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ACID-CATALYZED HYDROLYSES OF BRIDGED BI- AND TRICYCLIC COMPOUNDS–XII[†]

KINETICS OF HYDRATION OF 2-NORBORNENONE, A SPECIAL β,γ-UNSATURATED KETONE

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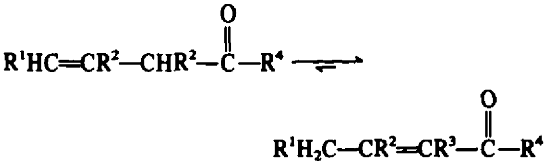
Abstract—The reaction rates, activation parameters, solvent deuterium isotope effects, and dependences of rates on acid concentration measured for the hydration of 2-norbornenone and its four Me-substituted homologs in aqueous acid agree with the slow protonation of the C=C double bond (A–S_E2 mechanism). Thus the mechanism differs from that reported for the isomerization (to α,β-unsaturated ketones) of unbridged β,γ-unsaturated ketones, e.g. 3-cycloalkenones and Δ^5-3-ketosteroids, under catalysis by acid.

The rates of acid-catalyzed hydrolysis (hydration and/or rearrangement) for several norbornenes have been measured.[1,2] The present work extends the study to norborn-5-en-2-ones or 2-norbornenones. They are β,γ-unsaturated ketones, whose usual reaction catalyzed by acids, bases and enzymes is the isomerization to conjugated α,β-unsaturated ketones:



$$R^1HC{=}CR^2{-}CHR^2{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}R^4 \rightleftharpoons R^1H_2C{-}CR^2{=}CR^3{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}R^4$$

This isomerization reaction has received much attention and the effects of the substituents (R^i) on the reaction rates and mechanism have been studied.[3–7]

The methylene bridge between α- and δ-carbons (C-1 and C-4) in 2-norbornenone evidently, however, causes so great a structural change that the reaction or the reaction mechanism hardly remains the same as that of unbridged ketones, e.g. 3-cyclohexenone, 3-methyl-3-cyclohexenone, 2-cyclohexen-1-yl methyl ketone, 3-cyclopentenone, and Δ^5-3-ketosteroids. In order to test this idea the rates of acid-catalyzed disappearance of 2-norbornenone and its four Me-substituted homologs were measured, also the rates under standard conditions, activation parameters, solvent deuterium isotope effects, and plots for $\log k_1$ vs H_0 and $(\log k_1 + H_0)$ vs $(H_0 + \log c_{H^+})$ were calculated and compared with those reported for unbridged β,γ-unsaturated ketones.[3–7]

RESULTS

The disappearance rates of 2-norbornenones were measured in 1.00 or 5.00 mol dm^{-3} perchloric acid at four temperatures. The results are collected in Table 1 together with the activation parameters calculated from second-order rate constants ($= k_1/c_{HClO_4}$). No isomerization could be detected. The disappearance rates of 1- and 5-methyl-substituted 2-norbornenones were also measured in different acid concentrations (Table 2) and the fairly linear plots, $\log k_1 = -AH_0 + B$ and $(\log k_1 + H_0) = \phi(H_0 + \log c_{H^+})$,[8] were obtained with the following parameters (H_0 values are from Ref. 9; r = correlation coefficients): 1-Me (348 K): $A = 0.99 \pm 0.03$, $B = -6.37 \pm 0.04$, $r = 0.9989$, $\phi = 0.00 \pm 0.04$; if the value in 1 mol dm^{-3} is omitted (perhaps less accurate than others) $A = 1.04 \pm 0.01$, $B = -6.46 \pm 0.01$, $r = 0.9999$, $\phi = -0.06 \pm 0.01$ and 5-Me (298 K): $A = 1.23 \pm 0.02$, $B = -5.27 \pm 0.03$, $r = 0.9997$, $\phi = -0.34 \pm 0.05$. The solvent deuterium isotope effects were measured in 1.00 or 5.00 mol dm^{-3} perchloric acid ($HClO_4$ and $DClO_4$) generally at 348 K. The results are listed in Table 3.

The measured wavelengths (λ_{max}/nm) for the maximum carbonyl absorbances were as follows: 2-norbornanone 286, 2-norbornenone 300, 1-Me 299, 5-Me 298 and 6-Me (3% 4-Me) 300 (ϵ was between 240 and 330 dm^3 mol^{-1} cm^{-1}).

DISCUSSION

The protonation of 2-norbornenone may occur on three different sites illustrated in Scheme and this causes three imaginable reaction pathways (a – c). Route (a) represents the A–S_E2 mechanism with rate determining protonation of the C=C double bond, which mechanism was rejected in the reactions of unbridged β,γ-unsaturated ketones.[3–7] Ways (b) and (c) are initiated by the reversible protonation of the carbonyl oxygen. The former corresponds to the isomerization mechanism proposed for the unbridged ketones and the latter is possible owing to the homoconjugation present in 2-norbornenone between the ethylenic and carbonylic double bonds[10] or to the homoallylic participation of the ethylenic bond of the intermediate cations. The homoconjugation is alike in 2-norbornenone and its Me homologs, since the shift of the UV carbonyl absorption to the longer wavelength is quite similar in all cases (12–14 nm) with 2-norbornanone as reference compound (cf. Ref. 11). However, route (b) does not seem probable due to the very high internal strain present in the intermediate enol and the resulting ketone with the double bond at the bridgehead. In the case of the 1-methyl substrate this pathway is even impossible since the α-hydrogen lacks. Hence, routes (a) and (c) are more probable. They both produce

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[†] Part XI, see Ref. *1b*.

Table 1. Disappearance rates of 2-norbornenone (nil) and some methyl-substituted 2-norbornenones in perchloric acid at different temperatures and the calculated activation parameters at 298 K.

c_{HClO_4} mol dm^{-3}	Temp. K	$k_1/10^{-6}$ s^{-1} nil	1-Me	4-Me	5-Me	6-Me
1.00	298				12.2[a,b]	8.10[a]
5.00	298	0.0622[a]	0.139[a]	0.0602[a]		
1.00	318				150	98.5
1.00	328				480	282
5.00	328	3.91	8.76	4.20		
1.00	338				1290	757
5.00	338	13.1	29.0	12.1		
1.00	348				3780	2360
5.00	348	38.4	89.2	44.0		
5.00	358	124	274	131		
$\Delta S^{\neq}$/J mol^{-1} s^{-1}		-28 ± 6	-21 ± 3	-23 ± 12	-16 ± 5	-25 ± 10
$\Delta H^{\neq}$/kJ mol^{-1}		110 ± 2	110 ± 1	111 ± 4	96 ± 2	95 ± 3

a) Calculated from the activation parameters. b) The exp. value $12.6 \cdot 10^{-6}$ s^{-1}.

Table 2. Disappearance rates of 1- and 5-methyl 2-norbornenones in different acid concentrations.

c_{HClO_4} mol dm^{-3}	H_0 [a]	$k_1/10^{-7}$ s^{-1} 1-Me (348 K)	5-Me (298 K)
1.00	-0.32	9.64	126
2.00	-0.83	25.6	591
3.00	-1.32	80.5	2230
4.00	-1.80	256	9540
5.00	-2.31	892	35900

a) Ref. 9.

at least partly the same ketoalcohols, which may be, however, rearranged.[12]

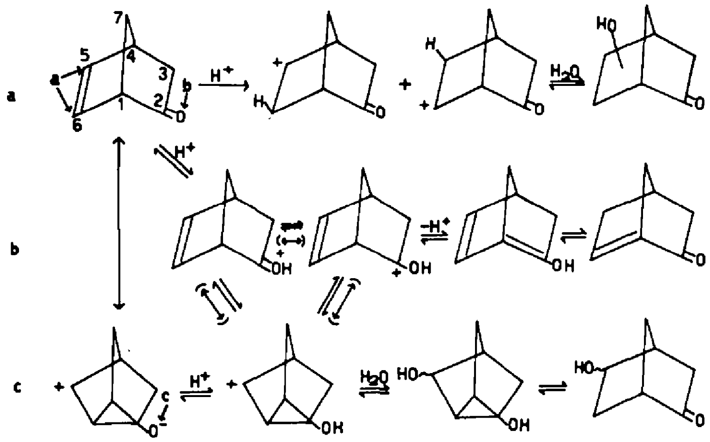
The activation entropies in Table 1 are typical of the A–S_E2 mechanism.[1,2] The only value reported for the acid-catalyzed isomerization of the β,γ-unsaturated ketones is -82 J mol^{-1} K^{-1} measured with a Δ^5-3-ketosteroid.[5] It is more negative than those observed for the substrates in this work (-16 to -28 J mol^{-1} K^{-1}). Route (c) evidently has a A-2 character and thus the water molecule in the transition state probably makes the activation entropy more negative than observed here.

Table 3. Disappearance rates of 2-norbornenones in deuterioperchloric acid and the solvent deuterium isotope effects (k_H values are from Table 1).

Subst.	Temp. K	c_{DClO_4} mol dm^{-3}	k_1 / 10^{-5} s^{-1}	k_D/k_H [a]
nil	348	5.00	3.02	0.786
1-Me	348	5.00	6.86	0.770
4-Me	348	5.00	3.54	0.805
5-Me	348	1.00	193	0.511
5-Me	298	5.00	237	0.658
6-Me	348	1.00	137	0.580

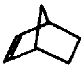
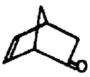
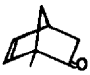
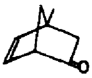
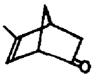
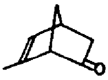
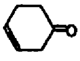
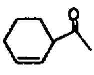
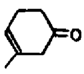
a) The error limits calculated from standard errors of the rate coefficients are 2 - 3 %.

The plots $\log k_1$ vs $-H_0$ are linear for the disappearance of the 1- and 5-methyl substrates, which is in agreement with the A–S_E2 mechanism.[1b,13] The plots reported for the isomerization of the unbridged ketones are all curved.[6] A non-linear plot can also be predicted for route (c).[8] The measured ϕ-values (-0.06 to -0.34) are in the range observed for the slow proton transfer to a C atom.[1b,8]



Scheme 1.

Table 4. Rate coefficients and relative rates of reactions of some norbornenes and cyclohexenes in the 1.0 mol dm^{-3} acid at 298 K.

						
$\frac{k_1}{10^{-6}\ s^{-1}}$ [a]	110	0.0007	0.0015	0.0007	12	8.1
k_{rel}	1	$6\cdot10^{-6}$	$14\cdot10^{-6}$	$6\cdot10^{-6}$	0.11	0.07
k_{rel}		1	2	1	$2\cdot10^4$	$1\cdot10^4$
						
$\frac{k_1}{10^{-7}\ s^{-1}}$ [b]	1.1	1000	1000			10000
k_{rel}	1	$1\cdot10^3$	$1\cdot10^3$			$1\cdot10^4$
k_{rel}		1	1			10

[a] Measured in perchloric acid. [b] Measured in sulfuric acid.

The solvent deuterium isotope effects measured here for the 2-norbornenones (k_D/k_H 0.51–0.81, see Table 3) are of the magnitude typical of the hydration of aliphatic, alicyclic and bicyclic olefins.[1,2,13] Quite different isotope effects have been measured for unbridged ketones (k_D/k_H 0.2–1.6).[4,6,7]

The most striking differences in the behavior of the unbridged and bridged β,γ-unsaturated ketones can be seen in the relative rates under standard conditions (the 1 mol dm^{-3} acid at 298 K; the rate coefficients are interpolated or extrapolated from the data in Refs 1*b*, 6 and 13, and in this work). The values are collected in Table 4. The keto group in norbornene causes a *retardation* of the rate by five orders of ten, but the same substitution in cyclohexene causes an *increase* of the rate by three orders of ten. The accelerating effect of the methyl group in the ethylenic bond is 10^4 in 2-norborneneone, but only 10 in 3-cyclohexenone. In both cases the substitution of α-hydrogen by an alkyl has only a slight effect on the reaction rate. On the contrary, the effects of the methyl substitution in 2-norbornenone are very similar to those in alkenes and cycloalkenes (H_2SO_4, $H_0 = 0$, 298 K): k(2 - methyl - 1 - butene)/k(2 - methyl propene) = 1.4, k(propene)/k(ethene) = 2×10^6, k(2 - methyl propene)/k(propene) = 2×10^5 and k(1 - methyl cyclohexene)/k(cyclohexene) = 7×10^3.[13]

Thus the slow protonation of the C=C double bond, i.e. the A-S_E2 mechanism, is evident in the hydration of 2-norbornenones. In the cases of the 5- and 6-methyl homologs the Markownikov addition can be assumed and so the protonation occurs at the unmethylated end of the double bond. A comparison of the rates of these isomers shows that the transition state (and the intermediate carbocation) of the former with a positive charge at C-5 has only a slightly lower relative energy than those of the latter with a positive charge at C-6. Thus it is probable that the protonation of 2-norbornenone may occur both at C-6 and C-5, but the former is somewhat more favored. This is in agreement with the inductive effect of the carbonyl group and the partial positive charge at C-5 due to the hyperconjugation. Krieger has also observed the formation of both 5- and 6 - *exo* - acetoxy - 2 - norbornanones when adding acetic acid to 2-norbornenone under catalysis by sulfuric acid.[12]

EXPERIMENTAL

Preparations. 2-Norbornenone was prepared by hydrolyzing the Diels–Alder adduct of monomerized cyclopentadiene and 2-chloroacrylonitrile in alkaline dimethyl sulfoxide.[14] Four Me-substituted 2-norbornenones (1-Me, 4-Me, 5-Me and 6-Me) were obtained as a mixture from monomerized methyl cyclopentadiene and 2-chloroacrylonitrile by the method of Goering and Chang.[15] The 1-Me and 5-Me isomers could be separated on a preparative GLC (a Carbowax 20 M column), but the 4-Me and 6-Me isomers were collected as a mixture consisting of 3% of the former. The purities of the other substrates were ≥99% (by GLC). The ketones were identified from their IR, ^{1}H NMR and mass spectra.[16] The wavelengths of UV absorption maximum for carbonyl group were recorded in EtOH employing a ketone concentration of *ca.* 1 mmol dm^{-3}.

Kinetic measurements. The disappearance rates of the ketones were measured by the GLC method reported earlier.[1] In every case cyclohexanone was used as internal standard. The 4-Me and 6-Me isomers were studied using their mixture, since the ratio of their rates was so high that the rates could be measured separately with good accuracy. The first order kinetics was always observed with standard errors ≤2% (average 1%). The product of the 5-Me homolog, probably 5-hydroxy-5-methyl-2-norbornanone, easily dehydrated partly in the injection block of the analytical GLC, but this could be eliminated by exchanging the glass injection tube after every injection. The reaction products were not analyzed.

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