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ANALYTICAL SEPARATION OF HOMOALLYLIC AND SOLVENT PARTICIPATION

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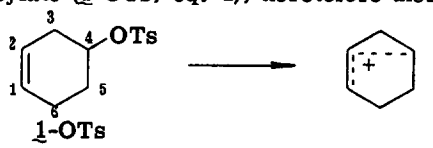
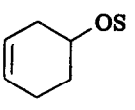
Although there have been numerous studies on the question of homoallylic assistance in cyclohexen-4-yl tosylate (1-OTs, eq. 1), heretofore there has been no definitive proof of the



1-OTs (1)

presence[1a] or absence[1b] of participation in this fundamental system. We report herein a new approach to this problem by determination of the substitution stereochemistry of reaction (1) through the use of a diastereomeric proton label. By this means we have been able to obtain the exact proportions of direct solvent attack (k_s) and homoallylic participation (k_Δ) in a variety of solvents. Such detailed elucidation of the mechanism of solvolysis of homoallylic systems has not previously been possible.

The major substitution product from the solvolysis of cyclohexen-4-yl tosylate is the ester, ether, or alcohol that corresponds to starting material (1), although lesser amounts of the bicyclic material (2) and the hydride shift product (3) are observed.[2] We have studied the



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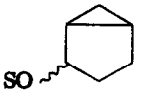

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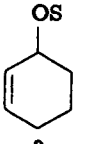

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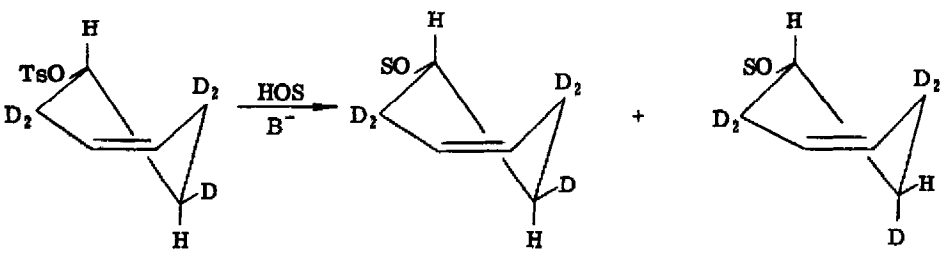
reaction in several solvents (buffered 70% 1,4-dioxane/water, acetic acid, formic acid, and hexafluoroisopropanol[3]) in order to have a wide range of solvent nucleophilicity and ionizing power. Direct solvent displacement or displacement on a tight ion pair (k_s) results in a product (1) with stereochemistry inverted from that of the starting tosylate, whereas homoallylic participation (k_Δ) results in retained stereochemistry.[4] A k_c mechanism for a secondary system is highly unlikely in water or acetic and formic acids,[5] but possible in HFIP.[6]

We have employed a diastereomeric proton label to monitor the stereochemistry at the 4 position of 1-OTs in order to avoid the introduction of a substituent (alkyl, aryl, etc.) that can alter the transition state structure. We prepared cyclohexen-4-yl-3,3,5,6,6-d_5 tosylate by the monoepoxidation of cyclohexa-1,4-diene-3,3,6,6-d_4, followed by ring opening with lithium aluminum deuteride and tosylation. The synthetic procedure should yield a product with a trans relationship between the protons at the 4 and 5 positions [1-OTs-trans(4H,5H)]. This stereochemistry was confirmed by observation of $J_{4,5}$ = 9.6 Hz.[8] Solvolysis with retention would produce 1-trans(4H,5H), whereas inversion would give 1-cis(4H,5H). The stereochemical



1-OTs-trans(4H,5H) 1-trans(4H,5H) 1-cis(4H,5H)

outcome can be determined from either of two nmr properties of the product 1-OS, which was isolated by preparative gas chromatography after work-up. (1) The large axial-axial splitting between the 4 and 5 protons in the starting tosylate should still be present in the retention product, whereas the splitting in the inversion product (axial-equatorial coupling) would be much smaller. If there is a mixture of mechanisms, the 4-proton resonance would then be a composite of two superimposed doublets, one with the large coupling (from the retention process), the other with the small coupling (inversion). (2) In the retention product, the 5 proton is predominantly axial, whereas in the inversion product it is equatorial. The different stereochemistries therefore yield not only different splittings in the 5-proton

resonance, but also different chemical shifts. The 4- and 5-proton resonances thus give independent measures of the reaction stereochemistry.

After 5 half-lives of acetolysis, we isolated 1-OAc, which comprised about 70% of the substitution product.[2] These products were tested and found to be stable to reaction conditions. With deuterium irradiation, the 4-proton resonance clearly showed two superimposed doublets (J = 9.8, 3.3 Hz) in the ratio 83/17, with the material corresponding to inverted stereochemistry in the larger amount. The 5-proton resonance consisted of a low field (equatorial) doublet with the 3.3-Hz splitting and a smaller high field (axial) doublet with the 9.8-Hz splitting, again in the ratio 83/17. The major pathway of acetolysis therefore is the direct solvent displacement reaction, but a retention pathway is observably competitive. On the other hand, in 70% dioxane/water only the 3.3-Hz doublet is observed in 1-OH (inverted product), so homoallylic participation is entirely lacking.

A solvent with lower nucleophilicity or higher ionizing power should be able to promote the homoallylic pathway at the expense of solvent assistance. After 5 half-lives for formolysis, we isolated 1-OF, which comprised essentially all of the substitution product. The superimposed 4-proton doublets were in the ratio 60/40, with the inverted material still in excess. The two 5-proton doublets yielded the same ratio. Thus formic acid indeed increases the proportion of the homoallylic pathway, at the expense of solvent displacement, hydride shift, and elimination, but the inversion process is still dominant. In HFIP (5 half-lives), substitution again is more important than elimination, and 1-O-HFIP is the major product. The retained isomer in this solvent is now the only observable product (>85%), so that nucleophilic attack is no longer the dominant pathway. Thus solvents of low nucleophilicity and high ionizing power tend toward a retention mechanism rather than racemization. We believe that homoallylic participation therefore offers the best explanation for the retention pathway. Detailed analysis of the rates in terms of N and Y shows that the increased proportion of the retention product is due to a diminution of the k_s process as well as an enhancement of the k_Δ process.

The method of the diastereotopic proton label has thus shown that the substitution component of the solvolysis of cyclohexen-4-yl tosylate passes from an entirely solvent participation pathway in dioxane/water through mixed mechanisms in acetic and formic acids to an entirely homoallylic participation pathway in hexafluoroisopropanol. Since 1-OTs solvolyzes by a mixture of mechanisms in acetic acid, it is not surprising that previous

interpretations have been somewhat conflicting.[1] This method therefore provides a subtle but accurate method for the determination of the relative amounts of homoallylic and solvent participation.

Acknowledgments. This work was supported by the National Science Foundation (Grant No. MPS 72-05006), the Chevron Research Company, and the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 2970-AC4).

References and Notes

1. Previous approaches have used standard considerations of rates and products. (a) M. Hanack and H.-J. Schneider, Angew. Chem. Intern. Ed. Engl., 6, 666 (1967). These authors argue from the observation of a small rate acceleration and a few per cent of bicyclic products that participation is present in acetolysis. (b) K. B. Wiberg, B. A. Hess, Jr., and A. J. Ashe, III, "Carbonium Ions," Vol. III, G. A. Olah and P. v. R. Schleyer, ed., Wiley-Interscience, New York, 1972, p. 1337. These authors report a small rate deceleration in acetolysis and imply that participation is quite weak or even absent.

2. E. C. Friedrich, M. A. Saleh, and S. Winstein, J. Org. Chem., 38, 860 (1973). These authors report the unpublished product studies of two other groups that examined the acetolysis of this compound earlier. Elimination products comprise better than half the reaction mixture in acetolysis, but considerably less in the other solvents.

3. F. L. Schadt and P. v. R. Schleyer, Tetrahedron Lett., 2335 (1974). We thank Professor Schleyer for suggesting this solvent to us.

4. P. R. Story and B. C. Clark, Jr., "Carbonium Ions," Vol. III, G. A. Olah and P. v. R. Schleyer, ed., Wiley-Interscience, New York, 1972, pp. 1007f.

5. (a) J. B. Lambert and G. J. Putz, J. Amer. Chem. Soc., 95, 6313 (1973); (b) J. L. Fry, C. J. Lancelot, L. K. M. Lam, J. M. Harris, R. C. Bingham, D. J. Raber, R. E. Hall, and P. von R. Schleyer, J. Amer. Chem. Soc., 92, 2538 (1970).

6. The "free" cyclohexen-4-yl cation has been found to rearrange rapidly in $FSO_3H-SbF_5-SO_2ClF$ to the 1-methylcyclopenten-3-yl cation.[7] No products corresponding to such an intermediate were observed in the present study.

7. G. A. Olah, G. Liang, and Y. K. Mo, J. Amer. Chem. Soc., 94, 3544 (1972).

8. The antiperiplanar relationship still holds between the 4- and 5-axial protons of cyclohexene, despite the fact that the conformation is a half-chair. The displacement from the vertical is about 11°; see F. R. Jensen and C. H. Bushweller, Adv. Alicyclic Chem., 1, 191 (1970).