cis-3,3-Dimethylcyclopentyl-5-*d*-trimethylammonium Iodide. This compound and the corresponding undeuterated material were prepared by the method of Cooke and Coke.[9] The amine contained 89 ± 1% d_1 by mass spectrometry.

Elimination Reactions in Solution. Reactions were carried out in stainless steel ampoules[13] for at least ten half-lives. Rate constants were not known for the dimethylcyclopentyl salts, so reactions were run for twice to three times the period used for the cyclopentyl salts. An amount of the salt sufficient to give an approximately 0.1 *M* solution was weighed into the ampoule and 10 ml of 0.2 *M* base solution (at least a 100% excess) was added. The ampoule was heated in a thermostat for the specified time, cooled, and the contents were added to 10 ml of 2 *N* hydrochloric acid and 1 ml of *n*-pentane. In a few cases the reaction mixture was neutralized and analyzed directly by glpc.

Hofmann Elimination of Cyclopentyl-1-*d*-trimethylammonium Hydroxide. The aqueous solution of the hydroxide was evaporated *in vacuo* and the resulting syrup pyrolyzed at 120–130° in a stream of nitrogen. The products were collected in a Dry Ice trap. The cyclopentene was isolated and analyzed for deuterium at an ionizing voltage of 11 eV in the manner described below. It contained at least 0.99 atom of deuterium per molecule, thus demonstrating the absence of exchange at the α position prior to reaction.

Isolation and Analysis of Products. Cyclopentene from the Hofmann eliminations was purified by glpc on a 12 ft × 0.25 in. column of 20% tri-*o*-cresyl phosphate on Chromosorb P, using the gas inlet system. The olefin was collected in a liquid nitrogen trap. Cyclopentene from the reaction in dilute aqueous solution was distilled from the neutralized reaction mixture at −25° (carbon tetrachloride slush) to a liquid nitrogen trap on a high vacuum line. Cyclopentene was isolated from the reaction in *t*-butyl alcohol by neutralizing the reaction mixture, distilling 0.5–1.0 ml, and injecting the distillate on the glpc column described above. All other samples of cyclopentene were extracted into *n*-pentene (see above) and the extract injected on a 15 ft × 0.25 in. column of 20% adiponitrile on Chromosorb P. Under the conditions used (35°, 30 psi of helium), retention times were 3 min for *n*-pentane and 8 min for cyclopentene.

The dimethylcyclopentenes were in all cases extracted into *n*-pentane. Both collections and analyses (for the proportions of 3,3- and 4,4-dimethylcyclopentene) were performed on a 10-ft column of 40% silver nitrate–ethylene glycol on Chromosorb W. A 0.25-in. column at room temperature was used for collections, and a 1/8-in. column at 50° for analyses. For analyses of products from reactions in *t*-butyl alcohol, a 10 ft × 1/8 in. column of 20% Carbowax 20M on Chromosorb P was used in series with the silver nitrate column to hold back traces of *t*-butyl alcohol. All analyses were performed on a F & M Model 700 glpc equipped with a flame ionization detector and a Disc integrator. Measurement of relative peak areas with the integrator and with a planimeter gave the same results within experimental error.

Determination of Mass Spectra. The procedure was essentially the same as that previously described.[13] At least two ionizing voltages over the range of 70–13 eV (where no P − 1 peak is observed) were used and the spectra analyzed, according to standard methods.[25] Results at different ionizing voltages were indistinguishable. Appropriate corrections were made for the isotopic contents of the starting materials. In the case of the dimethylcyclopentenes, the deuterium content of the 3,3-dimethylcyclopentene (which cannot have lost deuterium during reaction) was used to correct the deuterium content of the 4,4-dimethylcyclopentene. The deuterium contents of the cyclopentenes and the dimethylcyclopentenes are given in Tables III and IV, respectively.

(25) K. Biemann, "Mass Spectrometry: Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 5.

Stereochemical Aspects of R_2O-3 Participation. Solvolytic Studies of the Epimeric 9-Oxabicyclo[4.2.1]nonan-2-yl Brosylates

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Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received December 31, 1969*

Abstract: Acetolysis of *endo*-9-oxabicyclo[4.2.1]nonan-2-yl *p*-bromobenzenesulfonate (**15**) is accompanied by direct interaction between the developing p orbital at C_2 and the lone pair orbital on oxygen. The oxonium ion so produced (**21a**) suffers ion-pair return to **15** and *endo*-9-oxabicyclo[3.3.1]nonan-2-yl brosylate (**17**) and concomitant passage to *endo* acetates **18** ad **19a**. The results are consistent with the observation that the first-order rate of solvolysis of **15** exhibits significant curvature through approximately one half-life whereupon the rate becomes steady. In the case of *exo*-9-oxabicyclo[4.2.1]nonan-2-yl brosylate (**16**), participation of the oxygen bridge by backside displacement is geometrically prohibited. Although its rate of solvolysis is steady, product analysis indicates that migration of the C_1–C_8 (which would provide the stereoelectronic backside shielding at C_2 in the manner truly characteristic of carbocyclic systems) does not occur because of the adverse inductive effect of the oxygen bridge. Rather, oxonium ion formation follows upon the rate-determining ionization. A number of other factors are organized and interpreted in terms of the high level of control exerted in unprecedented fashion by the oxygen atom in the solvolysis of **15** and **16**.

Because of the unique structural features associated with bridged bicyclic hydrocarbons, much attention has been given to solvolytic reactions of derivatives of such systems. The variety of available structural types has provided opportunity for assessment of the relative importance of participation by carbon–carbon σ electrons,[1] carbon–hydrogen σ electrons,[1] homoallylic π electrons,[1] remote π electrons,[2] and cyclopropane carbon–carbon σ electrons.[3] More recent develop-

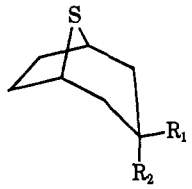
(1) For a review, see J. A. Berson in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, Part 1, p 213.

(2) (a) H. L. Goering and M. F. Sloan, *J. Amer. Chem. Soc.*, 83, 1992 (1961); (b) H. L. Goering, R. W. Greiner, and M. F. Sloan, *ibid.*, 83, 1391 (1961); (c) H. L. Goering and D. L. Towns, *ibid.*, 85, 2295 (1963); (d) N. A. LeBel and J. E. Huber, *ibid.*, 85, 3193 (1963); (e) N. A. LeBel and R. J. Maxwell, *ibid.*, 91, 2307 (1969).

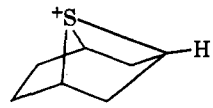
(3) (a) M. A. Battiste, C. L. Deyrup, R. E. Pincock, and J. Haywood-Farmer, *ibid.*, 89, 1954 (1967); (b) H. Tanida, T. Tsuji, and T. Irie,

ments have shown that certain pairs of cationic intermediates maintain their structural and conformational integrity and afford products characteristic of the stereochemical alignment of the leaving group in each instance.[4]

Although this area of study has provided much quantitative and qualitative insight into carbonium ion chemistry, only very limited attention has been given to systems containing atoms other than carbon. Ireland and Smith have shown that **1a** and **1b** solvolyze more

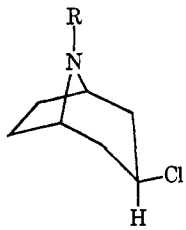


1a, $R_1 = H$; $R_2 = OTs$
b, $R_1 = OTs$, $R_2 = H$

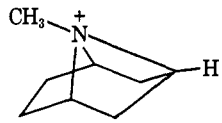


2

slowly in aqueous ethanol ($k_{rel}^{77°}$ = 0.46 and 0.21, respectively) than *trans*-4-*t*-butylcyclohexyl tosylate ($k_{rel}^{77°}$ = 1.00).[5] These workers concluded that direct participation by sulfur was not operative in the rate-determining step since facilitation of ionization was not encountered. On the other hand, the high stereospecificity of these solvolyses (only *endo* alcohol from either tosylate) was interpreted to mean that sulfonium ion **2** intervened after ionization had taken place.[6] 3-β-Chlorotropane (**3a**) and 3-β-chloronortropane (**3b**) undergo quantitative fragmentation in 80% ethanol.[7] In contrast, kinetic[7] and product analyses[7,8] of the behavior of 3-α-chloronortropane has been interpreted on the basis of carbonium ion **5**.[7]



3a, R = CH_3
b, R = H



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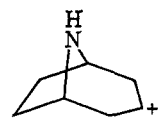
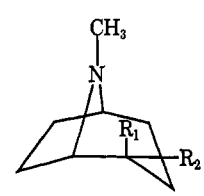
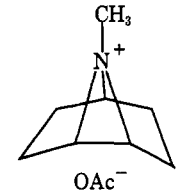


5

(+)-2-α-Tropanol (**6a**) undergoes racemization in refluxing acetic anhydride through the intermediacy of symmetrical ion **7**.[9] Interestingly, 2-β-chlorotropane (**6b**) is seen to rearrange in aqueous acetone with carbon migration to afford products *via* immonium ion **8**.[10,11]



6a, $R_1 = H$; $R_2 = OH$
b, $R_1 = Cl$; $R_2 = H$



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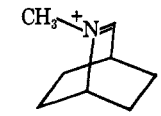
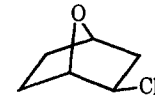
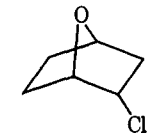


8

Of particular relevance to the present study is the work of Martin and Bartlett which showed that *exo*-7-oxanorbornyl chloride (**9a**) is substantially (2×10^3) less reactive than *exo*-norbornyl chloride and that the



9a



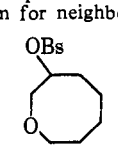
9b

endo counterpart (**9b**) solvolyzes 160 times more slowly at 140° than **9a**.[12] In either case, the solvolysis product (*cis*-3-formylcyclopentanol) was seen to be that resulting from Wagner–Meerwein rearrangement. This behavior was interpreted to be a reflection of the adverse inductive effect of the oxygen atom with no capability for R_2O-3 participation, particularly in the case of **9b**.

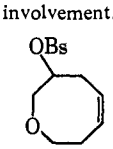
Thus, solvolysis of such bridged bicyclic heterocycles provides a unique opportunity to observe possible internal competition between at least four different phenomena: (a) unassisted ionization (*cf.* **5**); (b) unassisted ionization followed by bonding of the electron-deficient center to the heteroatom (*cf.* **2** and **4**); (c) preferred participation by carbon–carbon σ electrons (*cf.* **8** and **9a**); and (d) direct neighboring group participation by the heteroatom (*cf.* **7**). As yet, however, no clear definition of the relative efficiency of these various alternatives has emerged; in fact, even the qualitative order of nucleophilicity remains to be established.[13] As a result, we have initiated a systematic examination of ring size and geometrical effects in bridged bicyclic oxygen-containing molecules, and the present study describes the stereochemical aspects of R_2O-3 participation in the 9-oxabicyclo[4.2.1]nonan-2-yl system.

Results

9-Oxabicyclo[4.2.1]nonan-2-one (**12**) was prepared by bromination of 5-hydroxycyclooctanone (which exists almost exclusively in hemiketal form **10**)[16] and exposure



i



ii

relative order of nucleophilicity exhibited by these medium-sized rings is apparently not shared by acyclic ethers.[15]

ibid., 89, 1953 (1967); (c) R. M. Coates and J. L. Kirkpatrick, *ibid.*, 90, 4162 (1968).

(4) (a) J. A. Berson, J. J. Gajewski, and D. S. Donald, *J. Amer. Chem. Soc.*, 91, 5550 (1969); (b) J. A. Berson, M. S. Poonian, and W. J. Libbey, *ibid.*, 91, 5567 (1969); (c) J. A. Berson, D. S. Donald, and W. J. Libbey, *ibid.*, 91, 5580 (1969); (d) J. A. Berson, D. Wege, G. M. Clarke, and R. G. Bergman, *ibid.*, 91, 5594 (1969); (e) J. A. Berson, R. G. Bergman, G. M. Clarke, and D. Wege, *ibid.*, 91, 5601 (1969).

(5) R. E. Ireland and H. A. Smith, *Chem. Ind.* (London), 1252 (1959).

(6) For evidence that such behavior is not representative of sulfur's capability for electronic interaction, see L. A. Paquette, G. V. Meehan, and L. D. Wise, *J. Amer. Chem. Soc.*, 91, 3231 (1969).

(7) A. T. Bottini, C. A. Grob, E. Schumacher, and J. Zergenyi, *Helv. Chim. Acta*, 49, 2516 (1966).

(8) S. Archer, M. R. Bell, T. R. Lewis, J. W. Schulenberg, and M. J. Unser, *J. Amer. Chem. Soc.*, 79, 6337 (1957).

(9) S. Archer, T. R. Lewis, M. R. Bell, and J. W. Schulenberg, *ibid.*, 83, 2386 (1961).

(10) J. D. Hobson and W. D. Riddell, *Chem. Commun.*, 1180 (1968).

(11) For related behavior of isoquinuclidones, see J. W. Huffman, T. Kamiya, and C. B. S. Rao, *J. Org. Chem.*, 32, 700 (1967).

(12) J. C. Martin and P. D. Bartlett, *J. Amer. Chem. Soc.*, 79, 2533 (1957).

(13) In an earlier investigation,[14] it was shown that oxocan-3-yl brosylate (i) solvolyzes with R_2O-3 anchimeric assistance, but that the homoallylic participation available to ii overwhelms the capability of the oxygen atom for neighboring group involvement. However, the

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

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

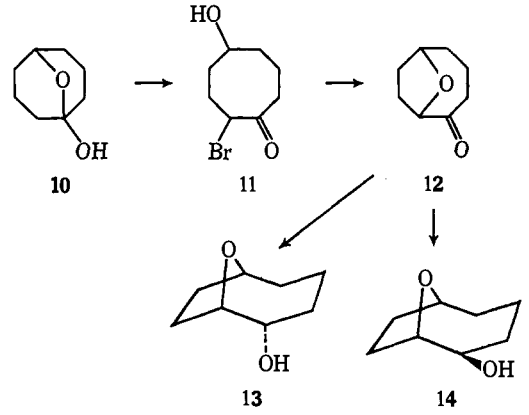
(16) We wish to thank Badische Anilin und Soda Fabrik, Ludwigshafen, Germany, for a generous supply of this material.

Table I. Acetolysis Rate Data for **15** and **16**

Compound	Rate constant designation	T, °C	Rate constant, $\times 10^5$ sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
15	k_i	39.98 ± 0.02	1.28 ± 0.02	24.5	−3.1
		50.05 ± 0.03	3.47 ± 0.03		
		65.00 ± 0.03	24.7 ± 1.5		
		25.00[a]	0.153		
		70.00[a]	39.7		
	k_1	39.98 ± 0.02	0.513	25.5	−1.4
		50.05 ± 0.03	1.70		
		65.00 ± 0.03	11.4		
		25.00[a]	0.0595		
		70.00[a]	19.5		
	k_2	39.98 ± 0.02	0.767	23.7	−6.7
		50.05 ± 0.03	1.77		
		65.00 ± 0.03	13.3		
		25.00[a]	0.0936		
		70.00[a]	20.4		
	k_3	50.05 ± 0.03	0.192 ± 0.009	32.4	15.4
		65.00 ± 0.03	1.87 ± 0.04		
		25.00[a]	0.00254		
		70.00[a]	3.83		
16	k	50.05 ± 0.03	0.242 ± 0.005	27.0	−0.8
		65.00 ± 0.03	1.61 ± 0.01		
		80.00 ± 0.12	9.37 ± 0.12		
		25.00[a]	0.00645		
		70.00[a]	2.96		

[a] Extrapolated values.

of the resulting bromo ketone (**11**) to methanolic potassium hydroxide.[17] Reduction of **12** with sodium borohydride in cold methanol solution afforded *endo* (axial) alcohol **13** in greater than 98% isomeric purity (vpc analysis). Dissolving lithium in liquid ammonia reduction[18] of **12** failed to produce the desired *exo* alcohol **14**. Rather, rupture of the oxygen bridge



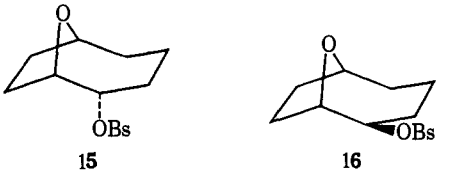
occurred to give 1,5-cyclooctanediol. Alternatively, Meerwein–Ponndorf–Verley reduction of **12** gave a 3:2 mixture of alcohols **14** and **13**, respectively. As it was not possible to separate efficiently these isomers by preparative vpc, the reaction mixture was converted to the *p*-nitrobenzoates. The two esters crystallized in distinctly different crystalline forms, making possible the manual separation of the *exo*-*p*-nitrobenzoate. Subsequent saponification of the purified *exo* ester gave isomerically pure **14**. To establish that no skeletal rearrangement had transpired during the conversion of **12** to **13** and **14**, these alcohols were oxidized and found to give rise exclusively to **12**.

(17) A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *J. Org. Chem.*, **34**, 2229 (1969). Appreciation is expressed to Dr. McKervey for making available the experimental procedure and an authentic sample of **12** prior to publication.

(18) A. A. Youssef, M. E. Baum, and H. M. Walborsky, *J. Amer. Chem. Soc.*, **81**, 4709 (1959).

Support for the configurational assignments of **13** and **14** is available from three convincing observations. First, the known responsive nature of sodium borohydride to steric development control[19] would be expected to give chiefly **13** from **12**, and this is observed. Also, the ability of aluminum isopropoxide to equilibrate **13** to **14** (ratio 2:3) serves to indicate that **14** is the thermodynamically favored *exo* isomer.[20] Last, by analogy to studies of nmr spectra of cyclohexane derivatives which reveal that equatorial protons are downfield shifted by about 0.48 ppm relative to axial protons,[21] the H_2 proton in **13** (δ 3.8, pseudoequatorial) should appear downfield from that of H_2 in **14** (δ 3.4, pseudoaxial). As indicated, the pertinent chemical shifts are in good agreement ($\Delta\delta$ = 0.4 ppm) with this prediction.

Brosylates **15** and **16** were prepared in cold pyridine and solvolyzed in sodium acetate–buffered acetic acid



at three different temperatures. The pertinent kinetic data are summarized in Table I. For **16**, graphs of log ($[HOBs]_\infty - [HOBs]_t$) *vs.* time were clearly linear through a time corresponding to at least three half-lives. The rate constants for **16** (k) were calculated using a computer program for the least squares treatment of the data applied to eq 1. Activation param-

(19) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *ibid.*, 78, 2579 (1956).

(20) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 244.

(21) (a) F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N. Y., 1969, p 77; (b) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, 80, 6098 (1958).

eters and extrapolated rate constants were computed

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

with the aid of the ACTENG computer program.[22]

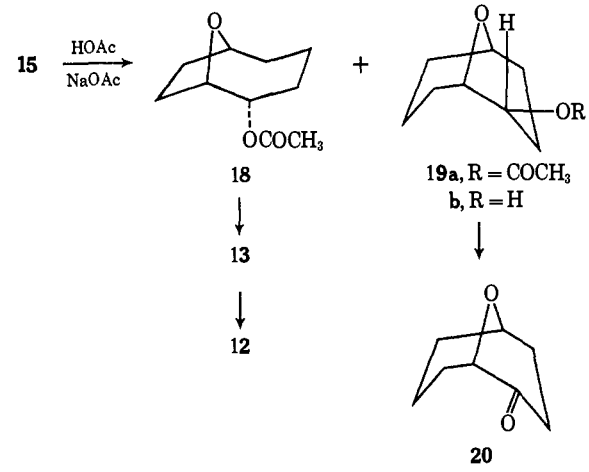
In contrast, the acetolysis of **15** was found to proceed to partial completion and then to form *p*-bromobenzenesulfonic acid at a slower rate. Graphs of log ($[\text{HOBs}]_\infty - [\text{HOBs}]_t$) *vs.* time exhibited significant curvature through approximately one half-life whereupon the plot became linear. This behavior, which was highly reproducible, is suggestive of concomitant internal return to a less reactive brosylate. In such a case, calculation of the initial rate constant can be accomplished using eq 1; however, because the disappearance of **15** proceeds at a rate faster than the appearance of *p*-bromobenzenesulfonic acid, use of the experimental infinity titer value would cause the calculated rate constant to be too small unless the rearranged sulfonate were unreactive.[23] In the present situation, the rearranged brosylate, while solvolyzing at a rate slower than **15**, does nevertheless contribute *p*-bromobenzenesulfonic acid in significant amounts as the reaction progresses. As a result, rate constant k_i must be evaluated in terms of a theoretical infinity titer obtained by a successive approximation treatment.[24] Of the four rate constants given for **15** in Table I, k_i is therefore its initial rate of disappearance and represents the sum of the rate constants for *p*-bromobenzenesulfonic acid production (k_1) and rearrangement (k_2, eq 2).[25] Since the ratio of acid produced to rearranged ester is equal to k_1/k_2 and as this is conveniently evaluated from the amount of acid produced at estimated infinity, k_1 and k_2 are readily obtained.

$$\begin{array}{l} \text{ROBs} \xrightarrow{k_1} \text{HOBs} + \text{ROAc} \\ \quad \mathbf{15} \\ \quad \downarrow k_2 \\ \text{R'OBs} \\ \quad \mathbf{17} \end{array} \quad (2)$$

$$k_i = k_1 + k_2$$

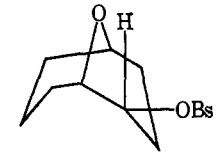
For the latter part of the acetolysis during which a plot of log ($[\text{HOBs}]_\infty - [\text{HOBs}]_t$) *vs.* time was linear, the first-order rate constant is termed k_3. If rearranged brosylate **17** solvolyzes without significant ion return to **15**, then k_3 corresponds to the rate of acetolysis of **17**. If, however, a pseudo equilibrium between **15** and **17** is maintained, then k_3 corresponds to the rate constant for the acetolysis of that equilibrium mixture. For the acetolysis of **15**, this rearrangement is reversible and does reach equilibrium (*vide infra*).[26]

The product mixture formed in the acetolysis of **15** was found to consist of equal parts of acetates **18** and **19a**. This acetate mixture was reduced with lithium aluminum hydride to alcohols **13** and **19b** which, in common with the acetates, were not efficiently separated by vapor phase chromatography. However, this alcohol mixture did not display any of the nmr absorptions characteristic of *exo* isomer **14**, thereby



confirming its absence. Oxidation of the alcohol mixture afforded two ketones that were separated by preparative vpc and identified as **12** and **20**.

That the downward drift in the rate was indeed due to isomerization to the less reactive bicyclo[3.3.1] isomer **17** was demonstrated by isolation of the unsolvolyzed



17

tosylate from an acetolysis experiment after incomplete reaction. Cleavage of the *p*-bromobenzenesulfonyl group in **17** with a solution of sodium naphthalene anion radical in tetrahydrofuran gave **19b** which was reoxidized to **20** for final characterization. Significantly, although this incomplete solvolysis had been allowed to proceed until the production of *p*-bromobenzenesulfonic acid was clearly first order, a significant amount of **15** was isolated along with **17**. Resubmission of **17** to the acetolysis conditions likewise gave rise to an equal mixture of **18** and **19a**. Such data attest to the interconversion of **15** and **17** during solvolysis by way of ion pair return.

Because both isomeric brosylates afford the same product mixture, it is most reasonable that the two processes are related to common oxonium ion intermediate **21a** (Scheme I). In the absence of solvent interference, this intimate ion pair can partition itself between **15** and **17** by internal ion return.[27] Sub-

(22) This program was developed by D. F. DeTar and adapted to Fortran IV by D. H. Slater.

(23) For a case in which this situation obtains, see E. L. Allred and S. Winstein, *J. Amer. Chem. Soc.*, 89, 4012 (1967).

(24) In the present work, the theoretical infinity values were calculated with an IBM System 360 computer program whose function is to increment successively the particular infinity value until the ratio of the standard deviation, obtained from a least squares treatment of the data applied to eq 1, to the rate constant reaches a minimum. This technique is essentially equivalent to the rate equation

$$[\text{HOBs}]_t = [\text{ROBs}]_0\left[1 - \frac{k_2}{k_1 + k_2 - k_3} e^{-k_3 t} - \frac{k_1 - k_3}{k_1 + k_2 + k_3} e^{-(k_1+k_2)t}\right]$$

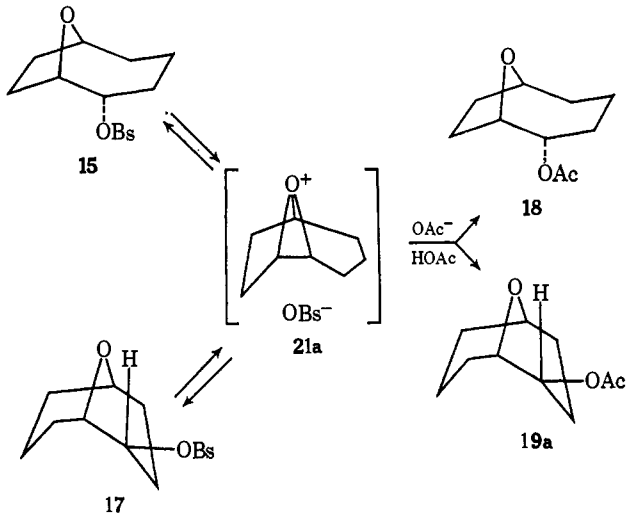
where k_{-2} is assumed to be zero.

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

(26) A related phenomenon has been observed with bicyclo[2.2.2]-octan-2-yl and axial bicyclo[3.2.1]octan-2-yl tosylates: H. L. Goering and M. F. Sloan, *J. Amer. Chem. Soc.*, 83, 1992 (1961).

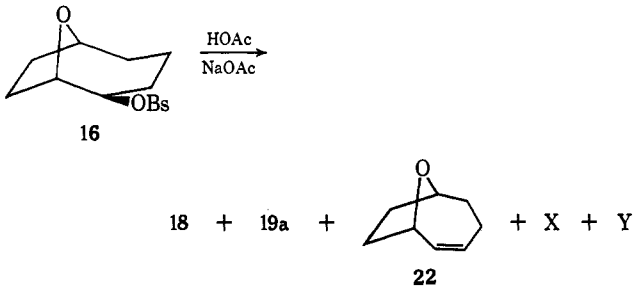
(27) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck, and G. C. Robinson, *ibid.*, 78, 328 (1956).

Scheme I



sequent ionization of **15** and **17** repeats the formation of **21a**, solvent attack on which produces *endo* acetates **18** and **19a**. That no products were obtained from solvent attack at the rearside C–O bond in **21a** is in agreement with the prediction that nucleophilic attack to open a five-membered ring will be significantly slower than the rate of attack on the strained three-membered ring.

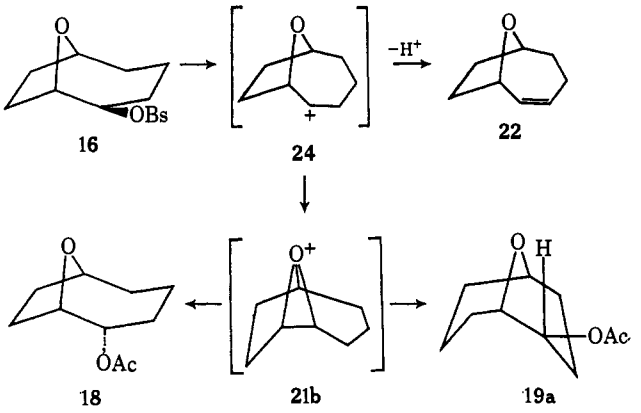
The product mixture obtained from the acetolysis of **16** consisted of five components. The three major constituents were readily identified as *endo* acetates **18** (35%) and **19a** (35%), and olefin **22**. The minor constituents X (8%) and Y (7%) were not characterized



because of limited quantities and their high volatility; however, it was clear that neither substance was *exo*-9-oxabicyclo[4.2.1]nonan-2-yl acetate (**23**) or *exo*-9-oxabicyclo[3.3.1]nonan-2-yl acetate. The latter two acetates as well as **18** and **19a** were stable to the solvolysis conditions.

Participation of the oxygen bridge by backside displacement of the departing brosylate ion in the rate-determining step as observed with **15** and **17** is structurally prohibited in **16** because of geometrical constraints produced by the tetrahydrofuran ring. Rather, concomitant with the departure of brosylate ion, C_2 must experience rehybridization from sp^3 to sp^2. Loss of a proton from C_3 serves to give olefin **22**. We feel that intermediate **24** must have only a fleeting existence, as solvent attack would be predicted to produce both *exo* and *endo* products. The ultimate acetate ratio discounts this possibility. However, the observed product distribution reveals that bonding of the oxygen bridge to the cationic site in **24** predominates and leads to **21b** from which acetates **18** and **19a** are formed in equal amounts (Scheme II).

Scheme II



Discussion

Comparison of the acetolysis rate constants for *endo*-brosylate **15** and *exo*-brosylate **16** (Table I) shows that solvolysis of **15** proceeds at a rate 24 times faster than **16** at 25°. This observation is in direct contrast to related bicyclic systems where the *exo* isomer is clearly more reactive. For example, *exo*-norbornyl brosylate (**25**) liberates brosylate ion 350 times faster than its *endo* counterpart (**26**) at 25° under acetolysis conditions (Table II). The bicyclo[3.2.1]oct-2-yl isomers **27** and **28** display a similar tenfold reactivity difference (50°).[28] Consideration need also be given to the 7-oxanorbornyl chlorides **9a** and **9b**, since they represent the only other oxygen-containing bicyclic system to be examined to date. Interestingly, the *exo*/*endo* reactivity ratio (318 at 25°) in this instance is very nearly comparable to that of the epimeric norbornyl chlorides, a result which forced the conclusion that an oxonium ion does not intervene in the *endo* transition state.[12]

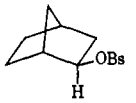
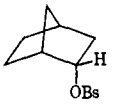
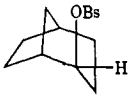
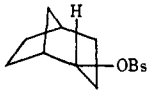
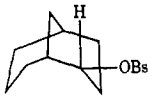
Examination of Tables I and II shows that the acetolysis rate constant for **16** is 2×10^{-2} times as large as the rate constant for **27** at 50°. This retardation is viewed to be the result of the adverse inductive effect of the proximate ether oxygen atom which, *in the absence of anchimeric assistance*, would be expected to cause a 100-fold reduction in rate.[14,15,29] Clearly, this rate comparison and the *exo*/*endo* ratio discussed earlier attest to the absence of R_2O-3 participation during the rate-determing ionization step of **16**. Once ion **24** is formed, however, slight geometric changes (and possibly a concomitant lowering in potential energy) give rise to **21** as evidenced by the formation of equal amounts of **18** and **19a**.

The analogous scheme is incompatible with the behavior of **15**. Specifically, it is noted that the solvolytic rate constant for **15** is roughly comparable to that of **28** at 50°. If the anticipated rate reduction caused by the inductive effect of neighboring oxygen is included, the adjusted rate constant for **15** becomes approximately 100 times greater than that of **28**. This factor of 10^2, which corresponds closely to the

(28) Unfortunately, kinetic data for derivatives of the bicyclo[4.2.1]-nonan-2-yl system do not yet seem to be available. However, there is no reason to expect a reversal of the *endo*/*exo* reactivity order demonstrated by **25**–**28** in this strictly homologous situation (note the behavior of **29**).

(29) (a) S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Amer. Chem. Soc.*, 70, 821 (1948); (b) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber, and J. Corse, *ibid.*, 74, 1113 (1952); (c) D. D. Roberts and W. Hendrickson, *J. Org. Chem.*, **34**, 2415 (1969).

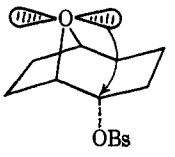
Table II. Selected Acetolysis Rates

Compound	T, °C	k, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	Ref
 25	25.0	8.82×10^{-5}			*a*
 26	25.0	2.52×10^{-7}	26.0	−1.5	*a*
 27	49.3	1.2×10^{-4} [e]			*b*
 28	48.9	1.0×10^{-5} [e]	27.1	0.2	*c*
 29	49.3 62.5	3.3×10^{-5} [e] 1.8×10^{-5} [e]			*d*

[a] S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan, and H. Marshall, *J. Amer. Chem. Soc.*, **74**, 1127 (1952). [b] H. L. Goering and G. N. Fickes, *ibid.*, **90**, 2848 (1968). [c] H. L. Goering and M. F. Sloan, *ibid.*, **83**, 1992 (1961). [d] M. Hanack, W. Kraus, W. Rothenwöhrer, W. Kaiser, and G. Wentrup, *Ann.*, **703**, 44 (1967). [e] Values obtained by multiplication of the acetolysis rate constant of the corresponding tosylate by a factor of 3.

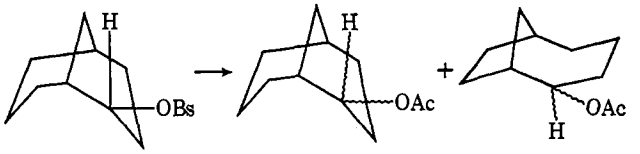
driving force observed in MeO-6 neighboring group participations,[2,3] is entirely compatible with oxonium ion intervention at the transition state which, in turn, is in complete agreement with the acetate product distribution.

Such direct interaction between a developing p orbital at C_2 and the lone pair orbital on oxygen in **15** (*cf.* **30**) is evidently not shared by **9b**. Also, the



30

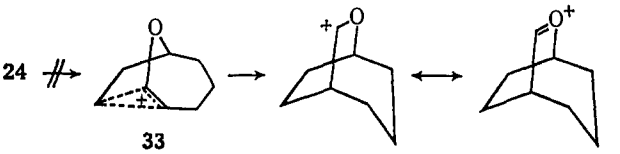
exclusive formation of *endo* acetates attests to the significant control exerted by the oxygen bridge in the solvolysis of both **15** and **17**. By contrast, acetolysis of **29** has been reported to afford all four acetates



29 **31** **32**

derivable from **31** and **32** in a nonequimolar ratio.[30]

Finally, it is significant to note that whereas carbobicyclic tosylates and brosylates generally exhibit a marked resistance to interconversion of their derived carbonium ions from one system to another,[2,4] introduction of an oxygen bridge as in **15** and **16** results in total loss of the memory effect. In the case of cation **24**, this "amnesia" is the result of inability on the part of the C_1–C_8 bond to provide the necessary stereoelectronic backside shielding of C_2 (*cf.* **33**) because of the inductive effect of the proximate oxygen center. Since the high energy requirements for this 1,2-carbon migration are not readily overcome, the stabilizing resonance effects available to **34** are not realized and



33 **34**

oxonium ion intervention dominates the scene. The causes of the marked difference in behavior between **9b** and **15** are presently the subject of investigation in this laboratory.

Experimental Section[31]

endo-**9-Oxabicyclo[4.2.1]nonan-2-ol (13).** To a solution of 4.5 g (0.032 mol) of ketone **12**[17] in 100 ml of absolute methanol at ice temperature was added 5.7 g (0.15 mol) of sodium borohydride in small portions. After being stirred overnight at ambient temperature, this solution was diluted with 100 ml of water, stirred for 1 hr, and extracted with dichloromethane. The combined extracts

(30) M. Hanack, W. Kraus, W. Rothenwöhner, W. Kaiser, and G. Wentrup, *Ann.*, 703, 44 (1967).

(31) Melting points are corrected, whereas boiling points are uncorrected. The microanalytical determinations were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark, and Galbraith Laboratories, Inc., Knoxville, Tenn. Nmr spectra were recorded with Varian A-60, A-60A, and HA-100 spectrometers. The vapor phase chromatographic analyses and separations were carried out with a Varian-Aerograph A-90P3 gas chromatographic unit.

were dried, concentrated, and sublimed to give 4.3 g (95%) of **13** (greater than 98% isomeric purity by vpc analysis) as hygroscopic white crystals: mp 60–62°; $\delta_{TMS}^{CCl_4}$ 1.1–2.3 (m, 10, H-3,4,5,7,8), 3.6–4.0 (m, 2, H-6 and –OH), and 4.1–4.6 (m, 2, H-1,2).

The phenylurethan of **13** was obtained as white crystals, mp 98–99°, from hexane.

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.94; H, 7.29; N, 5.47.

***exo*-9-Oxabicyclo[4.2.1]nonan-2-ol (14).** A solution containing 14.0 g (0.10 mol) of **12** and 20.4 g (0.10 mol) of aluminum isopropoxide in 125 ml of 2-propanol (freshly distilled from calcium oxide) was refluxed overnight. A distillation head was attached to the reaction flask and the solution was slowly distilled until the distillate gave a negative 2,4-dinitrophenylhydrazine test. The solution was then concentrated under reduced pressure and the residual oil was diluted with 200 ml of 1 *N* hydrochloric acid and extracted with dichloromethane. The combined extracts were dried and concentrated to give 17.0 g of a mixture of **14** and **13** in a ratio of 3:2 (vpc analysis).

To a solution of 4.3 g (0.03 mol) of this mixture in 25 ml of cold pyridine was added 7.5 g (0.04 mol) of *p*-nitrobenzoyl chloride, and the mixture was stirred for 2 hr at ambient temperature. This solution was poured into 75 ml of ice water and the solid was collected on a filter. The product was washed successively with 20 ml of saturated sodium bicarbonate solution and two 25-ml portions of water. The crude ester was air dried to afford 7.2 g (83%) of yellow crystals, mp 62–74°. Recrystallization of this material from ether–hexane gave a mixture of two distinctly different crystalline solids. The mushroomlike crystals were separated and recrystallized from ether–hexane to constant melting point, mp 83–85°.

A solution of 1.6 g (5.5 mmol) of pure *p*-nitrobenzoate and 1.5 g (28.0 mmol) of potassium hydroxide in 30 ml of methanol was refluxed for 36 hr. The solution was then cooled, poured into 50 ml of ice water, and extracted with dichloromethane. The combined extracts were dried, concentrated, and sublimed to give 0.7 g (90%) of **14** as very hygroscopic white crystals of greater than 99% purity (vpc analysis): $\delta_{TMS}^{CCl_4}$ 1.1–2.2 (m, 10, H-3,4,5,7,8), 3.3–3.6 (m, 2, H-6 and –OH), and 4.0–4.5 (m, 2, H-1,2).

The phenylurethan of **14** was obtained as white crystals, mp 159–160°, from hexane.

Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.07; H, 7.50; N, 5.37.

Epimerization of 13. A solution of 4.7 g (0.03 mol) of **13** in 40 ml of anhydrous 2-propanol was heated at reflux for 48 hr in the presence of 2.0 g (0.01 mol) of aluminum isopropoxide and 0.5 ml of acetone. The solution was cooled, concentrated, and treated with 90 ml of 1 *N* hydrochloric acid. The acidic solution was extracted with dichloromethane and the combined organic extracts were dried and concentrated to give 4.7 g (100%) of a mixture of **14** and **13** in the ratio of 3:2 (vpc analysis).

Oxidation of 13. A solution of chromic acid reagent (prepared by dissolving 26.72 g of chromium trioxide in 23 ml of concentrated sulfuric acid and diluting to 100 ml with water) was added dropwise to a solution of 250 mg (1.8 mmol) of **13** in 50 ml of a acetone until the red color persisted for at least 5 min. A few drops of 2-propanol were then added to destroy excess oxidant. The supernatant liquid was decanted, and the salts were washed with acetone. The combined acetone solutions were neutralized with sodium bicarbonate, filtered, and concentrated. The resulting oil was treated with 10 ml of water and extracted with dichloromethane. The combined extracts were dried and concentrated to give 170 mg (68%) of an oil with spectra identical with those of **12**.

Oxidation of 14. A solution of 80 mg (0.6 mmol) of **14** in 50 ml of acetone was treated with chromic acid as above to give 80 mg (100%) of an oil with spectra identical with those of **12**.

***endo*-9-Oxabicyclo[4.2.1]nonan-2-yl *p*-Bromobenzenesulfonate (15).** A solution of 5.1 g (0.02 mol) of *p*-bromobenzenesulfonyl chloride in 20 ml of cold pyridine was added to a solution of 1.4 g (0.01 mol) of **13** in 10 ml of cold pyridine and the resulting solution was allowed to stand overnight at 5°. Ice was added to hydrolyze excess sulfonyl halide and the mixture was diluted with 50 ml of water. This solution was extracted with two 50-ml portions of ether and the combined organic layers were washed repeatedly with 25-ml portions of cold 1 *N* hydrochloric acid until the wash remained acidic. This was followed by consecutive washing with one 25-ml protion of 5% sodium carbonate solution, drying, and evaporation to give 3.3 g (92%) of crude **15**. Recrystallization of this solid from ether–hexane afforded pure **15** as white crystals, mp 76–77°.

Anal. Calcd for $C_{14}H_{17}BrO_4S$: C, 46.54; H, 4.74; S, 8.88. Found: C, 46.43; H, 4.86; S, 8.93.

***exo*-9-Oxabicyclo[4.2.1]nonan-2-yl *p*-Bromobenzenesulfonate (16).** Using the same procedure as above, 1.5 g (1.5 mmol) of **14** was converted to **16** (3.5 g, 92%), mp 114–115°.

Anal. Calcd for $C_{14}H_{17}BrO_4S$: C, 46.54; H, 4.74; S, 8.88. Found: C, 46.45; H, 4.72; S, 9.08.

Acetolysis of 15. A solution containing 3.6 g (10.0 mmol) of brosylate **15** and 0.9 g (8.5 mmol) of anhydrous sodium carbonate dissolved in 55 ml of acetic acid was heated at 80° overnight. The solution was then cooled, diluted with 150 ml of water, and extracted with three 100-ml portions of ether. The combined extracts were washed with 50-ml aliquots of saturated sodium bicarbonate solution until neutral, dried, and concentrated to give 1.7 g (92%) of a mixture of acetates **18** and **19a** (vpc and nmr analysis).

A solution containing 500 mg (2.7 mmol) of this acetate mixture in 5 ml of dry ether was added dropwise to a slurry of 400 mg (10 mmol) of lithium aluninum hydride in 10 ml of the same solvent. After being stirred for 2 hr, the mixture was cooled and decomposed in the customary alkaline fashion to give 400 mg (100%) of alcohol mixture. The nmr spectrum of this material excluded the possibility of the presence of alcohol **14**.

A solution containing 350 mg (2.5 mmol) of this alcohol mixture dissolved in 50 ml of acetone was treated with chromic acid reagent in the predescribed fashion. The product obtained from this oxidation (220 mg, 64%) was shown by vpc retention times and nmr spectra to be a 1:1 mixture of ketones **12** and **20**.

Interrupted Acetolysis of 15. A solution containing 3.6 g (10.0 mmol) of **15** and 0.9 g (8.5 mmol) of sodium carbonate dissolved in 55 ml of acetic acid was heated at 65° for 12,000 sec (4 half-lives). The solution was quickly cooled and extracted as above to give an oil. From this oil dissolved in ether–pentane was deposited 0.9 g of crystals, mp 85–100°. Repeated recrystallizations of this solid from the same solvent system gave pure brosylate **17**, mp 113–114°.

Anal. Calcd for $C_{14}H_{17}BrO_4S$: C, 46.54; H, 4.74; S, 8.88. Found: C, 46.73; H, 4.81; S, 8.81.

A solution containing 200 mg (0.55 mol) of crude brosylate from above in 2 ml of dry tetrahydrofuran was treated under nitrogen with 9 ml of 0.3 *M* sodium naphthalene anion radial solution[32] prepared by adding 0.345 g (0.015 g-atom) of sodium metal to a solution of 1.92 g (0.015 mol) of naphthalene in dry tetrahydrofuran. Subsequently, a few drops of water were added and the solution was dried, filtered, and evaporated. The crude oil was purified with chromic acid solution in the above fashion to give a mixture of ketones **12** and **20** as shown by nmr and vpc.

A solution containing 0.55 g (1.5 mmol) of crude brosylate mixture and 140 mg (1.3 mmol) of sodium carbonate in 9 ml of acetic acid was heated overnight at 80°. Work-up of this solution in the usual manner gave 250 mg (91%) of an oil whose composition consisted of a 1:1 mixture of **18** and **19a** (vpc and nmr analysis).

Acetolysis of 16. A solution of 3.6 g (0.01 mol) of **16** and 0.9 g (8.5 mmol) of sodium carbonate in 55 ml of acetic acid was heated at 80° for 24 hr. The solution was cooled, diluted with 150 ml of water, and extracted with three 100-ml portions of ether. The combined extracts were neutralized by washing with 50-ml aliquots of a saturated sodium bicarbonate solution. The organic layer was dried and concentrated to give 1.5 g of crude product which was separated by preparative vpc on a 5 ft × 0.25 in. column packed with 10% SF-96 on 60–80 mesh Chromosorb G into four major peaks.

Peak 1 (15%) was found to be 9-oxabicyclo[4.2.1]non-2-ene (**22**): $\delta_{TMS}^{CCl_4}$ 1.4–2.5 (m, 8, H-4,5,7,8), 4.3–4.7 (m, 2, H-1,6), and 5.3–5.9 (m, 2, H-2,3).[33] Peaks 2 (8%) and 3 (7%) were not characterized. Peak 4 actually consisted of a 1:1 mixture of acetates **18** and **19a**, a conclusion which was verified by nmr analysis and by vpc separation (10% SF-96 column).

General Acetylation Procedure. A solution of 300 mg (2.1 mmol) of **13** and 300 mg (3.0 mmol) of acetic anhydride in 240 mg (3.9 mmol) of pyridine was allowed to stand overnight at room temperature. Ice water (10 ml) was added and the mixture was extracted with ether. The combined extracts were washed with 10-ml portions of 1 *N* hydrochloric acid until the wash remained acidic. After a final wash with 10 ml of saturated sodium bicarbonate

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

(33) A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *J. Org. Chem.*, **34**, 2229 (1969). The chemical shift data reported by Cope and coworkers were not corrected for significant distortions in field width. After such corrections, the spectra of the two samples were superimposable. Appreciation is expressed to Dr. Weinshenker for making the original spectrum available to us.

Table III. Acetolysis Rate Calculations for **15** at Various Temperatures[a]

39.98 ± 0.02°		50.05 ± 0.03°		65.00 ± 0.03°	
Time, sec	0.02001 *M* $HClO_4$, ml	Time, sec	0.02001 *M* $HClO_4$, ml	Time, sec	0.02001 *M* $HClO_4$, ml
0	4.473	0	4.440	0	4.332
5,000	4.408	7,250	4.172	600	4.179
12,000	4.332	14,500	3.948	1,200	4.048
19,000	4.246	21,000	3.794	2,400	3.840
31,000	4.127	27,000	3.692	∞	1.793
40,000	4.060	∞	1.770	Calcd ∞	3.290[b]
∞	1.777	Calcd ∞	3.195[b]		
Calcd ∞	3.450[b]				
$k_i = 1.30 \times 10^{-5}$ sec^{-1}		$k_i = 3.44 \times 10^{-5}$ sec^{-1}		$k_i = 2.61 \times 10^{-4}$ sec^{-1}	
$k_1 = 5.1 \times 10^{-6}$ sec^{-1}		$k_1 = 1.7 \times 10^{-5}$ sec^{-1}		$k_1 = 1.1 \times 10^{-4}$ sec^{-1}	
$k_2 = 7.7 \times 10^{-6}$ sec^{-1}		$k_2 = 1.7 \times 10^{-5}$ sec^{-1}		$k_2 = 1.3 \times 10^{-4}$ sec^{-1}	

[a] Aliquots of 0.923 ml were employed. [b] Value obtained by successive approximation method outlined in text.

solution, the ether layer was dried and concentrated to give 400 mg (100%) of **18**. The oil was purified by preparative vpc (10% SF-96 column): $\delta_{TMS}^{CCl_4}$ 1.1–2.3 (m, 13, H-3,4,5,7,8, and $-CH_3$), 4.2–4.6 (m, 2, H-1,6) and 4.7–5.1 (m, 1, H-2).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.10; H, 8.75.

In analogous fashion, 200 mg of **14** afforded acetate **23** in quantitative yield. Similar vpc purification afforded the analytical sample: $\delta_{TMS}^{CCl_4}$ 1.4–2.4 (m, 13, H-3,4,5,7,8, $-CH_3$) and 4.1–4.8 (m, 3, H-1,2,6).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.07; H, 8.82.

9-Oxabicyclo[3.3.1]nonan-2-one (20). A solution of 15.0 g (0.06 mol) of 2-iodo-9-oxabicyclo[3.3.1]nonane,[34] 29.4 g (0.3 mol) of potassium acetate, and 20 ml of water in 100 ml of glacial acetic acid was refluxed overnight. The solution was cooled, diluted with 100 ml of cold water, and extracted with dichloromethane. The combined dried extracts were evaporated and the resulting oil was heated with 100 ml of acetic anhydride and 5.0 g of potassium acetate. After being stirred overnight, the solution was diluted with 150 ml of cold water, stirred for 1 hr, and extracted with dichloromethane. The combined extracts were washed with four 25-ml portions of saturated sodium bicarbonate solution until neutral, concentrated, dried, and distilled to give 5.7 g (52%) of an oil, bp 110–112° (2.3 mm), composed of a mixture of **18** (40%) and **19a** (60%) by vpc and nmr analysis.

A sample of this acetate mixture (4.5 g, 0.024 mol) dissolved in 25 ml of anhydrous ether was added dropwise to a slurry of 1.1 g (0.03 mol) of lithium aluminum hydride in 50 ml of the same solvent, and the resulting mixture was stirred overnight at ambient temperature. The solution was cooled and successively treated with 1.1 ml of water, 1.1 ml of 25% sodium hydroxide solution, and 3.3 ml of water. The slurry was filtered and concentrated to give 3.3 g (97%) of alcohol mixture.

A solution of 300 mg (2.0 mmol) of this mixture in 50 ml of acetone was oxidized with chromic acid reagent in the usual manner to give 140 mg (50%) of an oil. Preparative scale vpc separation (10 ft × 0.25 in. Al column packed with 10% QF-1 on 60–80 mesh Chromosorb G) led to the successful isolation of **12** (40%) and **20** (60%): $\delta_{TMS}^{CCl_4}$ 1.2–2.9 (m, 10, H-3, 4, 6, 7, 8), 3.8–4.1 (m, 1, H-5), and 4.1–4.5 (m, 1, H-1).

The 2,4-dinitrophenylhydrazone of **20** was obtained from ethanol–water as yellow crystals, mp 153–155°.

Anal. Calcd for $C_{14}H_{16}N_4O_5$: C, 52.49; H, 5.04; N, 17.49. Found: C, 52.47; H, 5.07; N, 17.11.

The synthesis of *exo*-9-oxabicyclo[3.3.1]nonan-2-yl acetate will be described in a subsequent paper.

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 removed, sealed in glass ampoules, and immersed in a constant-temperature bath. After 10 min, the first ampoule was removed, an accurate timer started, and the ampoule quickly cooled in an ice–water bath. The ampoule was then placed in a vessel of water at room temperature. After 4 min, exactly 0.923 ml of solution was removed with 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

Table IV. Acetolysis Rate Calculations for **15** ⇌ **17** at 50.05 and 65.00° [a]

50.05 ± 0.03°		65.00 ± 0.03°	
Time, sec	0.02001 *M* $HClO_4$, ml	Time, sec	0.02001 *M* $HClO_4$, ml
162,000	2.913	0	4.317
169,000	2.883	24,000	2.883
176,000	2.876	31,500	2.754
183,000	2.861	38,500	2.625
194,000	2.835	45,500	2.536
201,000	2.824	52,500	2.433
∞	1.791	59,500	2.350
		∞	1.800
$k_3 = 1.84 \times 10^{-6}$ sec^{-1}		$k_3 = 1.91 \times 10^{-5}$ sec^{-1}	

[a] Aliquots of 0.923 ml were employed.

Table V. Acetolysis Rate Calculations for **16** at Various Temperatures[a]

50.05 ± 0.03°		65.00 ± 0.03°		80.00 ± 0.04°	
Time, sec	0.02001 *M* $HClO_4$, ml	Time, sec	0.02001 *M* $HClO_4$, ml	Time, sec	0.02001 *M* $HClO_4$, ml
0	4.535	0	4.456	0	4.384
19,000	4.409	5,000	4.274	6,000	3.273
40,700	4.251	12,000	3.998	12,000	2.614
79,500	4.032	19,000	3.744	18,000	2.236
103,000	3.886	26,000	3.537	24,000	2.025
126,700	3.777	33,000	3.348	30,000	1.900
173,700	3.555	40,000	3.198	36,000	1.844
∞	1.719	∞	1.760	∞	1.753
$k = 2.47 \times 10^{-6}$ sec^{-1}		$k = 1.60 \times 10^{-5}$ sec^{-1}		$k = 9.48 \times 10^{-5}$ sec^{-1}	

[a] Aliquots of 0.923 ml were employed.

(34) L. A. Paquette and P. C. Storm, *J. Org. Chem.*, in press.

at appropriately timed intervals, immediately cooled in ice water, and titrated as previously described (see Tables III–IV).

In each case an ampoule was allowed to remain in the heated bath for a period of at least 10 half-lives. The sample was then titrated as above to give the infinity point.

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Stereoisomerism in Some Derivatives of the 2-Substituted 3-Phospholene System[1]

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Abstract: *trans*-1,3-Pentadiene and *trans,trans*-2,4-hexadiene form cycloadducts with phosphonous dihalides (CH_3PCl_2 or $C_6H_5PBr_2$) which on reduction with magnesium give mixtures of *cis,trans*-1,2-disubstituted 3-phospholenes. Hydrolysis of the cycloadducts gives the *cis,trans*-3-phospholene oxides. The configuration of the 3-phospholenes has been deduced from their nmr properties. For the 1-phenyl-2-methyl systems, the *cis* configuration was assigned to that isomer showing an upfield 2-CH_3 signal, occasioned by phenyl shielding. This isomer had a much smaller value for J_{PCCH} (10 Hz) than the *trans* isomer (18 Hz). Similar values were obtained for other isomer pairs; configurations were assigned on this basis and were supported by other data. Assignments were also made to the isomeric benzyl bromide salts and oxides of the phospholenes. The nmr spectra of the cycloadducts, which are largely ionic, do not show the presence of *cis,trans* isomers, and this was attributed to a rapid equilibration through pentacovalent structures (intermediates or transition states).

In 1965, we announced the first instance of the separation of stable *cis,trans* forms of a five-membered ring (3-phospholene) where trivalent phosphorus provided one chiral center.[2] In this paper, other cases of isomeric 3-phospholenes are reported, and assignment of structure to the *cis* and *trans* forms is made. Consideration is also given to the structure of the diene–phosphonous dihalide cycloadducts, from which the isomeric pairs are formed by reduction (dehalogenation).

Synthesis. The cycloaddition of dienes and phosphonous dihalides[3] was used to construct the 3-phospholene ring. The reactions and structures prepared are summarized in Chart I.

Methylphosphonous dichloride has been used extensively in earlier cycloadditions, and the products of hydrolysis or reduction of the adducts have been proven to contain the 3-phospholene ring.[4] When 1,3-pentadiene is used in the cycloaddition and the adduct **1a** reduced, a mixture of *cis*- and *trans*-1,2-dimethyl-3-phospholenes is possible. This isomerism is due to the configurational stability of trivalent phosphorus.[5] That an isomer mixture was obtained was readily apparent from the gas chromatogram, which contained two peaks in a 3:1 ratio, and the proton nmr spectrum, which had two P–CH_3 doublets and two C–CH_3 signals (four lines, due to coupling with the methine proton and ^{31}P). The isomer mixture was separated by preparative gc as well as by fractional distillation. The isomers were analyzed as their more readily handled benzyl bromide salts. As will be discussed below, the major isomer, having the lower boiling point and shorter gc retention time, proved to be the *trans* form of **3a**.

In the first synthesis[2] of the isomeric phospholenes, a commercial mixture of *trans*(73%)- and *cis*(27%)-1,3-pentadiene had been used in the cycloaddition. The individual dienes have now been subjected to the reaction and it has been found, as predicted on steric grounds,[3] that only the *trans* isomer reacted. The *cis* isomer failed to give any cycloadduct even after several months.[6]

Hydrolysis of adduct **1a** has already been reported[2] to give a mixture of stereoisomeric 3-phospholene oxides. Gc analysis of the distilled product indicated the ratio *cis*-**2a**:*trans*-**2a** to be 1:2. Fractional distillation provided a sample of the lower boiling (*trans*) isomer of good purity; however, some rearrangement to the higher boiling 2-phospholene oxide[4] isomer accompanied the distillation, and the best sample of the *cis* form obtained was of 85% purity. Other experiments have indicated a *cis*:*trans* ratio of about 1:1 to be more descriptive of the steric outcome of the hydrolysis.

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(2) L. D. Quin, J. P. Gratz, and R. E. Montgomery, *Tetrahedron Lett.*, 2187 (1965).

(3) W. B. McCormack, U. S. Patents 2,663,736 and 2,663,737 (1953); for a review, see L. D. Quin, "1,4-Cycloaddition Reactions," J. Hamer, Ed., Academic Press, New York, N. Y., 1967, Chapter 3.

(4) L. D. Quin, J. P. Gratz, and T. P. Barket, *J. Org. Chem.*, 33, 1034 (1968).

(5) (a) L. Horner, H. Winkler, A. Rapp, A. Mentrup, H. Hoffmann, and P. Beck, *Tetrahedron Lett.*, 161 (1961); (b) for a recent review of phosphorus stereochemistry, seem M. J. Gallagher and I. D. Jenkins, "Topics in Stereochemistry," Vol. 3, E. L. Eliel and N. L. Allinger, Ed., Interscience Publishers, New York, N. Y., 1968, Chapter 1.

(6) An earlier suggestion[2] that the isomeric dienes might give different cycloadducts, thus accounting for the isomerism in the reduction product, may now be discarded.