the mechanism proposed earlier[2] is thus confirmed. Accordingly, the extension of the α-halo ketone optical rotatory dispersion rule to α-oxygenated ketones has become a matter of continuing interest in these laboratories.

Experimental Section

α-(+)-1-(10-Camphorsulfonyl)-3-benzoyl-3-chloropiperidine [α-(+)-VII] from (−)-I.—A solution of 1.1 g. of (−)-I (4.40 mmoles based on optical purity), $[\alpha]^{26}D$ −3.8 ± 0.3° (*c* 10.00, absolute ethanol), lit.[2] $[\alpha]^{25}D$ −4.2°, was slowly added to a warm (40–45°) solution of 1.5 g. (14 mmoles) of cyanogen bromide in 20 ml. of benzene. After 48 hr. the solid quaternary bromide (50 mg., 0.15 mmole) was filtered off and the benzene was removed under reduced pressure to give the levorotatory (benzene) cyanamide: infrared, 2212 (–CN), 1660 cm.$^{-1}$ (C=O). The cyanamide and 20 ml. of concentrated hydrochloric acid were refluxed for 48 hr. Following removal of the excess acid at the water pump, the syrup was treated with aqueous sodium bicarbonate and extracted with chloroform. A solution of the labile[5a] free amine VI in benzene is levorotatory. The chloroform extracts were added to a benzene solution (40 ml.) of the sulfonyl chloride, prepared as described earlier,[5a] from 2.5 g. (10.8 mmoles) of (+)-10-camphorsulfonic acid. The solution was refluxed for 3 hr., treated with an aqueous slurry of sodium bicarbonate, and stirred for an additional 1 hr. After washing with diluted aqueous hydrochloric acid, the dried organic solution separated from the reaction mixture was evaporated under reduced pressure. The resulting gum was crystallized from methanol and afforded 0.98 g. (2.3 mmoles, 54%) of α-(+)-VII, m.p. 131–132°, lit.[5a] m.p. 131–132°.

(+)-1-Methyl-3-benzoyl-3-benzoyloxypiperidine [(+)-X] from (+)-III.—To 13.0 g. (59.3 mmoles) of optically pure (+)-III, $[\alpha]^{25}D$ +11.1 ± 0.3° (*c* 5.00, absolute ethanol), lit.[2] $[\alpha]^{25}D$ +11.4°, was added 18 g. (80 mmoles) of benzoic anhydride in 100 ml. of pyridine. After refluxing for 24 hr., the pyridine was removed under reduced pressure, and the syrup was treated with ether and 10% hydrochloric acid. The resulting precipitate was filtered off, washed with ether, and dissolved in water. Both aqueous solutions were extracted with ether, neutralized with excess sodium bicarbonate, and extracted with chloroform. The organic phase was dried over sodium sulfate, filtered, and evaporated to give an oil which afforded crystals of (+)-X, 9.0 g. (28.7 mmoles, 47%), m.p. 65–66°, $[\alpha]^{25}D$ +61.4 ± 0.4°, (*c* 4.00, absolute ethanol), from petroleum ether (b.p. 40–60°): infrared, 1676 (ketone), 1705 cm.$^{-1}$ (ester), no OH bands.

Anal. Calcd. for $C_{20}H_{21}NO_3$: C, 74.41; H, 6.54; N, 4.33. Found: C, 74.00; H, 6.62; N, 4.14.

(+)-3-Hydroxy-3-benzoylpiperidine *p*-Toluenesulfonic Acid Salt [(+)-XI] from (+)-X.—When subjected to the von Braun conditions described above, 8.0 g. (25.7 mmoles) of (+)-X afforded a dextrorotatory cyanamide [infrared, 2205 (–CN), 1678 (ketone), 1718 cm.$^{-1}$ (ester)] and 0.40 g. (1.0 mmole) of the quaternary bromide. Hydrolysis of the cyanamide afforded the corresponding desmethyl α-hydroxy ketone, isolated as its (+)-*p*-toluenesulfonic acid salt, (+)-XI, 4.0 g. (10.6 mmoles, 41%), m.p. 124–125°, $[\alpha]^{29}D$ +11.4 ± 0.4° (*c* 2.73, absolute methanol), from ethanol–ether.

Anal. Calcd. for $C_{19}H_{23}NO_5S$: C, 60.50; H, 6.16. Found: C, 60.59; H, 6.30.

α-(+)-1-(10-Camphorsulfonyl)-3-benzoyl-3-hydroxypiperidine [α-(+)-IX] from (+)-XI.—The free base, obtained from 3.11 g. (8.25 mmoles) of (+)-XI, was dissolved in 50 ml. of 1:1 benzene–chloroform and slowly added to a benzene solution (40 ml.) of the sulfonyl chloride, prepared as described earlier,[5a] from 1.90 g. (8.0 mmoles) of (+)-10-camphorsulfonic acid. After refluxing for 24 hr., 2.0 g. of sodium bicarbonate was added and refluxing was continued for an additional 2 hr. On cooling, the mixture was extracted with aqueous base and acid. The organic extract was removed under reduced pressure and replaced with benzene. After treating with anhydrous sodium sulfate and carbon, filtering through sintered glass, and completely removing the solvent under reduced pressure (0.01 mm.), there was obtained a colorless oil, **α-(+)-IX**, 2.07 g. (4.95 mmoles, 60%), $[\alpha]^{25}D$ +34.0 ± 0.4° (*c* 5.19, 0.2 *N* HCl in 4:1 acetone–water), which could not be crystallized and which had been obtained earlier[5a] from β-(+)-VII, through the total epoxy ether mixture, $[\alpha]^{25}D$ +34.5 ± 0.3° (*c* 5.54, 0.2 *N* HCl in 4:1 acetone–water). The infrared spectra (liquid films) were superimposable.

(6) Melting points were obtained in a Hershberg [*Ind. Eng. Chem., Anal Ed.*, **8**, 312 (1936)], silicone (550-Dow) filled melting point apparatus equipped with Anschutz full-immersion thermometers. The samples were placed in the circulating bath 10° below the reported melting points and heated at the rate of 1–2°/min. Elemental analyses were performed by Weiler and Strauss, Oxford, England. Infrared survey spectra (Nujol mulls) were determined with a Perkin-Elmer Model 421 spectrophotometer. Band assignments are believed accurate to within ±5 cm.$^{-1}$. Specific rotations were determined with a Zeiss 0.01° polarimeter in a modified [G. Hite and J. Lyons, *Chemist-Analyst*, **43**, 84 (1964)] 1-dm. (1-ml.) syringe-filling tube.

The Mechanism and Stereochemistry of Formation and Cleavage of Epoxy Ethers.[1] III[2]

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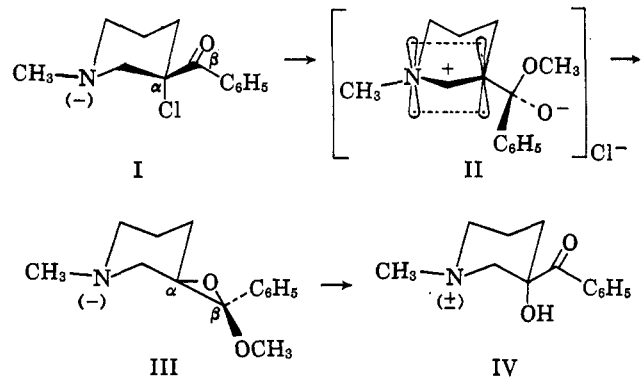
The work of Stevens, *et al.*,[3] indicates that epoxy ether cleavage[3c,f] and epoxy ether formation from α-halo ketones[3] are stereospecific processes resulting in retention and inversion of configuration of the α-carbon, respectively.

The *anomalous* α-C symmetrization in the epoxy ether, (−)-III, formation–cleavage sequence, (−)-I → [II] → (−)-III → (±)-IV, has been rationalized[4] by



invoking participation of the free electron pair of the piperidine nitrogen (*cf.* II). Accordingly, it was of interest to examine an analog of (−)-I in which the methyl group is replaced by an electronegative moiety designed to preclude such participation.

The syntheses and rationale for use in these studies of the two diastereoisomers, α-(+)- and β-(+)-1-(10-camphorsulfonyl)-3-benzoyl-3-chloropiperidine [α-(+)- and β-(+)-V], have been recorded.[5]

(1) See H. Patel and G. Hite, *J. Org. Chem.*, **30**, 4336 (1965), footnote 1.

(2) Paper II: T. B. Zalucky, S. Marathe, L. Malspeis, and G. Hite, *ibid.*, **30**, 1324 (1965).

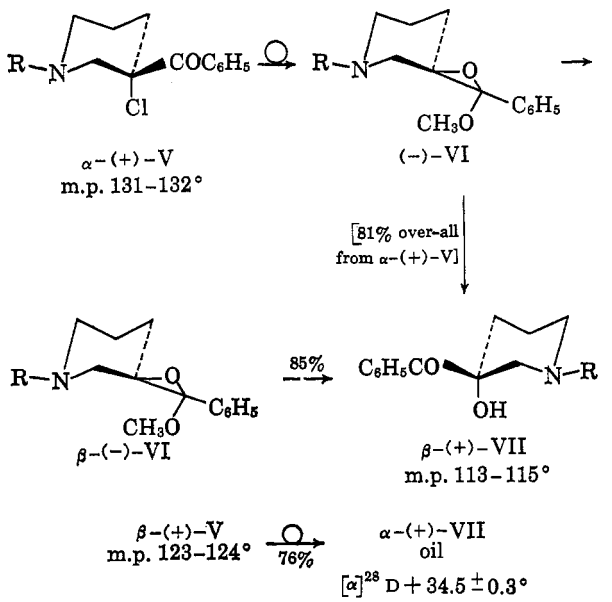
(3) (a) C. L. Stevens and A. J. Weinheimer, *J. Am. Chem. Soc.*, **80**, 4072 (1958); (b) C. L. Stevens, M. L. Weiner, and R. C. Freeman, *ibid.*, **75**, 3977 (1953); (c) C. L. Stevens and T. H. Coffield, *J. Org. Chem.*, **23**, 336 (1958); (d) C. L. Stevens, W. Malik, and R. Pratt, *J. Am. Chem. Soc.*, **72**, 4758 (1950); (e) C. L. Stevens and T. H. Coffield, *ibid.*, **80**, 1919 (1958); (f) C. L. Stevens and S. J. Dykstra, *ibid.*, **75**, 5975 (1953).

(4) T. B. Zalucky, L. Malspeis, and G. Hite, *J. Org. Chem.*, **29**, 3143 (1964).

(5) T. B. Zalucky, L. Malspeis, H. Patel, and G. Hite, *J. Pharm. Sci.*, **54**, 687 (1965).

Treatment of α-(+)-V with methanolic sodium methoxide afforded a levorotatory diastereoisomeric mixture of epoxy ethers, 2-methoxy-2-phenyl-5-(10-camphorsulfonyl)-1-ox-5-azaspiro[2.5]octanes (VI), from which an optically pure diastereoisomer, β-(−)-VI, was isolated in 28% yield by fractional crystallization. Isolation of an optically pure, *solid* α-hydroxy ketone, β-(+)-1-(10-camphorsulfonyl)-3-benzoyl-3-hydroxypiperidine [β-(+)-VII], m.p. 113–115°, in 85% yield, upon treatment of β-(−)-VI with 0.2 *N* hydrochloric acid in 1:4 aqueous acetone, confirms retention of configuration through β-C–O cleavage of the epoxy ether.[2,3f,4] Moreover, the quantitative polarimetric analysis of this reaction reveals total retention of configuration within the limits of experimental error.

The mechanism of epoxy ether formation from α-halo ketones was clearly demonstrated by conversion of α-(+)-V directly to the same solid, β-(+)-VII, through the total epoxy ether mixture (VI) in 81% over-all yield. Thus, inversion of configuration normally occurs in epoxy ether formation, while anchimeric assistance[4] is responsible for the anomalous symmetrization (−)-I. Finally, from the fact that β-(+)-V afforded an *oil*, α-(+)-VII, $[\alpha]^{28}D$ +34.5 ± 0.3°, lit.[6a] $[\alpha]^{28}D$ +34.0 ± 0.4° (optically pure), which we have been unable to crystallize, it can be concluded that both "normal" epoxy ether formation and cleavage are virtually, if not in fact, 100% optically specific.



R = 10-camphorsulfonyl moiety derived from (+)-10-camphorsulfonic acid

Experimental Section[6b]

α-(+)- and β-(+)-1-(10-Camphorsulfonyl)-3-benzoyl-3-chloropiperidine [α-(+)-V and β-(+)-V].—These solids, m.p. 131–132° and 123–124°, respectively, were prepared as described earlier.[5]

Epoxy Ether Formation from α-(+)-V [VI and β-(−)-VI].—To 50 ml. of methanolic sodium methoxide (from 0.7 g. of freshly cut sodium and absolute methanol) was added 5.0 g. (11.4 mmoles) of optically pure α-(+)-V in 25 ml. of anhydrous benzene. After standing for 24 hr. at room temperature, the solution was filtered and the solvent was removed under reduced pressure. The residual gum was partitioned between benzene and water. The benzene extracts were dried over sodium sulfate, treated with carbon, filtered through sintered glass, and evaporated to dryness under reduced pressure. The residue (VI) was recrystallized from hexane and then petroleum ether (b.p. 20–60°) to constant melting point, 135–137°, and specific rotation, $[\alpha]^{28}D$ −32.2 ± 0.3° (*c* 1.18, methanol), to give 1.40 g. (3.1 mmoles, 28%) of β-(−)-VI.

Anal. Calcd. for $C_{28}H_{31}NO_5S$: C, 63.71; H, 7.21; N, 3.23; S, 7.39. Found: C, 63.59; H, 7.39; N, 3.44; S, 7.38.

The carbonyl band at 1670 cm.$^{-1}$ (1740 cm.$^{-1}$, camphor carbonyl) in the infrared spectrum of α-(+)-V was absent in the spectrum of β-(−)-VI.

Epoxy Ether Cleavage [β-(−)-VI → β-(+)-VII].—To 0.3128 g. (0.724 mmole) of β-(−)-VI in 7 ml. of acetone, was added 2 ml. of 1 *N* hydrochloric acid and enough acetone to bring the final volume to 10.00 ml. No change (±0.01°) in rotatory power could be observed, undoubtedly owing to the speed of the acidolysis.[4] Assuming 100% conversion to α-hydroxy ketone VII (after 24 hr.), from the weight of β-(+)-VII equivalent to that of β-(−)-VI introduced and the observed rotation, the calculated specific rotation, $[\alpha]^{28}D$ +12.9 ± 0.3° (0.2 *N* hydrochloric acid–1:4 water–acetone), of product(s) in the solution indicated total formation, within experimental error, of β-(+)-VII. This could be isolated in 85% yield (0.258 g., 0.62 mmole), m.p. 113–115°, $[\alpha]^{28}D$ +13.2 ± 0.3° (*c* 3.88, 0.2 *N* hydrochloric acid–1:4 water–acetone), by evaporation of the solvent under a stream of dry nitrogen and recrystallization of the residue from hexane.

Anal. Calcd. for $C_{22}H_{29}NO_5S$: C, 62.98; H, 6.97; N, 3.34. Found: C, 62.83; H, 7.03; N, 3.55.

The infrared spectrum of β-(+)-VI exhibited carbonyl absorptions at 1660 and 1740 cm.$^{-1}$ and hydroxyl absorption at 3450 cm.$^{-1}$.

Epoxy Ether Formation and Cleavage [α-(+)-V → (−)-VI → β-(+)-VII].—Treatment of 1.028 g. (2.34 mmoles) of α-(+)-V with methanolic sodium methoxide followed by subjection of the total epoxy ether mixture (VI) to acidolysis afforded 0.800 g. (1.91 mmoles, 81%) of β-(+)-VII, m.p. 113–115°, $[\alpha]^{28}D$ +13.4 ± 0.5° (*c* 3.28, 0.2 *N* hydrochloric acid–1:4 water–acetone).

Epoxy Ether Formation and Cleavage [β-(+)-V → (+)-VI → α-(+)-VII].—After treatment of 1.6 g. (3.65 mmoles) of β-(+)-V as described for the α isomer, the solution was filtered. The water-soluble precipitate contained no organic material. The solvent was removed under reduced pressure. The total residue was dissolved in about 25 ml. of 0.2 *N* hydrochloric acid in acetone–water (4:1). After 24 hr. the solvent was removed under a stream of dry nitrogen. The resulting oil was dissolved in purified hexane. The solution was treated with carbon and sodium sulfate, filtered through sintered glass, and subjected to a stream of dry nitrogen to give 1.2 g. (2.86 mmoles, 76%) of a colorless oil, α-(+)-VII, $[\alpha]^{28}D$ +34.5 ± 0.3° (*c* 5.54, 0.2 *N* hydrochloric acid–1:4 water–acetone), lit.[6a] $[\alpha]^{28}D$ +34.0 ± 0.4° (0.2 *N* hydrochloric acid–1:4 water–acetone) (optically pure).

Anal. Calcd. for $C_{22}H_{29}NO_5S$: C, 62.98; H, 6.97. Found: C, 63.09; H, 7.11.

(6) (a) H. Patel and G. Hite, *J. Org. Chem.*, **30**, 4336 (1965); (b) *ibid.*, footnote 6.

Resin Acids. VII. Partial Synthesis of (−)-13-*epi*-Rimuane[1]

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Although our recently described[2] partial synthesis of (−)-rimuane (1) from isopimaric acid defined the absolute configuration of rimuene, we had determined at the outset, because of uncertainty about the stereochemistry at C-13,[3] to synthesize concurrently the

(1) Previous paper: W. Herz and R. N. Mirrington, *J. Org. Chem.*, **30**, 3198 (1965). Work was supported in part by grants from the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation (G.P.-1962).

(2) W. Herz and R. N. Mirrington, *ibid.*, **30**, 3195 (1965).

(3) The total synthesis[4] of *dl*-rimuene did not establish the configuration at this center unambiguously.

(4) R. E. Ireland and L. N. Mander, *Tetrahedron Letters*, **No. 46**, 3453 (1964).