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Synthesis of Nitrogen-containing Heterocyclic Compounds through Nitrilium Salt. II.[1] Reaction of Nitriles with 2-(2-Hydroxycyclohexyl)ethanol and 1-(2-Hydroxycyclohexyl)propan-2-ol in the Presence of Acid

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Reaction of 2-(2-hydroxycyclohexyl)- and 2-(2-hydroxycyclopentyl)-ethanols (VI and XX) with nitrile in the presence of stannic chloride afforded 4,4-pentamethylene- and tetramethylene-1,3-oxazine (VIII, XIX, and XXI). The same reaction of α-(2-hydroxycyclopentyl)-*t*-butanol (II) with a nitrile gave cyclopentenodihydropyridine (III). Reaction of 1-(2-hydroxycyclohexyl)propan-2-ol (XXV) and a nitrile in the presence of sulfuric acid gave 1,3-oxazine derivative (XXVI) and cyclohexanopyrroline (XXVII) which easily underwent oxidation to a 3-hydroxy compound (XXXI).

Meyers and others[3] obtained cyclopenteno-dihydropyridine (III) by the reaction of α-(1- and 3-cyclopentenyl)-*t*-butanol (I) or α-(2-hydroxycyclopentyl)-*t*-butanol (II) with nitrile under the so-called Ritter reaction conditions with little water activity.[3] The present authors[4] obtained 1-pyrroline (V) by the reaction of a glycol (IV) and a nitrile in the presence of stannic chloride, formed by the attack of nitrile on primary alcohol rather than on tertiary alcohol. Considering the formation of III and V, it was anticipated that the cyclization reaction between 2-(2-hydroxycyclohexyl)ethanol (VI) and benzyl cyanide by the latter conditions would give cyclohexano-dihydropyridine[5] (VII), an important starting material for the synthesis of morphinan. However, the base obtained by this reaction was not VII but a 1,3-oxazine derivative (VIII). The same reaction under the Ritter reaction conditions also gave the same product (VIII), which is also formed from cyclohexenylethanol (IX) under the same condition. At first, the structure of this base was variously considered as VIII, X, XI, or XII from its elemental analytical values, its infrared spectrum (IR) showing the presence of $-\overset{|}{C}=N-$ and $=\overset{|}{C}-O-$ bonds, without OH, and the absence of ultraviolet (UV) absorption for $-\overset{|}{C}=C-C=N-$. The nuclear magnetic resonance (NMR) spectral evidence for the absence of a signal for methine proton adjacent to nitrogen or oxygen denied the structures of XI and XII. On the other hand, X had already been synthesized and reported by Grewe,[5] and the present product did not agree with this compound. Finally, this base was determined as 2-benzyl-4,4-pentamethylene-4,5-dihydro-1,3-oxazine (VIII) because it was slowly hydrolyzed by moisture in the air to an amide alcohol (XIII) and its alkaline hydrolysis quantitatively afforded amino-alcohol (XIV) and phenylacetic acid. XIV can be derived to its N-dimethyl compound (XV) and further to its acetyl compound (XVI). Hofmann degradation of the methiodide of XV gives cyclohexenylethanol (IX). These evidences deny the structures of X and XII. This fact is also clear from the proof of the presence of primary alcohol by the NMR spectrum. The methylene proton signal adjacent to oxygen appears at 3.76 ppm in the NMR spectrum of XV and at 4.12 ppm in that of XVI, showing a shift of *ca.* 0.4 ppm

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[1] Part I: S. Ohki and M. Yoshino, *Chem. Pharm. Bull.* (Tokyo), **17**, 2142 (1969).

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[3] A.I. Meyers, J. Schneller and N.K. Ralhan, *J. Org. Chem.*, **28**, 2944 (1963).

[4] S. Ohki, F. Hamaguchi, T. Yanagi, and M. Yoshino, *Chem. Pharm. Bull.* (Tokyo), **14**, 187 (1966).

[5] R. Grewe, H. Pohlmann, and M. Schφnoor, *Chem. Ber.*, **84**, 527 (1951).

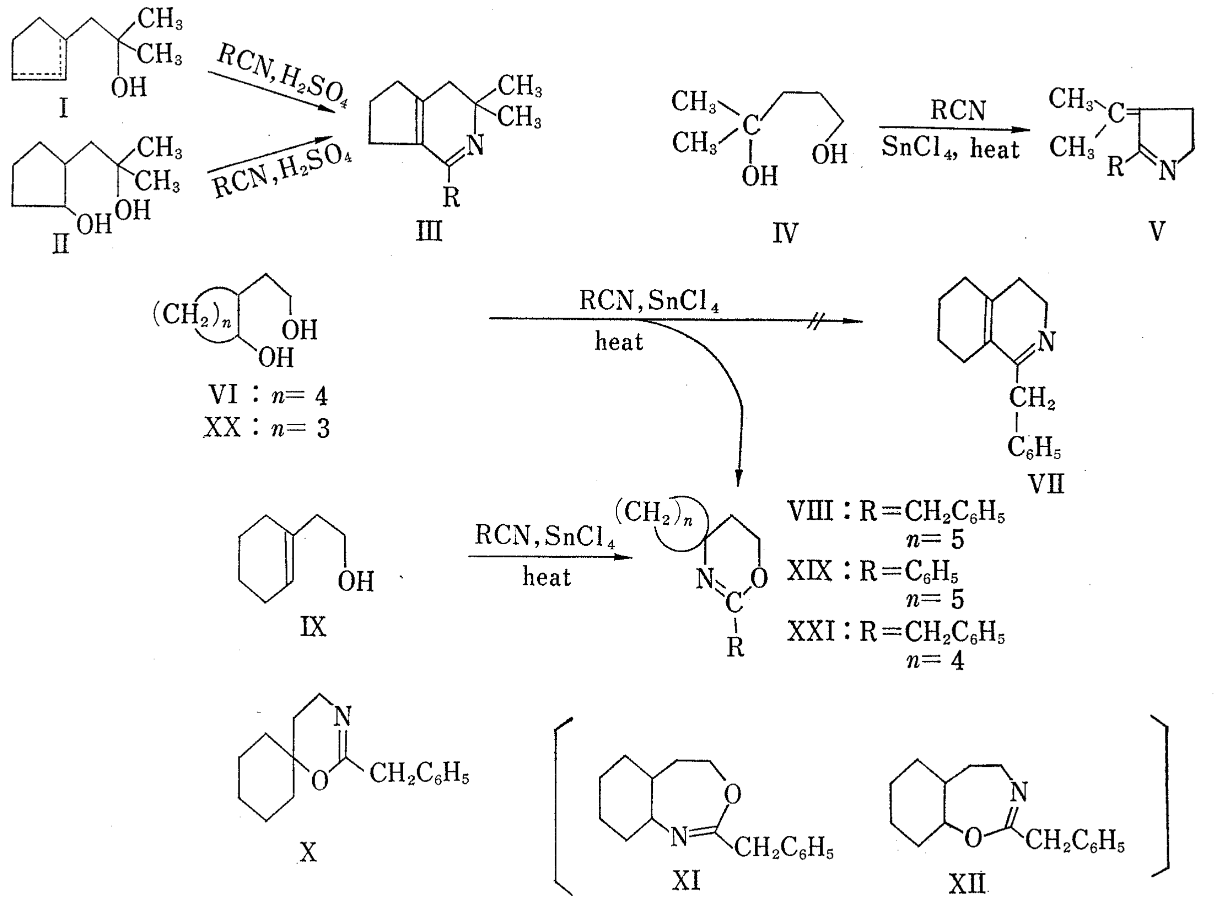


Chart 1

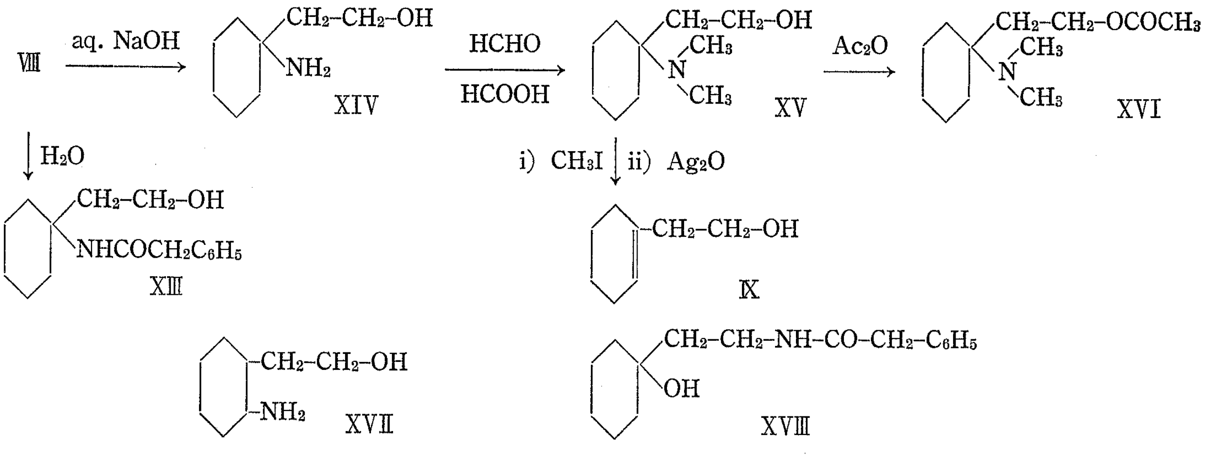


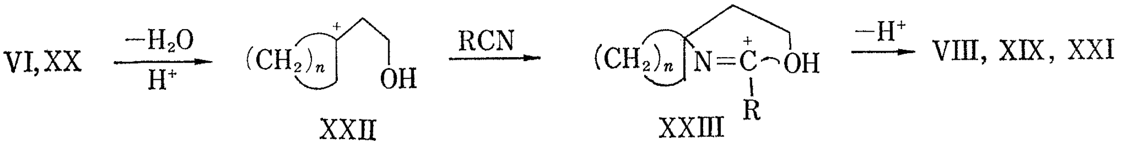
Chart 2

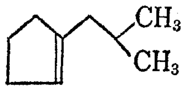
and indicating the presence of a primary alcohol. The product obtainable by hydrolysis of XI would be 2-aminocyclohexylethanol (XVII) but the product (XIV) obtained by hydrolysis of VIII and synthesized XVII (undetermined as to *cis* or *trans*) did not agree in every case and formula XI was also denied. This fact is also clear from the absence of methine proton signal adjacent to nitrogen or oxygen in any of XIV, XV, and XVI.

Grewe also reported that X, similar to VIII, is easily hydrolyzed by moisture in the air to form a product (XVIII) which has physical constants different from those of XIII.

The same reaction of VI and benzonitrile similarly afforded an oxazine (XIX) which, differing from VIII, was resistant to alkaline decomposition under the same condition, and only a small amount of benzoic acid was obtained. Formation of a dihydropyridine compound (dedimethyl compound of III) was anticipated from a five-membered ring compound (XX) but 1,3-oxazines (XXI) were obtained in practice. XXI underwent decomposition by moisture in air to form 1-(2-hydroxyethyl)-1-(phenylacetamido)cyclopentane.

Formation of 1,3-oxazines (VIII, XIX, and XXI) from VI and XX is considered to be the result of cyclization of a nitrilium salt (XXIII) formed from the tertiary carbonium cation (XXII).





XXIV

Chart 3

Reaction of II and acetonitrile in the presence of stannic chloride afforded III (R: CH_3), the same as in the case of the Ritter reaction conditions. In this case, formation of the side-chain *tert*-butyl cation (XXIV) must have taken priority. In the presence of stannic chloride, these reactions should tend to become an S_N2 type reaction,[4] and the above consideration should be taken merely as a model explanation.

The reaction was then extended to 1-(2-hydroxycyclohexyl)propan-2-ol (XXV) having a secondary alcohol in the side chain. Reaction of XXV with acetonitrile in the presence of sulfuric acid afforded two kinds of basic substance (XXVI and XXVII) in 44 and 20.3%

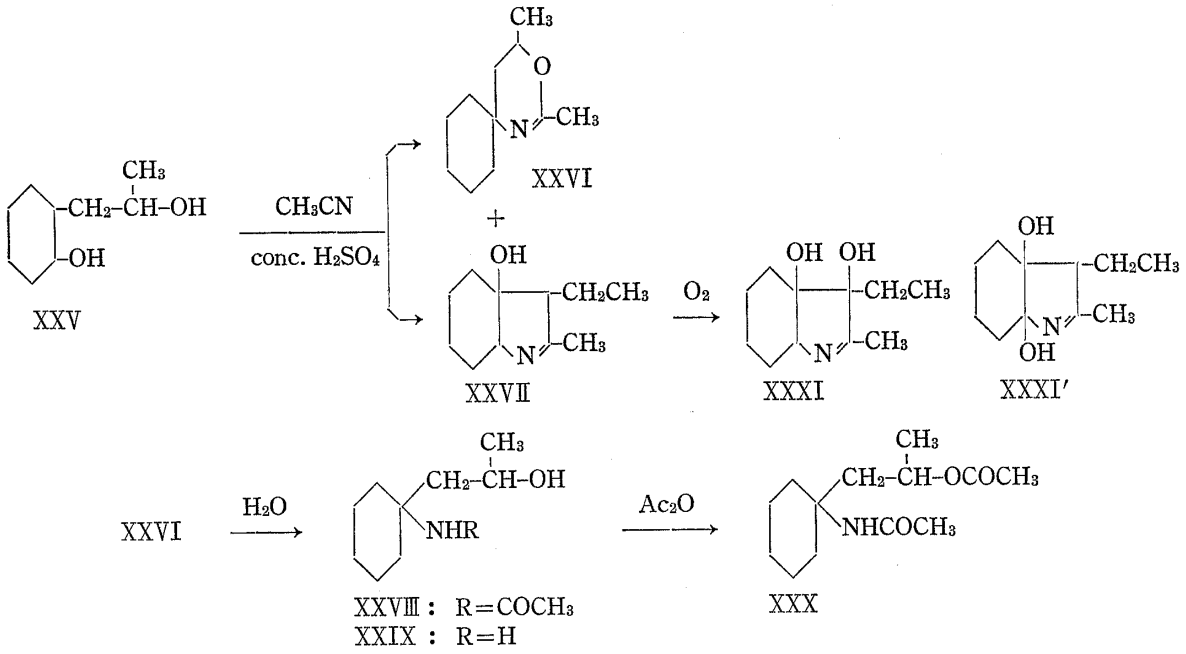


Chart 4

yield. IR spectrum of XXVI indicated the presence of $-\overset{|}{C}=N-$ and $=\overset{|}{C}-O-$ bonds, while its NMR spectrum indicated two methyl proton signals at 1.88 ppm (singlet) and 1.26 ppm (doublet), and only one methine proton signal adjacent to oxygen or nitrogen. Decoupling of this proton changed the methyl signal from a doublet to a singlet. With consideration of its elemental analytical values, the structure of this base was assumed to be an 1,3-oxazine (XXVI) of the same type as VIII or of the same type as X. Partial or complete hydrolysis of this product afforded N-acetamido-alcohol (XXVIII) or amino-alcohol (XXIX) and treatment of either of these with acetic anhydride gave the same N,O-diacetate (XXX), mp 87—88°. The methine proton signal shifted to 3.98 ppm in XXVIII and to 5.13 ppm in XXX, indicating the presence of a secondary hydroxyl. Consequently, this base is 2,6-dimethyl 4,4-pentamethylene-4,5-dihydro-1,3-oxazine (XXVI). XXVII has the same molecular formula as XXVI but its IR spectrum indicated the presence of $-\overset{|}{C}=N-$ and OH, and absence of $=\overset{|}{C}-O-$. Since its NMR spectrum indicated the methine proton signal at 4.15 and 2.45 ppm $(-C\underline{H}-N=\overset{|}{C}-\overset{|}{C}\underline{H}-)$ and a signal for ethyl group, XXVII was determined as 3-ethyl-3a-hydroxy-2-methyl-3a,4,5,6,7,7a-hexahydro-3*H*-indole. XXVII, similar to 2,3-dimethyl-3a-hydroxy 3a,4,5,6,7,7a-hexahydro-3*H*-indole reported in the preceding paper,[1] easily undergoes oxidation by oxygen in the air and similarly forms a diol compound (XXXI) whose NMR spectrum shows one methine proton signal at 4.13 ppm $(-\overset{|}{C}\underline{H}-N=\overset{|}{C}-)$ but the proton signal for $-N=\overset{|}{C}-\overset{|}{C}\underline{H}-$ in XXXI has disappeared and in its stead, one hydroxyl group has been added. Decoupling of $-CH-N=\overset{|}{C}-$ does not affect the methylene proton signal of ethyl group so that a partial structure of $-\overset{|}{C}H-N=C(CH_3)-\overset{|}{C}(OH)-C_2H_5$, with a hydroxyl group substituted at the base of ethyl group, can be assumed. This makes the formula XXXI more appropriate and the formula XXXI′ must be denied. XXXI comes as crystals of mp 115.5—116.5°, $M^+=197$.

In the Ritter reaction of XXV, formation of a carbonium cation (XXXII and XXXIII) can be first considered. This will be followed by the polar cycloaddition[6] of the nitrile, and XXVI and XXVII would be formed.

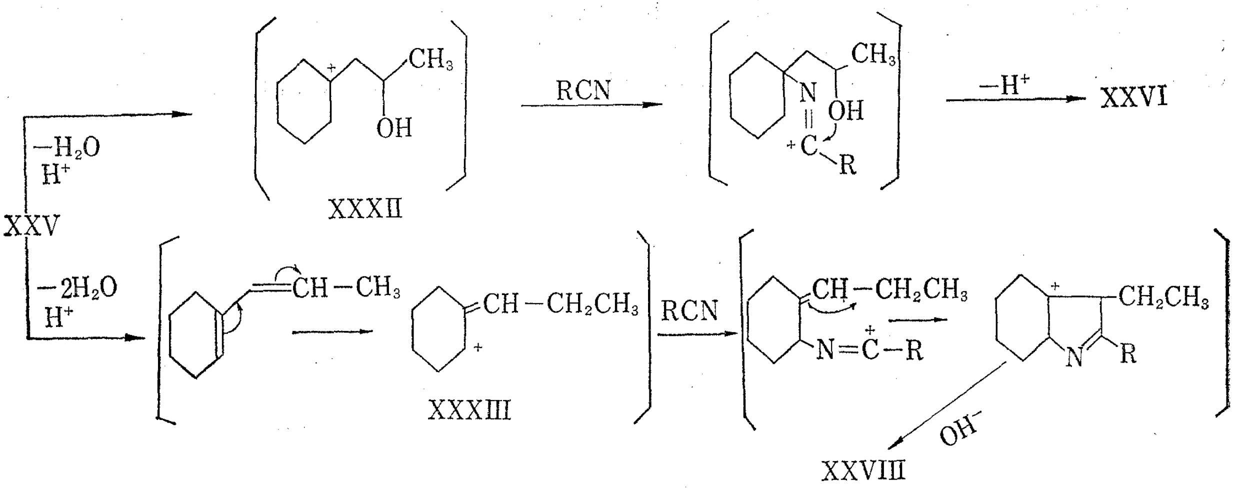


Chart 5

Syntheses of the starting glycols (VI, XX, and XXV) were carried out as depicted in Chart 6. Cycloalkanone was derived to ethyl 2-oxocycloalkylacetate[7] by the enamine

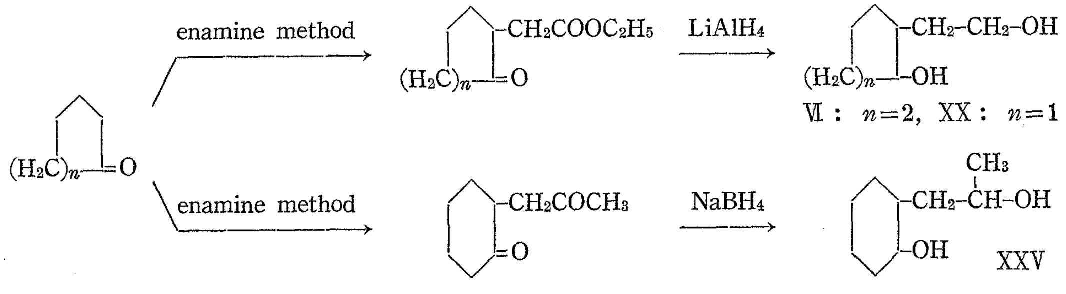


Chart 6

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6) R.R. Schmidt, *Tetrahedron Letters*, **1968**, 3443.

7) H.E. Baumgarten, P.L. Creger, and C.E. Villars, *J. Am. Chem. Soc.*,**80**, 6609 (1958).

method, and reduced with lithium aluminum hydride to VI and XX. Similarly, cyclohexanone was derived to α-(2-oxocyclohexyl)acetone[7] and reduced with sodium borohydride to XXV. *Cis* and *trans* forms of VI were not separated by thin-layer chromatography (TLC) and vapour phase chromatography (VPC), but its NMR spectrum indicated VI as the mixture of *cis* and *trans* forms (1:1.75). Similarly, XXV was the mixture of *cis* and *trans* forms (1:19—2.1). No detailed examinations were made on the steric structure of XXVII and XXXI derived from XXV.

Experimental

2-(2-Hydroxycyclohexyl)ethanol (VI)——To a stirred suspension of $LiAlH_4$ (0.47 g) in anhyd. ether was added a solution of ethyl 2-oxocyclohexylacetate (1.16 g) in anhyd. ether at room temperature. The mixture was stirred for 3 hr and then heated under reflux for 0.5 hr before decomposing the excess $LiAlH_4$ by adding H_2O under ice cooling. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether layer was dried over Na_2SO_4 and ether was distilled off, leaving 0.76 g (85%) of a colorless liquid of bp 104° (3 mmHg). *Anal.* Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.76; H, 11.12. NMR (in $CDCl_3$) ppm: 3.2 (0.64H, axial-C$\underline{H}$-OH in the *trans* form of VI, $J=17$ cps) 3.88 (0.36H, equatorial-C$\underline{H}$-OH in the *cis* form of VI, $J=10$ cps) 4.38 (2H, singlet, -OH).

2-Benzyl-4,4-pentamethylene-4,5-dihydro-1,3-oxazine (VIII)——(a) To a solution of 2.13 g of 2-(2-hydroxycyclohexyl)ethanol (VI) dissolved in $POCl_3$, 2.1 g of benzyl cyanide was added under cooling, followed by addition of 2.3 ml of $SnCl_4$, and the mixture was heated at 130—140° for 3—4 hr. $POCl_3$ and excess $SnCl_4$ were removed by low-pressure distillation, 20% NaOH was added to the residue to decompose, and the mixture was extracted with ether. The extract was shaken with 20% HCl, the acid layer was basified with 20% NaOH, and extracted with ether. After drying over Na_2SO_4, ether was evaporated and the residue was distilled to obtain a viscous liquid of bp 117—119° (2 mmHg), which was contaminated with phenylacetamide. Removal of the latter crystals afforded 1.4 g (39%) of VIII. Picrate of VIII: mp 152° from MeOH. *Anal.* Calcd. for $C_{16}H_{21}ON \cdot C_6H_3O_7N_3$: C, 55.92; H, 5.12; N, 11.86. Found: C, 56.28; H, 5.14; N, 11.41. IR cm^{-1}: 1670 (-C=N-), 1242 (=C-O-).

(b) A solution of 0.82 g of benzyl cyanide dissolved in 10 ml of conc. H_2SO_4 was chilled to 0—2°, 1 g of VI was added slowly under stirring, and the mixture was stirred at 0—5° for 2 hr. This was poured into 25 g of ice water and the mixture was extracted with $CHCl_3$. The aqueous layer was basified with 30% NaOH solution, extracted with ether, and ether was evaporated after drying over Na_2SO_4. Distillation of the residue at bp 117—119° (2 mmHg) and removal of contaminating phenylacetamide afforded 0.4 g (23.4%) of VIII.

(c) In exactly the same way as method (a), 0.4 g (41%) of VIII was obtained from 0.5 g of cyclohexenylethanol (IX) using 0.5 g of benzyl cyanide and 6 ml of $SnCl_4$.

2-Phenyl-4,4-pentamethylene-4,5-dihydro-1,3-oxazine (XIX)——Reaction was carried out as in above (a) method with 1.17 g of VI, 0.9 g of benzonitrile, and 2.8 ml of $SnCl_4$, and 0.72 g (39%) of XIX was obtained as a viscous liquid of bp 138° (8 mmHg). Picrate: mp 179—180° from acetone. *Anal.* Calcd. for $C_{15}H_{19}ON \cdot C_6H_3O_7N_3$: C, 55.02; H, 4.84; N, 12.22. Found: C, 55.48; H, 4.88; N, 12.40. Hydrochloride of XIX: mp 176—177° from acetone and $CHCl_3$. *Anal.* Calcd. for $C_{15}H_{19}ON \cdot HCl$: O, 6.02. Found: O, 5.80. IR cm^{-1}: 1653 (-N=C-), 1282 (=C-O-). UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ: 237. NMR (in $CDCl_3$) ppm: 4.24 (2H, triplet, $-CH_2-O-$), 7.28, 7.88 (3H, 2H, multiplet, multiplet, aromatic protons).

2-Benzyl-4,4-tetramethylene-4,5-dihydro-1,3-oxazine (XXI)——In the same way as above (a) method, 0.5 g of 2-(2-hydroxyethyl)cyclopentanol (XX) afforded 0.37 g (42%) of XXI as a viscous liquid, together with 22 mg of phenylacetamide as a by-product. Picrate, mp 139—140° from acetone. *Anal.* Calcd. for $C_{15}H_{19}ON \cdot C_6H_3O_7N_3$: C, 55.02; H, 4.84; N, 12.22. Found: C, 55.16; H, 5.02; N, 12.29.

1-(2-Hydroxyethyl)-1-(phenylacetamido)cyclohexane (XIII)——An ether solution of VIII was left to stand in air for 1 week and the crystals that separated out were recrystallized from acetone to lustrous plates, mp 135—136°. *Anal.* Calcd. for $C_{16}H_{23}O_2N$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.85; H, 8.77; N, 5.41. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1655, 1565 (-NHCO). XXI was similarly hydrolyzed and formed 1-(2-hydroxyethyl)-1-(phenylacetamido)cyclopentane which recrystallized from iso-Pr_2O to lustrous plates, mp 88—89°. *Anal.* Calcd. for $C_{15}H_{21}O_2N$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.57; H, 8.54; N, 5.70. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1645, 1551 (NHCO).

1-Amino-1-(2-hydroxyethyl)cyclohexane (XIV)——A solution of 154 mg of VIII dissolved in 7.5 ml of 80% EtOH, added with 80 mg of NaOH, was refluxed for 6 hr, EtOH was distilled off in reduced pressure, and the residue was extracted with ether. The extract solution was dried over Na_2SO_4 and ether was distilled off, leaving 87 mg (96%) of an oily substance (XIV), bp 96—98° (12 mmHg). The aqueous solution left after extraction with ether was acidified with HCl and extracted with ether. After drying over Na_2SO_4, ether was evaporated and 56 mg (83%) of plates, mp 76.5°, was obtained which corresponded to phenylacetic acid. Picrate of XIV, mp 142—143° from acetone. *Anal.* Calcd. for $C_8H_{17}ON \cdot C_6H_3O_7N_3$: C, 45.16; H, 5.41; N, 15.05. Found: C, 45.21; H, 5.57; N, 14.97. IR cm^{-1}: 3390, 3320, 1598 (NH). NMR (in $CDCl_3$) ppm: 2.75 (2H, broad, NH_2), 3.81 (2H, triplet, $-CH_2-O-$).

1-(Dimethylamino)-1-(2-hydroxyethyl)cyclohexane (XV)——A solution of 1.5 g of XIV in 2.0 g of HCOOH and 1.5 g of HCHO was refluxed for 6 hr, allowed to stand overnight, and *ca.* 1.0 g of conc. HCl was added. The mixture was heated for 40 min, concentrated in a reduced pressure, basified with 40% NaOH, and extracted with ether. The extract solution was dried over Na_2SO_4 and evaporation of ether left 1.4 g (79%) of a colorless liquid of bp 125° (12 mmHg). Picrate, mp 186—188° from acetone. *Anal.* Calcd. for $C_{10}H_{21}ON \cdot C_6H_3O_7N_3$: C, 47.99; H, 6.04; N, 13.99. Found: C, 48.21; H, 6.40; N, 14.41. NMR (in $CDCl_3$) ppm: 1.78 (2H, triplet, $-C\underline{H}_2-CH_2-O-$), 2.27 $\left(\text{6H, singlet, } -N\Big\langle\begin{matrix}CH_3\\CH_3\end{matrix}\right)$, 3.76 (2H, triplet, $-C\underline{H}_2-OH$).

Hofmann Degradation of XV Methiodide——Methiodide of XV: Addition of *ca.* 2 g of MeI to the abs. ether solution of 484 mg of XV immediately produced white turbidity. The mixture was allowed to stand overnight, heated in a water bath for 1 hr, and crystals that precipitated out were collected. The quantitatively formed methiodide was recrystallized from acetone and $CHCl_3$ to crystals which sintered at 142°, browned at 192°, and melted at 257°.

Hofmann Degradation: Ag_2O prepared from 1 g of $AgNO_3$ was added to a solution of 164 mg of the above methiodide dissolved in 4 ml of water, the mixture was allowed to stand overnight under agitation, and water was distilled under a reduced pressure by warming in a water bath of 37—40°. The residual solution was heated at 90° at ordinary pressure and extracted with ether. The extract solution was dried over Na_2SO_4 and ether was evaporated, leaving 17 mg (26%) of cyclohexenylethanol (IX). This compound agreed in IR spectrum and TLC with the compound obtained by reduction of phenethyl alcohol with Li-$MeNH_2$.[8]

2,6,6-Trimethyl-3,4-cyclopentano-5,6-dihydropyridine (III: R=Me)——To a mixture of 1.05 g of α-(1-cyclopentenyl)-*t*-butanol (I) in $POCl_3$, 1.27 g of MeCN was added under cooling, followed by addition of 2.8 ml of $SnCl_4$, and the mixture was heated at 130—140° for 3.5 hr. Excess $POCl_3$, $SnCl_4$, and MeCN were removed by low-pressure distillation, the residue was decomposed with 20% NaOH, and extracted with ether. The extract layer was extracted with 20% HCl, the acid layer was basified, and extracted with ether. After drying over Na_2SO_4, ether was evaporated and 0.25 g (20.2%) of III (R=Me), bp 90—100° (1 mmHg) was obtained which agreed entirely with this substance reported in literature.[3]

1-(2-Hydroxycyclohexyl)propan-2-ol (XXV)——MeOH solution of 0.5 g of $NaBH_4$ was added to the stirring MeOH solution of 1.19 g of α-(2-oxocyclohexyl)acetone[7] and the mixture was stirred for 5 hr at room temperature. Excess $NaBH_4$ was decomposed with 10% HCl, MeOH was evaporated, and the residue was extracted with ether. The extract solution was washed with 10% Na_2CO_3 and H_2O, dried over Na_2SO_4, and ether was evaporated to give 1.04 g (85%) of XXV as a colorless liquid, bp 115—117° (2 mmHg). *Anal.* Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.27; H, 11.20. NMR (in $CDCl_3$) ppm: 1.17 (3H, doublet, $J=6$ cps, $C\underline{H}_3-\overset{|}{C}H-$), 3.2 (0.65H, multiplet, $J=17.5$ cps, $C\underline{H}-OH$ axial, in the *trans* form of XXV), 3.2—4.1 (1.35—1.3H, multiplet, $C\underline{H}$ (eq)-OH in the *cis* form of XXV$+$$-C\underline{H}_2-\underset{\underset{OH}{|}}{CH}-CH_3$), 4.15 (2H, singlet, OH).

Reaction of XXV and Acetonitrile——To 10 ml of conc. H_2SO_4 chilled to 0—5°, 0.27 g of MeCN was added, and 1.01 g of XXV was added slowly with stirring. Viscous XXV was washed into with 0.2 g of MeCN, the mixture was stirred at 0—7° for 3 hr, and poured into 23 g of ice water. This mixture was shaken with $CHCl_3$ to remove the starting material and resinous substance, the acid layer was basified with 30% NaOH under cooling, and extracted with ether. After drying over Na_2SO_4, ether was evaporated, and 0.51 g (44%) of 2,6-dimethyl-4,4-pentamethylene-4,5-dihydro-1,3-oxazine (XXVI), bp 96° (12 mmHg), and 0.24 g (20.3%) of 3-ethyl-3a-hydroxy-2-methyl-3a,4,5,6,7,7a-hexahydro-3*H*-indole (XXVII) as a viscous liquid of bp 180° (1 mmHg) (bath temp.) were obtained. Picrate of XXVI: mp 118—119° from MeOH. *Anal.* Calcd. for $C_{11}H_{19}ON \cdot C_6H_3O_7N_3$: C, 49.75; H, 5.40; N, 13.65. Found: C, 49.59; H, 5.60; N, 13.86. IR cm^{-1}: 1668 ($-N=C-$), 1236 ($=C-O-$). NMR (in $CDCl_3$) ppm: 1.26 (3H, doublet, $C\underline{H}_3-CH-$), 1.88 (3H, singlet, $CH_3-C=N-$), 4.11 (1H, multiplet (12), $>C\underline{H}-O-$). Picrate of XXVII: mp 194—195.5° from MeOH. *Anal.* Calcd. for $C_{11}H_{19}ON \cdot C_6H_3O_7N_3$: C, 49.75; H, 5.40; N, 13.65. Found: C, 49.60; H, 5.54: N, 13.26. IR ν_{max}^{KBr} cm^{-1}: 1652 ($-N=C-$), 3348 (OH).

1-Acetamido-1-(2-hydroxypropyl)cyclohexane (XXVIII), 1-Amino-1-(2-hydroxypropyl)cyclohexane (XXIX) and 1-Acetamido-1-(2-acetoxypropyl)cyclohexane (XXX)——A solution of 59 mg of XXVI dissolved in 2 ml of 80% EtOH, added with 25 mg of NaOH, was refluxed in a water bath for 2 hr, EtOH was evaporated, and the residue was extracted with ether. After drying over Na_2SO_4, ether was evaporated and the residue was distilled to obtain 20 mg (31%) of XXVIII as an oil. IR cm^{-1}: 1653, 1548 (NHCO): NMR (in $CDCl_3$) ppm: 1.18 (3H, doublet, $C\underline{H}_3-\overset{|}{C}H-$), 1.96 (3H, singlet, $CH_3-C=O$), a signal at 3.98 ppm (1H, $-C\underline{H}-OH$) which branched out into 12 which decreased to six on addition of D_2O.

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[8] *a*) R.A. Benkeser, C. Arnold, J. Rogers, F. Lambert, and O.H. Thomas, *J. Am. Chem. Soc.*, 77, 6042 (1963); *b*) R.A. Benkeser, R.E. Robinson, D.M. Sauve, and O.H. Thomas, *J. Am. Chem. Soc.*, 77, 3230 (1963).

A solution of 0.3 g of XXVI dissolved in 14 ml of 80% EtOH, added with 0.32 g of NaOH, was refluxed in a water bath for 4 hr, EtOH was evaporated, and the residue was extracted with ether. Ether layer was extracted with 10% HCl, the acid layer was basified, and extracted with ether. After drying over Na_2SO_4, ether was evaporated and 190 mg (73%) of XXIX was obtained as a colorless liquid of bp 126—127° (16 mmHg). This compound quite easily formed a carbonate. IR cm^{-1}: 3323, 3253, 1601 (NH). A mixture of 15 mg of XXIX and 30 mg of Ac_2O was heated in a water bath for 4 hr, excess Ac_2O was distilled off, and residual crystals were recrystallized from iso-Pr_2O to 18 mg (100%) of XXX as plates mp 86—87°.

Similarly, excess Ac_2O was added to 19 mg of XXVIII, the mixture was allowed to stand overnight, and then heated in a water bath for 10 min and excess Ac_2O was distilled off. The same compound (XXX) was obtained in 28 mg (98%) amount. *Anal.* Calcd. for $C_{13}H_{23}O_3N$: C, 64.70; H, 9.61; N, 5.80. Found: C, 64.33; H, 9.43; N, 5.65. IR ν_{max}^{KBr} cm^{-1}: 1642, 1567 (NHCO); 1736 (>C=O). NMR (in $CDCl_3$) ppm: 1.21 (3H, doublet, $C\underline{H}_3CH-$), 1.93 (3H, singlet, CH_3COO), 1.98 (3H, singlet, $NHCOC\underline{H}_3$), 5.13 (1H, broad, $-C\underline{H}-O-C=O$).

3,3a-Dihydroxy-3-ethyl-2-methyl-3a,4,5,6,7,7a-hexahydro-3*H*-indole (XXXI)——XXVII underwent crystallization when left to stand (for *ca.* 5 days) and its recrystallization from iso-Pr_2O afforded colorless plates, mp 115—116.5°. The picrate of XXVII, when left standing for 2 days and then the free base liberated, also formed the same crystals. *Anal.* Calcd. for $C_{11}H_{19}O_2N$: C, 66.97; H, 9.71; N, 7.10. Found: C, 67.20; H, 9.74; N, 7.05. IR ν_{max}^{KBr} cm^{-1}: 1645 (C=N), 3083 (OH shoulder), 3552 (OH). NMR (in $CDCl_3$) ppm: 1.13 (3H, triplet, $C\underline{H}_3-CH_2-$), 2.13 (3H, singlet, $CH_3-C=N$), 2.22 (2H, singlet, OH), 4.13 (1H, multiplet, $-C\underline{H}-N=$). Mass Spectrum *m/e*: 197 (M^+).

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