Acid-catalysed Hydration of 3-Substituted Nortricyclanes

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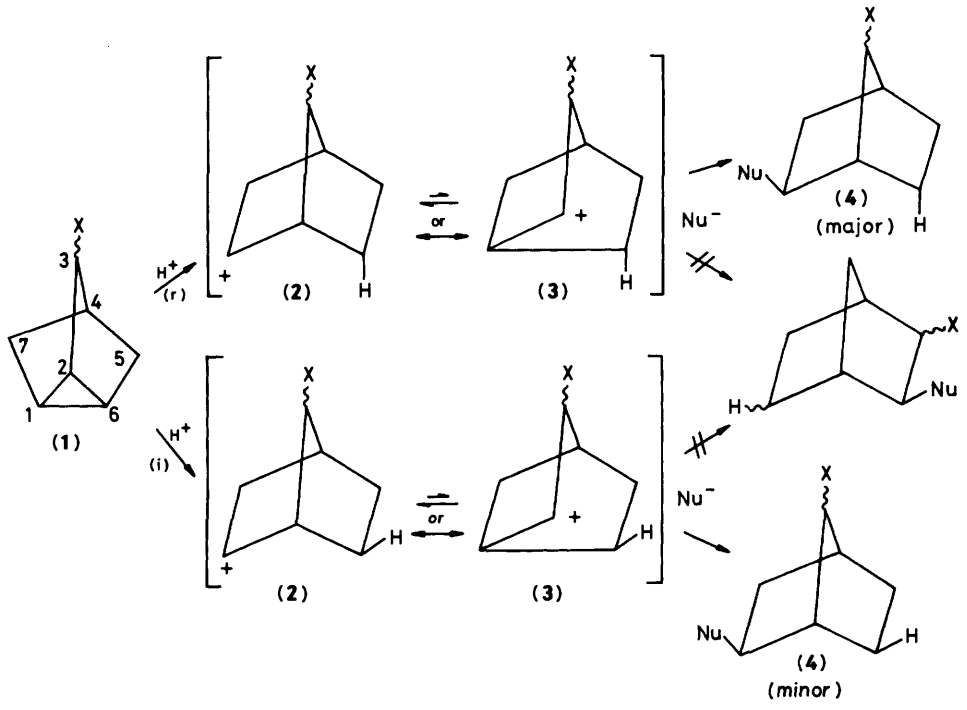
Disappearance rates of several 3-X-substituted nortricyclanes [X = H, CH_2OH, CH_2Cl, Ac, OH, $(CH_3)OH$, OAc, CN, NO_2, and oxo] were measured in aqueous perchloric acid by g.l.c. According to activation parameters, solvent deuterium isotope effects, and log k_1 *versus* H_0 and log k_1 *versus* σ_1^q correlations, the hydration mechanism is in most cases A-S_E2 (or Ad_E2), *i.e.*, protonation of the cyclopropane ring is the rate-determining stage of the reaction. The mechanism is different in the case of 3-methyl-3-hydroxynortricyclane (*A*-1) and 3-acetoxy- and 3-oxo-nortricyclane (*A*-2). The slope of the linear log k_1 *versus* σ_1^q correlation (−1.30 in 1 mol dm^{-3} $HClO_4$ at 348.2 K) is between those measured for separate protonations of two olefinic carbons of 5-X-substituted norbornenes. The contradiction between the normal inductive effects of the 3-X-substituents and the weak effects of the methyl groups at the cyclopropane carbons can be rationalized by formation of an edge-protonated nortricyclane in the rate-determining stage of the reaction.

The electrophilic cleavage of cyclopropane, generally initiated by a proton, has been extensively studied.[1,2] Probable intermediates are corner- and/or edge-protonated cyclopropanes whose calculated energies are roughly similar.[2,3] The mechanisms of protonation are not changed in the case of symmetrically alkyl-substituted cyclopropanes.[4] One such compound is nortricyclane (tricyclo[2.2.1.$0^{2,6}$]heptane), the investigation of which is also of interest owing to the formation of a 2-norbornyl cation, whose character (classical or nonclassical) has long been the object of controversy.[5,6] The proton (deuteron) which initiated the reaction is found mainly at the *exo*- and *endo*-6-positions of the product, an *exo*-2-norbornyl derivative, roughly in 1 : 1 ratio.[7–10]

An electron-withdrawing substituent at the 3-position of nortricyclane (**1**), however, changes the situation markedly (Scheme 1).[11] In this case the rupture of the C(1)–C(6) bond dominates ($\gtrsim$80%, when X = Cl or Br)[11] and produces a 7-X-substituted 2-norbornyl cation (**2**). This cation could rearrange (Wagner–Meerwein) to a 3-X-substituted cation (**3**), but the energy of the latter is high due to the location of the electron-withdrawing substituent adjacent to the positive charge. The reaction-initiating proton (deuteron) is now situated mainly at the *endo*-6 position ($\gtrsim$90%) of product (**4**), which strongly supports the initial edge protonation of 3-X-substituted nortricyclanes.[11]

Characteristic of the electrophilic cleavage of cyclopropane and nortricyclane is a slight rate-increasing effect of methyl (or ethyl) groups at the cyclopropane carbons [Chart; a Cl, Br, or OH group at C(3) of nortricyclane does not change the reaction mechanism].[2,11–13] This effect can be compared with that of a methyl group at an olefinic carbon of norbornene or bicyclo[2.2.1]heptene (**5**) since this bicyclic substrate also



Scheme 1.

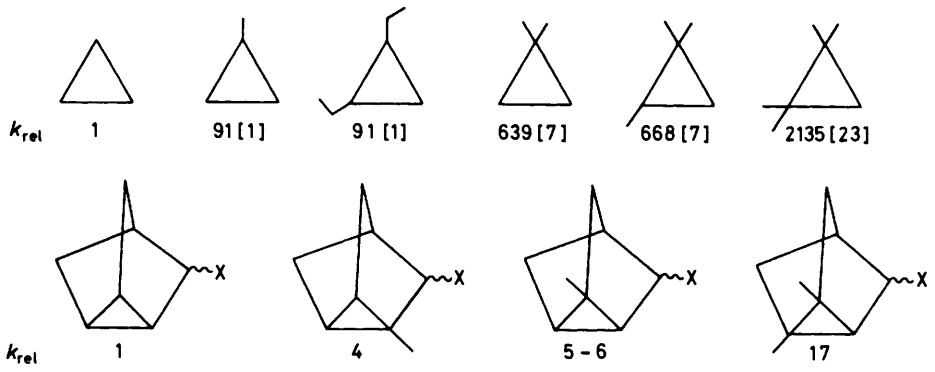
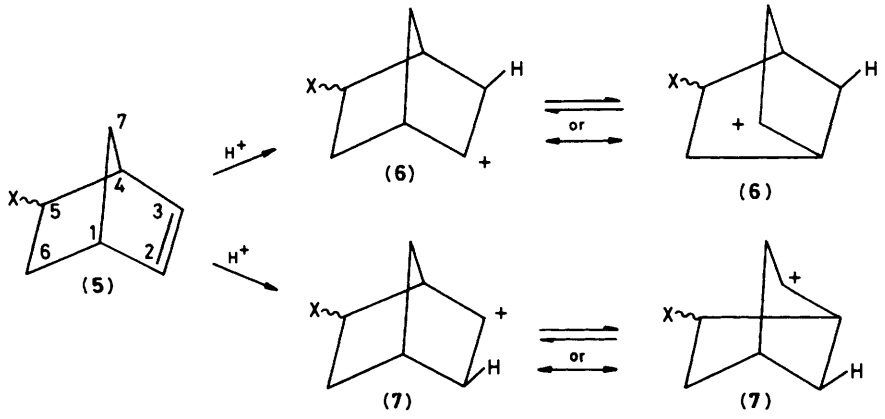


Chart.



Scheme 2.

produces the 2-norbornyl cation (*via* the rate-determining protonation of the double bond; the A–S_E2 or Ad_E2 mechanism) and solely *exo*-2-norbornyl products (Scheme 2; X = H).[6,13] A methyl group at an olefinic carbon increases the hydration rate by a factor of 10^4.[14]

The slight accelerating effects of methyl groups at the cyclopropane ring as well as a poor correlation between the protonation rates and initial strain energies of cyclopropanes have been explained by a slight development of the positive charge at the three-carbon ring and an early transition state.[2] On the other hand, in the hydration (protonation) of alkenes the transition state is probably late, *i.e.*, carbocation-like,[15,16] thus a hyperconjugative effect of the methyl group is significant.

If this transition state hypothesis is correct, the effects of substituents at other parts of a cyclopropane compound than at the three-carbon ring should also be slight. This gives a goal for the present work, which deals with the effects of 3-substituents on the rate and mechanism of disappearance of nortricyclane in aqueous acid with 5-substituted 2-norbornenes[17] as reference compounds.

Results and Discussion

Disappearance rates of ten 3-X-substituted nortricyclanes were measured in perchloric acid under different conditions by g.l.c. The rate constants in 1 mol dm^{-3} $HClO_4$ at 348.2 K as well as activation parameters, solvent deuterium isotope effects, and slopes for linear log k_1 *versus* H_0 correlations were calculated. The results are collected in Table 1 together with the inductive substituent constants (σ_I^q) of X.[18]

When X = H, CH_2OH, CH_2Cl, Ac, OH, CN, or NO_2, the activation entropies, isotope effects (*cf.* k_H/k_D = 1.56 in the hydration of cyclopropane),[19] and slopes for log k_1 *versus* H_0 are all typical of an A–S_E2 or Ad_E2 mechanism, in which proton transfer from an oxonium ion to a carbon atom of the three-membered ring is the rate-determining stage of reaction.[13,20] In the case when X = OH, no general acid catalysis was detected,[21] but the results of rate measurements in acidic H_2O–D_2O mixtures were in agreement with the slow proton transfer to a carbon atom.[12a,16] Thus the mechanism does not change in the case of the above mentioned substituents although the hydration rate varies by almost five powers of ten.

According to the kinetic parameters (Table 1) an acetoxy or oxo group or an α-hydroxy α-methyl function at the 3-position of nortricyclane causes a change of mechanism: protonation now occurs at an oxygen atom of the substituent in a fast pre-equilibrium followed by a rate-limiting bimolecular (OAc* and oxo) or monomolecular ($\langle^{OH}_{Me}$) stage.[20a,22,23] Paasivirta[24] has also proposed a similar (A-2) mechanism for the reaction of 1-methyl-3-nortricyclanone in sulphuric acid–acetic acid. The results of rate measurements in acidic H_2O–D_2O mixtures are also in agreement with the unimolecular (A-1) mechanism in the case of 3-methylnortricyclan-3-ol.[25]

Before examination of the effects of the 3-X-substituents on the hydration rates of nortricyclanes, possible protonation of a substituent must be considered. If X is protonated its ability to withdraw electrons increases and thus electrophilic attack on the cyclopropane ring is retarded. Comparison of the basicities

* The reaction is a normal ester hydrolysis ($A_{AC}2$), which yields the corresponding alcohol (X = OH).[23]

Table 1. Disappearance rate constants of 3-X-substituted nortricyclanes in 1.00 mol dm^{-3} aqueous perchloric acid at 348.2 K as well as activation parameters, solvent deuterium isotope effects and slopes for log k_1 *versus* H_0 at the same temperature if not otherwise noted. σ_I^q = inductive substituent constant [18]

X	σ_I^q	k_1/s^{-1}	$\Delta H^{\neq}$/kJ mol^{-1}	$\Delta S^{\neq}$/J mol^{-1} K^{-1}	k_H/k_D	Slope for log k_1 *versus* H_0	Ref.
H	0	0.117	82	−29		−1.17[a]	13
CH_2OH	0.66	8.09×10^{-3}	92	−21	1.54[b]		This work
CH_2Cl	1.02	3.90×10^{-3}	90	−34	1.42[c]		20*e*
Ac	1.69	6.31×10^{-4}	104	−9	1.35	−1.19[d]	20*d*
OH	1.74	8.64×10^{-4}	97	−27	1.49		20*a*
	1.85	4.00×10^{-3}	113	+33	0.48		20*a*
OAc	2.12	2.18×10^{-3}	63[e]	−113[e]	0.68	curved[a]	This work, 23
CN	3.04	1.23×10^{-5}	97	−32	1.38[b]	−1.11	20*b*
NO_2	3.52	2.05×10^{-6}	99	−41	1.22	−1.04[f]	20*c*
Oxo	3.66[g]	1.86×10^{-6}	105	−41	0.62	−0.65	22

[a] 298.2 K. [b] 328.2 K. [c] 338.2 K. [d] 318.2 K. [e] Measured in 60% dioxane–water.[23] [f] 358.2 K. [g] Calculated by means of a linear correlation between the substituent constants of Siegel and Komarmy [18b] and the σ_I^q values.[18a]

Scheme 3.

of X-substituted alkanes and cycloalkanes, however, suggests that the portion of X-protonated substrates is insignificant ($\lesssim 1\%$ in 1 mol dm^{-3} $HClO_4$).[26]

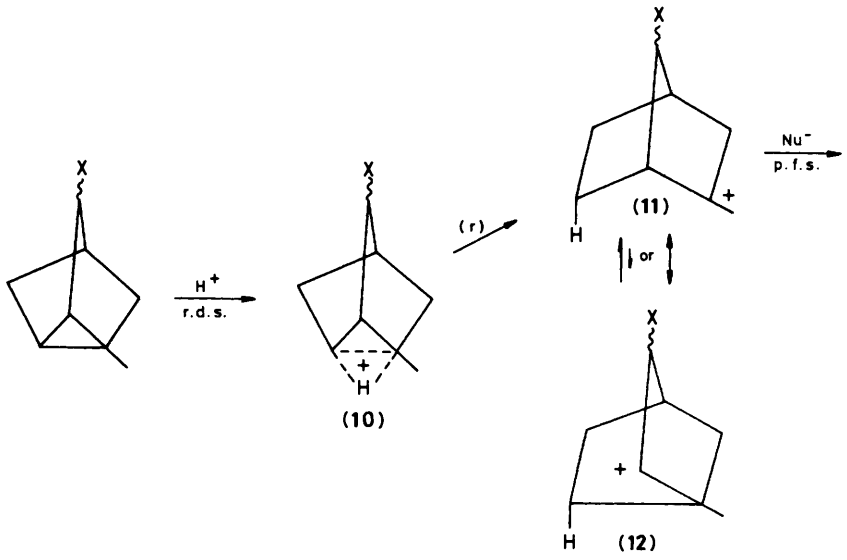
The logarithms of the hydration rate constants (at 348.2 K) of the 3-X-substituted nortricyclanes which react by the A–S_E2 mechanism correlate with inductive substituent constants σ_I^q [18] [equation (1); $r = -0.996$; slope $= -1.40$ and $r = -0.994$ at

$$\log (k_1/s^{-1}) = -(1.30 \pm 0.05)\sigma_I^q - (1.02 \pm 0.10) \quad (1)$$

298.2 K; the correlations are almost as good when employing σ_I values [27]]. The points for 3-acetoxy-and 3-methyl-3-hydroxy-nortricyclanes deviate about one logarithmic unit upwards from the regression line due to their different mechanisms of reaction, but that for 3-oxonortricyclane is on the line although its mechanism is also different (see above). An explanation for the latter phenomenon is possibly conjugative interaction between the oxo group and the three-membered ring,[28] which reduces the energy of the initial state and retards the protonation of the cyclopropane ring. (A corresponding retardation was observed in the protonation of norbornen-2-one, in which homo-conjugation between the oxo group and the carbon–carbon double bond exists.[17]) However, the rate for another mechanism, *i.e.*, protonation of the oxo group, is by accident such that the point does not deviate from the regression line calculated for A–S_E2 hydration.

Now we can consider whether the effects of the substituents are normal or exceptional. A small absolute value of the slope of equation (1) (reaction constant ρ_I) would be in agreement with an early or otherwise slightly charged transition state. Let us take the inductive reaction constants of the A–S_E2 hydration (protonation) of the double bond of 5-X-substituted norbornenes (**5**) as reference values (Scheme 2; ρ_I is practically independent of the position, *exo* or *endo*, of 5-X).[17] The reaction constants have been determined separately for the protonation of the two olefinic carbons of 5-X-norbornenes: $\rho_I = -1.56$ for C(2) protonation and −0.92 for C(3) protonation under similar conditions as for nortricyclanes.[17] As we can see, the reaction constant of hydration of the nortricyclanes (−1.30 at 348.2 K) is between those measured for the norbornenes and slightly closer to that for C(2) protonation.

Let us consider the norbornyl cations formed *via* rupture of different carbon–carbon bonds of the cyclopropane ring of the 3-X-nortricyclanes (Scheme 3). Cation (**6**) formed *via* cleavage of the C(1)–C(2) or C(2)–C(6) bond is similar to that formed *via* C(3) protonation of 5-X-norbornene [(**5**); Scheme 2]. The formation of another possible cation (**9**) *via* cleavage of the same bonds is not probable due to generation of the positive charge



Scheme 4.

Table 2. Tentative assignments of ^{13}C n.m.r. chemical shifts for 3-X-substituted nortricyclanes in $CDCl_3$ (tetramethylsilane as internal reference). The position of X is *cis* to C(5)

X	C(1)[a]	C(2)[a]	C(3)	C(4)	C(5)[b]	C(6)[a]	C(7)[b]	X
H	9.7	9.7	33.0	29.6	33.0	9.7	33.0	
CH_3	11.8	16.4	39.0	34.8	28.8	9.3	34.4	14.5
CH_2OH	11.2	12.3	47.8	30.9	29.0	9.6	34.1	62.8
CH_2Cl	12.0	14.0	45.2	32.1	28.9	9.7	34.0	48.1
$COCH_3$	11.5	12.3	57.9	29.1	33.1	10.1	34.7	209.8 and 30.3
CO_2H	11.4	12.7	49.5	33.5	34.5	10.3	30.7	180.8
CN	10.7	14.2	33.9	33.9	31.1	9.7	32.9	119.0
OH	13.5	16.2	77.4	35.6	29.4	10.6	30.7	
$\langle^{OH}_{CH_3}$	13.2	21.8	82.0	40.5	31.8	12.5	31.8	21.8
$OCOCH_5$	12.9	13.8	79.9	33.3	30.2	11.2	30.5	170.9 and 21.2
Oxo	19.2	17.3	214.1	37.7	31.6	19.2	31.6	
Cl	13.7	17.7	65.2	37.0	30.1	11.1	31.6	
NO_2	13.1	11.5	89.8	35.3	32.4	13.4	30.3	

[a] Signals are possibly to be interchanged. [b] Signals are possibly to be interchanged.

adjacent to the electron-withdrawing substituent.[11] Cation (**8**) formed *via* rupture of the C(1)–C(6) bond is not similar to that (**7**) formed *via* C(2) protonation of 5-X-norbornene, but the substituent is, however, at the γ position from the positively charged carbon atom in both of them. Thus, the reaction constants of hydration of nortricyclanes is in accord with those measured for the norbornenes. According to Werstiuk and his co-workers,[11] major products are formed *via* the initial cation (**8**) and minor products *via* cation (**6**) when addition of acetic acid occurs to 3-chloro- or 3-bromo-nortricyclane under catalysis by sulphuric acid. This product analysis is thus also in agreement with the reaction constant measured in this work.

What is the explanation for the contradiction between the slight accelerating effect of a methyl group at a cyclopropane carbon and the normal retarding effect of an electron-withdrawing substituent at C(3) upon the hydration (protonation) rate of nortricyclane? Evidently it cannot be a slight development of the positive charge in an (early) transition state since the absolute value of the reaction constant should be small in this case. Besides, measurements of hydration rates in acidic H_2O–D_2O mixtures have given results according to which the degree of proton transfer at the transition state ($0 \leq \alpha \leq 1$) is very similar in the hydrations of nortricyclanes ($\alpha = 0.78 \pm 0.07$) and norbornenes ($\alpha = 0.75 \pm 0.05$) and refers to a late transition state.[16] Neither can it be the poor ability of the cyclopropane ring to transmit electronic effects.[29]

Perhaps the explanation is an existance of different intermediates [(**10**) and (**11**)] in the rate-determining (r.d.s.) and product-forming (p.f.s) stages (Scheme 4) as Depuy has proposed for the electrophilic cleavage of substituted cyclopropanes.[4] If the former intermediates (**10**) are the edge-protonated cyclopropanes, the positive charge, although largely developed in the transition state, is not localized at one carbon atom having a methyl substituent as in (**11**) but delocalized in a two-carbon one-hydrogen system (two-electron three-centre bond). The methyl group has no marked hyperconjugative effect in this case, but the inductive effect of the electron-withdrawing substituent works normally since there is a positive charge at the three-membered carbon ring. The good linearity of the equation suggests that protonation occurs at one edge of the ring in the case of the 3-substituted nortricyclanes and the slope (-1.30) suggests that the edge is the C(1)–C(6) bond (Scheme 4), since the positive charge is delocalized between two carbon atoms at the γ-positions and one hydrogen atom at the δ-position from the substituent.

Experimental

Syntheses.—The preparations of 3-X-substituted nortricyclanes have been reported.[13,20,22] Their purities (by g.l.c.) were mostly 99% or better. In the cases when X = CH_2Cl, CN, or NO_2 the purities were *ca.* 95%. The retention times of impurities were such that they did not disturb kinetic measurements by g.l.c. The ^{13}C n.m.r. spectra of the substrates were recorded on a JEOL FX 60 or JEOL JNM-GX-400 spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. The chemical shifts are listed in Table 2. They are in the case when X = H, OH, oxo, or $\langle^{OH}_{Me}$ in agreement with published data.[30]

Kinetics.—Disappearance rates of the substrates (initial concentration 4×10^{-5} to 3×10^{-3} mol dm^{-3}) in thermostatted aqueous perchloric acid were followed by taking samples after appropriate intervals during *ca.* 2.5 half-lives, by neutralizing them with ammonia (and phosphate buffer if necessary) and by analysing them on a Perkin-Elmer F 11 gas chromatograph (FFAP, Carbowax 20 M, or XE 60 packed columns). An inert ketone, mostly norcamphor, was used as internal standard. The peak areas were measured on a Hewlett-Packard 3380S integrator. The fair first-order kinetics was generally observed with standard errors of 1–3%, although poor solubility of some substrates (X = H or CH_2Cl) decreased accuracy of analyses. In these cases the analyses and runs were repeated several times.

Acknowledgements

I am grateful to Mr. J. Tallgren for assistance in the kinetic measurements and to Mrs. M. Samppala and Mr. J. Mattinen for recording the n.m.r. spectra.

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Received 23*rd December* 1985; *Paper* 5/2257