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Synthetic Studies on Securitinine and Related Compounds. I. Stereochemistries of the Catalytic Hydrogenation Products of 6-(4-Methoxy-2-pyridyl)-1,4-dioxaspiro[4,5]decan-6-ol[1)]

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The catalytic hydrogenation of 6-(4-Methoxy-2-pyridyl)-1,4-dioxaspiro[4,5]decan-6-ol (V) gave VIa as a major product and VIb as a minor product. Their stereochemistries were determined by the nuclear magnetic resonance spectra of their oxathiazolidine derivatives (XIIIa and XIIIb, respectively).

Securitinine, a minor alkaloid isolated from the roots of *Securinega suffruticosa* REHD. grown in Hou-lung (Formosa), was assigned to have the structure as 9α-methoxyallosecurinine (I) by our group.[3)] On the other hand, Parello, *et al.*[4)] isolated a new alkaloid phyllantine from *Phyllanthus discoides* MUELL. ARG. and assigned the structure as 9β-methoxysecurinine (II), a diastereoisomer of securitinine. We have investigated the synthetic studies on securitinine and related compounds.

The present paper describes the stereochemistries of the catalytic hydrogenation products of 6-(4-methoxy-2-pyridyl)-1,4-dioxaspiro[4,5]decan-6-ol (V), which would serve a useful intermediate[5)] for syntheses of securitinine and related compounds.

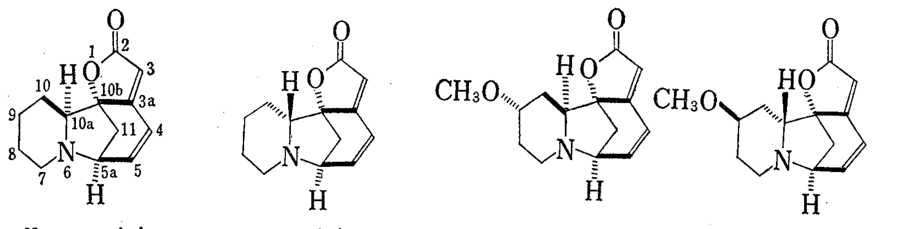


Chart 1

Condensation of 2-bromo-4-methoxypyridine (III)[6)] with 1,4-dioxaspiro[4,5]decan-6-one (IV)[7)] in dry ether in the presence of *n*-butyl lithium at −20° gave 6-(4-methoxy-2-pyridyl)-1,4-dioxaspiro[4,5]decan-6-ol (V) in 60—70% yield. In general, pyridine derivatives are reduced to the corresponding piperidines by means of catalytic hydrogenation over platinum

1) Part of this work was reported at the 91th, Annual Meeting of Pharmaceutical Soceity of Japan, Fukuoka, April 1971.
2) Location: *6-1-1, Toneyama, Toyonaka, Osaka.*
3) Z. Horii, M. Ikeda, M. Hanaoka, M. Yamauchi, Y. Tamura, S. Saito, T. Tanaka, K. Kotera, and N. Sugimoto, *Chem. Pharm. Bull.* (Tokyo), **14**, 918 (1966); *idem, ibid.*, **15**, 1633 (1967).
4) J. Parello and S. Munavalli, *Compt. Rend.*, **260**, 337 (1965); J. Parello, *Bull. Soc. Chim. France*, **1968**, 1117.
5) Z. Horii, M. Hanaoka, Y. Yamawaki, Y. Tamura, S. Saito, N. Shigematsu, K. Kotera, H. Yoshikawa, Y. Sato, H. Nakai, and N. Sugimoto, *Tetrahedron*, **23**, 1165 (1967).
6) Z. Talik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **9**, 561 (1961) [*C.A.*, **60**, 2884f (1964)].
7) R.H. Jaeger and H. Smith, *J. Chem. Soc.*, **1955**, 160.

oxide or sodium-alcohol reduction.[8] Though 4-methoxypyridine can not be reduced to 4-methoxypiperidine under these conditions, it can be reduced by means of catalytic hydrogenation over ruthenium dioxide.[9] But hydrogenation of V over ruthenium dioxide was unsuccessful. Recently, there are a few reports that rhodium catalysts are excellent for hydrogenations of pyridines.[10] Hydrogenation of V in ethanol in the presence of 5% rhodium on alumina proceeded slowly to give three products; VIa (51%), VIb (19%), and VII (trace). The product (VII) was derived to the amino-ketone (VIII) by hydrolysis, which was identical with an authentic sample.[5] The major product (VIa), colorless needles, mp 143—144°, possesses a molecular formula $C_{14}H_{25}O_4N$ and the minor product (VIb), colorless plates, mp 82—84°, also possesses the same molecular formula as VIa. These products, VIa and VIb, are diastereoisomeric with each other having the structure (A), as they have analogous fragmentation patterns in their mass spectra.

The piperidine compound (A) have four diastereoisomers theoretically as shown in Chart 2; both B and C are *cis*-2,4-disubstituted piperidines, and both D and E are *trans*-2,4-disub-

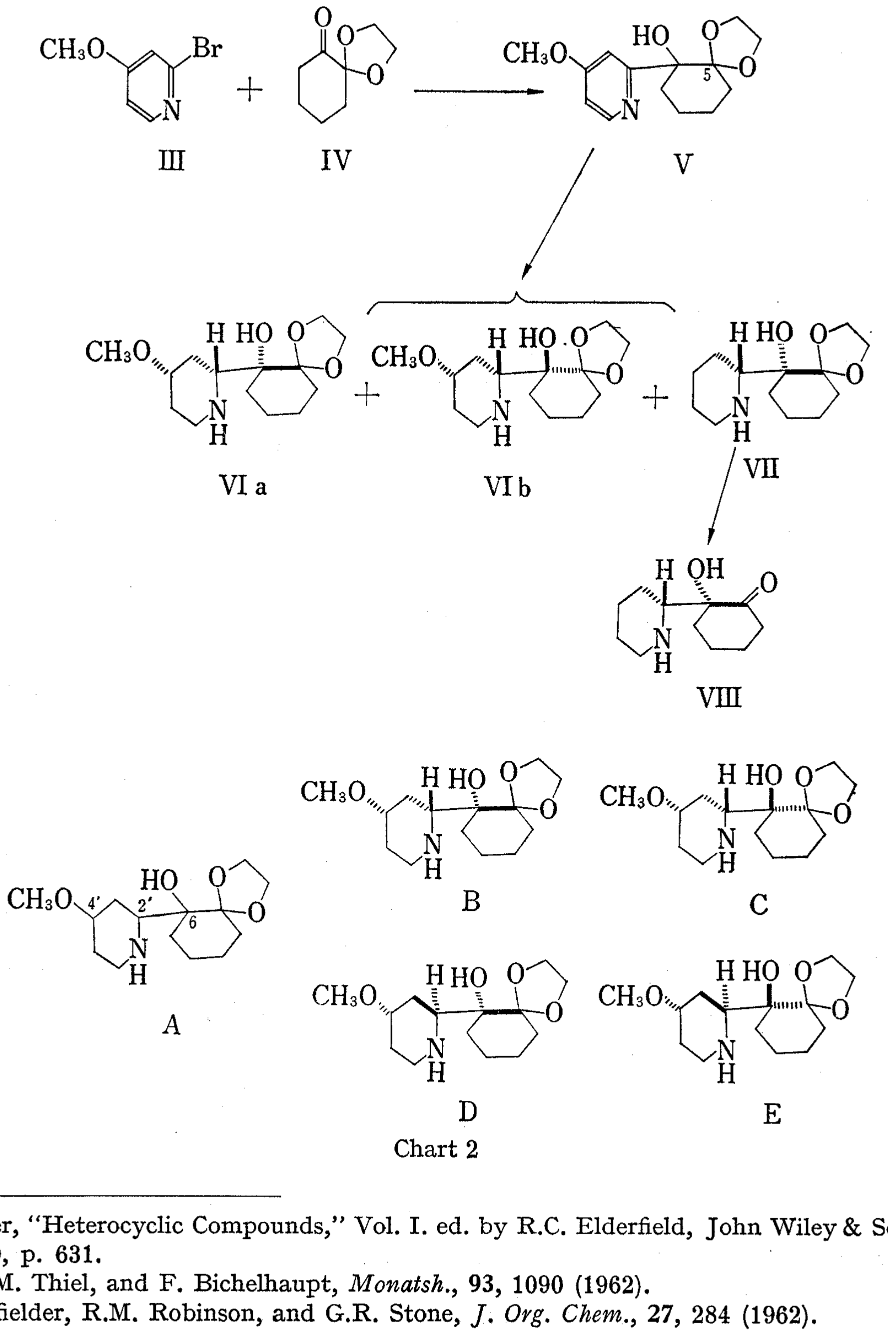


Chart 2

8) H.S. Mosher, "Heterocyclic Compounds," Vol. I. ed. by R.C. Elderfield, John Wiley & Sons, Inc., New York, 1950, p. 631.
9) K. Stach, M. Thiel, and F. Bichelhaupt, *Monatsh.*, 93, 1090 (1962).
10) *cf.* M. Freifielder, R.M. Robinson, and G.R. Stone, *J. Org. Chem.*, 27, 284 (1962).

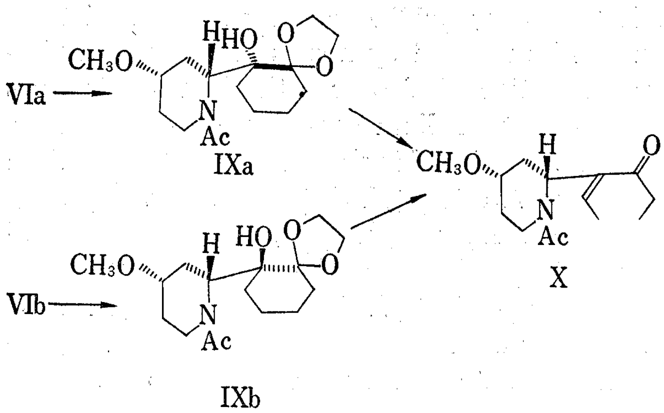
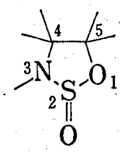


Chart 3



2-oxo-1,2,3-oxathiazolidine

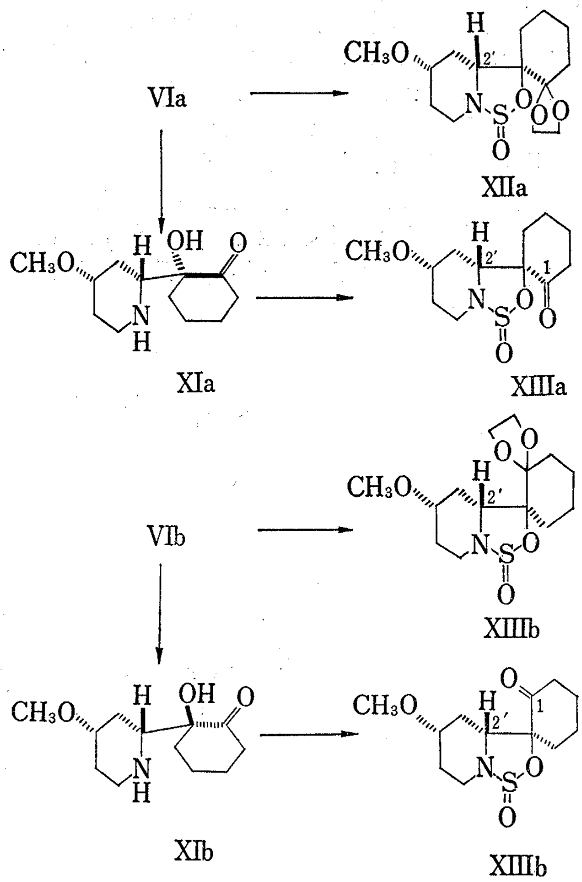


Chart 4

stituted piperidines. In order to determine the stereochemistries of VIa and VIb, initially we tried to determine the relative configuration between the methoxyl group at $C_{4'}$ and the cyclohexane ring at $C_{2'}$ in these compounds. After acetylations of the products (VIa and VIb) with acetic anhydride, the amides (IXa and IXb, respectively) were dehydrated with thionyl chloride-pyridine to give the same product (X), in which the position of double bond was assigned to locate at *endo*-position by the following spectral data. The nuclear magnetic resonance (NMR) spectrum of X shows one olefinic proton signal at 3.35τ and its ultraviolet (UV) spectrum shows the absorption maximum at 237 mμ due to a 2-substituted 2-cyclohexenone system.[11] These results show that VIa and VIb have the same configurations of $C_{2'}$ and $C_{4'}$. Since catalytic hydrogenations of disubstituted pyridine derivatives give *cis*-disubstituted piperidines as major products,[12] it could beconcluded that these compounds (VIa and VIb) are *cis*-2,4-disubstituted piperidines (B and C, or *vice versa*).

In order to determine the relative configuration of $C_{2'}$ and C_6, it is desired to fix the $C_{2'}$-C_6 bond. Recently, Deyrup and Moyer[13] reported that 2-oxo-1,2,3-oxathiazolidines were formed by the reactions of β-amino-alcohols with thionyl chloride in the presence of tertiary amines. Accordingly, the β-amino-alcohols (VIa, b and their hydrolyzed derivatives, XIa, b) were converted to the 2-oxo-1,2,3-oxathiazolidines (XIIa, b, and XIIIa, b, respectively) by the treatment of thionyl chloride in pyridine. Their physical data are summarized in Table I. The NMR spectrum of XIIIb exhibits one proton signal at 6.05 τ, which was assigned to $C_{2'}$-H. On the other hand, the NMR spectra of XIIa, XIIb, and XIIIa exhibit no corresponding signal at the lower field than 6.3 τ. In NMR spectra of alkyl substituted 2-oxo-1,2,3-oxathiazolidines, it was reported that the protons at C_4 appeared in 6.3—7.3 τ region.[13] In XIIIb the proton at $C_{2'}$ is coplanar with the carbonyl group at C_1, thus induc-

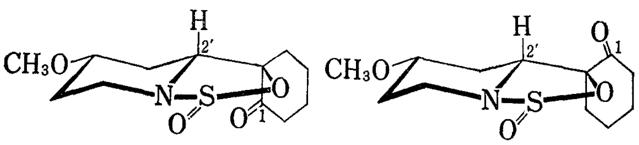
11) C.N.R. Rao, "Ultra-Violet and Visible Spectroscopy, Chemical Applications," Butterworths, London, 1961, p. 48.
12) *cf.* Y. Kawazoe, M. Tsuda, and T. Horie, *Chem. Pharm. Bull.* (Tokyo), **19**, 427 (1971); J.G. MaConnell, M.S. Blum, and H.M. Fales, *Tetrahedron*, **26**, 1129 (1971).
13) J.A. Deyrup and C.L. Moyer, *J. Org. Chem.*, **34**, 175 (1969).

Table I. The Physical Data of the 2-Oxo-1,2,3-oxathiazolidines

Compound	XIIa	XIIb	XIIIa	XIIIb
mp (°C)	95—96	117—118	129—131	75—76
IR (KBr; cm^{-1}) CO			1725	1732
SO	1180	1170	1180	1188
NMR ($CDCl_3$; τ) $-OCH_3$	6.60	6.61	6.66	6.63
$C_{2'}$ -H				6.05
Mass spectrum (m/e)	317 (M^+)	317 (M^+)	273 (M^+)	273 (M^+)

ing shift of the signal to lower field and in XIIIa, on the contrary, the proton at $C_{2'}$ is too far from the carbonyl group to be affected by the above interaction as shown in Chart 5. Thus it could be concluded that VIa has the structure (B) and VIb has the structure (C).

The fact that the catalytic hydrogenation of V gave VIa as a major product and VIb as a minor product is explained as follows; VIa was predominantly obtained by the *cis* attack of hydrogen from the less hindered side (α-side) and VIb was obtained by the *cis* attack of hydrogen from the hindered side (β-side) in the hydrogen bonded conformation (V')[14] as shown in Chart 6.



XIIIa XIIIb

Chart 5

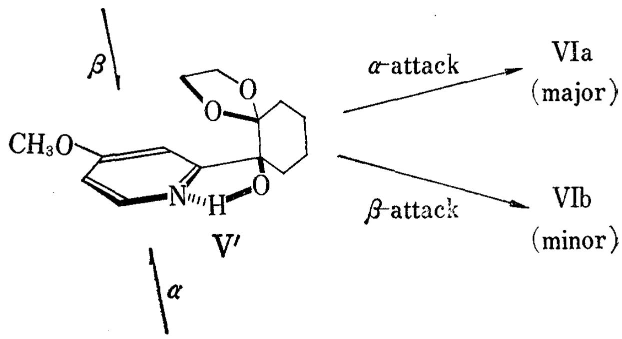


Chart 6

In order to examine the influence of C_5-substituents on the hydrogenation of V, the ketal (V) was converted to the diol (XV) *via* the ketone (XIV). The catalytic hydrogenation of XV under similar conditions to those employed for V gave the piperidine (XVI) as a diastereoisomeric mixture in quantitative yield. Jones oxidation of XVI, followed by chromatographic separation gave XIa and XIb in 38% and 21% yields, respectively and no other isomer was obtained. These compounds (XIa and XIb) were identical with the samples prepared by hydrolyses of VIa and VIb, respectively.

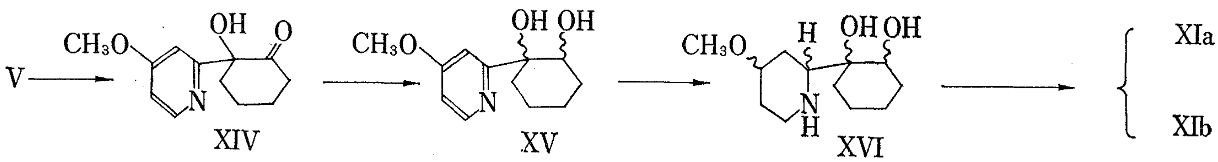


Chart 7

Further work on the syntheses of securitinine and its stereoisomers *via* these hydrogenated products (VIa and VIb) is in progress.

14) *cf.* H.J. Liu, Z. Valenta, and T.T.J. Yu, *Chem. Commun.*, **1970**, 1116.

Experimental[15]

6-(4-Methoxy-2-pyridyl)-1,4-dioxaspiro[4,5]decan-6-ol (V)——To a stirred solution of *n*-BuLi[16] (prepared from 3.0 g of *n*-BuBr and 0.30 g of Li) in dry ether was added a solution of 2-bromo-4-methoxypyridine[6] (III, 3.8 g) in dry ether (10 ml) dropwise over a period of 15 min at $-20°$, and then to the reaction mixture was added a solution of 1,4-dioxaspiro[4,5]decan-6-one[7] (IV, 3.1 g) in dry ether (10 ml) over a period of 15 min. After stirring for 3 hr at this temperature, to the reaction mixture was added satd. NH_4Cl solution at 0°. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether layers were washed with brine, dried and evaporated. Distillation of the residue gave 3.5 g (65%) of V as a pale yellow viscous oil, bp 160—170° (0.001 mmHg), which was soildified on standing and recrystallized from *n*-hexane to give colorless plates, mp 57.5—59°. IR ν_{max}^{KBr} cm^{-1}: 3289 (OH), 1600 and 1567 (pyridine ring). *Anal.* Calcd. for $C_{14}H_{19}O_4N$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.38; H, 7.11; N, 5.64. NMR τ: 6.25 (4H, m, -OC$\underline{H}_2$C$\underline{H}_2$O-), 6.15 (3H, s, -OC$\underline{H}_3$), 3.25 (1H, d of d, J=2.5 and 5.5 cps, pyridine ring proton), 2.91 (1H, d, J=2.5 cps, pyridine ring proton), 1.62 (1H, d, J=5.5 cps, pyridine ring proton).

Catalytic Hydrogenation of V——The pyridine (V, 10.0 g) was hydrogenated in EtOH (100 ml) over 5% Rh-Al_2O_3 (15 g) at 100° and 140 atm for 32 hr. After the catalyst was filtered off, the filtrate was evaporated to dryness. The solidal residue was extracted with boiling *n*-hexane. The solvent was evaporated and the residue was recrystallized from *n*-hexane twice to give 5.2 g (51%) of VIa as colorless needles, mp 143—144°. IR ν_{max}^{KBr} cm^{-1}: 3333, 3125 (OH, NH). *Anal.* Calcd. for $C_{14}H_{25}O_4N$: C, 61.96; H, 9.29; N, 5.16. Found: C, 62.07; H, 9.17; N, 5.23. NMR τ: 6.02 (4H, m, -OC$\underline{H}_2$C$\underline{H}_2$O-), 6.64 (3H, s, -OC$\underline{H}_3$). Mass Spectrum *m/e*: 271 (M^+), 114. The mother liquor was evaporated and recrystallization of the residue from petr. ether gave 2.0 g (19%) of VIb as colorless plates, mp 82—84°. IR ν_{max}^{KBr} cm^{-1}: 3330, 3122 (OH, NH). *Anal.* Calcd. for $C_{14}H_{25}O_4N$: C, 61.96; H, 9.29; N, 5.16. Found: C, 61.97; H, 9.32; N, 5.36. NMR τ: 5.98 (4H, s, -OC$\underline{H}_2$C$\underline{H}_2$O-), 6.61 (3H, s, -OC$\underline{H}_3$). Mass Spectrum *m/e*: 271 (M^+), 114. Hydrolysis of the *n*-hexane insoluble residue with 15% HCl at 90° for 3 hr, followed by chromatographic separation gave a small amount of VIII as colorless crystals, mp 89—90°, identical with an authentic sample[5] in comparison with IR, TLC and mp.

2-(1-Acetyl-4-methoxy-2-piperidyl)-2-cyclohexenone(X)——a) From VIa: A solution of the amine (VIa, 0.40 g) in Ac_2O (10 ml) was heated at 90° and the reaction mixture was evaporated *in vacuo* at 90°. To the residue was added water and K_2CO_3, and the resulting alkaline solution was extracted with $CHCl_3$. Evaporation of the dried extract gave an oily residue (0.58 g), which was chromatographed on silica gel (10 g). Elution with $CHCl_3$ afforded 0.40 g of the amide (IXa) as a colorless viscous oil, which was homogeneous on TLC. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3280 (OH), 1621 (amide). To a stirred solution of thionyl chloride (1.5 ml) in dry pyridine (10 ml) was added a solution of the amide (IXa, 0.40 g) in dry pyridine (5 ml) dropwise over a period of 25 min under ice-water cooling. After stirring for 2 hr under cooling and for 1.5 hr at room temperature, the reaction mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed with water, 10% HCl and water, and dried. Evaporation of the solvent gave a brown oily residue (275 mg), which was chromatographed on silica gel (4 g). Elutions with $CHCl_3$ and then with EtOH-$CHCl_3$ (1:100 v/v) afforded 170 mg (46%) of the α,β-unsaturated ketone(X) as a colorless oil, homogenous on TLC. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1665 (α,β-unsaturated ketone). 1628 (amide). Mass Spectrum *m/e*: 251 (M^+), 208, 176. NMR τ: 7.98 (3H, s, -NCOC$\underline{H}_3$), 6.81 (3H, s, -OC$\underline{H}_3$), 5.10 (1H, m, N-C$\underline{H}$〈), 3.35 (1H, m, 〉C=C$\underline{H}$-). UV λ_{max}^{EtOH} mμ (log ε): 237 (4.10). The semicarbazone of X, mp 175° (from AcOEt). *Anal.* Calcd. for $C_{15}H_{24}O_3N_4$ (1/2 H_2O): C, 56.76; H, 7.94; N, 17.62. Found: C, 57.04; H, 8.13; N, 17.43.

b) From VIb: A solution of the amine (VIb, 0.21 g) in Ac_2O (10 ml) was treated by the same manner as described above. Chromatography of the crude product gave 195 mg of the amide (IXb) as a colorless viscous oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3280 (OH), 1620 (amide). To a stirred solution of the amide (IXb, 105 mg) in dry pyridine (4.5 ml) was added thionyl chloride (0.1 ml) under ice-water cooling. Stirring was continued for 6 hr under cooling and the reaction mixture was treated by the same manner as described above. The crude product was subjected to preparative thin-layer chromatography on silicagel (30 g) using 5% MeOH-ether as a developing solvent to give 48 mg (47%) of the α,β-unsaturated ketone(X), as a colorless oil, which was identical with the sample obtained from VIa in comparison with IR, TLC, UV and mass spectrum.

2-(4-Methoxy-2-piperidyl)-2-hydroxycyclohexanone(XIa)——A solution of the ketal (VIa, 3.4 g) in 20% HCl (30 ml) was heated at 90° for 4 hr. After neutralization with aqueous NaOH, the resulting mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water and dried. Evaporation of

15) All melting points and boiling point are uncorrected. NMR spectra were taken on Hitachi Perkin-Elmer H-60 type spectrometer at 60 Mc in $CDCl_3$ with $(CH_3)_4Si$ as an internal standard. Mass spectra were taken on Hitachi RMU-60 spectrometer. Silica gel (Mallinckrodt) and Kiesel gel PF_{254} (Merck) were used for column chromatographies and preparative thin-layer chromatography (TLC), respectively. Organic extracts were dried over anhydrous $MgSO_4$.

16) R.G. Jones and H. Gilman, *Org. Reactions*, 6, 352 (1951).

the solvent gave 2.5 g (90%) of the ketone(XIa) as a colorless solid, which was recrystallized from *n*-hexane to give colorless leaflets, mp 114—115°. IR ν_{max}^{KBr} cm^{-1}: 3300, 3215 (OH, NH), 1701 (CO). *Anal.* Calcd. for $C_{12}H_{21}O_3N$: C, 63.41; H, 9.31; N, 6.16. Found: C, 63.71; H, 9.29; N, 6.27. NMR τ: 6.68 (3H, s, -OCH_3).

2-(4-Methoxy-2-piperidyl)-2-hydroxycyclohexanone(XIb)——A solution of the ketal(VIb, 1.0 g) in 20% HCl (15 ml) was treated by the same manner as for XIa. The crude product (820 mg) was chromatographed on silica gel (10 g) using $CHCl_3$ as a eluent to afford 650 mg (79%) of the ketone(XIb) as a viscous colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3380, 3240 (OH, NH), 1703 (CO). The picrolonate of XIb, mp 190° (from EtOH). *Anal.* Calcd. for $C_{22}H_{29}O_8N_5$: C, 53.76; H, 5.95; N, 14.25. Found: C, 53.91; H, 5.99; N, 13.76.

2-Oxo-1,2,3-oxathiazolidines——a) XIIa: To a stirred solution of thionyl chloride (1.0 ml) in dry pyridine (4 ml) was added a solution of the β-amino-alcohol (VIa, 0.30 g) in dry pyridine (4 ml) dropwise under ice–water cooling. After stirring for 5 hr under cooling, the reaction mixture was poured into ice–water. The resulting mixture was extracted with $CHCl_3$ (20 ml × 3) and the combined $CHCl_3$ extracts were washed with water, 10% HCl and water. Evaporation of the dried extract gave an oily residue (315 mg), which was chromatographed on silica gel (5 g). Elution with $CHCl_3$ afforded a solid, which was recrystallized from *n*-hexane to give 230 mg (66%) of XIIa as colorless needles, mp 95—96°. IR ν_{max}^{KBr} cm^{-1}: 1180 (SO). *Anal.* Calcd. for $C_{14}H_{23}O_5NS$: C, 52.99; H, 7.31; N, 4.41. Found: C, 53.19; H, 7.11; N, 4.38. Mass Spectrum *m/e*: 317 (M^+), 161, 114. NMR τ: 6.3—5.7 (4H, m, -$OC\underline{H}_2C\underline{H}_2O$-), 6.60 (3H, s, -$OC\underline{H}_3$).

b) XIIb: The β-amino-alcohol (VIb, 0.30 g) was treated according to the method in the reaction of VIa with thionyl chloride-pyridine to give 214 mg (61%) of the 2-oxo-1,2,3-oxathiazolidine (XIIb) as colorless plates, mp 117—118°. IR ν_{max}^{KBr} cm^{-1}: 1170 (SO). *Anal.* Calcd. for $C_{14}H_{23}O_5NS$: C, 52.99; H, 7.31; N, 4.41. Found: C, 52.84; H, 7.33; N, 4.40. Mass Spectrum *m/e*: 317 (M^+), 161, 114. NMR τ: 6.15—5.90 (4H, m, -$OC\underline{H}_2C\underline{H}_2O$-), 6.60 (3H, s, -$OC\underline{H}_3$).

c) XIIIa: The β-amino-alcohol (XIa, 420 mg) was treated according to the method in the reaction of VIa with thionyl chloride–pyridine to give 350 mg (69%) of the 2-oxo-1,2,3-oxathiazolidine(XIIIa) as colorless fine needles, mp 129—131°. IR ν_{max}^{KBr} cm^{-1}: 1725 (CO), 1180 (SO). *Anal.* Calcd. for $C_{12}H_{19}O_4NS$: C, 52.74; H, 7.01; N, 5.13. Found: C, 53.02; H, 6.92; N, 5.30. NMR τ: 6.66 (3H, s, -$OC\underline{H}_3$). Mass Spectrum *m/e*: 273 (M^+), 161, 114.

d) XIIIb: The β-amino-alcohol (XIb, 310 mg) was treated according to the method in the reaction of VIa with thionyl chloride–pyridine to give 210 mg (55%) of the 2-oxo-1,2,3-oxathiazolidine(XIIIb) as colorless needles, mp 75—76°. IR ν_{max}^{KBr} cm^{-1}: 1732 (CO), 1188 (SO). *Anal.* Calcd. for $C_{12}H_{19}O_4NS$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.66; H, 6.96; N, 4.99. NMR τ: 6.63 (3H, s, -$OC\underline{H}_3$), 6.05 (1H, d of d, J=4 and 13 cps, $C_{2'}$-H). Mass Spectrum *m/e*: 273 (M^+), 161. 114.

2-(4-Methyl-2-pyridyl)-2-hydroxycyclohexanone(XIV)——A solution of the ketal (V, 0.50 g) in 10% HCl (10 ml) was heated at 60° for 4 hr. After cooling, the reaction mixture was made alkaline with aqueous NaOH under cooling. The resulting mixture was extracted with $CHCl_3$ and the $CHCl_3$ extract was washed with water and dried. Evaporation of the solvent gave an oily residue (475 mg), which was chromatographed on silica gel. Elution with $CHCl_3$ afforded 358 mg (91%) of the ketone(XIV) as a solid, which was recrystallized from petr. ether to give colorless prisms, mp 84—85°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710 (CO), 1600 and 1570 (pyridine ring). *Anal.* Calcd. for $C_{12}H_{15}O_3N$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.26; H, 7.02; N, 6.45.

1-(4-Methoxy-2-pyridyl)cyclohexane-1,2-diol(XV)——To a stirred solution of the ketone(XIV, 175 mg) in MeOH (10 ml) was added $NaBH_4$ (25 mg) portionwise and stirring was continued for 1.5 hr at room temperature. After addition of water (20 ml), the resulting mixture was extracted with $CHCl_3$. Evaporation of the dried extract gave 169 mg (96%) of the diol (XV) as a solid, which was recrystallized from *n*-hexane to give colorless plates, mp 90—91°. IR ν_{max}^{KBr} cm^{-1}: 3225 (OH, NH). *Anal.* Calcd. for $C_{12}H_{17}O_3N$: C, 64.55; H, 7.68; N, 6.27. Found: C, 64.81; H, 7.55; N, 6.14.

1-(4-Methoxy-2-piperidyl)cyclohexane-1,2-diol(XVI)——The pyridine (XV, 1.03 g) was hydrogenated in EtOH (30 ml) over 5% Rh-Al_2O_3 (1.5 g) at 80° and 100 atm for 9 hr. The catalyst was filtered off and the filtrate was concentrated to dryness *in vacuo* to give 1.12 g (quantitative yield) of the piperidine (XVI) as a solid, which was used to the next step without further purification. A sample for analysis was obtained by recrystallization from *n*-hexane–C_6H_6, mp 150—152°, as colorless crystals. IR ν_{max}^{KBr} cm^{-1}: 3225 (OH, NH). *Anal.* Calcd. for $C_{12}H_{23}O_3N$: C, 62.85; H, 10.11; N, 6.11. Found: C, 62.95; H, 9.97; N, 6.09.

Oxidation of XVI with Jones Reagent——To a stirred solution of the diol (XVI, 720 mg) in purified acetone (15 ml) was added dropwise 2 ml of standard chromic acid reagent[17] under ice–water cooling. After 30 min, MeOH was added to the reaction mixture to decompose excess oxidant and the mixture was diluted with water, made alkaline with K_2CO_3 and extracted with $CHCl_3$. The extract was washed with water and dried. Evaporation of the solvent gave an oily residue (490 mg), which was chromatographed on silica gel (10 g). Elution with 3% EtOH–$CHCl_3$ afforded 150 mg (21%) of the ketone(XIb) as a colorless oil. Elution with 5% EtOH–$CHCl_3$ afforded 280 mg (38%) of the ketone(XIa) as a solid, which was recrystallized from *n*-hexane to give colorless leaflets, mp 114—115°. The products (XIa and XIb) were identical with the samples obtained from VIa and VIb, respectively in comparison with TLC, IR and mp.

17) A. Bowers, T.G. Halsall, E.R.H. Jones, and A.J. Lemin, *J. Chem. Soc.*, **1953**, 2548.