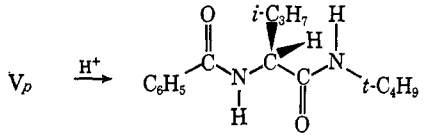
Table II. The Nmr Spectra of V (Varian A-60, TMS, $CDCl_3$)

Assignment of protons	Rel area	Multiplicity	V_p τ	V_p J, Hz	V_n τ	V_n J, Hz	V_p τ	V_p J, Hz	V_n τ	V_n J, Hz
			R = Fc				R = Ph			
C_6H_5CO	5	Pseudo s	2.53		2.54		2.52		2.55	
$C_6H_5CH(CH_3)$	5	Pseudo s					2.79		2.72	
$C_6H_5CH(CH_3)$	1	q					4.90	7.0	4.92	7.0
$-CH(CH_3)$	1	q	5.04	7.0	5.12	7.0				
$C_5H_4(Fe)C$	4	m	~5.8		~5.7					
			~5.95		~5.85					
$C_5H_5(Fe)$	5	s	6.17		6.09					
$-CHCH(CH_3)_2$	2	m	~7.1		7.0		~6.95		~7.0	
$-CH(CH_3)-$	3	d	8.50	7.0	8.49	7.0	8.39	7.0	8.40	7.0
$-C(CH_3)_3$	9	s	**8.83**		**8.64**		**8.86**		**8.61**	
$-CH(CH_3)_2$	6	m	~**9.05**		**9.18**	6.0	**8.93**	6.5	**9.20**	6.0
					9.50	6.0	**9.01**	6.5	**9.66**	6.0

((*S*)-VI), and V_n the corresponding (*R*) antipode. This result implies that V_p is the (*S*)(*S*) diastereomer and V_n is the (*S*)(*R*) diastereomer.



(4)

(*S*)-VI

Hence (+)-α-ferrocenylethylamine, one of the key compounds in the stereochemistry of ferrocene derivatives,[16] has the (*S*) configuration, in contrast to a previous assignment,[10] which was based on optical rotation data.

(16) The present authors will report in the near future on the synthesis and assignment of the absolute configurations of optically active ferrocene derivatives with *planar chirality*[17] by highly stereoselective metalation of (*S*)-N-dimethyl-α-ferrocenylethylamine and subsequent reactions with electrophiles, which is followed by further transformations of the primary products.

(17) K. Schlögl, "Topics in Stereochemistry," Vol. I, N. L. Allinger and E. L. Eliel, Ed., Interscience Publishers, New York, N. Y., 1967 p 39.

A Study of Competitive R_2O-3 and Homoallylic Participation in a Medium-Sized Ring. Acetolysis of Oxocan-3-yl and 3,4,7,8-Tetrahydro-2H-oxocin-3-yl Brosylates[1]

Leo A. Paquette, Robert W. Begland, and Paul C. Storm

Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received July 7, 1969*

Abstract: The products of acetolysis of oxocan-3-yl brosylate and 3,4,7,8-tetrahydro-2H-oxocin-3-yl brosylate were studied. First-order rate constants for the solvolysis of these oxygen-containing medium-sized ring compounds were determined and compared with values previously reported for cyclooctyl, 4-cycloocten-1-yl, and 3-cycloocten-1-yl brosylates. Oxocan-3-yl brosylate yielded products which arise exclusively from an intermediate bicyclic oxonium ion, while 3,4,7,8-tetrahydro-2H-oxocin-3-yl brosylate afforded products explicable on the basis of the derived homoallylic cation. Oxocin-3-yl brosylate exhibits a 70-fold rate retardation relative to cyclooctyl brosylate. Analysis of the significance of this result is shown to be complex, chiefly because of the unknown rate acceleration anticipated because of steric decompressions introduced by the hetero atom. The rate of solvolysis of 3,4,7,8-tetrahydro-2H-oxocin-3-yl brosylate was only 45 times slower than that of its carbocyclic congener (the expected rate retardation was approximately 10^2), indicating the lesser steric requirements of ether oxygen when compared to a ring methylene group. Additional aspects of the R_2O-3 participation question in these systems are discussed. One of the significant conclusions concerns the fact that homoallylic participation overwhelms R_2O-3 neighboring group assistance in a medium-sized ring.

The solvolyses of several oxygenated molecules related structurally to 4-methoxy-1-butyl (**1**) and 5-methoxy-1-pentyl brosylates (**2**) have provided a fund of information concerning the nature of RO-5 and RO-6 neighboring group participation.[2,3] Struc-

(1) Unsaturated Heterocyclic Systems. LVII. For the previous paper, see L. A. Paquette and R. W. Begland, *J. Org. Chem.*, **34**, 2896 (1969).

(2) For a recent review of this subject, see B. Capon, *Quart. Rev.* (London), **18**, 45 (1964).

(3) (a) R. Heck, J. Corse, E. Grunwald, and S. Winstein, *J. Amer. Chem. Soc.*, **79**, 3278 (1957); (b) S. Winstein, E. Allred, R. Heck, and

$CH_3OCH_2CH_2CH_2CH_2OBs$ (1) $CH_3OCH_2CH_2CH_2CH_2CH_2OBs$ (2)

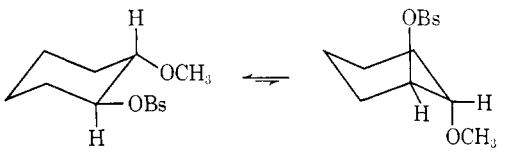
tures involving tetrahydrofuranium and tetrahydropyranium cations have been proposed to account for the substantial rate enhancement (k/k_H) exhibited by **1**, **2**, and related systems. The principal difference between **1** and **2** is the rate of ring closure with five-membered ring formation being favored by a factor of 14 in acetic acid.[3d] In view of comparable $\Delta H^{\ddagger}$ values, this rate difference has been attributed to an entropy effect, a more negative $\Delta S^{\ddagger}$ (by 4.7 eu) for six-ring formation, and the expected greater restriction in atomic motion which must develop in passing from **2** to the oxonium ion.

The situation with regard to RO-3 participation is less clearly defined. Thus, the slower rate of solvolysis of **3** relative to *n*-butyl brosylate has been interpreted to

$CH_3OCH_2CH_2OBs$ (3) $CH_3-C(OCH_3)(CH_3)-CH_2OBs$ (4)

mean that anchimeric assistance by ether oxygen in the rate-determining step is essentially negligible.[3b] In contrast, **4** ionizes in acetic acid at a rate 15 times faster than neopentyl tosylate.[4] The full extent of anchimeric assistance to ionization in **4** can be more fully appreciated after allowing for the inductive effect of oxygen which, in the absence of participation, has been shown[5] to reduce a given rate by a factor of approximately 10^2. The rate enhancement observed in the case of **4** may result principally from added stabilization of the transition state produced by increased alkyl substitution on the three-membered cyclic oxonium ion.

In the case of *trans*-2-methoxycyclohexyl brosylate (**5**), there also appears to be a modest (4.3-fold)[6] rate enhancement superimposed on the rate-retarding inductive effect.[5] The participation by neighboring oxygen in this example is somewhat surprising since **5** can be



5a **5b**

expected to exhibit substantial conformational bias away from **5b**, the diaxial conformer required for effective MeO-3 involvement at the transition state.[7]

R. Glick, *Tetrahedron*, **3**, 1 (1958); (c) G. T. Kwiatkowski, S. J. Kavarnos, and W. D. Closson, *J. Heterocycl. Chem.*, **2**, 11 (1965); (d) E. L. Allred and S. Winstein, *J. Amer. Chem. Soc.*, **89**, 3991, 3998, 4012 (1967); (e) E. R. Novak and D. S. Tarbell, *ibid.*, **89**, 73 (1967); J. R. Hazen, *Tetrahedron Lett.*, 1897 (1969).

(4) S. Winstein, C. R. Lindegren, and L. L. Ingraham, *J. Amer. Chem. Soc.*, **75**, 155 (1953). These workers have applied a correction factor of 1/3 to reduce the rate of **4** to that expected for the corresponding tosylate.

(5) S. Winstein, E. Grunwald, and L. L. Ingraham, *ibid.*, **70**, 821 (1948).

(6) Winstein's estimate of the acceleration was 4.3,[5] while a revised estimate using Taft's σ^*[OMe] = +0.52 and Streitwieser's ρ^* = −3.49 for secondary arenesulfonate solvolyses gives a value of 3.5.

(7) It should be noted that solvolysis of the bromide corresponding to **5** in acetic acid containing silver nitrate affords product of retained configuration [S. Winstein and R. B. Henderson, *J. Amer. Chem. Soc.*, **65**, 2196 (1943)]. However, the precise stage of oxygen involvement is obviously not revealed in this example.

Because of the obvious difficulties in correlating the above data, additional work on RO-3 participation seemed in order. The purpose of the present study was to determine to what extent ether oxygen, when positioned β to an incipient carbonium ion in a medium-sized ring, would affect the rates and products of solvolysis. To this end, brosylates **6** and **7** have been prepared. The investigation of these systems was of

6 **7**

special interest to us because of its obvious direct bearing on several important questions. First, the medium-sized rings represent a new variation which was expected to reveal useful information about the influence of structural factors on ring closure and subsequent product formation. Most importantly, brosylate **7** is so constructed that it provides an important calibration point for our understanding of the interrelationship of oxonium and homoallylic ions. In another respect, the differing steric requirements of ether oxygen and a methylene group in a medium-sized ring[8] were expected to shed new light on our knowledge of transannular behavior.

Results

Alcohols **8** and **9** were prepared by lithium aluminum hydride reduction of oxocan-3-one and 7,8-dihydro-2H-oxocin-3(4H)-one, respectively, the syntheses of which have been described.[9] Conversion to the respective

8 **9**

brosylates was achieved without difficulty with *p*-bromobenzenesulfonyl chloride in pyridine.

The rate data for the acetolysis of **6** and **7** together with those of related compounds[10] are summarized in Table I. Whereas the acetolysis rate constant for 3,4,7,8-tetrahydro-2H-oxocin-3-yl brosylate (**7**) was cleanly first order for at least three half-lives, plots of log *M* *vs.* time in the case of **6** showed substantial upward curvature. Such observations were suggestive that **6** and **7** were reacting by quite different pathways. The behavior of **6** indicated that concurrently with normal solvolysis, internal return of *p*-bromobenzenesulfonate ion was occurring with rearrangement to afford a second brosylate which was solvolyzing at a slower rate (Scheme I). Measurement of the rate

Scheme I

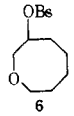
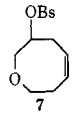
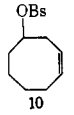
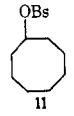
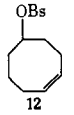
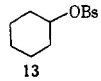
$$\begin{array}{ccc} ROBs & \xrightarrow[k_1]{HOAc} & ROAc + HOBs \\ \downarrow k_2 & & \\ R'OBs & \xrightarrow[k_3]{HOAc} & R'OAc + HOBs \end{array} \qquad k_1 > k_3$$

(8) For information bearing on this point, see (a) L. A. Paquette and R. W. Begland, *J. Org. Chem.*, **32**, 2723 (1967); (b) L. A. Paquette and R. W. Begland, *J. Amer. Chem. Soc.*, **88**, 4685 (1966).

(9) L. A. Paquette, R. W. Begland, and P. C. Storm, *ibid.*, **90**, 6148 (1968).

(10) A. C. Cope and P. E. Peterson, *ibid.*, **81**, 1643 (1959).

Table I. Rates of Acetolysis

Compd	T, °C	k_i, sec^{-1}	Relative rate, 70°	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
 6	39.8	4.45×10^{-6}	2.7	26.7	+2.30
	51.0	2.04×10^{-5}			
	64.0	1.04×10^{-4}			
	70.0	2.15×10^{-4} [a]			
 7	39.8	2.20×10^{-5}	8.1	23.2	−5.84
	50.7	8.13×10^{-5}			
	64.0	3.41×10^{-4}			
	70.0	6.45×10^{-4} [a]			
 10	70.0	2.97×10^{-2} [b]	370	19.0	−13.4
 11	70.0	1.48×10^{-2} [b]	185	21.0	−3.9
 12	70.0	2.32×10^{-4} [b]	2.9	26.2	+2.0
 13	70.0	8.02×10^{-5} [b]	1.0		

[a] Extrapolated values. [b] Values taken from ref 10.

Table II. Acid Production (k_1) and Rearrangement Rates (k_2) of Oxocan-3-yl Brosylate (**6**)

Rate	T, °C	k, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
k_1	39.8	2.63×10^{-6}	27.7	+4.30
	51.0	1.39×10^{-5}		
	64.0	6.89×10^{-5}		
	70.0	1.49×10^{-4} [a]		
k_2	39.8	1.82×10^{-6}	25.2	−4.56
	51.0	6.45×10^{-6}		
	64.0	3.56×10^{-5}		
	70.0	6.64×10^{-5} [a]		

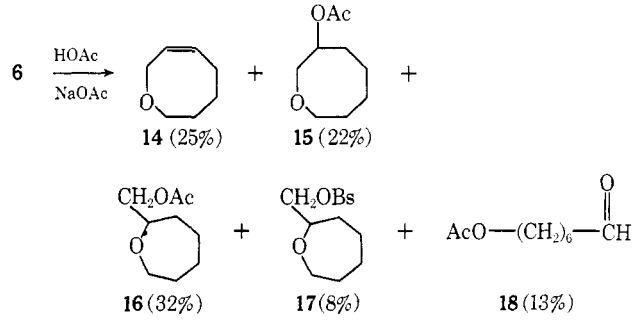
[a] Extrapolated values.

constant of this second compound (**17**, see below) was readily accomplished by initiating titrations only after all of **6** had reacted; calculations in this instance were based on the experimental infinity titer for acid production. The initial rate constant observed for the disappearance of **6** (k_i) is the sum of the rate constants for acid production (k_1) and rearrangement (k_2).[11]

Rate constant k_i was evaluated by means of the differential kinetic analysis approach[12a] with the aid of an IBM System 360 computer program.[12b] This treatment is well suited to the present situation, since the acetolysis reactivity of **6** and **17** (see below) are fairly closely matched, the k_1/k_3 ratio being 6.5 at 51° and 16 at 64°. Since the ratio of acid produced to rearranged ester is equal to the ratio of the rate constants k_1/k_2, and since this product ratio is most conveniently evaluated from the amount of acid produced at the calculated infinity, k_1 and k_2 are thereby obtainable (Table II).

The products of the acetolysis of oxocan-3-yl brosylate (**6**) in buffered acetic acid are shown in Scheme II. The product studies were carried out by running the

Scheme II

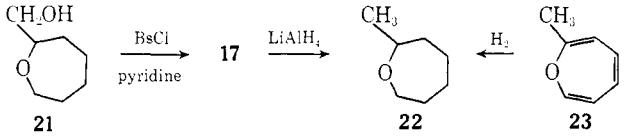


reaction through a time corresponding to 10 half-lives of **6**, diluting with water, and extracting with ether. Careful distillation of the solvolysis product mixture gave a low-boiling fraction, a high-boiling fraction, and a crystalline residue which remained in the distillation flask. The overall yield of recovered products was 94%. The low-boiling fraction proved to be one component (vpc analysis) which was assigned structure **14** on the basis of its nmr spectrum (see Experimental Section) and its ready hydrogenation to the known oxocane molecule (**19**).[8a] In particular, the

(11) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1961, p 160.

(12) (a) J. S. Fritz and G. S. Hammond, "Quantitative Organic Analysis," John Wiley & Sons, Inc., New York, N. Y., 1957, pp 158–166. (b) This program was written and made available to us by Dr. John C. Craig, Jr., whom we thank.

nonidentity of **14** and 3,4,5,6-tetrahydro-2H-oxocin (**20**)[8a] was unequivocally established by comparison of pertinent spectra. Preparative scale vpc analysis of the higher boiling fraction yielded a pure sample of **18**. The presence of aldehyde and acetate groups was apparent from the infrared spectrum which exhibited peaks at 2760 and 1750 cm^{-1} and the nmr spectrum which displayed a triplet (J = 1.7 Hz) at δ 9.97 and a singlet at 2.07. In addition, **18** gave a 2,4-dinitrophenylhydrazone of the proper chemical composition. The more rapidly eluted fraction from the gas chromatogram was a difficultly separable mixture of acetates **15** and **16**. Lithium aluminum hydride reduction of this acetate mixture gave the two corresponding alcohols which were readily separated by vpc. The lesser alcohol was identical with **8** and therefore **15** is the derived acetate. The proposed structure for **16** was confirmed by conversion of **21** to its brosylate (**17**) which upon reduction with lithium aluminum hydride gave 2-methyloxepane (**22**). An unequivocal synthesis of **22** was accomplished by catalytic hydrogenation of 2-methyloxepin (**23**).[13] The solid recovered from the distillation flask exhibited spectral characteristics which

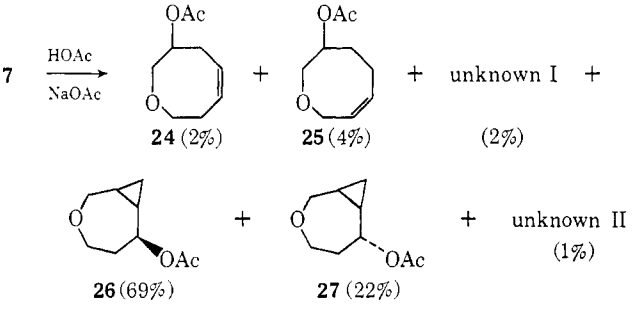


21 22 23

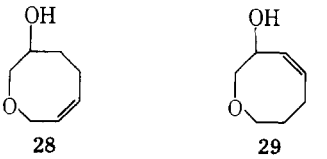
were superimposable upon those of brosylate **17**. Further structure proof was derived from the reduction of this solid to **21** with sodium naphthalene anion radical.[14]

Solvolysis of brosylate **7** led to a mixture of acetates which were isolated in 99.5% yield. Distillation in this instance gave no low-boiling olefin fraction and no residue remained in the distillation flask. Scheme III lists the products obtained and their

Scheme III

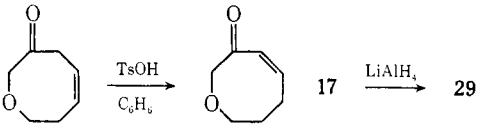


respective percentages. The products were examined gas chromatographically both as acetates and as the corresponding alcohols, following a preliminary reductive cleavage with lithium aluminum hydride. The identity of **24** was established by comparison of vpc retention times and infrared spectra with those of an authentic sample. The gross structure of alcohol **28** (derived from acetate **25**) was established by catalytic hydrogenation to **8**. Its nmr spectrum displayed six protons in the δ 3.5–4.3 region, two vinyl protons, two allylic protons, and two protons at higher field. These features are compatible only with structures **28** and



28 29

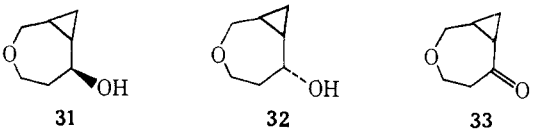
29.[15] An independent synthesis of **29** was achieved by acid-catalyzed equilibration of 7,8-dihydro-2H-oxocin-3(4H)-one to its conjugated isomer (**30**) with *p*-toluenesulfonic acid in benzene[16] and subsequent careful lithium aluminum hydride reduction (0°, 5 min).



30

The absence of skeletal rearrangement in the production of **30** was confirmed by catalytic hydrogenation to oxocan-3-one. Alcohol **28** proved not to be identical with **29** and thus the first structure is uniquely in accord with the above observations. Additional evidence in support of structure **28** is found in the great similarity of its nmr spectrum with that of olefin **14**.

The structures of *exo*-and *endo*-cyclopropyl acetates **26** and **27** and their derived alcohols (**31** and **32**) were assigned on the basis of elemental analysis and spectral data (see Experimental Section). To confirm that **31** and **32** were indeed epimers, a mixture of **31** and **32**



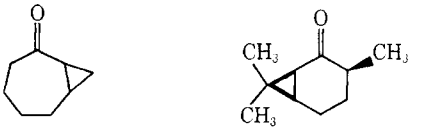
31 32 33

was oxidized with Jones' reagent; ketone **33** was the sole product. This ketone exhibited an unusual double carbonyl peak with maxima at 1720 and 1695 cm^{-1} which was also observed in its carbocyclic analog.[10] Reduction of **33** with lithium aluminum hydride gave a mixture of **31** and **32** in the ratio of 41:59, respectively. The predominance of **32** in this reduction,[17] the lower relative vpc retention time of **26** as compared to **27**,[18] mechanistic analysis of the

(15) The nmr spectrum of the remaining double bond isomer, *i.e.*, **9**, differs appreciably from that of **28** (see Experimental Section).

(16) N. Heap and G. H. Whitham, *J. Chem. Soc., B*, 164 (1966).

(17) The reduction of cyclic conjugated cyclopropyl ketones with lithium aluminum hydride or sodium borohydride results in predominant attack of hydride from that side of the ring on which the cyclopropane ring is situated to give chiefly the *exo* isomer. To illustrate, reduction of iii with $NaBH_4$ affords 70% *exo* alcohol and 30% *endo* alcohol [A. C. Cope, S. Moon, and P. E. Peterson, *J. Amer. Chem. Soc.*, **84**, 1935



iii iv

(1962)] whereas iv provided 67% *exo* and 33% *endo* alcohols upon treatment with $LiAlH_4$ [S. P. Acharya and H. C. Brown, *ibid.*, **89**, 1925 (1967)].

(18) Examination of models of **26** and **27** indicates that the acetate group of the *endo* isomer (**26**) is considerably more hindered than that of the *exo* isomer (**27**). In view of the widely accepted notion that the more hindered the substituent group, the more weakly adsorbed is the molecule on polar surfaces,[19] **26** is expected to be more rapidly eluted than **27** under the vpc conditions employed.

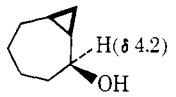
(19) (a) E. M. Kosower and S. Winstein, *J. Amer. Chem. Soc.*, **78**, 4347 (1956); (b) S. Winstein and H. J. Holness, *ibid.*, **77**, 5562 (1955); (c) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

(13) E. Vogel and H. Günther, *Angew. Chem.*, **79**, 429 (1967).

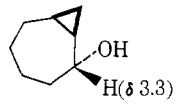
(14) W. D. Closson, P. Wriede, and S. Bank, *J. Amer. Chem. Soc.*, **88**, 1581 (1966).

solvolysis of **7** (see below), and nmr shift data for **26** and **27** combine to establish the assigned *exo–endo* relationship for these compounds.

In order to permit a more meaningful comparison of nmr spectra, further comment on this point is necessary. The absorptions of protons in the immediate vicinity of oxygenated substituents are, in general, downfield shifted.[20] Thus, when a hydroxyl or acetoxyl group is positioned *cis* to a cyclopropyl group, the protons of the three-membered ring are substantially deshielded.[21,22] Examination of the nmr spectra of **26** and **27** clearly establishes that the cyclopropyl protons of the major product (δ 0.52–1.43) are shifted downfield when compared to the cyclopropyl protons of the minor product (δ 0.28–1.32). Such an analysis reinforces the conclusion that **26** is indeed the *endo* isomer. However, the anomalous chemical shift of the α-acetoxy proton in **27** remains to be explained. The nmr spectra of **34** and **35** display α-carbinol hydrogen peaks at δ 4.2 and 3.3, respectively.[23] Because earlier evi-

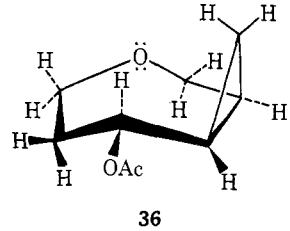


34



35

dence had substantiated the fact that axial protons positioned α to an oxygen atom in a six-membered ring are observed at higher field than their equatorial counterparts,[24] this argument was utilized by Cope to explain the high-field position of the α-carbinol proton in *exo* isomer **35**.[23] Similar diamagnetic shifts of protons *cis* to a cyclopropyl function have been attributed to a shielding effect of the cyclopropane ring.[22b,25] On this basis, the α-acetoxy proton of **26** would be expected to appear at lower field than the same proton in **27**. In actual fact, the opposite is seen (for **26**, δ 4.95; for **27**, δ 5.28). This apparent inconsistency was quickly resolved upon examination of models of **27** which show that although the proton in question is undoubtedly shielded by the cyclopropane ring, it is also held in very close proximity to one of the nonbonded pairs of electrons on the transannularly disposed ether oxygen (see **36**). The deshielding of the α-acetoxy proton of **27** is then a product of the effect exerted by the paramagnetic current associated with this ether oxygen which is apparently overriding the shielding caused by the cyclopropane ring.



36

(20) See, for example, H. C. Brown and A. Suzuki, *J. Amer. Chem. Soc.*, **89**, 1933 (1967); G. Zweifel and H. C. Brown, *ibid.*, **86**, 393 (1964).

(21) See Acharya and Brown (ref 17).

(22) (a) W. G. Dauben and W. T. Wipke, *J. Org. Chem.*, **32**, 2976 (1967); (b) L. Birladeanu, T. Hanafusa, and S. Winstein, *J. Amer. Chem. Soc.*, **88**, 2315 (1966).

(23) A. C. Cope, S. Moon, and C. H. Park, *ibid.*, **84**, 4843 (1962).

(24) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *ibid.*, **80**, 6098 (1958).

(25) H. Prinzbach and E. Druckrey, *Tetrahedron Lett.*, 2959 (1965).

Discussion

Examination of Table I shows that the rate of acetolysis of cyclooctyl brosylate (**11**) is significantly enhanced over that of cyclohexyl brosylate (**13**), the latter being an appropriate standard whose rate of solvolysis is comparable to that of acyclic brosylates. This enhancement is viewed to be the result of steric strain relief in the transition state for formation of a planar carbonium ion in an eight-membered ring.[10] The solvolysis rate of 4-cyclooctenyl brosylate (**12**) is considerably slower than that of **11** since introduction of a double bond in a medium-sized ring removes several eclipsed hydrogen interactions and lessens much of the strain inherent in the fully saturated derivative. Accordingly, the kinetic behavior of **12** can be expected to compare favorably with that of cyclohexyl brosylate (**13**); this is, in fact, observed. For the same reason, a like relative reactivity is to be expected from 3-cycloctenyl brosylate (**10**). However, because homoallylic participation is important in this system, **10** solvolyzes more rapidly than **12**, the 130-fold rate enhancement being a measure of the anchimeric acceleration provided by the β,γ-double bond.

In discussing the significance of the behavior of **6** and **7**, we must keep in mind that the introduction of the oxygen substituent, the very factor required to provide added driving force to ionization, alters other factors which affect rate, such as inductive and steric effects, and these need to be considered in interpreting the rates obtained. It is clear from the behavior of **5**, for example, that the ether oxygen in **6** can be expected to reduce the rate of acetolysis by a factor of approximately 10^2 relative to **11** because of the adverse inductive effect. An additional important key to understanding the R_2O-3 phenomenon in **6** is the assessment of the magnitude of the driving force to ionization which is available to cyclooctyl brosylate (**11**) but which is lost to **6** because of the significantly lesser steric demands of an ether oxygen atom (relative to $-CH_2-$). If the assumption is made that the presence of an oxygen atom in an eight-membered ring is roughly comparable to the diminution in steric compression caused by the introduction of a double bond,[26] then a further reduction in the solvolysis rate of **6** by approximately 10^2 could be operative (compare **11** and **12**). Unfortunately, however, there is no way at the present time to estimate *accurately* the magnitude of this anticipated rate acceleration.[28] In actuality, factors anywhere up to 10^2 might be reasonable. Therefore, the situation is such that two interpretative extremes are possible. In the first of these, **6** is expected to

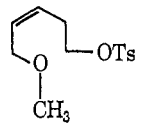
(26) Considerable recent chemical evidence supports this conclusion. Thus oxocane (**19**) exhibits an invariant nmr spectrum down to $-160°$ in contrast to cyclooctane and its derivatives which undergo at least two visible changes on the nmr time scale, indicating that the oxygen atom in **19** introduces strain minimization which makes possible very rapid averaging processes even at very low temperatures.[8a] A similar effect has been noted for medium-sized cyclic β-keto esters in which replacement of a ring CH_2 group by O results in an enhancement in enol content because of relief of several nonbonded intracyclic steric compressions.[27] Finally, attention should also be called to the preferred axial orientation of the *t*-butyl group in molecules such as the *cis*-2-alkyl-5-*t*-butyl-1,3-dioxanes, again demonstrating that the space requirements of oxygen electron pairs are much less than those of carbon-bonded hydrogen atoms.[27]

(27) E. L. Eliel and M. C. Knoeber, *J. Amer. Chem. Soc.*, **88**, 5347 (1966); **90**, 3444 (1968).

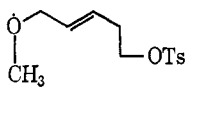
(28) Research into this question is presently being initiated by M. K. Scott in these laboratories.

solvolyze 10^4 times more slowly than **11**; the observed rate retardation of approximately 70 would therefore clearly implicate substantial ether oxygen participation, the factor of 10^2 corresponding closely to that observed in MeO-6 neighboring group participations.[29] On the other hand, the rate retardation of 70-fold is only slightly less than the expected factor of 100 expected from the inductive effect alone. To account for this small difference, it is necessary only to assume that there is a small reduction in transannular steric compression in **6** relative to **11**. Then an R_2O-3 rate acceleration of approximately 2 (instead of 10^2) would be operative. This latter estimate is probably too low, but at any rate it is clear that any attempt to assess the magnitude of the acceleration would be speculative until an accurate estimate of the effect of the ether oxygen on steric compressions in eight-membered rings becomes available.[28]

It is pertinent that R_2O-3 participation does *not* compete well with homoallylic participation in **7**. This observation is in direct contrast to the acetolysis behavior of acyclic tosylate **37** in which the 10^2-fold rate acceleration due to ether oxygen participation is sufficient to overcome homoallylic participation.[30] The related *trans*-isomer **38**, however, reacts *via* homoallylic participation to give a 72% yield of the cyclopropyl derivative.

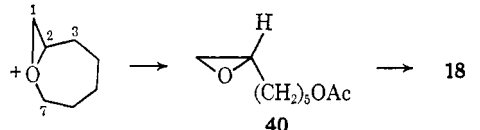


37



38

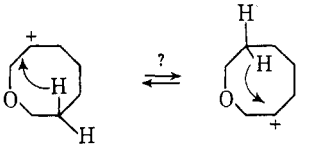
A large kinetic rate acceleration is, of course, not a necessary condition for the formation of products exclusively *via* the R_2O-3 pathway simply because oxygen participation may not yet be great at the transition state of the rate-determining ionization. In the case of **6**, however, it is clear (*cf.* Table II) that the rate of internal return *via* **39** (k_2) lags behind that of acid production (k_1) by the relatively small factor of approximately 2. Also, the five isolated products are most logically derived from this same intermediate oxonium ion. Thus, loss of a proton from C-3 would lead to olefin **14**, whereas attack of acetate ion at C-1 and C-2 would afford **16** and **15**, respectively. Internal return of brosylate ion to C-1 would eventuate in the



39 40

formation of **17**, the presence of which primary brosylate accounts for the progressive decrease in rate noted during the acetolysis. Aldehyde **18** could arise by attack of acetate at C-7 with ring opening to give epoxy acetate **40**, which subsequently undergoes acid-catalyzed rearrangement.[31]

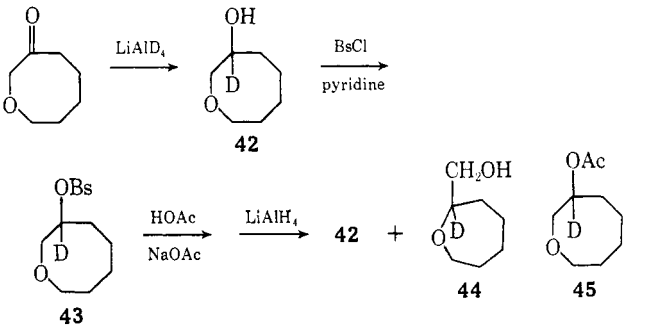
Because cyclooctyl carbonium ions are well recognized to be subject to transannular 1,5-hydride shifts,[32] it was deemed important to determine if such a process was occurring during the acetolysis of **6**, perhaps by leakage of oxonium ion **39** to carbonium ion **41**. The observation of this mechanism would not be possible under the conditions employed because the



41

1,5-hydride shift in this instance is degenerate. Therefore, to determine to what extent, if any, such shifts were occurring, the deuterium labeled brosylate **43** was prepared and the pertinent solvolysis products were carefully examined subsequent to lithium aluminum hydride reduction of the crude acetate mixture (Scheme IV). Alcohols **42** and **44** were separated by preparative

Scheme IV



vpc; integration of their nmr spectra showed only five protons at low field, thereby indicating that no appreciable 1,5-hydride shift had taken place. Further evidence that the deuterium label had remained in its initial environment was obtained by acetylation of the isolated sample of **42**. The nmr spectrum of **45** exhibited no measurable absorption in the δ 4.85 region which is the established position for the absorption of the α-acetoxy proton in **15**. At the mechanistic level, the absence of hydride shift may mean that no leakage from **39** to **41** takes place or that the presence of an oxygen atom in the ring lowers the compression caused by nonbonded hydrogen–hydrogen interactions to a degree where shifts of this type will not occur readily.

Indication of ether oxygen participation was further derived from solvolysis of brosylate **17** ($k_3^{51.0°} = 2.15 \times 10^{-6}$ sec^{-1}; $k_3^{63.0°} = 4.27 \times 10^{-6}$ sec^{-1}).[33] In addition

(29) See ref 3d and references cited therein.

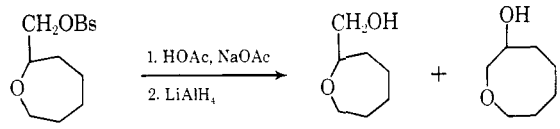
(30) J. R. Hazen and D. S. Tarbell, *Tetrahedron Lett.*, 5927 (1968).

(31) For reviews of this phenomenon, see: (a) L. A. Paquette, "Principles of Modern Heterocyclic Chemistry," W. A. Benjamin, Inc., New York, N. Y., 1968, pp 41–42; (b) A. Rosowsky, "Heterocyclic Compounds with Three- and Four-Membered Rings, Part One," A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1964, pp 231–270.

(32) A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev.* (London), **20**, 119 (1966).

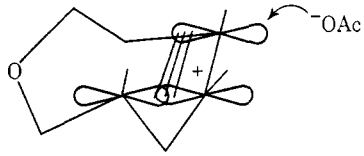
(33) It is interesting that the k_3 values show a small temperature dependence corresponding to a $\Delta H^{\ddagger}$ of approximately 12–14 kal/mol, a value about 15 kcal smaller than that of the more reactive isomer **6**. On this basis, the $\Delta S^{\ddagger}$ for **17** is required to be quite large. Three explanations can be advanced to account for this fact. Firstly, in the titrimetric rate analysis for **17**, the changes in acid production were small and somewhat larger errors than usual could therefore have entered into the quantitative evaluation. Secondly, it is possible that **17** solvolyzes with a significant SN2 component; this would be consistent with the larger **21**:**8** ratio compared with the **16**:**15** ratio for the acetolysis of **6**. Thirdly, the rate constant for this portion of the reaction could very well be that for the equilibrated unsolvolyzed mixture of **6** and **17** [see H. L. Goering and M. F. Sloan, *J. Amer. Chem. Soc.*, **83**, 1992 (1961)].

to **21** (56%) and an unknown compound (21%),[34] there was produced the ring-expanded alcohol **8** in 23% yield.



17 21 (56%) 8 (23%)

Turning our attention now to **7**, we can expect that this brosylate will solvolyze 100 times more slowly than 3-cyclooctenyl brosylate (**10**) if the ether oxygen exerts its customary inductive effect.[5] From the data of Table I, it is seen that **7** reacted only 44 times more slowly than its carbocyclic congener. Such a result is congruent with the concept that relief of ring strain produced by the ether oxygen atom facilitates participation of the β,γ-double bond and formation of homoallylic cation **46**. A comparison of the acetolysis products of **7** and **10** lends additional support to this



46

proposal; thus, cyclopropyl acetates constitute only 52% of the product mixture from **10**, whereas the cyclopropyl acetates from **7** comprise 91% of the total. The preferential formation of *endo*-acetate **26** is to be expected on the basis of a concerted reaction from cation **46** (see formulation). The indications from the present work suggest that homoallylic cation intervention is strongly preferred to R_2O-3 participation, at least when such a choice is available to a medium-sized ring.

Experimental Section[35]

Oxocan-3-ol (8). To a stirred slurry of 1.15 g (0.030 mol) of lithium aluminum hydride in 70 ml of anhydrous ether was added dropwise a solution of 1.85 g (0.015 mol) of oxocan-3-one[9] in 30 ml of ether. The resulting mixture was stirred for 4 hr and worked up by the careful sequential addition of 1.1 ml of water, 1.1 ml of 30% sodium hydroxide solution, and 3.5 ml of water. The precipitated salts were filtered and washed thoroughly with ether. The combined filtrate and washings were evaporated and distilled to give 1.67 g (89%) of **8** as a clear liquid, bp 110–112° (9 mm), n^2D 1.4750; $\delta_{max}^{CCl_4}$ 4.43 (singlet, 1 H, –OH), *ca.* 3.7 (multiplet, 5 H, C*H*O–), and 1.67 (broad peak, 8 H, $-CH_2-$).

The α-naphthylurethan of **8** was obtained as white crystals from ether, mp 112.5–113.5°.

Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.21; H, 7.07; N, 4.68. Found: C, 72.32; H, 7.03; N, 4.77.

Oxocan-3-yl Brosylate (6). A cold (0°) solution of 1.67 g (0.013 mol) of **8** in 10 ml of pyridine was added to a cooled solution of 6.60 g (0.026 mol) of *p*-bromobenzenesulfonyl chloride in 20 ml of pyridine. The solution was allowed to stand in a refrigerator for 19 hr and was then worked up in the usual manner (see below) to give 4.32 g (96%) of white solid, mp 56–58°. Recrystallization from ether–hexane gave white crystals, mp 58.0–59.0°. This substance has also been obtained in a polymorphic form, mp 67–68.5°.

Anal. Calcd for $C_{13}H_{17}BrO_4S$: C, 44.71; H, 4.91; S, 9.18. Found: C, 44.81; H, 4.90; S, 9.13.

3,4,7,8-Tetrahydro-2H-oxocin-3-ol (9). To a stirred slurry of 2.0 g (0.053 mol) of lithium aluminum hydride in 50 ml of dry ether was added dropwise a solution of 3.4 g (0.027 mol) of 7,8-dihydro-2H-oxocin-3(4H)-one[9] in 20 ml of ether. The mixture was stirred for 4 hr and product isolation was achieved in the predescribed manner. There was obtained 3.4 g (98%) of **9** as a clear colorless liquid, bp 94–96° (18 mm); $\delta_{TMS}^{CCl_4}$ *ca.* 5.8 (multiplet, 2 H, vinyl protons), 4.29 (singlet, 1 H, –OH), *ca.* 3.6 (multiplet, 5 H, C*H*O–), and *ca.* 2.3 (multiplet, 4 H, allylic protons).

The α-naphthylurethan of **9** was obtained as white crystals from carbon tetrachloride–ether, mp 143.0–144.5°.

Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.60; H, 6.45; N, 4.76.

3,4,7,8-Tetrahydro-2H-oxocin-3-yl Brosylate (7). A solution of 3.0 g (0.023 mol) of **9** in 20 ml of pyridine was cooled in ice and added to a solution prepared by dissolving 12.0 g (0.047 mol) of *p*-bromobenzenesulfonyl chloride in 40 ml of cold pyridine. After 19 hr at 5°, the excess sulfonyl chloride was hydrolyzed by the addition of ice. Finally, water (100 ml) was added and the mixture was extracted with ether (2 × 100 ml). The combined ether layers were washed with 50-ml portions of iced 1 *N* hydrochloric acid until the washings remained acidic, followed with 50 ml of 5% sodium carbonate solution. Evaporation of the dried ether solution gave 7.57 g (93%) of a white solid, mp 74–77°. Recrystallization from ether–hexane gave white crystals, mp 79–80°.

Anal. Calcd for $C_{13}H_{15}BrO_4S$: C, 44.96; H, 4.35; S, 9.23. Found: C, 44.99; H, 4.31; S, 9.19.

Solvolysis of 6. A solution of 4.45 g (0.0127 mol) of **6**, 55 ml of glacial acetic acid, and 0.80 g (8.5 mmol) of sodium carbonate was stirred at 70° for 22 hr (10 half-lives). The solution was cooled, 150 ml of ice–water was added, and the resulting mixture was extracted with ether (3 × 100 ml). The combined ether extracts were washed with saturated sodium bicarbonate solution until neutral, dried, and carefully evaporated. Careful distillation of the residual liquid afforded 340 mg (23.6%) of **14**, bp 52–53° (30 mm); $\delta_{TMS}^{CCl_4}$ 5.43 (multiplet, 2 H, vinyl protons), 4.05 (multiplet, 2 H, $-OCH_2CH=$), 3.62 (multiplet, 2 H, $-OCH_2CH_2-$), 2.45 (multiplet, 2 H, allylic protons), and *ca.* 1.62 (multiplet, 4 H).

In addition, there was obtained 1.34 g (62.3%) of a mixture of acetates, bp 66–67° (0.10 mm), and a distillation pot residue consisting of 350 mg (7.9%) of brosylate **17**, mp 78.0–79.0° (from ether–pentane). The overall yield of isolated material was 93.8%.

The acetate fraction was subjected to vpc analysis[36] and two peaks in the ratio of 81:19 were displayed. The 81% peak was a mixture of **15** and **16**. The 19% component was found to be pure **18**; $\nu_{max}^{CCl_4}$ 2760 and 1750 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 9.97 (triplet, J = 1.7 Hz, 1 H, –C*H*O), 4.14 (triplet, J = 6.5 Hz, 2 H, $AcOCH_2-$), 2.50 (triplet of doublets, J = 7.0 and 1.7 Hz, 2 H, $-CH_2CHO$), 2.07 (singlet, 3 H, $-OCOCH_3$), and 1.20–1.90 (complex absorption, 8 H).

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.48; H, 9.33.

The 2,4-dinitrophenylhydrazone of **18** was obtained as orange crystals from ethanol–water, mp 77.0–77.5°.

Anal. Calcd for $C_{15}H_{20}N_4O_6$: C, 51.13; H, 5.72; N, 15.90. Found: C, 51.21; H, 5.83; N, 15.95.

Hydrogenation of 5,6,7,8-Tetrahydro-2H-oxocin (14). A 50-mg sample of **14** in ether (20 ml) was hydrogenated over 10% palladium on charcoal catalyst at atmospheric pressure for 2 hr. The solution was filtered and the ether was carefully removed to give a compound with identical vpc retention times[36,37] and infrared and nmr spectra with those of an authentic sample of oxocane (**19**).[8a]

Oxocan-3-yl Acetate (15). To a solution of 160 mg (1.6 mmol) of acetic anhydride and 130 mg (1.6 mmol) of pyridine cooled in an ice bath was added 150 mg (1.15 mmol) of **8**. The resulting solution was allowed to stand at room temperature for 18 hr; water and ether were added and the ether layer was separated, washed with dilute hydrochloric acid, until neutral, and then with water, and dried. Evaporation of the solvent gave 180 mg (92%) of **15**,

(34) Insufficient quantities of this substance precluded its complete characterization.

(35) Melting points were determined in open capillaries and are corrected, whereas boiling points are uncorrected. The microanalytical determinations were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Infrared spectra were recorded on a Perkin-Elmer Model 237 spectrophotometer. Ultraviolet spectra were determined with a Cary Model 14 spectrometer and the nmr spectra were obtained with a Varian A-60 spectrometer. The vapor phase chromatographic analyses and separations were carried out with a Varian-Aerograph A-700 gas chromatographic unit.

(36) A 5 ft × 0.25 in aluminum column packed with 20% Carbowax 20M on 60–80 mesh Chromosorb P was employed for this purpose.

(37) A 5 ft × 0.25 in. aluminum column packed with 10% SF-96 on 60–80 mesh Chromosorb P was employed for this purpose.

a pure sample of which was obtained by preparative vpc;[36] $\nu_{max}^{CCl_4}$ 1730 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 4.85 (multiplet, 1 H, -C*H*(OAc)-), 3.62 (multiplet, 4 H, -CH_2OCH_2-), 2.02 (singlet, 3 H, -OCOCH$_3$), and 1.50–1.90 (multiplet, 8 H).

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.75; H, 9.31.

Reduction of Acetates 15 and 16. A 580-mg (3.4 mmol) sample of a mixture of **15** and **16** which had been isolated by preparative vpc was reduced with 1.13 g (0.030 mol) of lithium aluminum hydride in 40 ml of anhydrous ether to give 430 mg (97%) of a mixture of alcohols **8** and **21**. The two alcohols were separated by preparative vpc;[36] the lesser alcohol was identical in all respects with an authentic sample of **8**.

The major alcohol (**21**) displayed the following nmr spectrum: $\delta_{TMS}^{CCl_4}$ 3.20–4.15 (complex multiplet, 6 H, -CH_2OC*H*CH_2O*H*-) and *ca.* 1.61 (broad peak, 8 H).

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.45; H, 10.92.

2-Oxepanylmethyl Brosylate (17). From 100 mg (0.77 mmol) of **21** and 410 mg (1.6 mmol) of *p*-bromobenzenesulfonyl chloride in 3 ml of pyridine, there was obtained 260 mg (97%) of **17** as white crystals from ether–pentane, mp 78.0–79.0°. The infrared spectrum of this material was superimposable upon that of the brosylate recovered from the acetolysis of **6**.

Cleavage of 2-Oxepanylmethyl Brosylate (17). A solution of 120 mg of **17** (which had been isolated from the solvolysis of **6**) in 2 ml of tetrahydrofuran under nitrogen was treated with 3 ml (6 equiv) of a green solution of sodium naphthalene anion radical [prepared from 310 mg (0.014 g-atom) of sodium and 1.80 g (0.015 mol) of naphthalene in 30 ml of tetrahydrofuran] added by means of a syringe. A few drops of water and a spatula of magnesium sulfate were added, the solution was filtered, the solvent was evaporated, and the resulting alcohol was collected by preparative vpc.[36] The alcohol thus obtained was identical with **21**.

2-Methyloxepane (22). A. Reduction of 17. To a solution of 1.04 g (4.0 mmol) of *p*-bromobenzenesulfonyl chloride in 2 ml of pyridine at 0° was added 250 mg (1.9 mmol) of a mixture of alcohols obtained from the solvolysis of **6**. The resulting solution was allowed to stand overnight at 5° and worked up in the usual manner to give 480 mg of a mixture of brosylates. The crude brosylate mixture was treated with 380 mg (10 mmol) of lithium aluminum hydride in ether and stirred for 12 hr. Isolation in the predescribed fashion gave 130 mg (60%) of a mixture of two reduction products (vpc analysis[38]). The high retention time peak corresponded to oxocane (**19**) and the low-retention time peak was found to be 2-methyloxepane (**22**); $\delta_{TMS}^{CCl_4}$ 3.30–3.80 (multiplet, 3 H, -CH_2OCH), *ca.* 1.60 (broad peak, 8 H, ring -CH$_2$-), and 1.10 (doublet, J = 6.5 Hz, 3 H, -CH$_3$).

Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.33; H, 12.30.

B. Hydrogenation of 2-Methyloxepin (23). A crude sample of 2-methyloxepin (**23**)[13] (approximately 1.5 g of 80% purity) dissolved in 30 ml of ether containing 2 ml of triethylamine and 0.10 g of platinum oxide was hydrogenated in a Parr hydrogenator. After filtration of the catalyst and evaporation of the solvent, the remaining liquid was subjected to preparative vpc[38] which gave 330 mg of 2-methyloxepane (**22**), identical in all respects with the previously prepared sample.

Solvolysis of 7. A solution of 4.75 g (0.013 mol) of **7**, 60 ml of glacial acetic acid, and 0.95 g (9.0 mmol) of sodium carbonate was stirred for 2 hr 50 min (10 half-lives) at 70°. The products were isolated as above; distillation of the residual liquid gave 2.32 g (99.5%) of a mixture of acetates, bp 82–84° (0.8 mm). Analysis by vpc[36] showed three peaks in the ratio of 74.5:2.2:23.3. Preparative vpc[38] separated the three constituents and the 2.2% component was found to have identical infrared spectrum and vpc retention times with those of an authentic sample of **24**. The 23.3% component (an impurity consisting of approximately 1% yield based on starting brosylate was present in this cut) was assigned the *exo*-cyclopropyl acetate structure (**27**); $\nu_{max}^{CCl_4}$ 1740 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 5.28 (multiplet, 1 H, C*H*OAc), 3.4–4.1 (multiplet, 4 H, -C*H*OCH_2-), 2.01 (singlet, 3 H, -OCOCH$_3$), *ca.* 1.7 (multiplet, 2 H, methylene group), and 0.28–1.32 (multiplet, 4 H, cyclopropyl protons).

The 74.5% component (two very minor components were found to be present in this fraction subsequent to hydride reduction) was characterized as the *exo*-cyclopropyl acetate **26**; $\nu_{max}^{CCl_4}$ 1740 cm^{-1}; δ 4.95 (multiplet, 1 H, C*H*OAc), 3.3–4.2 (multiplet, 4 H, -CH_2OCH_2-), 2.06 (singlet, 3 H, -OCOCH$_3$), 1.4–2.0 (multiplet, 2 H, methylene group), and 0.52–1.43 (complex multiplet, 4 H, cyclopropyl protons).

3,4,7,8-Tetrahydro-2H-oxocin-3-yl Acetate (24). Acetylation of 300 mg (2.3 mmol) of **9** with 300 mg of acetic anhydride and 240 mg of pyridine at room temperature for 18 hr gave 380 mg (96%) of **24**; $\nu_{max}^{CCl_4}$ 1730 cm^{-1}; $\delta_{TMS}^{CCl_4}$ *ca.* 5.8 (multiplet, 2 H, vinyl protons), 4.87 (multiplet, 1 H, C*H*OAc), 3.2–4.1 (complex multiplet, 4 H, -CH_2-OCH_2-), 2.1–2.9 (multiplet, 4 H, allylic protons), and 2.03 (singlet, 3 H, -OCOCH$_3$).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.42; H, 8.35.

Reduction of Acetate 26. Reduction of 980 mg (5.8 mmol) of the major acetate component from the solvolysis of **7** with 1.90 g (50 mmol) of lithium aluminum hydride in 40 ml of anhydrous ether gave 730 mg (99%) of a mixture of alcohols. Vpc analysis[38] of the mixture showed three peaks which when based on starting brosylate amounted to 1.5, 4.1, and 68.9%. The 1.5% product was not isolated in quantities sufficient for characterization.

The 4.1% component was assigned structure **28**; $\delta_{TMS}^{CCl_4}$ 5.59 (multiplet, 2 H, vinyl protons), 3.4–4.3 (multiplet, 6 H, -CH_2-OCH_2C*H*(O*H*)-), *ca.* 2.6 (multiplet, 2 H, allylic protons), and *ca.* 1.8 (multiplet, 2 H, methylene group). A small sample of this material when hydrogenated over platinum oxide gave **8**.

The major component was **31**; $\delta_{TMS}^{CCl_4}$ 2.95–4.6 (complex pattern, 6 H), 1.55–2.10 (multiplet, 2 H), and 0.33–1.40 (multiplet, 4 H, cyclopropyl protons). A sample of **31** was reacetylated to give pure **26**.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.28; H, 8.32. Found: C, 63.51; H, 8.29.

Oxidation of a Mixture of 31 and 32. To a solution of 1.50 g (11.7 mmol) of a mixture of **31** and **32** in 100 ml of acetone was added dropwise with stirring a solution of Jones' reagent[39] (prepared from 26.7 g of chromium trioxide in 23 ml of concentrated sulfuric acid diluted to 100 ml with water) until a yellow color persisted. The resulting mixture was stirred for 5 min and isopropyl alcohol was added until the yellow color had faded. The mixture was filtered, the insoluble solids were washed with acetone, the organic layers were combined, and the acetone was evaporated. Ether (100 ml) was added and the resulting solution was washed with saturated sodium bicarbonate solution, dried, and evaporated. There was obtained 1.10 g (75%) of **33**; $\nu_{max}^{CCl_4}$ 1720 and 1695 cm^{-1}.

The 2,4-dinitrophenylhydrazone of **33** was obtained as red-orange crystals from 95% ethanol, mp 189–191°.

Anal. Calcd for $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 50.65; H, 4.71; N, 18.32.

Reduction of 33. A solution of 1.10 g (8.75 mmol) of **33** in 50 ml of anhydrous ether was treated with 610 mg (16 mmol) of lithium aluminum hydride for 3 hr at room temperature. Work-up in the predescribed manner gave 1.11 g (99%) of a mixture of alcohols which was acetylated directly to permit vpc analysis.[36] The composition of the acetate mixture was seen to consist in 41% of **26** and 59% of **27**.

7,8-Dihydro-2H-oxocin-3(6H)-one (30). A solution of 2.0 g (15.6 mmol) of 7,8-dihydro-2H-oxocin-3(4H)-one and 1.72 g (10 mmol) of anhydrous *p*-toluenesulfonic acid in 40 ml of anhydrous benzene was heated at reflux for 15 min, cooled, and poured into 100 ml of saturated sodium carbonate solution. The layers were separated and the benzene phase was dried and evaporated. Distillation gave 1.1 g of colorless liquid, bp 82–84° (11 mm), vpc analysis[37] of which indicated the presence of 84.8% of starting β,γ-unsaturated ketone and 15.2% of **30**. Preparative vpc gave a sample of **30** of 80% purity; ν_{max}^{EtOH} 229.5 mμ (ϵ 8000). The ϵ_{max} value was corrected for the actual concentration of **30**.

Hydrogenation of 30. A solution of 34 mg (0.26 mmol) of **30** in 30 ml of ether containing 10 mg of 10% palladium on carbon was hydrogenated under 40 psig of hydrogen for 5 hr. Filtration of the catalyst and evaporation of the solvent afforded 30 mg (88%) of oxocan-3-one.

3,6,7,8-Tetrahydro-2H-oxocin-3-ol (29). To a stirred slurry of 320 mg (8.45 mmol) of lithium aluminum hydride in 40 ml of anhydrous ether at 0° was added dropwise a solution of 1.05 g (8.20 mmol) of an equilibrium mixture of **30** (15%) and 7,8-dihydro-2H-oxocin-3(4H)-one (85%) in 20 ml of ether. After stirring for 5 min at 0°, the reaction mixture was processed in the customary fashion

(38) A 5 ft × 0.25 in. aluminum column packed with 10% Carbowax 6000 on 60–80 mesh Chromosorb G was employed for this purpose.

(39) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

to give 1.00 g (93.5%) of a mixture of **9** (85.2%) and **29** (14.8%). A pure sample of **29** was isolated by preparative scale vpc;[36] $\delta_{TMS}^{CCl_4}$ 5.62 (multiplet, 2 H, vinyl protons), *ca.* 4.5 (multiplet, 1 H, $-CH-$(OH)–), 4.33 (singlet, 1 H, –OH), 2.9–4.0 (multiplet, 4 H, $-CH_2-OCH_2-$), and 1.3–2.5 (complex multiplet, 4 H, allylic and methylene protons).

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.30; H, 9.54.

Solvolysis of 2-Oxepanylmethyl Brosylate (17). A solution of 210 mg (0.60 mmol) of **17** and 43 mg (0.40 mmol) of sodium carbonate in 3 ml of glacial acetic acid was heated at 110° for 65 hr in a sealed tube. When the reaction mixture was processed in the predescribed manner, there was obtained 90 mg (88%) of a mixture of acetates which were reduced directly with lithium aluminum hydride to the corresponding alcohols. Vpc analysis of the alcohol mixture showed 56% of **21**, 23% of **8**, and 21% of an unknown alcohol. Samples of **8** and **21** which were isolated by preparative vpc[36] of this mixture exhibited infrared spectra which were identical with those of authentic samples.

Oxocan-3-ol-3-*d* (42). To a slurry of 360 mg (9.0 mmol) of lithium aluminum deuteride in 30 ml of dry ether was added 2.0 g (15.6 mmol) of oxocan-3-one in 20 ml of the same solvent. After stirring for 5 hr, the reaction mixture was worked up as above to give 2.0 g (99%) of **42**, $n^{25}D$ 1.4755; $\delta_{TMS}^{CCl_4}$ 3.96 (singlet, 1 H, –OH), *ca.* 3.5 (multiplet, 4 H, $-CH_2OCH_2-$), and 1.61 (broad peak, 8 H, methylene protons).

Oxocan-3-yl-3-*d* Brosylate (43). From 1.95 g (14.9 mmol) of **42** and 7.65 g (30 mmol) of *p*-bromobenzenesulfonyl chloride, there was obtained 5.15 g (99%) of **43** as white crystals from ether–pentane, mp 57.5–58.5°; $\delta_{TMS}^{CDCl_3}$ 7.71 (singlet, 4 H, aromatic protons), 3.60 (singlet, 4 H, $-CH_2OCH_2-$), and *ca.* 1.6 (multiplet, 8 H, methylene protons).

Solvolysis of Brosylate 43. A 4.0-g sample of **43** was solvolyzed in the same manner as its nondeuterated analog. After work-up, the acetates were converted directly to their corresponding alcohols with lithium aluminum hydride and separated by preparative vpc. The sample of **42** thus isolated had identical spectral properties with those of the authentic sample. This alcohol was converted to its corresponding acetate with acetic anhydride in pyridine in 84% yield. The nmr spectrum of this acetate displayed no peak in the δ 4.85 region.

The sample of **44** which was isolated in this fashion differed from **21** in its infrared, nmr, and mass spectra. Particularly significant was the presence of only five protons at low field which indicated that no 1,5-hydride shift had occurred.

Kinetic Procedure. Anhydrous acetic acid was prepared by refluxing a solution of acetic anhydride in glacial acetic acid for 24 hr and subsequent fractional distillation in a dry atmosphere. Standard perchloric acid in acetic acid (*ca.* 0.051 *M*) used in titrating aliquots was prepared by the addition of an accurately weighed amount of standard 70% perchloric to a known volume of anhydrous acetic acid. Standard sodium acetate in acetic acid (*ca.* 0.03 *M*) was prepared by the addition of anhydrous acetic acid to anhydrous sodium carbonate; the water of neutralization was not removed. The sodium acetate solution was standardized against the perchloric acid solution using bromophenol blue as the indicator. A *ca.* 0.02 *M* solution of brosylate (accurately weighed) in acetic acid–sodium acetate was prepared and aliquots (*ca.* 2.2 ml) were removed and sealed in glass ampoules. The ampoules were placed in a constant temperature bath and after 10 min the first ampoule was removed and quenched in ice–water. At this point an accurate timer was started. The ampoule was then placed in a beaker of water at room temperature for 4 min, whereupon exactly 1.925 ml of solution was removed from the ampoule by means of an automatic pipet and titrated with the standard perchloric acid solution. The remaining ampoules were removed at appropriately timed intervals, immediately quenched in ice–water, and titrated in the same fashion.

In the cases of **7** and **17**, the various rate constants were calculated by means of a least-squares computer program whereas the activation parameters and extrapolated rate constants were computed with the aid of the ACTENG computer program developed by Professor D. F. DeTar, Florida State University, and adapted to Fortran IV by D. H. Slater, The Ohio State University (IBM System 7094). For **6**, k_i, k_1, and k_2 were calculated as indicated in the text.

Acknowledgment. We thank the Army Research Office, Durham, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the funds employed in support of this research.