46 min, 2.2 g (30%). The yields were poorer when a mixture of benzene–V of 1:5 was used.

Major Adduct. Mixture of Pentacyclo[8.3.0.0^{2,8}.0^{3,7}.0^{9,11}]trideca-4(or 5),12-dienes (VI and XV): mass spectrum parent peak 170, other intense peaks at 155, 105, 104, 91, and 76; infrared spectrum (liquid film) 3020 (s), 2900 (vs), 1590 (w), 1345 (m), 826 (s), 786 (m), 730 (vs), and 710 (vs) cm^{-1}; ultraviolet spectrum (pentane) shoulder at 220 nm (ϵ 2000); nmr spectrum (CCl_4 solution), TMS as internal reference, see text.

Anal. Calcd for $C_{13}H_{14}$: C, 91.73; H, 8.29. Found: C, 91.45; H, 8.17.

Minor Adduct. Mixture of Pentacyclo[9.2.0.0^{2,9}.0^{3,7}.0^{6,8}]trideca-4,12-diene (XIIIa) and Pentacyclo[9.2.0.0^{3,10}.0^{4,8}.0^{7,9}]trideca-5,12-diene (XIIIb): mass spectrum parent peak 170, other intense peaks at 155, 129, 105, 104, 92, 91, 90, and 39; infrared spectrum (liquid film) 3030 (s), 2900 (vs) 1600 (w), 1350 (m), 855 (m), 775 (s), 752 (vs), and 732 (vs) cm^{-1}; ultraviolet spectrum (pentane) shoulder at 223 nm (ϵ 2080); nmr spectrum (CCl_4 solution), TMS as internal reference, see text.

Anal. Calcd for $C_{13}H_{14}$: C, 91.73; H, 8.29. Found: C, 91.80; H, 8.09.

Pyrolysis of the Major Adduct (VI and XV). The reaction was carried out in exactly the same way as the pyrolysis of IX except that the temperature was maintained at 230° for 90 min. The products were separated by preparative glc at 155°. VII (retention time 34 min) was collected as a colorless liquid (50%).

endo-**Tetracyclo[8.2.1.0^{2,6}.0^{7,13}]trideca-3,8,11-triene (VII)**: mass spectrum parent peak 170, other intense peaks at 155, 105, 104, 76, 75, and 39; infrared spectrum (liquid film) 3030 (s), 2860 (vs), 1600 (w), 1445 (m), 1350 (m), 848 (m), 830 (m), 743 (vs), 723 (vs), and 705 (s) cm^{-1}; ultraviolet spectrum (pentane) 230 nm (ϵ 240) 220 (1800), and 210 (6700); nmr spectrum (CCl_4 solution, TMS as internal reference) see Figures 2 and 3.

Anal. Calcd for $C_{13}H_{14}$: C, 91.73; H, 8.29. Found: C, 91.42; H, 8.19.

Acknowledgment. The author wishes to express his gratitude to the Air Force Office of Scientific Research (AFSC), U. S. Air Force, for Contract No. F 44620-72-C-0024 under which this work was carried out. He also thanks Dr. J. N. C. Hsu for many useful discussions.

Stereochemical Aspects of Ether Oxygen Participation. VIII. Kinetic, Polarimetric, and Deuterium Isotope Effect Analysis of Oxygen Lone-Pair Involvement during Solvolysis of 8-Oxabicyclo[3.2.1]octan-2-yl Derivatives[1]

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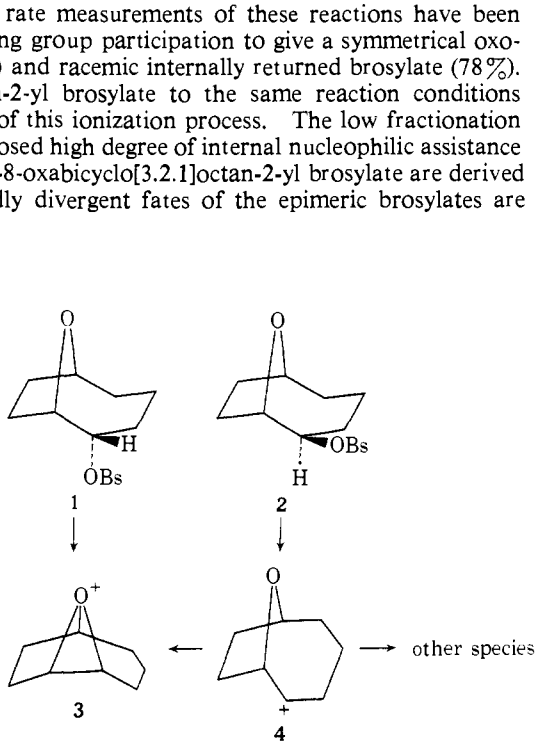
Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received April 12, 1972*

Abstract: Upon solvolysis in buffered acetic acid, *endo*-8-oxabicyclo[3.2.1]octan-2-yl brosylate gives rise uniquely to the corresponding endo acetate. The endo acetate arising from acetolysis of chiral endo brosylate, $[\alpha]_{365}^{25°}$ +54.7°, is completely racemic. Titrimetric and polarimetric rate measurements of these reactions have been made. These studies indicate the operation of R_2O-3 neighboring group participation to give a symmetrical oxonium ion which partitions itself between racemic acetate (22%) and racemic internally returned brosylate (78%). Subjection of (+)-*exo*-2-deuterio-*endo*-8-oxabicyclo[3.2.1]octan-2-yl brosylate to the same reaction conditions allows for the determination of the α-deuterium isotope effect of this ionization process. The low fractionation factor ($k_H/k_D = \sim 1.08$) is particularly compatible with the proposed high degree of internal nucleophilic assistance in the rate-determining step. The products of acetolysis of *exo*-8-oxabicyclo[3.2.1]octan-2-yl brosylate are derived exclusively from carbon skeletal rearrangement. The markedly divergent fates of the epimeric brosylates are discussed in the light of the above data.

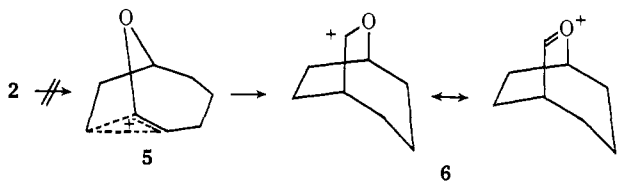
In an earlier paper of this series[3] it was shown that acetolysis of *endo*-9-oxabicyclo[4.2.1]nonan-2-yl brosylate (**1**) proceeds with direct intervention of oxonium ion **3**. Comparable solvolysis of **2** also results in appreciable formation of **3**, although stereochemical, kinetic, and product development considerations attest to the formation of **4** prior to covalent bonding of the neighboring oxygen atom in this instance.[3] The dominating influence of oxonium ion intervention in the [4.2.1] bicyclic series is reflected particularly in the almost complete lack of 1,2-carbon migration (*cf.* **5** and **6**), especially during ionization of **2**. These observations contrast with those reported by Martin and Barlett for hydrolysis of the isomeric 7-oxanorbornyl



(1) For part VII of this series, see L. A. Paquette and M. K. Scott, *J. Amer. Chem. Soc.*, **94**, 6760 (1972).

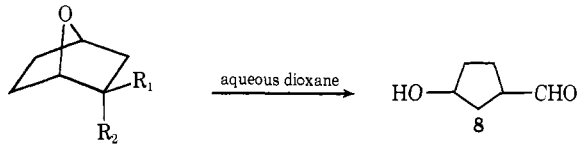
(2) American Chemical Society Petroleum Research Fund Graduate Fellow, 1968–1969; National Science Foundation Graduate Fellow, 1966–1968.

(3) L. A. Paquette and P. C. Storm, *J. Amer. Chem. Soc.*, **92**, 4295 (1970).



5 6

chlorides (**7a** and **7b**), where the product **8** is exclusively

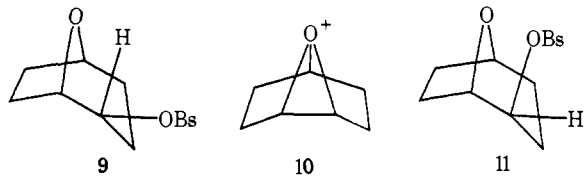


8

7a, $R_1 = Cl$; $R_2 = H$
b, $R_1 = H$; $R_2 = Cl$

that resulting from carbon framework rearrangement.[4] The purpose of this phase of our investigation was to obtain information about the carbonium ion systems intermediate between these two apparent extremes, *i.e.*, those derived from the epimeric 8-oxabicyclo[3.2.1]-octan-2-yl brosylates.

The endo epimer **9** was anticipated to undergo accelerated acetolysis directly to oxonium ion **10**. Be-



9 10 11

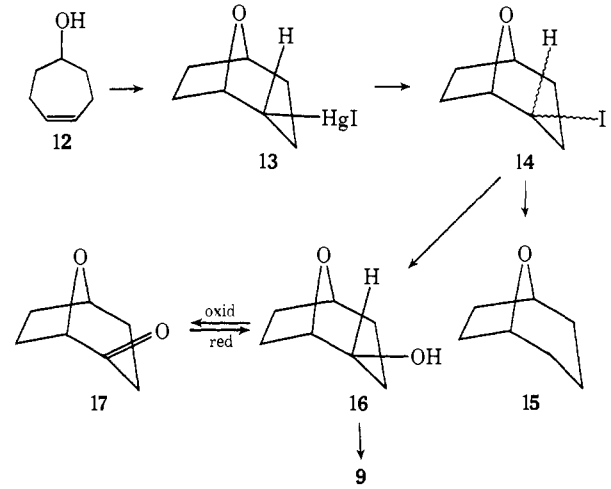
cause this intermediate species is symmetrical, internal return of brosylate ion, a prevalent process in the ionization of functionalized bicyclic ethers of this type,[3] would lead to no net reaction and thereby render unassessable the precise determination of the rate acceleration due to R_2O-3 participation. This difficulty may be circumvented, however, by making recourse to optically active **9**. In the present work, we have determined the titrimetric and polarimetric acetolysis rates of *rac*- and (+)-**9**, respectively, and in addition have elucidated the α-deuterium isotope effect of this reaction. These data establish that kinetic acceleration due to R_2O-3 participation in a relatively rigid system possessing an ideal stereoelectronic arrangement is appreciable.

The behavior of exo isomer **11** was less predictable. In view of the marked proclivity of the related carbocyclic system for 1,2 carbon migration,[5] some participation of this type was expected. The extent to which the proximate oxygen center could effectively deter this process by means of its inductive effect (as in **2**) was not immediately apparent.

Results

Synthetic Considerations. The readily accessible 4-cyclohepten-1-ol (**12**), obtained through reaction of 1-piperidinocyclopentene with acrolein followed by quaternization, hydroxide-promoted ring opening, and lead tetraacetate decarboxylation of the initially isolated bicyclic amino ketone,[6,7] proved to be a most serviceable precursor to both **9** and **11**. Oxymercuration of **12** with buffered mercuric acetate and subsequent iodide ion exchange afforded the stable crystalline bicyclic mercurial iodide **13**. The formation of an ether bridge in this step was substantiated by several lines of evidence. Firstly, neither hydroxyl nor carbonyl absorption was apparent in the infrared spectrum of **13**. Secondly, iodination of **13**[8] gave iodide **14**, lithium aluminum hydride reduction of which led uniquely to known ether **15**[9] (Scheme I).

Scheme I



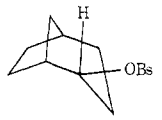
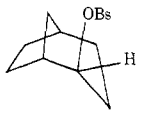
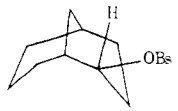
12 13 14 17 16 15 9

Acetolysis of iodide **14** followed by saponification produced alcohol **16** whose stereochemistry was subsequently found to be exclusively endo. Oxidation of **16** gave rise to ketone **17** of known structure,[10] thereby establishing that no new structural alterations had occurred. Sodium borohydride reduction of **17** in cold methanol produced chiefly (~90%) alcohol **16**, exo attack of hydride being heavily favored as observed also with its carbocyclic congener[11] and azalog.[12] Meerwein–Ponndorf–Verley reduction of **17** likewise gave rise to **16** as the almost exclusive isomer. Crystalline brosylate **9** was prepared in the customary manner.

The synthesis of **11** was achieved by means of the sequence outlined in Scheme II. Dehydrohalogenation of iodide **14** with potassium *tert*-butoxide in dimethyl sulfoxide led to volatile unsaturated ether **18** in good yield. Subsequent epoxidation of **18** with *m*-chloroperbenzoic acid afforded an 80:20 mixture of *exo*- and *endo*-2,3-epoxy-8-oxabicyclo[3.2.1]octanes (**19** and **20**). The two epoxides were separated by preparative vpc. Structural assignments were initially designated on the basis of kinetically favored exo attack on **18**[13] and were subsequently substantiated by their nmr spectra (see

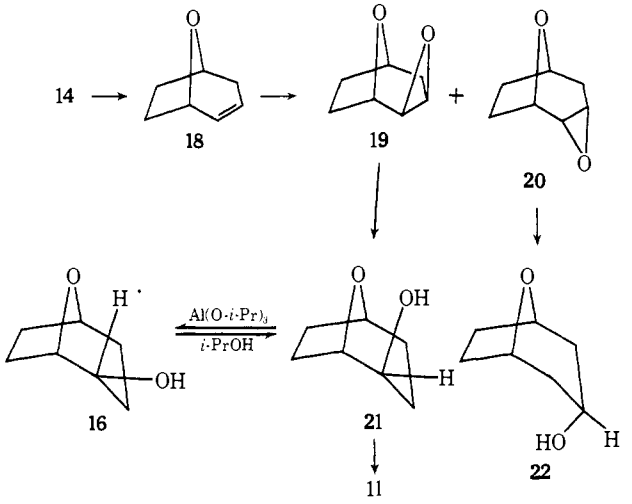
(4) J. C. Martin and P. D. Bartlett, *J. Amer. Chem. Soc.*, 79, 2533 (1957).
(5) H. L. Goering and G. N. Fickes, *ibid.*, 90, 2856, 2862 (1968).
(6) G. Stork and H. K. Landesman, *ibid.*, 78, 5129 (1956).
(7) A. C. Cope, C. H. Park, and P. Scheiner, *ibid.*, 84, 4862 (1962).
(8) (a) F. R. Jensen, L. H. Gale, and J. E. Rodgers, *ibid.*, 90, 5793 (1968); (b) F. R. Jensen and L. H. Gale, *ibid.*, 82, 148 (1960); (c) S. Winstein and T. G. Traylor, *ibid.*, 78, 2597 (1956); (d) for a review of this subject consult F. R. Jensen and B. Rickborn, "Electrophilic Substitution of Organomercurials," McGraw-Hill, New York, N. Y., 1968, Chapter 4.
(9) A. C. Cope, M. Gordon, S. Moon, and C. H. Park, *J. Amer. Chem. Soc.*, 87, 3119 (1965).
(10) W. A. M. Davies, A. R. Pinder, and J. G. Morris, *Tetrahedron*, 18, 405 (1962).
(11) A. A. Youssef, M. E. Baum, and H. M. Walborsky, *J. Amer. Chem. Soc.*, 81, 4709 (1959).
(12) M. R. Bell and S. Archer, *ibid.*, 80, 6147 (1958).
(13) For the behavior of a related azabicyclic system, see: (a) D. E. Ayer, J. Toth, P. Reynolds-Warnhoff, and D. M. White, *ibid.*, 80, 6146 (1958); (b) W. A. M. Davis, J. B. Jones, and A. R. Pinder, *J. Chem. Soc.*, 3504 (1960).

Table I. Acid Production Rates Arising from Acetolysis of **9**, **11**, and Related Compounds

Compound	T, °C	k, sec^{-1}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu	Ref
9	25.0	2.45×10^{-7} [a]	26.0	−1.6	
	50.00	8.01×10^{-6}			
	64.98	4.94×10^{-5}			
	70.0	8.94×10^{-5} [b]			
	79.96	2.71×10^{-4}			
11	25.0	1.65×10^{-8} [a]	28.2	+0.4	
	50.0	7.12×10^{-7} [a]			
	65.04	5.18×10^{-6}			
	70.0	9.75×10^{-6} [b]			
	79.97	3.30×10^{-5}			
	94.96	1.70×10^{-4}			
 23	48.9	1.0×10^{-5} [c]	27.1	+0.2	*d*
 24	49.3	1.2×10^{-4} [c]			*e*
1	50.05	3.47×10^{-5}	24.5	−3.1	*f*
2	50.05	2.42×10^{-6}	27.0	−0.8	*f*
 25	49.3	3.3×10^{-6} [c]			*g*

[a] Extrapolated values using activation parameters. [b] Interpolated values using activation parameters. [c] Values obtained by multiplication of the acetolysis rate constant of the corresponding tosylate by a factor of 3. [d] H. L. Goering and M. F. Sloan. *J. Amer. Chem. Soc.*, **83**, 1992 (1951). [e] H. L. Goering and G. N. Fickes, *ibid.*, **90**, 2848 (1968). [f] L. A. Paquette and P. C. Storm, *ibid.*, **92**, 4295 (1970). [g] M. Hanack, W. Kraus, W. Rothenwöhrer, W. Kaiser, and G. Wentrup, *Justus Liebigs Ann. Chem.*, **703**, 44 (1967).

Scheme II



Experimental Section) and vpc retention times (endo isomer **20** with the more hindered epoxide oxygen was eluted first). Reduction of this epoxide mixture with lithium aluminum hydride proceeded under the control of trans diaxial opening of the oxirane rings as expected. *exo*-8-Oxabicyclo[3.2.1]octan-2-ol (**21**) was isolated as the major product and *endo*-8-oxabicyclo-[3.2.1]octan-3-ol (**22**) as the less dominant alcohol. Pure **19** gave exclusively **21**. Equilibration of **21** by means of aluminum isopropoxide in isopropyl alcohol at 155° gave a mixture consisting of 62% of **16** and 38% of **21**.

Titrimetric Rate and Product Studies of Racemic Brosylates. Acetolysis of **9** in buffered acetic acid exhibited normal first-order kinetic behavior through a time corresponding to at least 3 half-lives (>93% reaction) at three different temperatures. Similar uncomplicated behavior was observed in the case of exo brosylate **11**. The pertinent kinetic data are summarized in Table I together with that for a number of related compounds included for comparison purposes. Values of the thermodynamic quantities $\Delta H^{\pm}$ and $\Delta S^{\pm}$ have also been mathematically derived. The titrimetric rate constants were calculated using a computer program for the least-squares treatment of the data applied to eq 1. The activation parameters and extrapolated

$$k = \left(\frac{1}{t}\right) \ln \left(\frac{[\mathrm{HOBS}]_{\infty} - [\mathrm{HOBs}]_0}{[\mathrm{HOBS}]_{\infty} - [\mathrm{HOBs}]_t}\right) \qquad (1)$$

rate constants were computed with the aid of the ACTENG computer program.[14] Endo brosylate **9** is seen to be more reactive than exo epimer **11** by a factor of 9 at 70° and by a factor of 15 at 25°.

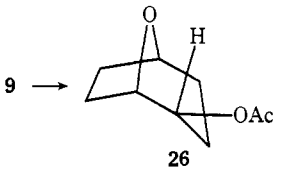
Preparative scale acetolysis of **9** for a time sufficient to achieve complete solvolysis afforded a quantitative yield of endo acetate **26**. Authentic **26** was available from acetylation of **16**. The observed retention of stereochemistry is compatible with the intervention of oxonium ion **10**. Since ion pair return from such an intermediate would regenerate only starting endo

(14) This program, initially developed by Professor D. F. Detar, was adapted for use with the Wang system in these laboratories by Michael Epstein.

Table II. Polarimetric and Titrimetric First-Order Rate Constants for Acetolysis of *endo*-8-Oxabicyclo[3.2.1]octan-2-yl Brosylates (0.1 *M* NaOAc in HOAc)

Starting ester	*T*, °C	Rate	Rate constant, sec^{-1}	Other
(±)-**9**	50.00 ± 0.03	Titrimetric	$k_{t\text{-H}} = (8.01 \pm 0.09) \times 10^{-6}$	$\frac{k_{\alpha\text{-H}}}{k_{t\text{-H}}} = 4.64$
(+)-**9**	50.04 ± 0.1	Polarimetric	$k_1 = k_{\alpha\text{-H}} = (3.72 \pm 0.03) \times 10^{-5}$	
(+)-**37**	50.04 ± 0.1	Polarimetric	$k_{\alpha\text{-D}} = (3.56 \pm 0.03) \times 10^{-5}$ $k_4 = (3.46 \pm 0.03) \pm 0.03) \times 10^{-5}$	$\frac{k_H}{k_D} = \frac{k_1}{k_4} = \sim 1.08$
(+)-**23**	48.86	Polarimetric	$k = 4.7 \times 10^{-5}$ [a]	

[a] Value obtained by multiplying tosylate rate constant by 3 [H. L. Goering and G. N. Fickes, *J. Amer. Chem. Soc.*, **90**, 2848 (1968).

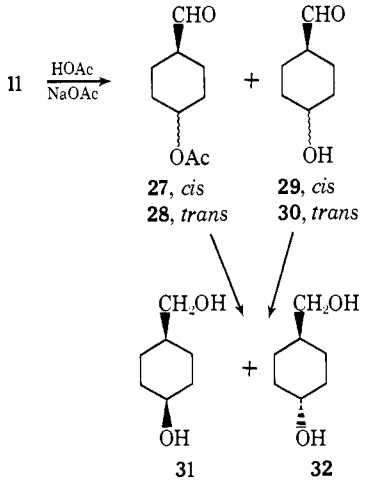


26

brosylate, the first-order kinetic plots for disappearance of **9** do not exhibit curvature of the type frequently encountered in related oxygen-containing systems.[1,3]

When a solution of brosylate **11**, an excess of sodium acetate, and anhydrous acetic acid was refluxed for 10 half-lives, a mixture of four products was obtained in 95% yield. While the first two of these (**27** and **28**, 58%) were readily extracted from aqueous solution with ether, the remaining two (**29** and **30**, 42%) could be isolated only by continuous ether extraction. The four products were identified by means of their nmr and mass spectra, conversion to 2,4-dinitrophenylhydrazones, and by reduction to the known[15] *cis*- and *trans*-4-hydroxymethylcyclohexanols (**31** and **32**). Of these latter

Scheme III

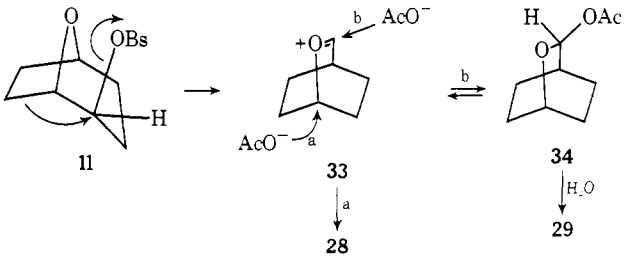


31 **32**

compounds, *trans*-diol **32** was identified by its melting point[15] and that of its bistosylate,[15a,c] while *cis*-diol **31** was characterized as its bistosylate.[15a] From these data, it is apparent that the acetolysis of **11** proceeds exclusively with skeletal rearrangement. Presumably oxonium ion intermediate **33** is involved in the product-forming step (see Scheme IV). Ring opening of **33** by path a is undoubtedly much less favored than path b. However, the likely reversibility of path b under the solvolysis conditions could allow a substantial amount of product to arise *via* path a. Epimerization of the

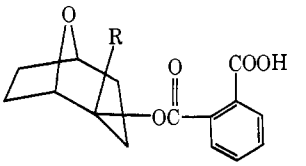
(15) (a) L. N. Owen and P. A. Robins, *J. Chem. Soc.*, 326 (1949); (b) H. Pines, H. G. Rodenberg, and V. N. Ipatieff, *J. Amer. Chem. Soc.*, 76, 771 (1954); (c) S. F. Birch, R. A. Dean, N. J. Hunter, and E. V. Whitehead, *J. Org. Chem.*, 22, 1590 (1957); (d) H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959).

Scheme IV



initially formed aldehydes, either during the reaction or during work-up, accounts for the cis–trans mixtures isolated.

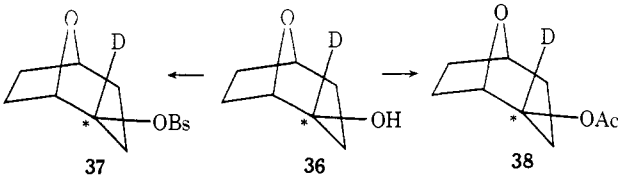
Preparation of Optically Active 9 and 9-*2-d*. The synthesis of chiral **9** began with the conversion of alchol **16** to its acid phthalate (**35**, R = H). Treatment



35, R = H, D

of **35** with (−)-cinchonidine and fourfold fractional recrystallization produced a salt of mp 169–171.5° which yielded an acid phthalate of $[\alpha]^{25}_{365}$ +63.7° ($CHCl_3$). Alkaline hydrolysis of resolved ester afforded (+)-**16**, $[\alpha]^{25}_{365}$ 51.0° ($CHCl_3$), which when treated with *p*-bromobenzenesulfonyl chloride in pyridine gave (+)-**9**, $[\alpha]^{25}_{365}$ +50° ($CHCl_3$ or HOAc).

Reduction of **17** with sodium borodeuteride produced a mixture of monodeuterated **16** (90%) and **21** (10%). Although this mixture could be separated readily by preparative vpc, it proved more economical to convert the mixture directly to crude acid phthalate **35**-*d*. Resolution was effected as above to give cinchonidine salt of mp 168.5–170.5°, from which (+)-**35**-*d*, $[\alpha]^{25}_{365}$ 68.7°, was subsequently derived. Saponification of the half-ester gave **36**, $[\alpha]^{25}_{365}$ +52.7°, from which brosylate **37**, $[\alpha]^{25}_{365}$ +54.7°, and acetate **38**, $[\alpha]^{25}_{365}$ +76.4°, were readily synthesized.

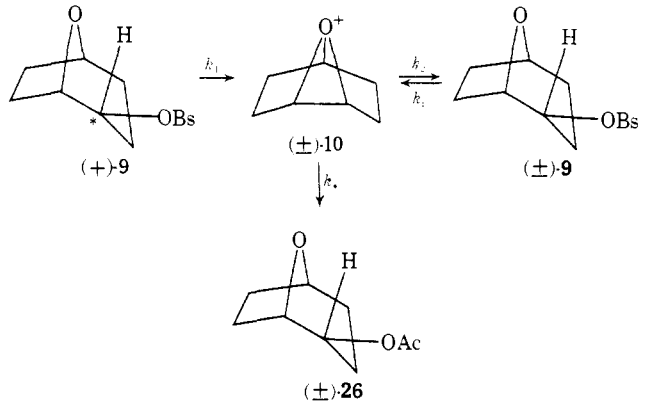


Polarimetric Rate Studies. The first-order polarimetric rate constant for acetolysis of (+)-**9** in 0.1 *M* sodium acetate–glacial acetic acid at 50° is given in Table II. The racemization rates were determined at

the 365-nm line of mercury and are the averages of at least two individual determinations. No unusual trends in the rate constants were observed. Rotations could be easily measured to 0.002° and thus the reactions could be followed with good precision as reflected in the small average standard deviations. Significantly, chiral (+)-endo acetate (in actuality, **38** was employed) proved to be optically stable under the reaction conditions.

Analysis of the solvolytic behavior of *endo*-8-oxabicyclo[3.2.1]octan-2-yl brosylate can now be substantially refined and in fact actually segmented into three rate constants, k_1, k_2, and k_3 (see Scheme V). The

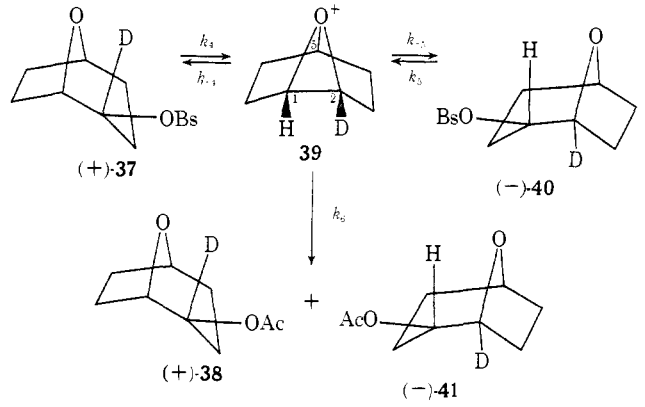
Scheme V



experimental polarimetric rate constant determined for (+)-**9** ($k_{\alpha\text{-H}}$) is a direct quantitative assessment of k_1 (the rate constant for formation of intermediate **10** which is, at least on the average, symmetrical) and the true kinetic measure of R_2O participation in this system. Since the experimental titrimetric rate constant ($k_{t\text{-H}}$) derived from (±)-**9** equals $k_{\alpha\text{-H}}k_3/(k_2 + k_3)$ and the $k_{\alpha\text{-H}}/k_{t\text{-H}}$ ratio equals 4.64, it follows that $k_2/k_3 = 3.64$. Thus, intermediate oxonium ion **10** reacts under the stipulated conditions to yield 22% of the product of acetolysis [(+)-**26**] and 78% of returned racemic *endo*-brosylate **9**.

The presence of a deuterium atom in *endo*-brosylate (+)-**37** imparts an asymmetry to the derived oxonium ion (**39**, see Scheme VI) that introduces an added

Scheme VI



parameter to the polarimetric kinetics. For (+)-**37**, the rate constant required to achieve a direct measure of the α-deuterium isotope effect is k_4. However, oxonium ion **39** is partitioned between stable acetate products [(+)-**38** and (−)-**41**] and reactive brosylates [(+)-**37** and (−)-**40**], both pairs of compounds having net optical activity as a consequence of the partition factor arising from the presence of the deuterium atom. In entirely expected fashion, (+)-**37** and (−)-**40** experience ionization at somewhat different rates such that as reaction progresses the instantaneous rate constant for loss of optical activity will be subject to slight variation. In fact, plots of ln α *vs.* *t* were linear within experimental error through about 1 half-life, after which slight curvature became apparent. The results derived from a least-squares treatment of polarimetric behavior during the first half-life afforded a rate constant whose value was reduced by merely 3% when these complications were included in the mathematical model as outlined below.

The acetate product (**38** and **41**) isolated after complete solvolysis of (+)-**37** was found to be levorotatory, $[\alpha]^{25}_{365}$ −2.5°, corresponding to 3.3% net inversion.[16] Accordingly, oxonium ion **39** exhibits a 1.068:1 preference for attachment of acetate to the unlabeled site (C-1). The plausible assumption that brosylate anion exhibits the same partition factor in its reaction with **39** gives $k_5/k_{-4} = 1.068$ or $k_{-4} = 0.94k_{-5}$. We then assign k_{-5} as equal to $k_2/2$ (see Scheme V) and $k_6 = {}^1/_2(1 + 0.94)k_3$. This yields the ratio $k_{-4}:k_{-5}:k_6 = 0.94:1.00:0.97$.

The observed rotation during solvolysis can be expressed as the sum of the products of the individual molar rotations and concentrations of **37**, **38**, **40**, and **41**; differentiation with respect to time gives eq 2. The

$$\frac{d\alpha}{dt} = [M_{37}]\frac{d[\mathbf{37}]}{dt} + [M_{40}]\frac{d[\mathbf{40}]}{dt} + [M_{\text{acetates}}]\frac{d[\text{acetates}]}{dt} \quad (2)$$

relationships expressed by eq 3 and 4 and their incorporation in eq 2 afford eq 5. Application of the

$$[M_{37}] = -[M_{40}] \quad (3)[16]$$

$$\frac{[M_{\text{acetates}}]}{[M_{37}]} = -\frac{2.5°}{54.7°}\frac{171}{348} = -0.022 \quad (4)$$

$$\frac{1}{[M_{37}]}\frac{d\alpha}{dt} = \frac{d[\mathbf{37}]}{dt} - \frac{d[\mathbf{40}]}{dt} - 0.022\frac{d[\text{acetates}]}{dt} \quad (5)$$

steady-state approximation to oxonium ion **39** (d[**39**]/d*t* = 0) permits derivation of expression for d[**37**]/d*t*, d[**40**]/d*t*, and d[acetates]/d*t*. Substitution of these into eq 5 and simplification give eq 6. At $t = 0$, the values

$$\frac{d\alpha}{dt} = -1.03k_4[M_{37}][\mathbf{37}] + 0.97k_5[M_{37}][\mathbf{40}] \quad (6)$$

for [**40**] and [acetates] equal zero; hence, $\alpha = [M_{37}][\mathbf{37}]$ and

$$\left[\frac{d\alpha}{dt}\right]_0 = -1.03k_4(\alpha) \quad (7)$$

The initial linearity of plots of ln α *vs.* *t* allows a refined estimate of k_4 which, as indicated by eq 7, differs by only 3% from the unrefined polarimetric rate constant.

The small isotope effect on ionization caused by C-2 deuteration of chiral *endo*-8-oxabicyclo[3.2.1]octan-2-yl brosylate [(+)-**37**] ($k_H/k_D = \sim 1.08$) is consistent with

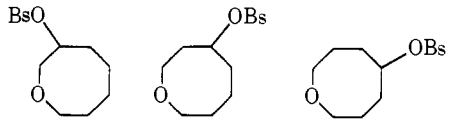
(16) In this and all such ensuing calculations, it has been necessary to neglect any possible variations in magnitude of optical rotation attributable to the position of deuterium.

a solvolysis mechanism involving rate limiting formation of oxonium ion **10**.[17] Such R_2O-3 participation imparts substantial SN2 character to the reaction and does away with the need of $sp^3 \rightarrow sp^3$ rehydridization at the seat of reaction. Despite this high degree of internal nucleophilic assistance in the rate-determining step, however, the oxabicyclic experiences ionization somewhat more slowly than its all-carbon analog (Tables I and II) owing to the undiminished nature of the adverse inductive and dipolar field effects of this electronegative atom under such circumstances.

Discussion

Examination of the solvolytic behavior of **9** and **11** has provided significant information on the role played by neighboring ether oxygen during heterolytic bond cleavage reactions of this type. Availability of the chiral endo derivative (+)-**9**, for example, has permitted establishment of the fact that oxonium ion **57** suffers internal return of brosylate ion some four times faster than solvent capture. As a result, the titrimetric rate constant for acetolysis of **9**, as expected, is not a realistic measure of R_2O-3 participation, a better value arising instead directly from the polarimetric rate data obtained with (+)-**9**.

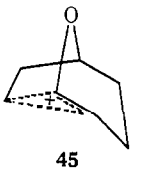
Notwithstanding the fact that oxonium ion intermediate **10** is formed directly under conditions of kinetic control, (+)-**9** is seen to ionize at a slightly slower rate than **23**. These data clearly reflect the significant rate-retarding inductive and dipolar field effects of the proximate oxygen atom. The observed rate in actuality represents a counterbalancing of these adverse influences and the positive rate acceleration arising from anchimeric assistance. To dissect accurately such contributing factors is at best complex at the present time. A recent case in point may be found in the oxocanyl series (**42**–**44**)[1,18] Although both **42**



	42	**43**	**44**
rel rate (70°)	1	10	48,500

and **44** give evidence of experiencing solvolysis by respective R_2O-3 and R_2O-5 participation pathways, the relative rate of acetolysis of **42** attests to the importance of negative kinetic contributions arising from inductive and dipolar forces. These conclusions receive added support from the behavior of **43**; although transannular oxygen participation is nonoperative at the transition state of the rate-determining ionization in this instance, ionization occurs ten times faster than for **42**, and **43** itself is not entirely devoid of nonbonded interactions as revealed by its sevenfold slower acetolysis rate relative to cyclooctyl tosylate.[1]

It is necessary only to compare the rates of acetolysis of **11** and **24** (Table I) to see that the effects unfavorable to ionization persist also in the exo series. Although both bicyclic systems show a high propensity for Wagner–Meerwein shift, the oxa derivative **11** undergoes solvolysis some 100 times more slowly than **24** showing that in **45** the heteroatom is electronically in-



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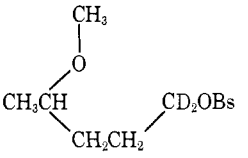
hibiting the 1,2 shift. Interestingly, this skeletal rearrangement operates to the apparent exclusion of alternative possible pathways. Intrinsically, therefore, the *exo*-8-oxabicyclo[3.2.1]octan-2-yl system seems more closely allied to norbornane derivatives of related type[4] than to higher structural homologs.[3]

The α-deuterium isotope effect derived from the kinetic behavior of (+)-**37** provides convincing evidence for the incursion of minimal bond order change at C-2 during solvolysis of this endo derivative, particularly since the entire α effect is expected to be associated with the generation of ion **39**.[19] The experimentally derived fractionation factor (k_H/k_D = ~1.08) is somewhat larger than that experienced by **46** (k_H/k_D = 1.01),[19] a



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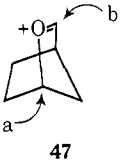
molecule which otherwise does not suffer from detractive electronic and strain effects.

Lastly, it is apparent that solvent attack on rearranged oxonium ion **33** results in appreciable bonding at position a with attendant ring opening. While the present data give no information concerning the relative efficiencies of acetate bonding at the two possible sites (a and b), it is clear that oxonium ions such as **3** and **10** do not share this propensity for multisite solvent capture. This is in line with expectation, since formation of epoxides in the latter cases would certainly be more highly endothermic than the alternative pathways which regenerate the particular oxabicylic nucleus. Unfortunately, since Martin and Bartlett[4] examined the solvolytic behavior of **7a** and **7b** only in 80% ethanol and 50% dioxane, the possible operation of multiple-site reactivity in ion **47** was masked to them. On the basis



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of the present results, however, we would expect that the two reactions in question also operate competitively in this intermediate.

Experimental Section

Melting points are corrected. Proton magnetic resonance spectra were obtained with a Varian A-60A spectrometer and apparent coupling constants are cited. Elemental analyses were

(17) C. J. Collins and N. S. Bowman, Ed., "Isotope Effects in Chemical Reactions," Van Nostrand-Reinhold, New York, N. Y., 1971, particularly p 179.

(18) L. A. Paquette, R. W. Begland, and P. C. Storm, *J. Amer. Chem. Soc.*, **92**, 1971 (1970).

(19) K. Humski, R. Malojcic, S. Borcic, and D. E. Sunko, *ibid.*, **92**, 6534 (1970).

performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

8-Oxabicyclo[3.2.1]octan-2-ylmercuric Iodide (13). To a well-stirred solution containing 47.8 g (0.15 mol) of mercuric acetate and 20.4 g (0.15 mol) of sodium acetate hydrate in 150 ml of water was added 16.8 g (0.15 mol) of 4-cyclohepten-1-ol (**12**)[7] over a 15-min period. This solution was stirred for an additional 15 min, at which time a solution containing 33.2 g (0.20 mol) of potassium iodide and 6.0 g (0.15 mol) of sodium hydroxide in 150 ml of water was added dropwise. The precipitated product was filtered, washed with 25 ml of water, and air-dried to give 69 g (>100%) of crude solid. Recrystallization of this material from methanol afforded **13** as white platelets, mp 133–134°.

Anal. Calcd for $C_7H_{11}HgIO$: C, 19.16; H, 2.53. Found: C, 18.94; H, 2.22.

2-Iodo-8-oxabicyclo[3.2.1]octane (14). A mixture of 3.5 g (8.0 mmol) of **13** and 2.2 g (8.0 mmol) of iodine in 50 ml of carbon tetrachloride was stirred overnight at ambient temperature. The solution was filtered, decolorized with aqueous sodium thiosulfate, dried, and concentrated to give 1.8 g (94%) of **14**. Because of its lability, this iodide was not further purified: $\delta_{TMS}^{CCl_4}$ 4.2–4.7 (m, 3, H-1, -2, -5) and 1.2–2.6 (m, 8, H-3, -4, -6, -7).

8-Oxabicyclo[3.2.1]octane (15). A solution containing 1.8 g (8.0 mmol) of **14** dissolved in 10 ml of anhydrous ether was added dropwise to a slurry of 0.4 g (10 mmol) of lithium aluminum hydride in 40 ml of ether, and the mixture was stirred overnight. After work-up in the usual manner, the resulting oil was distilled to give 0.35 g (41%) of **15** as a waxy solid: bp 58–60° (20 mm); mp 45–46° (lit.[9] mp 46.5–47°); $\delta_{TMS}^{CCl_4}$ 4.1–4.4 (m, 2, H-1, -5) and 1.1–2.1 (m, 10, CH_2).

endo-**8-Oxabicyclo[3.2.1]octan-2-ol (16).** A solution containing 33.2 g (0.15 mol) of **14** and 45.0 g (0.45 mol) of potassium acetate in 200 ml of water was heated at reflux overnight. After the solution had cooled, 8.0 g (0.14 mol) of potassium hydroxide was added and the heating was resumed for 24 hr. The cooled solution was extracted with dichloromethane and the combined organic layers were dried and concentrated to give 16.5 g (92%) of crude alcohol. Sublimation gave **16** as a very hygroscopic white solid: mp 93–95°; $\delta_{TMS}^{CCl_4}$ 3.9–4.4 (m, 3, H-1, -5, and OH), 3.4–3.8 (m, 1, H-2), and 1.1–2.2 (m, 8, CH_2).

The *p*-nitrobenzoate of **16** was obtained from ether–pentane as pale yellow crystals, mp 130–131°.

Anal. Calcd for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.53; H, 5.49; N, 5.05.

8-Oxabicyclo[3.2.1]octan-2-one (17). A solution containing 15.0 g (0.12 mol) of **16** in 400 ml of acetone was treated with chromic acid solution. Work-up in the usual manner gave 10.0 g (66%) of **17**: bp 96–99° (14 mm) [lit.[10] bp 89° (13 mm)]; $\nu_{max}^{CCl_4}$ 1725 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 4.3–4.6 (m, 1, H-1), 3.9–4.2 (m, 1, H-5), and 1.3–2.6 (m, 8, CH_2).

The 2,4-dinitrophenylhydrazone was obtained from ethanol-ethyl acetate as yellow crystals, mp 202–204° [lit.[10] mp 207° (from benzene–ethanol)].

Anal. Calcd for $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 50.76; H, 4.68; N, 18.29.

Borohydride Reduction of 17. A solution of 2.5 g (0.02 mol) of **17** in 75 ml of absolute methanol at ice temperature was treated with 3.8 g (0.10 mol) of sodium borohydride in small portions. After being stirred overnight at room temperature, the solution was diluted with 75 ml of water, stirred for an additional 60 min, and extracted with dichloromethane. The combined extracts were dried, concentrated, and sublimed to give 2.3 g (90%) of **16**, mp 93–95°.

Meerwein–Ponndorf–Verley Reduction of 17. A solution containing 2.5 g (0.02 mol) of **17** and 4.0 g (0.02 mol) of aluminum isopropoxide in 25 ml of dry isopropyl alcohol was heated overnight at reflux. The solution was then slowly distilled until the distillate failed to give a positive 2,4-DNPH test whereupon it was concentrated *in vacuo*. The residue was treated with 30 ml of 1 *N* hydrochloric acid solution and extracted with dichloromethane. The combined extracts were dried, concentrated, and sublimed to give 2.5 g (100%) of **16**, mp 92–94°.

endo-**8-Oxabicyclo[3.2.1]octan-2-yl *p*-Bromobenzenesulfonate (9).** A solution of 15.3 g (0.06 mol) of *p*-bromobenzenesulfonyl chloride dissolved in 40 ml of cold pyridine was added to a solution of 3.8 g (0.03 mol) of **16** in 20 ml of cold pyridine, and the resulting solution was allowed to stand at 5° overnight. Ice was added, followed by 50 ml of water. This solution was extracted with two 50-ml portions of ether. The combined extracts were repeatedly washed with 25-ml portions of cold 1 *N* hydrochloric acid until the wash remained acidic. The ether layer was washed with 25 ml of a 5% sodium carbonate solution, dried, and concentrated to give 9.5 g (92%) of crude brosylate. Recrystallization of this solid from ether–hexane afforded **9** as white crystals, mp 94.5–95.5°.

Anal. Calcd for $C_{13}H_{15}BrO_4S$: C, 44.96; H, 4.35; S, 9.24. Found: C, 45.07; H, 4.46; S, 9.25.

8-Oxabicyclo[3.2.1]oct-2-ene (18). A stirred, ice-cooled solution of 25.7 g (0.108 mol) of **14** in 250 ml of anhydrous dimethyl sulfoxide (distilled directly from calcium hydride into the reaction vessel) was treated portionwise during 25 min with 24.7 g (0.22 mol) of potassium *tert*-butoxide under dry nitrogen. The rate of addition was such as to maintain the temperature of the mixture at 15–20°. An immediate blackening was observed. Upon completion of the addition, the mixture was allowed to warm to room temperature and stirred for 14.5 hr. At this time, it was poured into 750 ml of ice water and extracted with pentane. The combined organic layers were washed with 250 ml of saturated brine, dried, and carefully distilled through a short Vigreux column. The residue was fractionated under reduced pressure to give 5.70 g (48%) of **18**, bp 92–97° (90 mm), as a colorless liquid, 96–98% pure by vpc analysis. An analytical sample was obtained by preparative vpc purification: $\delta_{TMS}^{CDCl_3}$ 5.3–6.2 (m, 2, olefinic), 4.2–4.9 (m, 2, H-1, -5), and 1.4–3.0 (m 6, CH_2).

Anal. Calcd for $C_7H_{10}O$: C, 76.33; H, 9.15. Found: C, 75.99; H, 9.26.

***exo*- and *endo*-2,3-Epoxy-8-oxabicyclo[3.2.1]octanes (19 and 20).** A solution of 6.3 g (*ca.* 40% excess) of *m*-chloroperbenzoic acid (89% by titration) in 70 ml of dichloromethane was added during 15 min to a stirred, ice-cooled solution of 2.93 g (0.0266 mol) of **18** in 15 ml of dichloromethane. The mixture was allowed to stand overnight at room temperature, the precipitated *m*-chlorobenzoic acid was filtered, and the clear filtrate was washed with 50 ml of 20% aqueous sodium bisulfite, 80 ml of saturated aqueous sodium bicarbonate, and 50 ml of brine solutions. The dried dichloromethane solution gave 3.07 g (91%) of crude epoxides on evaporation.

Vpc analysis (10% SE-30 or 10% FFAP on Chromosorb G) of this mixture showed the presence of a more rapidly eluting minor component (20%) and a major product (80%). The substances were separated by preparative vpc on these columns.

The major product, identified as **19**, was obtained as a very deliquescent, low-melting solid: $\delta_{TMS}^{CDCl_3}$ 4.0–4.5 (partially coalesced, br s and t, 2, H-1, -5), 2.8–3.2 (m, 2, H-2, -3), and 1.2–2.5 (m, 6, CH_2).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.59; H, 8.06.

The minor component, identified as **20**, was likewise a very deliquescent, low-melting solid: $\delta_{TMS}^{CDCl_3}$ 4.45–4.7 (t, J = 5 Hz, 1, H-1), 4.05–4.35 (t, J = 5 Hz, 1, H-5), 3.25–3.5 (t, J = 5 Hz, 1, H-2), 3.0–3.25 (t, J = 5 Hz, 1, H-3), and 1.2–2.4 (m, 6, CH_2).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.41; H, 8.12.

***exo*-8-Oxabicyclo[3.2.1]octan-2-ol (21) and *endo*-8-Oxabicyclo-[3.2.1]octan-3-ol (22).** A solution of 3.05 g (0.0242 mol) of the epoxide mixture in 125 ml of anhydrous ether was added during 12 min to an ice-cold, stirred suspension of 0.85 g (0.0224) mol) of lithium aluminum hydride in 60 ml of the same solvent. The mixture was allowed to warm to room temperature and then stirred for 20 hr, cooled, and treated successively with 0.85 ml of water, 0.85 ml of 15% aqueous sodium hydroxide solution, and 2.55 ml of water. The granular solid was filtered and washed thoroughly with ether. The combined organic layers were dried and evaporated to a colorless, mobile oil (2.84 g). Preparative vpc on a 1/4 in. × 5.5 ft column of 10% FFAP on Chromosorb G at 180° gave 1.68 g (54%) of **21** and 0.365 g (11.8%) of **22**.

The major, more rapidly eluting alcohol **21** was a very deliquescent white solid which melted at 75–78°, with softening occurring 20° lower: $\delta_{TMS}^{CDCl_3}$ 4.0–4.5 (br, 2, H-2 and OH), 3.25–3.4 (br, 1, H-1), 2.8–3.2 (br, 1, H-5), and 1.0–2.3 (m, 8, CH_2). This compound was characterized as its brosylate **11** which was obtained as colorless needles, mp 113–114°, from ether–hexane.

Anal. Calcd for $C_{13}H_{15}BrO_4S$: C, 44.97; H, 4.35; S, 9.23. Found: C, 44.99; H, 4.44; S, 9.25.

The minor component **22** was again a very deliquescent white solid: ν_{max}^{neat} 3250 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.1–4.4 (m, 2, H-1,5), 3.9–4.1 (br, 1, H-3), 3.40 (br, 1, OH), and 0.8–2.6 (m, 8). This alcohol gave a crystalline brosylate, mp 118–120° dec.

Hydride Reduction of 19. A solution of 108 mg (0.86 mmol) of pure **19** in 3 ml of anhydrous ether was added to an ice-cold, stirred suspension of 50 mg (1.3 mmol) of lithium aluminum hydride in 2

ml of the same solvent. The mixture was allowed to stir at room temperature for 21 hr, and work-up as above gave 103 mg (94%) of a colorless gum which was shown by vpc methods to contain only exo alcohol **21** and a small amount of unchanged epoxide.

Equilibration of 16 and 21. A mixture of 61.8 mg (0.482 mmol) of **21**, 310 mg (1.52 mmol) of aluminum isopropoxide, and 0.005 ml of acetone in 3 ml of anhydrous isopropyl alcohol was heated in a sealed tube at 155° for 70 hr. After cooling, the contents of the tube were dissolved in the minimum amount of 3 *N* hydrochloric acid (*ca.* 2.5 ml), and the solution was diluted with 5 ml of water and 10 ml of saturated aqueous sodium chloride solution and extracted with dichloromethane (4 × 10 ml). Evaporation of the combined dried extracts gave 59.0 mg (95% recovery) of a yellow oil shown by vpc analysis to contain 39% of **21** and 61% of **16**.

A second tube containing a similar mixture was heated at 155° for 315 hr and gave upon work-up a mixture containing 37% of **21** and 63% of **16**.

The *endo*-alcohol **16** from the combined equilibrations was isolated by preparative vpc (the 10% FFAP column, 175°) and gave the corresponding brosylate **9**, mp 94.5–95.5°, after two recrystallizations from ether–hexane. The melting point was undepressed on admixture with an authentic sample.

Titrimetric Kinetic Procedure. Anhydrous acetic acid was prepared by refluxing a solution of acetic anhydride in glacial acetic acid overnight and subsequent fractional distillation in a dry atmosphere. Standard 0.02 *M* perchloric acid in acetic acid was prepared by dilution of an accurately weighed quantity of standard 70% perchloric acid with anhydrous acetic acid to a known volume. Sodium carbonate which had been heated over an open flame and cooled in a desiccator was accurately weighed and diluted to a known volume with anhydrous acetic acid to prepare the standard 0.1 *N* sodium acetate solution; the water of neutralization was not removed.

A 0.06 *M* solution of brosylate in the sodium acetate solution was prepared. Aliquots of this solution (*ca.* 1.1 ml) were sealed in glass ampoules and immersed simultaneously in a constant-temperature bath. After 10 min, one ampoule was removed, an accurate timer started, and the ampoule quickly cooled in an ice–water bath. The ampoule was then placed in a water bath at 20° for 4 min. Exactly 0.923 ml (for endo brosylate) or 0.927 ml (for exo brosylate) of solution was removed by means of an automatic pipet, treated with 1 drop of a saturated solution of Bromophenol Blue indicator in acetic acid, and titrated with standard perchloric acid using a Fisher Accumet pH meter and microprobe combination electrode to determine potentiometrically the end point. The remaining ampoules were removed at appropriate intervals, cooled, and titrated as before. In each run, one ampoule was allowed to remain in the oil bath for a period of at least 10 half-lives. The sample was then titrated to give the infinity titer. In all runs, the infinity titers corresponded to calculated values within 3% of the total sodium acetate consumed. Duplicate runs were conducted at each temperature.

Acetolysis of (±)-9. A solution containing 3.4 g (10.0 mmol) of (±)-**9** and 0.90 g (8.5 mmol) of anhydrous sodium carbonate in 55 ml of acetic acid was stirred overnight at 80°. The solution was cooled, diluted with 150 ml of ice water, and extracted with three 100-ml portions of ether. The combined extracts were washed with aliquots of a saturated sodium bicarbonate solution until neutral, dried, and concentrated to afford 1.8 g (100%) of an oil whose vpc retention time and nmr spectrum were superimposable upon those of authentic **26**.

***endo*-8-Oxabicyclo[3.2.1]octan-2-yl Acetate (26).** A solution containing 250 mg (2.0 mmol) of **16** and 300 mg (3.0 mmol) of acetic anhydride dissolved in 240 mg (3.0 mmol) of pyridine was allowed to stand at room temperature overnight. Ice was added and the mixture was extracted with ether. The combined extracts were washed with cold 1 *N* hydrochloric acid and saturated sodium bicarbonate solutions, dried, and evaporated. The 300 mg (90%) of crude product so obtained was purified by preparative vpc to give **26**, a colorless liquid: $\delta_{TMS}^{CDCl_3}$ 4.6–5.0 (m, 1, H-2), 4.1–4.4 (m, 2, H-1, -5), and 1.2–2.3 (m, 11, methylenes and C*H*$_3$).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51: H, 8.29. Found: C, 63.34; H, 8.22.

Acetolysis of 11. A solution of 3.47 g (10.0 mmol) of **11** and 0.90 g (8.5 mmol) of anhydrous sodium carbonate in 55 ml of anhydrous acetic acid was heated at 95° for 63,000 sec (*ca.* 15 half-lives). The cooled solution was diluted with 350 ml of water and neutralized by addition of sodium carbonate and finally sodium bicarbonate. The resulting mixture was continuously extracted with ether for 42 hr under nitrogen. Upon evaporation, the dried extracts gave 1.47 g of a pale yellow oil. Vpc analysis of this product (1/4 in. × 6 ft 10% FFAP on Chromosorb G) showed it to contain two components: A (shorter retention time), 58%, and B, 42%.

Component A reduced Fehling's solution and gave a precipitate with 2,4-dinitrophenylhydrazine in 1:1 85% phosphoric acid–ethanol: ν_{max}^{neat} 2740, 1730, and 1250 cm^{-1}; mass spectrum, M$^+$ 170 as required for $C_9H_{14}O_3$; $\delta_{TMS}^{CCl_4}$ 9.6 (br s, 1, CHO), 4.5–5.1 (br m, 1, H-4), and 1.2–2.6 (complex pattern, 12). The complexity of the spectrum was indicative of a mixture. The 2,4-dinitrophenylhydrazone was obtained as lemon-yellow needles: mp 150–153° dec; ν_{max}^{Nujol} 1730 cm^{-1}; *m/e* calcd, 350.1226; found, 350.1219.

Anal. Calcd for $C_{15}H_{18}N_4O_6$: C, 51.43; H, 5.18; N, 15.99. Found: C, 51.22; H, 5.16; N, 15.84.

Component B likewise reduced Fehling's solution and gave a precipitate with 2,4-dinitrophenylhydrazine: ν_{max}^{neat} 3400, 2740, and 1740 cm^{-1}; *m/e* calcd, 128.0837; found, 128.0834.

Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.59; H, 9.46.

Reduction of Component A. A solution of 82 mg (0.48 mmol) of component A in 5 ml of anhydrous ether was added at room temperature to a stirred suspension of 100 mg (2.64 mmol) of lithium aluminum hydride in 1 ml of anhydrous ether, and the mixture was stirred for 45 hr. Work-up in the usual alkaline fashion gave 52 mg (83%) of a pale yellow, viscous oil. Preparative scale vpc analysis and separation of the two components of this oil (on the 10% FFAP column) afforded pure **31** (first to elute) and **32**, mp 101–102.5°. Additionally, **32** was converted to its bistosylate, mp 93.5–95° (lit.[15a,c] mp 94–95°), and **31** was converted to its bistosylate, mp 98.5–99.5° (lit.[15] mp 98.5°).

Reduction of component B in identical fashion also furnished a mixture of **31** and **32** which were likewise separated and characterized by infrared methods.

***endo*-8-Oxabicyclo[3.2.1]octan-2-yl Hydrogen Phthalate (35, R = H).** A solution of 2.0 g (0.0156 mmol) of **16** and 2.31 g (0.0156 mmol) of phthalic anhydride in 2.68 g (0.034 mol) of pyridine was stirred overnight at room temperature and poured onto 25 ml of 2 *N* hydrochloric acid. The crude precipitate was collected and recrystallized from benzene–hexane to give 3.6 g (84%) of white crystals, mp 142.5–144.5°.

Anal. Calcd for $C_{15}H_{16}O_5$: C, 65.21; H, 5.84. Found: C, 65.56; H, 5.92.

Resolution of 35 (R = H). Optically inactive **35** (6.35 g, 22.6 mmol) was dissolved in 160 ml of hot acetone and 6.66 g (22.6 mmol) of (−)-cinchonidine was added. Excess insoluble solid (unchanged cinchonidine) was separated by filtration, 160 ml of anhydrous methanol was added, and the solution was allowed to stand overnight at 0°. No precipitate resulted. All solvent was then removed and the residue fractionally crystallized from ethyl acetate. Four successive recrystallizations produced cinchonidine salt of mp 169–171.5°.

Free acid phthalate was regenerated by dissolving the above salt in chloroform (*ca.* 25 ml/g) and extracting the solution with three portions of 5% hydrochloric acid. The chloroform solution was dried and concentrated to give an oil which slowly crystallized upon standing: yield, 91%; $[\alpha]^{25}D$ +20.40° (*c* 3.510, $CHCl_3$); $[\alpha]^{25}_{365}$ +63.68 (*c* 3.510, $CHCl_3$). Recrystallization of the acid phthalate from benzene–hexane did not improve its melting point or optical rotation.

(+)-*endo*-8-Oxabicyclo[3.2.1]octan-2-ol [(+)-16]. Optically active acid phthalate ester (0.75 g, 2.72 mmol) of average rotation, $[\alpha]^{25}_{365}$ +62°, was stirred with 10 ml of 10% sodium hydroxide solution (0.025 mol) at 60–70° for 9 hr. This solution was cooled and stirred vigorously with three 7-ml portions of ether. The combined organic layers were dried and evaporated to give 0.30 g (88%) of white solid alcohol: $[\alpha]^{25}D$ +19.8° (*c* 1.607, $CHCl_3$); $[\alpha]^{25}_{365}$ +51.0° (*c* 1.607, $CHCl_3$). This solid was directly converted to brosylate.

(+)-*endo*-8-Oxabicyclo[3.2.1]octan-2-yl *p*-Bromobenzenesulfonate [(+)-9]. The above sample of (+)-**16** (0.30 g, 2.38 mmol) was added to an ice-cold, stirred solution of 1.3 g of *p*-bromobenzenesulfonyl chloride in 15 ml of pyridine. After standing at 0° for 36 hr, the reaction mixture was poured into 45 ml of an ice–water mixture and stirred vigorously with a pinch of racemic brosylate. Crystallization began at once. When the ice had melted, the white brosylate was filtered, washed with fresh water, and dried to give 0.51 g (62%) of (+)-**9**, mp 97.5–99.5°. Recrystallization from hexane–tetrahydrofuran gave 0.46 g of colorless needles: mp 99.5–101°; $[\alpha]^{25}D$ +16.2° (*c* 1.367, $CHCl_3$); $[\alpha]^{25}_{365}$ +50.0° (*c* 1.367, $CHCl_3$); $\delta_{TMS}^{CDCl_3}$ 7.75 (s, 4, aryl), 4.1–4.8 (m, 3, H-1, -2, -5) and 1.3–2.1 (m, 8, C*H*$_2$).

(±)-*exo*-2-Deuterio-*endo*-8-oxabicyclo[3.2.1]octan-2-yl Hydrogen Phthalate (**35**, R = D). Sodium borodeuteride (0.80 g, 0.019 mol) was added portionwise at room temperature to a stirred solution of 4.80 g (0.038 mol) of **17** in 50 ml of anhydrous ethanol. The solution which became warm was stirred at room temperature for 19 hr, treated with 50 ml of water, and stirred for a further 60 min. Additional water (40 ml) was introduced and the solution was extracted with dichloromethane (4 × 50 ml). The combined, dried extracts were concentrated to give a colorless, viscous oil (4.40 g, 90%) which gradually crystallized on standing. Vpc analysis showed this product to consist of the desired endo isomer (90%) admixed with 10% of the exo epimer.

A mixture of 4.30 g (0.0333 mol) of the above mixture, 5.00 g (0.0338 mol) of phthalic anhydride, and 5.88 g (0.0743 mol) of anhydrous pyridine was stirred at room temperature for 24 hr. Processing as in the protio case gave, after one recrystallization from ethyl acetate–hexane, 6.03 g (65%) of **35** (R = D): mp 136–142°; *m/e* calcd, 277.1060; found, 277.1065. The major portion of this crude material was directly resolved without further purification; sixfold recrystallized (ethyl acetate–hexane) material melted at 144.5–146.5°.

(±)-*exo*-2-Deuterio-*endo*-8-oxabicyclo[3.2.1]octan-2-ol (**36**). The unpurified, deuterated acid phthalate (5.81 g, 0.0210 mol) was dissolved in 50 ml of hot acetone and 6.18 g (0.210 mol) of (−)-cinchonidine was added portionwise with swirling together with 20 ml of acetone. The resulting hot solution was filtered, concentrated to *ca.* 50 ml, and allowed to cool. The crystallized salt (7.22 g) obtained was collected and recrystallized three times from acetate–acetone and ethyl acetate. This procedure yielded 4.09 of resolved salt, mp 168.5–170.5°.

This salt (4.00 g) was dissolved in 100 ml of chloroform and the solution was extracted with ice-cold 2 *M* hydrochloric acid (3 × 100 ml). The resulting organic layer was washed with 100 ml of brine, dried, and evaporated to give a colorless oil. Trituration with ethyl acetate–hexane led to the isolation of 1.78 g (92%) of impure acid phthalate: mp 100–120°; $[\alpha]^{25}_{365}$ +68.7° (*c* 3.07, $CHCl_3$).

A solution of 1.76 g (6.25 mmol) of crude, resolved acid phthalate and 2.4 g (60 mmol) of sodium hydroxide in 25 ml of water was stirred at 65° for 16 hr. Work-up as above gave 0.63 g (77%) of **36** as a colorless, viscous oil, $[\alpha]^{25}_{365}$ +52.7° (*c* 1.71, $CHCl_3$). Vpc analysis revealed that the product contained only a trace of the exo isomer.

(+)-*exo*-2-Deuterio-*endo*-8-oxabicyclo[3.2.1]octan-2-yl *p*-Bromobenzenesulfonate (**3**). A solution of 2.00 g (7.83 mmol) of *p*-bromobenzenesulfonyl chloride in 6 ml of cold, anhydrous pyridine was added to a solution of 0.50 g (3.87 mmol) of **36** in 4 ml of the same solvent, and the mixture was allowed to stand at 5° for 2 days. Normal processing furnished 1.24 g (92%) of **37**: mp 100.5–102° (from ether–petroleum ether); $[\alpha]^{25}_{365}$ +54.7° (*c* 1.112, $CHCl_3$).

(+)-*exo*-2-Deuterio-*endo*-8-oxabicyclo[3.2.1]octan-2-yl Acetate (**38**). A solution of 36.0 mg (0.279 mmol) of **36** in 2 ml of pyridine was treated with 0.5 ml of acetic anhydride, and the mixture was allowed to stand at room temperature for 19 hr. There was obtained after molecular distillation the pure colorless acetate: $[\alpha]^{25}_{365}$ +76.4° (*c* 0.238, $CHCl_3$).

Polarimetric Kinetic Procedure. Chiral brosylate (0.0992 g) was weighed into a 6.00-ml volumetric flask and the flask was filled to the mark with a 0.10065 *N* solution of sodium acetate in dry acetic acid (substrate concentration, 0.0476 *M*; *c* 1.6533 g/100 ml). After shaking to dissolve the brosylate, the solution was quickly transferred to a 1-dm, jacketed Perkin-Elmer Model 141 polarimeter cell (5+ ml volume) and the cell was placed in the closed compartment of the polarimeter, the latter operating with the mercury lamp and 365-nm filter setting. An initial reading was made after 7–8 min to allow for thermal equilibration. Subsequent polarimeter readings were then recorded at appropriate intervals. Plots of the log of observed rotation *vs.* time gave excellent straight lines indicative of good first-order behavior.

Acetolysis of (+)-9. The cell contents from a kinetic run and the additional 0.9 ml of solution which had remained at room temperature were combined and heated in a sealed tube at 75° for 75 min. The solution was cooled, 25 ml of water was added, and the resulting solution was extracted with ether (3 × 25 ml). The combined organic layers were washed with saturated sodium bicarbonate solution until neutralized, dried, and concentrated. Molecular distillation of the residual yellowish liquid at 90° (11 mm) gave a colorless oil which by vpc analysis (10% FFAP) was shown to be pure **26**. This material was racemic.

Acetolysis of 37. The acetate product from the combined solutions of two kinetic runs which had been allowed to proceed to complete solvolysis was isolated and purified as above: ν_{max}^{neat} 1740 and 1240 cm^{-1}; $[\alpha]^{25}_{365}$ −2.5° (*c* 0.910, $CHCl_3$).

Stability of 38 to Solvolysis Conditions. Pure **38** was dissolved in 0.1008 *M* sodium acetate in acetic acid: $[\alpha]^{25}_{365}$ +88.7° (*c* 0.238, HOAc). This solution was heated in a stoppered vessel for 18 hr at 75°. No change in optical activity was detected.

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