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TEMPERATURE EFFECT ON THE STERIC COURSE OF THE ACID-CATALYSED SOLVOLYSIS OF ARYLOXIRANES. A RELATIONSHIP BETWEEN THE ENTHALPIC AND THE ENTROPIC CONTENTS OF THE TRANSITION STATES AND THE STEREOSELECTIVITY.

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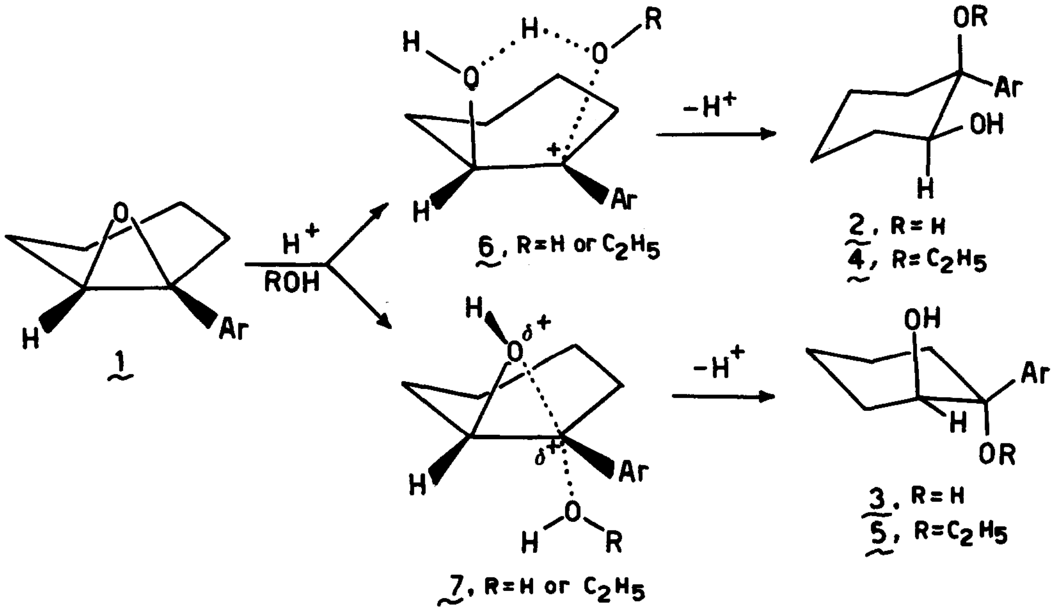
The stereoselectivity of the ring opening of aryloxyranes under acidic conditions is strongly dependent on the structure, configuration and conformation of the epoxides, the nature of the aryl group, the solvent, the acid catalyst, *etc.*[1-3] Recently[3] an application of the Hammett free energy relationship to the ratios of *cis* (**2**) to *trans* diols (**3**) formed in the acid-catalysed hydrolysis of 1-arylcyclohexene oxides (**1**) has clearly shown that the transition state leading to the *cis* product has a higher degree of carbocationic character than the one relative to the formation of the *trans* diol. According to these results it was suggested[3] that the transition state (T.S.) leading from the protonated epoxide to the *trans* adduct should be of a borderline A-1 type (**7**) in which the incomplete breaking of the epoxidic C-O bond causes the preferential attack of the nucleophile from the *anti* side. The *cis* adduct should be formed on the contrary from the collapse of a nucleophile-carbenium ion complex (**6**) in which the cation and the nucleophile are held together by hydrogen bonding; the complete rupture of the benzylic C-O bond appears to be prerequisite for a *syn* attack.[2,3]

In order to get further confirmation for these mechanistic hypothesis and to be able to assess the relative importance of entropic and enthalpic factors in determining the steric course of these reactions we used an approach similar to the one applied by us with the Hammett equation.[3] Term by term substraction of the logarithm of the rate constant expression obtained according to the transition state theory[4] relative to the formation of the *trans* adducts (**3** and **5**) from that one of the parallel reaction relative to the formation of the *cis* adducts (**2** and **4**) affords equation (1). In the present case the differences between the activation enthalpies and entropies can be taken as equal respectively to the differences between the enthalpic and entropic contents of the corresponding transition states and the ratios (k_C/k_T) can be equated to the concentration ratios ($[C]/[T]$) of the *cis* and *trans* adducts formed in the reaction[3,5], which can be easily determined by GLPC. Equation (2) is obtained, that allows to deduce the differences in the activation parameters from the ratio $[C]/[T]$.



a, (Ar= C_6H_5); b,(Ar = m-Cl-C_6H_5)

The stereoselectivity of the hydrolysis of epoxide 1a in aqueous H_2SO_4[6] changed markedly with the temperature and the ratios of cis to trans diols ([C]/[T]) fitted very satisfactorily equation (2) (see figure 1 and Table 1). Similarly good results were obtained in the acid-catalysed ethanolysis of the same epoxide (1a)[6] (the reaction was entirely regiospecific, giving only the hydroxy ethers 4 and 5) and in the hydrolysis of the m-chloro substituted epoxide 1b[6] (see Table 1). The data of Table 1 reveal positive differences of both the enthalpic and the entropic contents between the transition states 6[7] and 7 leading respectively to the syn and the anti adducts. While the entropic factor favors the formation of the syn adducts, the enthalpic one favours the anti products. Therefore the stereoselectivity of these reactions is linked to the prevalence of the one or the other factor in determining the difference of free energy between the two transition states ($F_C^{\ddagger}-F_T^{\ddagger}$). However

$$\ln \frac{k_C}{k_T} = -\frac{(\Delta F_C^{\ddagger}-\Delta F_T^{\ddagger})}{RT} = -\frac{(\Delta H_C^{\ddagger}-\Delta H_T^{\ddagger})}{RT} + \frac{(\Delta S_C^{\ddagger}-\Delta S_T^{\ddagger})}{R} \qquad (1)$$

$$2.3\,R \log \frac{[C]}{[T]} = -\frac{(F_C^{\ddagger}-F_T^{\ddagger})}{T} = -\frac{(H_C^{\ddagger}-H_T^{\ddagger})}{T} + (S_C^{\ddagger}-S_T^{\ddagger}) \qquad (2)$$

because the differences of entropies are practically constant, clearly the stereoselectivity changes observed in the different reactions are to be ascribed almost entirely to the enthalpic factors. All these results agree with the mechanism suggested and strengthen the structures previously hypothesized for the transition states **6** and **7**. As a matter of fact the three membered ring, still present in **7**, is expected to have a lower entropic content than the five-membered ring occuring in **6**, in which there are more degrees of freedom. On the other hand also the positive differences of enthalpy ($H^{\ddagger}_{C}-H^{\ddagger}_{T}$) are in agreement with the higher amount of breaking of the epoxidic C–O bond in **6** than in **7**. In accordance with this scheme, the increase of the enthalpy difference ($H^{\ddagger}_{C}-H^{\ddagger}_{T}$) when the solvent is changed from water to ethanol can be ascribed to the lower polarity and solvating power of the organic solvent; these effects should lead in the reaction carried out in the latter solvent to a more difficult breaking of the benzylic C–O bond, and therefore should increase the enthalpic contents of the transition state (**6**) in which such bond is completely broken. However it is also possible that the higher nucleophilic character of ethanol can at the same time lower the enthalpy of **7** and thus contribute to the increase in the enthalpy difference obtained in this solvent. Finally the increase of $H^{\ddagger}_{C}-H^{\ddagger}_{T}$ observed in the hydrolysis of **1** when the phenyl group is changed to *m*-chlorophenyl, must be attributed, in

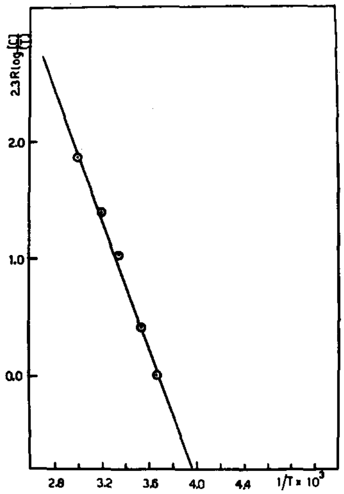


Figure 1. Plot of 2.3Rlog[C]/[T] *vs*. 1/T for the hydrolysis of **1a**

Table 1. Ratios of *cis* to *trans* adducts formed in the acid-catalysed solvolysis of epoxides of type **1** at different temperatures and differences of the activation parameters.

t(°C)	**2a** : **3a**$^{i)}$	**2b** : **3b**$^{ii)}$	**4a** : **5a**$^{iii)}$
−30	—	—	11.5 : 88.5
−20	—	—	15.4 : 84.6
−10	—	—	17.5 : 82.5
0	50.0 : 50.0	22.5 : 77.5	21.2 : 78.8
+10	55.1 : 44.9	28.2 : 71.8	26.1 : 73.9
+25	62.6 : 37.4	36.2 : 63.8	32.5 : 67.5
+40	66.9 : 33.1	41.8 : 58.2	40.3 : 59.7
+60	71.9 : 28.1	49.1 : 50.9	—
$H^{\ddagger}_{C}-H^{\ddagger}_{T}$(Kcal mol^{-1})	+ 2.85	+ 3.60	+ 3.47
$S^{\ddagger}_{C}-S^{\ddagger}_{T}$(cal K^{-1}mol^{-1})	+10.5	+10.8	+10.2
$F^{\ddagger}_{C}-F^{\ddagger}_{T}$(Kcal mol^{-1}, at 25°C)	− 0.28	+ 0.38	+ 0.43
$r^{iv)}$	0.9963	0.9951	0.9967

i) **1a** in water. ii) **1b** in water. iii) **1a** in ethanol. iv) correlation coefficient.

agreement with the previous results[3], to the lower capability of the m-chlorophenylsubstituent to delocalize the positive charge[8]. The effect of the electron-withdrawing substituent(m-Cl) makes the breaking of the C-O benzylic bond more difficult and therefore increases the enthalpic content of the more polar transition state (6).

In conclusion it may be stressed that the high tendency of aryloxiranes towards syn addition under acidic conditions[1-3] is mainly due to the favourable entropic content of the transition state leading to the syn adduct and to the relatively low enthalpic barrier to the breaking of the benzylic C-O bond. On the contrary, the high ionization enthalpy of the C-O bond that should be observed for purely aliphatic or cycloaliphatic oxiranes should be responsible for the practically complete anti stereoselectivity generally found for these compounds[1,9].

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Footnotes and References

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5. The ratio k_C/k_T can be made equal to [C]/[T] on admitting that the two parallel reactions follow the same kinetic equation, a very likely hypothesis in the case of solvolytic reactions.
6. The reactions were carried out in the following way: a suspension (water) or solution (ethanol) of 1 (50 mg) in 0.2N H_2SO_4 in the solvent (5ml) was stirred at the chosen temperature long enough to allow for complete reaction of 1, quenched with $NaHCO_3$ and thoroughly extracted with ether, and the products were analyzed by GLPC. The addition products (2-5) were completely stable under the reaction conditions and their overall yields were almost quantitative (> 97%). The only side products were 2-arylcyclohexanones, 1-arylcyclopentane-1-carbaldehydes and 2-arylcyclohex-2-en-1-ols.
7. Formula 6 can actually be considered as an intermediate, whose structure must be very near to that of the transition state leading to it; in order to simplify the discussion this transition state is referred to as 6 in the text.
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