Acta Chemica Scandinavica A 35 (1981) 139–143

Acid-catalyzed Hydrolyses of Bridged Bi- and Tricyclic Compounds. XVIII. Kinetics of Isomerization (Fragmentation) of 6-Methyl- and 2,6-Dimethyl-*endo*-2-norbornenols to (3-Methylcyclopent-3-enyl)acetaldehyde and -acetone

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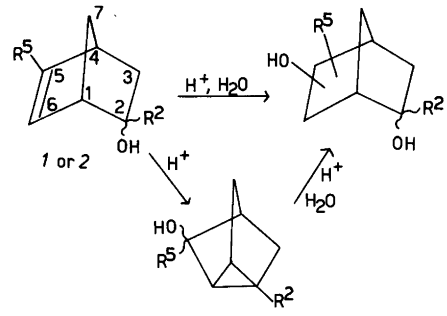
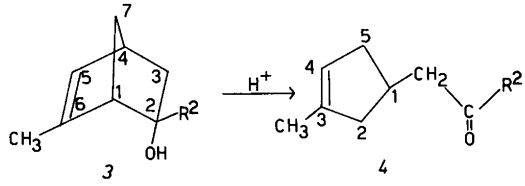
A replacement of the 6-hydrogen by methyl changes the mainly hydration reaction of *endo*-2-norbornenol and 2-methyl-*endo*-2-norbornenol to an isomerization reaction (fragmentation), which produces (3-methylcyclopent-3-enyl)ethanal and -2-propanone, respectively. The reaction rate increases by a factor of 2×10^4. In both the reactions the rate-determining stage is, however, the same, the protonation of the 5,6-double bond (A-S_E2 mechanism). The solvent deuterium isotope effects (k_D/k_H 0.54 to 0.58) and reaction rates (30 % smaller than those measured for the corresponding 5-methyl-2-norbornenols) support this mechanism. The activation entropies (21 to 27 J mol^{-1} K^{-1}) are somewhat more positive than values typical of the $A-S_E2$ mechanism.

In our preceding paper[1] the effect of a 5-methyl group on the hydration rates of the 5,6-double bond of *exo*- and *endo*-2-norbornenols (*1* and *2*, $R^2=H$ or Me, $R^5=H$ or Me; $k_a^h(5\text{-Me})/k_a^h(5\text{-H}) = 3 \times 10^4$ to 7×10^4) was found to be similar to the effect of methyl substitution at the ethylenic bond on the hydration rate of aliphatic and alicyclic alkenes. This agrees with the protonation of the 6-carbon (Markovnikov rule) from the *exo* direction. The solvent deuterium isotope effects (k_D/k_H 0.5 to 0.6) indicate that the protonation is the rate-determining stage of the reaction ($A-S_E2$ mechanism). The products are mainly norbornanediols. Isomerization to tricyclic alcohols, however, competes with the hydration (Scheme 1).



Scheme 1.

A replacement of the 6-hydrogen by methyl, however, seems to eliminate the hydration reaction and yield unsaturated monocyclic carbonyl compounds (Scheme 2). In the presented report the



Scheme 2.

syntheses and the kinetics and the product analyses of the hydrolysis of 6-methyl- and 2,6-dimethyl-*endo*-2-norbornenol (*3*, $R^2=H$ or Me, respectively) are presented.

0302-4377/81/020139-05$02.50

EXPERIMENTAL

Syntheses. 6-Methyl-2-norbornenone was prepared from methylcyclopentadiene and vinyl acetate by the method of Krieger and Masar.[2,3] A reduction of the ketone with lithium aluminium hydride in ethyl ether produced 92 % of 6-methyl-*endo*-2-norbornenol and 8 % of 6-methyl-*exo*-2-norbornenol. A treatment of the ketone with methyl magnesium iodide yielded 97 % of 2,6-dimethyl-*endo*-2-norbornenol and 3 % of 2,6-dimethyl-*exo*-2-norbornenol. The *endo*-epimers were purified on a preparative gas chromatograph (Carbowax 20 M column). Attempts to purify the *exo* epimers were not succesful. The alcohols were identified from their IR, ^{1}H and ^{13}C NMR spectra.[4,5]

Product analyses. The hydrolysis products were isolated from the reaction mixture (0.1 mol dm^{-3} $HClO_4$) after ten half-lives of the substrates by extracting into ethyl ether. The ether solutions were washed with 0.5 mol dm^{-3} Na_2CO_3 and water and dried with Na_2SO_4. The ether was distilled off in weak vacuum. The remainder was investigated by GLC and spectroscopic methods. The hydrolysis product of 6-methyl-*endo*-2-norbornenol was concluded to be (3-methylcyclopent-3-enyl)ethanal (acetaldehyde): ^{1}H NMR (60 MHz, CCl_4): δ 9.6 (*CH*O), 5.15 (*CH*=C), 1.7 (CH_3); ^{13}C NMR (15 MHz, $CDCl_3$): δ 206.3 (*C*HO), 139.6 (C3), 123.4 (C4), 43.4 (C2), 41.1 (CH_2-CHO), 39.2 (C5), 33.7 (C1), 16.7 (CH_3 – C3) [and several smaller peaks probably caused by 3-methylenecyclopentyl)acetaldehyde]. The product of hydrolysis of 2,6-dimethyl-*endo*-2-norbornenol was concluded to be (3-methylcyclopent-3-enyl)-2-propanone (-acetone): ^{13}C NMR (15 MHz, $CDCl_3$): δ 209.1 (C=O), 139.2 (C3), 123.1 (C4), 50.7 (CH_2–CO-), 43.2 (C2), 39.1 (C5), 33.5 (C1), 30.1 (CO – CH_3), 16.6 (CH_3 – C3).

Kinetics. Disappearance of substrates and formation of products were followed by GLC (FFAP and Carbowax 20 M columns) with cyclohexanone as inert internal standard.[6] The disappearance of the substrates always obeyed fair first-order kinetics, with standard errors of the mean from 1 to 2 % (av. 1.5 %).

RESULTS AND DISCUSSION

The disappearance rates of 6-methyl- and 2,6-dimethyl-*endo*-2-norbornenols (*3*, R^2 = H or Me, respectively) were measured in 0.1 mol dm^{-3} perchloric acid. The rate constants, activation parameters and solvent deuterium isotope effects are presented in Table 1. The activation parameters have

Table 1. Disappearance rate constants of 6-methyl-*endo*-2-norbornenol (*3*, R^2 = H) and 2,6-dimethyl-*endo*-2-norbornenol (*3*, R^2 = Me) in aqueous perchloric acid, and activation parameters (at 298.2 K) and solvent deuterium isotope effects.

Substrate	c_{HClO_4}/ mol dm^{-3}	T/K	$k \times 10^3$/ dm^3 mol^{-1} s^{-1}	Activation parameters and deuterium isotope effects
3, R^2 = H	0.100	283.2	0.993	
	1.00	283.2	2.51	
	0.100	293.2	3.87	$\Delta G^{\neq}$ = 85.17(9) kJ mol^{-1}
	0.102[a]	293.2	2.25	$\Delta H^{\neq}$ = 93(2) kJ mol^{-1}
	(1.00	298.2	7.47)[b]	$\Delta S^{\neq}$ = +27(8) J mol^{-1} K^{-1}
	1.00	298.2	18.9[c]	k_D/k_H = 0.581(20)
	0.100	303.2	13.0	
	0.100	313.2	50.1	
3 R^2 = Me	0.100	283.2	1.21	
	1.00	283.2	2.71	
	0.100	293.2	4.93	$\Delta G^{\neq}$ = 84.68(4) kJ mol^{-1}
	0.103[a]	293.2	2.65	$\Delta H^{\neq}$ = 91(1) kJ mol^{-1}
	(1.00	298.2	9.08)[b]	$\Delta S^{\neq}$ = +21(3) J mol^{-1} K^{-1}
	1.00	298.2	20.4[c]	k_D/k_H = 0.538(19)
	0.100	303.2	17.0	
	0.100	313.2	54.2	

[a] Deuterioperchloric acid. [b] Calculated from the activation parameters, not h_o corrected. [c] Calculated from the activation parameters, h_o corrected.

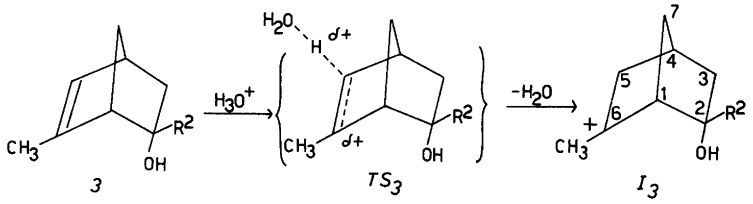
been calculated from the second-order rate constants (k_a/c_{HClO_4}). The rate constants at 298.2 K have been calculated from the activation parameters and corrected (*cf.* Ref. 1) to correspond to the reference state: 1.00 mol dm^{-3} $HClO_4$ at 298.2 K.

The hydrolysis product of 6-methyl-*endo*-2-norbornenol was found to be (3-methylcyclopent-3-enyl)ethanal (-acetaldehyde) [with some (3-methylenecyclopentyl)acetaldehyde (see Experimental)], which did not seem to react further during ten half-lives of the substrate. Its formation was estimated to be quantitative (99 ± 1 %) by the method of consecutive reactions.[6] The product of hydrolysis of 2,6-dimethyl-*endo*-2-norbornenol was deduced to be (3-methylcyclopent-3-enyl)-2-propanone (-acetone), which reacted slowly with the solvent (disappearance rate was roughly 0.01 times that of the substrate). Its formation was estimated to be nearly quantitative (ca. 90 %), but the difficulty in measuring the disappearance rate of the product made the estimate inaccurate.

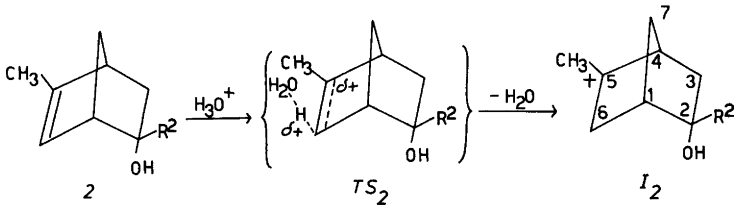
The solvent deuterium isotope effects (k_D/k_H 0.54 to 0.58) are very similar to those measured for the hydration of 5-methyl-2-norbornenols (0.5 to 0.6) and typical of the $A-S_E2$ mechanism, whose rate-determining stage is the protonation of the carbon-carbon double bond.[1] The activation entropies (21 to 27 J mol^{-1} K^{-1}) are somewhat more positive than values typical of the $A-S_E2$ mechanism (≤ 0), but agree with those of the hydration of 5-methyl-2-norbornenols.[1] This could in part be due to the rigid structure of 2-norbornenols, possibly also to experimental error and/or unnoticeable side reactions.

The rate constants of 6-methyl- and 2,6-dimethyl-*endo*-2-norbornenols (1.89×10^{-2} and 2.04×10^{-2} dm^3 mol^{-1} s^{-1}, respectively) are *ca.* 30 % smaller than those of the corresponding 5-methyl-substituted *endo*-2-norbornenols (2.62×10^{-2} and 3.00×10^{-2} dm^3 mol^{-1} s^{-1}, all in 1.00 mol dm^{-3} $HClO_4$ at 298.2 K).[1] This agrees, at least qualitatively, with the slow protonation of the 5,6-double bond, since in the protonation of the 6-methylated substrates a proton attacks carbon 5 (Markovnikov rule) and the positive charge develops at carbon 6 (Scheme 3). The charge of this atom is nearer the electronegative substituent (OH) at carbon 2 than the developing positive charge at carbon 5 in the transition state of the protonation of the 5-methyl-2-norbornenols (Scheme 4). The effect of 2-methyl is slight in both cases (*cf.* Ref. 1).

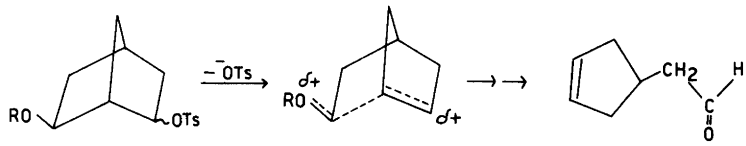
If the transition state of the reaction, *i.e.* the transition state of the rate-determining stage, would lie after the intermediate (I_3 and I_2 in Schemes 3 and 4; *cf.* Ref. 1), the rate-determining step could be isomerization (*e.g.* Wagner-Meerwein rearrangement or fragmentation, an *A*-1 mechanism) or addition of a water molecule (an *A*-2 mechanism). In this case the solvent deuterium isotope effects should be greater than unity,[7] not smaller as observed in this work and in Ref. 1. There is, however, a small possibility that the replacement of 5- or 6-hydrogen by methyl decreases the energy of the intermediate (changes from secondary to tertiary) so much that the energy barriers before and after the intermediate in the reaction coordinate come close to each other. In this case there would be two



Scheme 3.



Scheme 4.



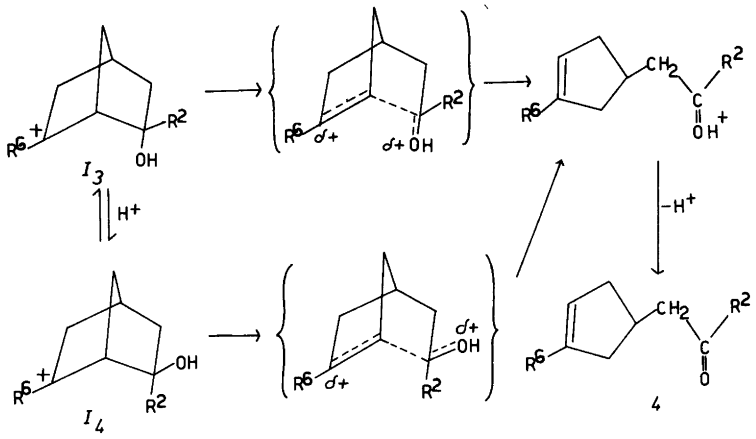
Scheme 5.

rate-limiting stages. The positive activation entropies observed in this work and in Ref. 1 hint that the latter would be unimolecular rather than bimolecular. The very normal deuterium isotope effects do not, however, support this possibility. Thus it is evident that the reaction steps which cause the formation of norbornanediols in the case of 5-methyl-2-norbornenols and the formation of (3-methylcyclopent-3-enyl)acetaldehyde and -acetone in the case of 6-methyl-2-norbornenols are fast stages after the rate-determining protonation of the 5,6-double bond.

Grob *et al.*[8,9] recently observed that the hydrolysis of *exo*-6 substituted *exo*- and *endo*-2-norbornyl *p*-toluenesulfonates produces quantitatively (cyclopent-3-enyl)acetaldehyde if the 6-substituent is *e.g.* hydroxyl or methoxyl (R = H or Me, Scheme 5). Besides, the rate of solvolysis is in the case of the *exo* epimers from 84 to 97 times greater than "normal" (estimated from the linear regression line between log k_1 and σ_I^q of several 6-substituted tosylates). This acceleration of rate is due to the carbon-carbon hyperconjugation and/or to the so-called fragomeric effect (derived from fragmentation) and is typical of strongly conjugating donor substituents.

In the present work no acceleration can be seen, although the formation of the fragmentation products is totally or nearly quantitative. It is true that the replacement of 6-hydrogen by methyl causes an enhancement of rate by a factor of 2×10^4,[10,11] but this increase is slightly smaller than that caused by the replacement of 5-hydrogen by methyl (3×10^4 in the cases of the *endo*-2-norbornenols).[1] The ratio of the effects is similar to the ratio of effects of 5-methyl (2×10^4) and 6-methyl (1×10^4) on the hydration rate of 2-norbornenone.[12]

The results of the present work and Ref. 1 can be used to estimate the portions of protonation of 5- and 6-carbons in the hydration of *endo*-2-norbornenol and 2-methyl-*endo*-2-norbornenol.[10,11] The reaction rate of 5-methyl-*endo*-2-norbornenol (protonation occurs at carbon 6, Scheme 4) is 1.39 times greater than that of 6-methyl-*endo*-2-norbornenol (protonation occurs at carbon 5, Scheme 3). This gives the estimate that 58 % of the protonation of *endo*-2-norbornenol occurs at carbon 6 and 42 % at carbon 5. In the case of 2-methyl-*endo*-2-norbornenol the estimated percentages are 60 and 40, respectively, equal to those in the hydration of 2-norbornenone,[12] although the protonation rates of 2-norbornenols are *ca.* 10^3 times greater than



Scheme 6.

those of the corresponding 2-norbornenones. The energy difference between the transition states of protonation of 5- and 6-carbons is only 1 kJ mol^{-1} and it is probably also very small between the 2-norbornyl cations with an electronegative substituent (OH or =O) at the 5- or 6-positions, provided that the 5- and 6-methyl substrates are equal in energy. More work is needed in order to clarify this.

The kinetic data above do not tell anything about the stages after the formation of the carbocation intermediate (Scheme 3, I_3). However, something can be assumed on the basis of the products of hydrolysis. The mechanism in Scheme 6 is probably the simplest imaginable way from the first intermediate to the fragmentation (isomerization) products. According to the reports of Grob *et al.*,[8,9] the fragmentation occurs quantitatively when $R^2 = R^6 = H$ and OH or OMe is at the *exo* position (I_4). The present works shows that the quantitative or nearly quantitative fragmentation also occurs when $R^2 = H$ or Me, $R^6 = Me$ and the hydroxyl group is at the *endo* position (I_3). It is possible that the position of OH and R^2 can interchange *via* a dication making the fragmentation easier. However, it is surprising that a replacement of 6-hydrogen by methyl does not seem to prevent the delocalization of charge from carbon 6 to the hydroxylic oxygen bonded to carbon 2.

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Received September 9, 1980.