The ultraviolet spectrum in Spectrograde hexane, obtained on a Cary Model 14 spectrophotometer, showed a peak at 215 mμ, ascribable to a conjugated nitrile.[24] The infrared spectrum showed an ether group[25a] at 9.15 (s), a nitrile group at 4.50 (w) (the weakness possibly being caused by the nearby ether group[25b]), and a conjugated C=N at 6.27 μ (m).[25c] The n.m.r. spectrum in deuteriochloroform showed only two peaks at τ 8.27 (s) and 8.35 (s), relative areas 1:1. From this information the compound is presumed to be 2,2,5,5-tetramethyl-4-cyano-Δ^3-oxazoline, perhaps formed as shown in Scheme III.

The cleavage of oximes to nitriles is well known.[26] Fragmentation[27] with loss of cyanide ion would be followed by Michael addition and a second Beckmann rearrangement to give a carbimonium ion which is finally trapped by cyanide ion.[27,28]

Acknowledgment.—The author is deeply indebted to Mrs. Janet Willoughby and Miss Helen Anderson for excellent technical assistance, to Mr. P. Baiocco for the n.m.r. spectra, to Professor C. S. Marvel, Dr. R. G. Beaman, Dr. D. R. Wilson, and Dr. R. A. Clement for helpful discussions, and to a referee for a suggestion about the reduction mechanism.

(24) M. St. C. Flett, "Physical Aids to the Organic Chemist," American Elsevier Publishing Co., New York, N. Y., 1962, p. 88.

(25) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed. John Wiley and Sons, Inc., New York, N. Y., 1958, (a) p. 118, (b) p. 266, (c) p. 263.

(26) L. G. Donaruma and W. Z. Held, *Org. Reactions*, **11**, 28 (1960).

(27) C. A. Grob, H. P. Fischer, H. Link, and E. Renk, *Helv. Chim. Acta*, **46**, 1190 (1963).

(28) (a) P. Oxley and W. F. Short, *J. Chem. Soc.*, 1514 (1948); (b) I. Ugi, F. Beck, and U. Fetzer, *Chem. Ber.*, **95**, 127 (1962).

The Mechanism and Stereochemistry of Formation and Cleavage of Epoxy Ethers. I[2,3]

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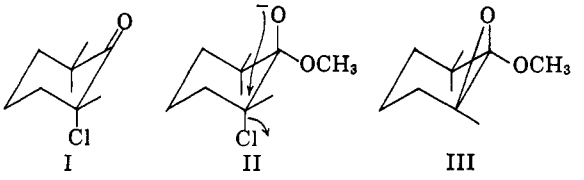
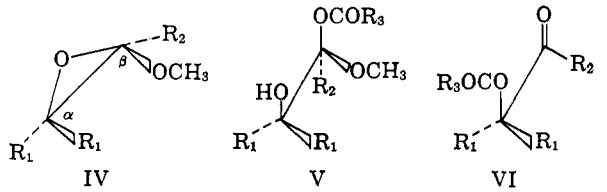
The optical activity of dextrorotatory and levorotatory epoxy ethers (XI) prepared from (−)-1-methyl-3-benzoyl-3-chloropiperidine (X) by treatment with sodium methoxide in xylene and methanol, respectively, is attributed to asymmetry at the ketal carbon and not at the carbon common to both rings. Both epoxides are regarded as mixtures. Ring opening with acids led, in both cases, to racemic 1-methyl-3-benzoyl-3-hydroxypiperidine (XII). The mechanisms of these transformations are discussed.

It was suggested by Stevens and Weinheimer[4] that ring closure of the α-halo ketone, I, to form the *cis*-epoxy ether, III, proceeds with inversion of configuration through II. Further, Stevens and Dykstra[5] have



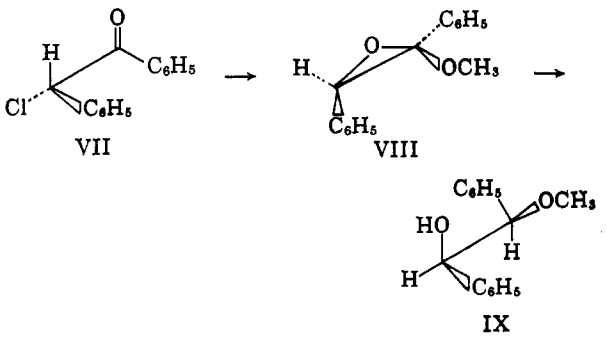
I II III

shown that acid-catalyzed cleavage of epoxy ethers, *e.g.*, IV → V → VI, involves O–β-C scission followed by O-to-O acyl migration. That epoxy ether formation and



IV V VI

cleavage are highly stereospecific processes is supported by the work of Stevens and Coffield.[6] They have reported that treatment of racemic chlorodesoxybenzoin (VII) with methanolic sodium methoxide affords only *one* of the diastereoisomeric 1,2-diphenyl-1-methoxyethylene oxides (VIII). Reduction of the latter with lithium borohydride gives chiefly (*ca.* 60:1) the *threo* monomethyl ether of hydrobenzoin (IX).



VII VIII IX

This sequence of reactions was of interest for the preparation of optically active 1-methyl-3-benzoyl-3-hydroxypiperidine (XII) of known configuration relative to (−)-X. However, while treatment of (−)-X with methanolic sodium methoxide gave a levorotatory, halogen-free oil (XI), subjection of this oil to acidolysis in aqueous acid afforded racemic α-hydroxy ketone (XII) as the only isolable product. When warmed with glacial acetic acid, the oil afforded an ester (XIII) which was hydrolyzed to racemic XII.

Earlier,[7] the synthesis of a dextrorotatory oil (XI) from (−)-X was effected with a slurry of methanol-free sodium methoxide in refluxing xylene. The synthesis was repeated. However, acidolysis of the epoxy ether again afforded only racemic XII.

Racemization was shown not to occur subsequent to formation of XIII and/or XII under the conditions

(1) Author to whom inquiries should be addressed at Columbia University.

(2) This investigation was supported by Public Health Service Research Grant B-3593 (Cl) from the Institute of Neurological Diseases and Blindness, NIH.

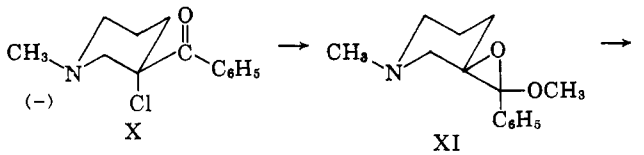
(3) Presented at the 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April, 1963.

(4) C. L. Stevens and A. J. Weinheimer, *J. Am. Chem. Soc.*, **80**, 4072 (1958).

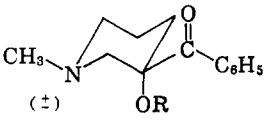
(5) C. L. Stevens and S. J. Dykstra, *ibid.*, **75**, 5975 (1953).

(6) C. L. Stevens and T. H. Coffield, *J. Org. Chem.*, **23**, 336 (1958).

(7) E. E. Smissman and G. Hite, *J. Am. Chem. Soc.*, **82**, 3375 (1960).



X XI (optically active)



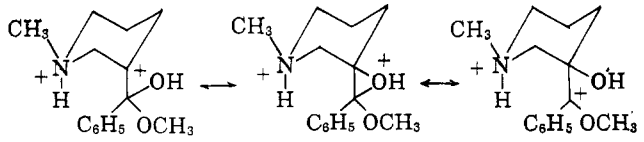
XII, R = H-
XIII, R = CH_3CO-
XIV, R = CH_3O-

used in the acidolyses. This was accomplished by conversion of (+)-XII to the corresponding dextrorotatory acetate (XIII) followed by hydrolysis with acid or base to regenerate α-hydroxy ketone (XII) with total retention of configuration.

That the optical activity of the oils assigned the structure XI was related to asymmetry in the epoxy ether and not to *traces* of the optically active, isomeric α-methoxy ketone (XIV) was demonstrated by following the optical course of the acidolysis. The rotatory power of a solution of the dextrorotatory oil in aqueous hydrochloric acid reached 0.00 ± 0.01° in 2 min. or less while, under identical conditions, the rotatory power of the α-methoxy ketone, (+)-XIV, prepared from (+)-XII by selective O-methylation with potassium *t*-butoxide and methyl *p*-toluenesulfonate, remained unchanged.

Accordingly, the isolation of racemic α-hydroxy ketone (XII) is a reflection of processes occuring during epoxy ether formation and/or cleavage.

Although the Stevens mechanism[4-6] for epoxy ether cleavage predicts retention of configuration at α-C, racemization of (−)-XI through a mesomeric ion such as XV is a possibility. However, under the influence of

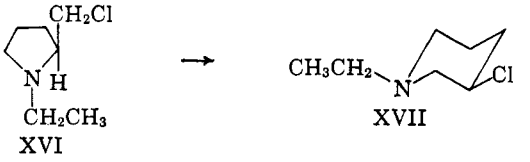


XV

acids, epoxides cleave chiefly by an SN2-cA mechanism.[8] This stereospecificity will undoubtedly be amplified by the cationoid character of the amine under the conditions employed for acidiolysis, since generation of a second positive center would be suppressed (*cf.* SN2-cA transition state).

Thus, if epoxy ether formation occurs with inversion (or retention) of configuration at α-C, the products (XII and XIII) would have been optically active. Since this rules out *total* racemization during epoxy ether cleavage, any degree of stereoselectivity or stereospecificity with respect to α-C, during epoxy ether formation, is untenable.

It is pertinent to the rationalization of the stereochemistry of the apparently anomalous epoxy ether formation that the large rate differential between α-halogenated amines and their nonnitrogenous analogs in solvolysis reactions has been attributed to the formation of internally solvolized carbonium ions.[9] Further, the exceptional facility of ring expansion of 1-ethyl-2-chloromethylpyrrolidine (XVI) to 1-ethyl-3-chloropiperidine (XVII), noted by Fuson and Zirkle,[10] also



XVI XVII

suggests that the stereochemistry of α-C formation of the epoxy ether (XI) is influenced by the anchimeric effect of the β-amino moiety in X.

It is proposed that asymmetric induction of the carbonyl carbon, by methoxide attack upon rotamers[7,11] (−)-Xa and (−)-Xb, is followed by or occurs concurrently with anchimeric ejection of the chloride atom to give XVIIIa and XVIIIb, respectively. The resulting planarity of α-C in the proposed transition states[12] (XVIIIa and b) requires that ring closure from above and below this plane will result in a 1:1 ratio (α-C symmetrization) of the two diastereoisomers, XIa and XIb (or XIc and XId) from XVIIIa (or XVIIIb) (Scheme I).

As product composition (XIa,b and c,d) is dependent upon the rates of reaction of the ground-state conformations, Xa and Xb, the ratio of the rates and, consequently, the ratio (XIa,b:XIc,d) depends only upon the relative free energies of the proposed transition states, XVIIIa and XVIIIb.[13] Accordingly, the dextrorotatory and the levorotatory epoxy ethers isolated from the methanol and the xylene reactions are undoubtedly equimolar mixtures of two diastereoisomers, partially racemic, the XIa,b couple predominating in one case and the XIc,d couple predominating in the other. This difference in asymmetric induction of α-C is considered to be a reflection of the effect of solvent on the free energies of formation of XVIIIa and XVIIIb. Thus, XVIIIa would be favored in polar solvents and XVIIIb in nonpolar solvents (or at the surface of molecular aggregates of the nucleophile), a not unprecedented conclusion.[14]

Although the chemistry of halopiperidines restricts generalization of the suggested mechanism for epoxy ether formation from α-halo ketones, it seems likely that epoxy ether (XI) cleavage results in retention of configuration.

(8) S. Winstein and R. B. Henderson in "Heterocyclic Compounds," Vol. 1, R. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 22-46.

(9) C. A. Grob and F. A. Jenny, *Tetrahedron Letters*, **No. 23**, 25 (1960). *Cf. Bull. soc. chim. France*, 1360 (1960); A. T. Bottini, C. A. Grob, and E. Schumacher, *Chem. Ind.* (London), 757 (1958).

(10) R. C. Fuson and C. L. Zirkle, *J. Am. Chem. Soc.*, **70**, 2760 (1948).

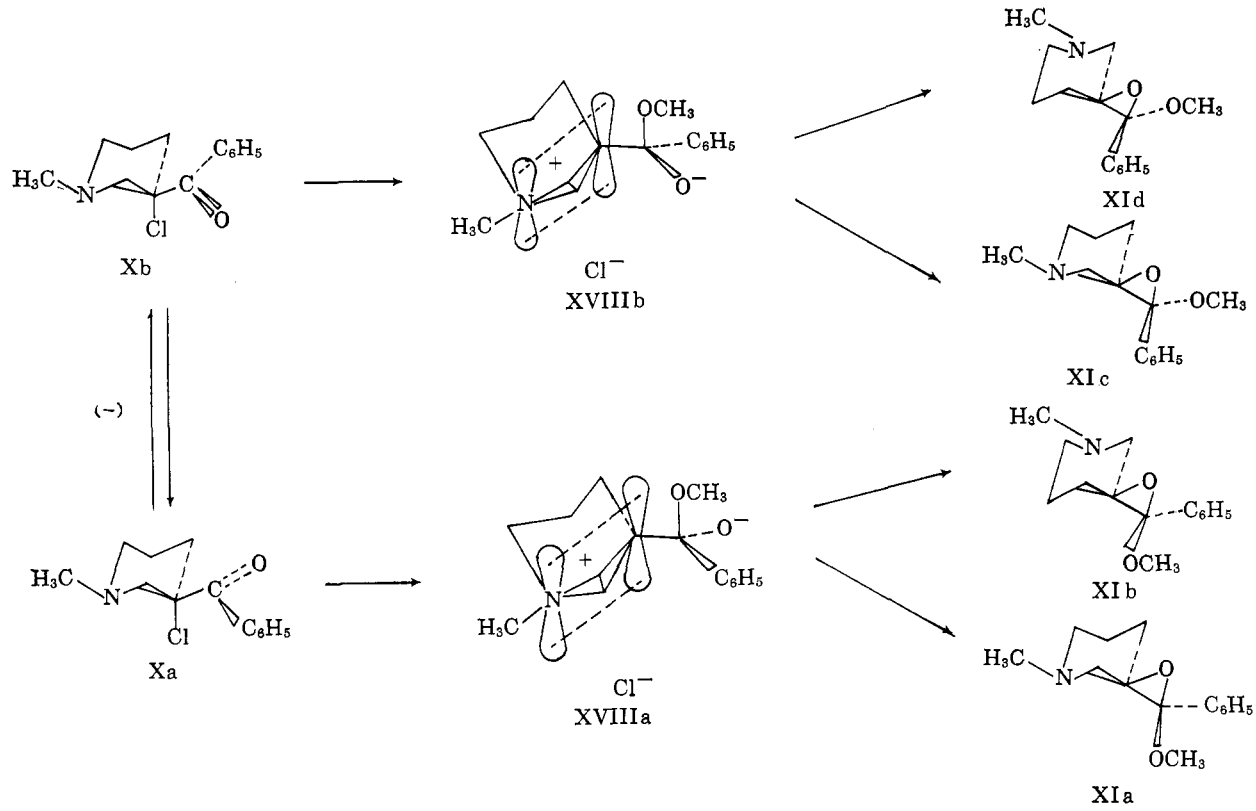
(11) It is implicit in this treatment that the nucleophilic attack occurs perpendicular to the plane of the carbonyl group [M. L. Bender, *Chem. Rev.*, **60**, 53-113 (1960)] and *trans* to the halogen [E. L. Eliel, in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 103-126; A. Streitweiser, Jr., "Solvolytic Displacement Reactions at Saturated Carbon Atons," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 13-29].

(12) For simplicity, a single composite intermediate is employed to designate the transition state(s) involved in the over-all process. The rationalizations and results are unaffected by a more complicated treatment.

(13) W. G. Dauben and K. S. Pitzer, in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 44-47. As required in this treatment, the products XIa-d are not in equilibrium under the conditions of the reaction: *cf.* C. L. Stevens, W. Malik, and R. Pratt, *J. Am. Chem. Soc.*, **72**, 4758 (1950); C. L. Stevens, M. S. Weiner, and R. C. Freeman, *ibid.*, **75**, 3977 (1953).

(14) L. L. McCoy, *ibid.*, **82**, 6416 (1960).

SCHEME I



Experimental[15]

(−)-1-Methyl-3-benzoyl-3-chloropiperidine [(−)-X].—An analytically pure sample of the free base was prepared from nicotinic acid as previously described[7,16]: m.p. 25–6°, $[\alpha]^{28}D$ (absolute ethanol) −4.1° (*c* 12.40); lit.[7] m.p. 25–26°, $[\alpha]^{27}D$ (absolute ethanol) −4.2°.

(+)-1-Methyl-3-benzoyl-3-hydroxypiperidine [(+)-XII].—An analytically pure sample of the free base was prepared as previously described[7,16]: m.p. 72.5–73°, $[\alpha]^{28}D$ (absolute ethanol) +10.9° (*c* 5.00); lit.[7] m.p. 72.5–73°, $[\alpha]^{25}D$ (absolute ethanol) +11.4°.

(−)-2-Methoxy-2-phenyl-5-methyl-1-ox-5-azaspiro[2.5]octane [(−)-XI].—To 50 ml. of freshly prepared anhydrous methanol was added 1.70 g. (74 mg.-atoms) of clean sodium. Upon completion of the reaction, the solution was cooled to room temperature (25°). A solution consisting of 25 ml. of anhydrous methanol and 5.94 g. (25 mmoles) of the levorotatory (−3.3°) α-halo ketone (X) was added. After 48 hr., the sodium chloride precipitate was filtered off and the methanol was removed with a stream of dry nitrogen leaving a paste which was partitioned between water and petroleum ether (b.p. 40–60). The organic layer was dried over sodium sulfate, treated with carbon, and filtered through sintered glass. Upon removal of the solvent under reduced pressure and subsequent distillation, 4.7 g. (20 mmoles, 80%) of epoxy ether, (−)-XI, b.p. 70–71° (0.08 mm.), was obtained. The halogen-free distillate, $[\alpha]^{25}D$ (absolute ethanol) −1.0° (*c* 25.80), exhibited neither carbonyl nor hydroxyl bands in the infrared spectrum of a liquid film or chloroformic solution. These bands are prominent at 1665 and 3458 $cm.^{-1}$, respectively, in the spectrum of the α-hydroxy ketone measured under identical conditions.

Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.12; H, 8.18; N, 5.87.

(+)-2-Methoxy-2-phenyl-5-methyl-1-ox-5-azaspiro[2.5]octane [(+)-XI].—To 50 ml. of anhydrous methanol was added 1.70 g. (74 mg.-atoms) of clean sodium. Upon completion of the reaction, the methol was removed at the steam table under reduced pressure (0.01 mm.) and replaced with 40 ml. of anhydrous xylene. A solution of 1.19 g. (5 mmoles) of (−)-X (−3.3°) in 25 ml. of anhydrous xylene was added. The mixture was refluxed for 20 min., cooled, and extracted with water. The organic phase was dried. The xylene was removed under reduced pressure. The resulting oil yielded 0.70 g. (3 mmoles, 60%) of epoxy ether, (+)-X1, after distillation: b.p. 70–71° (0.08 mm.), $[\alpha]^{25}D$ (absolute ethanol) +1.3° (*c* 18.78).

Acidolyses of (+)- and (−)-XI. Method A.—A solution of 4.67 g. (20 mmoles) of epoxy ether, (−)-XI, in 100 ml. of 2 *N* hydrochloric acid was refluxed for 24 hr. After cooling, the solution was made basic with sodium hydroxide and extracted with petroleum ether. The organic extract was treated with sodium sulfate and carbon and filtered through sintered glass. The solvent volume was reduced to about 30 ml. at the steam table. Upon cooling, there was obtained 3.94 g. (18 mmoles, 90%) of racemic XII: m.p. and m.m.p. 56–57°; lit. m.p. 53–53.5°,[16] 52–54°.[5] In our apparatus the melting point and mixture melting point of a sample of (±)-1-methyl-3-benzoyl-3-hydroxypiperidine, prepared earlier,[16] and our product were identical. Infrared spectra of these samples in chloroform taken under identical conditions were superimposable. Acidolysis of (+)-XI in this way also afforded (±)-XII, m.p. and m.m.p. 56–57°.

A solution of (+)-XI, 10.0%, $[\alpha]^{26}D$ (absolute ethanol) +1.3° (*c* 17.60), in 2 *N* hydrochloric acid exhibited a rotation of 0.00° ± 0.01° 2 min. after preparation of the solution. After 48 hr. at 25° the solution was still optically inactive. Racemic XII, m.p. and m.m.p. 56–57°, was isolated after the usual work-up.

Method B.—A solution of 2.33 g. (10 mmoles) of epoxy ether, (−)-XI, in 10 ml. of glacial acetic acid was heated for 10 hr. on a steam bath. The solution was poured into saturated aqueous sodium bicarbonate solution overlaid with petroleum ether. The organic extract was treated with sodium sulfate and carbon and filtered through sintered glass. The solvent volume was reduced to about 15 ml. at the steam table. On cooling, there was obtained 2.50 g. (8.9 mmoles, 89%) of racemic XIII, m.p. 83.5–

(15) All melting points were obtained in a Hershberg-type [E. B. Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 312 (1936)] silicone-filled (550 Dow) melting point apparatus equipped with Anschutz full-immersion thermometers. The samples were placed in the circulating silicone bath 10° below the reported melting points and were heated at the rate of 1–2°/min. Elemental analyses were performed by Weiler and Strauss, Oxford, England. Infrared spectra were determined with a Perkin-Elmer Model 421, double-grating spectrophotometer. Specific rotations $[\alpha]^{t}D$ were determined with a Zeiss 0.01° polarimeter in a modified [G. Hite and J. Lyons, to be published] 2-dm. (2-ml.) syringe filling tube. The criterion for racemic products, obtained from optically active starting materials, was a level base line in the range 700–320 mμ which was determined with a Rudolph manual spectropolarimeter.

(16) E. E. Smissman and G. Hite, *J. Am. Chem. Soc.*, **81**, 1201 (1959).

84.5°, lit.[17] m.p. 88–89°. Hydrolysis of the ester in 2 *N* hydrochloric acid afforded (±)-XII, m.p. and m.m.p. 56–57°. Identical results were obtained by subjection of (+)-XI to this sequence.

(+)-1-Methyl-3-acetoxy-3-benzoylpiperidine (XIII).—To 10 ml. of acetic anhydride was added 3.29 g. (15 mmoles) of (+)-XII, $[\alpha]^{27}D$ (absolute ethanol) +10.9° (*c* 5.25). After refluxing for 1 hr. the solution was cooled and poured into 100 ml. of 0.2 *N* hydrochloric acid. The aqueous layer was extracted with ether. The ether layers were discarded. The aqueous layer was treated with excess saturated sodium bicarbonate and extracted with petroleum ether. The organic phase was dried over sodium sulfate, treated with carbon, filtered through sintered glass, and evaporated to a final volume of about 15 ml. On cooling, 2.60 g. (10 mmoles, 67%) of XIII was obtained: m.p. 66–67°, $[\alpha]^{25}D$ (absolute ethanol) +34.7° (*c* 10.56), $[\alpha]^{25}D$ (0.5 *N* hydrochloric acid) +72.3° (*c* 11.14).

Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.78; H, 7.41; N, 5.44.

Hydrolysis of (+)-1-Methyl-3-acetoxy-3-benzoylpiperidine (XIII).—After refluxing a solution of 1.31 g. (5 mmoles) of the ester in 25 ml. of 2 *N* hydrochloric acid for 24 hr. and cooling, the reaction mixture was poured into a saturated solution of sodium bicarbonate and extracted with petroleum ether. The extract was dried over sodium sulfate, decolorized with carbon, filtered through sintered glass, evaporated to a final volume of about 10 ml. on the steam bath, and cooled to give 0.92 g. (4.2 mmoles, 84%) of (+)-XII: m.p. 72.5–73°, $[\alpha]^{25}D$ (absolute ethanol) +10.9° (*c* 5.00); lit.[7] m.p. 72.5–73°.

To 1.31 g. (5 mmoles) of the ester in 10 ml. of 5% alcoholic potassium hydroxide was added 10 ml. of water. After refluxing for 1 hr. the mixture was diluted with 100 ml. of water and worked up as above to give 0.98 g. (4.5 mmoles, 90%) of (+)-XII, m.p. 72.5–73°, $[\alpha]^{25}D$ (absolute ethanol) +10.9° (*c* 5.00).

(+)-1-Methyl-3-methoxy-3-benzoylpiperidine [(+)-XIV].—To 20 ml. of freshly prepared anhydrous *t*-butyl alcohol was added 1.0 g. (25.6 mg.-atoms) of freshly cut potassium shavings. When the potassium was consumed, the mixture was cooled to room temperature. To this was added a solution of 3.07 g. (14 mmoles) of (+)-XII, $[\alpha]^{26}D$ (absolute ethanol) + 10.9° (*c* 5.30), in 30 ml. of anhydrous ethyl ether. To the solution, cooled in an acetone–Dry Ice bath, was introduced a solution of 4.66 g. (25 mmoles) of methyl *p*-toluenesulfonate in anhydrous ethyl ether. The mixture was stirred for 3 hr. and then poured over ice, acidified to pH 3 with concentrated hydrochloric acid, and extracted first with chloroform and then with petroleum ether. The extracts were discarded. The aqueous portion was made basic with sodium hydroxide solution and extracted with petroleum ether. The combined extracts were dried over sodium sulfate, treated with carbon, filtered through sintered glass, and evaporated on the steam table to give an oil which was distilled under reduced pressure (0.1 mm.). The distillate was dissolved in ethanol and treated with anhydrous hydrochloric acid. On cooling there was obtained 1.35 g. (5 mmoles, 36%) of a dextrorotatory material, m.p. 268–269° dec., $[\alpha]^{22}D$ (water) +42.7° (*c* 1.227), which exhibited a carbonyl band (1667 $cm.^{-1}$) but no hydroxyl band in the infrared spectrum. Good yields of the pure salt were obtained in subsequent runs in which distillation was omitted.

Anal. Calcd. for $C_{14}H_{20}ClNO_2$: C, 62.33; H, 7.47; Cl, 13.14; N, 5.19. Found: C, 61.95; H, 7.44; Cl, 13.42; N, 5.50.

The free amine, b.p. 106–109° (0.9 mm.), isolated from an analytically pure sample of the salt, exhibited an $[\alpha]^{27}D$ (absolute ethanol) of +10.0° (*c* 8.00). The observed rotation of a 2.00% solution of (+)-XIV in 2 *N* hydrochloric acid was constant at +1.71 ± 0.01° for 48 hr. at 25°.

Acknowledgment.—We are indebted to Dr. H. Fales and Miss Katherine Warren of the National Institutes of Health for the rotatory dispersion measurements, to Mr. J. Lyons for his expert technical assistance, and to both Bristol Laboratories and the Schering Corporation for funds which made possible the acquisition of a Zeiss polarimeter.

(17) R. E. Lyle and G. H. Warner, *J. Med. Pharm. Chem.*, **3**, 597 (1961).

Epoxy Ethers. XX.[1] Synthesis of Diamines, Morpholines, and Piperazines

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Received August 12, 1964

Epoxy ether Ia was converted to 1,2-diamine III by reaction with excess methylamine and subsequent reduction of the intermediate imine IIb. Epoxy ethers Ia and b were converted *via* reaction with aziridine to the corresponding α-amino ketones IVa and b. Treatment of IVa with butylamine, followed by reduction, produced diamine VI. Amino ketones IVa and b were also converted, *via* their corresponding carbinols, to morpholines IXa and b by acid treatments. Epoxy ether Ia was converted to hydroxymorpholines Xa and b by reaction with the appropriate ethanolamine. Epoxy ethers Ia, c, and d reacted with ethylenediamine forming tetrahydropyrazines XIIa, c, and d, which were readily reduced to their corresponding piperazines.

The treatment of epoxy ethers with secondary amines has been shown to produce α-amino ketones in high yield.[1] This present work reports illustrative reactions of epoxy ethers with primary amines, ethylenimine, ethanolamines, and ethylenediamine to demonstrate the utility of these reactions in the synthesis of diamines, morpholines, hydroxymorpholines, and piperazines, respectively.

1,2-Diamines.—Numerous methods for the preparation of substituted ethylenediamines are recorded in the chemical and patent literature. However, for those ethylenediamines with unsymmetrical carbon skeletons few syntheses have been recorded. One such synthesis[3] used the reaction of a β-chloramine with a second amine. Such a reaction could well proceed through an ethyleniminium ion[4] which could be opened by attack of the second amine at the two different carbon atoms of the intermediate to give two isomeric products. Thus, the β-chloramine starting material is not ideal for either synthesis or structure proof. The utility of an epoxy ether starting material results from the stepwise and directional incorporation of amines into molecules of unsymmetrical carbon skeleton.

Two successive treatments[5] of epoxy ether Ia with methylamine at and above 150° formed the α-iminoamine IIb, which was isolated in 68% yield. Imino-

(1) Paper XIX of this series: C. L. Stevens and C. H. Chang, *J. Org. Chem.*, **27**, 4392 (1962).

(2) (a) Parke, Davis and Co. Postdoctorate Research Fellow, Jan., 1959, to Jan., 1960. (b) Abstracted in part from the Ph.D. Dissertation of K. G. Taylor and the M.S. Thesis of A. L. Schy, Wayne State University, 1963.

(3) Roche Products Ltd., British Patent 729003 (April 27, 1955).

(4) R. C. Fuson and C. Zirkle, *J. Am. Chem. Soc.*, **70**, 2760 (1948).

(5) Successive treatments were necessary to convert all of the intermediate α-amino ketone, IIa, to the imine.