

Acid-Catalyzed Hydrolysis of Bridged Bi- and Tricyclic Compounds. XXX. 7-Oxabicyclo[2.2.1]heptane: Kinetics and Mechanism

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7-Oxabicyclo[2.2.1]heptane (7-oxanorbornane) produces in concentrated (5.5–7.0 mol dm⁻³) aqueous perchloric acid mainly 3-cyclohexen-1-ol and a mixture (1:1) of *cis*- and *trans*-1,4-cyclohexanediols. The activation entropy, the solvent deuterium isotope effect and the slope parameter m^* of the linear excess acidity plot as well as the products are in agreement with the A-1 hydrolysis mechanism. The data are compared with those recently measured for 7-oxa-5-oxo-2-bicyclo[2.2.1]heptene.

The acid-catalyzed hydrolysis of 7-oxa-5-oxo-2-bicyclo[2.2.1]heptene (**1**) was recently studied.¹ According to the results, the reaction, which is an isomerization, is initiated by the pre-equilibrium protonation of the ether oxygen atom, the O(7)–C(1) bond is broken in the rate-limiting step, and the later fast stages yield 1,2-dihydroxybenzene (catechol) as the main product. However, the kinetic parameters, e.g. the activation entropy ($-32 \text{ J K}^{-1} \text{ mol}^{-1}$), the solvent deuterium isotope effect ($k_{\text{H}}/k_{\text{D}} = 0.34$) and the slopes of some linear correlations between $\log k$ and acidity functions, are not in agreement with one reaction mechanism only, but have features typical of both A-1 and A-2 mechanisms. This kind of behaviour is not unique, but has been observed earlier in the acid-catalyzed hydrolyses of epoxides and some other small ring ethers.^{2,3}

In order to see which mechanism is probable for the rupture of the O(7)–C(1) bond of the simplest member of 7-oxabicyclo[2.2.1]heptane family, the acid-catalyzed hydrolysis of the first member, 7-oxanorbornane (**2**), was studied in the present work. The kinetic parameters, such as activation entropy, solvent deuterium isotope effect and excess acidity correlations, were evaluated and the reaction products were analyzed.

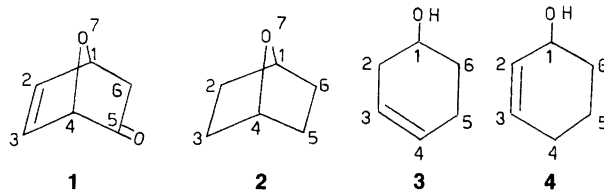
Experimental

Material. 7-Oxanorbornane was a commercial product from Aldrich (purity 99% by GLC). Its IR and ¹³C NMR spectra were identical with the literature data.^{4,5}

Kinetic measurements. The disappearance of 7-oxanorbornane (ca. $7 \times 10^{-3} \text{ mol dm}^{-3}$) in concentrated aqueous perchloric acid solutions was followed by a GLC method de-

scribed earlier with cyclopentanone as an internal standard.¹ First-order kinetics were always strictly obeyed, and parallel runs gave rate constants equal within 6% (av. 2%).

Product analysis. A mixture of 7-oxanorbornane (0.5 cm³) and cyclohexanone (internal standard; 0.1 cm³) was stirred with 7 mol dm⁻³ HClO₄ (aq) (50 cm) in a stoppered bottle for 20 half-lives at ca. 318 K, and several samples were neutralized with concentrated ammonia and centrifuged to remove the precipitated salt. The solutions were then analyzed by GLC by using a packed Carbowax 20 M column. The substrate and two main products were analyzed quantitatively by using response ratios measured separately. According to the retention times (RT) and the IR and ¹³C NMR spectra, the product with a short RT is 3-cyclohexen-1-ol (**3**, ca. 68% during the first seven half-lives, but decreasing slowly later), whose data were slightly different from those of 2-cyclohexen-1-ol (**4**; Aldrich; Table 1). Their ¹³C NMR spectra were also compared with those of the corresponding acetates.^{6,7} The product with a long RT is 1,4-cyclohexanediol (**5**; ca. 32% during the first seven half-lives, but increasing slowly later), whose data were identical to those of an authentic 1:1 mixture of *cis*- and *trans*-1,4-cyclohexanediols (Aldrich). GLC analyses (made from a CH₂Cl₂ extract) with a Carbowax 20 M capillary column showed that the diol produced by the hydrolysis of 7-



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Table 1. Tentative assignments of ^{13}C NMR chemical shifts for 3-cyclohexenol (**3**), 2-cyclohexenol (**4**) and the corresponding acetates in CDCl_3 (TMS).

Substrate	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	Ref.
3	66.7	34.1	126.6	124.1	23.8	30.8	
3 -OAc	69.7	30.8	126.8	123.7	23.4	27.4	6
4	64.7	130.0	129.0	24.6	18.8	31.4	
4 -OAc	68.1	132.8	126.0	25.0	19.0	28.4	7

oxanorbornane is also a 1:1 mixture of the *cis* and *trans* isomers (actually a $54:46 \pm 1$ mixture or *vice versa*, but the partitioning of the isomers between the organic solvent and aqueous solution may be slightly different). The separate experiments showed that the diols are practically stable under the reaction conditions during at least 20 half-lives of 7-oxanorbornane, although small peaks of 7-oxanorbornane ($< 0.1\%$) and 3-cyclohexen-1-ol ($< 1\%$) could be found in the reaction solution of the diols by GLC. They may be due to dehydration of the diols during the GLC analysis.

Several minor products (total max. ca. 15%) were also found by GLC and some of them dyed the reaction solution red (cf. Ref. 1). These products are evidently dimeric and polymeric cyclohexane compounds with or without a hydroxyl group according to their gas-phase FTIR spectra. A small amount of a precipitate was also formed when the initial concentration of 7-oxanorbornane was great enough (ca. 0.1 mol dm^{-3}). It is probably a mixture of 1,4-cyclohexanediols according to its IR spectrum.

Results and discussion

The disappearance rate constants of 7-oxabicyclo[2.2.1]heptane (7-oxanorbornane, **2**) were measured in aqueous perchloric acid at different temperatures and acid concentrations, and in deuterioperchloric acid. The results are collected in Table 2, together with activation parameters and a kinetic solvent deuterium isotope effect. The activation entropy ($7 \pm 2 \text{ J K}^{-1} \text{ mol}^{-1}$) is positive, in contrast to that of 7-oxa-5-oxo-2-bicyclo[2.2.1]heptene (**1**; $-32 \text{ J K}^{-1} \text{ mol}^{-1}$),¹ and thus in agreement with a unimolecular hydrolysis mechanism (A-1 mechanism). The isotope effect ($k_{\text{H}}/k_{\text{D}} = 0.54 \pm 0.02$) is closer to unity than that of **1** (0.34),¹ which seems strange. It is between the values estimated to be typical of the A-1 ($0.3 \leq k_{\text{H}}/k_{\text{D}} \leq 0.5$) and A-2 ($0.5 \geq k_{\text{H}}/k_{\text{D}} \geq 0.7$ at 298 K) mechanisms (cf. Ref. 1). It is, however, of the same magnitude as those (0.44 to 0.50) measured in concentrated perchloric acid solutions for the A-1 hydrolyses of several alkyl phenyl ethers^{8,9} (cf. also Ref. 2).

The reaction rate in the cases of the A-1 and A-2 mechanisms depends on the excess acidity (X_0)¹⁰ of the medium according to eqn. (1),¹¹ where the water activity term $\log a_w$

$$\log k_{\psi} - \log c_{\text{H}^+} - \log [c_{\text{S}}/(c_{\text{S}} + c_{\text{SH}^+})] (-\log a_w) = m^* X_0 + \log (k_0/K_{\text{SH}^+}) \quad (1)$$

is included in the A-2 mechanism but excluded in the A-1 mechanism. In the equation, c_{H^+} is equal to the concentration of perchloric acid, the parameter m^* depends on the transition state, m^* is a slope parameter of eqn. (2), k_0 is a

$$\log (c_{\text{SH}^+}/c_{\text{S}}) - \log c_{\text{H}^+} = m^* X_0 + pK_{\text{SH}^+} \quad (2)$$

medium-independent rate constant of the rate-limiting stage, and K_{SH^+} is a thermodynamic dissociation constant of the protonated substrate (SH^+).

The latter equation allows the evaluation of the correction term $\log [c_{\text{S}}/(c_{\text{S}} + c_{\text{SH}^+})]$ in different acid concentrations if the parameters m^* and pK_{SH^+} are known. The value -2.80 has been measured for the pK_{SH^+} of 7-oxanorbornane in aqueous sulfuric acid at room temperature,¹² and the value 1.0 can be estimated for m^* on the grounds of

Table 2. Disappearance rate constants of 7-oxabicyclo[2.2.1]heptane in aqueous perchloric acid solutions as well as activation parameters and solvent deuterium isotope effect at 298 K.

T/K	$c(\text{HClO}_4)/\text{mol dm}^{-3}$	X_0^a	$k_{\psi}/10^{-5} \text{ s}^{-1}$
289.2	6.92 ^b		4.52(5)
298.2	6.90 ^b		16.2(2)
298.2	6.90 ^b		16.4(3) ^c
298.2	7.26		48.0(9) ^d
308.2	6.88 ^b		63.1(10)
318.2	6.85 ^b		232(2)
298.2	5.48	1.75	1.08(9)
298.2	6.10	2.07	3.27(4)
298.2	6.51	2.31	7.42(5)
298.2	6.92	2.56	16.2(2)
298.2	7.29	2.80	30.1(3)
298.2	7.45	2.91	43.9(14)
298.2	7.96	3.25	106(5)

Kinetic parameters:

$$\begin{aligned} \Delta H^\ddagger &= 101.6(6) \text{ kJ mol}^{-1} \\ \Delta S^\ddagger &= 7(2) \text{ J K}^{-1} \text{ mol}^{-1} \\ k_{\text{H}}/k_{\text{D}} &= 0.54(2) \end{aligned}$$

^aExcess acidity.¹⁰ ^bTemperature corrected. ^cCalculated from the activation parameters. ^dMeasured in $\text{DClO}_4(\text{D}_2\text{O})$.

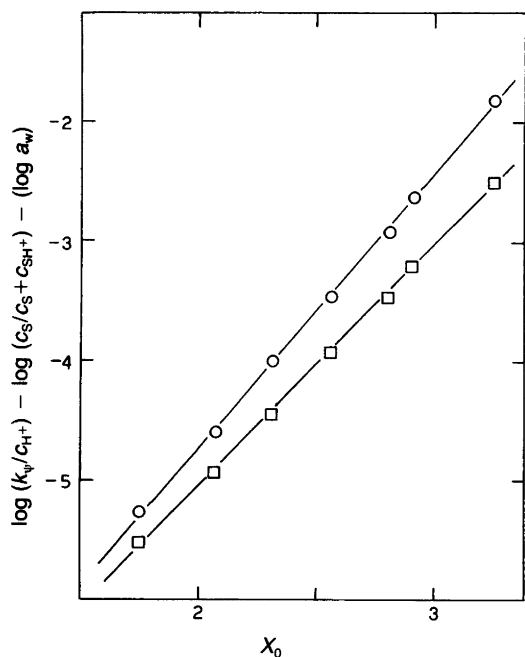
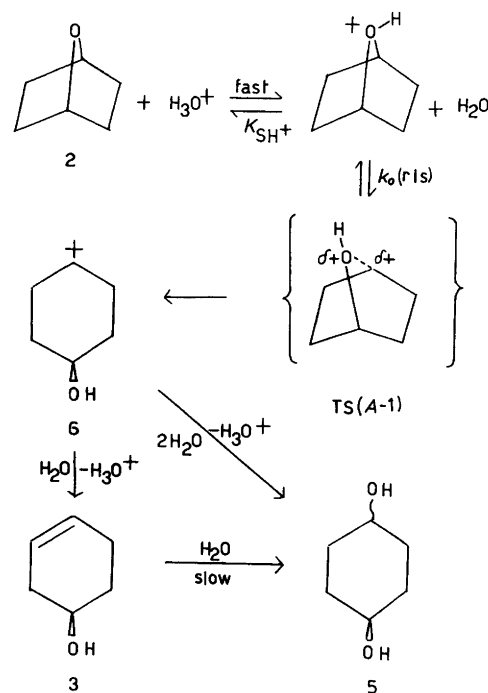


Fig. 1. Excess acidity plots for the hydrolysis of 7-oxabicyclo[2.2.1]heptane in $\text{HClO}_4(\text{aq})$ at 298.2 K with inclusion (○) and exclusion (□) of the activity of water [eqn. (1)].

measurements with alkyl phenyl ethers in perchloric acid.^{8,9} The correction term is significant at the acid concentrations used in the present kinetic measurements.

The excess acidity plots [eqn. (1)] are almost equally linear if the term $\log a_w$ is excluded (A-1 mechanism): $m^*m^* = 2.02 \pm 0.02$, $\log(k_0/K_{\text{SH}^+}) = -9.11 \pm 0.05$ and $r = 0.9997$, or if the term $\log a_w$ is included (A-2 mechanism): $m^*m^* = 2.29 \pm 0.03$, $\log(k_0/K_{\text{SH}^+}) = -9.32 \pm 0.07$ and $r = 0.9996$ (Fig. 1). However, the value m^* , 2.02, in the former case is typical of the A-1 mechanism, but that in the latter case, 2.29, is not in agreement with the A-2 mechanism (it should be ca. 1).¹¹ Thus the excess acidity studies support the unimolecular rupture of the O(7)–C(1) bond.

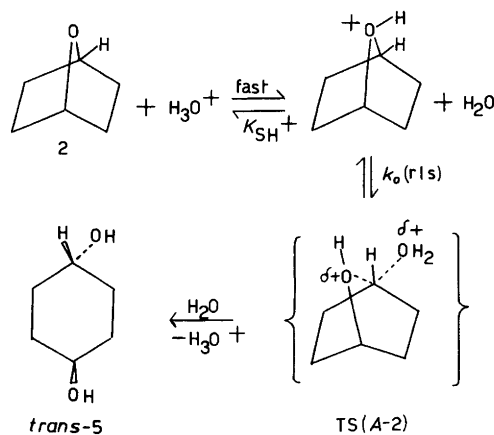
According to the product analysis (see Experimental), the acid-catalyzed hydrolysis of 7-oxanorbornane yields 3-cyclohexen-1-ol (3; the reaction is an isomerization) and 1,4-cyclohexanediols (5) as main products. The former alcohol is unstable in the reaction solution and also produces cyclohexanediols slowly. Both products are easily formed from the 4-hydroxycyclohexyl cation (6), which is an expected intermediate generated by the protonation of the ether oxygen atom and by the subsequent unimolecular rupture of the O(7)–C(1) bond (Scheme 1). The equal formation of the *cis* and *trans* isomers of the diol also supports the existence of 6, because the participation of a water molecule in the rupture (A-2 mechanism) should mainly produce the *trans* isomer (Scheme 2). The formation of 6 by dehydration of the diols probably does not occur, because the diols do not produce 3-cyclohexen-1-ol (3) significantly under the reaction conditions. The minor



Scheme 1.

products are evidently formed from cation 6 and/or alcohol 3 by polymerization.

In summary, the positive activation entropy, the value (2.0) of the slope parameter m^* of the linear excess acidity plot [eqn. (1)] and the product analysis support the A-1 mechanism (Scheme 1) in the acid-catalyzed hydrolysis of 7-oxabicyclo[2.2.1]heptane (2). The kinetic parameters are rather different from those measured for the hydrolysis of 7-oxa-5-oxo-2-bicyclo[2.2.1]heptene (1).¹ The mutual values of solvent deuterium isotope effects are slightly strange. An explanation, proposed by a referee, might be a reverse formation of the substrate (2) from the intermediate carbocation (6), which reaction evidently increases the



Scheme 2.

value of the isotope effect. In the acid-catalyzed hydrolysis of **1**, the electronegative groups, i.e. the carbonyl group and the carbon double bond, markedly reduce the hydrolysis rate [$k(2)/k(1) \approx 10^3$] and make the intermediate cation corresponding to **6** so unstable that the participation of water in the rupture of the O(7)–C(1) bond evidently becomes significant, although the total reaction is the acid-catalyzed isomerization. Thus the kinetic parameters of **1** gain some features typical of the A-2 mechanism.¹

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