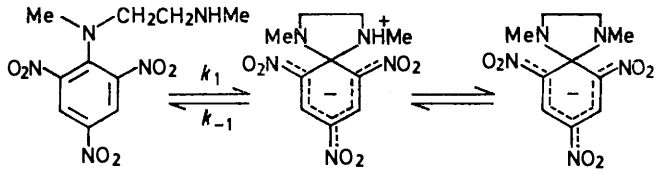
The Stabilities of Meisenheimer Complexes. Part IX.[1] The General Acid Catalysed Ring Opening of Spiro-complexes

By **Michael R. Crampton,*** and **Michael J. Willison,** Chemistry Department, The University, Durham

The ring opening of two spiro-Meisenheimer complexes to give respectively 1-(2-hydroxyethoxy)-2,4,6-trinitrobenzene and 1-(2-hydroxyethoxy)-2,4-dinitronaphthalene is found to be subject to general acid catalysis in water. The α value of the Brønsted equation is 0·5. The isotope effect of the hydronium ion catalysed reaction $k_{D_3O^+}/k_{H_3O^+} = 1{\cdot}5$. A mechanism is proposed involving concerted oxygen protonation and C–O bond breaking. The uncatalysed reaction is shown to proceed by a unimolecular mechanism rather than a bimolecular reaction with water. The results are compared with those for non-cyclic analogues.

SEVERAL studies have been reported of the formation of spiro-Meisenheimer complexes.[1-4] These are of particular interest since they have been used [3,4] as models



(I) (II) (III)

for the intermediates in aromatic nucleophilic substitution reactions. Recently Bernasconi and Gehriger in a kinetic study [4] of the formation of the complex (III) found the reaction to be subject to general base catalysis. This is a consequence of the unexpectedly high value for the rate constant k_{-1} for reversion of the zwitterionic intermediate (II) to parent (I) so that in the overall reaction the deprotonation of (II) may be rate limiting. This led to the suggestion that in some cases general base catalysis in nucleophilic aromatic substitution reactions may result from slow proton transfer rather than slow leaving group departure. While not disputing

[1] Part VIII, M. R. Crampton and M. J. Willison, preceding paper.

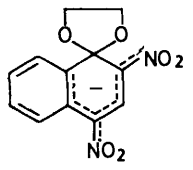
[2] M. R. Crampton, *J.C.S. Perkin II*, 1973, 2157; references to earlier structural studies of spiro-complexes are in this paper.

[3] C. F. Bernasconi and R. H. de Rossi, *J. Org. Chem.*, 1973, **38**, 500; C. F. Bernasconi, R. H. de Rossi, and C. L. Gehriger, *ibid.*, p. 2838; C. F. Bernasconi and H. S. Cross, *ibid.*, 1974, **39**, 1054; S. Sekiguchi and T. Shiojima, *Bull. Chem. Soc. Japan*, 1973, **46**, 693.

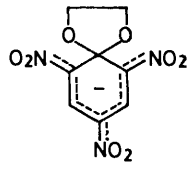
[4] C. F. Bernasconi and C. L. Gehriger, *J. Amer. Chem. Soc.*, 1974, **96**, 1092.

this latter inference we suggest that spiro-complexes may be subject to special factors not present in non-cyclic analogues.

In previous work [1,2] we have compared equilibrium and kinetic data for the spiro-complexes (IV) and (V) with those for similarly activated 1,1-dimethoxy-complexes. Our results indicated important differences



(IV)



(V)

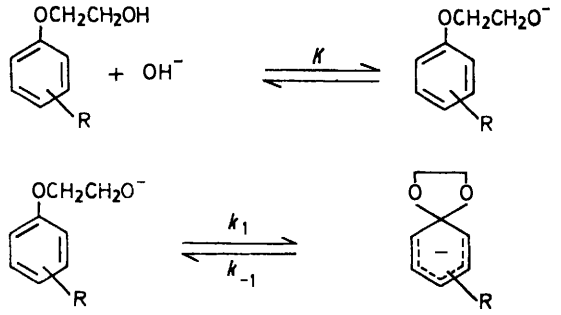
between these two types of complex. In particular the values for the rate constants for ring opening of the spiro-complexes are orders of magnitude higher than those for their non-cyclic analogues. This may indicate the presence of steric interactions in the dioxolan ring of the spiro-complexes.[5] A probable consequence of this ease of ring opening of the spiro-complexes is the observation discussed in the present work of general acid catalysis in their reversal to parent glycol ether.

EXPERIMENTAL

1-(2-Hydroxyethoxy)-2,4-dinitronaphthalene and 1-(2-hydroxyethoxy)-2,4,6-trinitrobenzene were prepared as before.[1] Kinetic measurements were made with a 'Canterbury' stopped-flow spectrophotometer described previously.[2]

RESULTS

Kinetic data have previously been reported for the formation of complexes (IV) and (V) in aqueous alkaline buffers.[1] The proposed mechanism involved formation of glycolate anion from glycol and hydroxide ions in a fast equilibrium followed by ring closure to give the spiro-complex (Scheme 1). The first order rate constant for



SCHEME 1

spiro-complex formation is given by equation (1). No buffer catalysis was observed in phosphate, borax, or phenol buffers.

$$k_{obs} = k_{-1} + k_1K[OH^-]/(1 + K[OH^-]) \quad (1)$$

In the present work the rates of ring opening of the spiro-complexes (IV) and (V) to give the parent glycol ethers were measured in acidic buffers and in dilute hydrochloric acid solutions. Measurements were made by stopped-flow spectrophotometry in the visible region of the absorption spectrum where the spiro-complexes, but not the glycol ethers, absorb. Experimental data were obtained by mixing solutions of spiro-complex (*ca.* 10^{-5}M) in very dilute aqueous sodium hydroxide (*ca.* 10^{-4}M) with appropriate buffer solutions. The acidities of the mixed solutions were measured with a pH meter. The fading of colour was in all cases an accurately first-order process. Rate constants are accurate to ±5%. In these acidic solutions it was found that the observed rate constant, k_{obs} can be expressed by equation (2) as a pH independent term k_{-1} together with terms due to catalysis by proton and undissociated acids.

$$k_{obs} = k_{-1} + k_{H^+}a_{H^+} + \Sigma k_{HA}[HA] \quad (2)$$

The results in Table 1 show that in acetic acid–sodium acetate buffers the observed rate constant depends linearly on the concentration of undissociated acid but is unaffected by acetate ions. Catalytic coefficients for acidic species were calculated and are given in Table 1. The value

TABLE 1

Kinetic data for the ring opening of complex (IV) in acidic buffers and in hydrochloric acid in water at 25°

Acid	$[HA]_{Stoich}$/M	$[Na^+A^-]_{Stoich}$/M	pH	k_{obs}/s^{-1}	k_{calc} [a]/s^{-1}
Acetic	0·026	0·026	4·65	3·4	3·4
	0·105	0·105	4·7	5·3	5·3
	0·26	0·26	4·7	8·8	9·2
	0·026 [b]	0·026 [b]	4·4	3·2	3·6
	0·105 [b]	0·015 [b]	4·45	5·1	5·5
	0·26 [b]	0·26 [b]	4·65	8·8	9·2
	0·026	0·013	4·3	3·8	3·8
	0·105	0·052	4·45	5·6	5·5
	0·26	0·13	4·45	9·6	9·4
	0·052	0·105	4·9	3·7	3·8
Formic	0·026	0·026	3·6	7·6	8·3
	0·104	0·104	3·6	12·9	13·0
	0·26	0·26	3·55	23·1	22·8
Chloroacetic	0·025	0·025	2·9	38	34
	0·10	0·10	2·9	54	56
	0·25	0·25	2·9	100	100
Hydrochloric	0·01			187	182
	0·018			300	320

[a] Calculated from equation (2) with k_{-1} 2·3 s^{-1}, and with the following values for the catalytic coefficients for acidic species: proton (1·8 ± 0·3) × 10^4 l mol^{-1} s^{-1}; acetic, 25 l mol^{-1} s^{-1}; formic, 60 l mol^{-1} s^{-1}; chloroacetic, 300 l mol^{-1} s^{-1}. [b] Ionic strength *I* 0·3M, with sodium chloride.

TABLE 2

Solvent isotope effect on the uncatalysed ring opening of (IV)

Solvent	pH	Conditions	k_{obs}/s^{-1}
H_2O	6·2	*a*	2·4 ± 0·1
	7·1	*a*	2·3
	7·1	*b*	2·2
	8·0	*a*	2·4
	pD [c]		
D_2O	7·5	*a*	1·7 ± 0·1
	7·6	*a*	1·75

[a] Phosphate buffer, 0·05M. [b] Phosphate buffer, 0·025M. [c] pD = pH + 0·4 (P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, 1960, **64**, 188).

2·3 s^{-1} required for the uncatalysed ring opening is in precise agreement with that obtained for k_{-1} from previous measurements [1] in alkaline media.

[5] J. F. Bunnett, quoted in ref. 4.

In the case of complex (IV) the value of k_{-1}, the rate constant corresponding to uncatalysed ring opening was

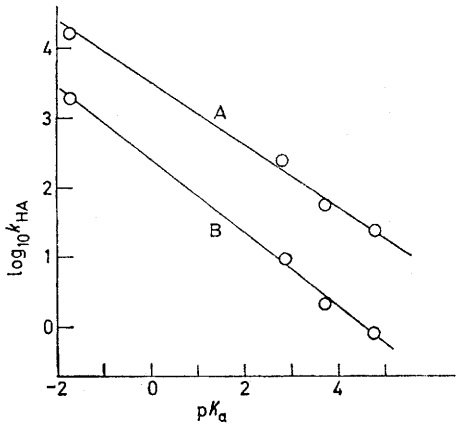
TABLE 3

Kinetic data for the acid catalysed ring-opening of complex (V) in buffers and in hydrochloric acid in water at 25°

Acid	$[HA]_{stoich}$/ M	$[Na^+A^-]_{stoich}$/ M	pH	k_{obs}/ s^{-1}	k_{calc} [a]/ s^{-1}
Acetic	0·025	0·025	4·65	0·16	0·16
	0·10	0·10	4·7	0·22	0·23
	0·25	0·25	4·7	0·35	0·36
	0·25	0·125	4·4	0·41	0·41
	0·125	0·25	5·0	0·21	0·22
Formic	0·026	0·026	3·65	0·61	0·63
	0·104	0·104	3·6	0·85	0·87
	0·26	0·26	3·6	1·25	1·25
Chloro-acetic	0·025	0·025	2·9	3·6	3·3
	0·10	0·10	2·85	4·7	4·4
	0·25	0·25	2·9	5·9	6·0
Hydro-chloric	0·0093			20·8	20·5
	0·0186			39·3	40
	0·030			60	60
DCl in D_2O	0·0093			31·7	31
	0·0186			60·5	61

[a] Calculated using equation (2) with k_{-1} 0·095 s^{-1} and with the following values for the catalytic coefficients for acidic species: acetic, 0·9 l mol^{-1} s^{-1}; formic, 2·3 l mol^{-1} s^{-1}; chloroacetic, 12 l mol^{-1} s^{-1}; H_3O^+, 2·2 × 10^3 l mol^{-1} s^{-1}; D_3O^+, 3·3 × 10^3 l mol^{-1} s^{-1}.

also determined in deuterium oxide. Measurements in media where $6 < pH < 8$ give the value of k_{-1} directly since terms due to catalysis by hydroxide ions, protons, or buffer are negligible. The data in Table 2 give a value for the solvent isotope effect $k_{-1}(H_2O)/k_{-1}(D_2O)$ of 1·3.



Brønsted plots for acid catalysed ring opening of A, complex (IV); B, complex (V)

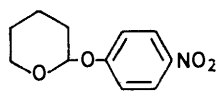
The results for the acid catalysed ring opening of (V) are in Table 3. Again the results indicate catalysis by protons and undissociated acid in addition to a spontaneous process. The calculated values of catalytic coefficients are collected at the foot of Table 3. Comparison of the rates of reaction in the presence of HCl in water and DCl in deuterium oxide gives a value for the isotope effect $k_{D_3O^+}/k_{H_3O^+}$ of 1·5.

[6] E. H. Cordes, *Progr. Phys. Org. Chem.*, 1967, **4**, 1.
[7] T. H. Fife, *Accounts Chem. Res.*, 1972, **5**, 264.
[8] E. Anderson and B. Capon, *J. Chem. Soc.* (*B*), 1969, 1033.
[9] R. F. Atkinson and T. C. Bruice, *J. Amer. Chem. Soc.*, 1974, **96**, 819.

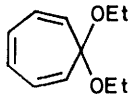
Brønsted plots of $\log_{10}k_{HA}$ *versus* the pK_a values for the catalysing acids are shown in the Figure. The slopes of these lines give values for the Brønsted coefficient α of 0·5 ± 0·1. From these graphs we may estimate the catalytic effects to be expected from weaker acids such as the dihydrogen phosphate ion. These estimates confirm that under the experimental conditions used in the present or previous [1] work no catalytic effects would be observable due to phosphate or borax buffers.

DISCUSSION

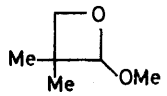
The spiro-complexes (IV) and (V) are structurally related to acetals. These normally react with acid by an *A*1 mechanism involving pre-equilibrium protonation followed by rate-limiting breakdown of the protonated substrate.[6] General acid catalysis has only been observed [7-9] when C–O bond breaking is facilitated by a good leaving group, *e.g.* (VI), or by formation of an especially stable oxocarbonium ion as in (VII), or by ring strain as in (VIII). It should be noted that the



(VI)



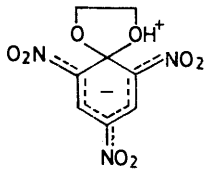
(VII)



(VIII)

spiro-complexes (IV) and (V) differ from normal acetals in that they are negatively charged so that reaction with acid involves charge neutralisation rather than charge formation.

Our results show that the ring opening of the complexes (IV) and (V) to give the parent glycol ethers is subject to general acid catalysis. This in itself excludes an *A*1 mechanism. In addition the value of 1·5 observed for the isotope effect $k_{D_3O^+}/k_{H_3O^+}$ for complex (V) is too low for reaction by the *A*1 mechanism where values [6] are usually >2·7. General catalysis indicates that proton transfer is involved in the rate-determining step. One mechanistic possibility is that slow proton transfer to give (IX) is followed by fast C–O bond breaking.



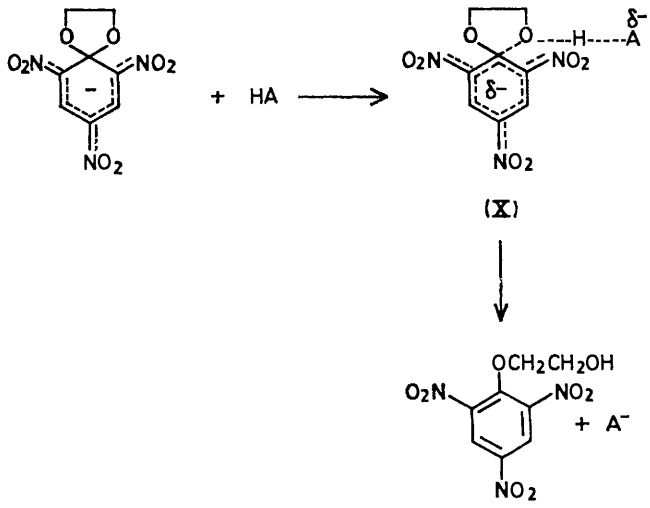
(IX)

This is the mechanism shown to be operative in the case of complex (III). However the acidity of (IX) is likely to be many orders of magnitude higher than that of the corresponding acid (II) (pK_a 6·64).[4] Thus protonated ethers and alcohols typically [10] have pK_a values of −3 to −4. It might be argued that the acidity of (IX) will be decreased relative to a normal protonated ether because of its zwitterionic nature. Nevertheless evidence [11,12] suggests that the $C_6H_2(NO_2)_3^-$ entity is

[10] E. M. Arnett, *Progr. Phys. Org. Chem.*, 1963, **1**, 223.
[11] M. R. Crampton, *J. Chem. Soc.* (*B*), 1971, 2112.
[12] E. Buncel and J. G. K. Webb, *Canad. J. Chem.*, 1974, **52**, 630.

electron demanding relative to hydrogen. We conclude that (IX) would be very much more acidic than the catalysing acids. However our results indicating values of 0·5 for the Brønsted coefficient α imply that the proton is about half-way between catalyst and substrate in the transition state. This renders the above mentioned mechanism very unlikely. A much more probable mechanism is one previously postulated [7,8] for the general acid catalysed hydrolysis of acetals in which proton transfer and C–O bond cleavage are concerted (A–S_E2). This is shown in Scheme 2. The effect of partial C–O bond breaking in the transition state will be to increase greatly the basicity of the oxygen in the dioxolan ring, making a value of $\alpha = 0{\cdot}5$ reasonable. An additional piece of evidence in favour of a concerted process comes from comparison of complexes (IV) and (V). Previous results indicate a faster rate of spontaneous ring opening of (IV) than (V), thus the greater susceptibility to acid catalysis of (IV) suggests that C–O bond breaking is involved in the rate-determining step.

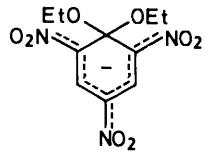
The principle of microscopic reversibility dictates that a pathway exists *via* the reverse of Scheme 2 for



SCHEME 2

the formation of spiro-complex from the parent glycol ether. The possibility must be considered that this rather than the alternative path described in Scheme 1 is the *major* pathway for spiro-complex formation in alkaline solutions. This would imply that hydroxide ion catalysis of ring closure involves a transition state (X; A = OH) while the uncatalysed ring opening involves a bimolecular reaction of the spiro-complex with water. There are two pieces of evidence that this is not the case. First the data in Table 2 show that the uncatalysed ring opening of (IV) proceeds at rather similar rates in H_2O and in D_2O with $k_{-1}(H_2O)/k_{-1}(D_2O)$ 1·3; if water were acting as a general acid the reaction should be much slower in D_2O.[13] Secondly we may calculate, using the Brønsted plots in the Figure, the values expected for catalysis by water. The value predicted for reaction of (V) is 1×10^{-4} compared with an experimental value of 0·095 s^{-1} while the predicted value for (IV) is $1{\cdot}7 \times 10^{-2}$ compared with the observed 2·3 s^{-1}. These results show that the uncatalysed ring-opening is a unimolecular reaction and that the major path in alkaline media is as shown in Scheme 1.

Comparison with Dialkoxy-Meisenheimer Complexes.— There have been several reports [14-16] of the acid catalysed decomposition of 1,1-dialkoxy-complexes such as (XI). General catalysis was not observed [14] and an $A1$ mechanism has been postulated.[15] The failure



(XI)

to observe general acid catalysis here might result from less ready C–O bond breaking and/or easier protonation of the ether oxygen. Evidence that C–O bond breaking is facilitated in spiro-complexes relative to 1,1-dialkoxy-complexes has been presented previously [1,2] and may be due to the relief of steric interactions in the ground state of the spiro-complex.[5] This is probably the major effect contributing to the difference in behaviour between the two types of complex. Nevertheless comparison of the hydronium ion catalysed decomposition of (XI) ($k_{H_3O^+}$ $1{\cdot}2 \times 10^4$ l mol^{-1} s^{-1}) [15] with that of (V) ($k_{H_3O^+}$ $2{\cdot}2 \times 10^3$ l mol^{-1} s^{-1}) indicates that the dialkoxy-complex is more readily protonated than the spiro-complex. This implies that the basicity of the ether oxygen in (XI) is greater than that in (V). It is of interest to speculate on the reasons for this increased basicity. We have shown previously [17] that in methanol 1,1-dimethoxy-complexes interact with alkali-metal cations by ion-pair interaction. It was suggested that a favourable site existed between the oxygen atoms of the methoxy-groups where a cation might be held by a cage effect. No such interaction with cations was observed for spiro-complexes.[2] A stabilising effect in the case of the proton similar to that observed with other cations would account for the increased basicity of (XI).

The question arises whether general catalysis would be expected to be the exception or the norm in the acid decomposition of σ-complexes. We note that the decomposition of the sodium ethoxide adduct of 1,3,5-trinitrobenzene is subject to general catalysis [18] and that

[13] B. Capon, 'Organic Reaction Mechanisms,' Interscience, New York, 1972, p. 389.
[14] J. B. Ainscough and E. F. Caldin, *J. Chem. Soc.*, 1956, 2528.
[15] J. Murto and J. Vainionpaa, *Suomen Kem.*, 1966, **B39**, 133; J. Murto and A. Viitala, *ibid.*, p. 138.
[16] J. H. Fendler, E. J. Fendler, W. E. Byrne, and C. E. Griffin, *J. Org. Chem.*, 1968, **33**, 977; J. H. Fendler, E. J. Fendler, and C. E. Griffin, *ibid.*, 1969, **34**, 689; J. H. Fendler and E. J. Fendler, *ibid.*, 1970, **35**, 3378.
[17] M. R. Crampton and H. A. Khan, *J.C.S. Perkin II*, 1972, 2286; 1973, 1103.
[18] J. B. Ainscough and E. F. Caldin, *J. Chem. Soc.*, 1956, 2540.

buffer catalysis has been observed in the reactions of several hydroxide ion adducts.[19] The specific base–general acid mechanism of base catalysis in nucleophilic aromatic substitution reactions requires the decomposition of a σ-complex to be subject to general acid catalysis;[20] that this is the case has been demonstrated in at least one instance.[20]

We thank the S.R.C. for financial support.

[4/1153 *Received*, 13*th June*, 1974]

[19] J. H. Fendler, E. J. Fendler, and L. M. Casilio, *J. Org. Chem.*, 1971, **36**, 1749; J. W. Bunting and W. G. Meathrel, *Canad. J. Chem.*, 1973, **51**, 1965.

[20] J. A. Orvik and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 2417.