−16.1° ($c$ 1.38, chloroform), and (−)-($S$,$S$)-VI[5] in 35% yield, mp 133–134°, $[\alpha]^{25}$D −64.6° ($c$ 1.96, chloroform). The nmr spectra of these diastereomers were distinctly different and were used to demonstrate the absence of less than 5% diastereomeric impurity in each sample.

Similar amide–ester interchanges were carried out that involved substitutions at sulfur (see Chart I). When (−)-($S$)-VII ($[\alpha]^{25}$D −197.3° ($c$ 1.22, acetone) (lit.[8] $[\alpha]^{25}$D −202°)) was treated with 1 mole of lithium anilide in ether at 0° (inverse addition), (+)-($S$)-VIII[5] was produced in 41% yield after chromatography (silica gel, pentane–ether), mp 131–133° (nonfractionally crystallized), $[\alpha]^{25}$D +216.9° ($c$ 1.02, chloroform). After several recrystallizations of this material from ether, a maximum rotation of $[\alpha]^{25}$D +224.4° ($c$ 2.0, chloroform) was reached; mp 116–117°. This reaction appears to have been highly stereospecific. When carried out with excess lithium anilide by addition of ester to anilide salt, totally racemic VIII[9] was obtained, mp 133–135° (mixture melting point with (+)-($S$)-VIII 106–125° dec). The two results provide strong evidence that the substitution reaction occurred essentially stereospecifically with inversion and that in the presence of excess anilide ion optically active sulfinanilide was converted to racemic material by multiple substitutions of anilide ion by anilide ion with inversion. Comparison of the ord curves of optically pure (+)-($S$)-benzyl $p$-tolyl sulfoxide,[8] $\lambda_{\max}$ 277 m$\mu$, $[\phi]$ +27.8 × 10$^3$ ($c$ 0.027, methanol), and that of (+)-($S$)-VIII, $\lambda_{\max}$ 285 m$\mu$, $[\phi]$ +9.9 × 10$^3$ ($c$ 0.016, methanol), provides direct evidence for the configuration of (+)-VIII since that of the sulfoxide has been established.[8] Others have demonstrated that Grignard reagents react with menthyl sulfinates stereospecifically[10a] and with inversion of configuration.[10b]

A second amide–ester interchange was performed with the more hindered lithium salt of (−)-($S$)-V (see Chart I). When (−)-($S$)-VII ($[\alpha]^{25}$D −200.6 ($c$ 1.22, acetone))[8] was added to 2 moles of optically pure (−)-($S$)-V[7] in ether at 25°, (+)-($S$,$S$)-IX was produced in 70% yield after chromatography (silica gel, pentane–ether): mp 116.5–119.5° (nonfractionally crystallized), $[\alpha]^{25}$D +37.2° ($c$ 3.89, chloroform). The nmr spectrum of this material demonstrated the absence of more than 5% of the other diastereomer (see below). Apparently the more hindered anion of V does not displace amide ion from (+)-($S$,$S$)-IX to give (−)-($S$,$R$)-IX once the former diastereomer formed, as did anilide anion under the same conditions. A mixture of optically pure diastereomers (−)-($S$,$R$)-IX and (+)-($S$,$S$)-IX was prepared by treating optically pure (−)-($S$)-V[7] (2 moles) with $p$-toluenesulfinyl chloride (1 mole) in ether at 25° for 1 hr. The product was chromatographed (silica gel, pentane–ether 8:1) to give (+)-($S$,$S$)-IX:[5] yield 5%; mp 119.5–120°; $[\alpha]^{25}$D +41.2° ($c$ 0.85, chloroform). A clear separation of diastereomers was not accomplished by chromatography, and the low isolated yield reflects this fact. The isomer (−)-($S$,$R$)-IX was not obtained free of (+)-($S$,$S$)-IX. However, a comparison of the nmr spectra of pure (+)-($S$,$S$)-IX in deuteriochloroform ($\tau$ 8.42, d, 3 H, $J_{\mathrm{H-H}}$ = 7 cps; 7.70, s, 3 H; 5.35, m, 2 H; 2.35–2.90, m, 9 H) and of the diastereomeric mixture ($[\alpha]^{25}$D −40.5° ($c$ 1.72, chloroform)) provided the spectrum of (−)-($S$,$R$)-IX ($\tau$ 8.58, d, 3 H, $J_{\mathrm{H-H}}$ = 7 cps; 7.66, s, 3 H; 2.35–2.90, m, 9 H). From integration of the methyl doublets of the two diastereomers present in the mixture and its rotation, the rotation of pure (−)-($S$-$R$)-IX was estimated to be $[\alpha]^{25}$D −95° ($c \sim 2$, chloroform).

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(8) C. J. M. Stirling, *J. Chem. Soc.*, 5741 (1963).

(9) J. von Braun and W. Kaiser, *Chem. Ber.*, 56, 553 (1923).

(10) (a) K. K. Andersen, *Tetrahedron Letters*, 93 (1962); (b) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, 87, 1958 (1965).

(11) This author wishes to acknowledge gratefully nonresident tuition grants from Dow Chemical Co. and U. S. Rubber Co.

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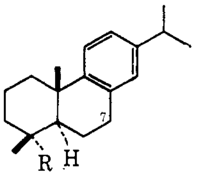
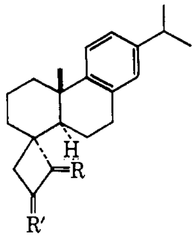
## Anomalous Wolff Rearrangements

*Sir:*

Treatment of the diazomethyl ketone Ib, mp 99–101°, derived from dehydroabietic acid (Ia), with a suspension of silver oxide in methanol[1] has afforded methyl homodehydroabietate (Ic;[1] 55% yield), the liquid ketone Id [20%; infrared (neat): 5.82 $\mu$ (C=O, s); nmr ($CDCl_3$): two-proton singlet at $\delta$ 4.31 (ketomethylene), three-proton singlet at 3.38 (OMe)]—the exclusive product of the interaction of Ib with acidic methanol—and the ketone IIa [22%; mp 84–85°; infrared (Nujol): 5.65 $\mu$ (C=O, s); nmr ($CDCl_3$): three-proton singlet at $\delta$ 1.08 (C-10 methyl), six-proton doublet at 1.19 ($J$ = 7.0 cps, isopropyl methyls)].[2–4] This observation invited an investigation of further examples of rearrangements of sterically compressed diazo ketones.



Ia, R = $CO_2H$
b, R = $COCHN_2$
c, R = $CH_2CO_2Me$
d, R = $COCH_2OMe$



IIa, R = O; R′ = $H_2$
b, R = O; R′ = $CHC_6H_5$
c, R = HOH; R′ = $CHC_6H_5$

Treatment of a methanolic solution of diazomethyl $t$-butyl ketone (IIIa)[5] with silver oxide yielded methyl homopivalate (IIIb;[6] 53%)—also the product of photolysis of a methanolic solution of IIIa—and two stereoisomers of IV, solids, mp 106° [13%; infrared ($CCl_4$):

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(1) For a previous study of this reaction, *cf.* G. Stork and J. W. Schulenberg, *J. Am. Chem. Soc.*, 84, 284 (1962).

(2) Satisfactory elemental analyses were obtained for all new compounds.

(3) Similar treatment of the diazomethyl ketone of 7-ketodehydroabietic acid produced the homoester 7-keto-Ic (61%; mp 90–90.5°), the methoxymethyl ketone 7-keto-Id (20%), and the cyclobutanone 7-keto-IIa (16%; mp 146°).

(4) The only previous example of cyclobutanone formation by intramolecular carbon–hydrogen bond insertion in an attempted Wolff rearrangement of a diazo ketone has been cited by H. O. House, S. G. Boots, and V. K. Jones, *J. Org. Chem.*, 30, 2519 (1965).

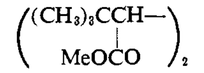
(5) K. B. Wiberg and T. W. Hutton, *J. Am. Chem. Soc.*, 76, 5367 (1954).

(6) A. H. Homeyer, F. C. Whitmore, and V. H. Wallingford, *ibid.*, 55, 4209 (1933).

5.76 $\mu$ (C═O, s); nmr ($CDCl_3$): 18-proton singlet at $\delta$ 0.95 (Me), two-proton singlet at 2.71 (methine), six-proton singlet at 3.66 (OMe)] and mp 48° [10%; infrared ($CCl_4$): 5.76 $\mu$ (C═O, s); nmr ($CDCl_3$): 18-proton singlet at $\delta$ 1.00 (Me), two-proton singlet at 2.48 (methine), six-proton singlet at 3.62 (OMe)].[7] Similar treatment of diazomethyl $\alpha$-methylcyclohexyl ketone (Va) gave the liquid homoester Vb (51%)—also a product of the photolysis of Va in methanol—the two stereoisomers of VI, solids of mp 105–106° [18%; infrared ($CCl_4$): 5.77 $\mu$ (C═O, s); nmr ($CDCl_3$): six-proton singlet at $\delta$ 1.09 (Me), two-proton singlet at 2.92 (methine), six-proton singlet at 3.61 (OMe)] and mp 84–86° [17%; infrared ($CCl_4$): 5.77 $\mu$ (C═O, s); nmr ($CDCl_3$): six-proton singlet at $\delta$ 1.06 (Me), two-proton singlet at 2.55 (methine), six-proton singlet at 3.62 (OMe)], and the liquid ketone VII [6%; infrared ($CCl_4$): 5.73 $\mu$ (C═O, s); nmr ($CDCl_3$): three-proton singlet at $\delta$ 0.97 (Me), two-proton multiplet at 2.17 (ketomethylene), one-proton multiplet at 2.50 (methine); semicarbazone mp 221–233°].[7]

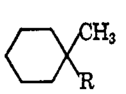
$(CH_3)_3CR$

IIIa, R = $COCHN_2$
b, R = $CH_2CO_2Me$

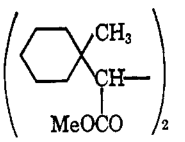


$$\left(\begin{array}{c}(CH_3)_3CCH{-}\\ |\\ MeOCO\end{array}\right)_2$$

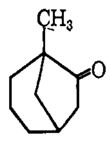
IV



Va, R = $COCHN_2$
b, R = $CH_2CO_2Me$

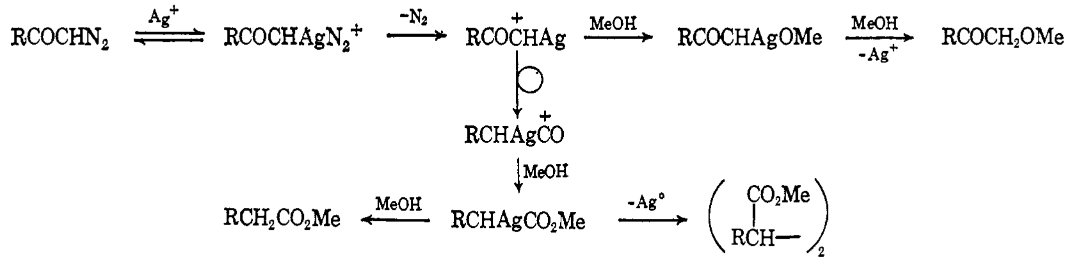


VI

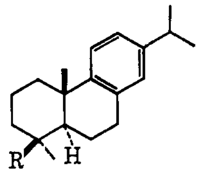


VII

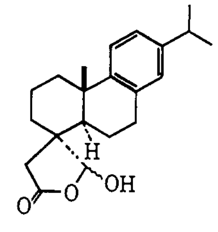
Both the carbon–hydrogen bond insertion and the coupling processes are suggestive of the intermediacy of organosilver species in the rearrangements. In analogy with RCHMX intermediates in carbenoid reactions[8] the complexes $RCOCHAgN_2^+$ or $RCOCAgN_2$[9] can be envisaged as important species in the bond-insertion process. Further, alkylsilver systems are known to dimerize.[10] These points lead to a simple, albeit not exclusive, rationale of the Wolff rearrangement (*vide supra*).[11]



The ease of cyclobutanone formation in the Wolff rearrangement of the dehydroabietic acid derivative Ib[12] recommends this reaction as a method of preparation of difunctionalized geminal dialkyl groups or of inversion of quaternary carbon centers—both important problems in di- and triterpene chemistry. The conversion of IIa into a derivative of callitrisic acid (VIIIa)[13] illustrates such an application. Base-catalyzed condensation of the cyclobutanone IIa with benzaldehyde yielded IIb, mp 148–150°. Sodium borohydride reduction of the latter followed by oxidation of the resultant alcohol IIc with osmium tetroxide and sodium periodate afforded the lactol IX [mp 160–161°; infrared ($CCl_4$): 2.75 (OH, m), 5.59 and 5.85 $\mu$ (C═O, s)]. Wolff–Kishner reduction and diazomethane treatment led to liquid methyl homocallitrisate (VIIIb) [infrared ($CCl_4$): 5.76 $\mu$ (C═O, s); nmr ($CDCl_3$): three-proton singlets at $\delta$ 1.05, 1.18 (C-4 and C-10 methyls, respectively), six-proton doublet at 1.19 ($J$ = 7.0 cps, isopropyl methyls), two-proton AB pair of doublets centered at 2.37 ($J$ = 13.0 cps), three-proton singlet at 3.60 (OMe)].



VIIIa, R = $CO_2H$
b, R = $CH_2CO_2Me$



IX

The unexpected production of ketones IIa and VII during Wolff rearrangements led to a general study of intramolecular, carbon–hydrogen bond insertions of diazo ketones catalyzed by copper sulfate[14] whose early outgrowth is the following facile preparation of bicyclo-[2.1.*n*] alkanones.[15]

Cyclohexane solutions of the diazo ketones were added dropwise at exceedingly low rate to refluxing suspensions of anhydrous cupric sulfate in cyclohexane. Under these conditions the formation of undesired ene dione dimers were fully suppressed. Decomposi-

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(7) Minor products were not isolated.

(8) W. Kirmse, "Carbene Chemistry," Academic Press Inc., New York, N. Y., 1964.

(9) The ester equivalent, $N_2AgCCO_2Et$, has been isolated recently [V. Schöllkopf and N. Reiber, *Angew. Chem.*, 79, 238 (1967)].

(10) H. C. Brown and C. H. Snyder, *J. Am. Chem. Soc.*, **83**, 1002 (1961); W. Reusch and R. Starkey, *J. Org. Chem.*, **32**, 931 (1967).

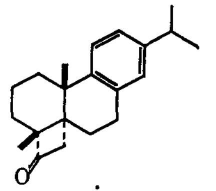
(11) Except for the variation by M. S. Newman and P. F. Beal, *J. Am. Chem. Soc.*, **72**, 5163 (1950) ($RCOCHN_2 \rightarrow RCO\bar{C}N_2 \rightarrow RCO\dot{C}N_2 \rightarrow R\dot{C}{=}C{=}O \rightarrow RCH{=}C{=}O \rightarrow RCH_2CO_2Me$), the original suggestion of G. Schroeter, *Ber.*, **42**, 2336 (1909) ($RCOCHN_2 \rightarrow RCO\ddot{C}H \rightarrow RCH{=}C{=}O \rightarrow RCH_2CO_2Me$), appears to have been accepted universally.

(12) More surprisingly, photolysis of Ib in methanol solution produced some IIa alongside the expected homoester Ic.

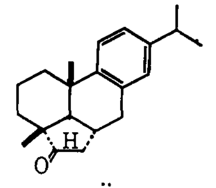
(13) L. J. Gough, *Tetrahedron Letters*, 295 (1968); R. M. Carman and H. C. Deeth, *Australian J. Chem.*, 20, 2789 (1967).

(14) While such reactions appear uncommon, intramolecular double-bond addition of diazo ketones and diazo esters induced by copper or its salts is now a common method of construction of polycyclic compounds [G. Stork and J. Ficini, *J. Am. Chem. Soc.*, **83**, 4678 (1961); H. O. House and C. J. Blankley, *J. Org. Chem.*, **33**, 53 (1968), and references cited therein].

(15) Decomposition of Ib in cyclohexane solution under the influence of copper sulfate has yielded mainly ketones i (mp 79–80°) and ii (mp 136–138°; 2,4-dinitrophenylhydrazone mp 208–209°).

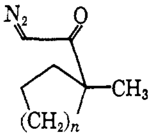


i

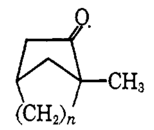


ii

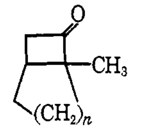
tion of diazomethyl $\alpha$-methylcycloheptyl ketone (Xa)[16] led to 1-methyl-8-bicyclo[4.2.1]nonanone (XIa) [72% yield; liquid; infrared (neat): 5.75 $\mu$ (C=O, s); nmr ($CDCl_3$): three-proton singlet at $\delta$ 1.02 (Me)] and 1-methyl-9-bicyclo[5.2.0] nonanone (XIIa) [9%; liquid; infrared ($CCl_4$): 5.63 $\mu$ (C=O, s); nmr ($CDCl_3$): three-proton singlet at $\delta$ 1.23 (Me), three-proton multiplet at 2.2–3.5 (bridgehead H and $\alpha$-ketomethylene)].[7] Decomposition of diazomethyl $\alpha$-methylcyclohexyl ketone (Xb) produced a 62% yield of 1-methyl-7-bicyclo[3.2.1]octanone (XIb).[7] Decomposition of diazomethyl $\alpha$-methylcyclopentyl ketone (Xc) afforded 1-methyl-2-bicyclo[2.2.1]heptanone (XIc;[17,18] 19%; semicarbazone mp and mmp[17] 212–214°) and 1-methyl-7-bicyclo[3.2.0]heptanone (XIIc) [3%; liquid; infrared ($CCl_4$): 5.63 $\mu$ (C=O, s); nmr ($CDCl_3$): three-proton singlet at $\delta$ 1.24 (Me), three-proton multiplet at 2.2–3.5 (bridgehead H and $\alpha$-ketomethylene); semicarbazone mp 176–178°; 2,4-dinitrophenylhydrazone mp 93–95°].[19-21]



X



XI



XII

a, $n = 4$; b, $n = 3$; c, $n = 2$; d, $n = 1$

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[16] The authors are indebted to Dr. S. Shulman for his preparation of the precursor, $\alpha$-methylcycloheptanecarboxylic acid, mp 43–45°.

[17] H. Toivonen, *Suomen Kemistilehti*, **33b**, 66 (1960); T. Gibson and W. F. Erman, *J. Org. Chem.*, **31**, 3028 (1966).

[18] The authors are indebted to Dr. T. Gibson for a sample of this substance.

[19] The solvent insertion product, hexahydrobenzyl $\alpha$-methylcyclopentyl ketone (bp 87° (0.45 mm); semicarbazone mp 174°), was obtained in 9% yield.

[20] Decomposition of diazomethyl $\alpha$-methylcyclobutyl ketone (Xd) has yielded *inter alia* 1-methyl-2-bicyclo[2.1.1]hexanone (XId) [liquid; infrared ($CCl_4$): 5.68 $\mu$ (C=O, s); nmr ($CDCl_3$): three-proton singlet at $\delta$ 1.18 (Me), two-proton multiplet at 2.05–2.25 ($\alpha$-ketomethylene), one-proton multiplet at 2.72 (bridgehead H)].

[21] The authors are indebted to the National Science Foundation for support of this work.

[22] National Science Foundation Undergraduate Research Participant, summer 1967.

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*Received February 29, 1968*

## Distinguishing Diastereotopic Hydrogens by Mass Spectrometry. A Direct Probe into the Transition State of an Electron-Impact-Induced Elimination Reaction

*Sir:*

It has been recognized for some time that acyclic diastereomers exhibit mass spectral differences which are usually small and difficult to interpret.[1] While consistent differences are found for the intensities of ions formed in the fragmentation of double-bond stereoisomers they are also minor and not easily rationalized.[2] Cyclic diastereomers on the contrary have been the subject of many varied and continuing studies on the effect of stereochemistry on mass spectral fragmentations.[3]

We now report that two acyclic diastereomers, which are isomers *only* by virtue of isotopic substitution, can be distinguished by a stereoselective electron-impact-induced elimination reaction.

Racemic 2,4-pentanediol[4] was allowed to react with 1 equiv of *p*-toluenesulfonyl chloride in pyridine. Reduction of the derived tosylate with lithium aluminum deuteride in ethyl ether leads by stereospecific reaction[5,6] to (*S*,*R*)-2-deuterio-4-hydroxypentane (I).[7] Treatment of *meso*-2,4-pentanediol in exactly the same manner leads to (*S*,*S*)-2-deuterio-4-hydroxypentane (II). Conversion of I and II to their chlorosulfite esters and subsequent heating in dioxane produces III and IV, respectively.[8] Dissolution of I and II in pyridine and treatment with 1 equiv of thionyl chloride leads, respectively, by inversion of configuration,[9] to the chlorides IVa and IIIa. The reaction sequences are summarized in Scheme I while the mass spectral data are shown in Table I.

**Table I.**[a] Mass Spectral Data for Loss of HCl, DCl, and Cl from the Molecular Ions of III, IIIa, IV, and IVa[b]

| | III | IIIa | IV | IVa |
|---|---|---|---|---|
| *A* | 29.5 | 30.2 | 25.8 | 26.0 |
| *B* | 4.3 | 4.1 | 4.3 | 4.2 |

[a] Data were taken on a CEC-103-C mass spectrometer at a nominal 9-eV ionizing voltage with inlet at ambient temperature and ion source at ~28°. The molecular ion is undetectable under these conditions. The low source temperature was attained by scanning the region of interest immediately after starting the filament. The temperature was measured just before and after the run. The spectra were indistinguishable on various runs. At 130° and 70 eV the relative difference between III (IIIa) and IV (IVa) is close to 50% of that shown in table. [b] $A = \{(M - DCl)/[(M - DCl) + (M - HCl)]\}10^2$; $B = \{(M - Cl)/[(M - DCl) + (M - HCl) + (M - Cl)]\}10^2$.

It is apparent from the results shown in Table I that the two chlorides produced from I (Scheme I) eliminate different amounts of DCl. Further, the chlorides from

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[1] K. Biemann, "Mass Spectrometry, Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 144–151. See, though, H. E. Audier, H. Felkin, M. Fétizon, and W. Vetter, *Bull. Soc. Chim. France*, 3236 (1965).

[2] For a comprehensive review, see P. Natalis in "Mass Spectrometry," R. I. Reed, Ed., Academic Press Inc., New York, N. Y., 1965, p 379 ff. See also S. W. Staley and D. W. Reichard, *J. Am. Chem. Soc.*, 90, 816 (1968).

[3] For a review of early work see ref 1. For more recent reviews see J. M. Wilson, *Ann. Rept. Progr. Chem.* (Chem. Soc. London), **63**, 275 (1966); H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, p 110 ff. More recent publications with leading references are: W. M. Bryant, III, A. L. Burlingame, H. O. House, C. G. Pitt, and B. A. Tefertiller, *J. Org. Chem.*, **31**, 3120 (1966); H. E. Audier, M. Fétizon, H. B. Kagan, and J. L. Luche, *Bull. Soc. Chim. France*, 2297 (1967); V. I. Zarettskii, N. S. Wulfson, and V. G. Zaikin, *Tetrahedron*, 23, 3683 (1967); J.-L. Imbach, E. Doomes, N. H. Cromwell, H. E. Baumgarten, and R. G. Parker, *J. Org. Chem.*, **32**, 3123 (1967); M. Shamma and K. F. Foley, *ibid.*, **32**, 4141 (1967); L. Dolejš and V. Hanuš, *Collection Czech. Chem. Commun.*, **33**, 332 (1968).

[4] The diols were prepared following the procedure of J. G. Pritchard and R. L. Vollmer, *ibid.*, **28**, 1545 (1963). We are grateful to Professor C. G. Overberger for a sample of *d*,*l*-2,4-pentanediol.

[5] G. K. Helmkamp and B. F. Rickborn, *ibid.*, **22**, 479 (1957).

[6] Anchimeric assistance is not involved in this reaction; see H. B. Henbest and B. B. Millward, *J. Chem. Soc.*, 3575 (1960). Assistance through four-membered rings has been shown to be poor or nonexistent; see B. Capon, *Quart. Rev.* (London), **18**, 45 (1964).

[7] Unless otherwise specified all compounds are racemic mixtures. All deuterated compounds were found to be identical with authentic protium materials by vapor phase chromatography.

[8] This reaction is known to occur with retention of configuration; see C. E. Boozer and E. S. Lewis, *J. Am. Chem. Soc.*, **75**, 3182 (1953).

[9] W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman, and A. D. Scott, *J. Chem. Soc.*, 1252 (1937).