

Acid-catalyzed Hydrolysis of Bridged Bi- and Tricyclic Compounds. XXIII. Kinetics of Hydration and Hydrolysis of *exo*- and *endo*-5-Chloromethyl-2-norbornenes and 3-Chloromethylnortricyclane

MARTTI LAJUNEN

Department of Chemistry and Biochemistry, University of Turku, SF-20500 Turku 50, Finland

Total disappearance rates of *exo*- and *endo*-5-chloromethyl-2-norbornenes (*1* and *2*) and 3-chloromethylnortricyclane (*3*) in aqueous perchloric acid have been divided between two competing reactions, hydrolysis of the chloromethyl group and hydration of the double bond or the cyclopropane ring. The rate constants for the hydrolysis have been estimated from the disappearance rates of *exo*- and *endo*-2-chloromethylnorbornanes (*4* and *5*). The hydrolysis is evidently an acid-catalyzed reaction (an A-2 mechanism). The hydrations of the double bond and the cyclopropane ring occur by A-S_E2 mechanisms and their rate constants agree with those of other substituted norbornenes and nortricyclanes. The portions of hydrolysis are ca. 15, 33 and 4 % of the total disappearance rates of *1*, *2* and *3*, respectively in 1 mol dm⁻³ HClO₄ at 348 K.

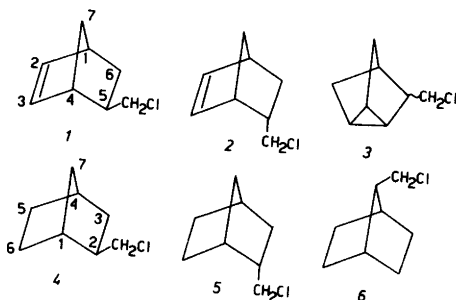
Primary alkyl halides, especially chlorides, are generally hydrolyzed very slowly in water (e.g. $k=6.6 \times 10^{-6} \text{ s}^{-1}$ at 348.2 K for n-butyl chloride).^{1,2} If, however, formation of a carbocation is possible, the hydrolysis rates are much greater (e.g. $k=2.1 \times 10^{-3} \text{ s}^{-1}$ for benzyl chloride and ca. 0.14 s^{-1} for cyclopropylmethyl chloride at 348.2 K).^{1,2} Acid catalysis has been observed in the hydrolysis of primary alkyl halides only when formation of a carbocation is probable, e.g. in the case of benzyl halides.^{2,3} In the case of primary aliphatic chlorides the effect of perchloric acid is similar to that of sodium perchlorate: it retards the reaction rate (a linear relationship prevails between log k and the concentration of the electrolyte).² Some cations, such as Ag⁺ and Hg²⁺, have a special promoting effect on the hydrolysis rates of alkyl halides.^{4,5}

A bromomethyl group has recently been used as a substituent in the hydrolysis of 6-substituted 2-norbornyl tosylates without any side reactions caused by the substituent.^{6,7} Thus a chloromethyl group might also be a stable substituent in the acid-catalyzed hydrations of 5-substituted 2-norbornenes and 3-substituted nortricyclanes.^{8,9} This idea is tested in the present work by measuring the total disappearance rates of *exo*- and *endo*-5-chloromethyl-2-norbornenes (*1* and *2*) and 3-chloromethylnortricyclane (*3*) in aqueous perchloric acid and by estimating the hydrolysis rates of the chloromethyl group by measuring the disappearance rates of the substrates in aqueous sodium perchlorate and the

disappearance rates of their saturated analogues, *exo*- and *endo*-2-chloromethylnorbornanes (4 and 5), in aqueous HClO_4 and NaClO_4 . However, the main aim is to get more data for the investigation of substituent effects on the hydration of norbornenes and nortricyclanes.^{8,9}

EXPERIMENTAL

Syntheses. An effort was made to enrich a commercial mixture of 5-hydroxymethyl-2-norbornenes (Fluka AG, *exo/endo*=15/85) on a Perkin Elmer Auto Annular Still. The separation was, however, poor. The best fractions were separated twice on a Perkin Elmer F



21 Preparative Gas Chromatograph (FFAP column). Part of the two pure ($\geq 98\%$) epimers was treated with thionyl chloride in pyridine, which reaction produced the corresponding 5-chloromethyl-2-norbornene (1 and 2) with about 20% of 2-oxatricyclo[4.2.1.0]nonane, an *endo* ether, whose retention time (FFAP and Carbowax 20 M columns) was nearly the same as those of the chloromethylnorbornenes. The impurity is stable in concentrated mineral acids,¹⁰ thus no effort was made to remove it. Part of the epimeric chlorides was hydrogenated in acetone into the corresponding saturated chlorides (4 and 5) using palladium on carbon as catalyst.

3-Chloronortricyclane^{9,11} was transformed into nortricyclyl magnesium chloride with magnesium turnings in diethyl ether. Bubbling of carbon dioxide through the solution on an ice bath and addition of aqueous hydrogen chloride produced 3-nortricyclane carboxylic acid. It was reduced by lithium aluminium hydride in diethyl ether into 3-hydroxymethylnortricyclane, which was turned into 3-chloromethylnortricyclane (3) by thionyl chloride in pyridine.

The substrates were identified from their IR ($-\text{Cl}$ 710–735 cm^{-1}), ^1H NMR ($\delta_{\text{CH}_2\text{Cl}}$ 3.3–3.6), and ^{13}C NMR ($\delta_{\text{CH}_2\text{Cl}}$ 47–50) spectra.^{12,13}

Kinetics. The disappearance of a substrate was followed by taking samples after appropriate intervals from an aqueous solution of the substrate, by neutralizing and diluting (1:1) the acidic samples (LClO_4 solutions, $\text{L}=\text{H}$ or D) with cold ammonia or diluting (1:1) the neutral samples (NaClO_4 and pure L_2O solutions) with cold Sørensen phosphate buffer (pH 7.0), by chilling the sample tubes in crushed ice, and by analyzing them by GLC (FFAP and Carbowax 20 M columns). The reaction solutions were very dilute in regard to the poor solubilities of the substrates (7×10^{-5} – 4×10^{-4} mol dm^{-3}). The solution also contained about the same amount of cyclopentanone, cyclohexanone, norcamphor, or camphor, which were used as internal standards in GLC analyses. When pure water was used as reaction medium, it was redistilled before use.

Precautions were made to prevent evaporation of the substrates by keeping the air volume of the reaction vessel small and the stopper tightly closed between the samplings. The reaction vessel was protected from light during the runs. The GLC analyses demanded the highest available sensitivity of the GLC apparatus (Perkin Elmer F 11) and were not very accurate. Therefore they were repeated at least once, often twice or more times, and each rate constant was measured 2–4 times.

Table 1. Rate constants of disappearance for *exo*- and *endo*-5-chloromethyl-2-norbornenes (1 and 2), 3-chloromethylnortricyclane (3), and *exo*- and *endo*-2-chloromethylnorbornanes (4 and 5) in aqueous solutions, and activation parameters (at 298.2 K) and solvent deuterium isotope effects ($M = \text{mol dm}^{-3}$).

Substrate	Solution	Temp./K	$k_1/10^{-5} \text{ s}^{-1}$	Activation parameters and solvent isotope effects
1	1 M HClO ₄	298.2	0.54(6) ^a	$\Delta H^\ddagger = 94(3) \text{ kJ mol}^{-1b}$ $\Delta S^\ddagger = -29(8) \text{ J mol}^{-1} \text{ K}^{-1b}$ $k_H/k_D = 0.69(3)$
	1 M HClO ₄	318.2	6.3(4)	
	1 M HClO ₄	328.2	19.5(6)	
	1 M HClO ₄	338.2	50.1(8)	
	1 M DClO ₄	338.2	72(2)	
	1 M HClO ₄	348.2	151(4)	
	1 M HClO ₄	348.2	148(8) ^a	
	1 M NaClO ₄	348.2	7.6(2)	
2	1 M HClO ₄	298.2	0.295(4) ^a	$\Delta H^\ddagger = 91(1) \text{ kJ mol}^{-1b}$ $\Delta S^\ddagger = -45(1) \text{ J mol}^{-1} \text{ K}^{-1b}$ $k_H/k_D = 0.73(4)$
	1 M HClO ₄	318.2	3.16(10)	
	1 M HClO ₄	328.2	9.2(2)	
	1 M HClO ₄	338.2	25.1(5)	
	1 M DClO ₄	338.2	34.4(10)	
	1 M HClO ₄	348.2	65.8(12)	
	1 M HClO ₄	348.2	67.2(5) ^a	
	1 M NaClO ₄	348.2	7.3(2)	
	H ₂ O	348.2	2.45(10)	
3	1 M HClO ₄	298.2	1.79(8) ^a	$\Delta H^\ddagger = 90(1) \text{ kJ mol}^{-1b}$ $\Delta S^\ddagger = -32(4) \text{ J mol}^{-1} \text{ K}^{-1b}$ $k_H/k_D = 1.32(6)$
	1 M HClO ₄	318.2	19(2)	
	1 M HClO ₄	328.2	53(4)	
	1 M HClO ₄	338.2	146(3)	
	1 M DClO ₄	338.2	110(3)	
	1 M HClO ₄	348.2	387(16)	
	1 M HClO ₄	348.2	380(8) ^a	
	1 M HClO ₄	348.2	4.8(4)	
4	1 M HClO ₄	298.2	0.33(5) ^a	$\Delta H^\ddagger = 70(3) \text{ kJ mol}^{-1}$ $\Delta S^\ddagger = -114(10) \text{ J mol}^{-1} \text{ K}^{-1}$ $k_H/k_D = 0.60(3)$
	1 M HClO ₄	318.2	1.96(3)	
	1 M HClO ₄	328.2	5.2(1)	
	1 M HClO ₄	338.2	10.2(3)	
	1 M DClO ₄	338.2	17.1(5)	
	1 M HClO ₄	348.2	21.2(3)	
	1 M HClO ₄	348.2	22.4(14) ^a	
5	1 M HClO ₄	298.2	0.47(4) ^a	$\Delta H^\ddagger = 64(2) \text{ kJ mol}^{-1}$ $\Delta S^\ddagger = -132(6) \text{ J mol}^{-1} \text{ K}^{-1}$ $k_H/k_D = 0.54(3)$ $k_H/k_D = 1.08(10)$ $k_H/k_D = 1.27(9)$
	1 M HClO ₄	318.2	2.45(9)	
	1 M HClO ₄	328.2	5.6(1)	
	1 M HClO ₄	338.2	10.6(1)	
	1 M HClO ₄	348.2	21.5(5)	
	1 M HClO ₄	348.2	21.9(8) ^a	
	1 M DClO ₄	348.2	39.8(14)	
	1 M NaClO ₄ (H ₂ O)	348.2	7.5(4)	
	1 M NaClO ₄ (D ₂ O)	348.2	6.9(2)	
	H ₂ O	348.2	3.0(1)	
	D ₂ O	348.2	2.4(1)	

^a Calculated from the activation parameters; rate constants in $\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. ^b Apparent values due to two competing reactions.

RESULTS AND DISCUSSION

The total disappearance rate constants for *exo*- and *endo*-5-chloromethyl-2-norbornenes (1 and 2), 3-chloromethylnortricyclane (3), and *exo*- and *endo*-2-chloromethylnorbornanes (4 and 5) in aqueous 1.00 mol dm⁻³ HClO₄ at different temperatures are listed in Table 1. The activation parameters and the solvent deuterium isotope effects are also presented.

Earlier measurements of hydrolysis rate constants for primary alkyl halides have been made titrimetrically (AgNO₃) or conductometrically.^{1,2} From the results by Koskikallio² the hydrolysis rate constant can be estimated for *n*-butyl chloride in 1 mol dm⁻³ HClO₄ at 348.2 K to be *ca.* 4.7 × 10⁻⁶ s⁻¹ (no acid catalysis, see above). The uncatalyzed hydrolysis rate of isobutyl chloride is roughly six times slower.^{1,14} Thus the hydrolysis rates measured in this work for *exo*- and *endo*-2-chloromethylnorbornanes (Table 1, 4 and 5) are *ca.* 280 times higher than that of isobutyl chloride, an aliphatic analogue of the bicyclic chlorides. It is improbable that this large deviation is due to the difference in methods of measurement. It is easier to suppose that the high rate of hydrolysis of 2-chloromethylnorbornanes is due to an acid catalysis (see above). To study the hydrolysis more extensively the disappearance rate constants were measured for the *endo* epimer in aqueous HClO₄-NaClO₄ solutions (Fig. 1), in NaClO₄(D₂O), and in ordinary and heavy water (Table 1). Some measurements were also made for the other substrates in these solutions (Table 1).

The hydrolysis rate of *endo*-2-chloromethylnorbornane (5) is 2.5 times as high in 1 mol dm⁻³ NaClO₄(H₂O) and 7 times as high in 1 mol dm⁻³ HClO₄(H₂O) as in ordinary water. This kind of behavior is different from that of *e.g.* benzyl chloride, but resembles that of benzyl fluoride.^{2,3} The solvent deuterium isotope effects for 5 in L₂O (L=H or D, $k_H/k_D=1.3$) and in aqueous NaClO₄ ($k_H/k_D=1.1$) are normal for the hydrolysis of alkyl halides in water,^{1,14} but those measured for 4 and 5 in perchloric acid ($k_H/k_D=0.5$ to 0.6) are exceptional. The last values are, however, typical of the acid-catalyzed hydrolyses of many oxygen and nitrogen compounds, which reactions occur via a fast pre-equilibrium protonation of the hetero atom followed by a monomolecular (A-1 mechanism) or bimolecular (A-2 mechanism) rate-limiting stage.¹⁵⁻¹⁸ The values are, however, different from that measured for benzyl fluoride ($k_H/k_D=0.98$ at 323.2 K).³

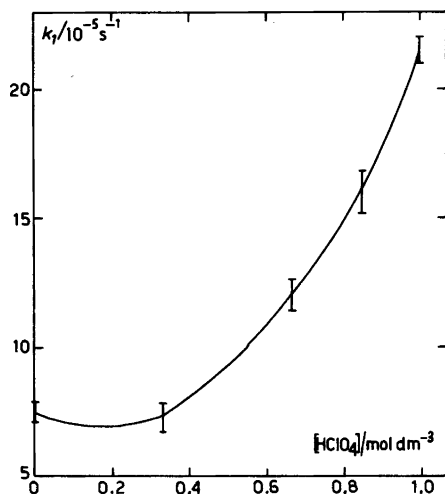
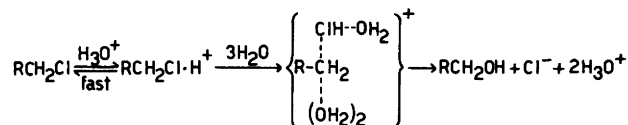


Fig. 1. Disappearance rate constants of *endo*-2-chloromethylnorbornane (5) versus HClO₄ concentration of the solution. Ionic strength=1.00 mol dm⁻³ with the aid of NaClO₄.

The rate constants measured in HClO_4 – NaClO_4 solutions (ionic strength 1 mol dm^{-3}) at 348.2 K for **5** (Fig. 1) show that the acid-catalyzed portion of the hydrolysis is still minimal in 0.33 mol dm^{-3} acid, but becomes more observable in higher acid concentrations. The activation enthalpies and entropies measured for the hydrolysis of chloromethylnorbornanes (**4** and **5**) in 1 mol dm^{-3} HClO_4 (Table 1) are typical of the *A*-2 type acid-catalyzed reaction where one or more water molecules participate in the rate-limiting stage of reaction, *e.g.* according to eqn. (1).¹⁶



Comparison of the disappearance rate constants measured in 1 mol dm^{-3} HClO_4 for *exo*- and *endo*-5-chloromethyl-2-norbornenes (**1** and **2**) and for *exo*- and *endo*-2-chloromethylnorbornanes (**4** and **5**) shows that the hydrolysis of the chloromethyl group may be a noteworthy reaction of **1** and **2**. In order to estimate its portion, the disappearance rates of **1** and **2** were measured in 1 mol dm^{-3} NaClO_4 , where the acid-catalyzed hydration of the double bond does not occur. The rate constants at 348.2 K (Table 1) are 9–20 times slower than in 1 mol dm^{-3} HClO_4 . They are equal in the limits of experimental error to the disappearance rate constant of *endo*-2-chloromethylnorbornane (**5**) in 1 mol dm^{-3} NaClO_4 . The hydrolysis rates of **2** and **5** in water are also close to each other.

If it is assumed that the replacement of the 1 mol dm^{-3} NaClO_4 solution by the 1 mol dm^{-3} HClO_4 solution causes a similar increase of rate ($\times 2.9$ at 348.2 K) in the hydrolysis of the chloromethyl group of norbornanes (**4** and **5**) and norbornenes (**1** and **2**), the hydrolysis rates of **1** and **2** can be estimated from the disappearance rates of **4** and **5** measured under the same conditions. The portions of the hydrolysis of the chloromethyl group in the total disappearance of **1** and **2** are, when estimated in this way, 15 and 33 %, respectively, in 1 mol dm^{-3} HClO_4 at 348.2 K .

In the case of 3-chloromethylnortricyclane (**3**) the best reference compound for the estimation of the hydrolysis rate of the chloromethyl group would be 7-chloromethylnorbornane (**6**). Its synthesis, however, failed. So the rate constants measured for **4** and **5** and multiplied by the ratio of the hydrolysis rate constants of **3** and **1** or **2** (very similar) in 1 mol dm^{-3} NaClO_4 at 348.2 K (*i.e.* $4.8 \times 10^{-5}/7.5 \times 10^{-5}$) were used as the rate constants of hydrolysis of the chloromethyl group of **3**. The portion of hydrolysis is quite small, *ca.* 4 % in 1 mol dm^{-3} HClO_4 at 348.2 K .

Now we can calculate the approximate hydration rate constants for substrates **1**–**3** (Table 2): *e.g.* $k_{\text{hydrat.}}(\text{1}) \approx k_{\text{disapp.}}(\text{1}) - k_{\text{disapp.}}(\text{4})$. The activation parameters and solvent deuterium isotope effects have also been calculated. The value of the activation entropy is in the case of **1** and **3** typical of the slow protonation of the double bond or the cyclopropane ring (*A*–*S_E2* mechanism), but exceptional (>0) in the case of the *endo* epimer (**2**).^{8,9} The method of estimation of the rate constants and the experimental inaccuracy are probable reasons for the last value, but it might also be effected by the *endo*-5-chloromethyl group close to the double bond. The hydration rate of **2** is 2.5 times slower than that of **1** in 1 mol dm^{-3} HClO_4 at 348.2 K . The deuterium solvent isotope effects for the hydration of **1** and **2** are somewhat exceptional ($k_{\text{H}}/k_{\text{D}} \leq 1$), evidently due to the reasons mentioned above, but that measured for **3** is normal for the slow protonation of the cyclopropane ring.^{8,9} Comparison of the hydration rate constants of **1**–**3** with those of other 5-X-substituted

Table 2. Rate constants of hydration for *exo*- and *endo*-5-chloromethyl-2-norbornenes (1 and 2) and 3-chloromethylnortricyclane (3) in 1.00 mol dm⁻³ HClO₄, and activation parameters (at 298.2 K) and solvent deuterium isotope effects.

Substrate	Temp./K	$k_1/10^{-5} \text{ s}^{-1}$	Activation parameters and solvent isotope effects
1	298.2	0.31(4) ^a	$\Delta H^\ddagger = 101(3) \text{ kJ mol}^{-1}$ $\Delta S^\ddagger = -11(8) \text{ J mol}^{-1} \text{ K}^{-1}$
	318.2	4.3(5)	
	328.2	14.3(6)	
	338.2	39.9(9)	$k_{\text{H}}/k_{\text{D}} = 0.72(5)$
	338.2	55(2) ^b	
	348.2	130(5)	
	348.2	127(7) ^a	
2	298.2	0.030(6) ^a	$\Delta H^\ddagger = 125(5) \text{ kJ mol}^{-1}$ $\Delta S^\ddagger = 51(15) \text{ J mol}^{-1} \text{ K}^{-1}$
	318.2	0.71(14)	
	328.2	3.6(3)	
	338.2	14.5(5)	$k_{\text{H}}/k_{\text{D}} = 0.95(11)$
	338.2	15.2(12) ^b	
	348.2	44.3(13)	
	348.2	50(5) ^a	
3	298.2	1.58(8) ^a	$\Delta H^\ddagger = 92(1) \text{ kJ mol}^{-1}$ $\Delta S^\ddagger = -28(4) \text{ J mol}^{-1} \text{ K}^{-1}$
	318.2	17.5	
	328.2	49.2	
	338.2	139	$k_{\text{H}}/k_{\text{D}} = 1.42$
	338.2	98 ^b	
	348.2	373	
	348.2	377(9) ^a	

^a Calculated from the activation parameters; rate constants in dm³ mol⁻¹ s⁻¹. ^b Measured in 1.00 mol dm⁻³ DClO₄.

2-norbornenes and 3-X-substituted nortricyclanes (X=H, CH₂OH, OH, COCH₃, CN, and NO₂, cf. Ref. 8) shows that also the rate constants calculated for the hydration of the double bond of the 5-chloromethyl-2-norbornenes and the cyclopropane ring of 3-chloromethylnortricyclane are of the order of magnitude expected.

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REFERENCES

- Robertson, R.E. *Prog. Phys. Org. Chem.* 4 (1967) 213.
- Koskikallio, J. *Acta Chem. Scand.* 21 (1967) 397.
- Swain, C.G. and Spalding, R.E.T. *J. Am. Chem. Soc.* 82 (1960) 6104.
- Bender, M.L. *Mechanisms of Homogeneous Catalysis from Protons to Proteins*, Wiley, New York 1971, Chapter 8.
- Rudakov, E.S., Kozhevnikov, I.V. and Zamashchikov, V.V. *Usp. Khim.* 43 (1974) 707; *Chem. Abstr.* 81 (1974) 24536c.
- Fischer, W., Brob, C.A., Hanreich, R., von Sprecher, G. and Waldner, A. *Helv. Chim. Acta* 64 (1981) 2298.
- Grob, C.A., Günther, B. and Hanreich, R. *Helv. Chim. Acta* 64 (1981) 2312.

8. Lajunen, M. and Kukkonen, H. *Acta Chem. Scand. A* 37 (1983) 447 and references therein.
9. Lajunen, M. and Hintsanen, A. *Acta Chem. Scand. A* 37 (1983) 545.
10. Kablaoui, M.S. *Ph. Thesis*, University of South Carolina, Columbia 1967.
11. Reetz, M.T. and Sauerwald, M. *Chem. Ber.* 114 (1981) 2355.
12. Moen, R.V. and Makowski, H.S. *Anal. Chem.* 39 (1967) 1860.
13. Lippmaa, E., Pehk, T., Paasivirta, J., Belikova, N. and Plate, A. *Org. Magn. Reson.* 2 (1970) 581.
14. Laughton, P.M. and Robertson, R.E. *Can. J. Chem.* 37 (1959) 1491.
15. Schowen, R. L. *Prog. Phys. Org. Chem.* 9 (1972) 275.
16. Willi, A.V. In Bamford, C.H. and Tipper, C.F.H., Eds., *Comprehensive Chemical Kinetics*, Elsevier, Amsterdam 1977, Vol. 8, Chapter 1.
17. Lajunen, M. and Wiksten, P. *Finn. Chem. Lett.* (1980) 17.
18. Lajunen, M. and Tallgren, J. *Finn. Chem. Lett.* (1981) 106.

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