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Acid-catalyzed Hydrolyses of Bridged Bi- and Tricyclic Compounds. XXII. Kinetics of Epimerization and Hydration of *exo*- and *endo*-5-Acetyl-2-norbornenes and Hydration of 3-Acetylnortricyclane

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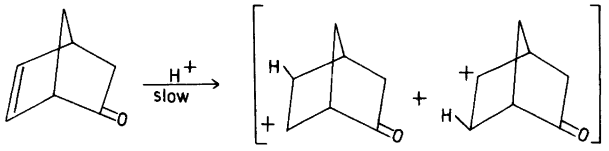
In aqueous perchloric acid *exo*- and *endo*-5-acetyl-2-norbornenes react by competing epimerization of the acetyl group and hydration of the carbon-carbon double bond. The four rate constants which control the reactions are evaluated at different temperatures. 3-Acetylnortricyclane reacts under similar conditions by hydration of the three-membered carbon ring. Kinetic parameters indicate that epimerization occurs via enolic intermediates and that the mechanism of hydration is $A-S_E2$, *i.e.* slow protonation of a carbon atom. The reaction products support the conclusions.

In a recent study 5-oxo-2-norbornene (dehydronorcamphor) was observed to disappear in aqueous acid by slow protonation and subsequent hydration of the carbon-carbon double bond ($A-S_E2$ mechanism, eqn. 1).[1] Thus its reaction differs from the acid-catalyzed reactions of other β,γ-unsaturated ketones, which generally isomerize to α,β-unsaturated ketones by initial pre-equilibrium protonation of the carbonyl oxygen followed by deprotonation and protonation steps, one of which is rate-limiting (A-2 mechanism, eqn. 2).[2,3]

In the case of other 5-x-substituted 2-norbornenes (x=H, CH_2OH, OH, CN, and NO_2) the mechanism of hydration is $A-S_E2$.[4–9] Thus 5-oxo-2-norbornene reacts similarly as the other bicyclic compounds.

In the acid-catalyzed hydration of 3-x-substituted nortricyclanes (x=H, CH_2OH, OH, CN, and NO_2) protonation of the cyclopropane ring is also the rate-determining step ($A-S_E2$ mechanism, eqn. 3).[5,7–9] The hydration mechanism of



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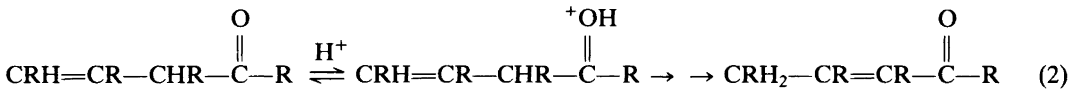

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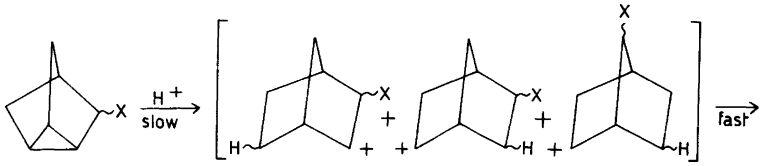

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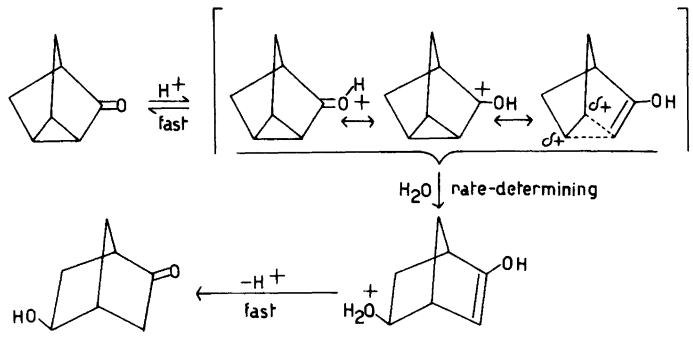
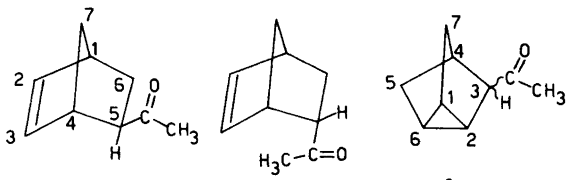


Scheme 1.

3-oxonortricyclane (3-nortricyclanone) is, however, different: it occurs mainly by fast initial protonation of the carbonyl oxygen followed by rearrangement and hydration steps (*A*-2 mechanism, Scheme 1).[10,11] Thus the carbonyl group may account for the different routes of the hydration reactions.

The aim of the present work is to study the effect of the carbonyl group situated outside but second to the bi- and tricyclic skeleton upon the hydration mechanisms of norbornenes and nortricyclanes. Therefore *exo*- and *endo*-5-acetyl-2-norbornenes (*1* and *2*) and 3-acetylnortricyclane



1 *2* *3*

(*3*) were prepared, their disappearance rates in perchloric acid were measured, and reaction products were identified in the case of acetylnorbornenes.

EXPERIMENTAL

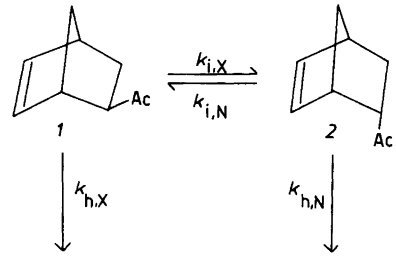
Syntheses. A 1:4 mixture of *exo*- and *endo*-5-acetyl-2-norbornenes was prepared by the Diels-Alder reaction of monomerized cyclopentadiene and methyl vinyl ketone.[12] The isomers were enriched by distillation and separated on a preparative gas chromatograph (FFAP column).

3-Acetylnortricyclane was synthesized as follows. A 27:73 mixture of *exo*-5-acetoxy-2-norbornene and 3-acetoxynortricyclane was obtained by addition of acetic acid to norbornadiene.[13] The mixture was hydrolyzed in aqueous potassium hydroxide to the corresponding alcohols, which were turned into the corresponding chlorides by treating them with thionyl chloride in pyridine. The chlorides were isomerized totally to 3-chloronortricyclane with titanium tetrachloride in methylene chloride.[14] The chloride was transformed into nortricyclyl magnesium chloride with magnesium turnings in diethyl ether and addition of acetaldehyde into the solution produced 3-(1-hydroxyethyl)nortricyclane, which was oxidized to 3-acetylnortricyclane with chromic acid.[15] The yield was 33 % from the starting materials.

A 3:7 mixture of *exo*- and *endo*-2-acetylnorbornanes for a ^{13}C NMR spectrum was obtained by hydrogenating the corresponding mixture of acetylnorbornenes in acetone with palladium on carbon as catalyst at room temperature and in atmospheric pressure.

The products were identified from their IR (C=O 1710 cm^{-1}), ^1H and ^{13}C NMR spectra.[12,16]

Kinetics. The disappearance of the substrates (initial concentration *ca.* 2×10^{-3} mol dm^{-3}) in aqueous $HClO_4$, was followed by taking samples after appropriate intervals, by neutralizing them with concentrated ammonia (final pH ca. 7), and by analyzing them by GLC (FFAP column) using norcamphor or 1-methylnorcamphor as inert internal standard. In the case of acetylnorbornenes, where mutual isomerization occurred, the peak areas of both epimers were measured and the rate constants of isomerization (k_i) and hydration (k_h, Scheme 2) were computed from



Scheme 2.

$$(1)= \frac{k_{1,N}(2)_o-(k_{i,X}+k_{h,X}+m_2)(1)_o}{m_1-m_2} \exp(m_1t) + \frac{(k_{i,X}+k_{h,X}+m_1)\ (1)_o-k_{i,N}(2)_o}{m_1-m_2} \exp(m_2t) \quad (4)$$

$$(2)= \frac{(k_{i,X}+k_{h,X}+m_1)\ [k_{i,N}(2)_o-(k_{i,X}+k_{h,X}+m_2)\ (1)_o]}{k_{i,N}(m_1-m_2)} \exp\ (m_1t) + \frac{(k_{i,X}+k_{h,X}+m_2)\ [(k_{i,X}+k_{h,X}+m_1)\ (1)_o-k_{i,N}(2)_o]}{k_{i,N}(m_1-m_2)} \exp(m_2t) \quad (5)$$

$$m_1=\tfrac{1}{2}\left\{-(k_{i,X}+k_{i,N}+k_{h,X}+k_{h,N})-[(k_{i,X}+k_{i,N}+k_{h,X}+k_{h,N})^2 -4(k_{i,N}k_{h,X}+k_{i,X}k_{h,N}+k_{h,X}k_{h,N})]^{\frac{1}{2}}\right\} \quad (6)$$

$$m_2=\tfrac{1}{2}\left\{-(k_{i,X}+k_{i,N}+k_{h,X}+k_{h,N})+[(k_{i,X}+k_{i,N}+k_{h,X}+k_{h,N})^2 -4(k_{i,N}k_{h,X}+k_{i,X}k_{h,N}+k_{h,X}k_{h,N})]^{\frac{1}{2}}\right\} \quad (7)$$

eqns. (4) and (5)[17] by iteration.

In these equations (*1*) and (*2*) are the peak areas of the *exo* and *endo* epimers divided by the peak area of the internal standard at time t, the subindex 0 refers to the first sample (t=0), and m_1 and m_2 are defined by eqns. (6) and (7).

Each sample was analyzed several times and the mean values were used in the calculations. Measurements at different temperatures were made three or more times by starting with the pure epimers (purity ≥ 99 % by GLC). The means of $k_{i,X}$, $k_{i,N}$, $k_{h,X}$, and $k_{h,N}$ and their standard deviations were calculated.

Efforts to measure the rate constants in 1.00 mol dm^{-3} $DClO_4(D_2O)$ for solvent deuterium isotope effects were unsuccesful in the case of acetylnorbornenes, but there were no difficulties in the case of 3-acetylnortricyclane. The measurements of the rate constants for acetylnortricyclane (purity > 99 %) were much more accurate than those for acetylnorbornenes.

Equilibration of acetylnorbornenes. 5-Acetyl-2-norbornenes (0.05 mol dm^{-3}) were equilibrated in methanol under catalysis of sodium methoxide (0.1 mol dm^{-3}). The ratio of isomers was analyzed by GLC from samples neutralized by aqueous perchloric acid (final pH *ca.* 7).

Product analysis. 1.00 g of the 24:76 mixture of *exo*- and *endo*-5-acetyl-2-norbornenes was hydrolyzed for over ten half-lives by stirring efficiently in 70 cm^3 of 1 mol dm^{-3} $HClO_4$ at 75 °C. The solution became brown and a black tarry substance was formed. The mixture was cooled and extracted with CH_2Cl_2 three times when the tarry material was dissolved as well. The organic phase was washed with water three times and dried on sodium sulphate. The solvent was distilled off in vacuo and the black residue (0.75 g) was analyzed by GLC and by IR and ^{13}C NMR spectroscopy. The product is mainly a mixture of 5- and 6-acetyl-*exo*-2-norborneols and its ^{13}C NMR spectrum agrees with the following positions of the acetyl group: 37 % of *exo*-5, 23 % of *endo*-5, 22 % of *exo*-6, and 18 % of *endo*-6 (±3 %, see Table 1). There are several other minor signals which do not fit in the calculated chemical shifts of 5- and 6-acetyl-*endo*-2-norborneols and are, at least partly, due to the unidentified impurity (5 %) of the acetylnorbornenes used as starting material.

RESULTS AND DISCUSSION

The aqueous acid causes both *exo-endo* isomerization (epimerization) and disappearance of *exo*- and *endo*-5-acetyl-2-norbornenes (*1* and *2*). The isomerization (k_i) and disappearance (k_h)

Table 1. Comparison of the ^{13}C chemical shifts for *exo*- and *endo*-5- and -6-acetyl-*exo*-2-norborneols (calculated by addition of the effects of the *exo*-2-hydroxyl and *exo*- and *endo*-5- and -6-acetyl groups on the chemical shifts of norbornane) with the observed ^{13}C chemical shifts in $DCCl_3$ for the hydration products of *exo*- and *endo*-5-acetyl-2-norbornenes.

	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C=O	CH_3	Ref.
Norbornane	36.8	30.1	30.1	36.8	30.1	30.1	38.7			15
$\Delta\delta$ (*exo*-2-OH)	+7.7	+44.3	+12.3	−1.0	−1.3	−5.2	−4.1			15
$\Delta\delta$ (*exo*-5-Ac)	−0.8	−0.6	−1.2	+3.9	+24.8	+2.3	+1.2	+209.9	+29.8	[a]
exo-5-acetyl-*exo*-2-norborneol (calc.)	43.7	73.8	41.2	39.7	53.6	27.2	35.8	209.9	29.8	
exo-5-acetyl-*exo*-2-norborneol (obs.)	44.1	74.2	42.2	39.2	53.7	27.1	36.8	209.5	28.9	[a]
$\Delta\delta$ (*endo*-5-Ac)	+0.4	−1.0	−5.6	+3.9	+24.7	−0.3	+1.6	+209.6	+29.8	[a]
endo-5-acetyl-*exo*-2-norborneol (calc.)	44.9	73.4	36.8	39.7	53.5	24.6	36.2	209.6	29.8	
endo-5-acetyl-*exo*-2-norborneol (obs.)	45.8	73.9	37.8	39.4	53.0	25.3	35.3	209.3	29.8	[a]
$\Delta\delta$ (*exo*-6-Ac)	+3.9	−1.2	−0.6	−0.8	−0.3	+24.8	+1.2	+209.9	+29.8	[a]
exo-6-acetyl-*exo*-2-norborneol (calc.)	48.4	73.2	41.8	35.0	28.5	49.7	35.8	209.9	29.8	
exo-6-acetyl-*exo*-2-norborneol (obs.)	48.9	74.5	42.0	34.4	28.1	51.2	35.1	209.0	29.5	[a]
$\Delta\delta$ (*endo*-6-Ac)	+3.9	−5.6	−1.0	+0.4	+2.3	+24.7	+1.6	+209.6	+29.8	[a]
endo-6-acetyl-*exo*-2-norborneol (calc.)	48.4	68.8	41.4	36.2	31.1	49.6	36.2	209.6	29.8	
endo-6-acetyl-*exo*-2-norborneol (obs.)	47.5	71.9	41.8	37.2	31.2	50.4	37.1	208.7	28.7	[a]

[a] This work.

Table 2. Rate constants of isomerization (k_i) and disappearance (k_h) for *exo*- and *endo*-5-acetyl-2-norbornenes (Scheme 2) in 1.00 mol dm^{-3} $HClO_4$ at different temperatures and activation parameters at 25 °C.

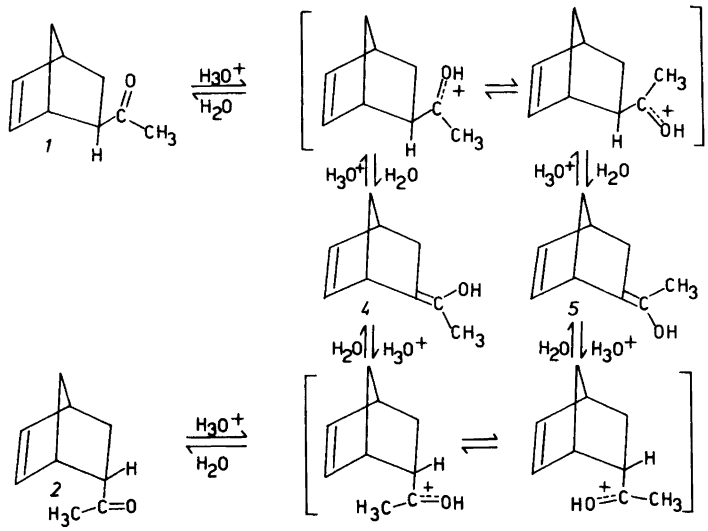
Reaction	Temp./ °C	k_1/ 10^{-5} s^{-1} [a]	Activation parameters
exo→*endo*	25	0.40(4)[b]	
($k_{i,X}$)	55	9.9(5)	$\Delta H^{\neq}$=84(2) kJ mol^{-1}
	65	24(1)	$\Delta S^{\neq}$= −67(5) J mol^{-1} K^{-1}
	75	56(3)	
	85	137(3)	
endo→*exo*	25	0.24(5)[b]	
($k_{i,N}$)	55	7.0(5)	$\Delta H^{\neq}$=89(4) kJ mol^{-1}
	65	17.0(9)	$\Delta S^{\neq}$= −55(12) J mol^{-1} K^{-1}
	75	51(2)	
	85	107(4)	
exo→products	25	0.051(16)[b]	
($k_{h,X}$)	55	3.7(6)	$\Delta H^{\neq}$=114(6) kJ mol^{-1}
	65	11.7(11)	$\Delta S^{\neq}$=+17(17) J mol^{-1} K^{-1}
	75	49(4)	
	85	119(8)	
endo→products	25	0.14(3)[b]	
($k_{h,N}$)	55	6.8(4)	$\Delta H^{\neq}$=104(4) kJ mol^{-1}
	65	22(1)	$\Delta S^{\neq}$= −9(11) J mol^{-1} K^{-1}
	75	56(3)	
	85	184(17)	

[a] The standard deviations are given in parenthesis. [b] Calculated from the activation parameters.

rate constants (see Scheme 2) in 1.00 mol dm^{-3} aqueous $HClO_4$ are listed in Table 2 together with the activation parameters. The epimerization rates are somewhat greater than the disappearance rates at lower temperatures (*e.g.* 25 °C), but all the four rates are of the same magnitude at the higher temperature used (*e.g.* 75 °C). These results agree with the activation enthalpies being higher for disappearance (104 to 114 kJ mol^{-1}) than for isomerization (84 to 89 kJ mol^{-1}). The latter values are similar to those measured for the acid-catalyzed enolization of aliphatic and alicyclic ketones and aldehydes (82 to 87 kJ mol^{-1} in aqueous acids and 75 to 97 kJ mol^{-1} in 90 % acetic acid – HCl solutions).[18,19] The activation entropies of isomerization (−55 to −67 J mol^{-1} K^{-1}) are also in accordance with those measured for enolization of the ketones (−30 to −62 J mol^{-1} K^{-1} in 90 % acetic acid – HCl solutions).[19] Thus it is evident that the epimerization occurs via enolic structures (*4* and *5* in Scheme 3). Considering the equilibrium ratios for the corresponding methyl enol ethers (*6*–*9*) at 25 °C [20] the intermediates (*4* and *5*) are energetically close to each other and only somewhat less stable than the corresponding methylene enols, 5-(1-hydroxyvinyl)-2-norbornenes.

The ratio of the epimerization rate constants ($k_{i,X}$:$k_{i,N}$) differs slightly from the equilibrium ratio of the *exo* and *endo* epimers (K=[*endo*]/[*exo*]): $k_{i,X}$:$k_{i,N}$= 1.10±0.09 and K=0.96±0.02 at 75 °C. The equilibrium ratio of acetylnorbornenes is very similar to that measured for *exo* and *endo*-5-carbomethoxy-2-norbornenes (K=0.95±0.02 at 75 °C).[21] The discrepancy above may be due to the inaccuracy of the isomerization rate constants presented in Table 2.

The corresponding reaction via enolic structures is also probable in the case of 3-acetylnortricyclane (*3*), but it causes only a racemization of



Scheme 3.

the substrate. Since the tricyclic compound is already an optically inactive mixture of two enantiomers, there is no change in the composition of the substrate. Evidently the amounts of the enolic forms are so minor[22] that they have no effect on the disappearance rates of acetylnorbornenes (Table 2) and acetylnortricyclane (Table 3).

The activation entropies of disappearance for 5-acetyl-2-norbornenes are close to zero (−9 to +17 J mol^{-1} K^{-1}) and are thus in agreement with the slow protonation of the carbon-carbon double (A–S_E2 mechanism).[1,4–9] The activation entropy measured for the disappearance of 3-acetylnortricyclane is of the same magnitude (−7 J mol^{-1} K^{-1}, Table 3). The activation enthalpies for acetylnorbornenes and -nortricyclane are also similar (104 to 114 kJ mol^{-1}). The other kinetic parameters of disappearance measured only for acetylnortricyclane (the solvent deuterium isotope effect, k_H/k_D=1.35, and the slopes for log k_1 *vs.* $-H_o$, 1.19, and for log k_1+H_o *vs.* H_o+log c_{HClO_4}, −0.27) are also in accordance with the slow protonation of the three-membered carbon ring (A–S_E2 mechanism).[5,7–9] Besides, the rate constants of disappearance for 5-acetyl-2-norbornenes and 3-acetylnortricyclane are in agreement with the hydration rate constants of other 5-*x*-substituted 2-norbornenes and 3-*x*-substituted nortricyclanes (*x*=H, CH_2OH, CH_2Cl, OH, CN, and NO_2).[9]

The main reaction products of acid-catalyzed hydration of 5-acetyl-2-norbornenes were identified to be 5- and 6-acetyl-*exo*-2-norborneols (see Experimental). The observed amounts of the acetyl group at different positions are 60±4 % at C(5) and 40±4 % at C(6) [the acetyl group may evidently shift between the *exo* and *endo* positions as it does in the substrates, (*1* and *2*), and the Wagner-Meerwein rearrangement may occur, at least, in the 5-acetyl-2-norbornyl cation (see Scheme 4)].

The ratio indicates that about 60 % of protonation occurs at C(3) and about 40 % at C(2) of 5-acetyl-2-norbornenes, which is just the same ratio as was recently observed for the hydrations

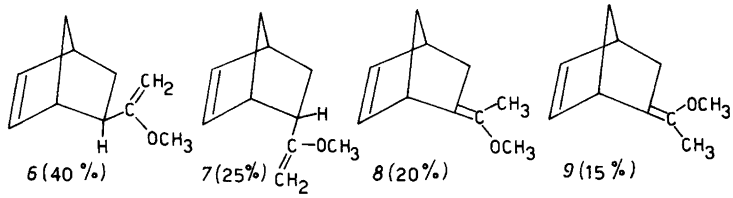


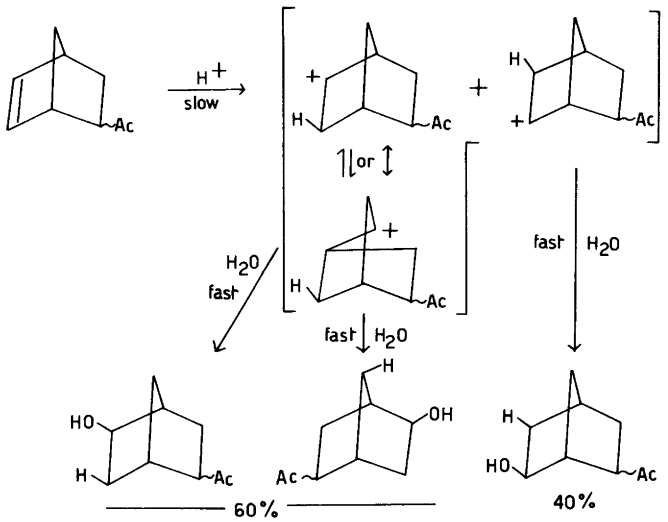
Table 3. Disappearance rate constants for 3-acetylnortricyclane in aqueous perchloric acid at different temperatures and acid concentrations, activation parameters at 25 °C, solvent deuterium isotope effect, and slopes for the plots log k_1 *vs.* $-H_o$ (Slope) and log k_1+H_o *vs.* $H_o+\log c_{HClO_4}$ (Ø).

Temp./ °C	$^cHClO_4$/ mol dm^{-3}	$-H_o$	k_1/ 10^{-5} s^{-1}	Activation parameters, isotope effect, and slopes
25	1.00		0.129(6)[a]	
45	1.01		1.89(4)	
55	1.01		6.73(12)	$\Delta H^{\neq}$=104.5(9) kJ mol^{-1}
65	1.01		20.6(4)	$\Delta S^{\neq}$= −7(3) J mol^{-1} K^{-1}
75	1.01		63.6(12)	k_H/k_D=1.35(6)
75	1.01		47.1(12)[b]	
85	1.01		168(3)	
45	1.01	0.33	1.89(4)	
45	2.02	0.83	9.50(7)	Slope=1.19(3)
45	3.03	1.33	34.6(2)	Ø= −0.27(7)
45	4.02	1.81	125(2)	
45	5.03	2.33	468(5)	

[a] Calculated from the activation parameters. [b] Measured in $DClO_4(D_2O)$.

of *endo*-5-hydroxy- and 5-methyl-*endo*-5-hydroxy-2-norbornenes.[23] The similarity of the ratios is rational considering the similar inductive effects of the acetyl and hydroxyl groups,[24] but it is strange that the same ratio was also measured for the hydration of 5-oxo-2-norbornene.[1] The oxo substituent is much more electronegative than the hydroxyl or acetyl groups, *e.g.* the hydration rates of 5-hydroxy- and 5-acetyl-2-norbornenes are *ca.* 10^3 times higher than that of 5-oxo-2-norbornene.[1,7] According to Carrupt and Vogel[25] the oxo group at C(5) may, however, stabilize the positive charge at C(3) by a hyperconjugative interaction, although the protonation of C(3) and the subsequent formation of a positive charge at C(2) would seem more probable in view of the homoconjugation present in the initial state of 5-oxo-2-norbornene, which already causes a partial positive charge at C(2).[26]

Thus both the kinetic and product-analytic results indicate that *exo*- and *endo*-5-acetyl-2-norbornenes and 3-acetylnortricyclane disappear



Scheme 4.

in the aqueous acid by the rate-determining protonation of the carbon-carbon double bond or the three-membered carbon ring (A-S_E2 mechanism, eqn. 3 and Scheme 4). In the case of acetylnorbornenes the epimerization of the *exo* and *endo* isomers via the enolic forms (A-2 mechanism, see Scheme 3), however, competes with the hydration reaction. The enolization in deuterioperchloric acid also results in an exchange of the hydrogen atom at C(5) to deuterium, which causes a primary isotope effect and is the reason for the failure in the attempt to measure solvent deuterium isotope effects for acetylnorbornenes (see Experimental).

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