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THE ACETOLYSIS OF CONSTRAINED CYCLOHEXYL TOSYLATES[1]

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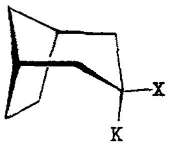
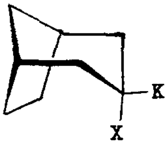
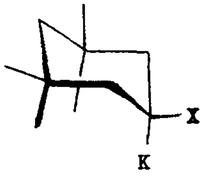
Recently[3] we have examined 3,3,5,5-tetramethylcyclohexanone (I) and bicyclo[3.2.1]octanone-3 (II) as models for the operation of the Reflex Effect.[4] As a continuation of this investigation we were interested in the solvolysis of the tosylates derived from I and II. Accordingly, we have prepared exo-3 and endo-3-bicyclo[3.2.1]octyl tosylates (III and IV) and 3,3,5,5-tetramethylcyclohexyl tosylate (V) and studied their acetolyses.[5] The kinetic data are assembled in Table 1.



III X = OTs
IIIa X = OH



IV X = OTs
IVa X = OH



V X = OTs
Va X = OH

K = Hydrogen in all cases

TABLE 1

Acetolysis Rates of Constrained Cyclohexyl *p*-Toluenesulfonates

Tosylate	Temp., °C	k_1, sec.$^{-1}$	ΔH kcal.	ΔS e.u.
Exo-3-Bicyclo-[3.2.1]octyl (III)	25.0[a]	4.87×10^{-7}	25.6	-2.4
	50.0	9.71×10^{-6}		
	70.0	1.07×10^{-4}		
	90.0	7.71×10^{-4}		
Endo-3-Bicyclo-[3.2.1]octyl (IV)	25.0[a]	5.32×10^{-6}	22.8	-6.2
	50.0	1.12×10^{-4}		
	70.0	8.87×10^{-4}		
	90.0	5.52×10^{-3}		
3,3,5,5-Tetramethylcyclohexyl (V)	25.0[a]	8.59×10^{-8}	27.4	1.0
	50.0	3.27×10^{-6}		
	70.0	3.96×10^{-5}		
	90.0	3.55×10^{-4}		

[a] Calculated rates

However, in order to evaluate the observed rate constants, knowledge of the ground state conformations of the tosylates is required. The steric effect of the ethane bridge and the two pairs of geminal methyl groups could generate boat-formed cyclohexane moieties, especially in the case of IV and V.

As can be seen from Table 2, the chemical shifts and vicinal coupling constants of the tertiary carbinyl proton K in the alcohols corresponding to III - IV, viz., IIIa - Va, are invariant with temperature.[6] Moreover, the mul-

TABLE 2

Chemical Shifts and Coupling Constants of Substituted Cyclohexanols, 0° - 120°[6]

Compound	Signal due to Proton K
IIIa	Septuplet at 225 c.p.s. Jaa = 10.5, Jae = 6.0 c.p.s.
IVa	Quintuplet at 237 c.p.s. Jea ≈ Jee ≃ 3.0 c.p.s.
Va	Triplet of Triplets at 228 c.p.s. Jaa = 11.25, Jae = 4.25 c.p.s.

tiplicities indicate that the cyclohexane moiety is locked firmly in the chair conformation. Therefore, by extension, the tosylate configurations in III - V are as depicted.

The acetolysis rate at 25° of tetramethylcyclohexyl tosylate (V) is about the same as that of cyclohexyl tosylate (VI).[7] Both 3-endo and 3-exo-bicyclo[3.2.1]octyl tosylate are one hundred, and ten times faster respectively than VI. Both these rate enhancements are quantitatively compatible with steric acceleration due to the ethane bridge.[8]

It is especially significant that the endo tosylate IV acetolyses faster than the exo (III) by a factor of ten. Brown has proposed that the rate of solvolysis of exo-2-norbornyl p-bromobenzenesulfonate is 'normal', whereas that of the endo isomer is uncommonly slow due to "steric hindrance to ionization".[9] Since models and the n.m.r. data indicate that III and IV resemble geometrically *exo*- and *endo*-2-norbornyl tosylate, it would appear that the aforementioned proposal, if true, must constitute a special case, as it clearly does not apply to the order of the difference in rate demonstrated by *exo*- and *endo*-3-bicyclo[3.2.1]octyl tosylates (III and IV).

Analysis[10] of the composition of the products formed from the acetolysis of III, IV and V is particularly informative (Fig. 1).[11] The formation of *endo* as well as *exo*-acetates from the *endo* tosylate (IV) indicates that there may be some degree of solvolytic epimerization of IV.[12] Nevertheless, the predominance of the *exo* acetate undoubtedly originates from the backside attack of solvent on IV.[13] It is remarkable that in the case of the *exo* tosylate (III) the

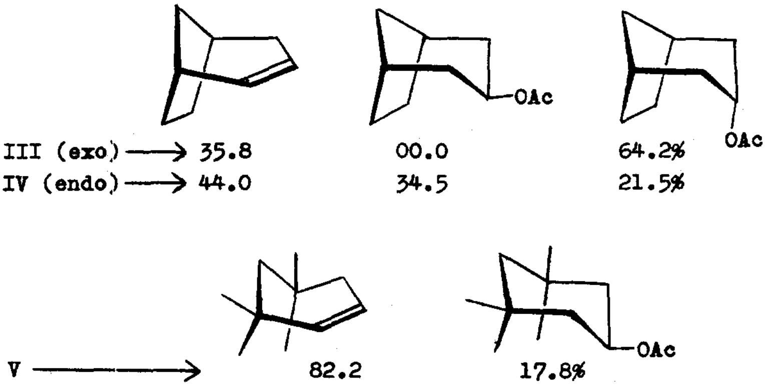


Figure 1. Products formed from III, IV and V on acetolysis[11]

substituted product is exclusively the endo acetate. Brown has attributed the predominant formation of exo product on solvolysis of exo-2-norbornyl p-bromobenzenesulfonate to "steric hindrance to endo substitution".[9,14] This interpretation is at variance with the stereochemical result of the solvolysis of exo-3-bicyclo[3.2.1]octyl tosylate (III), the endo side of which appears to be just as hindered as that of the 2-norbornyl system.

Acknowledgements

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References

1. To be regarded as Part VI of a series entitled "The Stereochemistry of the Bicyclo[3.2.1]octane System." For Part V see C. W. Jefford, S. Mahajan, J. Gunsher and B. Waegell, Tetrahedron Letters, No.28, 2333 (1965).
2. Visiting Lecturer for the Summer Session, 1964 on leave from the Institut de Chimie, Strasbourg, France.
3. a) C. W. Jefford and B. Waegell, Tetrahedron Letters, No. 28, 1981 (1963).
   b) B. Waegell and C. W. Jefford, Bull. Soc. chim.France, 844 (1964).
4. a) C. Sandris and G. Ourisson, Bull. Soc. chim. France, 1524 (1958).

b) B. Waegell and G. Ourisson, Bull. Soc. chim. France, 495, 496, 503 (1963).

5. All compounds reported herein gave acceptable elemental analyses.

6. The alcohols IIIa - Va were investigated as approximately 10% solutions in carbon tetrachloride at 60 Mc. on a Varian Associates model A-60 spectrometer. A variable temperature controller (model V 6040) and probe were used for the temperature measurements between 0° - 120°. Jaa signifies the vicinal coupling constant of axial proton K and its axial neighbour; e designates an equatorially disposed proton.

7. The acetolytic rate constant at 25° of cyclohexyl tosylate is 3.79×10^{-8} $sec.^{-1}$ (cf. S. Winstein and N.J. Holness, J. Amer. Chem. Soc., 77, 5562 (1955)).

8. The axial tosylate group in IV experiences steric interaction with the ethane bridge of an estimated 5.0 kcal./mole (cf. the 1,3-diaxial methyl-hydroxyl interaction of 2.4 kcal./mole; E. L. Eliel and H. Haubenstock, J. Org. Chem., 26, 3504 (1961)). However, not all this strain is relieved in the transition state so that the observed 100 fold rate enhancement is not unreasonable.

9. H. C. Brown, Special Publication No. 16, The Chemical Society, London, 1962 pp. 140-57, 176-78. H. C. Brown et al., J. Amer. Chem. Soc., 86, 1246,5008 (1964) and intervening papers.

10. The identity of the products was established through

their n.m.r. spectra and by comparison with authentic compounds.

11. For product analysis, the tosylates were acetolysed at 90° for about 20 half-lives.

12. IV may dissociate to an intimate ion pair which could suffer internal return to its exo isomer, III. Alternatively, IV could undergo SN2 attack by free tosylate ion to form III. These possibilities are under investigation.

13. There is no doubt that the solvolysis of 'normal' secondary sulfonates proceeds by solvent attack in an SN2 type process. (H. Weiner and R. A. Sneen, J. Amer. Chem. Soc., 87, 287, 292 (1965)).

14. H. C. Brown, K. J. Morgan and F. J. Chloupek, J. Amer. Chem. Soc., 87, 2137 (1965), footnote 73.