Mechanisms of solvolytic elimination reactions of tertiary substrates: stereospecific 1,2-elimination reactions

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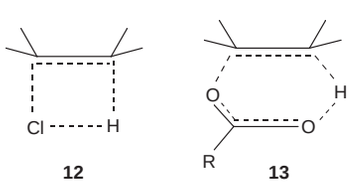
Solvolysis of (*R*,*S*)-1-chloro-1-(fluoren-9-yl)-2-methylcyclopentane (**1-Cl**) or the analogous 3,5-dinitrobenzoate ester **1-DNB** in largely aqueous solutions yields alkenes 1-(fluoren-9-yl)-2-methylcyclopentene (**4**) and 1-(fluoren-9-yl)-5-methylcyclopentene (**5**) as the main products. The chloride **1-Cl** gives a product ratio **4**:**5** of 35:65 in 25 vol% acetonitrile in water at 25 °C. The former product is formed by an *anti* elimination route, which shows that the elimination reaction does not have a concerted unimolecular mechanism. The reaction to give **4** is suggested to occur *via* a carbocation ion pair in which the leaving chloride ion abstracts the β-hydron. Alternatively, the reaction may have an enforced uncoupled concerted mechanism in which water acts as the hydron-abstracting base. Also, solvolysis of 2-methyl-1-phenylcyclopentyl *p*-nitrobenzoate (**8-PNB**) yields the more stable alkene **10** by *anti* stereochemistry.

Introduction

It was recently pointed out that there is no consensus about the dynamics of solvolytic substitution and elimination reactions at tertiary carbon.[1] For example, it is not clear what the lifetime of a simple tertiary carbocation is in aqueous solution. The rate constant for reaction of the *tert*-butyl carbocation with water has been estimated as $k_w \sim 4 \times 10^9$ s^{-1} [2–4] and $k_w \sim 1 \times 10^{10}$ s^{-1},[5–7] which suggests that the ion pair undergoes diffusional separation ($k_{-d} \sim 2 \times 10^{10}$ s^{-1}) before reaction with nucleophiles. A recent estimate is much larger, $\sim 4 \times 10^{12}$ s^{-1}.[1] This rate constant refers to reaction of the *tert*-butyl carbocation with water *in which water has already undergone rotation into a reactive conformation*. This very high reactivity of the *tert*-butyl carbocation suggests that the carbocation does not form a liberated intermediate in aqueous solution because the reaction of the ion pair with the solvent is much faster than its separation to free ions. The high reactivity of the carbocation has been used as one of several arguments for a concerted unimolecular mechanism for the competing elimination reaction.[1,8]

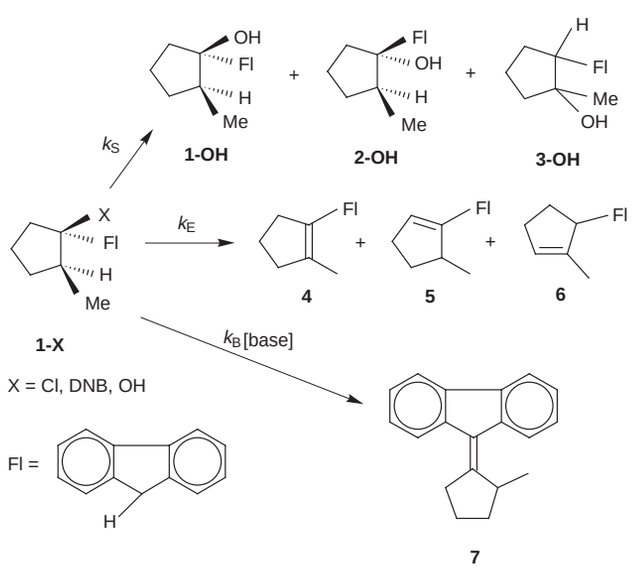
The proposed concerted unimolecular reaction mechanism is controversial because the generally accepted solvolytic elimination reaction mechanism for tertiary substrates is the ion-pair mechanism in which the leaving group acts as a base to abstract the hydron within the ion pair.[9,10] Experimental support for such a mechanism was recently reported for the solvolytic elimination of cumyl substrates having neutral leaving groups of different basicity; a Brønsted parameter of $\beta = 0.13$ was measured.[11] However, as has also been pointed out by Toteva and Richard,[1] it is not clear why chloride anion, which is much less basic than water, is such an efficient base in abstracting a hydron within the ion pair.

The concerted unimolecular elimination mechanism requires a cyclic transition state such as **12** and **13** providing *syn* stereochemistry. An investigation of the stereochemistry of the elimination is therefore essential for the mechanistic assignment.



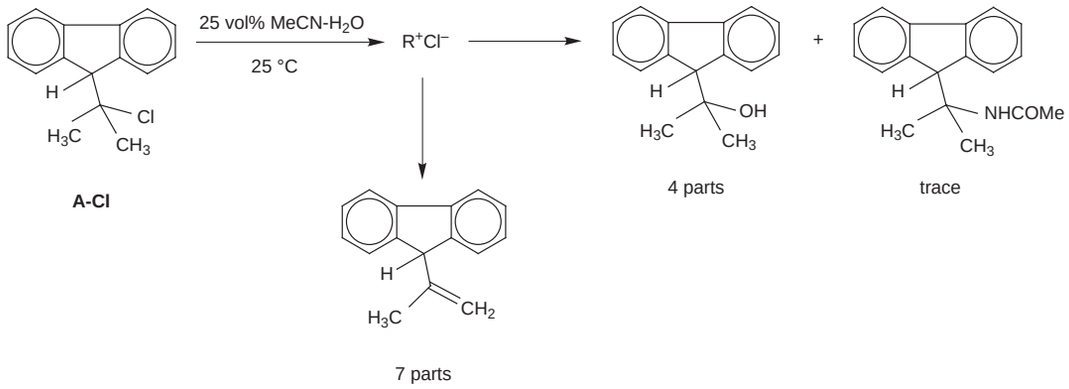
12 **13**

We report here a study of the kinetics, product distributions, and stereochemistry of solvolytic elimination reactions of the chloride **1-Cl** and the corresponding 3,5-dinitrobenzoate **1-DNB** (Scheme 1). The putative ion-pair intermediates of these



Scheme 1

reactions are concluded to have similar or shorter lifetimes than that formed from *tert*-butyl chloride. The closely related chloride **A-Cl** has been concluded to undergo solvolysis, yielding substitution and elimination *via* a common ion-pair intermediate as shown in Scheme 2.[12] This mechanistic assignment was based upon the measured kinetic deuterium isotope effects using the hexadeuterated analog of **A-Cl**, which indicated a branched mechanism *via* a common intermediate. The *anti* stereochemistry now reported for the elimination reaction to give alkene **4** from **1-Cl** and **1-DNB** supports this mechanistic assignment and the alternative concerted unimolecular mechanism can be ruled out. However, the estimated lifetime of the putative intermediate $\mathbf{1}^+\mathbf{X}^-$ is very short and an elimination reaction mechanism of uncoupled concerted type is also discussed. The paper also addresses the question of why chloride



Scheme 2

ion shows such a high reactivity as a Brønsted base in many solvolytic elimination reactions.

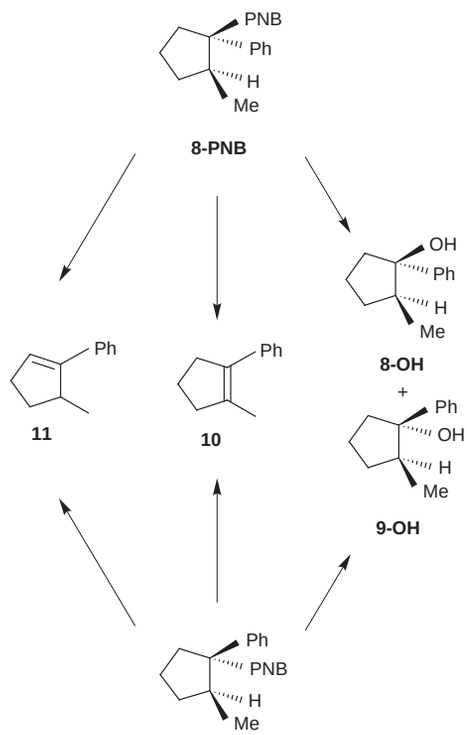
Results

Synthesis and structure assignment

(*R*,*S*)-1-(Fluoren-9-yl)-2-methylcyclopentanol (**1-OH**) was synthesized by treating fluorene with butyllithium in dry diethyl ether, followed by the addition of 2-methylcyclopentanone. The addition of fluorenyl anion to the carbonyl group of 2-methylcyclopentanone should occur by attacking the face opposite to the methyl group due to steric hindrance providing **1-OH** (Scheme 1) as the main diastereomer. This structure assignment was confirmed by ^{1}H NMR studies; NOESY spectra in DMSO-d_6 showed NOEs (5–10%) between the methyl and the hydroxy protons. (*R*,*S*)-1-Chloro-1-(fluoren-9-yl)-2-methylcyclopentane (**1-Cl**) was prepared from **1-OH** and dry hydrogen chloride gas in dichloromethane at 0 °C.

A mixture of the two diastereomers of 2-methyl-1-phenylcyclopentanol was prepared as above. The configurations of the two diastereomers were determined by ^{1}H NMR NOE difference spectra. One of the isomers showed NOEs between the methyl protons and the hydroxy proton, and between the *ortho*-protons of the phenyl group and the methine proton. The (*R*,*S*)-structure was assigned to this isomer (**8-OH**, Scheme 3).

(*R*,*S*)-1-(Fluoren-9-yl)-2-methylcyclopentyl 3,4-dinitrobenzoate (**1-DNB**) was synthesized from **1-OH**, butyllithium, and 3,5-dinitrobenzoyl chloride. This reaction is expected to proceed with complete retention of configuration; only one diastereomer was obtained. The same procedure was used for preparation of **8-PNB** from **8-OH**, and **9-PNB** from **9-OH**.



Scheme 3

Kinetics and product studies

The solvolysis of **1-Cl** or **1-DNB** in mixtures of water with acetonitrile, methanol, or trifluoroethanol at 25 °C provides mainly elimination products (Scheme 1). The predominant alkenes are those formed by 1,2-elimination: 1-(fluoren-9-yl)-2-methylcyclopentene (**4**) and 1-(fluoren-9-yl)-5-methylcyclopentene (**5**), the former by an *anti* elimination path. A minor amount of the 1,3-elimination product 5-(fluoren-9-yl)-1-methylcyclopentene (**6**) is also formed. The substitution products are (*R*,*S*)-1-(fluoren-9-yl)-2-methylcyclopentanol (**1-OH**), (*R*,*R*)-1-(fluoren-9-yl)-2-methylcyclopentanol (**2-OH**), and the rearranged alcohol 1-(fluoren-9-yl)-2-methylcyclopentanol (**3-OH**), along with the corresponding ethers. The product compositions and the kinetics of the reactions were studied by a sampling high-performance liquid chromatography procedure combined with GC analysis of the alkene compositions. The measured rate constants are recorded in Table 1 and the results of the product studies are shown in Table 2. Sodium perchlorate has a small rate-enhancing effect on the solvolysis of **1-Cl**. In contrast, chloride, bromide, and azide anions show negative salt effects (Table 1) on both k_S and k_E (Scheme 1). Fig. 1 shows the effect of azide anion. It is not clear why the fraction of alkene **4** increases with increasing azide ion concentration in 40 vol% acetonitrile in water. However, there is no such effect in 25 vol% acetonitrile (Table 2) or with acetate ion, which is of similar basicity as azide ion.

The substitution with solvent water predominantly occurs with retention of configuration, *e.g.* the amount of retention was measured with **1-Cl** as 81% in the water–acetonitrile mixtures and as *ca.* 92% in 50 vol% trifluoroethanol in water (Table 2). The bimolecular methoxide-promoted E2 reaction providing 1-fluoren-9-ylidene-2-methylcyclopentane (**7**) is relatively slow. The data in Table 1 yield an approximate second-order rate constant of $(34.7 - 8.2) \times 10^{-6}/0.10 = 265 \times 10^{-6}$ M^{-1} s^{-1}, which is about 6 times smaller than the corresponding rate constant for the closely related **A-Cl**.[12,13] It is difficult to study the hydroxide-promoted E2 reaction of **1-Cl** since even with a large concentration of base this reaction is relatively slow compared with the solvolysis. Moreover, the alkenes produced from the latter reaction are isomerized by the hydroxide ion to give the thermodynamically more stable alkene **7**. It is easier to study the methoxide-promoted elimination owing to the slower competing solvolysis in methanol (Tables 1 and 2).

Table 1 Rate constants for the reactions of **1-Cl**[a] at 25 °C

Salt	Solvent (vol%)[b]	$k_{obs}/10^{-6}$ s^{-1}[c,d]	$k_S/10^{-6}$ s^{-1}[d]	$k_E/10^{-6}$ s^{-1}[d]
None	MeCN (40)	519	22	497
0.50 M $NaClO_4$	MeCN (40)	743	33	710
0.50 M NaCl	MeCN (40)	312	11	301
0.50 M NaBr	MeCN (40)	450	17	433
0.50 M NaN_3	MeCN (40)	519	16	504
None	MeCN (25)	3.9×10^3	0.2×10^3	3.7×10^3
None	MeOH	8.2	0.5	7.7
0.10 M NaOMe	MeOH	34.7		

[a] Substrate concentration 0.01–0.1 mM. [b] By volume in water. [c] $k_{obs} = k_S + k_E + k_B$[base] (Scheme 1). [d] Estimated maximum error: ±10%.

Table 2 Product compositions for the solvolysis reactions of **1-Cl**, **1-DNB**, and the acid-catalyzed solvolysis of **1-OH** at 25 °C

			Product/mol%[c]					
Substrate[a]	Solvent (vol%)[b]	Salt	**1-OH**	**2-OH**	**3-OH**	**4**	**5**	**6**
1-Cl	MeCN (25)	none	2.8	0.6	2.5	30	55	9
1-Cl	MeCN (25)	0.75 M NaOAc	2.4	0.6	2.5	25	58	11
1-Cl	MeCN (25)	0.75 M NaN_3	2.9	0.5	2.8	31	56	7
1-Cl	MeCN (40)	none	2.1	0.5	1.6	24	61	11
1-Cl	MeCN (40)	0.50 M $NaClO_4$	2.4	0.5	1.5	22	61	13
1-Cl	MeCN (40)	0.50 M NaN_3	1.5	0.2	1.3	38	50	9
1-Cl	MeCN (40)	0.50 M NaBr	1.8	0.4	1.4	33	53	11
1-Cl	MeCN (40)	0.50 M NaCl	1.7	0.5	1.3	28	58	11
1-Cl	MeCN (60)	none	1.6	0.3	1.0	18	70	9
1-Cl	MeCN (75)	none	1.3	0.2	0.6	13	76	8
1-Cl	MeOH (50)[d]	none	1.5	0.3	1.4	39	50	7
1-Cl	CF_3CH_2OH (50)[d]	none	2.5	0.2	0.9	15	72	10
1-Cl	MeOH (100)[d]	none				34	58	8
1-DNB[e]	MeCN (40)	none	1.8	0.4	1.4	8	81	8
1-OH	MeCN (25)	0.75 M $HClO_4$		~9[f]	—	60	15	16
1-OH[g]	MeCN (25)	0.75 M $HClO_4$		<1	<1	84	7	7

[a] Substrate concentration 0.01–0.1 mM. [b] By volume in water. [c] Estimated maximum error is ±10%. [d] Ethers are formed in small amounts, but they are not included in the calculation of the product compositions. [e] $T = 70$ °C. [f] The yield of **2-OH** was determined by extrapolation to zero time of a plot of product yield ratio [**2-OH**]/([**2-OH**] + [**4**] + [**5**] + [**6**]) against time for 2–15% reaction during which the ratio of the alkenes does not change within experimental error. No **3-OH** was detected by HPLC analysis. [g] Product yields after 3 months, only 1.3 mol% of **1-OH** left.

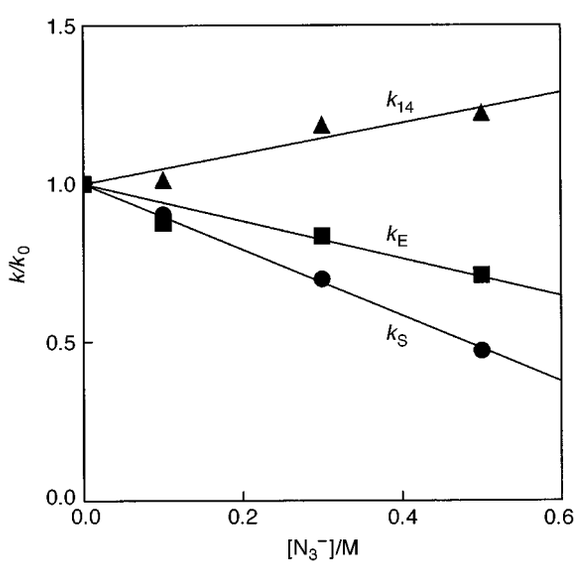


Fig. 1 The effect of added sodium azide on the reaction rates of **1-Cl** in 40 vol% acetonitrile in water at 25 °C. Ionic strength was kept constant (0.50 M) with sodium perchlorate. The rate constant k_{14} refers to formation of alkene **4** from **1-Cl**.

The acid-catalyzed solvolysis of **1-OH** in 25 vol% acetonitrile in water containing 0.75 M $HClO_4$ gives the alkenes **4**, **5**, and **6** as shown in Table 2. The product composition is time-dependent, showing that the initially formed products undergo slow isomerization, a long reaction time favouring the more stable alkene **4**. No interconversion of the products occurs under the neutral conditions used for the solvolysis of **1-Cl** and **1-DNB**.

The nucleophilic discrimination between azide ion and water is very small and only a very small amount of azide product is observed in the solvolysis of **1-Cl** in 40 vol% MeCN in water containing 0.50 M NaN_3 ($k_{N_3}/k_{HOH} = 3$). Thiocyanate also gives only one product; a discrimination value of $k_{SCN}/k_{HOH} = 3$ was measured with 0.75 M NaSCN in 25 vol% acetonitrile in water. These are dimensionless ratios of second-order rate constants calculated by means of eqn. (1). No traces of other isomeric

$$k_{Nu}/k_{HOH} = (\Sigma[RNu]/\Sigma[ROH])([H_2O]/[Nu^-]) \quad (1)$$

azide or thiocyanate products are detected by HPLC, ^{1}H NMR, and GC analyses.

The solvolysis of **8-PNB** and of the more reactive isomer **9-PNB** in 25 vol% acetonitrile in water yields the elimination products 2-methyl-1-phenylcyclopentene (**10**), 5-methyl-1-phenylcyclopentene (**11**) and the substitution products (*R*,*S*)-2-methyl-1-phenylcyclopentan-1-ol (**8-OH**) and the corresponding (*R*,*R*)-diastereomer **9-OH** (Scheme 3). The product compositions for the solvolysis reactions of the esters and the acid-catalyzed reactions of the alcohols, determined by HPLC analysis, are shown in Table 3. Alkene **10** is the thermodynamically more stable product, and after long reaction time in perchloric acid solution the alcohols have been converted to 94% of **10** and 6% of **11** (Table 3). No interconversion of the products occurs under the neutral conditions used for the solvolysis of **8-PNB** and **9-PNB**. The nucleophilic discrimination between thiocyanate ion and water is small: a discrimination ratio of $k_{SCN}/k_{HOH} = 63$ was measured with 0.75 M NaSCN in 25 vol% acetonitrile in water.

Table 3 Product compositions for the solvolysis reactions of **8-PNB**, **9-PNB** and the acid-catalyzed solvolysis of **8-OH** and **9-OH** in 25 vol% acetonitrile in water at 25 °C

		Product/mol%[b]			
Substrate[a]	$[HClO_4]$/M	**8-OH**	**9-OH**	**10**	**11**
8-PNB	—	9	66	6	19
9-PNB	—	9	60	9	22
8-OH	0.10		63[c,d]	20	17
8-OH	0.75			94[e]	6[e]
9-OH	0.10	51[d,f]		26	23
9-OH	0.75			94[e]	6[e]

[a] Substrate concentration 0.01–0.1 mM. [b] Estimated maximum error is ±10%. [c] The yield of **9-OH** was determined by extrapolation to zero time of a plot of product yield ratio [**9-OH**]/([**10**] + [**11**]) against time for 6–21% reaction, during which the ratio of the two alkene stereoisomers does not change within experimental error. [d] Estimated maximum error is ±20%. [e] Product yields after 3 months, no alcohol left. [f] The yield of **8-OH** was determined by extrapolation to zero time of a plot of product yield ratio [**8-OH**]/([**10**] + [**11**]) against time for 36–82% reaction, during which the ratio of the two alkene stereoisomers does not change within experimental error.

Discussion

The solvolysis of **1-Cl** in 25 vol% acetonitrile in water (Scheme 1) is about 27 times faster than that of the closely related substrate **A-Cl** (Scheme 2), and the elimination-to-substitution ratio is larger, 94 : 6 compared with 7 : 4.[12] Thus, the solvolytic substitution of **1-Cl** is about 4 times faster than that of **A-Cl** and the elimination reactions of **1-Cl** are 40 times faster than that of **A-Cl**. The reason is presumably steric; there is more crowding in **1-Cl** than in **A-Cl**, which is decreased in the elimination products. Consistently, alkenes with only traces of alcohols are the final products in acidic solution (*vide infra*). Accordingly, there is a large driving force favouring reaction of the carbocation to give the alkenes. This is in contrast to the partitioning of a simple acyclic carbocation where thermodynamics generally favours formation of the alcohol product.

Addition of azide anion does not increase the rate of disappearance of the substrate ($k_{obs} = k_S + k_E$, Fig. 1), and the amount of azide substitution product is very small, $k_{N_3}/k_{HOH} = 3$ [see Results, dimensionless ratio of second-order rate constants in 25 vol% acetonitrile in water, eqn. (1)]. The amount of substitution product with thiocyanate ion, which is also expected to give substitution products with a diffusion-limited rate, is also very small ($k_{SCN}/k_{HOH} = 3$). This is consistent with the results obtained for **A-Cl**, which showed an extremely low nucleophilic discrimination of $k_{N_3}/k_{HOH} = 5$ in 25 vol% acetonitrile in water.[12] The nucleophilic discrimination between methanol and water for reaction with the carbocation was also found to be unusually small ($k_{MeOH}/k_{HOH} \sim 0.6$).[12,14] The corresponding bromide **A-Br** showed a nucleophilic selectivity in 70 vol% methanol of $k_{SCN}/k_{HOH} = 3$ and $k_{N_3}/k_{HOH} \sim 4$.[14]

These results suggest that the carbocation $\mathbf{1}^+$ is very short-lived. The lifetime should be close to that of $\mathbf{A}^+$, which reacts with solvent water as a nucleophile with a rate constant estimated at $k_w \sim 4 \times 10^{10}$ s^{-1}.[12] This rate constant was determined by the "azide-clock" method,[15] *i.e.* it is based upon the measured product ratio [**A-N$_3$**]/[**A-OH**] and an assumed rate constant for reaction of $\mathbf{A}^+$ with azide ion of 5×10^9 M^{-1} s^{-1}. Direct measurement of second-order rate constants for diffusion-limited reaction of azide ion with more stable carbocations in aqueous acetonitrile confirms that this is a good estimate.[16] However, since the diffusional separation of an ion pair in water has a rate constant of about 2×10^{10} s^{-1},[17] the ion pair reacts with nucleophiles to some extent before separation. Therefore, the azide-clock method for estimation of k_w for the carbocation probably results in a lower limit owing to significant reaction of azide ion through a preassociation mechanism.†

Despite the uncertainties discussed above, let us use the results with azide ion and thiocyanate ion, $k_{N_3}/k_{HOH} = k_{SCN}/k_{HOH} = 3$, as a clock to estimate the lifetime of the carbocation. Thus, the carbocation $\mathbf{1}^+$ reacts to give products through the ion pair with a rate constant of $\geq 1.2 \times 10^{12}$ s^{-1}, which is the sum of the rate constants for formation of alcohol ($k_w \geq 7 \times 10^{10}$ s^{-1}) and alkenes ($k_e \geq 11 \times 10^{11}$ s^{-1}). A considerably longer lifetime of the intermediate is obtained if the main routes to the products **5** and **6** do not proceed through the same intermediate as the reactions giving **1-OH** and **4**, *i.e.* there are parallel reactions to these products. Thus, if the main reaction routes providing **5** and **6** do not proceed through the carbocation intermediate as the reactions which give **4** and **1-OH**, the lifetime of the putative intermediate may be much longer ($k_w \sim 4 \times 10^{10}$ s^{-1} and $k_e \sim 3 \times 10^{11}$ s^{-1}) which is far below the borderline ($\sim 10^{13}$ s^{-1}) where the intermediate does not exist as a discrete intermediate owing to the disappearance of the barrier for departure of the leaving group.

A roughly similar reactivity was estimated for the substitution reaction of the ion pair $\mathbf{A}^+\mathbf{Cl}^-$, $k_w = 4 \times 10^{10}$ s^{-1} in 25 vol% acetonitrile in water; the rate constant for the elimination was measured as $k_e = 7 \times 10^{10}$ s^{-1}.[12] For comparison, the nucleophilic selectivity for $PhCH_2C(Me)_2Cl$ under the same reaction conditions was determined as $k_{N_3}/k_{HOH} = 19$,[19] and the reaction *p*-$MeOC_6H_4CH_2C(Me)_2Cl$ in 50% trifluoroethanol or methanol in water shows selectivities of $k_{N_3}/k_{HOH} = 11$–15.[1] Nucleophilic selectivity values are expected to be somewhat smaller in these solvents because the viscosity of the alcohol–water mixtures are higher than those of acetonitrile–water.‡

Indirect evidence for stepwise carbocation reactions is also provided by the formation of significant amounts of **3-OH** and **6**. Formation of these products by concerted reactions would require a large number of changes in bonding occurring at single reaction steps. However, it is plausible that intramolecular transfer of a hydride is concerted with cleavage of the bond to the leaving group. This produces a somewhat more stable tertiary carbocation having a methyl instead of a fluorenyl substituent connected to the carbocation center. Also the predominant retention of substitution with solvent water supports the conclusion of stepwise reactions.

The fluorenyl hydron of **1-Cl**, despite its high acidity (pK_a of fluorene is ~22.5),[20] is abstracted much more slowly than the other β-hydrons. The reason for this behaviour, which is in sharp contrast to the behaviour with added strong bases but is similar to that of **A-Cl** and **A-Br**,[12] is probably that the β-hydrons of the cyclopentane ring provide stabilization of the ionization transition state as well as of the carbocation intermediate by hyperconjugation. Hyperconjugative stabilization from the fluorene 9-hydrogen is sterically unfavourable in this system. This small partial bond-breaking of the carbon-hydrogen bonds increases the acidity of the hydrogens in the carbocation ion pair. Therefore, it should be relatively easy for

† The ion pair does not necessarily show the same partitioning as the free carbocation. A shielding effect that decreases the rate constant for attack of negatively charged nucleophiles, even the potent azide ion, more than attack of a neutral nucleophile is likely. Experimental support for such a shielding has been discussed previously; it results in an *overestimation* of the rate constant for the water reaction.[18] The shielding effect should be more important in reactions showing predominant retention of configuration like that of **1-Cl** (Table 1) than in reactions which mostly give inversion.

‡ The viscosity of 50 vol% methanol in water is about 1.8 times higher than that of water. This means that the rate of diffusion is about 1.8 times slower in the methanol–water mixture than in the mixtures with acetonitrile. Ethanol–water mixtures show even higher viscosity. Accordingly, the value of $k_d = 5 \times 10^9$ M^{-1} s^{-1} for diffusion in water–alcohol solvent mixtures is probably too high. A value of 7×10^9 M^{-1} s^{-1} has been estimated for the diarylmethyl carbocation in 0–50 vol% acetonitrile water.[16]

the chloride leaving group to abstract one of these hydrons to give the elimination products **4** and **5**. The large secondary kinetic deuterium isotope effect of $k_{obs}^{H}/k_{obs}^{D_6} = 2.2$ measured for the hexadeuterated analog of **A-X** (Scheme 2) is consistent with a large amount of hyperconjugation in the rate-limiting ionization transition state.[12] Furthermore, the isotope effects on the solvolytic elimination and substitution reactions vary with solvent composition in a way which suggests coupled reactions *via* a common intermediate.[12]

The partial breaking of the bonds to the β-hydrogens is also manifested by a 1,2-hydride shift which gives rise to the rearranged alcohol **3-OH** and the alkene **6**. The π-orbitals of the fluorene moiety have been concluded to assist the ionization to the primary carbocation which is formed in the solvolysis of 9-(4′-bromophenylsulfonyloxymethyl)fluorene.[21] Stabilization of this type is expected to be small in the tertiary carbocations $\mathbf{1}^+$ and $\mathbf{A}^+$ for steric reasons and there is also less need for such participation. Therefore, the large amount of retention is most reasonably attributed to the larger stability of the **1-OH** diastereomer, and not to significant participation. Attack of the nucleophile from the less sterically hindered side of the carbocation gives rise to the more stable **1-OH** as the main substitution product. However, this side of the ion pair holds the negatively charged leaving group that may slow down the attack of the negatively charged nucleophile more than the reaction with the uncharged water molecule (which may involve the solvent-separated ion pair). The result is an overestimation of k_w for short-lived carbocations.[18]

The stereochemistry of the elimination reactions of **1-Cl** and **1-DNB** to give alkene **4** is *anti*, which shows that these reactions are *not* of the concerted unimolecular type, as suggested by Richard and co-workers for the elimination of HCl from *tert*-butyl chloride and related derivatives.[1,22]

Is a concerted *anti* elimination reaction a possible explanation for the formation of alkene **4**? An E2 reaction having a central transition state with a solvent water molecule acting as the hydron-abstracting base should involve loss of the more acidic of the β-hydrons, which is the 9-hydron of the fluorene moiety of the substrate ($pK_a \sim 22.5$). Moreover, strong base, *e.g.* hydroxide anion, abstracts the latter hydron giving rise to alkene **7** by a base-promoted E2 mechanism and there is no indication of a bimolecular reaction to give **4**. We have previously concluded that concerted solvent-promoted elimination reactions in aqueous solvents are only significant for a substrate having an acidic β-hydrogen and which relatively slowly ionizes to a carbocation intermediate.[21] However, in principal, an E2 reaction having a very carbocation-like transition state may show similar characteristics to an elimination reaction through a very unstable ion-pair intermediate. Accordingly, a concerted elimination reaction may be enforced by the non-existence of a barrier for departure of the leaving group. This corresponds to a reaction across a flat potential maximum with no energy well for the intermediate. Such a reaction may account for the relatively large amount of alkene **5** that is formed from **1-Cl** under kinetic control, compared to the more stable alkene **4** (Table 2). Alternatively, **5** may be formed by a concerted unimolecular mechanism.[22]

The elimination of HCl from the ion pair to give alkene **4** is apparently very fast, about 3×10^{11} s^{-1}, which is in fair agreement with the expected rate constant for such a process. The rate constant for rotation of the leaving group into reaction position should be in the order of 10^{11} s^{-1}.[23] The estimated rate constant for formation of **5** from the putative intermediate is larger, about 6×10^{11} s^{-1}. The studied system does not give any information about the stereochemistry of this elimination, *i.e.* which of the hydrons is abstracted. Therefore, it is not possible to exclude that the major reaction path to give **5** does not employ a carbocation intermediate but is a one-step reaction of the concerted unimolecular type.[22] The reaction to give alkene **6** is slower, about 1×10^{11} s^{-1}, but this hydron abstraction should occur from the rearranged carbocation intermediate which is formed either by hydride transfer from the initially formed carbocation, or is formed by a direct ionization involving concerted hydride transfer.

The esters **8-PNB** and **9-PNB** yield about 25% and 30%, respectively, of alkenes **10** and **11**. The fraction of the former, which is formed by an *anti* elimination route from **8-PNB**, is **10**/(**10** + **11**) = 24%. This is not much lower than the fraction of **10** (28%) formed from **9-PNB** by a *syn* elimination route. This shows that the elimination reaction to give **10** does not have a concerted unimolecular mechanism with a pericyclic transition state as **13**, but indicates a carbocation mechanism. *Anti* elimination has also been observed in the solvolysis of 2-aryl-*endo*-2-norbornyl trifluoroacetates in trifluoroethanol.[24]

The substitution reactions of the two diastereomeric esters with solvent water yield predominantly the alcohol **9-OH** (Table 3). The amount of retention for the reaction of **8-PNB** is 12% which might suggest a carbocation reaction with some leaving-group shielding. However, the two diastereomers give similar product compositions, indicating a common carbocation intermediate. Attack of the nucleophile from the less sterically hindered side gives rise to alcohol **9-OH** as the main product.

The lifetime of the carbocation has been determined by trapping experiments with **9-PNB** in 25 vol% acetonitrile in water. The measured nucleophilic discrimination ratio of $k_{SCN}/k_{HOH} = 63$ corresponds to a reactivity of $k_w = 3 \times 10^9$ s^{-1}. It is, as expected, close to that of the cumyl carbocation, $PhC(Me)_2^+$, which has a reactivity of $k_w = 5 \times 10^9$ s^{-1} based upon a measured nucleophilic discrimination ratio of $k_{N_3}/k_{HOH} = 42$ in the same aqueous solvent.[25]

The product data (Table 3) show that the carbocation is *not* a completely free, solvent-equilibrated carbocation since **9-OH** gives a quite different product spectra than the two esters **8-PNB** and **9-PNB**. Also solvolysis of cumyl compounds $PhC(Me)_2X$ gives an elimination fraction which varies with leaving group X.[11,25] This clearly shows that the leaving group is involved in the elimination process. The thermodynamic stabilities of the products are, however, quite different: the cyclic alkenes are thermodynamically much more stable relative to the alcohols than the corresponding acylic alkenes. This is reflected in the product compositions.

The major elimination product from the esters **8-PNB** and **9-PNB** is **11** owing to kinetic control; important factors here are the number of available β-hydrons and the extent of steric hindrance. In contrast, under thermodynamic control alkene **10** is predominant. The same behaviour is observed with **1-Cl**; the alkene product ratio **5** to **4** is much larger under kinetic control than under thermodynamic control (Table 2).

Why is chloride ion such an efficient base in solvolytic elimination reactions?

An important driving force of the ionization is of course the solvation of the chloride ion but it is not expected to be complete at the contact ion-pair stage. Thus, the chloride anion in the ion pair is not solvent-equilibrated and the pK_a of HCl in water may not reflect its kinetic basicity. A halide anion, which is not fully solvated, should be a relatively strong base. For example, it is well known that halide anions in aprotic solvents are strong bases. The stabilization of the positive charge of the carbocation partner by the negative leaving chloride ion of the ion pair may decrease the basicity of the leaving group but this effect is probably less important than the positive effect originating from incomplete solvation. The low catalytic activity of water as a hydron acceptor in E1 reactions and in water-promoted E2 reactions has been observed previously;[26] Brønsted plots generally show a negative deviation for water as base of about one order of magnitude.

It has been concluded that even substrates which solvolyze to give relatively stable carbocations in mostly aqueous solution produce alkene predominantly from the ion pair; the solvent-equilibrated carbocation yields almost exclusively the alcohol product.[27] Moreover, Bunton and co-workers have found that, even in highly aqueous solvents, added Cl^- promotes elimination from relatively stable carbocations.[28]

Conclusions

Our results show that the solvolysis of **1-Cl** does *not* produce alkene **4** by the recently proposed concerted unimolecular mechanism. The results are consistent with a mechanism in which the leaving chloride ion abstracts the β-hydron within an ion pair. The mechanistic conclusions for the solvolysis of the esters **8-PNB** and **9-PNB** are similar.

Experimental

General procedures

NMR spectra were recorded at 25 °C with a Varian Unity 400 spectrometer, for ^{1}H at 400 MHz and for ^{13}C at 100.6 MHz. Chemical shifts are indirectly referenced to TMS *via* the solvent signal (chloroform-d_1 7.26 ppm and 77.0 ppm; DMSO-d_6 2.49 and 39.5 ppm). *J* Values are given in Hz. The high-performance liquid chromatography analyses were carried out with a Hewlett-Packard 1090 liquid chromatograph equipped with a diode-array detector on an Inertsil 5 ODS-2 (3 × 100 mm) reversed-phase column. The mobile phase was a solution of acetonitrile in water. The reactions were studied at constant temperature in a HETO 01 PT 623 thermostat bath. The pH was measured using a Radiometer PHM82 pH meter with an Ingold micro glass electrode.

The GC analyses were carried out with a Varian 3400 capillary gas chromatograph equipped with a flame ionization detector. Nitrogen was used as carrier gas. The column was a fused-silica capillary column (Rescom, SE54, 25 m, 250 μm). The injection temperature was 250 °C, and the column temperature was maintained constant at 200 °C.

Materials

Merck silica gel 60 (240–400 mesh) was used for flash chromatography. Diethyl ether and tetrahydrofuran were distilled under nitrogen from sodium and benzophenone. Methanol and acetonitrile were of HPLC grade. All other chemicals were of reagent grade and used without further purification. The aqueous solutions of sodium azide, sodium chloride, sodium bromide, and sodium perchlorate were adjusted to pH ~6.5 with 1 M aqueous perchloric acid before use.

(*R*,*S*)-1-(Fluoren-9-yl)-2-methylcyclopentanol (1-OH)

A solution of butyllithium (12.5 ml of a 1.6 M solution in hexane, diluted with 30 ml of dry diethyl ether) was added to fluorene (3.3 g), dissolved in dry diethyl ether (60 ml), at room temperature under nitrogen. After addition, the reaction mixture was refluxed for 1 h. Then it was cooled to −40 °C, and a solution of 2-methylcyclopentanone (2.4 g, dissolved in 10 ml of dry diethyl ether) was added. The reaction mixture was stirred at this temperature for 20 min, and was then poured into a mixture of ice and 2 M hydrochloric acid. The mixture was extracted three times with diethyl ether. The combined diethyl ether fractions were washed with water to neutrality, followed by washing with brine and drying over sodium sulfate. After removal of solvent, the crude product was purified by flash chromatography (silica gel) with 10–15% ethyl acetate–pentane as eluent. Recrystallization twice from CH_2Cl_2–pentane gave pure material: mp 102–103 °C; ^{1}H NMR ($CDCl_3$) δ 7.20–7.90 (m, 8 H), 4.17 (s, 1 H), 2.16 (m, 1 H), 1.73 (m, 1 H), 1.71 (s, 1 H), 1.52 (m, 2 H), 1.25 (m, 1 H), 1.13 (d, *J* 6.9, 3 H), 1.08 (m, 2 H); ^{1}H NMR (DMSO-d_6) δ 7.20–7.90 (m, 8 H), 4.61 (s, 1 H), 4.10 (s, 1 H), 1.93 (m, 1 H), 1.56 (m, 1 H), 1.41 (m, 2 H), 1.04 (d, *J* 6.8, 3 H), 0.97 (m, 2 H), 0.79 (m, 1 H).

(*R*,*S*)-1-Chloro-1-(fluoren-9-yl)-2-methylcyclopentane (1-Cl)

A solution of **1-OH** (1 g) in dichloromethane (50 ml) containing anhydrous calcium chloride and lithium chloride was cooled to 0 °C. Dry hydrogen chloride was bubbled through the solution for 5 h. After filtration, the solvent was removed. Recrystallization several times from a mixture of ethanol and pentane gave pure material: mp 79–81 °C; ^{1}H NMR ($CDCl_3$) δ 7.26–8.22 (m, 8 H), 4.55 (s, 1 H), 2.43 (m, 1 H), 1.79 (m, 1 H), 1.68 (m, 2 H), 1.49 (m, 1 H), 1.41 (d, *J* 6.5, 3 H), 1.32 (m, 1 H), 1.09 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 145.48, 142.59, 142.09, 141.23, 127.93, 127.60, 127.19, 126.75, 126.73, 126.29, 119.81, 119.44, 89.42, 54.99, 43.29, 36.49, 31.33, 19.35, 14.93.

(*R*,*S*)-1-(Fluoren-9-yl)-2-methylcyclopentyl 3,5-dinitrobenzoate (1-DNB)

A solution of **1-OH** (0.34 g) in dry diethyl ether (20 ml) was cooled to −20 °C, and butyllithium (0.8 ml of 1.6 M solution in hexane) was added under nitrogen by means of a syringe. The mixture was stirred at this temperature for 30 min. Then 3,5-dinitrobenzoyl chloride (0.30 g), dissolved in dry diethyl ether (10 ml), was added at −20 °C. The mixture was stirred for another 1 h and was then poured into ice and water, followed by extraction three times with diethyl ether. The combined diethyl ether fractions were washed with saturated aqueous potassium carbonate solution, followed by washing with water and brine, and drying over sodium sulfate. After removal of solvent, the crude product was purified by flash chromatography (silica gel) with 5% ethyl acetate–pentane as eluent. Recrystallization twice from CH_2Cl_2–pentane–ethanol gave pure material: mp 149–151 °C; ^{1}H NMR ($CDCl_3$) δ 9.32 (t, *J* 2.2, 1 H), 9.27 (d, *J* 2.2, 2 H), 7.12–7.82 (m, 8 H), 5.44 (s, 1 H), 3.06 (m, 1 H), 2.52 (m, 1 H), 1.71 (m, 1 H), 1.62 (m, 1 H), 1.35 (m, 3 H), 0.62 (d, *J* 6.5, 3 H).

1-(Fluoren-9-yl)-2-methylcyclopentene (4), 1-(fluoren-9-yl)-5-methylcyclopentene (5) and 5-(fluoren-9-yl)-1-methylcyclopentene (6)

These were prepared by treatment of the alcohol **1-OH** with $ZnCl_2$–HCl in chloroform. After the reaction mixture had been stirred for 1 h at room temperature, it was extracted with pentane, followed by washing with water, brine, and drying over sodium sulfate. After removal of solvent, the residue was separated by flash chromatography (silica gel) with 1% ethyl acetate–pentane as eluent. The early fractions contained a mixture of **4** and **5** (4:1); **4**: ^{1}H NMR ($CDCl_3$) δ 7.20–7.90 (m, 8 H), 4.96 (s, 1 H), 2.45 (m, 2 H), 2.05 (m, 3 H), 1.67 (m, 4 H); **5**: ^{1}H NMR ($CDCl_3$) δ 7.20–7.90 (m, 8 H), 5.76 (m, 1 H), 4.80 (s, 1 H), 1.32–2.70 (m, 5 H), 0.51 (d, *J* 7.0, 3 H).

The later fractions contained only **6**: ^{1}H NMR ($CDCl_3$) δ 7.20–7.80 (m, 8 H), 5.54 (m, 1 H), 4.16 (d, *J* 3.5, 1 H), 3.50 (m, 1 H), 2.04 (m, 3 H), 1.99 (m, 1 H), 1.72 (m, 1 H), 1.53 (m, 1 H), 0.67 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 147.33, 144.68, 142.09, 141.41, 140.67, 127.79, 126.90, 126.74, 126.49, 125.37, 123.93, 119.57, 119.46, 51.81, 47.98, 31.31, 24.20, 15.38.

(*R*,*S*)- and (*R*,*R*)-1-Phenyl-2-methylcyclopentanol (8-OH) and (9-OH)

A solution of butyllithium in hexane (1.6 M, 8 ml) was added to a solution of bromobenzene (2 g) in dry diethyl ether (20 ml) at 0 °C under nitrogen. After addition, the reaction mixture was stirred for 30 min at 0 °C, followed by addition of a solution of 2-methylcyclopentanone (1.3 g, dissolved in 10 ml of THF). The reaction mixture was then allowed to reach room temperature. After 2 h, the reaction solution was poured into a mixture of ice and 2 M hydrochloric acid, and extracted with diethyl

ether three times. The combined diethyl ether fractions were washed with water to neutrality, followed by washing with brine and drying over sodium sulfate. After removal of solvent, the crude product was purified by flash chromatography (silica gel) with 10–15% ethyl acetate–pentane as eluent. The early fractions contained only **8-OH**: ^{1}H NMR ($CDCl_3$) δ 7.21–7.51 (m, 5 H), 2.23 (m, 1 H), 2.11 (m, 1 H), 1.97 (m, 3 H), 1.80 (m, 1 H), 1.66 (m, 1 H), 1.60 (s, 1 H), 0.86 (d, *J* 6.8, 3 H).

The later fractions contained only **9-OH**: ^{1}H NMR ($CDCl_3$) δ 7.20–7.55 (m, 5 H), 2.42 (m, 1 H), 2.22 (m, 1 H), 1.91 (m, 3 H), 1.60 (s, 1 H), 1.41 (m, 1 H), 0.87 (m, 1 H), 0.56 (d, *J* 7.1, 3 H).

(*R*,*S*)-1-Phenyl-2-methylcyclopentyl *p*-nitrobenzoate (8-PNB)

This was synthesized from **8-OH** and *p*-nitrobenzoyl chloride by the same method as described above for **1-DNB**: mp 130–133 °C; ^{1}H NMR ($CDCl_3$) δ 8.20–8.34 (m, 4 H), 7.21–7.36 (m, 5 H), 2.73 (m, 2 H), 2.06 (m, 2 H), 1.86 (m, 2 H), 1.68 (m, 1 H), 1.15 (d, *J* 6.4, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.19, 150.45, 141.99, 136.83, 130.54, 128.26, 126.91, 124.35, 123.58, 93.62, 48.80, 36.75, 32.35, 22.06, 12.89.

(*R*,*R*)-1-Phenyl-2-methylcyclopentyl *p*-nitrobenzoate (9-PNB)

This was synthesized from **9-OH** as described above: mp 109–111 °C; ^{1}H NMR ($CDCl_3$) δ 8.14–8.30 (m, 4 H), 7.23–7.37 (m, 5 H), 2.69 (m, 3 H), 2.16 (m, 1 H), 1.91 (m, 2 H), 1.47 (m, 1 H), 0.65 (d, *J* 7.1, 3 H).

1-Phenyl-2-methylcyclopentene (10)

This was prepared by stirring a mixture of **8-OH** with $ZnCl_2$–HCl in chloroform for 1 h at room temperature. The mixture was extracted with pentane, followed by washing with water, brine, and drying over sodium sulfate. Removal of solvent gave an oil. Analysis by NMR showed about 5% of 1-phenyl-5-methylcyclopentene (**11**) but no other impurity: ^{1}H NMR ($CDCl_3$) δ 7.15–7.40 (m, 5 H), 2.77 (m, 2 H), 2.53 (m, 2 H), 1.93 (m, 2 H), 1.88 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.73, 135.17, 134.76, 127.96, 126.12, 125.96, 40.10, 37.26, 21.87, 15.47.

Kinetics and product studies

The reaction solutions were prepared by mixing acetonitrile or methanol with water at room temperature, *ca.* 22 °C. The reaction vessel was a 2 ml HPLC flask, sealed with gas-tight PTFE septa, which was placed in an aluminium block in the water thermostat bath. The reactions were initiated by fast addition, by means of a syringe, of a few microlitres of the substrate dissolved in acetonitrile. The concentration of the substrate in the reaction solution was usually about 0.01–0.1 mM. At appropriate intervals, samples were analyzed using the HPLC apparatus. The rate constants for the disappearance of the substrates were calculated from plots of substrate peak area *versus* time by means of a nonlinear regression computer program. Very good pseudo-first-order behaviour was seen for all the reactions studied. The separate rate constants for the elimination and substitution reactions were calculated by combination of product composition data, obtained from the peak areas and the relative response factors determined in separate experiments, with the observed rate constants.

The pseudo-first-order rate constant for the reaction of **1-Cl** with sodium methoxide (0.1 M) in methanol was measured as above, except that samples (100 μl) of the reaction solutions were quenched by a mixture of aqueous acetic acid (20 μl, 1 M) and ethanol (500 μl) before HPLC analysis. The alkenes **4** and **5** isomerize to alkene **7** in the presence of strong base.

A control experiment showed that the alkene **6** is stable under solvolytic conditions. The stability of the alkenes **4** and **5** was checked in the following way: Solvolysis of **1-Cl** in 75 vol% acetonitrile in water gave alkenes **4** and **5** (ratio 15:85, GC analysis). After the reaction was finished, the reaction mixture was diluted with water to a final concentration of 25 vol% acetonitrile in water. After two days at 25 °C, GC analysis showed no change in the area ratio of the two alkenes **4** and **5**.

The product compositions for the acid-catalyzed reaction of **1-OH**, **8-OH** and **9-OH** were determined according to the following method: At appropriate times, samples were transferred to a 2 ml HPLC flask and quenched with a mixture of acetonitrile and aqueous sodium acetate (1 M), followed by HPLC analyses giving the mol% of each component, except **4** and **5** which eluted as one peak. Pentane was added to a part of the quenched reaction solutions. After vigorous shaking, the organic phase was transferred to a pear-shaped flask, and solvent was evaporated with a stream of nitrogen until ~10 μl were left. Aliquots of this solution were injected directly onto the GC column. The ratio of the two alkene stereoisomers **4** and **5** was determined from the peak areas. Comparison with ^{1}H NMR analysis showed that the relative response factors were the same within experimental error assuming that the NMR integrals exactly correspond to the expected number of protons. Control experiments showed that the alcohol **1-OH** and the alkenes **4**, **5**, **6** are stable under GC analyzing conditions, but **1-Cl** and **1-DNB** decompose to the alkenes. The fractions of **4** and **5** from the solvolysis of **1-Cl** and **1-DNB** were determined after at least five half-lives.

Determination of relative HPLC response factors

The relative response factors of **1-OH** and alkene **6**, **6-OH** and the mixture of alkene **4** and **5** (the relative response factors of **4** and **5** were assumed to be same), **8-OH** and **9-OH**, **8-OH** and alkene **10**, **8-OH** and **8-PNB**, **8-OH** and **9-PNB** were determined by a combination of NMR analysis and HPLC analysis. A mixture of an appropriate amount of the two materials was dissolved in chloroform-d_1 and analysed by ^{1}H NMR. The peak areas of the well-resolved signals, usually methyl signals, were integrated and used to calculate the relative ratio of the two components, assuming that the NMR integrals exactly correspond to the expected number of protons. A few microlitres of this solution were transferred to a 2 ml HPLC flask. The solvent was evaporated under a stream of nitrogen. The residue was dissolved in acetonitrile and analyzed by HPLC.

The relative response factor of **8-OH** and alkene **11** was determined as follows: Pure **8-OH** in acetonitrile was analyzed by HPLC. Then, 200 μl of this solution was transferred to a 2 ml measuring flask, after which aqueous perchloric acid solution (600 μl, 1 M) was added. After 1 h, the reaction was complete (products: **10** and **11**); aqueous sodium acetate solution (1000 μl, 1 M) was then added, the volume was adjusted to 2 ml with acetonitrile, and the sample was analyzed again. The data were used to calculate the relative response factors of **8-OH** and the corresponding alkene product **11**.

The response factors for **2-OH** and **3-OH** and for the substitution products with SCN^- were assumed to be the same as for **1-OH**.

The estimated errors are considered as maximum errors derived from maximum systematic errors and random errors. The maximum errors of the directly measured quantities were thus allowed to propagate as systematic errors into derived quantities, *e.g.* reaction rate constants.

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