Faculty of Pharmaceutical Sciences,
University of Tokyo
Hongo, Bunkyo-ku, Tokyo

National Institute of Hygienic Sciences
1-18-1, Kamiyoga, Setagaya-ku, Tokyo

Zenzo Tamura
Yoichi Iitaka

Hiroya Tanabe
Sadao Uchiyama

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Syntheses of Ten-membered Ring Amine Derivatives and 1-Azabicyclo[4,4,1]undecane from 3,4,6,7,8,9-Hexahydro-2*H*-quinolizine

It is known that the enamine reacted with trichloroacetic acid producing β,β,β-trichloroalkylamine, which, on treatment with ethanol, gave N,N-disubstituted α-chloro amide.[1,2] Its application has led us to develop syntheses of ten-membered ring amines and 1-azabicyclo[4,4,1]undecane (XVIII) from $\Delta^{1,10}$-hexahydro-quinolizine (II).

Reaction of the enamine[3] (II) obtained by mercuric acetate oxidation of octahydroquinolizine (I), with trichloroacetic acid in benzene afforded in 15% yield a chloro lactam (III), mp 92—92.5°. *Anal.* Calcd. for $C_{10}H_{16}ONCl$: C, 59.55; H, 8.00; N, 6.94. Found: C, 59.58; H, 7.91; N, 7.27. IR ν_{max}^{Nujol} cm^{-1}: 1665 (–CO–N<), but not the expected trichloro compound (IV). Hydrolysis of the lactam (III) in dilute hydrochloric acid gave an amino acid hydrochloride (V), mp >300°. *Anal.* Calcd. for $C_{10}H_{19}O_2NCl_2$: C, 46.88; H, 7.48; N, 5.47.

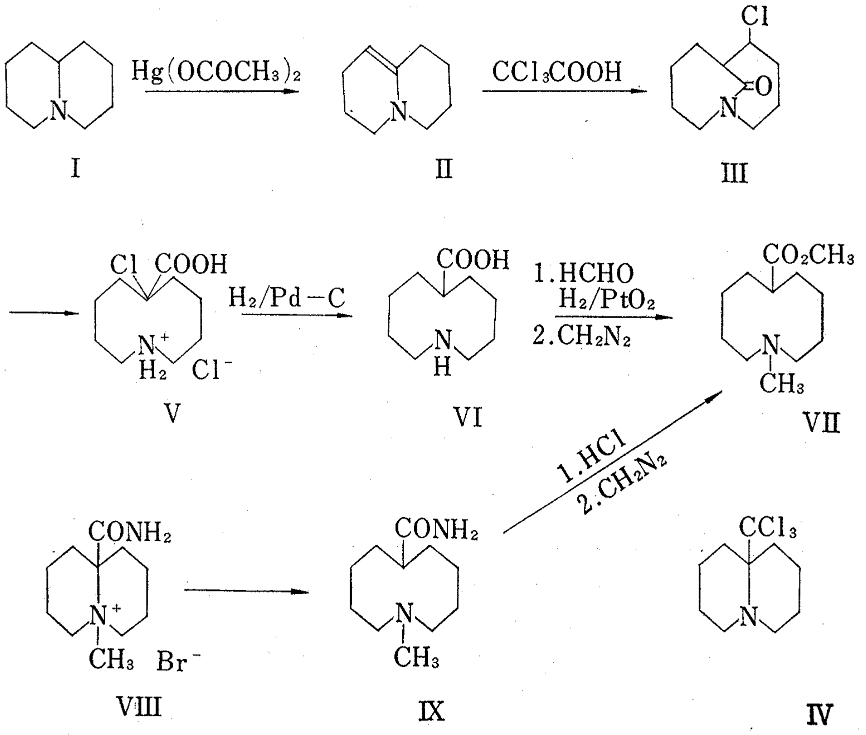

Chart 1

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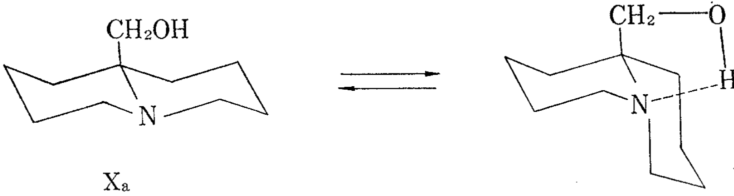
[1] A. Łukasiewicz and J. Lesnka, *Tetrahedron*, 24, 7 (1968).
[2] A. Łukasiewicz, *Tetrahedron*, 24, 513 (1968).
[3] N.J. Leonard and A.S. Hay, *J. Am. Chem. Soc.*, 78, 1984 (1956).

Found: C, 47.05; H, 7.44; N, 5.79. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1720 (-COOH). Catalytic reduction of V on palladium-charcoal afforded a dechlorinated product (VI), mp 250° (decomp.). *Anal.* Cacld. for $C_{10}H_{19}O_2N$: C, 64.83; H, 10.34; N, 7.56. Found: C, 64.80; H, 10.15; N, 7.43. Methylation of VI by formaldehyde and hydrogen in the presence of platinic oxide, followed by esterification with diazomethane, gave an N-methyl methylester (VII). IR $\nu_{\max}^{\text{Liq}}$ cm^{-1}: 1730 (ester), 2800 ($>$N-CH$_3$), which formed a picrate, mp 145—146°. *Anal.* Calcd. for $C_{18}H_{26}O_9N_4$: C, 48.86; H, 5.92; N, 12.66. Found: C, 48.96; H, 6.01; N, 12.63. The picrate of VII thus obtained did not show any melting point depression by the admixture with that (mp 145—146°) of 1-methyl-6-methoxycarbonyl-decahydroazecine,[4] derived from the known compound, 6-carbamoyl-1-methyl-decahydroazecine (IX).

Furthermore, reduction of the lactam (III) by lithium aluminium hydride produced an amino alcohol (X), mp 137—137.5°. *Anal.* Calcd. for $C_{10}H_{19}ON$: C, 70.96; H, 11.32; N, 8.28. Found: C, 70.87; H, 11.30; N, 7.99. NMR τ: 6.9 (1H, singlet, -OH), 6.4 (2H, singlet, $\geqslant$C-CH$_2$-O). The infrared spectrum of X in a dilute carbon tetrachloride solution showed bands, at 3400 (broad) and 3660 (sharp) cm^{-1}. The former was attributed to the OH$\cdots$N type bonded hydroxyl group, and the latter to the free hydroxyl. This fact indicated that X existed as the comformational equilibrium mixture $X_a \rightleftharpoons X_b$, as shown in Chart 2.



X_a X_b

Chart 2

Hydrolysis of III with aqueous sodium hydroxide gave an amino acid (XI), hydrochloride: mp $>$300°. *Anal.* Calcd. for $C_{10}H_{18}O_2NCl$: C, 54.66; H, 8.26; N, 6.38. Found: C, 54.94; H, 8.21; N, 6.46. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1720 (-COOH), which was esterified by diazomethane to yield a methyl ester (XII). IR $\nu_{\max}^{\text{Liq}}$ cm^{-1}: 1730 (ester), (picrate: mp 131—132°. *Anal.* Calcd. for $C_{17}H_{22}O_9N_4$: C, 47.88; H, 5.20; N, 13.14. Found: C, 47.85; H, 5.22; N, 13.11). Reduction of XII with lithium aluminium hydride also afforded the alcohol (X), mp 137—137.5°, in 80% yield. No melting point depression was observed by the admixture of the alcohol with X directly derived from III, and the infrared spectra of both alcohols did not show any difference. Hereupon, hydrogenation of III on palladium-charcoal gave in 74% yield a lactam (XIII), bp$_3$ 120° (bath temperature). IR $\nu_{\max}^{\text{Liq}}$ cm^{-1}: 1670 (-CO-N$<$), which, on reduction of lithium aluminium hydride, afforded azabicyclo undecane derivative (XIV), mp 89—90°. *Anal.* Calcd. for $C_{10}H_{19}ON$: C, 70.96; H, 11.32; N, 8.28. Found: C, 70.78; H, 11.36; N, 8.19, in 77% yield. The compound XIV easily reduced Fehling's solution. Reaction of III with sodium in liquid ammonia gave both the compound XIV, mp 89—90°, and a carbamoyl ten-membered ring amine (XV), mp 173—174°. *Anal.* Calcd. for $C_{10}H_{20}ON_2$: C, 65.17; H, 10.94; N, 15.21. Found: C, 65.13; H, 10.85; N, 15.06, in 74% and 3% yield, respectively. The former compound was found to be identical with XIV derived from XIII by mixed melting point determination and infrared spectral comparison. Methylation of the latter by formaldehyde and hydrogen in the presence of platinum oxide gave the compound, mp 177—179°, which did not show any melting point depression by the admixture with IX derived from VIII.[4] The action of *p*-toluenesulfonyl chloride on XIV, followed by reduction with lithium aluminium hydride, afforded, as expected, 1-azabicyclo[4,4,1]undecane (XVII) {picrate: mp 220—223° (decomp.). *Anal.* Calcd. for $C_{16}H_{22}O_7N_4$: C, 50.26; H, 5.80; N, 14.65. Found: C, 50.50; H, 5.93; N, 14.41}.

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4) Y. Arata, S. Yoshifuji and Y. Yasuda, *Chem. Pharm. Bull.* (Tokyo), **17**, 1363 (1969).

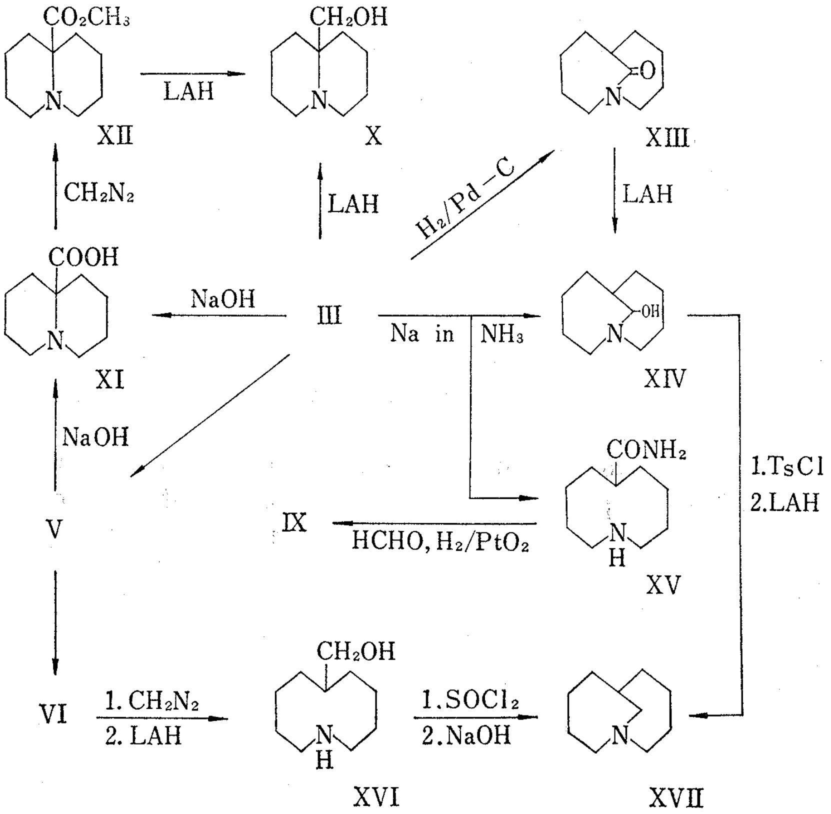

Chart 3

On the other hand, esterification of VI with diazomethane, and lithium aluminium hydride reduction of the resulting product, yield an amino alcohol (XVI), which formed a picrate, mp 180—183°. *Anal.* Calcd. for $C_{16}H_{24}O_8N_4$: C, 47.99; H, 6.04; N, 13.99. Found: C, 47.99; H, 5.98; N, 13.97. Reaction of XVI with thionyl chloride, followed by treatment with an alkaline solution, afforded the same product (XVII) {picrate: mp 220—223° (decomp.)}, as mentioned above. The infrared spectra of both amines (XVII) were completely coincident.

Faculty of Pharmaceutical Sciences,
Kanazawa University
Takara-machi, Kanazawa

Yoshio Arata
Toyohiko Kobayashi

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