# Synthesis and Solvolysis of *syn*- and *anti*-(6-Oxabicyclo[3.1.0]hex-3-yl)methyl *p*-Bromobenzenesulfonates[1]

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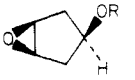
*syn*- and *anti*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexanes (**3a** and **4a**) have been prepared and the solvolysis rates of their *p*-bromobenzenesulfonate esters have been determined in aqueous ethanol. The solvolysis rate of **3c** was found to be $\sim 10^4$–$10^5$ times faster than the rate of its anti epimer **4c** but, unexpectedly, of similar order to the solvolysis rate of **6c**. Both **3c** and **6c** yielded the same mixture of products, **6a** and **6b**, exclusively. The $\alpha$- and $\beta$-deuterium isotope effects on the solvolysis of **5c** and **3c**-*3-d* were 1.034 and 1.084 per deuterium atom, respectively. Solvolysis of **6c**-*6-d* showed an $\alpha$-isotope effect of 1.086. Also, it yielded a mixture of exo-substitution products with an equal distribution of the deuterium atom at $C_1$ and $C_6$. On the basis of these experimental data, solvolysis of **3c** and **6c** must have proceeded by way of the common oxonium ion intermediate (**7**) which arises from participation of the nonbonded electrons on the oxygen atom. The solvolysis rate of **4c** is of similar magnitude to those of **1c** and **2c**; solvolysis yielded 80% substitution products and thus was interpreted to proceed via a solvent-assisted ionization pathway.

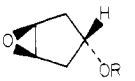
The solvolytic reactions of epoxy carbinyl systems have been widely investigated. Studies have been centered principally on the nature of the epoxy carbinyl cations,[2-6] relative to that of the corresponding cyclopropylcarbinyl systems.[7,8] Substitution of the methylene group in the cyclopropyl ring with ether oxygen affords a system which can potentially exert contrary effects. The inductive withdrawal of electrons by oxygen should destabilize the adjacent positive charge center while the available unshared pair electrons on oxygen could stabilize the electron-deficient carbon. The epoxide ring has an additional potential advantage in that its oxygen atom and the carbon–oxygen bond are more nucleophilic than the carbon–carbon bond of the ring.[9] Hence, if participation were to occur in the solvolysis of an epoxy carbinyl system it would involve the formation of oxabicyclobutonium ion[6] (arising from participation of the carbon–oxygen bond) or, more likely, an oxonium ion (resulting from the nonbonded electrons on the oxygen atom) rather than the intermediate arising from interaction of the carbon–carbon bond of the oxiryl group with carbinyl cation.[10] Replacement of a cyclopropyl group adjacent to the ionizing center by the oxacyclopropyl ring affects various factors considerably and thus, unfortunately, alters the overall outcome of the reaction. The available experimental evidence, therefore, does not allow an estimation of the magnitude contributed by the anchimeric assistance of the epoxide group alone.

In order to assess the magnitude of the anchimeric assistance by the epoxide ring in the solvolytic reaction, the reaction center should be placed further away from the epoxide group. The assumption was that, at least, if not completely, the inductive effect due to ether oxygen would be substantially diminished,[11] and hence the rate acceleration due to the epoxide group would provide useful information concerning the magnitude in question. In addition, the nature of the products could add some insight with regard to the role of the neighboring epoxide ring. Some evidence for these suppositions was already reported in the solvolysis of *syn*- and *anti*-6-oxabicyclo[3.1.0]hex-3-yl tosylates, **1d** and **2d**.[12] In these systems, the acetolysis rate (at 25 °C) of *anti*-**2d** is only 3.3 times slower than that of its syn epimer, **1d**, and thus was interpreted as lack of significant participation by the neighboring epoxide ring which probably resulted partly from the cancellation of the inductive withdrawal of electrons by oxygen atom over the rather weak driving force for the participation in this system.

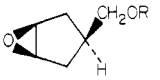
With the above-mentioned predictions regarding the behavior of the epoxide group in mine, we have undertaken initial studies involving the synthesis of *syn*- and *anti*-3-(hydroxymethyl)-6-oxabicyclo[3.1.0]hexanes (**3a** and **4a**), *syn*-3-(hydroxydideuteriomethyl)-6-oxabicyclo[3.1.0]hexane (**5a**), and *syn*-3-(hydroxymethyl)-6-oxabicyclo[3.1.0]-hexane-*3-d* (**3a**-*3-d*) and the solvolysis of their *p*-bromobenzenesulfonate esters.



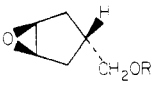
1a, R = H
b, R = $C_2H_5$
c, R = Bs
d, R = Ts



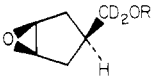
2a, R = H
b, R = $C_2H_5$
c, R = Bs
d, R = Ts



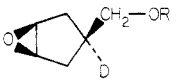
3a, R = H
b, R = $C_2H_5$
c, R = Bs



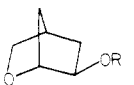
4a, R = H
b, R = $C_2H_5$
c, R = Bs



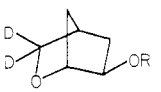
5a, R = H
b, R = $C_2H_5$
c, R = Bs



3a-*3-d*, R = H
3c-*3-d*, R = Bs



6a, R = H
b, R = $C_2H_5$
c, R = Bs



6a-*3,3-d*$_2$, R = H
6c-*3,3-d*$_2$, R = Bs

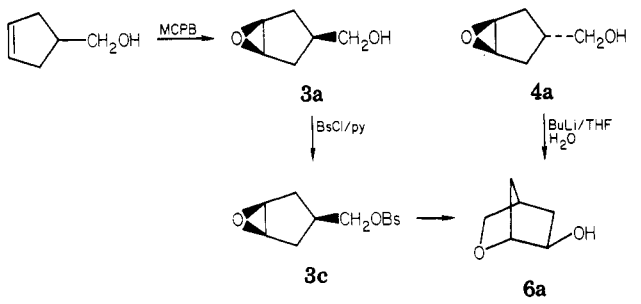
## Results and Discussion

**Synthesis.** 4-(Hydroxymethyl)cyclopentene was obtained from lithium aluminum hydride reduction of 4-cyclopentenecarboxylic acid which in turn was prepared

(1) A preliminary account of this work has been published: David, F. *J. Chem. Soc., Chem. Commun.* **1979**, 553.
(2) Peters, E. N. *J. Org. Chem.* **1978**, *43*, 4006.
(3) (a) Whalen, D. L.; Brown, S.; Ross, A. M.; Russel, H. M. *J. Org. Chem.* **1978**, *43*, 428. (b) Whalen, D. L.; Cooper, J. D. *Ibid.* **1978**, *43*, 432.
(4) (a) Santelli, M,; Viala, J. *Tetrahedron* **1978**, *34*, 2327. (b) Santelli, M. *J. Chem. Soc. C* **1974**, 214.
(5) Danen, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 4835.
(6) (a) Morita, H.; Oae, S. *Tetrahedron Lett.* **1969**, 1347. (b) Richey, H. G., Jr.; Kinsman, D. V. *Ibid.* **1969**, 2505. (c) Padwa, A.; Das, N. C.; Eastman, D. *J. Am. Chem. Soc.* **1969**, *91*, 5178.
(7) For recent reviews and references, see: (a) Wiberg, K. B.; Hess, B. A.; Ashe, A. J. "Carbonium Ions"; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. III, Chapter 26. (b) Richey, H. G., Jr. *Ibid.*, 1972; Chapter 25.
(8) Brown, H. C.; Rao, C. G.; Ravindanathan, M. *J. Am. Chem. Soc.* **1977**, *99*, 7663 and references cited therein.
(9) Walsh, A. D. *Trans. Faraday Soc.* **1949**, *45*, 179.
(10) References 3b and 4a.
(11) Waters, W. A. *J. Chem. Soc.* **1933**, 1551.
(12) Hornback, J. M. *J. Org. Chem.* **1973**, *38*, 4122.

0022-3263/81/1946-3512$01.25/0 

Scheme I




by the literature method.[13] Epoxidation of 4-(hydroxymethyl)cyclopentene with *m*-chloroperbenzoic acid in methylene chloride at temperatures below 5 °C afforded a mixture of syn/anti epoxides in a ratio of 1.1:1. This syn/anti product ratio is not significantly affected by changing solvent from methylene chloride to chloroform or ether. The epimeric epoxy alcohols were separated by distillation through an annular spinning-band column. The structure assignment was apparent from the following behavior: the brosylate ester of the lower boiling component (**3c**) solvolyzed facilely in aqueous acetone to give *exo*-2-oxabicyclo[2.2.1]heptan-6-ol (**6a**)[14] as the only VPC-detectable product in 55% yield. Under the same reaction conditions, the brosylate ester of the higher boiling component (**4c**) was inert. On the other hand, treatment of higher boiling epoxy alcohol (**4a**) with butyllithium solution followed by hydrolysis afforded only **6a** in 40% yield[15] (see Scheme I).

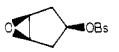
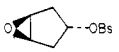
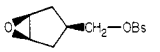
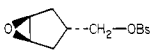
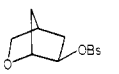
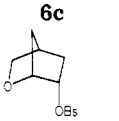
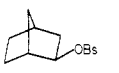
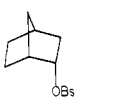
On the basis of these data, the first component must be *syn*-3-(hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (**3a**) and the other component its anti epimer (**4a**). The structure assignment was further substantiated by spectroscopic data.[16] Reduction of 4-(carbomethoxy)cyclopentene with lithium aluminum deuteride (Ventron) afforded 4-(hydroxydideuteriomethyl)cyclopentene which was epoxidized to a corresponding mixture of the syn and anti epoxy alcohols. *syn*-3-(Hydroxydideuteriomethyl)-6-oxabicyclo-[3.1.0]hexane (**5a**) was separated from the mixture in the same manner as that described for the corresponding protium compounds. Conversion of 4-(carbomethoxy)-cyclopentene to the carbanion with lithium diisopropylamide followed by addition of deuterium oxide (99.8% Ventron) afforded 4-(carbomethoxy)cyclopentene-*4-d*, the precursor for the preparation of **3a**-*3-d*.[17]

Oxidation of **6a** with chromic acid in acetone afforded the corresponding ketone (**12**) in 50–55% yield.[18] Oxidation with chromic acid in ether solution was also attempted, but no improvement in yield was obtained. Reduction of ketone **12** with lithium aluminum hydride in ether at room temperature afforded a mixture of exo and endo alcohols with the endo isomer predominating (90%). A small-scale reduction of ketone **12** with lithium trimethoxyaluminohydride resulted in the same exo/endo ratio. This insensitivity of the stereochemical outcome to the steric requirement of the reducing agent contrasts with the situation for reduction of bicyclo[2.2.1]heptan-2-one.[19] Reduction of ketone **12** with lithium aluminum deuteride gave 90% of the corresponding $\alpha$-deuterated endo alcohol and 10% of the exo epimer. Attempts to increase the exo/endo product ratio by trial reductions with other reducing agents, such as sodium borohydride and borane in tetrahydrofuran, were not successful. The $\alpha$-deuterated exo and endo alcohols, separated by preparative VPC, exhibit C–D stretching vibrations in the IR spectrum at 2150 and 2152 $cm^{-1}$, respectively.[20] Both isomers show $m/e$ 115 as the parent peak in the mass spectrum.

The alcohols **3a**, **3a**-*3-d*, **4a**, and **5a** were converted to their corresponding *p*-bromobenzenesulfonate esters by the standard method.[21] Structure assignment of all alcohols and esters was substantiated by spectroscopic data.

**Solvolysis.** The rates of solvolysis of **3c**, **6c**, and **10** were determined in 90% aqueous ethanol at 25 °C. Compounds **1c**, **2c**, and **4c** were inert under the above conditions, and hence their rates were determined in 50% aqueous ethanol at 70 °C. Except for compound **9**,[22] all determinations were

Table I. First-Order and Relative Rate Constants for the Solvolysis of Some *p*-Bromobenzenesulfonate Esters in Aqueous Ethanol

| compd | solvent (% EtOH) | temp, °C | $10^4k$,[d] $s^{-1}$ | $k_{rel}$[c] |
|---|---|---|---|---|
|  **1c** | 50 | 70 | 0.61 ± 0.03[a] | 1.8 |
|  **2c** | 50 | 70 | 1.38 ± 0.03[a] | 4.0 |
|  **3c** | 90 | 25 | 1.243 ± 0.001[b] | 1.1 × $10^5$ |
|  **4c** | 50 | 70 | 0.345 ± 0.05[a] | 1.0 |
|  **6c** | 90 | 25<br>15 | 4.560 ± 0.003[b]<br>1.244 ± 0.007[b] | 3.9 × $10^5$ |
|  **9** | 90 | 150 | 0.138 ± 0.01 | |
|  **10** | 90 | 25<br>15 | 3.240 ± 0.001<br>0.837 ± 0.016 | |
|  **11** | 90 | 60<br>70 | 0.501 ± 0.000[a]<br>1.461 ± 0.001[a] | |

[a] Conductometric method, from ref 27. [b] Spectrophotometric method. [c] Relative rate constants (50% EtOH, 70 °C) were obtained from extrapolation of rate constants of **3c** and **6c** to those in 50% aqueous ethanol at 70 °C, using the following parameters: $\Delta H^{\ddagger}$ = 21.6 kcal/mol; $\Delta S^{\ddagger}$ = −1.4 eu; $Y$ values of −0.727 and 1.604 for solvent of 90% and 50% aqueous ethanol, respectively. [d] Rates given are the average of two runs.

(13) (a) Murdock, K. C.; Angier, R. B. *J. Org. Chem.* **1962**, *27*, 2395. (b) Schmid, G. H.; Wolkoff, A. W. *Ibid.* **1967**, *32*, 254.

(14) The exo configuration of the product **6a** is a necessary consequence of an intramolecular displacement reaction that effects cyclization.

(15) It should be noted that all of these successful cyclization reactions were judged to be quantitative by VPC analysis. However, the isolated yield of **6a** was always in the range of 40–60%. The difficulty in obtaining a better yield of **6a** seems to arise from the nature of the compound which is rather volatile, very hygroscopic, and quite soluble in water; see: Giudice, T. A.; Bruice, T. C. *J. Org. Chem.* **1970**, *35*, 2386.

(16) See Experimental Section.

(17) The incorporation of the deuterium was shown to be ca. 95% by NMR analysis.

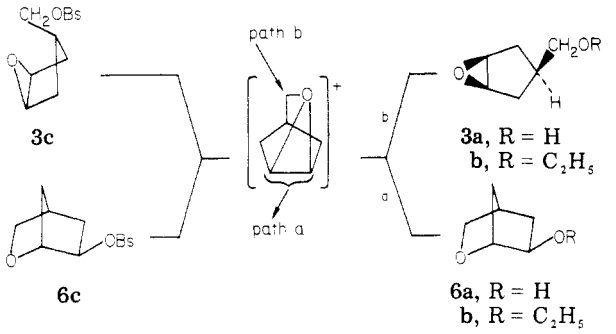
(18) Meinwald, J.; Crandall, J.; Hym, W. E. *Org. Synth.* **1965**, *45*, 77.

(19) Brown, H. C. "Hydroboration"; W. A. Benjamin, Inc.: New York, 1962.

(20) Winstein, S.; Sonnenberg, J. *J. Am. Chem. Soc.* **1961**, *83*, 3244.

(21) Tipson, R. S. *J. Org. Chem.* **1946**, *11*, 235.

Scheme II




run by either a precise conductometric or a spectrophotometric method. For each compound, the determination was run in duplicate and was followed at least for two half-lives. Compounds **3c**, **6c**, and **10** gave good first-order rate constants while those of **1c**, **2c**, and **4c** showed a slightly upward drift. All the rate data and the relative rate constants are summarized in Table I.

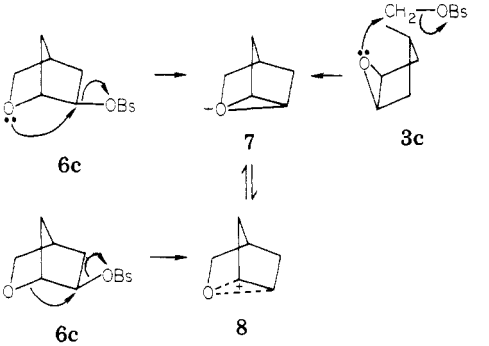
Three obvious conclusions emerge directly from the rate data in Table I: first, a similar reactivity in the solvolysis of **3c** and **6c**, despite the difference in the degree of substitution at the reaction centers; second, a large rate ratio in the solvolysis of **3c**/**4c** relative to that of **1c**/**2c**; third, a similar magnitude of rate constants of **4c**, **1c**, and **2c**.

For the product studies, the preparative solvolyses were run in the presence of suspended calcium carbonate to ensure kinetic control in the product formation. All epoxy compounds were shown to be stable under the conditions of solvolysis. The product studies were performed in either aqueous ethanol or aqueous acetone. The solvolysis products of all compounds studied here are quite simple. Solvolysis in aqueous ethanol of either **3c** or **6c** yielded the same mixture of products consisting of **6a** and **6b**, while their solvolysis in aqueous acetone yielded only **6a**. No elimination or other products were detected (by VPC) in the solvolysis of either substrate. The product mixture from solvolysis of **4c** in 50% aqueous ethanol consisted of substitution products (**4a** and **4b**) in yields up to 80%,[23] while those of **1c** and **2c** were the substitution products of inverted configuration.

Of significant interest in the solvolysis of **3c** is the large rate enhancement and the exclusive formation of products with the completely rearranged skeleton. A comparison of the solvolysis rate of **3c** with that of its anti epimer (**4c**) or of its analogue (**1c**) shows a rate acceleration of $10^4$–$10^5$, whereas comparison with *exo*-2-oxabicyclo[2.2.1]hept-6-yl brosylate (**6c**) shows a similar order of reactivity ($k_{6c}/k_{3c}$ = 3.6). Since rate acceleration and rearranged products are usually taken as evidence for neighboring-group participation in the solvolytic reaction,[24] the observed large rate enhancement and the exclusive formation of the rearranged products (**6a** and **6b**) in the solvolysis of **3c** are best explained in terms of the formation of the oxonium ion **7** (or its stereochemical equivalent) which arises from participation of the nonbonded electrons on the oxygen atom in the transition state of ionization of **3c** (see Scheme II). In principle, ion **7** can suffer solvent attack by any of two available paths (path a or b). Solvent attack at the oxiryl ring carbon (path a) gives rise to the observed **6a** and **6b**. Solvent attack at the rear side carbon (path b) would afford products having the 6-oxabicyclo[3.1.0]hexane skeleton (**3a** and **3b**). Neither **3a** nor **3b** was detected in the product mixture by VPC analysis. Since **3a** is shown to be stable under the reaction conditions, this product could not have been formed and undergone subsequent rearrangement to **6a**. The selectivity of solvent attack on the oxonium ion **7** is probably best explained in terms of the greater relief of strain achieved by cleavage of the three-membered ring rather than of the five-membered ring. This type of selectivity has been reported in many systems[25] and thus seems to be the rule rather than an exception.

Acetolysis of **6c** was reported to afford the *exo*-acetates as almost exclusive products.[26] No elimination product was observed but a trace of *endo*-acetate was detected. The *exo*-acetate mixture from acetolysis of *endo*-2-oxabicyclo[2.2.1]hept-6-yl-6-*d* brosylate showed the deuterium label to be equally distributed between $C_1$ and $C_6$ positions.

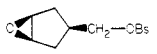
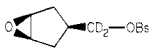
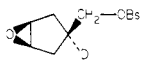
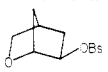
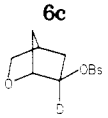
Solvolysis of **6c** in 90% aqueous ethanol was studied and found to afford the exo-substitution products (**6a** and **6b**) exclusively.[27] Neither elimination product nor endo epimer was detected in this solvent mixture. The solvolysis rate ratio for exo/endo isomers of 2-oxanorbornyl brosylate in 90% aqueous ethanol was ca. $10^6$, while that of syn/anti isomers (6-oxabicyclo[3.1.0]hex-3-yl)methyl brosylate in the same solvent was ca. $10^4$–$10^5$. On the basis of the data presented above and the exclusive formation of the same products in the solvolysis of **3c** and **6c**, one is led to conclude that both substrates solvolyzed via a common intermediate (oxonium ion **7** or its stereochemical equivalent, ion **8**). The true oxonium ion **7** is formed from participation by a lone pair of electrons on the oxygen atom, while the nonclassical ion **8** is a result of the carbon–oxygen $\sigma$-bond participation. Since these ions differ only in charge distribution, an experimental distinction between these to ions is not readily imagined. However, the true oxonium ion **7** seems more likely for the following reasons.




If oxonium ion **7** is the common intermediate (arising from the nonbonded electrons on the oxygen atom) for the solvolytic ionization of both **6c** and **3c**, the nonclassical ion **8** (arising from the carbon–oxygen $\sigma$ bond) could also represent the common intermediate for the ionization of both compounds. Assuming the polar effect of the ether oxygen atom to be approximately the same for the *exo*- and *endo*-oxanorbornyl system, one would predict the exo/endo rate ratio in the oxanorbornyl system to be of similar magnitude to that in the norbornyl system, if the nonclassical ion **8** were involved. This is contrary to the experimental fact that the exo/endo rate ratio was found to be $10^6$ for the oxanorbornyl series and only 192 in the norbornyl series.

(22) The solvolysis rate for compound **9** was determined by spectrophotometric using the ampule technique.
(23) The rest remained unidentified.
(24) Capon, B. *Q. Rev., Chem. Soc.* **1964**, *18*, 45.
(25) (a) Winstein, S.; Grundwald, E.; Ingraham, L.L. *J. Am. Chem. Soc.* **1948**, *70*, 821. (b) Paquette, L. A.; Dunkin, I. R.; Freeman, J. P.; Storn, P. C. *Ibid.* **1972**, *94*, 8124.
(26) Spurlock, L. A.; Fayter, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 2707.
(27) Amatavivadhana, F. Ph.D. Thesis, Ohio University, 1971.

Table II. Secondary Deuterium Isotope Effects on the Solvolysis of *syn*-6-Oxabicyclo[3.1.0]hex-3-yl and *exo*-2-Oxabicyclo[2.2.1]hept-6-yl *p*-Bromobenzenesulfonates in 90% Aqueous Ethanol at 25 °C

| compd | $10^4k$, $s^{-1}$ | $k_H/k_D$ |
|---|---|---|
|  **3c** | 1.243 ± 0.001 | |
|  **5c** | 1.163 ± 0.003 | 1.069 |
|  **3c-*3-d*** | 1.147 ± 0.003 | 1.084 |
|  **6c** | 4.560 ± 0.003 | |
|  **6c-*6-d*** | 4.200 ± 0.001 | 1.086 |

The magnitude of secondary $\alpha$-deuterium kinetic isotope effects has been used as a tool for distinguishing the solvolytic reactions which react by way of the carbonium ion mechanism ($S_N1$) from those reacting by the synchronous displacement mechanism ($S_N2$). The simple criterion is that a large deuterium isotope effect ($k_H/k_D$ = 1.15–1.20 per deuterium atom for a secondary alkyl arenesulfonates) signifies the $S_N1$ mechanism, whereas a small value ($k_H/k_D$ = 1.04 per deuterium atom for a primary substrate)[28,29] identifies the $S_N2$ pathway. Therefore the magnitude of $\alpha$-deuterium isotope effects on the solvolysis of **5c** and **6c**-*6-d* would provide further information on the mechanism discussed above. The $\alpha$- and $\beta$-deuterium isotope effects of **5c** were studied and the data are given in Table II, along with the isotope data on the solvolysis of **6c**-*6-d*. The solvolysis of **5c** in aqueous acetone yielded **3a**-*3,3-d*$_2$ as the sole product, while that of **6c**-*6-d* in 90% aqueous ethanol afforded an equal mixture of $C_1$-*d* and $C_6$-*d* exo-substitution products.

The magnitude of the $\alpha$-deuterium isotope effect of **6c**-*6-d* ($k_H/k_D$ = 1.086) is approximately half of the normal value[28] and that of *exo*-2-norbornyl brosylate ($k_H/k_D$ = 1.21 based on the data obtained during only the first 3–5% of the reaction,[29] or a value of 1.12 for the data taken for the whole reaction)[30] but is in good accord with that expected for the $S_N2$-like mechanism proposed for the solvolysis of **6c**-*d-d*. In fact Shiner has found that the $\alpha$-isotope effect on the solvolysis of isopropyl brosylate in 90% aqueous ethanol is 1.083.[31] On the basis of his isotope effect analysis, Shiner has concluded that the solvolysis of isopropyl brosylate in 90% aqueous ethanol involves more than 90% an $S_N2$ pathway.

Compound **6c** is the oxa analogue of the *exo*-2-norbornyl system, for which it has been shown that its low $\alpha$-isotope effect resulted from internal return, leading to scrambling of the deuterium (between $C_1$ and $C_2$), during the solvolysis.[29] Therefore it is less certain in this case that internal return could not be the cause of the diminished $\alpha$-isotope effect in the solvolysis of **6c**-*6-d*.[32] Even though internal return studies for **6c** have not been made, it is unlikely that internal return is important in the solvolysis of this sytem. If internal return were to occur to a great extent in the solvolysis of **6c**-*6-d*, the magnitude of 1.086 for $k_H/k_D$ would be too low.[33]

The reduced value for the $\alpha$-deuterium isotope effect of **5c** ($k_H/k_D$ = 1.034 per deuterium atom) is observed, as expected.[34] This magnitude is in fact compatible with that reported for the solvolysis of ethyl arenesulfonate in aqueous ethanol ($k_H/k_D$ = 1.020 per deuterium atom)[35] which is known to solvolyze by an $S_N2$ mechanism. Again, the diminished value of the $\alpha$-deuterium isotope effect of **5c** is consistent with the intramolecular displacement reaction[36] with the epoxide oxygen as internal nucleophile.

It is well accepted that anchimeric assistance can also reduce the magnitude of the expected $\beta$-isotope effect[37] in the solvolytic reactions. Therefore from the proposed mechanism discussed above, one might predict that the $\beta$-isotope effect of **3c** would be smaller than the normal value. In fact, a magnitude of 1.084 is obtained for $k_H/k_D$ in the solvolysis of **3c**-*3-d*. This value is considerably larger than expected for the solvolytic transition state discussed above, but not inconsistent with the mechanism proposed.

A comparison of the data on the solvolysis of **3c** and **6c** with those of 4-methoxy-1-pentyl (**13**) and 5-methoxy-2-pentyl (**14**) brosylates[38] reveals a similar situation. The acetolysis of **13** and **14** proceeded with almost the same rate and yielded the same mixtures of products. The secondary deuterium isotope data showed that for compound **13** both the $\alpha$- and $\beta$- effects are nil ($k_H/k_D$ = 1.0), while an $\alpha$-effect of 1.08 and a $\beta$-effect of 1.03 were observed for compound **14**. These data were interpreted as both substrates solvolyzing by way of the common oxonium ion (**15**) intermediate but different transition states, which possibly differ only in charge delocalization. Therefore the same conclusion could be made for the solvolyses of **3c** and **6c**.

Even thoud a precise estimate of the anchimeric effect of the epoxy oxygen in the solvolysis of **3c** can not be obtained from this study, it is likely that a factor of $10^4$–$10^5$ might correspond to the effect in question. This conclusion is based on the assumptions that (1) the electronic effect of the epoxy oxygen in **3c** and **4c** is either absent or ap-

(28) (a) Raaen, V. F.; Juhlke, T.; Brown, F. J.; Collins, C. J. *J. Am. Chem. Soc.* **1974**, *96*, 5928. (b) Shiner, V. J., Jr. *Ibid.* **1974**, *96*, 6187.

(29) (a) Sunko, D. E.; Borcić, S. "Isotope Effects in Chemical Reactions"; Collin, C. J., Bowman, N. S., Eds.; ACS Monograph No. 167; Van Nostrand Reinhold: New York, 1970; Chapter 3. (b) Humski, H.; Malojcic, R.; Borcić, S.; Sunko, D. E. *J. Am. Chem. Soc.* **1970**, *92*, 6534. (c) This magnitude was analyzed and criticized as incorrect, see: Maskill, H. *Ibid. Soc.* **1976**, *98*, 8482.

(30) (a) Murr, B. L.; Conkling, T. A. *J. Chem. Soc.* **1970**, *92*, 3464. (b) Lee, C. C.; Wong, W. C. *Can. J. Chem.* **1965**, *42*, 2254. (c) In the $S_N1$ process, the magnitude of the $\alpha$-deuterium isotope effect changes significantly with the leaving group while a slight change (1–2% per deuterium atom) was observed with a change in solvent. For the $S_N2$ mechanism the effect of leaving group of the $\alpha$-deuterium effect is similar to that in the $S_N1$ mechanism but over a much smaller range. See: Shiner, V. J., Jr.; Rapp, M. W.; Pinnick, H. R. *J. Am. Chem. Soc.* **1970**, *92*, 232; ref 25b.

(31) Shiner, V. J., Jr.; Fisher, R. D.; Dowd, W. J. *J. Am. Chem. Soc.* **1969**, *91*, 7748.

(32) The kinetic data were collected only after 15% reaction; therefore any reduced value of the $\alpha$-deuterium isotope effect (if it occurred) could not be detected.

(33) I thank one of the referees for his comments on this point.

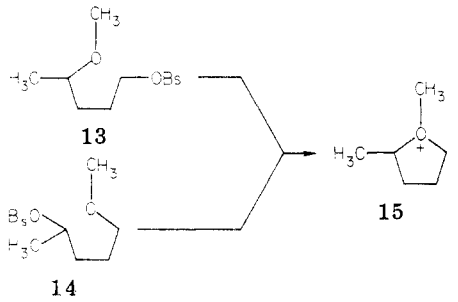
(34) The $\alpha$-deuterium isotope effect for the primary substrate is approximately 3–4% smaller than that of the corresponding secondary substrate which reacts by the $S_N2$ mechanism; see ref 25b.

(35) Leffek, K. T.; Llewllyn, J. A.; Robertson, R. E. *Can. J. Chem.* **1960**, *38*, 1505.

(36) One could argue that the small $\alpha$-deuterium isotope effect of **5c** might result from the solvent-assisted reaction. However, the complete absence of formation of substitution products in the solvolysis of **3c** does not favotr this argument.

(37) The $\beta$-deuterium isotope effect is approximately 10–20% per deuterium atom; see ref 25b, pp 119 and 137.

(38) (a) Allred, E. L.; Winstein, S. *J. Am. Chem. Soc.* **1967**, *89*, 3991, 3998, 4012. (b) References 29a, pp 177–181.



13 14 15

proximately independent of the geometrical arrangement of the leaving group and (2) participation by epoxy oxygen is stereoelectronically allowed in the syn system but prohibited in the anti epimer. Hence, this study clearly shows that a positionally remote epoxide ring, if spatially properly oriented (relative to the reaction center), can provide anchimeric assistance in a solvolytic reaction as a large factor.

The information at hand for the solvolysis of **4c** does not allow a detailed mechanistic intepretation. Based on the much retarded rate constant (relative to its syn isomer **3c**) and the large extent of substitution product formation, it is likely that the solvolysis of **4c** proceeds principally by the solvent-assisted mechanism.[39]

The acetolysis rates of **1d** and **2d** at 100 °C were reported to be of similar magnitude ($k_{1d}/k_{2d}$ = 2.4).[12] These data together with the acetolysis products were interpreted in terms of a lack of significant participation by the neighboring epoxide ring in the acetolysis of **1d** and **2d**. The solvolysis of **1c** and **2c** in aqueous ethanol at 70 °C was studied and the data at hand ($k_{2c}/k_{1c}$ = 2.3) showed a reversed order of reactivity to that reported in the literature.[12] This reactivity difference could possibly result from the effects of change of solvent and temperature. In view of the similar order of rate constants and almost exclusive formation of inverted products in the solvolysis of **1c** and **2c**, the solvolysis of both substrates presumably proceeds without participation of the epoxide group, but possibly by a solvent-assisted pathway.[39] In principle, this mechanistic interpretation can be confirmed from the data of a secondary deuterium isotope effect study. However, the lack of precision in the rate studes at high temperature renders this experimental confirmation impossible at the moment.

## Experimental Section

All boiling points and melting points are uncorrected. Melting points were taken on a Thomas-Hoover capilary melting point apparatus. Mass spectra were obtained with a Hitachi Perkin-Elmer RMu-6E mass spectrometer. Proton magnetic resonance spectra were obtained with a Varian A-60, HA-100, or JEOL-MH-100 spectrometer. The chemical shifts are recorded at $\tau$ values relative to tetramethylsialne as an internal standard (s, singlet; d, doublet; t, triplet; m, multiplet). Infrared spectra were determined with a Perkin-Elmer 237-B or Perkin-Elmer 267 grating infrared spectrophotometer. Characteristic absorptions were reported in wavenumbers ($cm^{-1}$) and intensities are designated as follows: vw = very weak, m = medium, s = strong, vs = very strong. Solvents used for recrystallization were purified by the appropriate methods.[40]

**4-Cyclopentenol** was prepared by the literature method:[41] bp 80–82 °C (80 mm); $n^{25}_D$ 1.4680 [lit.[41] bp 59–60 °C (27 mm); $n^{20}_D$ 1.4698].

**6-Oxabicyclo[3.1.0]hexan-3-ol.** To an ice-cooled solution of 1.95 g (23 mmol) of 4-cyclopentenol in 65 mL of methylene chloride was added 5.1 g (25 mmol) of *m*-chloroperbenzoic acid. Stirring was continued for 1 h in the ice bath and 2 h at room temperature. The resulting mixture was neutralized with excess calcium hydroxide,[42] and the solid was removed and washed thoroughly with methylene chloride. The combined solution was concentrated under reduced pressure to afford a crude yellow oil which was taken up in ether to precipitate any remaining inorganic material. VPC analysis of the crude material showed two components of 87% and 13%, respectively. Separation and purification were performed by preparative-scale VPC. The major component was identified as *syn*-6-oxabicyclo[3.1.0]hexan-3-ol (**1a**): $n^{25}_D$ 1.4595; NMR ($CCl_4$) $\tau$ 6.01 (m, 1), 6.44 (s, 2), 8.05 (m, 5); IR ($CCl_4$) 3355 (s), 3035 (m), 1077 (vs), 834. The minor component was assigned to its anti epimer (**2a**): NMR ($CCl_4$) $\tau$ 6.12 (m, 2), 7.61 and 8.48 (ABX, $J_{AX} = J_{BX}$ = 7 Hz, 4 H), 5.8–6.76 (m, 2 H); IR ($CCl_4$) 3410, 3031, 837.

**4-(Hydroxymethyl)cyclopentene** was prepared by lithium aluminum hydride reduction of 4-cyclopentenecarboxylic acid:[13] bp 82–83 °C (29 mm); $n^{25}_D$ 1.4700 [lit.[13] bp 82–85 °C (30 mm); $n^{29}_D$ 1.4665].

**3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (3a, 4a).** To a cooled solution of 44.2 g (0.45 mol) of 4-(hydroxymethyl)-cyclopentene in 150 mL of methylene chloride was added 100 g (85%; 0.49 mol) of *m*-chloroperbenzoic acid in one portion. The peracid dissolved almost instantaneously, resulting in a clear solution for several minutes before precipitation of the acid was observed. The reaction mixture was allowed to stir at 0 °C for 1 h and then at room temperature for 3 h. Excess calcium hydroxide (74 g) was added to neutralize the acid and methylene chloride was added to facilitate stirring which was continued for another 10 h. The inorganic salt was filtered and washed with solvent. The combined methylene chloride solutions were evaporated on a rotary evaporator, and the residue was taken up in 800 mL of ether from which a white solid precipitated at room temperature. After the solid had been removed the solution was concentrated under reduced pressure, and the residual oil was distilled to yield 44.3 g (86%) of a colorless liquid, bp 103–107 °C (9 mm). Analysis of the distillate by VPC (20% Carbowax 1500 on AW 60–80-mesh Chromosorb W) indicated that the material consisted of three components with the relative ratio of 2:47.5:50.5, respectively. Separation of the two major components was accomplished by distillation through an annular spinning-band column. First major component: bp 80–81 °C (2.3 mm); NMR ($CCl_4$) $\tau$ 5.87 (t, 1 H, OH), 6.58 (s, 2 H, epoxide ring) superimposed on 6.71 (t, 2 H, $CH_2$–O), 7.5–8.41 (m, 5 H, cyclopentyl ring); IR ($CCl_4$) 3418 (s), 3017 (m), 1034, 1016 (s), 837 (s). Second component: bp 91–92 °C (2.3 mm); NMR ($CCl_4$) $\tau$ 6.0–6.7 (m, 3 H, OH and $CH_2$–O) superimposed on 6.60 (s, 2 H, epoxide ring), 7.68–8.90 (m, 5 H, cyclopentyl ring). On the basis of these data, the first component was assigned to *syn*-3-(hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (**3a**) and the other one to its anti epimer (**4a**).

Anal. Calcd for $C_6H_{10}O_2$: C, 63.33; H, 8.74. Found: C, 62.67; H, 8.57.

***syn*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexyl *p*-Bromobenzenesulfonate (3c),**[21] A solution of 23 g (0.20 mol) of **3a** in 200 mL of dry pyridine, protected from the atmosphere with a drying tube, was cooled in an ice bath to maintain the temperature below 5 °C. *p*-Bromobenzenesulfonyl chloride (56 g, 0.22 mol) was added all at once, and the mixture was stirred in the ice bath until the acid chloride was completely dissolved. The reaction mixture was then placed in a refrigerator for 37 h. During this period pyridine hydrochloride crystallized from the solution. The contents were poured into 500 mL of ice–water to precipitate the crude product as a white solid. The precipitate was collected on a Büchner funnel and washed with 500 mL of ice-cold water in order to remove the bulk of pyridine. The crude product which had been dried under vacuum for 20 h amounted to 25 g (78%) and was used directly for the next step without further purification. An analytical sample was obtained by several recrystallizations from a chloroform–pentane mixture to yield

(39) (a) Streitwieser, A., Jr.; Waiss, A. C. *J. Org. Chem.* **1962**, *27*, 290. (b) Weiner, H.; Sucem, R. A. *J. Am. Chem. Soc.* **1965**, *87*, 287, 292. (c) Streitwieser, A., Jr.; Walsh, T. D.; Wolfe, J. R. *Ibid.* **1965**, *87*, 3682.

(40) (a) Fieser, L.; Fieser, M. "Reagents for Organic Chemistry"; John-Wiley: New York, 1967. (b) Perrin, P. D.; Armarego, L. F.; Perrin, D. R. "Purification of Laboratory Chemicals"; Pergamon Press: New York, 1966.

(41) Hess, H. M.; Brown, H. C. *J. Org. Chem.* **1967**, *32*, 4138.

(42) (a) Henbest, H. B.; Nicholls, B. *J. Chem. Soc.* **1957**, 4608. (b) Henbest, H. B.; Nicholls, B. *Ibid.* **1959**, 221.

white powder-like crystals: mp 93–95 °C; NMR ($CDCl_3$) $\tau$ 2.25 (s, 4 H, aromatic ring), 6.08 (d, 2 H, $CH_2OBs$), 6.54 (s, 2 H, epoxide ring), 7.71 (m, 1 H, $CHCH_2$), 8.18 (m, 4 H, cyclopentyl ring); IR ($CHCl_3$) 3055 (m), 1575 (m), 1468 (w), 1384, 1362 (s).

Anal. Calcd for $C_{12}H_{13}BrO_4S$: C, 43.26; H, 3.93; Br, 23.98; S, 9.62. Found: C, 43.37; H, 3.91; Br, 24.08; S. 9.45.

***exo*-2-Oxabicyclo[2.2.1]heptan-6-ol (6a). Hydrolysis of *syn*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexyl Brosylate (3c).** To a solution of 50 g (0.15 mol) of **3c** in 1500 mL of dioxane was added a solution of 6.5 g (0.16 mol) of sodium hydroxide in 20 mL of 1:1 dioxane–water mixture. The reaction mixture turned yellow and was homogeneous after refluxing for about 20 min. The mixture was maintained at reflux for an additional 2 h, during which time sodium *p*-bromobenzenesulfonate precipitated from the solution as fine shining crystals. After the salt had been removed by filtration, excess sodium chloride was added to the filtrate to salt out the aqueous layer. The organic layer was separated, the bulk of solvent was removed under reduced pressure, and the residue was dissolved in ether to precipitate any remaining salt. The ethereal solution was filtered and dried over anhydrous magnesium sulfate, and the ether was distilled through a Vigreux column to afford a crude product as a viscous oil. Analysis of this material by VPC (Carbowax 1500 on AW 60–80-mesh Chromosorb W) showed only one product. Initial purification was done by vacuum transfer at high temperature. Additional purification by the same technique afforded 9.3 g (53%) of **6a** as a hygroscopic white solid. Attempts to recrystallize **6a** from various solvents failed. An analytical sample of **6a** was obtained by preparative VPC: NMR ($CCl_4$) $\tau$ 6.01 (m, 1 H, O–CH), 5.86–6.4 (m, 2 H, CHOH), 6.46 (dt, 1 H, exo proton on $C_3$), 6.75 (d, 2 H, endo proton on $C_3$), 7.54 (m, 1 H, CH bridgehead), 7.73–8.92 (m, 4 H, methylene protons); IR ($CCl_4$) 3602 (m), 3412 (s), 1060, 1080 (vs); mass spectrum, *m/e* 114.

Anal. Calcd for $C_6H_{10}O_2$: C, 63.13; H, 8.74. Found: C, 63.23; H, 8.70.

***exo*-2-Oxabicyclo[2.2.1]heptan-6-ol (6a). Reaction of *anti*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (4a) and Butyllithium.** To a solution of 24.3 g (0.21 mol) of **4a** in about 450 mL of dry ether was added rapidly dropwise 580 mL (0.24 mol) of 0.42 N butyllithium solution. A white precipitate of lithium salt was formed almost immediately after the addition of butyllithium. Addition of 800 mL of purified THF effect solution of the salt. The mixture was heated at reflux for 69 h, at which time the reaction was shown (by VPC) to be 98% complete. Hydrolysis by dropwise addition of water resulted in two layers. The organic layer was removed, washed with sodium chloride, and dried over anhydrous sodium sulfate. The aqueous layer was saturated with sodium chloride followed by extraction with three 300-mL portions of ether and dried. The combined organic layers and the extract were distilled to remove the solvent, leaving a yellow viscous residue. Purification was accomplished by transfer under a high vacuum to afford 9.5 g (40%) of **6a** as a white semisolid. The NMR and IR spectra were identical with those of **6a** prepared by hydrolysis of **3c**.

**4-(Carbomethoxy)cyclopentene-*4-d*.** To a cooled (−60 °C) solution of 450 mL of dry tetrahydrofuran was added 50 mL (0.08 mol) of butyllithium solution[43] dropwise. The reaction was kept stirring below −60 °C for 1 h, after which 10.1 g (0.08 mol) of 4-carbomethoxy)cyclopentene in 10 mL of tetrahydrofuran was added. Stirring was continued in the dry ice–acetone bath for another hour. Then 8 mL of deuterium oxide (Ventron, 99.8%) in 10 mL of dry tetrahydrofuran was added and stirring in the cool bath was continued for 1 h more. The reaction was then slowly warmed up to ca. 10 °C, poured into a 2-L separatory funnel containing 500 mL of water and 250 mL of pentane, followed by addition of 150 mL of saturated sodium chloride, and extracted with two more portions of pentane. The pentane was washed with cold 10% hydrochloric acid, water, and saturated sodium chloride and finally dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure followed by distillation afforded a product which indicated the deuterium exchange of ca. 75%. The whole procedure was repeated two times, after which the product showed deuterium incorporation of ca. 95%: bp 55–56 °C (13 mm); NMR ($CCl_4$) $\tau$ 4.40 (s, 2 H, CH=CH), 6.38 (s, 3 H, $CO_2CH_3$), 7.40 (s, 4 H, $CH_2CCH_2$); IR (neat) 3060 (w), 1735 (s), 1618 (vw). It should be noted that the C–D stretching absorption is not observed in this compound.

**4-(Hydroxymethyl)cyclopentene-*4-d*** was prepared by reduction of 4-(carbomethoxy)cyclopentene-*4-d* with lithium aluminum hydride in ether which afforded a colorless liquid: bp 76–78 °C (22 mm); NMR ($CCl_4$) 4.40 (s, 2 H, CH=CH), 5.81 (s, 1 H, OH), 6.60 (s, 2 H, $CH_2O$), 7.58 and 7.96 (dd, 4 H, $CH_2CCH_2$); IR (neat) 3340 (s), 3055 (m), 2175 (w), 1618 (w).

***syn*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane-*3-d* (3a-*3-d*).** The procedure was as described in the epoxidation of 4-(hydroxymethyl)cyclopentene. Thus 3 g of 4-(hydroxymethyl)cyclopentene-*4-d* was converted to the corresponding mixture of syn and anti epoxides in 73% yield, bp 79–83 °C (2.2 mm). The syn isomer was separated by preparative VPC (20% Carbowax): IR (neat) 3410 (s, br), 3030 (m), 2175 (w); mass spectrum, *m/e* 115.

**4-(Hydroxydideuteriomethyl)cyclopentene** was obtained directly from reduction of 4-(carbomethoxy)cyclopentene with lithium aluminum deuteride in ether as a colorless liquid: bp 84–86 °C (36 mm); IR (neat) 3330 (s), 3055 (m), 2200, 2090 (m), 1619 (m).

***syn*-3-(Hydroxydideuteriomethyl)-6-oxabicyclo[3.1.0]hexane (5a).** The procedure was the same as that described for epoxidation of the corresponding protium compound. Thus 7 g of 4-(hydroxydideuteriomethyl)cyclopentene was converted to a mixture of syn and anti epoxy alcohols, bp 95–100 °C (7.5 mm). Separation and purification of the syn isomer **5a** was accomplished by distillation through a spinning-band column: IR (neat) 3400 (s), 3025 (m), 2200, 2100 (m); mass spectrum, *m/e* 116; NMR ($CCl_4$) $\tau$ 5.9 (s, 1 H), 6.51 (s, 2 H), a doublet centered at 8.14 (4 H) superimposed on a multiplet at 7.81 (1 H).

All *p*-bromobenzenesulfonate esters used for the rate and product studies were prepared by the Tipson method.[21] The following represents the general method.

To a cooled (5 °C) solution of 0.85 g (7.4 mmol) of the alcohol **6a** in 10 mL of dry pyridine in a 25-mL flask equipped with a drying tube and a magnetic stirrer was added 2.07 g (8.1 mmol) of recrystallized *p*-bromobenzenesulfonyl chloride in one portion. After all the solid had dissolved, the reaction mixture was stored in a refrigerator overnight during which time pyridine hydrochloride crystallized from the solution. The mixture was poured into 25 mL of ice–water with vigorous stirring. The product was immediately extracted into three 25-mL portions of ether, and the combined ether extract was washed with two 15-mL portions of cold 10% hydrochloric acid, two 15-mL portions of saturated sodium bicarbonate, and one 15-mL portion of saturated sodium chloride. After the extract had been dried over anhydrous sodium sulfate, ether was removed under reduced pressure to afford 1 g (40%) of a very viscous oil which solidified upon cooling in an ice bath. Three successive recrystallizations from purified pentane afforded pure **6c** as white crystals: mp 61.5–63 °C; NMR ($CDCl_3$) $\tau$ 2.15 (s, 4 H), 5.51 (m, 1 H), 5.75 (m, 1 H), 6.42 (td, 1 H), 6.70 (d, 1 H), 7.45 (br s, 1 H), 7.83–8.66 (m, 4 H); IR (KBr) 3070, 1574, 1467, 1387, 1373, 1187, 1173.

Anal. Calcd for $C_{12}H_{13}BrSO_3$: C, 43.26; H, 3.93. Found: C, 43.62; H, 3.68.

**Brosylate Ester of *exo*-2-Oxabicyclo[2.2.1]heptan-*6-d*-6-ol (6c-*6-d*).** The same procedure was used to convert 0.3 g (2.6 mmol) of *exo*-**6a**-*6-d* to 0.8 g (92%) of crude semisolid of **6c**-*6-d*. Three recrystallizations from purified pentane afforded **6c**-*6-d* as colorless crystals: mp 60.5–62.5 °C; NMR ($CDCl_3$) $\tau$ 2.24 (s, 4 H), 5.0–5.36 (m, 1 H), 7.48–9.31 (m, 10 H); IR (KBr) 1575 (m), 1470 (w), 1373, 1387, 1347 (s), 1187, 1175 (s).

**Brosylate Ester of *anti*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (4c).** The alcohol **4a** (1.95 g) was converted to 5 g (74%) of crude ester **4c**. Several recrystallizations from various solvents (pentane, petroleum ether, pentane–ether mixture, pentane–chloroform mixture) afforded colorless crystals of **4c**: mp 69–73 °C; NMR ($CDCl_3$) $\tau$ 2.25 (s, 4 H, aromatic ring), 5.95 (unresolved d, 2 H, $CH_2OBs$), 6.54 (s, 2 H epoxide ring), 7.47 (m, 1 H, CH), 7.86–8.82 (m, 4 H); IR ($CHCl_3$) 1575 (m), 1465 (w), 1386, 1365 (vs), 1174 (s).

**Brosylate Ester of *syn*-6-Oxabicyclo[3.1.0]hexan-3-ol (3c).** The alcohol **3a** (0.3 g) was transformed to 0.9 g (94%) of crude

(43) The butyllithium solution was sure-sealed (Aldrich, 1.6 M). The reaction mixture was kept below −60 °C all the time.

product, mp 148–151 °C. Three successive recrystallizations from a chloroform–pentane mixture gave **3c** as colorless crystals: mp 151–152 °C; NMR ($CDCl_3$) $\tau$ 2.24 (s, 4 H), 4.85 (m, 1 H), 6.47 (m, 2 H), 7.80 (br doublet-like, 4 H); IR (KBr) 1585 (s), 1481 (m), 1395, 1368 (s), 1202, 1177 (s).

Anal. Calcd for $C_{11}H_{11}BrSO_3$: C, 41.39; H, 3.47; O, 20.05. Found: C, 41.37; H, 3.29; O, 20.18.

**Brosylate Ester of *anti*-6-Oxabicyclo[3.1.0]hexan-3-ol (2c).** 4-Cyclopentenol (2.82 g) was converted to 10.2 g of crude corresponding brosylate ester which was recrystallized from pentane to afford colorless crystals, mp 57.5–58.5 °C. Epoxidation of 4-cyclopentenyl brosylate afforded crude product of mp 59–96 °C. Four successive recrystallization from pentane- afforded **2c** as colorless crystals: mp 75–76 °C; NMR ($CDCl_3$) $\tau$ 2.24 (s, 4 H), 5.42 (pentuplet, 1 H), 6.59 (s, 2 H), and an ABX pattern with $\tau_A$ at 7.49 and $\tau_B$ at 8.2; IR (KBr) 1571 (m), 1468 (w), 1386, 1736 (s), 1235 (vw), 1187, 1172 (s), 835 (m).

Anal. Calcd for $C_{11}H_{11}BrSO_3$: C, 41.39; H, 3.47; O, 20.05. Found: C, 41.37; H, 3.29; O, 20.18.

**Brosylate Ester of *syn*-3-(Hydroxydideuteriomethyl)-6-oxabicyclo[3.1.0]hexane (5c).** The same procedure was used to convert **5a** to **5c** in 75% yield. Recrystallization from a pentane–chloroform mixture afforded colorless crystals: mp 89–91 °C; NMR ($CDCl_3$) $\tau$ 2.2 (s, 4 H, aromatic ring), 6.54 (s, 2 H, epoxide ring), 7.57 (m, 1 H, ring methine), 8.16 (d, 4 H, $CH_2CCH_2$); IR (KBr) 1584 (s), 1478 (m), 1390, 1367 (s).

**Brosylate Ester of *syn*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane-*3-d* (3c-*3-d*).** The brosylate ester **3c**-*3-d* was prepared from the alcohol **3a**-*3-d* in 81% yield: mp 90–92 °C; NMR ($CDCl_3$) $\tau$ 2.19 (s, 4 H), 6.01 (m, 2 H), 6.51 (s, 2 H), 8.17 (m, 4 H); IR (KBr) 3100 (m), 3020 (m), 1578, 1470 (w), 1390, 1360 (s) 1188, 1175 (vs).

**Kinetics. A. Solvents.** All solvents were doubly distilled prior to use. Ethanol (90%)–water and ethanol (50%)–water were prepared by weight percent, using the appropriate conversion factors.[44]

**B. Procedures.** Rates of the solvolysis of various *p*-bromobenzenesulfonate ester used in this study have been determined by an ultraviolet spectrophotometric method[45] with a Cary Model 118A or Model 119 and 10-mm UV cell.

The clean cell was rinsed with the appropriate solvent mixture, filled, placed in the compartment of the spectrophotometer, and allowed to equilibrate for at least 1 h. After the instrument was zeroed the solvent was withdrawn from the cell without removing the cell from the compartment. The solution for the kinetic run was prepared in a 10-mL volumetric flask by dissolving 3.3 to 3.5 mg of ester sample in the solvent mixture. The solution was swirled in a constant-temperature bath (thermostated to within ±0.1 °C of the temperature studied) for 5 min (in order to bring the temperature of the solution as close as possible to the bath temperature) and was transferred to the cell. The solution was then allowed to equilibrate for an appropriate period (depending on the half-life of the substrate), after which points were taken for a period of 2–2.5 half-lives.

Rate constants were calculated by using a computer program for the least-squares analysis.[46] Except for **4c**, all compounds gave good first-order rate constants for at least 2–2.5 half-lives. Compound **4c** exhibited an upward rate constant.

**Product Studies.** The following represents the general procedure for product analysis in this study.

***exo*-2-Oxabicyclo[2.2.1]hept-6-yl *p*-Bromobenzenesulfonate (6c).** To a suspension of 0.3 g (3 mmol) of calcium carbonate powder in 150 mL of 90% aqueous ethanol was added 0.46 g (4.0 mmol) of **6c**. The mixture was allowed to stir at room temperature for 14 h, after which the solid was removed by filtration and the solution was directly analyzed by VPC (20% Carbowax 1500 on AW 60–80-mesh Chromosorb W). Besides the solvent peak, two peaks were shown at $t_{R_1}$ 2.1 min (72 ± 3%) and $T_{R_2}$ 17.3 min (28 ± 3%). The bulk of the ethanol was removed by distillation through a 130 × 10 mm Fenske column packed with $^1/_8$ in. Pyrex helices. The residue was extracted with seven 15-mL portions of ether, and the combined ether extract was washed successively with five 10-mL portions of water and dried over anhydrous magnesium sulfate. The solution was concentrated by distillation of the ether through the 130 × 10 mm Fenske column to afford a slightly yellow oil. Analysis of this concentrated solution by VPC on three other different columns confirmed that the solvolysis product mixture consisted of only two components. Purification and separation were accomplished by preparative VPC (20% Carbowax 20M on 20–30-mesh Chromosorb A). The minor component was assigned the structure of the starting alcohol (**6a**) on the basis of identical VPC retention time and infrared spectrum with the authentic sample. The major component exhibits the following spectral properties: NMR ($CCl_4$) a broad singlet at 5.86 (1 H), a complex multiplet between 6.36–6.67 (2 H), a quartet at 6.53, a triplet at 8.87 ($J$ = 7 Hz), a doublet at 6.78 (1 H, $J$ = 7 Hz), a very broad singlet at 7.57 (1 H), and a complex multiplet between 8.0 and 8.9 (4 H); IR (neat) 8.93, 9.07 (vs, C–O stretching of ether); mass spectrum, $m/e$ 142. Based on these spectral properties, the major component was assigned the structure of *exo*-2-oxabicyclo[2.2.1]hept-6-yl ethyl ether (**6b**).

***p*-Bromobenzenesulfonate Ester of *exo*-2-Oxabicyclo[2.2.1]heptan-*6-d*-6-ol (6c-*6-d*).** A mixture of 0.34 g (1 mmol) of **6c**-*6-d* and 0.2 g (2.0 mmol) of powdered calcium carbonate in 130 mL of 90% aqueous ethanol was stirred at room temperature for 24 h. The clear solution was directly analyzed by VPC (20% Carbowax 1500 on AW 60–80-mesh Chromosorb W); two components were observed as 72% and 28%, respectively. After the bulk of solvent was removed, the residue was saturated with sodium chloride followed by extraction with five 10-mL portions of purified pentane and dried over anhydrous sodium sulfate. Analysis of the pentane extract by VPC on the same column showed only the first component with traces of a second component. The aqueous layer was reextracted with four 10-mL portions of ether and dried. Analysis of this ether extract showed only the second component. Both pentane and ether extracts were separately concentrated by distillation. Purification was performed by preparative-scale VPC (20% Carbowax 20M on 20–30-mesh Chromosorb A). The major component was collected: NMR (100 MHz, $CDCl_3$), a broad singlet at 5.18 (0.5 H), a doublet and a quarted superimposed on a multiplet between 6.30 and 6.80 (4.5 H), a broad singlet at 7.54 (1 H), a complex multiplet between 8.2 and 9.0 (4 H), and a triplet at 8.85 (3 H). Based on these spectral data, the product was identified as a 50:50 (±) mixture of *exo*-2-oxabicyclo[2.2.1]hept-6-yl-*6-d* ethyl ether and *exo*-2-oxabicyclo[2.2.1]hept-6-yl-*1-d* ethyl ether. The minor component showed the following NMR spectrum (100 MHz, $CDCl_3$): a rather broad singlet at 5.92 (0.5 H), a broad unresolved doublet at 6.09 (0.5 H), a doublet of triplets at 6.43 ($J$ = 1.5 Hz, 1 H), a doublet at 6.70 ($J$ = 3.2 Hz, 1 H), a broad singlet at 7.49 overlapping with a very broad flat peak between 7.25 and 7.78 (2 H), and a complex multiplet between 7.93 and 8.80 (4 H). This minor product was identified as 50:50 (±) mixture of *exo*-2-oxabicyclo[2.2.1]heptan-*6-d*-6-ol and *exo*-2-oxabicyclo[2.2.1]heptan-*1-d*-6-ol.

***p*-Bromobenzenesulfonate Ester of *syn*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (3c).** To 300 mL of 90% aqueous ethanol was added 1.5 g (15 mmol) of powdered calcium carbonate and 1 g (0.01 mol) of **3c**. The reaction mixture was allowed to stir for 10 h at room temperature. The solution, after being filtered, was concentrated and analyzed by VPC (20% Carbowax 1500 on AW 60–80-mesh Crhomosorb W). Two products were shown as 75% and 25%, respectively. The concentrated solution was purified by vacuum transfer at room temperature which resulted in a clear colorless liquid. Separation of the two components was effected by preparative-scale VPC (20% Carbowax 20M on 20–30-mesh Crhomosorb A). The first component exhibited IR, NMR, and mass spectra that were identical with those of *exo*-2-oxabicyclo[2.2.1]hept-6-yl ethyl ether (**6b**) previously obtained from solvolysis of *exo*-2-oxabicyclo[2.2.1]hept-6-yl *p*-bromobenzenesulfonate. The second component appeared as a broad peak and was assigned to *exo*-2-oxabicyclo[2.2.1]heptan-6-ol (**6a**) on the basis of identical VPC retention time and infrared spectrum with those of an authentic sample.

***p*-Bromobenzenesulfonate Ester of *anti*-3-(Hydroxymethyl)-6-oxabicyclo[3.1.0]hexane (4c).** A solution of 2.2 g (7.0 mmol) of **4c** and 300 mL of 50% aqueous ethanol containing 2.0 g (0.02 mol) of solid calcium carbonate was heated at 70–75

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(46) The program was written by W. E. Buddenbaum and modified by J. G. Jewett.

°C for 65 h. Analysis of the clear solution by VPC (20% Carbowax 1500 on AW 60–80-mesh Chromosorb W) showed four components as 16%, 27%, 53%, and 4%, respectively. The first component (16%) was assigned the structure of *anti*-3-(hydroxymethyl)-6-oxabicyclo[3.1.0]hexyl ethyl ether (**4b**) on the basis of the following spectra properties: IR (neat) 3042 (CH stretching of epoxide ring), 1123, 1105 (vs, doublet, C–O stretching), 837 (CH bending of epoxide ring); mass spectrum, *m/e* 142. The third component (57%) was identified as *anti*-3-(hydroxymethyl)-6-oxabicyclo-[3.1.0]hexane (**4a**) on the basis of identical spectra and retention time with the authentic sample.

***p*-Bromobenzenesulfonate Ester of *syn*-3-(Hydroxydideuteriomethyl)-6-oxabicyclo[3.1.0]hexane (5c).** The same procedure was used for preparative solvolysis of **5c** in aqueous acetone which afforded a semisolid of *exo*-2-oxabicyclo[2.2.1]-heptan-3,3-$d_2$-6-ol as the sole product: NMR ($CCl_4$) a singlet at 6.95 (1 H), a broad singlet at 6.12 (1 H), an unresolved singlet at 7.49 (1 H), and a complex multiplet between 7.97 and 8.84 (5 H); mass spectrum, *m/e* 116. The alcohol **5a** was converted to its *p*-bromobenzenesulfonate ester: mp 62.5–64 °C; NMR ($CDCl_3$) a singlet at 2.20 (4 H), an unresolved doublet at 5.48 (1 H), a singlet at 5.74 (1 H), an unresolved singlet at 7.45 (1 H), and a complex multiplet between 7.88 and 8.45 (4 H).

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**Registry No. 1a**, 25494-14-8; **2a**, 25494-15-9; **2c**, 72598-09-5; **3a**, 72598-06-2; **3a**-*3-d*, 77662-16-9; **3c**, 72598-07-3; **3c**-*3-d*, 77662-17-0; **4a**, 72656-82-7; **4c**, 72598-08-4; **5a**, 77662-18-1; **5c**, 77662-19-2; **6a**, 36368-46-4; **6a**-*6-d*, 77662-20-5; **6a**-*1-d*, 77662-21-6; **6b**, 77662-22-7; **6b**-*6-d*, 77662-23-8; **6b**-*1-d*, 77662-24-9; **6c**, 36368-48-6; **6c**-*6-d*, 77680-03-6; 4-cyclopentenol, 14320-38-8; 4-(hydroxymethyl)cyclopentene, 25125-21-7; *p*-bromobenzenesulfonyl chloride, 98-58-8; 4-(carbomethoxy)cyclopentene-*4-d*, 77662-25-0; 4-(carbomethoxy)-cyclopentene, 58101-60-3; 4-(hydroxymethyl)cyclopentene-*4-d*, 77662-26-1; 4-(hydroxydideuteriomethyl)cyclopentene, 77662-27-2; 4-cyclopentenyl brosylate, 27721-58-0.

# Neutral Trichloroacetylations of Alcohols by Hexachloroacetone

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The addition of simple alcohols in hexachloroacetone (HCA) in the presence of strong hydrogen bond acceptors (e.g., dimethylformamide) results in a high yield of the corresponding trichloroacetate (via a haloform reaction scheme). The trichloroacetylation reactions are carried out under neutral conditions, and the resultant ester can easily be separated from the reaction mixture via extraction/distillation procedures. Kinetic evidence demonstrates that the trichloroacetylation of alcohols by HCA is a stereoselective process, and further studies suggest that the catalytic role of the acceptors is of a hydrogen bonding nature.

Reports within the literature have previously described neutral haloform reactions of hexachloroacetone (HCA) in such solvents as dimethyl sulfoxide,[1] formamide,[2] and pyridine.[3] These solvents are reportedly similar with respect to their hydrogen bond accepting capabilities.[4,5] In this study, we investigated the trichloroacetylation of various alcohols by HCA in the presence of these and other hydrogen bond accepting solvents. The addition of relatively weak hydrogen bond acceptors such as dioxane, tetrahydrofuran, acetone, ethyl acetate, and cyclopentanone to alcoholic HCA solutions which are heated at reflux for several hours do not result in the trichloroacetylation of the various alcohols studied; however, the addition of relatively strong hydrogen bond acceptors such as dimethyl sulfoxide, pyridine, hexamethylphosphoramide, and dimethyl formamide (DMF) to alcoholic HCA solutions at room temperature initiate exothermic reactions resulting in the rapid formation of trichloroacetate and chloroform.

Since DMF is a relatively available and fairly inexpensive solvent, trichloroacetylation yields were maximized by utilising this reagent. Yields obtained via gas–liquid chromatographic analysis (Table I) are superior to any yields obtained by previously reported trichloroacetylation procedures.[3,6–11] Chromatographic coelution of certain trichloroacetates with either HCA or DMF necessitated the aqueous extraction of these compounds from the organic esters prior to analysis. The efficient removal of unreacted HCA from pentane solutions of the reaction mixtures appeared to be effected by the formation of the

Table I. Trichloroacetylation of Alcohols by HCA

| alcohol | equiv of HCA | equiv of DMF | reaction time, h[a] | % yield[b] |
|---|---|---|---|---|
| methanol | 1.0 | 1.9 | 1.5 | 98[c] |
| ethanol | 1.5 | 4.0 | 9 | 98 |
| 1-propanol | 1.5 | 5.0 | 9 | 90 |
| 2-propanol | 1.5 | 5.0 | 48 | 74 |
| cyclohexanol | 1.5 | 7.0 | 48 | 75 |
| 2-methyl-2-propanol | 1.0 | 4.0 | 72 | 0 |

[a] Reaction temperature was 55 °C. [b] Determined by GLC with cyclohexyl chloride as the internal standard. [c] Product isolated with a yield of 93%.

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