27. Found: C, 67.38; H, 10.18; N, 14.38)in 10% yield. The former compound was found to be identical with the compound IX derived from VI by mixed melting point determination and infrared spectrum comparison. And hydrogenation of the latter (XI) using platinic oxide gave the dihydroamine, which did not show any melting point depression by the admixture with the compound X derived from VI.

Furthermore, the action of phosphorus pentoxide on X gave a nitrile which was identified with VII derived from IV, and lithium aluminum hydride reduction of X gave XII, bp 120° (4 mmHg) (bath temp.) (IR $cm^{-1}$: 3320, 3370 ($NH_2$), 2800 (N-$CH_3$); picrate: mp 172—174°, *Anal.* Calcd. for $C_{17}H_{27}O_7N_5$: C, 49.38; H, 6.58; N, 17.45. Found: C, 49.42; H, 6.58; N, 17.56).

The action of sodium hypobromide on VI afforded an amino compound, mp 222—224° (*Anal.* Calcd. for $C_{10}H_{21}N_2Br$: C, 48.20; H, 8.49; N, 11.20. Found: C, 47.19; H, 8.47; N, 10.83) which would be assumed to present formula XIII. Heating of XIII in an alkali solution afforded a ten-membered aminoketone (XIV),[5] bp 120° (18 mmHg) (bath temp.) (IR $cm^{-1}$: 2800 (N-$CH_3$), 1680 (C=O); picrate: mp 255—256°. *Anal.* Calcd. for $C_{16}H_{22}O_8N_4$; C, 48.24; H, 5.57; N, 14.07. Found: C, 48.38; H, 5.61; N, 13.83), whose ring appears in the majority of the medium sized ring alkaloids.

The infrared spectrum of hydrobromide (XV), mp 245—246° of XIV exhibited as expected band at 3120 $cm^{-1}$ attributable to a hydroxyl group, but not carbonyl band.

Wolff-Kishner reduction of XIV gave a ten-membered amine, which was identified with VIII derived from IV.

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[5] N.J. Leonald, M. Ōki, and S. Chiavarelli, *J. Am. Chem. Soc.*, **77**, 6234 (1955).