Transition State Structures in Ion-pair Base-promoted *syn*-Elimination Reactions

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The temperature dependence of the primary deuterium kinetic isotope effect has been applied as a criterion of transition state (TS‡) structure in the *syn*-elimination reaction of bicyclo[2.2.1]heptan-2-*exo*-yl toluene-*p*-sulphonate, caused by two different hindered bases in a low dielectric, aprotic solvent. The isotope effect (k_H/k_D = 3.43 ± 0.02) was temperature independent, and identical for the two bases used (t-butoxide and cyclohexylcyclohexyl oxide). These results are interpreted to indicate a non-planar, cyclic TS‡ involving non-linear hydrogen transfer. A comparison with the analogous Hofmann and amine oxide elimination reactions affords some understanding of the factors controlling TS‡ structure in cyclic *syn*- elimination processes.

The transition state (TS‡) for *syn*-elimination by strong, ion-paired bases, first recognized by Sicher,[1] Zavada,[2] and Bartsch,[3] and their associates, has been variously delineated as (1) [3] and (2).[2,4] These alternative TS‡ structures should be distinguishable by their deuterium kinetic isotope effects.[5] Model calculations on (2) assuming the sp^3, bx configuration have been carried out by Saunders [the models for which the bonding modes follow equations such as $F_{HC\ldots H} = 0.46(1 - z)$ (in the transition state) are labelled the bx configurations].[4] According to these theoretical considerations, independent of the nature of the leaving group X, a maximum value for k_H/k_D of *ca.* 2.8 might be realized in a TS‡ with 0.5 C–X cleavage and 0.3 C–H cleavage. The temperature dependence of k_H/k_D was not discussed. Similar calculations have not been carried out for the model (1). Moreover, since *syn*- and *anti*-eliminations are most often found to be competing pathways for a given substrate,[1] the experimental assignment of the components of the kinetic isotope effect the *syn* and *anti* processes is beset with difficulties.

Though such measurements have been carried out for some β-elimination reactions,[6] the temperature dependence of $(k_H/k_D)_{syn}$ has not previously been reported. Our objective was to apply the temperature dependence of k_H/k_D as a criterion of TS‡ structure in the *syn*-elimination reaction promoted by sterically hindered bases.

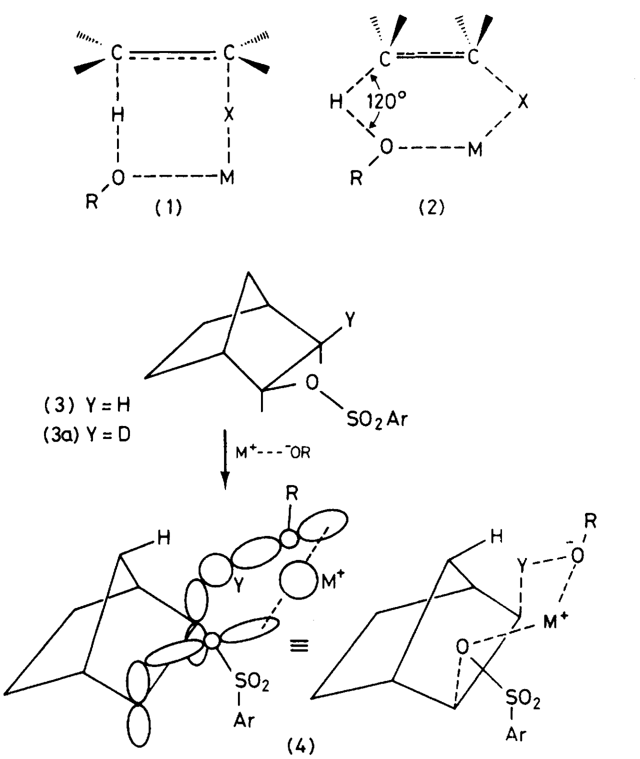

Figure. Bent TS‡ of *syn*-elimination

Results and Discussion

The case chosen for study was one for which Brown,[7] Bartsch,[8a] and others [8b] have established a (>98%) course of bimolecular *syn*-elimination, namely the reaction of bicyclo[2.2.1]heptan-2-*exo*-yl toluene-*p*-sulphonate (3) and its [3-^{2}H] isomer (3a) with the bulky sodium 2-cyclohexylcyclohexyl oxide in 2,5,8,11-tetraoxadodecane (triglyme). The same conditions were used in our case for determination of the rate constants and activation parameters for the bimolecular reaction of (3), and the same reaction was investigated using potassium t-butoxide, a somewhat stronger associated base. The resulting data are summarized in Table 1. The more hindered but weaker secondary alkoxide base exhibits a slightly higher activation free energy. The principal difference resides in the entropy factor, possibly reflecting a tighter association of the gegenions or greater difficulties in co-ordination of an ion pair as compared with potassium t-butoxide in this aprotic medium. The product formed with the t-butoxide was found to contain a negligible (<3%) amount of nortricyclene; this was also established [7,8] for the product from the cyclohexylcyclohexyl oxide base.

The values of k_H/k_D at several different temperatures spanning a 50—70 °C range were determined with each base (Table 2). The activation parameters computed [5] in each case are identical: $[\Delta E]_D^H \simeq 0$ and $A_H/A_D = 3.43$. Reactions having a single rate-determining step involving non-linear hydrogen transfer transition states are characterized by a virtually temperature-independent isotope effect: $([\Delta E]_D^H \longrightarrow 0)$.[5] Moreover, in contrast to linear hydrogen transfer, which appears to have a frequency factor ratio (A_H/A_D) limit of 1.2 (established by model calculations of Schneider and Stern [9]), it has been shown [10] that the value of A_H/A_D for a bent TS‡ frequently exceeds this limit, because of the differing amplitudes of vibration of corresponding hydrogen and deuterium bonds in a bent TS‡. These generalizations,[10] which are of

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Table 1. Rate constants and activation parameters for the elimination reaction bicyclo[2.2.1]heptan-2-*exo*-yl toluene-*p*-sulphonate

Temp. (°C ± 0.05)	$10^3 k_2$/l mol^{-1} s^{-1} [a,b]	Activation parameters [c]
(A) Promoted by sodium 2-cyclohexylcyclohexyl oxide in triglyme		
50	1.9 ± 0.1	$10^{-1} \ln A = 2.6 \pm 0.1$
80	26.7 ± 0.9	$E_A = 20.5 \pm 0.7$ kcal mol^{-1}
		$\Delta G^‡ = 23.3 \pm 0.2$ kcal mol^{-1} [d]
110	280 ± 10	$\Delta S^‡ = -9.9 \pm 0.1$ cal K^{-1} mol^{-1} [d]
(B) Promoted by potassium t-butoxide in triglyme		
40	4.0 ± 0.2	
		$10^{-1} \ln A = 2.81 \pm 0.09$
60	32 ± 1	$E_A = 20.9 \pm 0.6$ kcal mol^{-1}
		$\Delta G^‡ = 21.9 \pm 0.1$ kcal mol^{-1} [e]
90	410 ± 10	$\Delta S^‡ = -5.0 \pm 0.1$ cal K^{-1} mol^{-1} [e]

[a] Computed from the second-order kinetic data (stoicheiometric amounts of reagents) by least-squares analysis of $1/c$ (c = unchanged starting material concentration) at time t; $1/c = 1/c_0 + k_2t$ (c_0 = initial concentration of reagents = 0.05 mol l^{-1}). [b] Good linear behaviour was observed for these second-order plots. The standard deviations of the rate constants represented small percent errors ($2.4 \leqslant$ error $\leqslant 5.3$) and the correlation coefficients were close to unity (*e.g.* 0.9989). [c] The standard deviations of the activation parameters signified small percent errors ($0.2 \leqslant$ error $\leqslant 3.9$) and the correlation coefficients were close to unity (0.9999). [d] At 80 °C. [e] At 60 °C.

Table 2. Primary kinetic isotope effects determined by intermolecular competition in the reactions of bicyclo[2.2.1]heptan-2-*exo*-yl toluene-*p*-sulphonate and its [3-*exo*-^{2}H] analogue

Temp. (°C ± 0.05)	Fraction of reaction completed	Corrected isotopic ratio, R_{af} [a,b]	Isotope [a] effect, k_H/k_D	Mean k_H/k_D	Mean k_H/k_D over temp. range
(A) With sodium 2-cyclohexylcyclohexyl oxide in triglyme					
50	0.6412	0.317 ± 0.001	3.45 ± 0.01	3.45 ±0.01	3.43 ±0.02
50	0.7033	0.372 ± 0.002	3.44 ± 0.01		
50	0.8029	0.543 ± 0.001	3.45 ± 0.01		
80	0.6003	0.288 ± 0.001	3.42 ± 0.01	3.42 ±0.02	
80	0.7014	0.369 ± 0.001	3.40 ± 0.01		
80	0.8008	0.535 ± 0.001	3.45 ± 0.01		
110	0.5556	0.594 ± 0.002	3.41 ± 0.02	3.42 ±0.01	
110	0.6011	0.660 ± 0.001	3.42 ± 0.01		
110	0.6993	0.885 ± 0.001	3.442 ± 0.009		
(B) With potassium t-butoxide in triglyme					
40	0.6004	0.447 ± 0.005	3.40 ± 0.005	3.42 ±0.04	3.43 ±0.04
40	0.7004	0.588 ± 0.009	3.44 ± 0.96		
40	0.8001	0.882 ± 0.02	3.43 ± 0.01		
60	0.6007	0.450 ± 0.001	3.448 ± 0.003	3.436 ±0.005	
60	0.7004	0.587 ± 0.001	3.436 ± 0.007		
60	0.8013	0.888 ± 0.001	3.425 ± 0.003		
90	0.6004	0.449 ± 0.008	3.43 ± 0.06	3.434 ±0.009	
90	0.7078	0.602 ± 0.008	3.427 ± 0.009		
90	0.8007	0.885 ± 0.002	3.436 ± 0.007		

[a] Analysis of the deuterium content of this mixture of bicycloheptan-2-*exo*-ols was carried out by the mass spectrometric procedures discussed in the Experimental section. Mass spectrum corrections and calculations of the isotope effect were computed by application of the following equations:

$1/(k_H/k_D) = \ln(R_{af}/R_{a0})/\ln[(1-f)(1+R_{a0})/(I+R_{af})] + 1$, where R_{a0} is the ratio (corrected) of deuterium to proton at $t = 0$ and R_{af} is the deuterium to proton ratio after f fraction of reaction is completed.[22]

$$\text{Isotope ratio} \left(\frac{M_D}{M_H}\right)_{\text{corr}} = \frac{M_{113} - M_{H+1}}{M_{112} - M_{D-1}} = \frac{\left(1 + \frac{M_{D-1}}{M_D}\right)\left(\frac{M_H}{M_{H+1}} - \frac{M_{112}}{M_{113}}\right)}{\left(1 + \frac{M_H}{M_{H+1}}\right)\left(\frac{M_{112}}{M_{113}} - \frac{M_{D-1}}{M_D}\right)} = R_{af}$$

[b] (A). For the kinetic runs at 50 and 80 °C, the corrected, initial, isotopic ratio, $R_{a0} = 0.138 \pm 0.001$; for the runs at 110 °C $R_{a0} = 0.288 \pm 0.001$. (B). For the kinetic runs at 40, 60, and 90 °C, the corrected, initial isotopic ratio $R_{a0} = 0.206 \pm 0.001$.

empirical origin, can be applied to elucidation of TS‡ geometry. Thus, the results in Table 2 point to a non-linear hydrogen transfer in a bent TS‡ and appear to rule out the linear model (1). However, if a degree of double bond development has occurred in the TS‡ and we are dealing with an *sp*^{2}, rather than an *sp*^{3} model (2), the most likely orbital arrangement in keeping with the requirement of a non-linear hydrogen transfer may be represented as (4).

It is interesting that the corresponding planar five-membered cyclic TS‡ of Hoffmann elimination, which occurs with *N*-bicyclo[2.2.1]heptan-2-*exo*-yltrimethylammonium hydroxide, shows a kinetic isotope effect greater than 1.2, *i.e.* k_H/k_D = 1.86.[11] Such a process, involving a hydroxide base ion-paired to the ammonium centre as the H^+ abstracting agent, can be said to have structure and dimensions quite similar to the amine oxide elimination, for which a temperature-independent k_H/k_D of 2.2 has established [12] a non-planar TS‡ with non-linear hydrogen transfer. In view of the non-linear hydrogen abstraction of the TS‡, one would expect the isotope effect to be temperature-independent over a significant temperature range. Because the Hofmann elimination in this bicyclic system is a unimolecular *syn*-elimination process in that the ammonium hydroxide ion pair is an intramolecular reagent, there is no problem here in achieving the planar five-membered cyclic arrangement. In the associated base-promoted *syn*-elimination in (3), however, steric repulsion by the trans-annular (bridge) methylene prevents a linear, bimolecular approach of the ion pair from occurring in a planar array resembling that illustrated in (1). The kinetic isotope effects determined for the reaction of sodium pentyloxide in pentan-1-ol with 2,3-dibromobicyclo[2.2.1]heptane (*trans* and *endo, cis*) have been measured by LeBel and his co-workers.[13] The values of k_H/k_D for the *syn*- and *anti*-eliminations are given as 3.6 ± 0.1 at 96.3 and 3.4 ± 0.1 at 126.7 °C, respectively. These results are interpreted as support for a concerted, bimolecular pathway with a considerable degree of carbanion character *versus* a two-step, *E*lcB, carbanion process. The present results demonstrate that the kinetic isotope effect is not very sensitive to substituent effects, and is determined largely by TS‡ geometry. It also suggests, as contended by Sicher [1] and Zavada *et al.*,[14] that the geometries of *syn*- and *anti*-elimination effected by strong, associated bases are quite similar.

The same elimination was carried out in the presence of 18-crown-6, which greatly increases dissociation in the base.[8a] In this case, with the reduced steric requirements of the dissociated base, a TS‡ of linear hydrogen transfer may be realized. The coaxial arrangement of the three reaction centres involved in the hydrogen transfer would give rise to a temperature-dependent isotope effect. In the absence of 18-crown-6, the associated alkoxide base induces a non-planar, six-membered TS‡ of non-linear hydrogen transfer, resembling that depicted in the Figure. Such a TS‡ should yield a temperature-independent isotope effect, as observed in our work.

Finally, we note that the considerably greater base strength of t-butoxide as compared with cyclohexylcyclohexyl oxide appears to have no effect on the magnitude of A_H/A_D. The identity of the isotope effect for the two bases suggests that base strength also is not a factor determining the geometry of this ion-pair base-promoted, *syn*-elimination, although it is a factor determining the ease of proton transfer, *i.e.*, the rate of *syn*-elimination.

Experimental

Reagents and solvents were of commercial grade and were usually purified before use.

[3-exo-$^2H_1$]*Bicyclo*[2.2.1]*heptan*-2-exo-*ol and Bicyclo*[2.2.1]-*heptan*-2-exo-*ol*.—These were synthesized *via* hydroboration of bicyclo[2.2.1]hept-2-ene according to directions given by Brown and his co-workers.[15,16] These authors have already shown that addition of diborane or [$^2H_6$]diborane is stereospecific, both bonds being formed in the *exo*-orientation without rearrangement.

Bicyclo[2.2.1]*heptan*-2-exo-*yl Toluene*-p-*sulphonate*.—This was synthesized using the pyridine method of esterification by the procedure previously described,[17,18] the product showed δ ($CDCl_3$) 7.60 (4 H, q, aromatic), 4.45 (1 H, d, *endo*-2-H), 2.50—2.10 (5 H, s and m, Me and CH at C-1 and C-4, respectively), and 1.7—0.85 (8 H, m, CH_2).

[3-exo-$^2H_1$]*Bicyclo*[2.2.1]*heptyl*-2-exo-*yl Toluene*-p-*sulphonate*.—The procedure for synthesis has been previously described;[17,18] δ ($CDCl_3$) 7.60 (4 H, q, aromatic), 4.45 (1 H, d, *endo*-2-H), 2.50—2.10 (5 H, s and m, CH_3 and CH at C-1 and C-4), and 1.70—0.90 (7 H, m, CH_2 and *endo*-3-H).

Kinetic Procedure.—A typical kinetic run (second-order kinetics) was performed as follows. The vessel containing the base solution was placed in a well stirred oil bath regulated by a Hallikainen Thermotrol with the actual control temperature measured by a National Bureau of Standards thermometer, constant to within ± 0.05 °C. Once the base solution had thermally equilibrated at the reaction temperature, a minimal volume of substrate solution was injected into the vessel; the reaction mixture was vigorously shaken, and the timer was started simultaneously. A solution of bicyclo[2.2.1]heptan-2-*exo*-yl toluene-*p*-sulphonate in triglyme was readily hydrolysed when a quenching procedure was employed. In a prior study it was reported[19] that this reagent is hydrolysed quickly in water–ethanol to bicyclo[2.2.1]heptan-2-*exo*-ol ($k = 4.33 \pm 0.05 \times 10^{-3}$ s^{-1} at 25.18 °C). This hydrolysis was utilized in a slightly revised quenching procedure. The sample was cooled to −78 °C and the base neutralised; then the residual starting material was quantitatively hydrolysed to bicyclo[2.2.1]-heptan-2-*exo*-ol by warming the water–triglyme mixture at 70 °C for 2 h. The substrate concentration per sample was determined by comparing the g.l.c. peak area with that of the internal standard (1,2,4-trichlorobenzene).

Bicyclo[2.2.1]heptan-2-*exo*-yl toluene-*p*-sulphonate underwent elimination and hydrolysis when subjected to the typical g.l.c. analysis and purification methods. Moreover, its mass spectrum exhibited a negligible parent peak due to extensive fragmentation upon electron impact. Thus, it was advantageous to follow the extent of reaction and subsequently to determine the kinetic isotope effect by monitoring the alcohol concentration and its isotopic composition. The kinetic isotope effects were measured by exactly the same procedure as described above using 1 : 1 mixture of bicyclo-[2.2.1]heptyl-2-*exo*-yl toluene-*p*-sulphonate and its [3-*exo*-^{2}H] analogue as the starting material. In addition the product isolated from a given run by g.l.c. was condensed in a chilled capillary in the line emerging from the thermal conductivity detector. The capillary was sealed to protect its contents from contact with air, and the product was later subjected to mass spectrometric analysis.[20]

Instrumental and Analytical Procedure.—Quantitative g.l.c. analyses were conducted on a F and M 5750 chromatograph connected to a Hewlett–Packard 3370 A electronic integrator. Standard conditions were as follows: column 3.05 m × 0.32 cm of 10% Carbowax 20 M—2% KOH on 80—100 Chromosorb W-AW; oven temperature 135 °C; injection port and detector temperature 200 °C.

Preparative g.l.c. was performed on an F and M dual column gas chromatograph. Standard conditions were as follows: column 3.05 m × 0.64 cm of 20% Carbowax 20 M 60—80 Chromosorb W-AW; oven temperature 160 °C.

Mass spectral determinations were made with a Hewlett–Packard 5930 A spectrometer equipped with a 5932 data system. The high-precision isotope ratio measurement procedure used was origiaally described by Kwart and Stanulonis[21] and recently reviewed by Kwart.[5] Typical conditions called for a 70 eV ionizing energy, a 25 mA ionizing current, an analyser-inlet pressure of 5×10^{-7} to 1×10^{-6} Torr, a source temperature of 150 °C, and a filter temperature of 100 °C. Samples were introduced by direct insertion probe. Under equilibrium conditions, the parent peaks of the labelled and unlabelled compounds were scanned 180 000 times per sample to yield a mean isotropic ratio, M_D/M_H, of high precision (% error $\leqslant 0.3$).

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References

1 J. Sicher, *Angew. Chem., Int. Ed. Engl.*, 1973, **11**, 200, and references cited therein.
2 (*a*) J. Zavada and J. Svoboda, *Tetrahedron Lett.*, 1972, **23**; (*b*) M. Svoboda, J. Hapala, and J. Zavada, *Tetrahedron*, 1972, 265; (*c*) J. Zavada, M. Svoboda, and M. Pankova, *Tetrahedron Lett.*, 1972, 711.
3 R. A. Bartsch, *Acc. Chem. Res.*, 1975, **8**, 239.
4 W. H. Saunders, Jr., *Chem. Scripta*, 1975, **8**, 27; 1976, **10**, 82.
5 H. Kwart, *Acc. Chem. Res.*, 1982, **15**, 401.
6 K. C. Brown and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, 1970, **92**, 4292.
7 H. C. Brown and K. T. Lui, *J. Am. Chem. Soc.*, 1974, **96**, 4346.
8 (*a*) R. A. Bartsch and R. H. Kayser, *J. Am. Chem. Soc.*, 1974, **96**, 4346; (*b*) H. Kwart, T. Takeshita, and J. L. Nyce, *ibid.*, 1964, **86**, 2606.
9 M. E. Schneider and M. J. Stern, *J. Am. Chem. Soc.*, 1972, **94**, 1517.
10 H. Kwart and M. Brechbiel, *J. Am. Chem. Soc.*, 1981, **103**, 4650.
11 J. L. Coke and M. P. Cooke, Jr., *J. Am. Chem. Soc.*, 1967, **89**, 6701.
12 (*a*) H. Kwart, T. J. George, R. Louw, and W. Uttee, *J. Am. Chem. Soc.*, 1978, **100**, 3927; (*b*) H. Kwart, D. A. Benko, and M. E. Bromberg, *ibid.*, p. 7093; (*c*) H. Kwart and T. J. George, *J. Org. Chem.*, 1979, **44**, 162; (*d*) H. Kwart, A. G. Horgan, and Y. T. Lin, *J. Am. Chem. Soc.*, 1981, **46**, 1970.

13 N. A. LeBel, P. D. Beirne, E. R. Karger, J. C. Powers, and P. M. Subramanian, *J. Am. Chem. Soc.*, 1963, **86**, 1964,
14 J. Zavada, M. Pankova, and M. Svoboda, *J. Chem. Soc., Chem. Commun.*, 1973, 168.
15 H. C. Brown and J. Zweifel, *J. Am. Chem. Soc.*, 1961, **83**, 2544.
16 H. C. Brown, ' Organic Synthesis *via* Boranes,' Wiley, New York, 1975.
17 S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, 1952, **74**, 1154.
18 H. Kwart and J. Takeshita, *J. Org. Chem.*, 1963, **28**, 670.
19 T. W. Bentley and C. T. Bowen, *J. Chem. Soc., Perkin Trans. 2*, 1978, **6**, 557.
20 H. Kwart and T. Blazer, *J. Org. Chem.*, 1970, **35**, 2726.
21 H. Kwart and J. J. Stanulonis, *J. Am. Chem. Soc.*, 1976, **98**, 4009.

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