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Isoquinolines. I. Preparation and Stereochemistry of 9,10-Epoxy-1-(*p*-methoxybenzyl)-2-methyldecahydroisoquinolines

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Epoxidation of 1-(*p*-methoxybenzyl)-2-methyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (**7**) affords the two isomeric epoxides (**14** and **15**). Chemical evidence shows that performic acid exclusively attacks from the *cis*-side to the 1-substituent. The competitive reactions of **14** and **15** are qualitatively examined by gas chromatographic and thin-layer chromatographic analyses.

With the view of testing the pharmacological activities, attempts to synthesize 14-hydroxymorphinans have been carried out in our laboratory. Schnider, *et al.*[2] reported the synthesis of N-methylmorphinan (**2**) *via* the acid-catalyzed cyclization of 1-benzyl-2-methyl-1,2,3,4,-5,6,7,8-octahydroisoquinoline (**1**). This is the intramolecular Friedel-Crafts reaction. If the 9,10-epoxide of **1** is cyclized in the same manner, the 14-hydroxy derivative (**3**) will be expected. We have carried out a preparation of 9,10-epoxy-1-(*p*-methoxybenzyl)-2-methyldecahydroisoquinoline as a key compound.

1-(*p*-Methoxybenzyl)-2-methyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (**7**) was prepared from the amide (**4**) *via* several steps.[3] On epoxidation with performic acid, **7** afforded a mixture of the two epoxides (**14** and **15**) and the two diols (**16** and **17**).[4] The compounds (**14** and **15**) were hydrolyzed with 10% sulfuric acid to give **16** and **17**, respectively, in a nearly quantitative yield.

Treatments of **14** and **15** with potassium acetate in a acetic acid gave the diol monoacetates (**26** and **27**), respectively. The compounds (**26** and **27**) were converted into **16** and **17**, respectively, by hydrolyses with the Claisen's alkali. These facts reveal that the epoxides (**14** and **15**) undergo hydrolyses and acetolyses at the same position. Since it is generally well known that epoxide rings in cyclohexane system are opened to give a *trans* diaxially substituted product, the diols (**16** and **17**) and the diol monoacetates (**26** and **27**) are considered to contain the *trans* ring juncture. As recorded in Table I, **26** and **27** exhibit the intramolecular hydrogen bondings in their infrared (IR) spectra. The *trans* ring juncture with the 9-OH groups in these compounds can explain the existence of the intramolecular hydrogen bondings. Conclusively, the epoxides (**14** and **15**) undergo the regiospecific ring opening at C-10, and **16** and **17** therefore are the *trans*-9,10-diols.

The lithium aluminum hydride (LAH) reductions of **14** and **15** gave the alcohols (**29** and **30**), respectively, whose IR spectra showed the intramolecular hydrogen bondings at 3465 and 3525 cm^{-1}. This, also, shows that **14** and **15** are regiospecifically attacked by LAH at C-10 to give the *trans*-alcohols.

The observed nucleophilic attacks at C-10 remote from the substituents in **14** and **15** are consistent with the facts that 9,10-epoxy-2-methyldecahydroisoquinoline underwent

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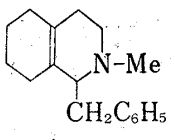
2) O. Schnider and A. Grussner, *Helv. Chim. Acta*, 32, 821 (1949).
3) O. Schnider and J. Hellerbach, *Helv. Chim. Acta*, 33, 1437 (1950).
4) The corresponded N-oxides must be afforded. However, we could not isolate these compounds.

nucleophilic attack at C-10[5] and 3-substituted *cis*- and *trans*-1,2-epoxycyclohexanes were attacked by nucleophiles at C-1.[6]



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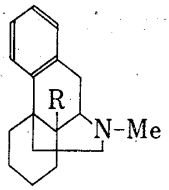
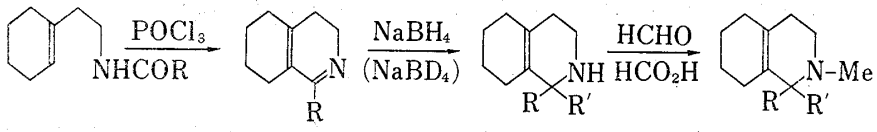
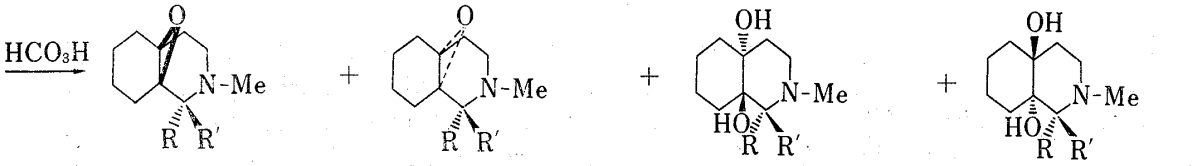


2 : R=H
3 : R=OH



4 : R=$ArCH_2$ 5 : R=$ArCH_2$ 6 : R=$ArCH_2$, R'=H 7 : R=$ArCH_2$, R'=H
10 : R=Me 11 : R=Me 8 : R=$ArCH_2$, R'=D 9 : R=$ArCH_2$, R'=D
12 : R=Me, R'=H 13 : R=Me, R'=H



14 : R=$ArCH_2$, R'=H 15 : R=$ArCH_2$, R'=H 16 : R=$ArCH_2$, R'=H 17 : R=$ArCH_2$, R'=H
18 : R=$ArCH_2$, R'=D 19 : R=$ArCH_2$, R'=D 20 : R=$ArCH_2$, R'=D 21 : R=$ArCH_2$, R'=D
22 : R=Me, R'=H 23 : R=Me, R'=H 24 : R=Me, R'=H 25 : R=Me, R'=H

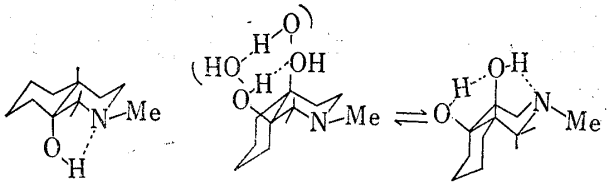
26 : R=AcO, R'=H 27 : R=AcO, R'=H Ar=*p*-$MeOC_6H_4$-
29 : R=R'=H 28 : R=AcO, R'=D
31 : R=H, R'=D 30 : R=R'=H
32 : R=H, R'=D

Chart 1

The nuclear magnetic resonance (NMR) spectra of the diols and the alcohols are recorded in Table II. Assignments of the 1-H and the $ArCH_2$[7] were ascertained by comparison of the NMR spectra of the corresponded 1-deuterio compounds derived from the 1-deuterioisoquinoline (**9**). Inspection of the NMR spectra of **17** and **30** shows that replacement of the hydrogen atom with the hydroxyl group at C-10 results in the shift of 1-H to a lower field by 0.7 ppm and approximately no change in the chemical shift of $ArCH_2$. This means that the $ArCH_2$ groups in **17** and **30** are equatorial. That the differences in the chemical shifts of $ArCH_2$ between **16** and **29** are 0.27 and 0.54 ppm, respectively, and the chemical shifts of 1-H in the two compounds remain approximately unchanged shows that the $ArCH_2$ groups in **16** and **29** are axial. On the basis of the structures of these compounds and the above chemical evidence, it is concluded that **14** is the *trans*-epoxide and **15** is the *cis*-epoxide.[8]

5) C.A. Grob and R.A. Wohl, *Helv. Chim. Acta*, **49**, 2175 (1966).
6) R.A.B. Bannard, A.A. Casselmann, E.J. Langstaff, and R.Y. Moir, *Can. J. Chem.*, **46**, 35 (1968); *idem*, *ibid.*, **45**, 1007 (1967).
7) Ar: *p*-$MeOC_6H_4$-.
8) *cis* and *trans* are referred to the steric relation of the 1-$ArCH_2$ group and the oxirane group.

TABLE I. The Intramolecular Hydrogen Bonding[a)]



	ν_f	ν_b		ν_f	ν_b
16	3614	3438	**17**	3616	3493
26	(3610)[b)]	3425	**27**	(3610)[b)]	3425
29	(3613)[b)]	3465	**30**	(3615)[b)]	3525
39	(3614)[b)]	3434	**40**		3490

a) 1.2×10^{-3} mole/liter (CCl_4); cm^{-1} *b*) weak band
ν_b: bonded hydroxyl band ν_f: free hydroxyl band

TABLE II. The NMR Spectra of *trans*-Diols and *trans*-Alcohols

	1-H	$ArCH_2$	
16	2.82 t J=4	3.13 q J=16 and 4	3.02 q J=16 and 4
17	2.77 t J=4	3.06 q J=16 and 4	2.54 q J=16 and 4
29	2.75 t J=4	2.86 q J=16 and 4	2.48 q J=16 and 4
30	2.07 m	3.13 q J=16 and 3	2.52 q J=16 and 5

On epoxidation with performic acid and subsequent hydrolysis, **7** gave a mixture of **16** and **17**, whose gas chromatography (GLC) showed the ratio of **16** and **17** to be approximately 1:15. The observed predominant formation of the *cis*-epoxide is of particular interest.

The spirano-form transition state for epoxidation with peracids appears to be generally accepted.[9)] Since the 2-Me group in **7** is considered to be equatorial in both the stable conformer (**33**) and another unstable conformer with the axial $ArCH_2$ group, preference for the *cis*-attack over the *trans*-attack by performic acid is unaffected by the 2-Me group remote from the reaction site.[10)] Inglis[11)] has investigated the epoxidation of 3-alkylcyclohexenes. When the alkyl group is methyl, the ratio of *cis*- and *trans*-epoxide is approximately 1:1. However, increasing the steric bulk of the alkyl group causes the exclusive formation of *trans*-epoxides owing to steric effects in the transition state. Epoxidation of 1,2-dimethyl-1,2,3,-4,5,6,7,8-octahydroisoquinoline (**13**), which was derived from the amide (**10**), afforded a mixture of the epoxides (**22** and **23**) and the diols (**24** and **25**), whose hydrolysis with 10% sulfuric acid gave a mixture of the diols (**24** and **25**) in approximately equal amounts. Since the ring openings in **22** and **23**, also, can be considered to occur regiospecifically at C-10 on the basis of the results of hydrolyses of the epoxides (**14** and **15**) and 9,10-epoxy-2-methyldecahydroisoquinoline,[5)] it is clear that, in this case, the *cis*- and *trans*-attack by performic acid are comparable. This result is in agreement with that of 3-methylcyclohexene[11)] and means that the amino group in the isoquinoline ring does not particularly participate in the formations of the epoxides. The interpretation of the result obtained with **7** is very difficult, al-

9) D.N. Kirk and M.P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier Publishing Company, Amsterdam 1968, p. 71.
10) B. Rickborn and S.-Y. Lwo, *J. Org. Chem.*, **30**, 2212 (1965); F. Marioni and A. Marsili, *Tetrahedron*, **28**, 3393 (1972).
11) D.B. Inglis, *Chem. Ind.* (London), **1971**, 1268.

though a particular role of the $ArCH_2$ group in the transition state would be suggested. The transition state (**34**) for **15** would proceed through **33**. The intramolecular hydrogen bonding depicted in the formula may depress the activation energy for **34**, leading to the predominant formation of **15** (Chart 2).

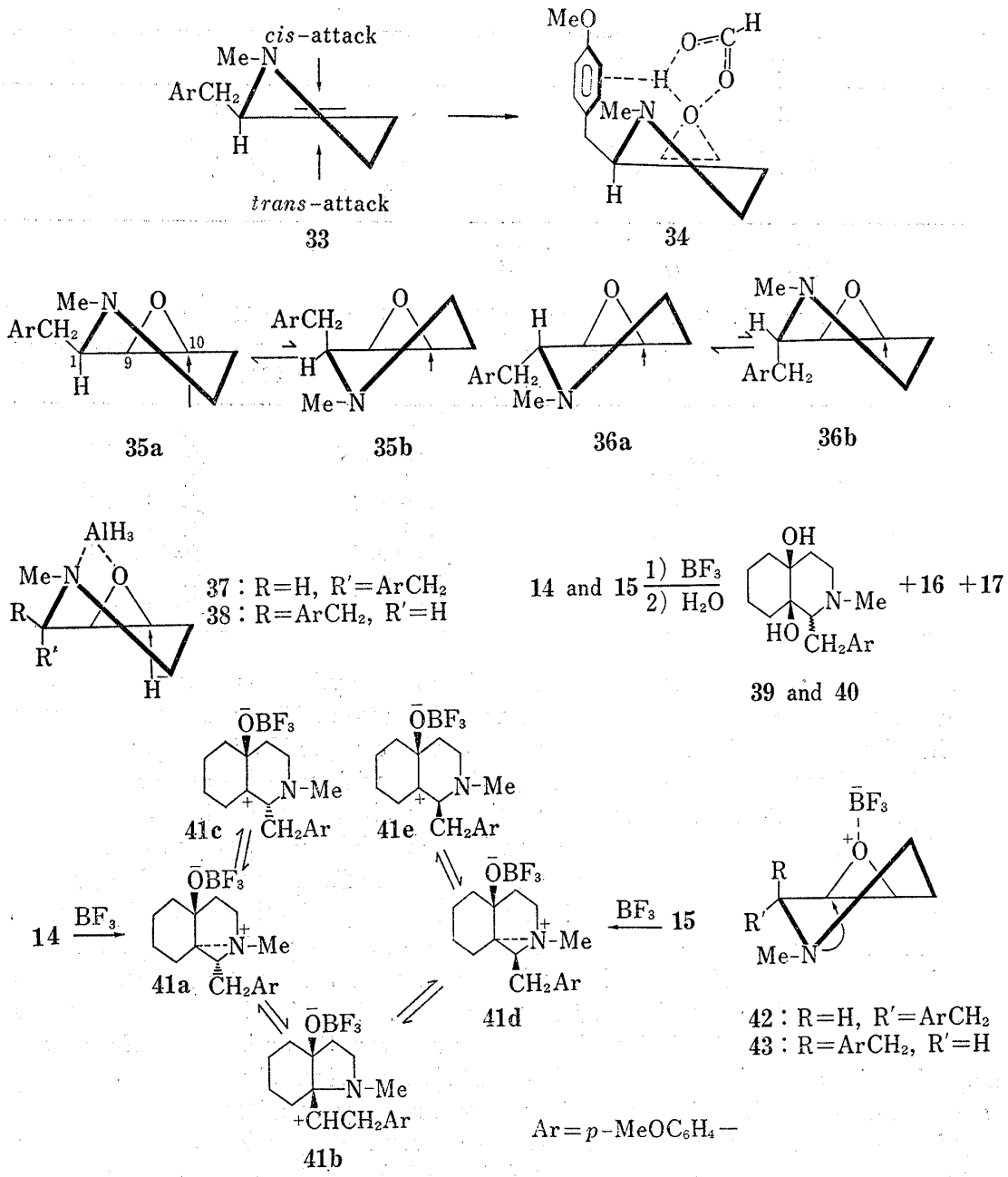


Chart 2

It seems worthwhile to examine qualitatively competitive reactions of **14** and **15**. When a mixture of **14** and **15** was hydrolyzed with 15% perchloric acid at room temperature, **15** reacted more quickly than **14**. Treatment of a mixture of **14** and **15** with potassium acetate in acetic acid at 55°, also, gave the same result. The compound (**15**) in its preferred conformer (**35a**) can readily open by nucleophilic attack at C-10 to give the compounds with the diaxial substituents. Attack at C-10 in **14** is disfavored by the facts that the diaxial ring opening in a conformer (**36a**) gives a quasi-boat product and the axial $ArCH_2$ group in another conformer (**36b**) sterically repulses approaching nucleophile.

On the LAH reduction of a mixture of **14** and **15**, conversely, **14** was reduced faster than **15**. Regiospecific reduction of the epoxides may mainly proceed through the aluminate transition states (**37** and **38**).[12] The transition state (**38**) contains the steric strain due to the aluminate group and the $ArCH_2$ group. Another one (**37**), insteadly, contains the steric strain due to the axial $ArCH_2$ group and the steric repulsion of the axial $ArCH_2$ group with the hydride ion. Difference in the steric factors between **37** and **38** may control over the reaction rates of **14** and **15**. Since the hydride ion is small in bulk, the steric repulsion concerned with it in **37** would not significantly influence upon the reaction rate of **14**. The steric strain in **37** would be less than that in **38** and consequently, this may be responsible for the faster reduction of **14**.

In order to obtain the 14-hydroxymorphinan derivative the epoxides (**14** and **15**) were treated with a Lewis acid, boron trifluoride, in inert solvents. A mixture of **14** and **15** gave, on the contrary to expectation, a mixture of the two *cis*-diols (**39** and **40**) and the two *trans*-diols (**16** and **17**). Competitive reaction of a mixture of **14** and **15** with boron trifluoride showed that **14** reacted more quickly than **15**. The ratio of the above four diols, which was obtained when **14** disappeared on the thin-layer chromatography (TLC), was approximately the same as that obtained when **15** disappeared on the TLC. This fact suggests that **14** and **15** give a mixture of **16**, **17**, **39**, and **40** in approximately same ratio, respectively. If reactions proceed through the same intermediates (**41**), in which the configurations at C-1 and C-9 are scrambled by equilibration, the above results can be reasonably accepted. The intermediates (**41a**) and (**41d**) may be derived from the conformer (**42**) in **14** and the conformer (**43**) in **15**, respectively, by the anchimeric assistance of nitrogen. The more stable conformer (**42**) compared to the conformer (**43**) would be able to explain that on treatment with boron trifluoride **14** reacted more quickly than **15**. We could not find the experimental data available for assignment of the configurations of the *cis*-diols.

Finally, we would like briefly to comment on the mass spectra of the above compounds. The fragmentation patterns are very simple and the base peaks, in common, due to the $(M-C_8H_9O)^+$ ion. The compounds (**17**, **27**, and **30**), whose structures have the *trans* ring juncture and the 9-OH group *trans* to the 1-H, show the peaks due to the $(M-H)^+$ ions more intense than the molecular ions.

Experimental

Melting points were determined on a micro hot-stage and were uncorrected. IR spectra were taken on a JASCO IR-G and intramolecular hydrogen bondings were measured with a JASCO DS-403G. NMR spectra were measured in $CDCl_3$ with a Varian HA-100 and a JEOL's JNM-4H-100. Mass spectra were taken on a JEOL's JMS-01SG by high resolution techniques. GLC was carried out with a Shimadzu Model GC-3AF. A glass column of 200 cm × 4 mm was packed with 1.5% OV-17 on Shimalite W (80—100 meshes). The operating conditions were as follows: sensitivity, 1000; range, 1.6. TLC was carried out on silica gel plates (0.25 mm) by using acetone–benzene (1:1).

1-(*p*-Methoxybenzyl)-2-methyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (**7**)——A solution of the amide (**4**) (5.0 g) and $POCl_3$ (6 g) in dry benzene (20 ml) was refluxed for 3 hr. After work-up, there was obtained the hexahydro compound (**5**) (4.0 g) as a syrup which gave the octahydro compound (**6**) (3.7 g) as a syrup by reduction with $NaBH_4$ (2.0 g) in methanol (70 ml). A mixture of **6** (2.1 g) and 37% HCHO (1.4 ml) in formic acid (2 ml) was heated at 70° for 30 min. After work-up, there was isolated **7** (2.0 g) as a syrup which gave the oxalate (1.9 g) of mp 163—164°.

1-Deuterio-1-(*p*-methoxybenzyl)-2-methyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (**9**)——To a solution of **5** (1.7 g) in methanol (20 ml) was added $NaBD_4$ (900 mg) in a small portion with cooling. After refluxing for 2 hr and removal of methanol, the residue was extracted with benzene. The benzene layer gave **8** (1.1 g) as a syrup. The compound (**8**) was treated by the same procedure as above and afforded the oxalate (500 mg) of **9**, mp 163—164°.

12) T.W. Craig, G.R. Harvey, and G.A. Berchtold, *J. Org. Chem.*, 32, 3743 (1967); B. Cooke, E.C. Ashby, and J. Lott, *ibid.*, 33, 1132 (1968); E.C. Ashby and B. Cooke, *J. Am. Chem. Soc.*, **90**, 1625 (1968).

1,2-Dimethyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (13)——The above procedure were carried out with the amide (**10**). There were obtained **11**, **12**, and **13** in 89%, 93%, and 76% yield, respectively. These compounds were syrupy. The **13**-picrate: yellow plates, mp 140—141°. *Anal.* Calcd. for $C_{18}H_{22}O_7N_4$: C, 51.78; H, 5.58; N, 14.21. Found: C, 51.45; H, 5.58; N, 14.11.

Epoxidation of 7——a) To a solution of the **7**-oxalate (1.8 g) in 99% formic acid (12 ml) was added dropwise 30% H_2O_2 (1.6 ml) at 30° with stirring and stirring was continued for 4 hr at 40°. The reaction mixture was made alkaline with 20% aq. KOH and then ethanol was added to obtain a clear solution. After refluxing for 30 min and removal of ethanol, the residue was extracted with ether. The ether residue (1.0 g) was chromatographed over neutral Al_2O_3 (Grade III) (100 g). The first fraction of *n*-hexane–benzene (1: 2) afforded the epoxide (**14**) (17 mg) as a syrup. NMR: δ 2.88 (1-H and $ArCH_2$), 2.72—2.49 (3-H_2), 2.32 s (N-Me). The picrate: yellow plates, mp 179—180° (from methanol). *Anal.* Calcd. for $C_{24}H_{28}O_9N_4$: C, 55.81; H, 5.46; N, 10.85. Found: C, 55.64; H, 5.36; N, 10.92. The second gave a mixture of the epoxides (**14** and **15**) (270 mg). The third afforded **15** (170 mg) as a syrup. NMR: δ −2.77 (1-H), −2.81 ($ArCH_2$), 2.95—2.66 (3-H_2), 2.34 s (N-Me). The picrate: yellow plates, mp 143—145° (from ethanol). *Anal.* Calcd. for $C_{24}H_{28}O_9N_4$: C, 55.81; H, 5.46; N, 10.85. Found: C, 55.68; H, 5.46; N, 10.90. The fraction of benzene–ethyl acetate (9: 1) gave the *trans*-diol (**16**) (23 mg) as colorless needles of mp 168—169° (from *n*-hexane–benzene). NMR: δ 2.90 dq (J=13.5, and 3)(3-He), 2.36 m (3-Ha), 2.23 s (N-Me). *Anal.* Calcd. for $C_{18}H_{27}O_3N$: C, 70.79; H, 8.90; N, 4.59. Found: C, 70.56; H, 8.84; N, 4.52. Mass Spectrum Calcd. for $C_{18}H_{27}O_3N$: mol. wt., 305.1990. Found: M^+, 305.1966. The subsequent fraction gave the *trans*-diol (**17**) (252 mg) as colorless plates of mp 132—134° (from *n*-hexane). NMR: δ 2.82—2.54 (3-H_2), 2.26 s (N-Me). *Anal.* Calcd. for $C_{18}H_{27}O_3N$: C, 70.79; H, 8.90; N, 4.59. Found: C, 70.65; H, 8.76; N, 4.51. Mass Spectrum Calcd. for $C_{18}H_{26}O_3N$: mol. wt., 304.1912. Found: $(M-H)^+$, 304.1895.

b) The oxalate (300 mg) was treated with 30% H_2O_2 (0.5 ml) and 99% formic acid (4 ml). There was obtained a mixture (150 mg) of **14**, **15**, **16**, and **17** in an approximate ratio of 1: 21: 1: 8.5 (GLC; column temperature, 170°). The subsequent hydrolysis of this mixture with 10% H_2SO_4 gave a mixture (112 mg) of **16** and **17** in an approximate ratio of 1: 15 (GLC; column temperature, 200°).

Epoxidation of 9——The **9**-oxalate (500 mg) was treated with 30% H_2O_2 (0.5 ml) and 99% formic acid (4 ml). The reaction mixture was worked-up by the above procedure to afford **18** (5 mg), **19** (62 mg), and a mixture of **20** and **21** (21 mg).

Epoxidation of 13——a) Five hundred mg of **13** was treated with 30% H_2O_2 (1.1 ml) and 99% formic acid (8 ml). The reaction mixture was treated by the above procedure. There were obtained the epoxides (**22** and **23**) (150 mg) as a syrup, whose picrate was yellow granules of mp 177—178° (from ethanol) and the *trans*-diols (**24** and **25**) (250 mg) as colorless prisms of mp 94—96° (from *n*-hexane), whose picrate was yellow granules of mp 235—236° (from ethanol). The picrates of **22** and **23**: *Anal.* Calcd. for $C_{17}H_{22}O_8N$: C, 49.75; H, 5.40; N, 13.65. Found: C, 49.68; H, 5.48; N, 13.65. The compounds (**24** and **25**): *Anal.* Calcd. for $C_{11}H_{21}O_2N$: C, 66.29; H, 10.62; N, 7.03. Found: C, 66.35; H, 10.66; N, 7.08. The picrates of **24** and **25**; *Anal.* Calcd. for $C_{17}H_{24}O_9N_4$: C, 47.80; H, 5.51; N, 12.86. Found: C, 47.66; H, 5.64; N, 13.08.

b) Five hundred mg of **13** was treated with 30% H_2O_2 (1.1 ml) and 99% formic acid (8 ml). There was obtained a syrup (280 mg), whose subsequent hydrolysis with 10% H_2SO_4 gave a mixture of **24** and **25** in an approximate ratio of 1: 1.2 (GLC; column temperature, 105°).

Hydrolyses of the Epoxides (14 and 18)——a) A solution of **14** (10 mg) in 10% H_2SO_4 (0.5 ml) was heated at 60° for 8 hr until **14** disappeared on TLC. The reaction mixture was made alkaline with 10% aq. NaOH and extracted with ether, giving **16** (8 mg) as colorless needles of mp 168—169°.

b) The compound (**18**) afforded **20** as colorless needles of mp 168—169° in a nearly quantitative yield by the above procedure.

Hydrolyses of the Epoxides (15 and 19)——a) A solution of **15** (47 mg) in 10% H_2SO_4 (2.5 ml) was heated at 60° for 4 hr until **15** disappeared on TLC. Work-up gave **17** (40 mg) as colorless plates of mp 132—134°.

b) The compound (**19**) afforded **21** as colorless plates of mp 132—134° in a nearly quantitative yield by the above procedure.

Acetolysis of 14——A mixture of **14** (150 mg) and AcOK (350 mg) in acetic acid (5 ml) was refluxed for 12 hr. The reaction mixture was made alkaline and extracted with ether. The ether residue was chromatographed over silica gel (10 g) by using benzene–ethyl acetate (1: 1) as eluent to give the diol monoacetate (**26**) (33 mg) as a syrup, which quantitatively gave **16** by treatment with the Claisen's alkali. IR ($CHCl_3$): 1725 cm^{-1} (AcO). NMR: δ −2.95 (1-H and $ArCH_2$), 2.82 m (3-He), 2.40 m (3-Ha), 2.17 s (N-Me), 2.08 s (10-OAc). Mass Spectrum Calcd. for $C_{20}H_{29}O_4H$: mol. wt., 347.2096. Found: M^+, 347.2074.

Acetolyses of the Epoxides (15 and 19)——a) A mixture of **15** (131 mg) and AcOK (300 mg) in acetic acid (4 ml) was refluxed for 7 hr. Work-up as above gave the diol monoacetate (**27**) (22 mg) as a syrup which quantitatively gave **17** by treatment with the Claisen's alkali. IR ($CHCl_3$): 1720 cm^{-1} (AcO). NMR: δ 2.60 t (J=3) (1-H), 3.03 q (J=16 and 3), 2.53 q (J=16 and 3) ($ArCH_2$), 2.80—2.48 (3-H_2), 2.21 s (N-Me), 2.04 s (10-OAc). Mass Spectrum Calcd. for $C_{20}H_{28}O_4N$: mol. wt., 346.2018. Found: $(M-H)^+$, 346.2037.

b) **19** (140 mg) gave **28** (26 mg) by the above procedure.

Reductions of the Epoxides (14 and 18)——a) To a solution of $LiAlH_4$ (14 mg) in dry ether (0.3 ml) was added dropwise a solution of **14** (72 mg) in dry ether (2 ml) and refluxing was continued for 2 hr. After

work-up, there was obtained the alcohol (**29**) (56 mg) as a syrup. NMR: δ 2.75—2.35 (3-H_2), 2.26 s (N-Me). Mass Spectrum Calcd. for $C_{18}H_{27}O_2N$: mol. wt., 289.2041. Found: M^+, 289.2087. The methiodide: colorless plates, mp 224—225° (from ethyl acetate–methanol). *Anal.* Calcd. for $C_{19}H_{30}O_2NI$: C, 52.93; H, 7.01; N, 3.25. Found: C, 53.22; H, 6.94; N, 3.32.

b) **18** (67 mg) gave **31** (51 mg) by the above procedure with $LiAlD_4$ (14 mg).

Reductions of the Epoxides (15 and 19)——a) To a solution of $LiAlH_4$ (150 mg) in dry tetrahydrofuran (10 ml) was added dropwise a solution of **15** (108 mg) in dry tetrahydrofuran (5 ml) and refluxing was continued for 16 hr. Work-up gave a syrup, whose chromatography over neutral Al_2O_3 (Grade III) (10 g) by using benzene as eluent afforded the alcohol (**30**) (55 mg) as a syrup. NMR: δ 2.80 dq (J=11, 5, and 3) (3-He), 2.07 m (3-Ha), 2.20 s (N-Me). Mass Spectrum Calcd. for $C_{18}H_{26}O_2N$: mol. wt., 288.1935. Found: $(M-H)^+$, 288.1958. The methiodide: colorless plates, mp 271—272°. *Anal.* Calcd. for $C_{19}H_{30}O_2NI\cdot H_2O$: C, 50.78; H, 7.17; N, 3.12. Found: C, 50.75; H, 6.89; N, 3.13.

b) One hundred and seven mg of **19** gave **32** (53 mg) as a syrup by the above procedure with $LiAlD_4$ (150 mg).

Reaction of the Epoxides (14 and 15) with $BF_3\cdot OEt_2$——a) A solution of a mixture of **14** and **15** (1.0 g) and $BF_3\cdot OEt_2$ (1 ml) in dry benzene (20 ml) was allowed to stand at room temperature for 4 days. The reaction mixture was made alkaline with 10% aq. NaOH and the benzene layer was washed wih H_2O. The benzene residue (1.1 g) was chromatographed over neutral Al_2O_3 (Grade III) (100 g) by using benzene–ethyl acetate (9: 1) as eluent. The first fraction gave the *cis*-diol (**39**) (300 mg) as colorless plates of mp 83—84° (from *n*-hexane). NMR: δ –2.96 (1-H and $ArCH_2$), 2.80—2.40 (3-H_2), 2.28 s (N-Me). *Anal.* Calcd. for $C_{18}H_{27}O_3N$: C, 70.79; H, 8.90; N, 4.59. Found: C, 70.64; H, 8.84; N, 4.46. Mass Spectrum Calcd. for $C_{18}H_{27}O_3N$: mol. wt., 305.1990. Found: M^+, 305.1940. The second gave the unreacted **15** (120 mg). The third afforded the *cis*-diol (**40**) (360 mg) as colorless plates of mp 117—118° (from *n*-hexane). NMR: δ 3.08 q (J=14 and 3) (ArCH), 2.80—2.40 (1-H, ArCH, and 3-H_2), 2.26 s (N-Me). *Anal.* Calcd. for $C_{18}H_{27}O_3N$: C, 70.79; H, 8.90; N, 4.59. Found: C, 70.59; H, 8.59; N, 4.37. Mass Spectrum Calcd. for $C_{18}H_{27}O_3N$: mol. wt., 305.1990. Found: M^+, 305.1950. The picrate: yellow needles, mp 158—160°. *Anal.* Calcd. for $C_{24}H_{30}O_{10}N_4$: C, 53.93; H, 5.66; N, 10.48. Found: C, 53.82; H, 5.83; N, 10.24. The fourth afforded a mixture of **14** and **15** (80 mg).

b) A mixture of **14** (145 mg) and $BF_3\cdot OEt_2$ (0.1 ml) in dry chloroform (5 ml) was refluxed for 5 hr. The reaction mixture was treated by the above procedure. There were obtained **39** (5 mg), **40** (40 mg), and a mixture of the *trans*-diols (16 mg).

Competitive Reactions of the Epoxides (14 and 15)[13]——(1) Hydrolysis: A solution of a mixture of **14** and **15** (1: 4) (50 mg) in 15% $HClO_4$ (5 ml) was allowed to stand at room temperature. After 55 hr, **15** disappeared on TLC. **14** did not disappear within 70 hr.

(2) Acetolysis: A solution of a mixture of **14** and 15 (6: 1) (30 mg) and AcOK (90 mg) in acetic acid (3 ml) was kept at 55° for 60 hr. After work-up, there was obtained a syrup (24 mg), whose TLC was as follows: **14** (positive), **15** (negative), **26** (negative), **27** (positive).

(3) Reduction: A solution of $LiAlH_4$ (8 mg) in dry ether (4 ml) was added a solution of a mixture of **14** and **15** (6: 1) (30 mg) in dry ether (5 ml) and stirring was continued for 40 hr at room temperature. After work-up, there was obtained a syrup (18 mg), whose TLC was as follows: **14** (negative), **15** (positive), **29** (positive), **30** (negative).

(4) Reaction with $BF_3\cdot OEt_2$: a) A solution of a mixture of **14** and **15** (1: 4) (40 mg) and $BF_3\cdot OEt_2$ (8 drops) in dry benzene (6 ml) was allowed to stand at room temperature. **14** and **15** disappeared on TLC within 7 days and 16 days, respectively. After work-up, there was obtained a syrup (21 mg) which contained **39**, **40**, **16**, and **17** in an approximate ratio of 44: 65: 1: 9 (GLC; column temperature, 200°).

b) When the reaction was ceased after 7 days in the above case, the ratio of products was, also, almost the same as above.

13) These reactions were carried out in quantitative sense. The ratios of the epoxides were determined by GLC (column temperature, 170°).