Acid-Catalyzed Hydrolysis of Bridged Bi- and Tricyclic Compounds. XXXIII. Hydration of exo- and endo-5-Methoxy-2-norbornenes and 3-Methoxynortricyclane

Martti Lajunen,* Jouni Jantunen and Päivi Koiranen

Department of Chemistry, University of Turku, FIN-20014 Turku, Finland

Acid-catalyzed hydrolysis of alkyl phenyl ethers has recently been of interest at our laboratory.1–6 The effect of a primary,5 secondary,1,2 and tertiary3 alkyl moiety on the rate (and mechanism) of reaction was generally observed to be large, whereas the effect of a substituent in the benzene ring was small.5 The hydrolysis rates of the alkyl phenyl ethers were either small or very small, thus high acid concentrations were usually used. In order to carry out rate measurements under different conditions, new types of substrates were desired. exo- and endo-5-methoxy-2-norbornenes (1 and 2) and 3-methoxynortricyclane (3) were selected, because their oxygen atoms are probably much more basic (pKₐ > -3)7,8 than those of alkyl phenyl ethers (mostly pKₐ < -6).1–7 These substrates are also interesting, since they have two reactive sites, the ether oxygen and the double bond or cyclopropane ring, for the proton attack. The latter alternative was found to be predominant; thus the reaction is an acid-catalyzed hydration.

Experimental

Materials. 5-Methoxy-2-norbornenes (1 and 2) were synthesized from a 1:1 mixture of exo- and endo-2-norbornen-5-ols9 with the aid of sodium hydride and methyl iodide in dry tetrahydrofuran.10 No attempt was made to separate the epimers (the exo/endo ratio was 53/47). 3-Methoxynortricyclane (3) was prepared in the same way from 3-nortricyclanol.9,10 The purities by GC were 99%. The substrates were identified from their ¹H and ¹³C NMR, mass and FTIR spectra.10

Kinetic measurements. The disappearance of the substrates (1 and 2 simultaneously) in HClO₄(aq) was followed by GC (an FFAP capillary column) using norcamphor as the internal standard and dichloromethane as the extracting solvent.5 The pseudo-first-order rate constants were calculated from the slopes of the linear (r = 0.998–0.99999) correlation log Sₜ vs. t (Sₜ = 0), in which Sₜ is the ratio of the GC integrals of the substrate and the internal standard at a time t. Parallel runs were always made, and gave rate constants which were at least equal within 6% (av. 1.4%).

* To whom correspondence should be addressed.
Product analyses. 0.3 g of the substrate (1:1 mixture of 1 and 2) was stirred with 50 cm³ of 1 M HClO₄(aq) in a tightly stoppered erlenmeyer flask at an elevated temperature (60–75 °C) for ca. 1 or 10 half-lives. The reaction solution was extracted with CH₂Cl₂ several times, the organic phase being neutralized by letting it flow through anhydrous K₂CO₃. The solvent was evaporated, and the residue was analyzed by GC, GC-FTIR and GC-MS, the components being mainly identified by comparing their spectra with those collected in the memories of the spectrometers.

Results and discussion

Rate constants of disappearance for exo- and endo-5-methoxy-2-norbornenes (1 and 2) and 3-methoxynortricyclane (3) in aqueous perchloric acid at different temperatures and acid concentrations, and in deuterioperchloric acid are shown in Table 1. They are in agreement with the rate constants measured earlier for the protonation and dehydration of several 5-exo- and -endo-substituted 2-norbornenes and 3-substituted nortricyclanes in 1 M HClO₄(aq) at 348.2 K. The activation parameters and solvent deuterium isotope effects are given in Table 2. The k_H/k₀ values are greater than unity, and the entropies of activation mostly slightly negative, which values are typical of the rate-determining proton transfer from the hydronium ion to the double bond or to the cyclopropane ring (Ad⁵ mechanism; Schemes 1 and 2). The slightly positive entropy of activation in the case of the exo-epimer is possibly due to the experimental scatter (Table 2), to a partial ring opening during the reaction and/or to a slight cleavage of the ether linkage (see later).

The rate constants of disappearance for the substrates increase steeply with increasing acid concentration. This effect can be analyzed quantitatively with the excess acidity theory, which offers eqn. (1)

\[ \log k_p - \log c_{H₂O} = m^* m X_0 + \log k_0 \]

for the pure rate-determining proton transfer (Ad⁵ mechanism). In the equation, k_p is the pseudo-first-order rate constant in the aqueous acid with a concentration c_{H₂O} and excess acidity X_0; m^* and m^* are slope parameters, the former being indicative of the transition state and the latter of the site of proton attack; while k_0

### Table 1. Rate constants of disappearance for exo- and endo-5-methoxy-2-norbornenes (1 and 2) and 3-methoxynortricyclane (3) in aqueous perchloric acid at different temperatures and acid concentrations and in deuterioperchloric acid.

<table>
<thead>
<tr>
<th>T/K</th>
<th>c(HClO₄)/[^a]</th>
<th>X₀[^b]</th>
<th>k_p/10⁻⁸ s⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mol dm⁻³</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>318.2</td>
<td>1.008</td>
<td>1.838(10)</td>
<td>3.434(6)</td>
</tr>
<tr>
<td>328.2</td>
<td>1.002</td>
<td>6.56(9)</td>
<td>11.53(13)</td>
</tr>
<tr>
<td>328.2</td>
<td>0.984</td>
<td>20.3(4)</td>
<td>35.4(6)</td>
</tr>
<tr>
<td>338.2</td>
<td>0.996</td>
<td>22.5(5)[^c]</td>
<td>37.0(4) [^c]</td>
</tr>
<tr>
<td>348.2</td>
<td>0.978</td>
<td>23.7(9)</td>
<td>38.5(3)</td>
</tr>
<tr>
<td>348.2</td>
<td>0.991</td>
<td>20.7(6)[^d]</td>
<td>30.5(2)[^d]</td>
</tr>
<tr>
<td>348.2</td>
<td>0.993</td>
<td>60.0(7)</td>
<td>101.5(2)</td>
</tr>
<tr>
<td>358.2</td>
<td>1.014</td>
<td>1.838(10)</td>
<td>3.43(6)</td>
</tr>
<tr>
<td>328.2</td>
<td>0.984</td>
<td>1.426</td>
<td>4.28(10)</td>
</tr>
<tr>
<td>328.2</td>
<td>0.999</td>
<td>29.5(3)</td>
<td>51.5(3)</td>
</tr>
<tr>
<td>328.2</td>
<td>2.440</td>
<td>29.5(3)</td>
<td>51.5(3)</td>
</tr>
<tr>
<td>328.2</td>
<td>2.919</td>
<td>57.0(5)</td>
<td>98.5(8)</td>
</tr>
<tr>
<td>328.2</td>
<td>3.421</td>
<td>96.7(13)</td>
<td>164.6(15)</td>
</tr>
<tr>
<td>328.2</td>
<td>3.821</td>
<td>198.0(11)</td>
<td>331(4)</td>
</tr>
<tr>
<td>328.2</td>
<td>4.351</td>
<td>1.349</td>
<td>382(3)</td>
</tr>
<tr>
<td>318.2</td>
<td>4.870</td>
<td>1.349</td>
<td>382(3)</td>
</tr>
</tbody>
</table>

[^a]Temperature corrected. [^b]Excess acidity. [^c]Temperature corrected. [^d]Calculated from the activation parameters (Table 2), corrected according to X₀ functions. [^e]Measured in DClO₄(D₂O)
Scheme 1.

Scheme 2.
Table 2. Activation parameters and solvent deuterium isotope effects at 348.2 K and parameters of the excess acidity equation [eqn. (3)] for the hydration of exo- and endo-5-methoxy-2-norbornenes (1 and 2 at 328.2 K) and of 3-methoxynortricyclane (3 at 318.2 K) in HClO₄(aq).

<table>
<thead>
<tr>
<th>Substrate</th>
<th>(\Delta H^\circ/kJ\ mol^{-1})</th>
<th>(\Delta S^\circ/J\ mol^{-1} \cdot K^{-1})</th>
<th>(k_H/k_o)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>110.9(11)</td>
<td>+2(3)</td>
<td>1.14(5)</td>
</tr>
<tr>
<td>2</td>
<td>107.9(4)</td>
<td>-2(1)</td>
<td>1.28(2)</td>
</tr>
<tr>
<td>3</td>
<td>105.5(1)</td>
<td>-2(1)</td>
<td>1.34(3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substrate</th>
<th>(m')</th>
<th>(pK_{S\text{H}^+})</th>
<th>(m^* m^*)</th>
<th>(\alpha^*)</th>
<th>(\log(k_0/M^{-1} s^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.99(2)</td>
<td>-2.05(5)</td>
<td>1.69(3)</td>
<td>0.94(7)</td>
<td>-5.086(11)</td>
</tr>
<tr>
<td>2</td>
<td>1.04(2)</td>
<td>-2.01(7)</td>
<td>1.71(2)</td>
<td>0.95(7)</td>
<td>-4.853(6)</td>
</tr>
<tr>
<td>3</td>
<td>1.05(3)</td>
<td>-1.94(7)</td>
<td>1.72(3)</td>
<td>0.95(7)</td>
<td>-5.044(8)</td>
</tr>
</tbody>
</table>

*\(\alpha^* = m^* = m^* / (1.80 \pm 0.10)\).17

stands for the medium-independent rate constant of the rate-determining step of the reaction.

The \(\log k_0\) values (\(k_0 = k_H/c_H^+\)) for the substrates are plotted versus the excess acidity in Fig. 1. All three plots are slightly curved. The reason is probably a partial protonation of the ether oxygen atom, which process reduces the protonation of the double bond or the cyclopropane ring at higher acid concentrations (Schemes 1 and 2). If one assumes that the oxygen-protonated substrate does not react further in any way, eqns. (1) and (2)16

\[
\log(c_{S\text{H}^+}/c_S) - \log(c_H^+) = m'X_0 + pK_{S\text{H}^+}
\]

(2)

can be joined together to form eqn. (3),

\[
\log k_0 - \log(c_H^+) = m^* m^* X_0 - \log[1 + (c_{H^+}/K_{S\text{H}^+})10^{m'X_0}] + \log k_0
\]

(3)

which is similar to that used earlier by Kresge.18,19 In the equations, \(c_S\) and \(c_{S\text{H}^+}\) are the concentrations of the substrate, unprotonated and protonated on the oxygen atom, \(m'\) is the slope parameter for this protonation, and \(K_{S\text{H}^+}\) stands for the thermodynamic dissociation constant of the methoxy-protonated substrate.

Equation (3) can be used to evaluate the values of parameters \(m' m^*\), \(m'\), \(K_{S\text{H}^+}\) (or \(pK_{S\text{H}^+}\)) and \(k_0\) (or \(\log k_0\)) from the experimental values of \(k_0\), \(c_H^+\) and \(X_0\) with the method of a nonlinear least-squares minimization. The evaluated parameters are given in Table 2. When the value of \(m^*\) for the formation of the carbocation is known (1.80±0.10),17 \(m^*\) can be calculated.

The parameters in Table 2 seem reasonable. The value of \(m'\) (av. 1.03±0.03) is typical of protonation of an ether oxygen in aqueous perchloric acid.1-6,19,20 The \(pK_{S\text{H}^+}\) values (ca. -2.0) are equal to that (−2.1±0.2)9 measured for cis-1,2-dimethoxyethene in aqueous perchloric acid, but less negative than those measured for dimethyl and diethyl ethers in sulfuric acid.7,18 The slope parameter \(m^*\) or \(\alpha^*\) (‘excess acidity’ \(\alpha\); av. 0.95±0.07), which indicates the progress of proton transfer (0 < \(\alpha < 1\)) in the transition state of the \(A_2d_2\) reaction,19,20 is close to unity. Accordingly, the transition state resembles the intermediate carbocation. The measured kinetic solvent deuterium isotope effects (Table 2), which are only slightly greater than unity, are also in agreement with the late transition state.21 The \(\alpha^*\) values of the present work are, however, mostly higher than the \(\alpha^*\) and \(\alpha_t\) (‘isotopic \(\alpha\)’) values measured earlier for the hydration of several 5-substituted 2-norbornenes (av. 0.77±0.08; \(N = 13\)) and 3-substituted nortricyclanes (av. 0.79±0.10; \(N = 8\).22 The values probably depend slightly on the temperature,23 but this fact does not explain the observed difference.

Equation (3) can be changed back to the linear form [eqn. (4)],

\[
\log k_0 - \log(c_H^+) - \log[(c_S/(c_S + c_{S\text{H}^+}))] = m^* m^* X_0 + \log k_0
\]

(4)

in which the correction term \(-\log[(c_S/(c_S + c_{S\text{H}^+}))]\) can be.

Fig. 1. Excess acidity plots for the hydration of exo-and endo-5-methoxy-2-norbornenes (1 and 2) at 328.2 K and 3-methoxynortricyclane (3) at 318.2 K in HClO₄(aq) \((k_0 = k_{S^+}/c_{S^+}; 0.3\) and 1.0 have been added to the log \(k_0\) values of 2 and 3, respectively, for clarity). □: eqn. (1) for 1; ■, eqn. (4) for 1; ▲, eqn. (1) for 2; △, eqn. (4) for 2; ●, eqn. (1) for 3 and †, eqn. (4) for 3. The correction term, log\((c_S/(c_S + c_{S\text{H}^+}))\), has been calculated with eqn. (2) from the \(m'\) and \(pK_{S\text{H}^+}\) values in Table 2.
calculated with eqn. (2) from the $m'$ and $pK_{a,H^+}$ values evaluated in Table 2. The corrected plots (Fig. 1) are strictly linear ($r=0.9997-0.99994$); thus the rate-reducing effect of the partial protonation of the ether oxygen atom is significant at the higher acid concentrations used.

The reaction products of the substrates (1–3) in 1 M HClO$_4$ (aq) are mainly methoxy-substituted $exo$-$2$-norbornenols (4, 5, 7 and 9–12), which are in accord with the protonation of the double bond or the cyclopropane ring and the subsequent attack of a water molecule on a methoxy-substituted norbornyl cation (Schemes 1 and 2). These hydration products are analogous to the methoxy-substituted $exo$-$2$-chloronorbornanes formed with the addition of HCl to 1–3 in dry CH$_2$Cl$_2$, as well as to the chloro-substituted $exo$-$2$-acetoxy-norbornanes formed with the addition of acetic acid to 3-chloronorcyclopane under catalysis of sulfuric acid. An exceptional product in the present work is, however, cyclopent-3-en-1-ylenan (8, 8%), which is formed via protonation of C-2 of 1 and 2 and via participation of the methoxy group and opening of the bicyclic ring system. [If the protonation and the ring opening processes are simultaneous, the activation entropy may be more positive than in the usual proton transfer reactions (see above)]. The amounts of products which would be formed via cleavage of the ether linkage, i.e. $exo$-5-hydroxy-2-norbornene and 3-nortricyclopanol (6), are small (<1%). Thus, the portion of the A-1 (or A-2) mechanism is negligible [it may, however, have a small increasing effect on the $\Delta S^*$ value of 1 (see above)], and accordingly the oxygen–carbon bond is much less reactive than the carbon–carbon double bond or the cyclopropane ring in acid media.

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References


