JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2001; **14:** 854–858
DOI:10.1002/poc.421

Acid-catalyzed hydrolysis of bridged bi- and tricyclic compounds. XXXVIII—Kinetics and mechanisms of 1- and 3-nortricyclanols

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Received 17 April 2001; accepted 6 June 2001

epoc ABSTRACT: The disappearance of 1- and 3-nortricyclanols (**1-OH** and **2-OH**) in aqueous perchloric acid was followed by capillary GC at different temperatures and acid concentrations. **1-OH** is ca 1000 times more reactive than **2-OH**. The activation parameters, solvent deuterium isotope effects and parameters of excess acidity equations were measured and the products were studied. Both isomeric nortricyclanols react according to the Ad_E2 mechanism, i.e. the cyclopropane ring is protonated at the rate-determining stage of the reaction. The protonation causes, in the case of **1-OH**, an isomerization called homoketonization with 2-norbornanone as the only product and, in the case of **2-OH**, hydration, i.e. the formation of hydroxyl-substituted norbornyl cations, the fast attack of which by water produces several norbornanediols. Copyright © 2001 John Wiley & Sons, Ltd.
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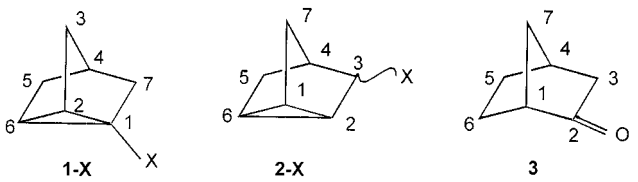
KEYWORDS: nortricyclanes; kinetics; acid catalysis; excess acidity; homoketonization; hydration; reaction mechanisms

INTRODUCTION

Recently, a mutual comparison of the kinetics and mechanisms of acid-catalyzed hydrolysis (hydration) of 1- and 3-X-substituted nortricyclanes or tricyclo[2.2,1.$0^{2,6}$]heptanes (**1-X** and **2-X**) was started at



our laboratory.[1] In the first case, when X = OAc, the disappearance rates and reaction mechanisms of the isomers were very similar, although the reaction was changed from $A_{AC}2$ ester hydrolysis[2] to the Ad_E2 or $A\text{-}S_E2$ hydration of the cyclopropane ring[3] with increasing acid concentration. Even the concentration [$c(HClO_4) \approx 6$ mol dm^{-3}] where the portions of the two reactions were equal was observed to be similar for both isomers.[1]

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This similarity is surprising, because **1-OAc** is a tertiary and **2-OAc** a secondary acetate. Evidently, the location of the acetoxyl group at a cyclopropane carbon in the tertiary isomer makes the normal $A_{AL}1$ ester hydrolysis in this case less probable.[2] 1-Nortricyclanol (**1-OH**) was considered to be a possible unstable intermediate product of the hydrolysis for **1-OAc**.[1,4] Therefore, it was chosen as the subject of additional studies on the comparison of 1- and 3-substituted nortricyclanes, when accordingly 3-nortricyclanol (**2-OH**) is the other isomer. Their disappearance rates were measured in aqueous perchloric acid at different temperatures and acid concentrations and in deuterioperchloric acid, and the products were analyzed in order to elucidate the reaction mechanisms.

EXPERIMENTAL

Materials. 1-Nortricyclanol (**1-OH**) was prepared by $LiAlH_4$ reduction of the corresponding acetate (**1-OAc**) in dry diethyl ether.[4] The substrate was unstable at room temperature, so it was stored in a freezer as a concentrated ether solution of the crude product. 3-Nortricyclanol (**2-OH**) was obtained by alkaline hydrolysis of **2-OAc**.[5] The purities by GC were 85% for **1-OH** [contains 7% of 2-norbornanone (**3**) and in total 8% of

three impurities] and 99.5% for **2-OH**. The substrates were identified from their ^{13}C NMR spectra [**1-OH** ($CDCl_3$, TMS) tentative assignments: C-1, 66.3; C-2 and C-6, 18.0; C-3 and C-5, 34.2; C-4, 32.6; and C-7, 38.9; **2-OH**;[6] and **3**[7]] and from GC–FTIR and/or GC–mass spectra.

Kinetic measurements. The disappearance of the substrates in aqueous perchloric acid was followed by GC (with a FFAP capillary column) using cyclohexanone (for **1-OH**) or 2-norbornanone (**3**, for **2-OH**) as the internal standard and dichloromethane as the extraction solvent.[1] The pseudo-first-order rate constants were obtained from the slopes of the strictly linear ($r = 0.9990$–0.99997) correlation of ln S_t vs $t(S_\infty = 0)$, where S_t is the ratio of the GC integrals of the substrate and the internal standard at time t. Each rate constant was measured twice, the values being equal to within at least 4% (average 1.4%) for both **1-OH** and **2-OH**. The impurities (8%, see above) did not affect the kinetic runs on **1-OH** by GC.

Product analyses. The only product of hydrolysis (and isomerization) of **1-OH** was identified by comparing its retention time with that of authentic 2-norbornanone (**3**). The formation of **3**-d_1 from **1-OH** was also observed in 0.25 M $DClO_4$ (D_2O) (1.3 h at ca 321 K; ca $10t_{1/2}$) by GC–MS. A ^2H NMR spectrum of the isolated (by CH_2Cl_2 extraction) **3**-d_1 was recorded in $CHCl_3$–$CDCl_3$ (9:1) with TMS-d_1 (not enriched according to D) as the internal reference and the spectrum was compared with those obtained by Nickon *et al.*[8]

About 0.2 g of **2-OH** was stirred magnetically with 50 cm^3 of 3 M $HClO_4$(aq.) for 0.5 h (ca $1t_{1/2}$) and 5 h ($\geq 10t_{1/2}$) at ca 318 K in a tightly stoppered Erlenmeyer flask. The solution was extracted several times with CH_2Cl_2 and the combined organic solution was neutralized and dried by allowing it to flow through anhydrous K_2CO_3. The solvent was evaporated almost totally and the residue was analyzed by GC, GC–FTIR and GC–MS, the components being mainly identified by comparing their spectra with those stored in the memories of the spectrometers.

RESULTS AND DISCUSSION

Rate constants, activation parameters and isotope effects

The rate constants of disappearance for 1- and 3-nortricyclanol (**1-OH** and **2-OH**) were measured in aqueous perchloric acid at different temperatures and acid concentrations and in deuterioperchloric acid. The pseudo-first-order rate constants (k_ψ) are shown in Table 1. **1-OH** is much more reactive than **2-OH** (990 times in 1.0 M $HClO_4$ at 298.2 K) and also clearly more reactive than 1-acetoxynortricyclane (**1-OAc**; 19 times).[1] Hence it is natural that **1-OH** could not be detected by GC in the hydrolysis of **1-OAc**. The rate constants measured for **2-OH** are in fair agreement with those measured earlier under similar conditions.[5] The activation parameters for **1-OH** were measured in 0.25 M $HClO_4$(aq.) and for **2-OH** in 1.0 and 5.4 M $HClO_4$(aq.). Their values are shown in Table 2 together with the solvent deuterium isotope effects. All values were calculated from the second-order rate constants [$k_a = k_\psi/c(HClO_4)$].

Table 1. Rate constants for disappearance of 1- and 3-nortricyclanol (**1-OH** and **2-OH**) in aqueous perchloric acid at different temperatures and acid concentrations and in deuterioperchloric acid

Substrate	T (K)	$c(HClO_4)$[a] (mol dm^{-3})	X_0[b]	k_ψ (10^{-4} s^{-1})[c]
1-OH	288.2	0.249		1.130 ± 0.005
	298.2	0.248		3.69 ± 0.05
	298.2	0.250		3.70 ± 0.07[d]
	298.2	0.249		1.360 ± 0.015[e]
	298.2	1.014		22.5 ± 0.3
	308.2	0.247		11.17 ± 0.07
	318.2	0.246		30.1 ± 0.6
2-OH	298.2	1.013		0.0227 ± 0.0003[d]
	318.2	1.005	0.257	0.336 ± 0.004
	328.2	1.000		1.148 ± 0.004
	338.2	0.994		3.546 ± 0.019
	348.2	0.988		10.59 ± 0.11
	288.2	5.459		2.252 ± 0.011
	298.2	5.427		8.39 ± 0.12
	298.2	5.427		8.1 ± 0.4[d]
	308.2	5.388		26.9 ± 0.4
	318.2	1.510	0.362	0.723 ± 0.004
	318.2	2.002	0.467	1.384 ± 0.004
	318.2	2.361	0.549	2.184 ± 0.008
	318.2	2.953	0.699	4.267 ± 0.025
	318.2	3.488	0.856	7.975 ± 0.026
	318.2	3.939	1.007	13.64 ± 0.08
	318.2	4.383		14.15 ± 0.07[e]
	318.2	4.381	1.173	22.97 ± 0.11
	318.2	4.904	1.392	43.8 ± 0.4
	318.2	5.358	1.602	74.3 ± 0.6

[a] Temperature corrected.
[b] Excess acidity, temperature corrected.[10,11]
[c] Error limits are standard deviations.
[d] Calculated from the activation parameters (Table 2).
[e] Measured in $DClO_4$ (D_2O).

The slightly or moderately negative entropies of activation, -5 to -27 J K^{-1} mol^{-1} at 298 K, and the isotope effects, $k_H/k_D = 1.62$–2.72, greater than unity are typical of the rate-determining protonation of the cyclopropane ring (Ad_E2 mechanism; Schemes 1 and 2).[6] In the case of **2-OH**, the decrease in $\Delta S^{\neq}$ from -5 to -27 J K^{-1} mol^{-1} with increasing acid concentration (1.0–5.4 M) seems normal for the Ad_E2 mechanism.[9] Thus, $\Delta S^{\neq}$, -27 J K^{-1} mol^{-1}, for **1-OH** in 0.25 M acid is unexpectedly negative. The reason for this is not known.

Table 2. Parameters of activation and solvent deuterium isotope effects at 298 K (unless noted otherwise) and parameters of the excess acidity equation [Eqn. (3)] at 318 K for the hydrolysis of 1- and 3-nortricyclanol (**1-OH** and **2-OH**) in $HClO_4$(aq.), with standard deviations

Substrate	$c(LClO_4)$[a] (mol dm^{-3})	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta S^{\neq}$ (J mol^{-1} K^{-1})	k_H/k_D
1-OH	0.25	81.2 ± 0.7	-27 ± 3	2.72 ± 0.07
2-OH	1.01	103.8 ± 0.4	-5.0 ± 1.2	
	5.43	86.9 ± 1.8[b]	-27 ± 6[b]	
	4.38			1.62 ± 0.02[c]
	m'	$pK_{S'H}{}^{+}$	$m^{\neq}\ m^*$	α_A[d]	$\log(k_0/M^{-1}\ s^{-1})$
2-OH	0.97 ± 0.07	-2.04 ± 0.26	1.52 ± 0.08	0.84 ± 0.05	-4.85 ± 0.03

[a] L = H or D.
[b] The Arrhenius plot is slightly curved; however, $r = 0.9996$ for the linear regression.
[c] 318.2 K.
[d] $\alpha_A = m^{\neq}\ m^*/1.80$.[10,13]

The excess acidity method

The excess acidity theory[10,11] was applied to the rate constants measured for the disappearance of 3-nortricyclanol (**2-OH; 1-OH** being too reactive for the corresponding measurements) at different acid concentrations at one temperature, 318.2 K (Table 1). The rate constant should follow the equation[10,11]

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

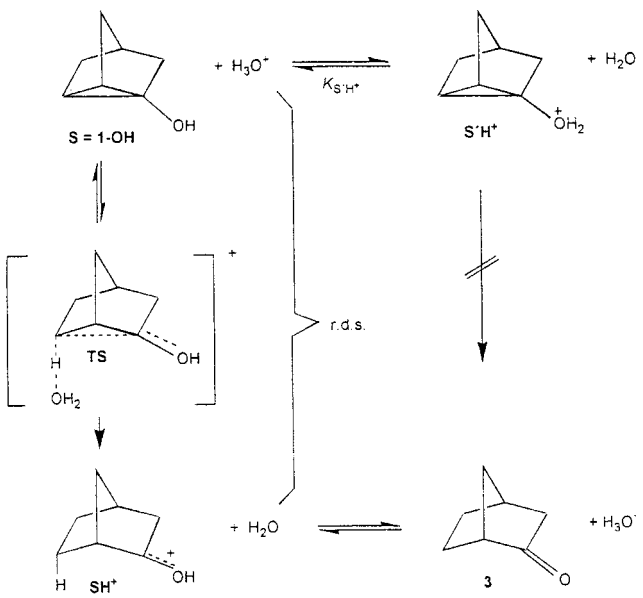
if no protonation of the substrate other than the rate-determining step on the cyclopropane ring occurs (the 'pure' Ad_E2 mechanism), and the equation[1,12]

$$\log k_\psi - \log[c_S/(c_S + c_{S'H^+})] - \log c_{H^+} = m^{\neq} m^* X_0 + \log k_0 \qquad (2)$$

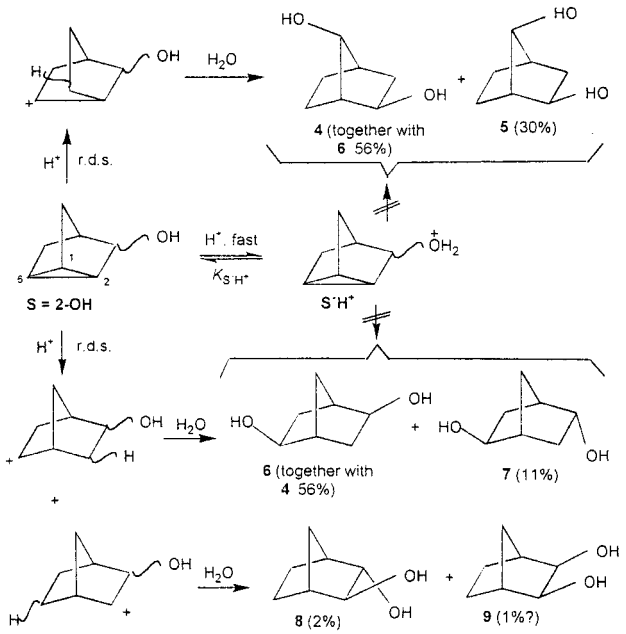
if the hydroxyl substituent of the substrate S is also protonated in a fast equilibrium producing $S'H^+$ (the 'impure' Ad_E2 mechanism; Scheme 2).

In the above equations, k_ψ is the pseudo-first-order rate constant measured in aqueous acid with concentration c_{H^+} [$= c(HClO_4)$] and excess acidity X_0 (c_{H^+} and X_0 are corrected according to temperature);[10,11] $m^{\neq}$ is the slope parameter indicative of the character of the transition state and m^* is the slope parameter dependent on the site of proton attack (the cyclopropane ring in this case, when $m^* = 1.80 \pm 0.10$);[11,13] k_0 is the medium-independent rate constant of the rate-determining step (r.d.s. in Scheme 2); and c_S and $c_{S'H^+}$ are the concentrations of the unprotonated substrate and of the substrate protonated on the substituent, respectively.

In the case of substrate **2-OH**, the hydroxyl group is



Scheme 1



Scheme 2

partly protonated in the moderately concentrated acids [$c(HClO_4)$ = 1.0–5.4 M] used in the present work. Thus, the plot log k_a vs X_0 ($k_a = k_\psi/c_{H^+}$) obeying Eqn. (1) is not linear (Fig. 1). In order to estimate the protonation correction term, $-\log[c_S/(c_S + c_{S'H})]$, of Eqn. (2), the equation is changed to a non-linear form:[1,12,14]

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

with the excess acidity equation:[10,11]

$$\log(c_{S'H^+}/c_S) - \log c_{H^+} = m'X_0 + pK_{S'H^+} \quad (4)$$

derived for the protonation equilibrium (Scheme 2). In these equations, m' is the slope parameter indicative of the protonation of the hydroxyl group and $K_{S'H^+}$ the thermodynamic dissociation constant of the substrate protonated on the substituent. Non-linear least-squares minimization can be used for the evaluation of the four parameters of Eqn. (3), i.e. $m^{\neq} m^*$, $K_{S'H^+}$ (or $pK_{S'H^+}$), m' and k_0 (or log k_0), by iteration from the experimental values of k_ψ, c_{H^+} and X_0 (Table 1) and from the estimated approximate values of the parameters. The iterated best values of the parameters are given in Table 2.

The excess acidity parameters for the Ad_E2 hydration of 3-nortricyclanol (**2-OH**) seem reasonable. The parameters dependent on the protonation of the hydroxyl group ($m' = 0.97$ and $pK_{S'H^+} = -2.0$ at 318 K) are very close to those measured earlier for other alcohols.[9,12,15] The combined parameter $m^{\neq} m^*$ consists of two terms, the latter being dependent on the protonation site (in this case a cyclopropane ring) and the former on the character of the transition state of the Ad_E2 mechanism, i.e. according to Kresge and co-workers,[16,17] on the progress of proton transfer from a hydroxonium ion (H_3O^+) to the substrate at the transition state ($0 \leq m^{\neq} \leq 1$; $m^{\neq} = \alpha_A$, i.e. the excess acidity Brönsted α). Thus $\alpha_A = m^{\neq} m^*/1.80 = 0.84 \pm 0.05$, which is a typical value for the protonation of nortricyclanes in $HClO_4$(aq.) and in excellent agreement with the isotopic Brönsted α ($\alpha_1 = 0.85 \pm 0.02$) measured for **2-OH** in 0.1 M $LClO_4$ (L_2O) (L = H or D) at 348.2 K.[18]

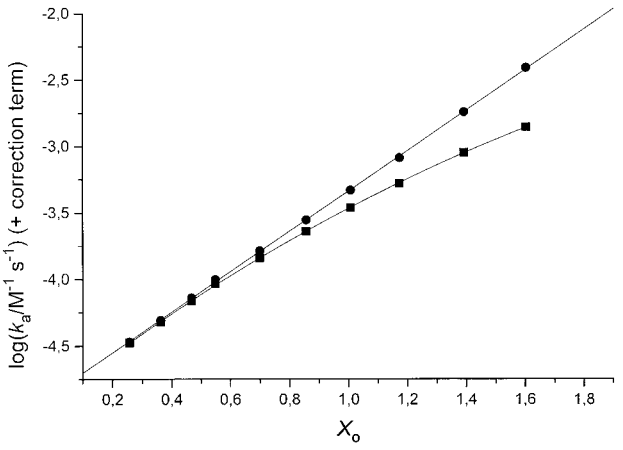


Figure 1. Excess acidity plots [Eqns (1) and (2)] for the Ad_E2 hydration of 3-nortricyclanol (**2-OH**) in $HClO_4$(aq.) at 318.2 K: (■) Eqn. (1); (●) Eqn. (2). The correction term, $-\log[c_S/(c_S + c_{S'H^+})]$, was calculated with Eqn. (4) from the m' and $pK_{S'H^+}$ values in Table 2

Now the correction term, $-\log[c_S/(c_S + c_{S'H^+})]$, of Eqn. (2) can be calculated by Eqn. (4) from the values of m' and $pK_{S'H^+}$ in Table 2. If the left-hand side of Eqn. (2) vs X_0 is drawn, a strictly linear ($r = 0.9992$) plot is obtained (Fig. 1). The difference between the two plots in Fig. 1 [according to Eqns (1) and (2)] shows that the effect of protonation of the hydroxyl oxygen is marked on the hydration rate of the cyclopropane ring of **2-OH**.

Hydrolysis products

According to the product analyses (see Experimental), the only product of hydrolysis for 1-nortricyclanol (**1-OH**) is 2-norbornanone (**3**), which was also slowly formed from **1-OH** during storage. The process (Scheme 1), called homoketonization,[4,8,19] is comparable with the keto–enol tautomerism,[20] both isomerizations being catalyzed by acids and bases. The mass spectrum of **3** formed in 0.25 M $DClO_4$ (D_2O) shows that it contains one deuterium atom per molecule and the ^2H NMR spectrum indicates that ca. 90% of deuterium is situated at the *endo*-6 position ($\delta_D = 1.31$) and ca. 8% at the *exo*-6 position ($\delta_D = 1.60$; besides 2% found at 1.84). The *exo/endo* ratio of 8:92 is in excellent agreement with that observed by Nickon *et al.*[8] for the hydrolysis of 1-acetoxynortricyclane (**1-OAc**) in D_2SO_4–DOAc–D_2O ([DOAc]:[D_2O] = 1:1 or 2:1) and shows that the rate-determining deuteration (protonation) occurs dominantly at C-2 or C-6 by retention in aqueous acids (Scheme 1). The formation of a thermodynamically stable oxocarbenium ion ($\mathbf{SH}^+$) is the probable reason for the relatively high protonation rate of **1-OH** [k_ψ(**1**−**OH**)/k_ψ(**2**−**OH**) ≈ 1000; see Table 1).

3-Nortricyclanol (**2-OH**) in $HClO_4$(aq.) probably produces five or six isomeric norbornanediols (**4**–**9**; Scheme 2), the proportions of which do not vary markedly within 1–10 half-lives of the substrate. Attemps were made to identify them by GC (retention times), by GC–FTIR (the isomers could not be separated, but two ν_{OH} absorptions were detected: 3653 cm^{-1} being typical of the free and 3601 cm^{-1} of the hydrogen-bonded hydroxyl group; cf. ν_{OH} = 3657 cm^{-1} for **2-OH**) and by GC–MS [the molecular ion ($M^{+\cdot}$ = 128) was sometimes hard to detect owing to the easy elimination of one or two water molecules]. The retention times and spectra were also compared with those recorded for six methoxynorborneols formed in the hydration of 3-methoxynortricyclane (**2-OMe**).[21] The approximate amounts of the

considered isomeric norbornanediols are shown in Scheme 2. Accordingly, the C-1—C-6 edge of the cyclopropane ring opposite to the 3-substituent is cleaved most easily, producing mainly 2,7-norbornanediols (**4** and **5**), in agreement with earlier observations.[6,21–23]

Acknowledgements

We are grateful to Dr Robin A. Cox for a copy of Ref. 11 and to Miss Kirsti Wiinamäki, Dr Martti Dahlqvist, Mr Petri Tähtinen and Mr Jaakko Hellman for recording the GC–mass, GC–FTIR, ^{2}H NMR and ^{13}C NMR spectra, respectively.

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