Influence of Substituents in the 3-Position of Cyclohexene Oxides on the Rates of their Reactions with Hydrogen Chloride in Low Polarity Aprotic Solvents

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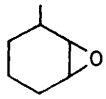
Rates of reactions of cyclohexene oxide and of its *cis*- and *trans*-3-methyl and 3-t-butyl derivatives with HCl were measured in toluene and CCl_4 by a calorimetric method. Although these rates are very sensitive to trace impurities, satisfactory second-order kinetics were obtained in the presence of small amounts of water or tetrahydrofuran. An equatorial substituent in the 3-position *trans* to the epoxide oxygen has a rate-retarding effect which is larger for t-butyl than for methyl. The qualitative agreement between the ratios of the rates of formation of the four *trans*-chlorohydrins from each *cis–trans* pair of the 3-alkylcyclohexene oxides and the molar ratios of the bromohydrins obtained in the reactions of the corresponding alkylcyclohexenes with NBS in DMSO–water supports the hypothesis that in the latter reaction the nucleophilic step, rather than the electrophilic one, is rate determining.

THE preference for electrophilic attack *syn* to 3-substituents in the additions of several reagents [*N*-bromoamides,[1-3] iodine azide,[4] mercury(II) acetate,[5] halogen–amine, and halogen–ether complexes,[6-8] *etc.*] to cyclohexene and dihydropyran derivatives has been interpreted[9] by assuming that these reactions involve a rapidly reversible electrophilic step, leading to a (probably) bridged intermediate, followed by a slow rate and product-determining nucleophilic step. Since this interpretation was based mainly on product distribution studies, it appeared desirable to complement the evidence with kinetic data that could demonstrate that nucleophilic attack on cyclohexene epihalogenonium ion or a similar species is slowed down by an equatorial substituent *trans* to the heteroatom in the 3-position. Because of the difficulty in working with epihalogenonium ions and since many data[8,9] indicate that the regioselectivity of nucleophilic attack on protonated epoxides is very similar to that of the analogous reactions on epihalogenonium ions, it appeared that a kinetic study of the reactions of substituted cyclohexene oxides with acids could provide a good model for obtaining relative rate data sufficiently valid for application to the nucleophilic step of additions to the corresponding olefins.

RESULTS

The *cis*- and *trans*-isomers of 3-methyl- and 3-t-butylcyclohexene oxide (1)—(4) were chosen as the substrates, since many data were already available on additions to the corresponding olefins.[9,10] The preparation of these epoxides has been described elsewhere.[10]

Several difficulties were encountered in this kinetic study and little help came from the literature since only very few papers deal with the kinetics of epoxide reactions in aprotic media. The use of spectrometric methods was prevented by the transparency of the substrates and products in the accessible u.v. region. The reactions with HCl were too fast for the use of titrimetric techniques; a recently reported method that was employed to follow the kinetics of the reaction of propene oxide with HCl[11] gave poor results in our hands and could not be applied to cyclohexene oxide, which reacts *ca.* 60 times faster. The use of weaker acids, such as chloroacetic, in order to slow down the rate, was ruled out when it was found that the reaction was complicated by the formation of substantial amounts of dimeric side-products.[12] The dilatometric method, often used in the study of epoxide reaction kinetics, could not be adopted because of the difficulty in preparing sufficient amounts of our diastereoisomeric substrates.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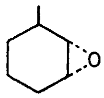
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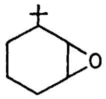
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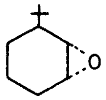
(4)

We therefore worked out a calorimetric method, based on a modification of a calorimeter described by one of us for the study of the hydration of pyridinecarbaldehydes.[13] The exothermicity of epoxide ring opening processes allows good results to be obtained for reactions conducted with 10^{-3}M solutions with half-lives of a few seconds.

Preliminary experiments on the reaction of propene oxide with HCl in toluene gave good second-order kinetics (Table

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[1] R. A. B. Bannard, A. A. Casselman, and L. R. Hawkins, *Canad. J. Chem.*, 1965, **43**, 2398.

[2] G. Bellucci, M. Ferretti, G. Ingrosso, F. Marioni, A. Marsili, and I. Morelli, *Tetrahedron Letters*, 1972, 3527.

[3] G. Berti, G. Catelani, M. Ferretti, and L. Monti, *Tetrahedron*, 1974, **30**, 4013.

[4] C. Freppel and J.-C. Richer, *Tetrahedron Letters*, 1972, 2321.

[5] D. J. Pasto and J. A. Gontarz, *J. Amer. Chem. Soc.*, 1971, **93**, 6909.

[6] P. L. Barili, G. Bellucci, F. Marioni, I. Morelli, and V. Scartoni, *J. Org. Chem.*, 1972, **37**, 4353.

[7] G. Bellucci, G. Ingrosso, F. Marioni, E. Mastrorilli, and I. Morelli, *J. Org. Chem.*, 1974, **39**, 2562.

[8] P. L. Barili, G. Bellucci, F. Marioni, and V. Scartoni, *J. Org. Chem.*, 1975, **40**, 3331.

[9] G. Bellucci, G. Berti, G. Ingrosso, and E. Mastrorilli, *Tetrahedron Letters*, 1973, 3911.

[10] G. Bellucci, G. Berti, M. Ferretti, G. Ingrosso, and E. Mastrorilli, *J. Org. Chem.*, 1978, **43**, 422.

[11] H. Kakiuchi and T. Iijima, *Bull. Chem. Soc. Japan*, 1973, **46**, 1568.

[12] P. L. Barili, G. Bellucci, G. Ingrosso, and A. Vatteroni, *Gazzetta*, 1977, **107**, 147.

[13] S. Cabani, G. Conti, and P. Gianni, *J. Chem. Soc. (A)*, 1969, 1363.

1) and a rate constant about double the reported value, obtained by the titrimetric method mentioned above. It was also observed that the rate depended very much on the presence of impurities; addition of small amounts of Cu^{II} salts increased the rate about three times, and the use of a copper stirrer *ca.* 80 times. A very strong catalytic effect by Cu^{II} salts on the hydrolysis of (2-pyridyl)oxiran has recently been reported.[14]

TABLE 1

Reaction of propene oxide with HCl in toluene at 20°

10^3[epoxide]/ M	10^3[HCl]/ M	k_{exp} [a]/ l mol^{-1} s^{-1}	r
11.55	63.42	0.074 ± 0.003 [b]	0.9990
12.64	60.85	0.072 ± 0.003	0.9988
9.75 [c]	65.68	0.21 ± 0.01	0.9997
13.14 [d]	67.30	0.26 ± 0.01	0.9996
1.23 [e]	6.88	5.70 ± 0.10	0.9999

[a] Errors are quoted as standard deviations estimated from the deviations of experimental points from the best-fit second-order straight line. [b] Lit.,[11] k_{exp} 0.038. [c] In the presence of CuO (20 mg). [d] In the presence of $CuCl_2$ (45 mg). [e] With a copper stirrer.

TABLE 2

Reaction of cyclohexene oxide with HCl in toluene at 20° [a]

10^3[epoxide]/ M	10^3[HCl]/ M	[HCl]: [epoxide]	k_{exp} [b]/ l mol^{-1} s^{-1}	r
1.16	2.44	2.1	5.7 ± 0.1	0.9998
1.30	3.93	3.0	5.8 ± 0.1	0.9995
1.17	3.91	3.3	3.4 ± 0.1	0.9994
1.86	6.34	3.4	3.0 ± 0.1	0.9995
2.03	7.65	3.8	4.8 ± 0.1	0.9993
4.77	20.38	4.3	5.4 ± 0.1	0.9998
1.91	8.33	4.4	3.3 ± 0.1	0.9999
4.77	21.85	4.6	3.7 ± 0.1	0.9999
		Average	4.4 ± 1.2 [c]	

[a] In the presence of added water (50 mg l^{-1}). [b] Errors are quoted as standard deviations estimated from the deviations of experimental points from the best-fit second-order straight line. [c] Standard deviations of k_{exp}.

A series of kinetic determinations was then carried out on the reaction of cyclohexene oxide with HCl in toluene. Rather poor results were obtained when carefully dried solvent was used. Single runs did not follow either second- or third-order kinetics. Furthermore, there was rather a wide variation in rate when different lots of solvent were used, probably because of traces of different catalytic impurities. The addition of small amounts of water improved the situation, since single runs gave a very satisfactory dependence on the second-order rate law, even if there was still a variation in the rate constants from one run to another (Table 2). It was found, however, that when the reaction was carried out with a sufficient excess of HCl, so that two consecutive additions of cyclohexene oxide could be made to the same solution in order to minimize variations due to solvent and adventitious impurities, similar values of the rate constants for the two additions were obtained. Since we were interested mostly in relative rates, we determined the rates for the substituted epoxides (1)—(4) immediately before or after those of a sample of cyclohexene oxide in the same solution. This method provided reproducible relative rates. Table 4 summarizes the results. The k_{exp} values in Table 4 are corrected by taking the ratio between the rate constants for the derivative and that for the run with cyclohexene oxide and multiplying by the average value of k_{exp} for cyclohexene oxide (4.4 l mol^{-1} s^{-1}).

The same reactions were examined more thoroughly in CCl_4, which was supposed to contain smaller amounts of trace metal impurities than toluene. Here again perfectly anhydrous solvents (checked by i.r.) did not give good second- or third-order kinetics. Results were better when small amounts of water were present. The presence of sulphur-containing impurities increased the rate considerably, particularly when the solvent was anhydrous. The best results were obtained when a little tetrahydrofuran (THF) (2×10^{-2}M) was added. Table 3 summarizes some of the results. Single runs on cyclohexene oxide gave a very satisfactory second-order rate dependence even if there was still some variation in rate constants from one run to another. In this case also we adopted the method of combining each rate measurement on a substituted epoxide

TABLE 3

Reactions of cyclohexene oxide with HCl in CCl_4 at 20°

10^3[epoxide]/ M	10^3[HCl]/ M	[HCl]: [epoxide]	k_{exp} [a]/ l mol^{-1} s^{-1}	r	Solvent
5.16	7.86	1.52	1.05 ± 0.03	0.9970	Anhydrous, <0.0005% CS_2
5.17	14.63	2.83	1.29 ± 0.02	0.9987	Anhydrous
5.89	21.03	3.57	3.44 ± 0.13	0.9949	Anhydrous (different lot of solvent)
5.80	9.81	1.69	2.60 ± 0.02	0.9995	3.6×10^{-3}M-H_2O
5.92	18.21	3.08	2.20 ± 0.03	0.9994	3.6×10^{-3}M-H_2O
5.18	12.68	2.45	6.25 ± 0.05	0.9998	H_2O and ~0.005% CS_2
			>10		Anhydrous, ~0.01% CS_2
7.50	7.50	1.00	3.50 ± 0.02	0.9990	Anhydrous, <0.0005% CS_2, 2×10^{-2}M-THF
5.50	9.48	1.72	4.14 ± 0.05	0.9995	
4.15	7.37	1.77	3.68 ± 0.02	0.9999	
3.69	8.16	2.21	4.31 ± 0.03	0.9999	
3.58	7.97	2.23	3.75 ± 0.02	0.9999	
3.75	8.62	2.30	3.45 ± 0.03	0.9998	
5.59	13.25	2.37	3.89 ± 0.02	0.9999	
3.42	8.51	2.49	3.48 ± 0.04	0.9997	
		Average	3.77 ± 0.32 [b]		
3.76	7.59	2.02	3.95 ± 0.02	0.9999	Anhydrous, <0.0005% CS_2, 4×10^{-2}M-THF
3.17	6.94	2.19	4.02 ± 0.03	0.9998	

[a] Errors are quoted as standard deviations estimated from the deviations of experimental points from the best-fit second-order straight line. [b] Standard deviation of k_{exp}.

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[14] R. P. Hanzlik and W. J. Michaely, *J.C.S. Chem. Comm.*, 1975, 113.

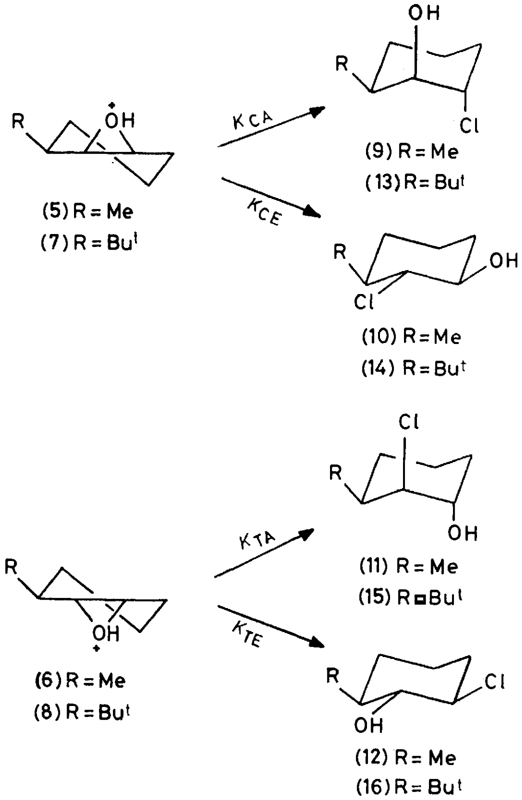
with one on cyclohexene oxide in the same solution and taking the average rate constant for cyclohexene oxide (3.77 l mol^{-1} s^{-1}) as reference. Table 4 summarizes the results. The rate of reaction of *trans*-3-t-butylcyclohexene oxide (4) with HCl was slow enough to be followed by a titrimetric method: the rate constant determined in this way was in fair agreement with that obtained by the calorimetric method. The effect of changing the concentration of THF was not examined in detail, but an increase from 2 to 4 × 10^{-2}M had practically no effect on the rate (Table 3). Lamaty and his co-workers [15] give for the reaction of cyclohexene oxide with HCl in pure THF at 0° a value of k_{exp} of 8 × 10^{-2} l mol^{-1} s^{-1}.

TABLE 4

Reaction rates of substituted cyclohexene oxides with HCl at 20° [a]

	In toluene [b]			In CCl_4 [c]		
Epoxide	k_{exp}	$k_{A(exp)}$	$k_{E(exp)}$	k_{exp}	$k_{A(exp)}$	$k_{E(exp)}$
(1)	5.20 ± 0.3	5.10 ± 0.3	0.10 ± 0.025	3.30 ± 0.25	3.17 ± 0.25	0.13 ± 0.02
(2)	2.20 ± 0.1	1.70 ± 0.1	0.50 ± 0.03	1.44 ± 0.01	0.92 ± 0.015	0.52 ± 0.015
(3)	1.00 ± 0.2	0.95 ± 0.2	0.05 ± 0.01	1.39 ± 0.05	1.29 ± 0.05	0.10 ± 0.01
(4)	0.076 ± 0.01	0.030 ± 0.005	0.046 ± 0.01	0.121 ± 0.01 [d]	0.050 ± 0.005	0.071 ± 0.005

[a] Each k_{exp}/l mol^{-1} s^{-1} is the average of at least three runs. Errors quoted for k_{exp} are maximum deviations from the average values. Errors quoted for $k_{A(exp)}$ and $k_{E(exp)}$ were obtained from those on k_{exp} and the maximum deviations from the averages of the product percentages (Table 5). [b] Containing 3 × 10^{-3}M-H_2O. [c] Containing 2 × 10^{-2}M-THF. [d] A titrimetric determination gave k_{exp} 0.10 [illegible] 0.02.



SCHEME 1

Analysis of the products from the kinetic runs described above showed that cyclohexene oxide gave exclusively *trans*-2-chlorocyclohexanol, the 3-methyl derivatives (1) and (2) and the 3-t-butyl derivatives (3) and (4) the corresponding *trans*-chlorohydrins as shown in Scheme 1 and Table 5.

DISCUSSION

The interpretation of the mechanism of acid catalysed ring opening reactions of epoxides is still open to discussion,[16] and data are particularly scarce for reactions conducted in aprotic solvents. Although our data do not yet allow precise mechanistic proposals (and this was not the main purpose of this work), they still give rise to some interesting points.

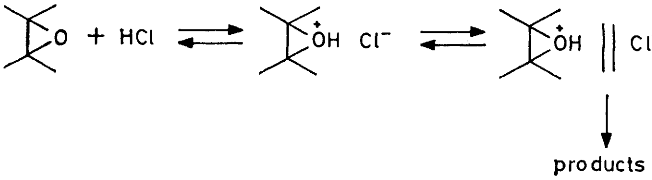
TABLE 5

Product compositions (%)

	In toluene [a]				In CCl_4 [b]			
Epoxide	(9)	(10)	(11)	(12)	(9)	(10)	(11)	(12)
(1)	98	2			96.2	3.8		
(2)			77.5	22.5			64	36
	(13)	(14)	(15)	(16)	(13)	(14)	(15)	(16)
(3)	95	5			92.5	7.5		
(4)			40	60			41	59

[a] Containing 3 × 10^{-3}M-H_2O. [b] Containing 2 × 10^{-2}M-THF.

A very recent hypothesis,[15] which tries to explain the apparently contradictory facts that in the reaction of several oxirans with HCl in THF, while the rate sequences go in the *A*1 sense, the product compositions are more consistent with an *A*2 mechanism and first-order dependence on HCl is observed, is that shown in part in Scheme 2 in which a tight oxonium–chloride ion pair is converted into a loose ion pair in the rate-determining step, in contrast with the usual assumption that the rate is determined during the step involving nucleophilic attack on the oxiran ring carbon.



SCHEME 2

Our results definitely confirm first-order dependence on HCl when there is some basic compound (water, THF)

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[15] G. Lamaty, R. Maloq, C. Selve, A. Sivade, and J. Wylde, *J.C.S. Perkin II*, 1975, 1119.

[16] R. A. Wohl, *Chimia*, 1974, **28**, 1 and references cited.

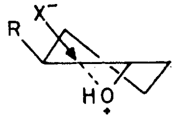
present in the solvent. They rule out, however, the possibility that, at least in our cases, the conversion of one ion pair into another is the rate-limiting step. If one considers the relative rates for the substituted cyclohexene oxides one sees that both in CCl_4 and in toluene the *cis*-3-methyl derivative (1) reacts with a rate close to that of the parent epoxide, but *ca.* 2.3 times faster than the *trans*-3-methyl derivative (2), while the ratio of the rate for the *cis*- (3) to that for the *trans*-3-t-butyl derivative (4) is >10. The decrease in rate constant in going from the *cis*- to the corresponding *trans*-derivative can in no way be justified by a mechanism involving the slow conversion of one ion pair into another, a process that should be very insensitive to steric effects by a 3-substituent. The observed trends, on the other hand, are in good agreement with a mechanism in which rate and product determination occurs during nucleophilic attack on the oxiran carbon, which can well be slowed down by a *trans*-equatorial substituent on the carbon α to the oxiran ring. We had expressed some time ago[9] the hypothesis that the direction of approach of the nucleophile is important in determining the course of epoxide ring opening and that this approach takes place in an oblique rather than in a perpendicular direction, that is collinearly with the breaking C–O bond as shown in (17).

TABLE 6

Ratios of rate constants

		Methyl derivatives	t-Butyl derivatives
$k_{CA} : k_{CE} : k_{TA} : k_{TE}$	In toluene	1 : 0.02 : 0.33 : 0.10	1 : 0.05 : 0.03 : 0.05
	In CCl_4	1 : 0.04 : 0.29 : 0.16	1 : 0.08 : 0.04 : 0.05
$k_{CA'} : k_{CE'} : k_{TA'} : k_{TE'}$ [a]		1 : 0.06 : 0.14 : 0.09	1 : 0.05 : 0.04 : 0.19

[a] Deduced from the ratios of products of the reactions of the olefins with NBS in aqueous DMSO; see refs. 9 and 10.



(17)

Our hypothesis was later confirmed by experimental results on the cyclization of epoxycarbanions[17,18] and recently rationalized by Baldwin.[19] An equatorial substituent R can interfere severely with the 'oblique' approach and thus decrease the rate of attack on the *trans*-epoxides. Diequatorial opening involving twist conformations or those with an axial alkyl group, normally unfavourable alternatives, can thus become competitive, resulting in an overall decrease in rate, as observed in the *trans*-3-methyl (2) and even more in the *trans*-3-t-butyl derivative (4).

The observed first-order dependence of the rate on HCl, on the other hand, implies that a second molecule of this reagent is not involved in the transition state of the rate-determining step and this leaves as an explanation of the experimental results the assumption that the nucleophilic attack by Cl^- takes place by an internal rearrangement of the epoxide–HCl intermediate (ion-pair?).

The situation is complicated by the fact that the measured rate constants (k_{exp}) are not the real k_2 but rather the product of k_2 by one or more of the equilibrium constants for the epoxide–HCl complex. If we simplify the problem, as usually done, by considering for cyclohexene oxide only one equilibrium constant in accordance with reaction (1) and assume that the concentration of the

$$E + HCl \overset{K}{\rightleftharpoons} E{\cdot}HCl \xrightarrow{k_2} \text{product} \qquad (1)$$

intermediate E·HCl is low and further that its formation and reversion to substrate are very fast by comparison with its conversion into products, the rate expression is given by (2). In the case of substituted cyclohexene

$$-dE/dt = k_2K[E][HCl] = k_{exp}[E][HCl] \qquad (2)$$

oxides (1)—(4) each k_2 is the sum of two constants referring to the diaxial (subscript A) and diequatorial (subscript E) opening reactions, respectively. Table 4 gives the values of $k_{A(exp)}$ and $k_{E(exp)}$ for each reaction, as deduced from the overall reaction rate and from the ratio of diaxial to diequatorial adducts in the products. While it would be difficult to measure the values of K, one would not expect them to be very different for the different cyclohexene oxides we have investigated, since electrophilic attack on oxygen should not be affected by inductive or steric effects of an equatorial substituent in the 3-position. A rough evaluation of the effect of these substituents on complexation with the oxiran oxygen was made by measuring the variation in chemical shift of the $CHCl_3$ proton on addition of an equimolar amount of the epoxide in CCl_4. Whereas this variation was exactly the same for cyclohexene oxide and its *trans*-3-t-butyl derivative, it was a little smaller for the *cis*-3-t-butyl epoxide, indicating a certain degree of hindrance to complexation only when the bulky substitient is *cis* to oxygen. We can therefore safely assume that the equilibrium constant for the *cis*-isomers (K_C) cannot be higher than that for the *trans*-epoxides (K_T) and that the higher values of k_{exp} found for the former must reflect higher values for k_C with respect to the corresponding k_T ones; in the case of the t-butyl epoxides the ratio k_C/k_T may even be larger than that of $k_{exp(cis)}/k_{exp(trans)}$, if $K_C/K_T < 1$, as could be inferred from the data on epoxide–$CHCl_3$ complexation.

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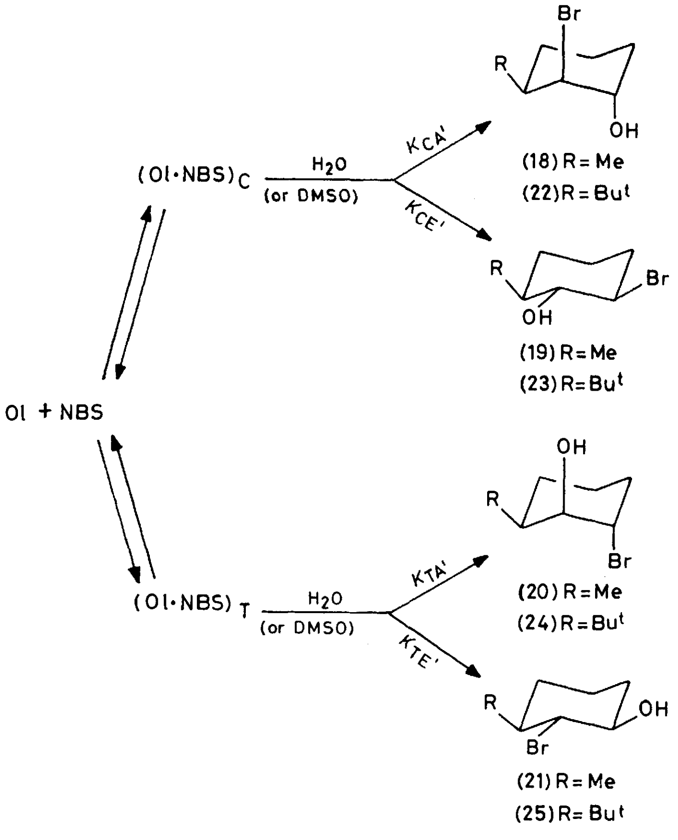
[17] G. Stork and J. F. Cohen, *J. Amer. Chem. Soc.*, 1974, **96**, 5270.

[18] J. H. Babler and A. J. Tortorello, *J. Org. Chem.*, 1976, **41**, 885.

[19] E. Baldwin, *J.C.S. Chem. Comm.*, 1976, 738.

The reason for the improvement in the second-order kinetics produced by the presence of small amounts of basic compounds (water, THF) and of the increase in rate caused by traces of metal ions or other impurities cannot be adequately explained on the basis of the available data. One may only assume that in low polarity solvents the breaking of the strong H–Cl bond requires some assistance which under high purity anhydrous conditions can be provided at the start only by a second HCl molecule, thus making the overall kinetics of third order. The fact that the reaction carried out in the drier and purer solvent actually did not follow either second- or third-order kinetics can be ascribed to the difficulty in rigorously excluding water or other impurities under our reaction conditions, and to the possibility that the product chlorohydrin itself may provide some nucleophilic assistance once it is formed.

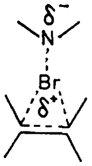
Products distributions (Table 5) are in accordance with our assumptions. They show a high preference for diaxial opening in the *cis*-epoxides (1) and (3), whereas the *trans*-derivatives (2) and (4) give more diequatorial products, particularly for the t-butyl derivative, in agreement with the assumed shielding of nucleophilic attack by the substituent.



SCHEME 3

We come now to our initial goal, that is to use the kinetic results on epoxides as a test for the mechanism of electrophilic additions of *N*-halogenoamides and similar reagents, and take the reactions of NBS in aqueous DMSO with the corresponding cyclohexenes, for which accurate data are available, as an example. Scheme 3 outlines the proposed mechanism. If the *cis*- and *trans*-intermediates (Ol·NBS) are in a rapid equilibrium with the olefins (Ol), and these intermediates are attacked by the nucleophile (H_2O or DMSO [20]) with rates that are much slower than those for the reversal of complex to reagents, the ratios of the bromohydrins (18)—(21) or (22)—(25) in the product should be equal to the ratios of the rate constants, $k_{CA'}$, $k_{CE'}$, $k_{TA'}$, and $k_{TE'}$.

On the other hand if the intermediates (Ol·NBS), which we believe may be roughly represented by (26),



(26)

can formally be assimilated to the protonated epoxides [(5), (6) or (7), (8) in Scheme 1] in their behaviour towards nucleophiles, steric effects during the nucleophilic attack should be similar in both systems, so that the ratios $k_{CA'} : k_{CE'} : k_{TA'} : k_{TE'}$ should not be too different from those, $k_{CA} : k_{CE} : k_{TA} : k_{TE}$, for the conversion of the epoxides into chlorohydrins. If we finally assume that the equilibrium constants K are similar (see above) and therefore that the latter ratio can be equated to that of the corresponding k_{exp} values, we obtain the comparative data shown in Table 6.

If one considers the many simplifying assumptions and the large difference in reaction media and reactants, the fact that the kinetic data obtained with the epoxides are in qualitative, even if in only fair quantitative, agreement with the product composition data for the olefin–NBS reactions provides further support for the hypothesis that these, and probably also the other addition reactions mentioned at the beginning of this paper, do not follow the normal Ad_E2 mechanism, but rather one in which rate and product composition are determined by steric effects operating in the nucleophilic step.

EXPERIMENTAL

Materials.—Commercial propene and cyclohexene oxides were purified by fractionation. The preparation and identification of epoxides (1)—(4) and of chlorohydrins (9)—(16) have been described elsewhere.[10] Toluene (Hoechst; Puranal) was refluxed over P_2O_5, distilled, refluxed over sodium, and fractionally distilled under nitrogen. Carbon tetrachloride (Hoechst; $<0.0005\%$ CS_2, except when stated differently) was refluxed over P_2O_5, fractionally distilled under nitrogen, and stored over molecular sieves. Tetrahydrofuran was distilled over $LiAlH_4$. Hydrogen chloride was dried by bubbling through concentrated H_2SO_4.

Kinetic Method.—The kinetic measurements were carried out using a Submarine calorimeter of a type already described,[13] and kept at 20 ± 0.01°. In this case, however, in

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[20] D. R. Dalton, V. P. Dutta, and D. G. Jones, *J. Amer. Chem. Soc*, 1968, **90**. 5498.

order to avoid catalytic effects due to metallic surfaces, all parts were made of glass and Teflon. A dry HCl solution (280 ml), prepared just before the experiment, was introduced into the calorimetric vessel through a calibrated glass bulb at 20° under pressure of dry nitrogen. The HCl concentration was determined on samples directly withdrawn from the calorimeter by titration with $0.01\text{M-Hg(ClO}_4)_2$ in the presence of diphenylcarbazone.[21] At the end of each experiment the residual HCl was checked and found to correspond to the difference between the initial acid and epoxide concentrations. The mixing system consisted of a glass tube containing a specially shaped Teflon hollow piston holding the liquid epoxide, immersed in the calorimetric solution. Reactions were started by rapidly pushing down a rod so causing the piston to bring the epoxide in contact with the stirred HCl solution. Separate experiments showed that the mixing time was negligible. The temperature variations due to the reaction were recorded by a thermistor (2 000 Ω at 20°) connected to a Wheatstone bridge and an electronic amplifier and were registered as a function of time with a Philips PM 8000 recorder.

The data were analysed as follows: heights h_t measured on the recorded calorimetric curve at different times t, and assumed to be proportional to the temperature increments, were corrected for the non-adiabatic nature of the calorimeter as well as for other effects extraneous to the reaction (stirring, vaporization heat) through equation (3) where

$$h_t^{\mathrm{corr}} = h_t - \chi h_c(t - t_0) + \chi \int_{t_0}^{t} h\,\mathrm{d}_t t \qquad (3)$$

h_t^{corr} are the corrected values of the observed h_t, χ is the constant of the Newton cooling law and h_c the convergence value of h_t. The values of χ and h_c were calculated by solving system (4), $(\mathrm{d}h_t/\mathrm{d}t)_{t_i}$ and $(\mathrm{d}h_t/\mathrm{d}t)_{t_f}$ being the slopes of

$$\begin{aligned}(\mathrm{d}h_t/\mathrm{d}t)_{t_i} &= \chi(h_c - h_{t_i})\\ (\mathrm{d}h_t/\mathrm{d}t)_{t_f} &= \chi(h_c - h_{t_f}) \qquad (4)\end{aligned}$$

the calorimetric curve for the linear parts before and after the reaction respectively, h_{t_i} the value of h_t just before mixing, and h_{t_f} the h_t value chosen beyond a time t_f at which the reaction could be considered complete.

The formal kinetic constants were obtained using equation (5) where c°_{HCl} and c°_{Ep} are the initial concentrations of the reagents and h_∞^{corr} the constant value h_t^{corr} obtained at the end of the reaction. All calculations and the best fit of equation (5) were carried out with a HP 2114 computer using the BASIC program.

$$\frac{1}{c^\circ_{\mathrm{HCl}} - c^\circ_{\mathrm{Ep}}} \ln \frac{h_\infty^{\mathrm{corr}} c^\circ_{\mathrm{HCl}} - h_t^{\mathrm{corr}} c^\circ_{\mathrm{Ep}}}{c^\circ_{\mathrm{Ep}}(h_\infty^{\mathrm{corr}} - h_t^{\mathrm{corr}})} = kt + \text{const.} \qquad (5)$$

Determination of the reaction rate of epoxide (4) with HCl in CCl_4 in the presence of 0.02M-THF at 20° was also made by a titrimetric method: samples (2—4 ml) were withdrawn at intervals from the calorimetric vessel, quenched in a 2.5 : 1 ethanol–water mixture (35 ml) at −10° and titrated with $0.01\text{M-Hg(ClO}_4)_2$. The second-order rate constant so obtained is reported in Table 4.

Product Analysis.—At the end of each kinetic run, the calorimetric solution was stirred with solid $CaCO_3$, filtered, and subjected to g.l.c. on a Fractovap 2300 gas chromatograph fitted with a 1.5 m glass column, 2.5 mm i.d., packed with 10% Carbowax 20 M on silanized Chromosorb W (80—100 mesh) under the following conditions: low isotherm 100° (3 min), high isotherm 170°, temperature increment 3° min^{-1}, evaporator and detector 175°, nitrogen flow 30 ml min^{-1}. The relative retention times of the pairs (9), (10); (11), (12); (13), (14); and (15), (16) were respectively 1.51 : 1, 1.73 : 1, 1.22 : 1, and 1.76 : 1. The product compositions reported in Table 5 are averages of at least three runs. Maximum deviations from the values quoted were estimated to be $\leqslant 0.5\%$ for percentages < 10 and $\leqslant 1\%$ for percentages > 10.

Complexation of Epoxides with $CHCl_3$.—The ^{1}H n.m.r. spectrum of a 2M solution of $CHCl_3$ in CCl_4 was compared with that of a solution that was 2M both in $CHCl_3$ and cyclohexene oxide. A downfield shift of 12.4 Hz was observed for the $CHCl_3$ proton in the latter solution. A similar comparison involving *trans*-3-t-butylcyclohexene oxide (4) also gave a downfield shift of 12.4 Hz, whereas with the *cis*-isomer (3) the shift was 9.9 Hz.

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[21] W. Schöniger, *Mikrochimica Acta*, 1955, 123; 1956, 869.