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# Studies on 1-Azabicyclo Compounds. XIV.[1] Synthesis of 1-Methyldecahydro-1,4-diazecin-5-one from Octahydropyrido[1,2-*a*]pyrazine Derivatives[2]

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Octahydropyrido[1,2-*a*]pyrazine (VI) and its N-benzyl derivative (I) were subjected to oxidation by mercuric acetate to afford 1,3,4,6,7,8-hexahydro-2*H*-pyrido[1,2-*a*]pyrazin-1-one (VII) and its N-benzyl compound (II), respectively. The former product (VII) was also obtained by similar oxidation of the lactam (V). Compound (V) was treated with methyl iodide in methanol to give two isomeric methiodides, *trans*-octahydropyrido[1,2-*a*]-pyrazin-1-one methiodide (Xa) and the corresponding *cis*-methiodide (Xb). On thermal treatment, the latter methiodide was converted into the former. Methiodides, IV, XI, Xa, and Xb were reduced with lithium-liquid ammonia giving the 10-membered ring lactam (XII) in 4%, 52%, 81%, and 82% yields, respectively. When treated with sodium amalgam, Xa gave XII in 59% yield, which, on reduction with lithium aluminum hydride, yielded XIII.

In connection with previous studies[1,4] on the syntheses of ten-membered ring amines from octahydroquinolizine system, we wish to report the conversion of derivatives of octahydropyrido[1,2-*a*]pyrazine (VI), one of azaoctahydroquinolizines, into a ten-membered amino lactam (XII) or the corresponding diamine (XIII). N-Benzyloctahydropyrido[1,2-*a*]-pyrazine (I), IR $\nu_{\max}^{\text{liq.}}$ cm$^{-1}$: 2800, 2760, 2670 (Bohlmann band[5]), the condensation product of 1-(2-chloroethyl)-2-chloromethylpiperidine[6] and benzylamine, was oxidized with mercuric acetate in 5% aqueous acetic acid to afford in 32% yield an unstable oily product, IR $\nu_{\max}^{\text{liq.}}$ cm$^{-1}$: 1653 (enamine), 1620 (amide), which formed a crystalline methiodide (IV), $C_{15}H_{18}ON_2 \cdot CH_3I$, mp 177—179°. The product was treated with sodium borohydride[7] in ethanol to yield a dihydro product, mp 111°. Its infrared (IR) spectrum showed bands at 2800, 2740, 2660 (Bohlmann band), and 1650 cm$^{-1}$ (amide). The reduction product was identified with an N-benzyl lactam (III), mp 110°, derived from octahydropyrido[1,2-*a*]pyrazin-1-one[8,9] (V) by direct comparison. Thus, the oxidation product was characterized as 2-benzyl-1,3,4,6,7,8-hexahydro-2*H*-pyrido[1,2-*a*]pyrazin-1-one (II). Similarly, when heated with mercuric acetate in aqueous acetic acid, octahydropyridopyrazine[8-10] (VI) derived from V afforded, as expected, an $\alpha,\beta$-unsaturated lactam (VII), $C_8H_{12}ON_2$, mp 146—148°, in 15% yield. The IR spectrum of VII in a KBr disk showed bands at 1670 (enamine) and 1625 cm$^{-1}$ (lactam), whereas that of the perchlorate (VIII), mp 186—188°, exhibited bands at 1711 (iminium) and 1680 cm$^{-1}$

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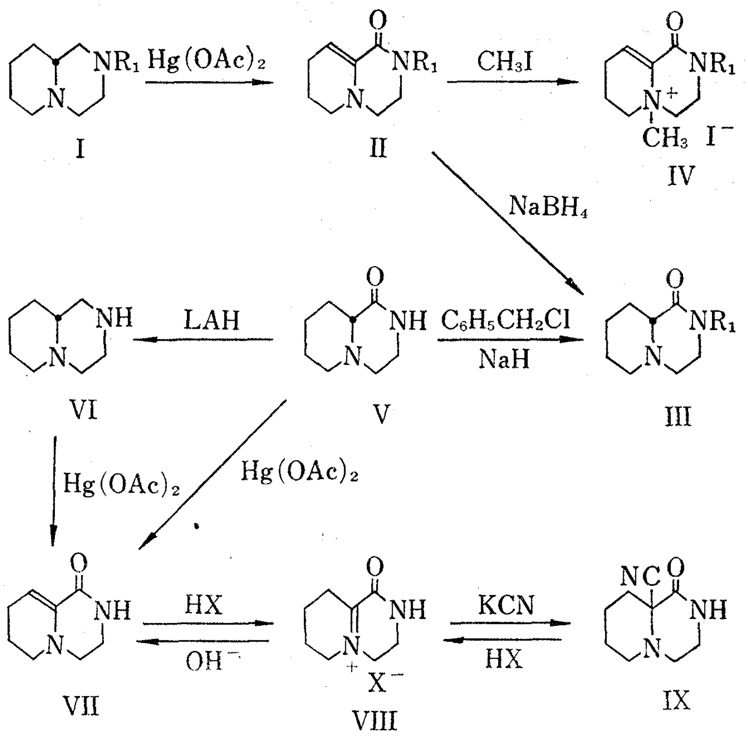
1) Part XIII: Y. Arata and Y. Oda, *Chem. Pharm. Bull.* (Tokyo), **21**, 752 (1973).
2) Reported at the 92nd Annual Meeting, Pharmaceutical Society of Japan, Osaka, April 1972.
3) Location: *13-1 Takara-machi, Kanazawa, 920, Japan.*
4) *a*) Y. Arata, S. Yoshifuji, and Y. Yasuda, *Chem. Pharm. Bull.* (Tokyo), **17**, 1363 (1969); *b*) Y. Arata, T. Kobayashi, M. Nakamura, and T. Yasuda, *Yakugaku Zasshi*, **90**, 1424 (1970); *c*) Y. Arata, S. Yoshifuji, and T. Shioda, *Yakugaku Zasshi*, **92**, 69 (1972); *d*) Y. Arata and T. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), **20**, 325 (1972); *e*) Y. Arata and T. Shioda, *Chem. Pharm. Bull.* (Tokyo), **20**, 783 (1972).
5) F. Bohlmann, *Angew. Chem.*, **69**, 641 (1957).
6) K. Winterfeld, K. Kullmar, and W. Gobel, *Chem. Ber.*, **92**, 1510 (1959).
7) *a*) Y. Arata, T. Nakanishi, and Y. Asaoka, *Chem. Pharm. Bull.* (Tokyo), **10**, 675 (1962); *b*) Y. Arata, T. Asai, and M. Tsukioka, *Yakugaku Zasshi*, **85**, 219 (1968).
8) M. Freed and A.R. Day, *J. Org. Chem.*, **25**, 2108 (1960).
9) T. Yamazaki, M. Nagata, K. Ogawa, and F. Nohara, *Yakugaku Zasshi*, **87**, 668 (1967).
10) K. Winterfeld and G. Gierenz, *Chem. Ber.*, **92**, 240 (1959).

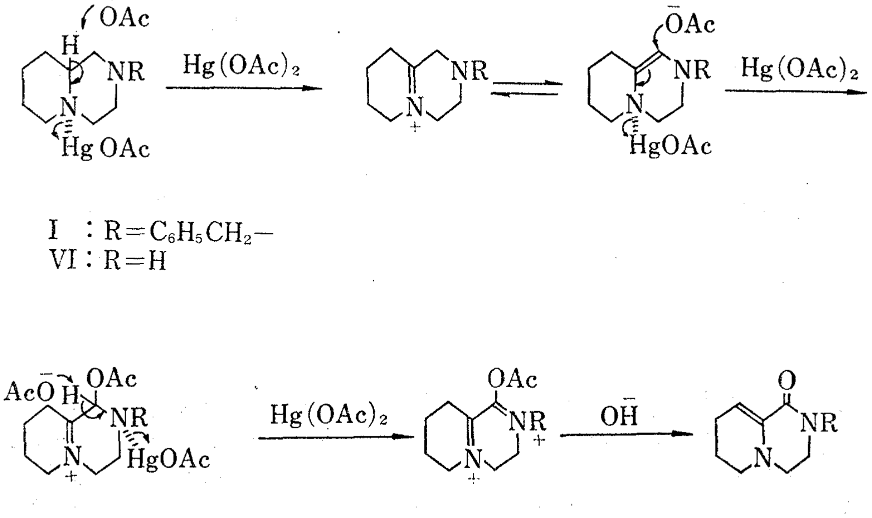
(lactam). The iminium salt (VIII) reacted with potassium cyanide to yield a nitrile (IX), mp 137—139°, IR $\nu_{\max}^{\text{CHCl}_3}$ cm$^{-1}$: 2220 (nitrile), which, on neutralization with perchloric acid, readily afforded VIII. The compound VII, mp 146—148°, was obtained by mercuric acetate oxidation of the lactam (V). The product (VII) thus obtained did not show any melting point depression on admixture with VII derived from VI and the IR spectra of both compounds were completely coincident. The mechanism of the conversion of I to II and of VI to VII may be regarded as similar to that[11] postulated for mercuric acetate oxidation of 1-methyldecahydroquinoline producing 10-hydroxy-1-methyl-$\Delta^8$-octahydroquinoline and as shown in Chart 2. All the IR spectra of compounds (I, III, V, and VI) showed Bohlmann bands[5] and, therefore, these compounds exist predominantly in *trans* ring-fused conformation.



$R_1 = C_6H_5CH_2-$

Chart 1

The compound (V) was treated with methyl iodide in methanol affording two isomeric methiodides, Xa and Xb, in the ratio of 1: 1.5; Xa, mp 221—223°, IR $\nu_{\max}^{\text{KBr}}$ cm$^{-1}$: 3100 (NH), 1670 (CON), sparing soluble in methanol; Xb, mp 177—178°, IR $\nu_{\max}^{\text{KBr}}$ cm$^{-1}$: 3200 (NH), 1670 (CON), comparatively soluble in methanol. The nuclear magnetic resonance (NMR) spectra



I : $R = C_6H_5CH_2-$
VI : $R = H$

II : $R = C_6H_5CH_2-$
VII : $R = H$

Chart 2

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11) N.J. Leonard, L.A. Miller, and P.O. Thomas, *J. Am. Chem. Soc.*, **78**, 3463 (1956).

of Xa and Xb exhibited N-methyl signals at $\tau$ 6.93 (3H, singlet) and $\tau$ 6.75 (3H, singlet), respectively. This observation[12,13] indicates that the former is *trans*-octahydropyrido[1,2-*a*]pyrazin-1-one methiodide and the latter, the corresponding *cis*-methiodide. In methanolic solution the compound V existed presumably as the conformational equilibrium mixture of Va and Vb, as shown in Chart 4, which then reacted with methyl iodide to give the methiodides, Xa and Xb, respectively. On thermal treatment, the *cis*-methiodide (Xb) was readily converted into the stable *trans*-methiodide (Xa).

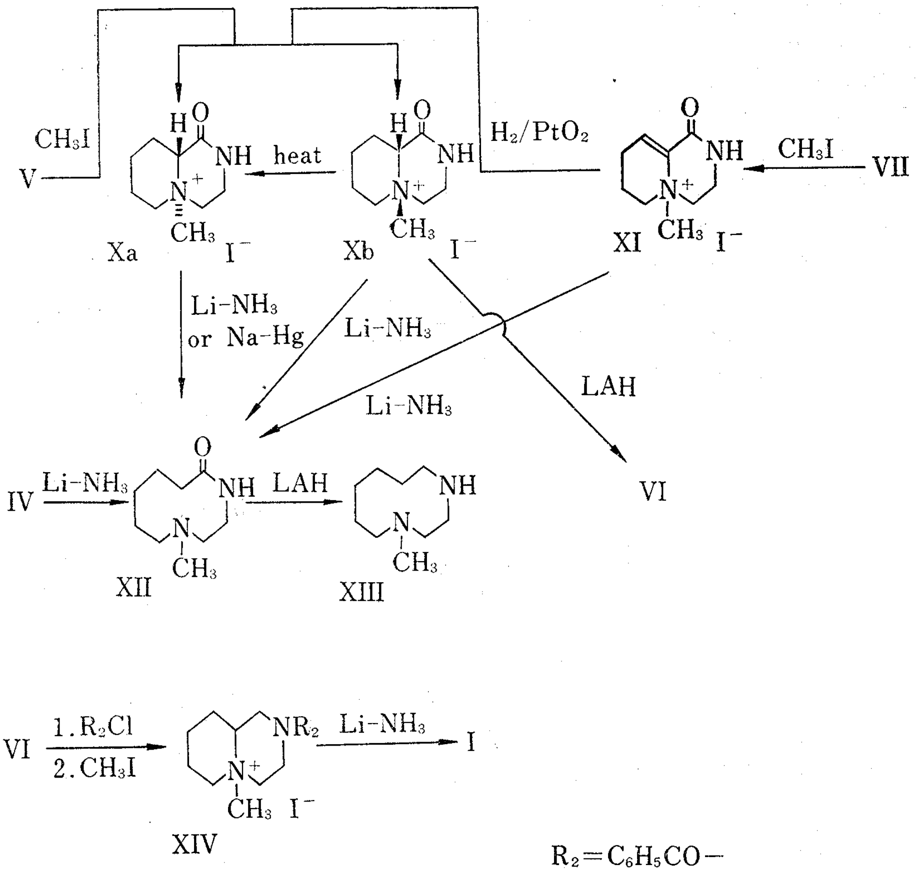

Chart 3

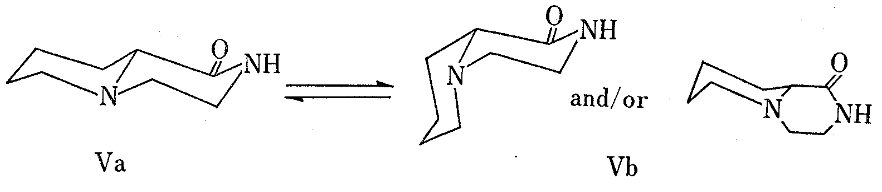

Chart 4

The fact that catalytic hydrogenation of 5-methyl-$\Delta^{1,10}$-hexahydroquinolizinium iodide produced only *cis*-5-methyloctahydroquinolizinium iodide was already reported by Schofield, *et al.*[14] However, when reduced over platinic oxide, $\Delta^{1,10}$-hexahydropyrido[1,2-*a*]pyrazin-1-one methiodide (XI), mp 209—211°, derived from VII, gave both Xa and Xb in 1: 2 ratio. Conformation of the methiodide (XI) would be more coplaner than that of 5-methyl-$\Delta^{1,10}$-

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[12] T.M. Moynehan, K. Schofield, A.Y. Jones, and A.R. Katritzky, *J. Chem. Soc.*, **1962**, 2637.
[13] J.D. England, D. Temple, and J. Sam, *J. Med. Chem.*, **11**, 353 (1968).
[14] K. Schofield and R.J. Well, *Chem. Ind.* (London), **1963**, 572.

hexahydroquinolizinium iodide because the double bond is conjugated with the lactam in the former. Consequently, the hydrogenation of XI would possibly occur from both sides giving both *cis*- and *trans*-methiodides.

Finally, attempts were made to produce the ten-membered lactam (XII) and the corresponding amine (XIII) from the methiodides, IV, XI, Xa, and Xb. Reaction of the N-benzyl methiodide (IV) with lithium in liquid ammonia effected selective cleavage of C(10)-N bond accompanied with hydrogenation of $\alpha,\beta$-unsaturated lactam and debenzylation to afford the expected product, 1-methyldecahydro-1,4-diazecin-5-one (XII), mp 116—117°, albeit in 4% yield. The IR spectrum of XII showed bands at 3250, 3090 (NH), 2800 (N-$CH_3$), 1638, and 1568 $cm^{-1}$ (CON) and its NMR spectrum exhibited an N-methyl signal at $\tau$ 7.7 (3H, singlet) and no C-methyl signal. Similar reduction of the methiodide (XI) gave XII in 52% yield. Although the reduction of $\alpha,\beta$-unsaturated ketones with lithium-liquid ammonia producing the corresponding saturated ketones has appeared in a number of literatures,[15–17] the present reduction of $\alpha,\beta$-unsaturated lactam provides a novel example. On treatment with lithium in liquid ammonia, both isomeric methiodides, Xa and Xb, gave XII in over 80% yield. On the other hand, treatment of Xa with sodium amalgam in aqueous ethanol gave the expected lactam (XII) in 58% yield. The lactam was further reduced with lithium aluminum hydride to yield 1-methyldodecahydro-1,4-diazecine (XIII), IR $\nu_{max}^{liq.}$ $cm^{-1}$: 3350 (NH), 2800 (N-$CH_3$); monopicrate, mp 212—214°.

Reduction of Xb with lithium aluminum hydride resulted in a demethylation product (VI). Benzoylation of the diamine (VI) with benzoyl chloride, followed by quaternization with methyl iodide afforded an N-benzoyl methiodide (XIV), mp 213—214°. When kept standing in liquid ammonia containing lithium, XIV yielded only the N-benzyl derivative (I); hydrobromide, mp 266—267°.

## Experimental[18]

**2-Benzyloctahydropyrido[1,2-*a*]pyrazine (I)**——To a solution of 1-(2-chloroethyl)-2-chloromethylpiperidine[6] (7.8 g) in 50% aqueous acetone was added benzylamine (17.1 g). The solution was refluxed for 16 hr, followed by evaporation of the solvent. The residue was made alkaline with aqueous NaOH and the oily substance that deposited was extracted with ether. The ether solution was washed, dried, and then evaporated. The residue was distilled to give a colorless liquid, bp 110—120° (bath temp.)/0.2 mmHg. Yield, 21% (4.2 g). IR $\nu_{max}^{liq.}$ $cm^{-1}$: 3050, 1600, 1500 (phenyl), 2800, 2760, 2670 (Bohlmann band).

Dihydrobromide: Recrystallized from EtOH to colorless needles, mp 266—267°. *Anal.* Calcd. for $C_{15}H_{24}N_2Br_2$: C, 45.94; H, 6.17; N, 7.14. Found: C, 46.15; H, 6.41; N, 7.10.

**Octahydropyrido[1,2-*a*]pyrazin-1-one (V)**——According to the method of Freed, *et al.*,[8] V was obtained from the reaction of ethyl 2-piperidinecarboxylate and ethyleneimine, as colorless prisms, mp 134—135° (from ligroin). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3400, 3200 (NH), 1660 (CON), 2800, 2760 (Bohlmann band).

Methiodide (X): To a solution of V (0.78 g) in MeOH was added MeI (0.8 g). The solution was kept standing for 3 days depositing a precipitate which was collected by filtration.

Xa: The precipitate was recrystallized from MeOH to colorless plates, mp 221—223°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3100 (NH), 1670 (CON). NMR (5% solution in $Me_2SO$) $\tau$: 6.93 (3H, singlet, $\geqslant N^+\text{-}C\underline{H}_3$), 1.65 (1H, broad, N$\underline{H}$). *Anal.* Calcd. for $C_9H_{17}ON_2I$: C, 36.50; H, 5.79; N, 9.46. Found: C, 36.59; H, 5.66; N, 9.63.

Xb: The filtrate was evaporated *in vacuo* and the residue was recrystallized from MeOH to colorless plates, mp 177—178°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3200, 3050 (NH), 1670 (CON). NMR (6% solution in $Me_2SO$) $\tau$: 6.75 (3H, singlet, $\geqslant N^+\text{-}C\underline{H}_3$), 1.55 (1H, broad, N$\underline{H}$). *Anal.* Calcd. for $C_9H_{17}ON_2I$: C, 36.50; H, 5.79; N, 9.46. Found: C, 37.06; H, 5.88; N, 9.23.

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15) D.H.R. Barton and C.H. Robinson, *J. Chem. Soc.*, **1954**, 3045.
16) G. Stork and S.D. Darling, *J. Am. Chem. Soc.*, **82**, 1512 (1960).
17) G. Stork and J. Tsuji, *J. Am. Chem. Soc.*, **83**, 2783 (1961).
18) All the melting points were measured with a Yanagimoto Micro-Melting Point Apparatus and are uncorrected. IR spectra were measured with a Spectrophotometer G, Japan Spectroscopic Co., Ltd., and NMR spectra with a Spectrometer H-60-C, Japan Electron Lab. Co., using tetramethylsilane as an internal standard.

**Conversion of Xb to Xa**——The methiodide Xb was heated at 245° for 10 min. The product was recrystallized from MeOH to colorless plates, mp 221—223°. No depression of the melting point was observed by admixture of the product with Xa.

**2-Benzyl-1,3,4,6,7,8-hexahydro-2*H*-pyrido[1,2-*a*]pyrazin-1-one (II)**——To a solution of mercuric acetate (32 g) in 5% aqueous AcOH (100 ml) was added 2.2 g of I with stirring. The solution was warmed at 65—75° for 5 hr with stirring in $N_2$ atmosphere to deposit HgOAc. The reaction solution was filtered and the precipitate was further washed with a small amount of EtOH. $H_2S$ was passed through the filtrate, precipitated HgS was filtered off, and the filtrate was evaporated to dryness in a reduced pressure. The residue was made alkaline with aqueous NaOH followed by extraction with ether. The ether layer was washed with $H_2O$, dried and then evaporated. The residue was distilled to give 0.73 g of a pale yellow liquid, bp 170—180° (bath temp.)/0.2 mmHg. Yield; 32%. Color of the product soon changed into brown. IR $\nu_{max}^{liq.}$ cm$^{-1}$: 1653 (enamine), 1620 (amide).

Methiodide (IV): Recrystallized from MeOH–EtOH (1: 1) to colorless needles, mp 177—179°. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1635 (CON). *Anal.* Calcd. for $C_{16}H_{21}ON_2I$: C, 50.17; H, 5.74; N, 7.26. Found: C, 50.15; H, 5.45; N, 7.02.

**2-Benzyloctahydropyrido[1,2-*a*]pyrazin-1-one (III)**——1) Reduction of II with $NaBH_4$: To a solution of 0.58 g of II in EtOH (30 ml), $NaBH_4$ (0.9 g) was added and the suspension was refluxed for 30 hr in $N_2$ atmosphere. After evaporation of the solvent, $H_2O$ was added to the residue, and the solution was extracted with ether. The ether layer was washed with $H_2O$, dried, and then evaporated to leave a colorless liquid which soon solidified. Yield, 31% (0.18 g). The crude product was recrystallized from hexane to colorless prisms, mp 111°. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3030, 1600, 1500 (phenyl), 1650 (CON), 2800, 2740, 2660 (Bohlmann band). *Anal.* Calcd. for $C_{15}H_{20}ON_2$: C, 73.73; H, 8.25; N, 11.47. Found: C, 73.91; H, 8.26; N, 11.43.

2) Benzylation of V: To a suspension of 0.2 g of 50% NaH in oil in benzene, 0.5 g of V was added in small portions. After the solution was refluxed for 5 hr, a solution of $C_6H_5CH_2Cl$ (0.43 g) in benzene (5 ml) was added dropwise to it followed by heating for 5 hr. The solution was evaporated *in vacuo*. To the residue $H_2O$ was added and extracted with ether. The ether layer was washed with $H_2O$, dried, and then evaporated to leave an oily product which soon solidified. Yield, 59% (0.47 g). The product was recrystallized from hexane to colorless prisms, mp 111°. No melting point depression was observed by admixture of this product with III derived from II, and the IR spectra of both compounds were coincident.

**Octahydropyrido[1,2-*a*]pyrazine (VI)**——According to the method of Freed, *et al.*,[8] VI was produced by $LiAlH_4$ reduction of V as a colorless liquid, bp 92°/15 mmHg. IR $\nu_{max}^{liq.}$ cm$^{-1}$: 3250 (NH), 2800, 2750, 2660 (Bohlmann band). Dipicrate: Recrystallized from $H_2O$ to yellow needles, mp 253—257° (decomp.).

**1,3,4,6,7,8-Hexahydro-2*H*-pyrido[1,2-*a*]pyrazin-1-one (VII)**——1) Oxidation of VI with Mercuric Acetate: VI (2 g) was oxidized with mercuric acetate (37 g) in 5% aqueous AcOH (150 ml) in the same way as described above for I, and VII obtained in 15% yield (0.32 g) was recrystallized from iso-$Pr_2O$ to colorless needles, mp 146—148°. IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 3160 (NH), 1670 (enamine), 1625 (CON). *Anal.* Calcd. for $C_8H_{12}ON_2$: C, 63.13; H, 7.95; N, 18.41. Found: C, 63.45; H, 7.86; N, 18.27.

2) Oxidation of V with Mercuric Acetate: Oxidation of V was carried out in the same way as above, using 13 g of V, mercuric acetate (128 g), and 5% aqueous AcOH (400 ml). The crude product obtained in 31% yield (4 g) was recrystallized from iso-$Pr_2O$ to colorless needles, mp 146—148°. This product did not show any melting point depression on admixture with VII derived from VI. Perchlorate (VIII): Recrystallized from EtOH to colorless needles mp 186—188°. IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 3300 (NH), 1710 (iminium), 1680 (amide).

Methiodide (XI): Recrystallized from MeOH to colorless needles, mp 209—211°. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3150 (NH), 1680 (olefin), 1635 (CON). *Anal.* Calcd. for $C_9H_{15}ON_2I$: C, 36.71; H, 5.13; N, 9.51. Found: C, 36.89; H, 5.15; N, 9.49.

**10-Cyano-octahydropyrido[1,2-*a*]pyrazin-1-one (IX)**——To a solution of the perchlorate (VIII) in MeOH 0.5 g of KCN was added, the solution was refluxed for 8 hr, and the solvent was evaporated *in vacuo*. The residue was shaken with benzene and then filtered. The filtrate was evaporated *in vacuo*, and the residue (0.3 g) was recrystallized from benzene to colorless plates, mp 137—139°. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3400 (NH), 2220 (CN), 1695 (CON). *Anal.* Calcd. for $C_9H_{13}ON_3$: C, 60.31; H, 7.31; N, 23.45. Found: C, 60.57; H, 7.26; N, 23.45. The product was neutralized with perchloric acid to give the iminium salt (VIII).

**Catalitic Hydrogenation of XI (Formation of Xa and Xb)**——Catalytic hydrogenation of 0.31 g of XI in 30% aqueous EtOH was carried out over $PtO_2$, and 24 ml of $H_2$ was absorbed. The catalyst was removed by filtration, the filtrate was evaporated to dryness, and the residue was treated with a small amount of MeOH to deposit a precipitate. The mixture was filtered. The precipitate (90 mg) was recrystallized from MeOH to colorless plates, mp 221—223°. No melting point depression was observed by admixture of this methiodide with Xa and the IR spectra of both methiodides were coincident.

The filtrate was evaporated to dryness *in vacuo* and the residue was recrystallized from MeOH to colorless plates, mp 177—178°. Yield, 170 mg. No melting point depression was observed by admixture of this methiodide with Xb.

**1-Methyldecahydro-1,4-diazecin-5-one (XII)**——1) Reduction of IV with Li in Liquid $NH_3$: To a solution of 1.2 g of IV in liquid $NH_3$ (400 ml) 400 mg of Li was added in small portions, the solution was stirred for 10 min, followed by evaporation of $NH_3$. To the residue were added $H_2O$ and ether with stirring. The ether layer was dried and evaporated to dryness. The residue was distilled to give a colorless liquid, bp 120—130° (bath temp.)/4 mmHg in 4% yield, which soon solidified. Recrystallization from hexane afforded colorless needles, mp 116—117°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3250, 3090 (NH), 2800 ($N\text{-}CH_3$), 1638, 1568 (amide). NMR (2.8% solution in $CDCl_3$) $\tau$: 7.7 (3H, singlet, $N\text{-}C\underline{H}_3$), 3.95 (1H, broad, $N\underline{H}$). *Anal.* Calcd. for $C_9H_8ON_2$: C, 63.49; H, 10.66; N, 16.46. Found: C, 63.47; H, 10.60; N, 16.57.

2) Reduction of XI with Li-Liquid $NH_3$: The methiodide (XI) (0.4 g) was reduced in the same way as for IV. The product obtained in 52% yield was recrystallized from hexane to colorless needles, mp 116—117°. No depression of the melting point was observed by admixture of this amine with XII derived from IV.

3) Reduction of Xa with Li in Liquid $NH_3$: Reduction of Xa (0.3 g) with Li (120 mg) in liquid $NH_3$ (400 ml) was carried out in the same way as above. The product obtained in 81% yield was recrystallized from hexane to colorless needles, mp 116—117°. No melting point depression was observed by admixture of this product with XII and the IR spectra of both compounds were coincident.

4) Reduction of Xb with Li in Liquid $NH_3$: The reduction was carried out in the same way as above. Colorless needles, mp 116—117°. Yield, 82%. No depression of the melting point was observed by admixture of the product with XII.

5) Reduction of Xa with Na-Hg: To a boiling solution of 500 mg of Xa in 80% aqueous EtOH (12 ml), 3% Na-Hg (25 g) was added in small portions with stiring and $CO_2$ was passed through the mixture. It took 24 hr to complete the reduction. Hg was filtered off and the filtrate was evaporated to dryness *in vacuo*. To the residue, ether and $H_2O$ were added and the mixture was shaken. The ether layer was washed with $H_2O$, dried, and then evaporated. The residue obtained in 59% yield (161 mg) was recrystallized from hexane to colorless needles, mp 116—117°. No depression of the melting point was observed by admixture of the product with XII, and the IR spectra of both compounds were coincident.

**1-Methyl-decahydro-1,4-diazecine (XIII)**——To a suspension of $LiAlH_4$ (0.2 g) in ether, a solution of XII (0.1 g) in ether was added with stirring and the mixture was refluxed for 20 hr. After the reaction, excess of $LiAlH_4$ was decomposed with $H_2O$ followed by extraction with ether. The ether layer was dried and evaporated. The residue was distilled to collect a colorless liquid, bp 90—100° (bath temp.)/17 mmHg. Yield, 73% (68 mg). IR $\nu_{max}^{liq.}$ $cm^{-1}$: 3350 (NH), 2800 ($N\text{-}CH_3$).

Monopicrate: Recrystallized from EtOH to yellow needles, mp 212—214°. *Anal.* Calcd. for $C_{15}H_{23}O_7N_5$: C, 46.75; H, 6.02; N, 18.17. Found: C, 46.82; H, 6.02; N, 18.08.

**Reduction of Xb with $LiAlH_4$ (Formation of VI)**——To a solution of 500 mg of Xb in dioxan (50 ml) $LiAlH_4$ (1.95 g) was added and the mixture was heated at reflux for 87 hr. After the reaction, an excess of $LiAlH_4$ was decomposed with $H_2O$ followed by evaporation of the solvent. The residue was shaken with ether, the ether solution was acidified with HCl. The aqueous layer was basified with $Na_2CO_3$ and extracted with ether. The ether layer was dried and evaporated. The residue was distilled to give a colorless liquid, bp 100—120° (bath temp.)/17 mmHg. Yield, 150 mg. The IR spectrum of this amine was coincident with that of VI.

Picrate: Recrystallized from $H_2O$ to yellow needles, mp 253—256° (decomp.).

**2-Benzoyl-octahydropyrido[1,2-*a*]pyrazine**——To a suspension of 0.5 g of VI in 15% NaOH (3 ml), a solution of $C_6H_5COCl$ (0.8 g) in ether was added and the mixture was shaken under cooling for 1 hr. The ether layer was washed with $H_2O$, dried, and then evaporated. The residue was distilled to afford a colorless liquid, bp 150—160° (bath temp.)/0.2 mmHg. Yield, 63% (0.53 g). IR $\nu_{max}^{liq.}$ $cm^{-1}$: 3050, 1580, 1500 (phenyl), 1635 (amide).

Picrate: Recrystallized from EtOH to yellow prisms, mp 203—204°. *Anal.* Calcd. for $C_{21}H_{23}O_8N_5$: C, 53.28; H, 4.90; N, 14.79. Found: C, 53.68; H, 5.15; N, 14.63.

Methiodide (XIV): Recrystallized from EtOH–AcOEt (3:1) to colorless prisms, mp 213—214°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1640 (CON). *Anal.* Calcd. for $C_{16}H_{23}ON_2I$: C, 49.75; H, 6.00; N, 7.25. Found: C, 49.71; H, 6.07; N, 7.19.

**Reduction of XIV with Li in Liquid $NH_3$ (Formation of I)**——To a solution of XIV (0.28 g) in liquid $NH_3$ (100 ml) Li (100 mg) was added, the solution was stirred for 10 min, and $NH_3$ was evaporated. To the residue, $H_2O$ and ether were added with stirring. The ether layer was washed with $H_2O$, dried, and then evaporated. The residue was distilled to yield a colorless liquid, bp 110—120° (bath temp.)/0.2 mmHg. Yield, 54% (90 mg). Its IR spectrum was in accordance with that of I.

Hydrobromide: Recrystallized from EtOH to colorless needles, mp 266—267°. The hydrobromide did not show any melting point depression on admixture with that of I.

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