

# Acid-catalyzed Hydrolyses of Bridged Bi- and Tricyclic Compounds.

## VII. Kinetics of 2-Methyl-2-norbornenols in Isotopically Different Waters \*

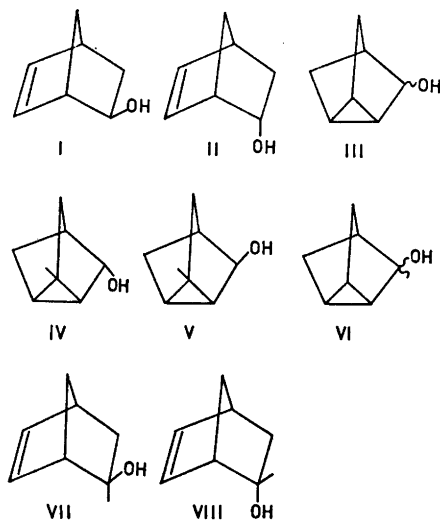
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Solvent deuterium isotope effects have been measured for the hydrolysis of 2-methyl-*exo*-2-norbornenol (VII) and 2-methyl-*endo*-2-norbornenol (VIII) in deuterium oxide-protium oxide mixtures. The data are best in accordance with the *A*-1 hydrolysis, in which a proton (deuteron) rapidly attacks the hydroxylic oxygen of the substrate and the rate-determining departure of a water molecule produces a carbocation, which yields, by reaction with the solvent, VII and rearranged alcohols (mainly 1-methyl-3-nortricyclanol). Besides, rate-determining protonation (deuteration) of the double bond occurs in the hydrolysis of VIII. Activation parameters support the same mechanism.

In recent papers <sup>1-4</sup> kinetics of acid-catalyzed hydrolysis of two epimeric 2-norbornenols (I and II) and four 3-nortricyclanol (III–VI) was discussed. Marked solvent effects,<sup>1</sup> slightly negative activation entropies,<sup>1,4</sup> and solvent deuterium isotope effects ( $k_D/k_H < 1$ )<sup>1,3,4</sup> are in accordance with the rate-determining protonation of the double bond of I and II and of the three-membered carbon ring of III–V (*A*-*S*<sub>E</sub>2 mechanism).<sup>5</sup> A slight general acid catalysis occurring in the hydration of I and II also supports the same mechanism.<sup>2</sup> In the case of III no general acid catalysis was observed in phosphoric acid-dihydrogen phosphate buffers (implying an *A*-1 mechanism), but its verification (< 10 % of the total disappearance rate) beside the dominating hydronium ion catalysis may have failed owing

to experimental inaccuracy.<sup>3</sup> The results are in agreement with the transition state structures which closely resemble the carbocation intermediates (*cf.* hydration of simple olefins).<sup>5</sup> The protonation of the hydroxylic group was, however, observed in the hydration of VI ( $k_D/k_H = 2.1$ ,  $\Delta S^\ddagger = 32 \text{ J mol}^{-1} \text{ K}^{-1}$ ) and to some extent also in the hydrolysis of I yielding the rearranged tricyclic product III ( $k_D/k_H \approx 1.6$ ).<sup>1,3</sup> In this work acid-catalyzed hydrolysis of two epimeric tertiary alcohols, 2-methyl-*exo*-2-norbornenol (VII) and 2-methyl-*endo*-2-norbornenol (VIII), was investigated in protium oxide-deuterium oxide mixtures under catalysis of perchloric acid. The corresponding



\* Part VI, see Ref. 4.

study concerning 3-methyl-3-nortricyclanol (VI) is under way.

## EXPERIMENTAL

2-Norbornenone was prepared by hydrolyzing the Diels-Alder adduct of cyclopentadiene and 2-chloroacrylonitrile in alkaline dimethyl sulfoxide.<sup>6</sup> The Grignard reaction between 2-norbornenone and methyl magnesium iodide produced 2-methyl-*endo*-2-norbornenol,<sup>7</sup> which also contained 8–10% of the *exo* alcohol. The isomers were separated by repeated distillations through an efficient column. The purity of the *endo* alcohol was *ca.* 99% and that of the *exo* alcohol *ca.* 97% (3% *endo* alcohol) as analyzed by GLC. The alcohols were identified on the basis of their IR and NMR spectra.<sup>7–9</sup>

Deuterium oxide was from Norsk Hydro (99.8 atom-% of D) and deuterioperchloric acid from E. Merck AG (*ca.* 70% of DC1O<sub>4</sub> in D<sub>2</sub>O, >99 atom-% of D).

Gas-chromatographic methods used for measuring the disappearance rates of the substrates and for evaluating the formation rates of unstable intermediate products (B) in consecutive reactions A→B→C (when A also yields other unstable products) were described earlier.<sup>10</sup>

## RESULTS AND DISCUSSION

The acid-catalyzed hydrolysis of 2-methyl-*exo*-2-norbornenol (VII in Scheme 1) produces in H<sub>2</sub>O–D<sub>2</sub>O mixtures containing 0.1 M LClO<sub>4</sub> (L=H,D) 1-methyl-3-nortricyclanols (*trans* and *cis* isomers, IV and V, in an approximate ratio of 14/1)<sup>11</sup> as major intermediate products, which are hydrated by solvent water to methyl-substituted norbornanediols (these were not identified).<sup>4</sup> Two unknown minor intermediate products were also

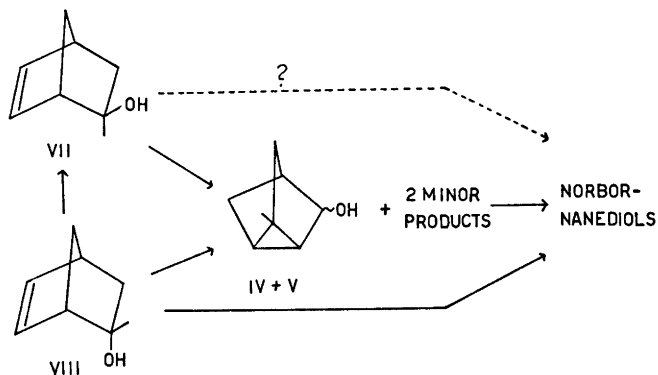
observed to form; their retention times were between those of VII and VIII when an FFAP column was employed for the GLC analyses. The formation of elimination products, diolefins, could not be detected.

The hydrolysis of 2-methyl-*endo*-2-norbornenol (VIII in Scheme 1) yields the same products as the *exo* isomer, but also VII is a probable intermediate product (a small GLC peak with the proper retention time could be seen), which, however, transforms so fast into IV+V (they had the same retention times) and into minor products that its concentration remains small. (Even half of VIII may hydrolyze *via* VII according to rough iterative calculations, which evaluated  $k_A$  in the consecutive

reactions VIII  $\xrightarrow{k_A}$  VII  $\xrightarrow{k_B}$  IV+V+ minor products. The formation rate of VII is roughly included in the formation rate of IV+V, because  $k_A \ll k_B$  and the portion of the unknown products yielded by VII is small.)

The disappearance rates of VII and VIII and the formation rates of IV+V from VII and VIII are presented in Table 1. (In the iterative calculations of the formation rates of IV+V, the disappearance rate of the *trans* alcohol, IV, was used,<sup>4</sup> since it is the main product<sup>11</sup> and the disappearance rates of V differ only slightly (10–20%) from those of IV.)<sup>4</sup>

The difference between the disappearance rates and the formation rates presented in Table 1 represents the part of reaction which occurs either *via* other intermediate products than IV and V or produces directly norbornanediols. In the hydrolysis of VII, these differences (<10% of the total rate) can be



Scheme 1.

Table 1. Total disappearance rates ( $k_{\text{tot}}$ ) of 2-methyl-*exo*- and -*endo*-2-norbornenols (VII and VIII) and formation rates ( $k_f$ ) of 1-methyl-3-nortricyclanols (IV and V) from VII and VIII in solutions of perchloric acid (0.10 M) in protium oxide-deuterium oxide mixtures ( $n$ = deuterium atom fraction) at 75 °C.

Substrate	$n$	$k_{\text{tot}}/10^{-5} \text{ s}^{-1}$	$k_f/10^{-5} \text{ s}^{-1}$	$k_f/k_{\text{tot}}$
VII	0.0	311 ± 8	298 ± 3	0.96
	0.2	369 4	341 5	0.92
	0.4	437 6	408 5	0.93
	0.6	518 6	452 7	0.87
	0.8	633 8	589 8	0.93
	1.0	737 9	688 18	0.93
VII-OAc <sup>a</sup>	0.0	10.1 ± 0.2		
	1.0	24.8 0.5		
VIII	0.0	7.17 ± 0.03	3.25 ± 0.11	0.45
	0.2	7.61 0.05	4.17 0.06	0.55
	0.4	8.42 0.06	5.16 0.09	0.61
	0.6	9.66 0.08	6.24 0.13	0.65
	0.8	11.12 0.06	7.45 0.17	0.67
	1.0	12.88 0.04	9.20 0.16	0.71

<sup>a</sup> 2-Methyl-*exo*-2-norbornenyl acetate, measured at 25 °C.

Table 2. Observed and calculated (eqn. 2) solvent deuterium isotope effects on the total disappearance rates (tot) of VII and VIII, on the formation rates (f) of IV + V from VII and VIII, and on the differences (d) of the two rates in the D<sub>2</sub>O-H<sub>2</sub>O mixtures (0.1 M LiClO<sub>4</sub>) at 75 °C.

Substrate	$n$	$(k_n/k_H)_{\text{tot}}$		$(k_n/k_H)_f$		$(k_n/k_H)_d^b$
		obs. <sup>a</sup>	calc.	obs.	calc.	obs.
VII	0.0	1.00	1.00	1.00		
	0.2	1.19	1.17	1.14		
	0.4	1.40 <sub>5</sub>	1.37	1.37		
	0.6	1.67	1.64	1.52		
	0.8	2.03 <sub>5</sub>	1.98	1.98		
	1.0	2.37	2.43	2.31		
VII-OAc <sup>c</sup>	1.0	2.46				
VIII	0.0	1.00	1.00	1.00	1.00	1.00
	0.2	1.06	1.10	1.28	1.21	0.82
	0.4	1.17	1.22	1.59	1.47 <sub>5</sub>	0.83
	0.6	1.35	1.37	1.92	1.82	0.87
	0.8	1.55	1.55	2.29	2.28	0.94
	1.0	1.80	1.77	2.83	2.90	0.94

<sup>a</sup> The maximum errors calculated from the standard errors of the rate coefficients in Table 1 are 1–5 % (av. 2.5 %). <sup>b</sup>  $(k_n/k_H)_d = (k_{\text{tot}} - k_f)/n / (k_{\text{tot}} - k_f)_H$ . <sup>c</sup> 2-Methyl-*exo*-2-norbornenyl acetate, measured at 25 °C.

explained by the formation of the minor products (and experimental error), but in the case of VIII the differences varying steadily with deuterium fraction (55 % in H<sub>2</sub>O and 29 % in D<sub>2</sub>O) seem too large to be explained in

this way. (Rough iterative calculations were performed to evaluate the formation rates of the minor products by setting their disappearance rates to zero. In this way their portions were estimated to be a few per cent. The

increase in the formation rates with the increasing deuterium fraction was detected.)

The isotope effects (Table 2) measured on the differences of the disappearance rates and the formation rates are larger than unity in the case of VII (very rough values, not listed in Table 2), but they are regularly a little smaller than unity in the case of VIII. These results agree with the idea that in the hydrolysis of VII the difference is due to the formation of the minor rearranged products, but in the hydrolysis of VIII, in addition to the formation of the minor products, a marked part of the reaction yields directly norbornanediols (see Scheme 1) by hydration of the homoallylic double bond. The isotope effect on this kind of addition reaction was measured to be 0.5–0.65 in the hydration of the secondary 2-norbornenols (I and II).<sup>1,3</sup> Separation of the reaction occurring *via* the minor products from the reaction yielding directly the norbornanediols was not attempted owing to inaccuracy in the experimental data, but an increase in the rates of the former reaction occurring with increasing deuterium fraction (see above) causes a decrease in the isotope effects of the latter reaction. Thus the  $k_D/k_H$  value for the latter will be fairly similar to those observed for the  $A-S_E2$  hydration of substrates I–V.<sup>1,3,4</sup> The hydration of the double bond of *exo* alcohol VII is probably an insignificant part of its hydrolysis (*cf.* hydration rates of I and II, Ref. 1).

The deuterium isotope effects observed (Table 2) can also be employed for discussing the reaction mechanism of the change of VII and VIII to the intermediate products. The total disappearance rates have been considered in the case of VII and the formation rates of IV+V have been included in the case of VIII unless otherwise noted. The isotope effects ( $k_D/k_H=2.4-2.8$ ) are similar to that measured for the hydrolysis of 2-methyl-*exo*-2-norbornenyl acetate (Table 2), which hydrolyzes *via* an  $A_{AL}1$  mechanism<sup>10</sup> (rapid equilibrium in the protonation of an oxygen atom before the rate-determining unimolecular reaction).<sup>12</sup> Thus the protonation of the hydroxylic oxygen is evident.

The total solvent deuterium isotope effect,  $k_n/k_H$ , for proton (deuteron) transfer reactions in aqueous medium with deuterium

atom fraction  $n$  can be expressed by eqn. (1).<sup>13,14</sup>

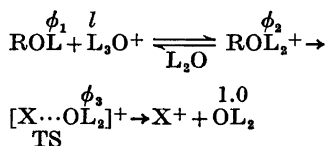
$$\frac{k_n}{k_H} = \frac{\prod (1-n+n\phi_j)}{\prod (1-n+n\phi_1)} \exp[\Delta(\Delta G^\ominus)/RT] \quad (1)$$

In the equation  $\phi_1$  is the fractionation factor of an exchangeable proton (deuteron) in the initial state,  $\phi_j$  is that in the transition state, and  $\Delta(\Delta G^\ominus)$  represents the standard free energy of transfer for the transition state from light to mixed water minus that for the initial state transferred in the same way.

Eqn. (1) can be transformed to eqn. (2) in the case of an  $A-1$  mechanism, if the rate-

$$\frac{k_n}{k_H} = \frac{(1-n+n\phi_3)^2}{(1-n+n\phi_1)(1-n+nl)^2} \quad (2)$$

determining step is assumed to be the elimination of a water molecule from the protonated substrate (fractionation factors are presented above the formulas):



or to eqn. (3), if the rate-determining step is assumed to be

$$\frac{k_n}{k_H} = \frac{1}{(1-n+n\phi_1)(1-n+nl)^2} \quad (3)$$

a rearrangement of the intermediate  $X^+$  into another intermediate  $Y^+$  with no exchangeable protons (deuterons) in either of them. Besides, we must assume that the structure of the hydronium ion is  $L_3O^+$  ( $L=H,D$ ) and that the free energy term  $\Delta(\Delta G^\ominus)=0$  (*cf.* Ref. 3). The  $A-2$  and  $A-S_E2$  mechanisms (slow proton transfer at the hydroxylic oxygen in the latter case) have been excluded since the former is improbable due to the activation entropies (see later) and marked solvent effects<sup>10,11</sup> and since the latter did not give any agreement between the observed and calculated isotope effects (*cf.* Ref. 15).

Eqn. (2) has been used for calculation of the values of the fractionation factor  $\phi_3$  ( $\phi_1$  was fixed as unity, *i.e.* the same as that of water, and the fractionation factor of the lyonium ion,  $l$ , was fixed as 0.72)<sup>3</sup> by search-

ing the best fits between the observed and calculated isotope effects by the method of least squares. Factor  $\phi_3$  is  $0.952 \pm 0.002$  for VII and  $1.041 \pm 0.006$  for VIII;  $0.813 \pm 0.002$  was calculated for the total disappearance rate of VIII. The calculated isotope effects are presented in Table 2 and they are regularly some per cent smaller than the observed ones in mixed water (*i.e.*  $0.2 \leq n \leq 0.8$ ) in the hydrolysis of VII and in the formation reaction of IV+V from VIII (the occurrence of VII as a short-living intermediate product may cause an error in the latter case), but some per cent larger than the observed ones in the total disappearance of VIII. In the hydration of 3-methyl-3-nortricyclanol (VI) under the same conditions, the calculated (eqn. 2) isotope effects are also regularly some per cent smaller than the observed ones ( $\phi_3 = 0.902$ ).<sup>15</sup> Hence, this behavior is probably "normal" and is possibly due to several approximations made.<sup>3,13,14</sup> That the value of  $\phi_1$  is some per cent larger or smaller than unity has no marked effect on the value of  $\phi_3$ . The behavior observed in the total disappearance of VIII is evidently "abnormal", agreeing with two competing reactions men-

tioned; thus the fractionation factor 0.813 has no meaning. The  $\phi_3$  value of VII seems reasonable ( $\phi_2 \lesssim \phi_3 \lesssim \phi_{L,HO}$  or  $0.72 \lesssim \phi_3 \lesssim 1.0$ ), but that of VIII (1.041) is possibly too large due to experimental inaccuracy.

The fractionation factor of the hydroxylic hydrogen of the substrates ( $\phi_1$ ) can be calculated from eqn. (3) in the  $H_2O-D_2O$  mixtures, if the transition states do not contain exchangeable protons (deuterons). In the hydrolysis of VII,  $\phi_1$  increases from 1.01 to 1.13 rather regularly with increasing deuterium content of the medium and in the formation of IV+V from VIII the increase is still more marked (from 0.64 to 0.95), which makes this mechanism improbable. The magnitude of  $\phi_1$  for VII, however, seems quite reasonable ( $\approx 1 = \phi_{L,HO}$ ).

The solvent deuterium isotope effects thus agree best with the A-1 mechanism in which elimination of a water molecule from the substrate, protonated at the hydroxylic oxygen, is the rate-determining step of the reaction. The value of  $\phi_3$  is probably a measure of the degree of departure of the water molecule (*i.e.*  $\phi_3 \approx 0.72$  in the beginning and  $\phi_3 \approx 1$  in the end). The values of  $\phi_3$  measured for

Table 3. Total disappearance rates ( $k_a^{\text{tot}}$ ), formation rates of IV+V ( $k_a^f$ ), and their differences ( $k_a^d$ ) for the hydrolysis of 2-methyl-2-norbornenols in 1.00 M perchloric acid, and the activation parameters at 25 °C.

Substrate	$t/^\circ\text{C}$	$k_a^{\text{tot}}/10^{-5} \text{ M}^{-1} \text{ s}^{-1}$	$k_a^f/10^{-5} \text{ M}^{-1} \text{ s}^{-1}$	$k_a^d/10^{-5} \text{ M}^{-1} \text{ s}^{-1} \text{ }^a$
VII	25	13.2 $\pm$ 0.7 <sup>b</sup>	12.8 $\pm$ 0.8 <sup>b</sup>	0.4 $\pm$ 1.1 <sup>c</sup>
	25	13.2 $\pm$ 0.3	12.5 $\pm$ 0.2	0.7 $\pm$ 0.4
	35	54.2 $\pm$ 0.4	51.7 $\pm$ 1.2	2.5 $\pm$ 1.3
	45	231 $\pm$ 3	209 $\pm$ 5	22 $\pm$ 6
	55	737 $\pm$ 12	662 $\pm$ 13	75 $\pm$ 18
$\Delta H^\ddagger/\text{kJ mol}^{-1}$		107.6 $\pm$ 1.1	104.4 $\pm$ 2.7	
$\Delta S^\ddagger/\text{J mol}^{-1} \text{ K}^{-1}$		42 $\pm$ 7	31 $\pm$ 9	
VIII	25	0.125 $\pm$ 0.002 <sup>b</sup>	0.033 $\pm$ 0.002 <sup>b</sup>	0.097 $\pm$ 0.003 <sup>b</sup>
	35	0.617 $\pm$ 0.003	0.185 $\pm$ 0.007	0.432 $\pm$ 0.008
	45	2.72 $\pm$ 0.01	1.06 $\pm$ 0.05	1.66 $\pm$ 0.05
	55	10.98 $\pm$ 0.11	4.58 $\pm$ 0.15	6.40 $\pm$ 0.19
	65	41.8 $\pm$ 0.4	20.3 $\pm$ 1.3	21.5 $\pm$ 1.4
$\Delta H^\ddagger/\text{kJ mol}^{-1}$		119.3 $\pm$ 0.4	132.5 $\pm$ 2.1	110.9 $\pm$ 1.0
$\Delta S^\ddagger/\text{J mol}^{-1} \text{ K}^{-1}$		42 $\pm$ 1	75 $\pm$ 6	11 $\pm$ 3

<sup>a</sup> Errors are calculated from eqn.  $\delta_a = (\delta_{\text{tot}}^2 + \delta_f^2)^{1/2}$ . <sup>b</sup> Calculated from the activation parameters. <sup>c</sup>  $(k_a^d)_{\text{calc.}} = (k_a^{\text{tot}})_{\text{calc.}} - (k_a^f)_{\text{calc.}}$

VII and VIII are thus in accordance with the Hammond principle<sup>16</sup> which states that the structure of the transition state at an energetically higher level is closer to that of an intermediate (formed in the rate-determining step) than is the structure of the transition state at an energetically lower level. However, the fact that  $\phi_s$  measured for one *exo* substrate is smaller than that measured for the corresponding *endo* substrate may be fortuitous and necessitates more studies. The carbocation  $X^+$  formed produces VII (also in the hydrolysis of VII) and rearranged products (mainly IV and V) in its reaction with the solvent.

The activation parameters have been measured for the hydrolyses of the substrates in aqueous 1.00 M perchloric acid. The results are presented in Table 3. The activation parameters calculated for the total disappearance rates are typical of the *A*-1 mechanism as are also those calculated for the formation of IV+V. However, the activation entropy computed for the difference of the former two rates in the case of VIII is only slightly positive and the subtraction of the formation rates of the minor products from the difference of the total disappearance rates of VIII and the formation rates of IV+V easily makes the activation entropy slightly negative, which is typical of the *A*- $S_E2$  hydration of the double bond and the three-membered carbon ring.<sup>1,4</sup>

The *exo/endo* rate ratios calculated for the formation rates of IV+V from VII and VIII are *ca.* 80 in  $D_2O-H_2O$  mixtures (0.1 M  $LCIO_4$ ) at 75 °C and *ca.* 390 in aqueous perchloric acid (1 M) at 25 °C, which are typical of the solvolysis reactions of 2-norbornyl and 2-norbornenyl esters.<sup>17,18</sup>

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