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

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The disappearance of *exo-* and *endo*-5-methoxy-2-norbornenes and 3-methoxy-nortricyclane in aqueous perchloric acid was followed by capillary GC at different temperatures and acid concentrations. The rate constants, activation parameters, solvent deuterium isotope effects, excess acidity plots and products accord with the rate-determining protonation of the double bond or the cyclopropane ring followed mainly by water attack on a methoxy-substituted 2-norbornyl cation (Ad_E2 mechanism). The excess acidity plots were corrected according to a partial protonation of the ether oxygen atom. No significant cleavage of the ether linkage was observed.

Acid-catalyzed hydrolysis of alkyl phenyl ethers has recently been of interest at our laboratory.[1-6] The effect of a primary,[6] secondary[1,2] and tertiary[3] 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-methoxy-nortricyclane (3) were selected, because their oxygen atoms are probably much more basic ($pK_a > -3$)[7,8] than those of alkyl phenyl ethers (mostly $pK_a < -6$).[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-ols[9] 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
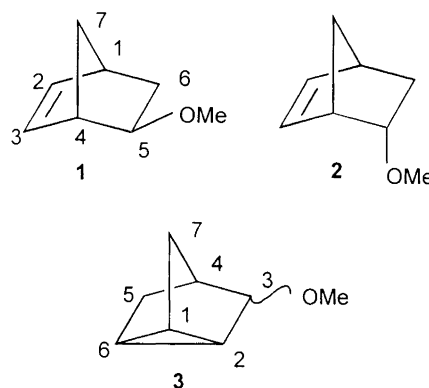
53/47). 3-Methoxynortricyclane (3) was prepared in the same way from 3-nortricyclanol.[9,10] The purities by GC were 99%. The substrates were identified from their ¹H and ¹³C NMR, mass and FTIR spectra.[10]

Kinetic measurements. The disappearance of the substrates (1 and 2 simultaneously) in $HClO_4$(aq) was followed by GC (an FFAP capillary column) using norcamphor as the internal standard and dichloromethane as the extracting solvent.[6] The pseudo-first-order rate constants were calculated from the slopes of the linear ($r = 0.998-0.99999$) correlation $\log S_t$ vs. t ($S_\infty = 0$), in which S_t 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%).

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Product analyses. 0.3 g of the substrate (1:1 mixture of
1 and 2) was stirred with 50 cm³ of 1 M $HClO_4$(aq) in
a tightly stoppered erlenmeyer flask at an elevated tem-
perature (60–75 °C) for ca. 1 or 10 half-lives. The
reaction solution was extracted with CH_2Cl_2 several
times, the organic phase being neutralized by letting it
flow through anhydrous K_2CO_3. The solvent was evapor-
ated, 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 mem-
ories of the spectrometers.

Results and discussion

Rate constants of disappearance for *exo*- and *endo*-5-
methoxy-2-norbornenes (1 and 2) and 3-methoxynor-
tricyclane (3) in aqueous perchloric acid at different
temperatures and acid concentrations, and in deuterio-
perchloric acid are shown in Table 1. They are in agree-
ment with the rate constants measured earlier for the
protonation and hydration of several 5-*exo*- and -*endo*-
substituted 2-norbornenes and 3-substituted nortricyc-
lanes in 1 M $HClO_4$(aq) at 348.2 K.[11,12] The activation

parameters and solvent deuterium isotope effects are
given in Table 2. The k_H/k_D 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 (Ad_E2 mechanism; Schemes 1
and 2).[11–15] 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,[16] which offers eqn. (1)

$$\log k_\psi - \log c_{H^+} = m^\neq m^* X_0 + \log k_0 \qquad (1)$$

for the pure rate-determining proton transfer (Ad_E2
mechanism). In the equation, k_ψ is the pseudo-first-order
rate constant in the aqueous acid with a concentra-
tion c_{H^+} and excess acidity X_0;[17] $m^\neq$ 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.

T/K	c(HClO₄)/[a] mol dm⁻³	X₀[b]	$k_\psi/10^{-5}\,s^{-1}$ 1	2	3
318.2	1.008				2.46(3)
328.2	1.002				8.47(3)
328.2	0.984		1.838(10)	3.434(6)	
338.2	0.996				27.30(12)
338.2	0.978		6.56(9)	11.53(13)	
348.2	0.991				82.3(6)
348.2	0.973		20.3(4)	35.4(6)	
348.2	1.000		22.5(5)[c]	37.0(4)[c]	83.0(3)[c]
348.2	1.017		23.7(9)	38.5(3)	
348.2	0.993				61.4(9)[d]
348.2	1.014		20.7(5)[d]	30.5(2)[d]	
358.2	0.967		60.0(7)	101.5(2)	
328.2	0.984	0.246	1.838(10)	3.43(6)	
328.2	1.426	0.340	4.28(10)	7.30(8)	
328.2	1.999	0.458	8.95(11)	16.07(9)	
328.2	2.440	0.557	15.9(4)	28.1(4)	
328.2	2.919	0.677	29.5(3)	51.5(3)	
328.2	3.421	0.823	57.0(5)	98.5(8)	
328.2	3.821	0.951	96.7(13)	164.6(15)	
328.2	4.351	1.138	198.0(11)	331(4)	
328.2	4.870	1.349	382(3)	625(4)	
318.2	1.008	0.258			2.46(3)
318.2	1.445	0.350			4.91(1)
318.2	2.016	0.471			11.00(3)
318.2	2.445	0.569			19.34(5)
318.2	2.926	0.692			35.73(12)
318.2	3.428	0.839			67.20(15)
318.2	3.826	0.969			111.7(3)
318.2	4.386	1.176			221.0(5)
318.2	4.872	1.378			415.9(4)

[a]Temperature corrected. [b]Excess acidity,[17] temperature corrected.[16] [c]Calculated from the activation parameters (Table 2),
corrected according to X_0 functions. [d]Measured in $DClO_4$(D_2O).
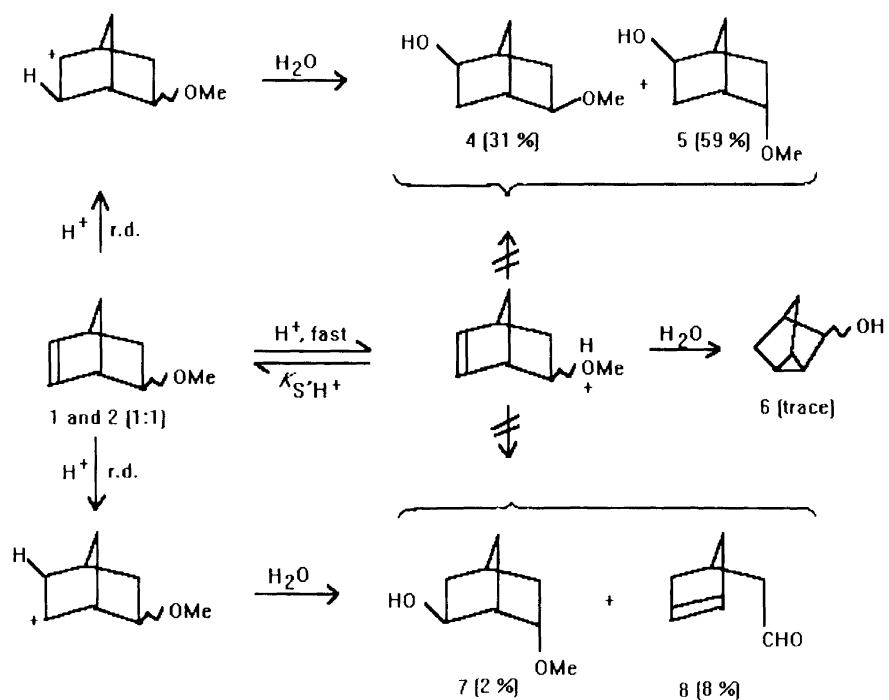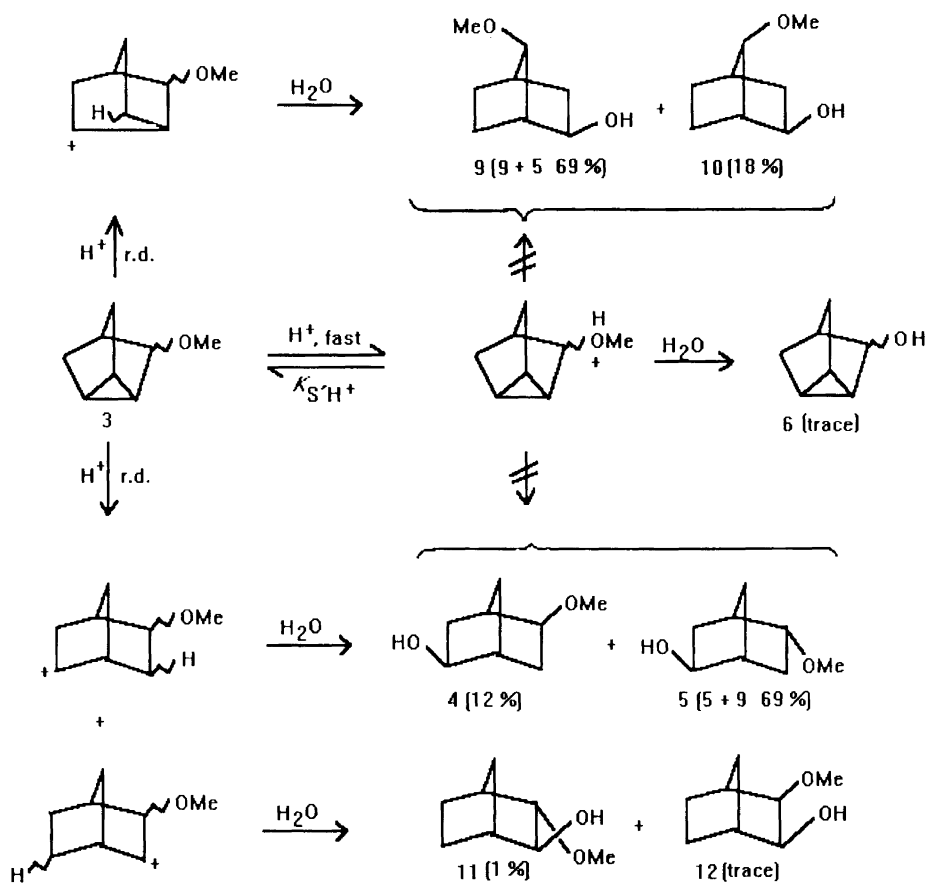
Scheme 1.

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 $HClO_4$(aq).

Substrate	$\Delta H^{\neq}$/kJ mol^{-1}	$\Delta S^{\neq}$/J mol^{-1} K^{-1}	k_H/k_D
1	110.9(11)	+2(3)	1.14(5)
2	107.9(4)	−2(1)	1.26(2)
3	105.5(1)	−2(1)	1.34(3)

Substrate	m'	p$K_{S'H^+}$	$m^{\neq} m^*$	α_A [a]	log(k_0/M^{-1} s^{-1})
1	0.99(2)	−2.05(5)	1.69(3)	0.94(7)	−5.086(11)
2	1.04(2)	−2.01(7)	1.71(2)	0.95(7)	−4.853(6)
3	1.05(3)	−1.94(7)	1.72(3)	0.95(7)	−5.044(8)

[a] $\alpha_A = m^{\neq} = m^{\neq} m^*/(1.80 \pm 0.10)$.[17]

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

The log k_a values ($k_a = k_\psi/c_{H^+}$) 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]

$$\log(c_{S'H^+}/c_S) - \log c_{H^+} = m'X_0 + pK_{S'H^+} \qquad (2)$$

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

$$\log k_\psi - \log c_{H^+} = m^{\neq} m^* X_0$$
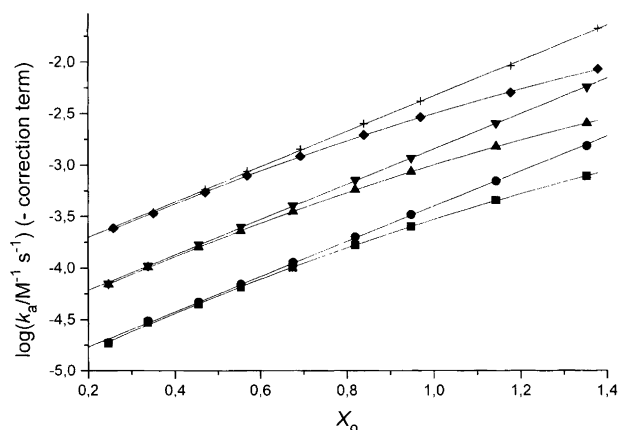$$- \log[1 + (c_{H^+}/K_{S'H^+})10^{m'X_0}] + \log k_0 \qquad (3)$$

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 $HClO_4$(aq) ($k_a = k_\psi/c_{H^+}$; 0.3 and 1.0 have been added to the log k_a 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/($c_S + c_{S'H^+}$)], has been calculated with eqn. (2) from the m' and p$K_{S'H^+}$ values in Table 2.

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

Equation (3) can be used to evaluate the values of parameters $m^{\neq} m^*$, m', $K_{S'H^+}$ (or p$K_{S'H^+}$) and k_0 (or log k_0) from the experimental values of k_ψ, 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] $m^{\neq}$ 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 p$K_{S'H^+}$ values (ca. −2.0) are equal to that (−2.1 ± 0.2)[19] measured for *cis*-1,2-dimethoxyethene in aqueous perchloric acid, but less negative than those measured for dimethyl and diethyl ethers in sulfuric acid.[7,8] The slope parameter $m^{\neq}$ or α_A ('excess acidity α'; av. 0.95 ± 0.07), which indicates the progress of proton transfer ($0 \leqslant \alpha \leqslant 1$) in the transition state of the Ad_E2 reaction,[16] 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 α_A values of the present work are, however, mostly higher than the α_A and α_I ('isotopic α') 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)],

$$\log k_\psi - \log c_{H^+} - \log[c_S/(c_S + c_{S'H^+})]$$
$$= m^{\neq} m^* X_0 + \log k_0 \qquad (4)$$

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

calculated with eqn. (2) from the m' and $pK_{S'H^+}$ values evaluated in Table 2. The corrected plots (Fig. 1) are strictly linear ($r = 0.9997-0.999\,94$); 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 subtrates (1–3) in 1 M $HClO_4$ (aq) are mainly methoxy-substituted exo-2-norborneols (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_2Cl_2,[10,24] as well as to the chloro-substituted exo-2-acetoxynorbornanes formed with the addition of. acetic acid to 3-chloronortricyclane under catalysis of sulfuric acid.[25] An exceptional product in the present work is, however, cyclopent-3-en-1-ylethanal (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.[26,27] [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)].[6] The amounts of products which would be formed via cleavage of the ether linkage, i.e. exo-5-hydroxy-2-norbornene and 3-nortricyclanol (6),[9] 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 $\Delta S^{\neq}$ 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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