Solvent-promoted E1cB/E2 reactions competing with stepwise solvolysis through homoallylic carbocations

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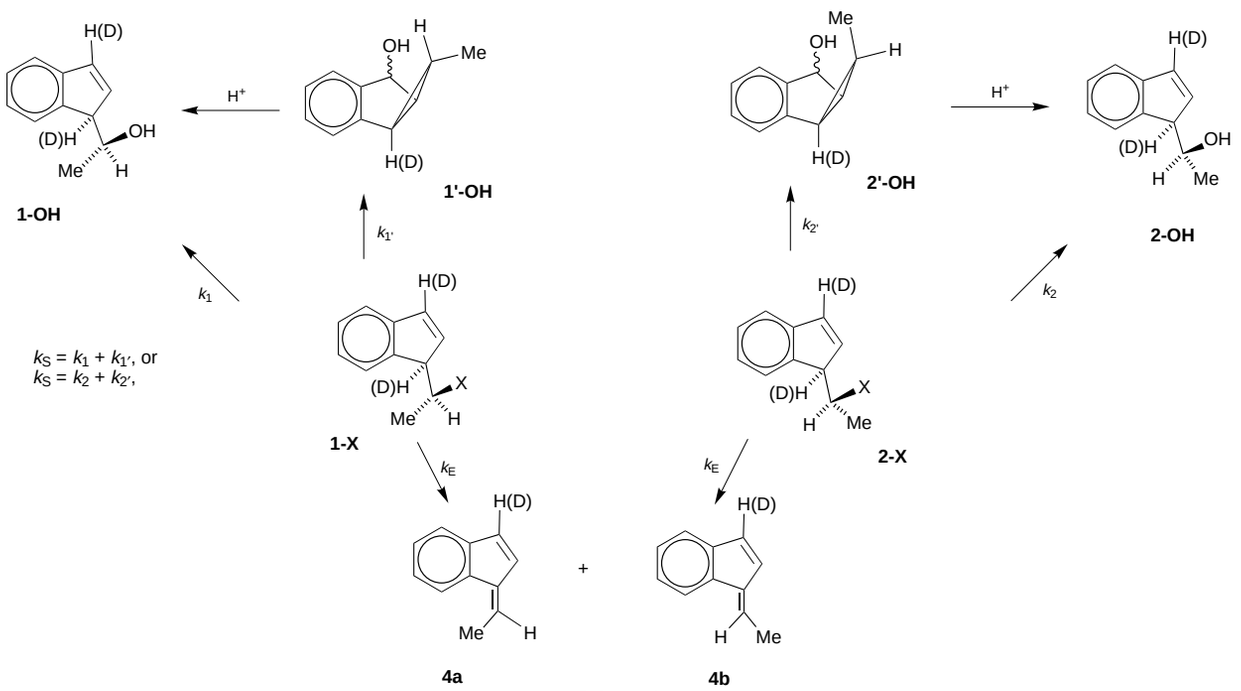
The water-promoted elimination reactions of (*R*,*S*)-1-(1-X-ethyl)indene 1-X [X = Cl, Br, I, OBs (4-bromophenylsulfonyloxy)] and the corresponding (*R*,*R*) isomers 2-X in 25 vol% acetonitrile in water exhibit non-stereospecific and stereospecific 1,2 elimination, respectively. The reactions are E1cB and E2 type reactions; the conclusion is based upon measured large kinetic deuterium isotope effects and Brønsted *β* parameters. The rate of the competing solvolytic substitution, which occurs through homoallylic carbocations, increases with the leaving group in the order Br^-, I^- and BsO^-. The spontaneous reactions in methanol are slow; the *anti* stereochemistry increases with increasing basicity of added base and is favored by negative charge of the base.

The classical view of base-promoted concerted E2 elimination reactions, *i.e.* reactions following the $A_{xh}D_HD_N$ mechanism,[1] is that a strong base is required and that the base and the leaving group are antiperiplanar to each other in the transition state.[2] However, it was recently shown that even water is able to function as an efficient base in concerted E2 reactions.[3] Evidence that the elimination is a one-step concerted reaction promoted by solvent water is provided by data showing large kinetic deuterium isotope effects. In addition, the reactions exhibit large Brønsted parameters of $\beta = 0.4 - 0.8$ for catalysis by general bases and low sensitivity to solvent polarity.[3] It was concluded from these data that high acidity of the β-hydrogen is required for the water-promoted E2 reaction, otherwise competing stepwise solvolytic elimination and substitution reactions are predominant.

In the present study we have made the β-hydrogen acidic by including an α-indenyl substituent in the ethyl halide and ethyl ester substrates (Scheme 1).[4] This increases the acidity of the β-hydrogen by 2–3 pK_a units compared to the unsubstituted fluorene system.[5] Therefore, it may be possible, at least for less efficient leaving groups, that the solvent-promoted reactions of these acidic compounds are of the irreversible E1cB type. The issue of distinguishing E1cB and E2 reactions and the E1cB–E2 borderline are discussed in this paper. The reason for the fast solvolytic substitution reactions, which compete with the elimination, is also addressed.

Results

The solvolysis of (*R*,*S*)- or (*R*,*R*)-1-(1-X-ethyl)indene **1-X** and **2-X** (X = Br, I, OBs) in 25 vol% acetonitrile in water yields the alkenes (*Z*)- and (*E*)-1-ethylideneindene (**4a** and **4b**). The substitution products (*R*,*S*)-1-(1-hydroxyethyl)indene **1-OH** and *anti*-1-methyl-1,1a,6,6a-tetrahydrocyclopropa[*a*]inden-6-ol **1′-OH** are formed from **1-X** in a 1:7 ratio, but **2-X** yields **2-OH** as the major alcohol product along with some *cis*-1-methyl-1,1a,6,6a-tetrahydrocyclopropa[*a*]inden-1-ol **2′-OH** (Scheme 1). The kinetics of the reactions were studied by a sampling HPLC procedure. The rate constants and reaction conditions are shown in Table 1. The homoallylic alcohol products **1′-OH**



Scheme 1

Table 1 Rate constants for the solvolyses of **1-X**, **2-X** and **3-OBs** in 25 vol% acetonitrile in water

Substrate[a,b]	T/°C	k_{obs}[c,d]/10^{-6} s^{-1}	k_E[e]/10^{-6} s^{-1}	k_S[e]/10^{-6} s^{-1}
1-I	55	250	50.4	200
1-Br	55	195	14.2	181
2-Br	55	75.8	50.5	25.3
1-OBs	25	605	2.2	603
2-OBs	25	118	5.0	113
3-OBs	25	1210		1210

[a] Substrate concentration 0.01–0.1 mmol dm^{-3}. [b] [$HClO_4$] = 1 mmol dm^{-3}. [c] $k_{obs} = k_E + k_S$. [d] Estimated maximum error ±5%. [e] Estimated maximum error ±10%.

Table 2 Rate constants for the reactions of **1-X**, **2-X** and **3-OBs** with bases

Substrate[a]	Base	T/°C	k_E/10^{-6} dm^3 mol^{-1} s^{-1}
25 vol% acetonitrile in water			
1-I	$NCCH_2COO^-$ [b]	55	547
1-I	$MeOCH_2COO^-$ [c]	55	1.39×10^3
1-I	AcO^- [d]	55	4.28×10^3
1-I	$(CF_3)_2CHO^-$ [e]	25	6.22×10^5
1-Br	$NCCH_2COO^-$ [b]	55	164
1-Br	$MeOCH_2COO^-$ [f]	55	514
1-Br	AcO^- [d]	55	1.20×10^3
1-Br	$(CF_3)_2CHO^-$ [e]	25	2.30×10^5
2-Br	CF_3COO^- [g]	55	39.8
2-Br	$NCCH_2COO^-$ [b]	55	509
2-Br	$MeOCH_2COO^-$ [c]	55	1.61×10^3
2-Br	AcO^- [d]	55	5.55×10^3
2-Br	$(CF_3)_2CHO^-$ [e]	25	1.21×10^6
2-OBs	$NCCH_2COO^-$ [h]	25	5.06
2-OBs	$MeOCH_2COO^-$ [i]	25	12.6
2-OBs	AcO^- [j]	25	44.2
Methanol			
1-OBs	HMTA [k,l]	25	2.49×10^3
1-OBs	DABCO [m,n]	25	5.09×10^4
1-OBs	Q [o,p]	25	3.01×10^5
2-OBs	HMTA [k,l]	25	3.30×10^3
2-OBs	DABCO [m,n]	25	1.21×10^5
2-OBs	Q [o,p]	25	8.50×10^5
3-OBs	HMTA [k,l]	25	224
3-OBs	DABCO [m,n]	25	6.38×10^3
3-OBs	Q [o,p]	25	4.26×10^4

[a] Substrate concentration 0.01–0.1 mmol dm^{-3}; all reactions were studied at constant ionic strength of 0.75 M maintained with $NaClO_4$. [b] Measured with 0.10–0.40 mol dm^{-3} $NCCH_2COO^-$. [c] Measured with 0.05–0.20 mol dm^{-3} $MeOCH_2COO^-$. [d] Measured with buffer conc. 25–100 mmol dm^{-3}, [AcO^-]:[HOAc] = 1. [e] Measured with 1–10 mmol dm^{-3} $(CF_3)_2CHO^-$, [$(CF_3)_2CHO^-$]:[$(CF_3)_2CHOH$] = 1. [f] Measured with 0.10–0.60 mol dm^{-3} $MeOCH_2COO^-$. [g] Measured with 0.25–0.75 mol dm^{-3} CF_3COO^-. [h] Measured with buffer conc. 0.10–0.50 mol dm^{-3}. [$NCCH_2COO^-$]:[$NCCH_2COOH$] = 10. [i] Measured with buffer conc. 0.10–0.50 mol dm^{-3}, [$MeOCH_2COO^-$]:[$MeOCH_2COOH$] = 4. [j] Measured with buffer conc. 0.10–0.30 mol dm^{-3}, [AcO^-]:[HOAc] = 100. [k] Hexamethylenetetramethane. [l] Measured with base conc. 0.29 mol dm^{-3}, [Base]:[$BaseH^+$] = 7.6. [m] Diazabicyclo[2,2,2]octane. [n] Measured with base conc. 10 mmol dm^{-3}, [Base]:[$BaseH^+$] = 1. [o] Quinuclidine. [p] Measured with base conc. 2 mmol dm^{-3}, [Base]:[$BaseH^+$] = 1.

and **2′-OH** are stable under the solvolytic reaction conditions but isomerize to the thermodynamically more stable alcohols **1-OH** and **2-OH**, respectively, in perchloric acid solution.

The substitution reactions show very high configuration retention, >95% retention with **1-X** and >98% with **2-X**. These results were obtained after converting **1′-OH** in the product mixture to **1-OH** and **2′-OH** to **2-OH**, respectively. No epimerization of the substrates was found during the reactions.

The solvolysis of 3-[1-(4-bromophenylsulfonyloxy)ethyl]-indene (**3-OBs**) gives exclusively alcohol products 3-(1-hydroxyethyl)indene **3-OH** and 2-hydroxy-1-ethylideneindan (Scheme 2).

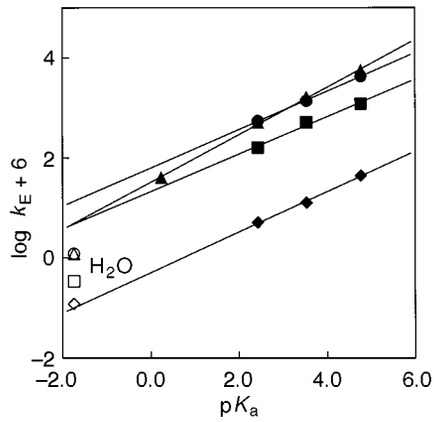


Fig. 1 Brønsted plots for the eliminations of **1-I** (●), **2-Br** (▲), **1-Br** (■) at 55 °C and **2-OBs** (◆) at 25 °C with substituted acetate anions in 25 vol% acetonitrile in water; ionic strength 0.75 M was maintained with sodium perchlorate

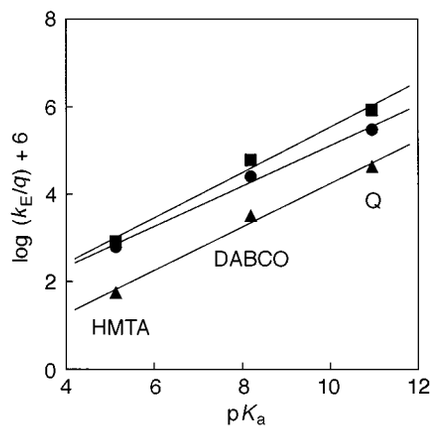
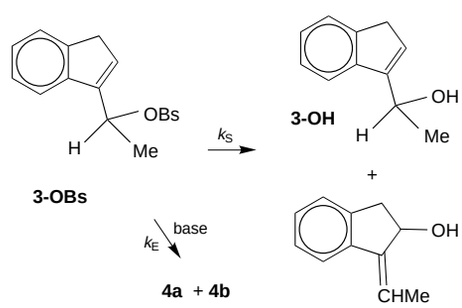


Fig. 2 Brønsted plots for the eliminations of **2-OBs** (■), **1-OBs** (●) and **3-OBs** (▲) with tertiary amines in methanol at 25 °C. The measured slopes are β = 0.52, 0.46 and 0.50, respectively. Data from Table 2.



Scheme 2

Table 2 shows the kinetic data for the reactions with added buffer bases. The fast reactions with sodium hexafluoropropan-2-oxide at 25 °C were studied by following the increase in absorbance at 312 nm for **1-X** and 308 nm for **2-X** by UV spectrophotometry. The reactions of **1-OBs**, **2-OBs** and **3-OBs** with tertiary amine buffers in methanol were studied by a sampling-quenching technique using HPLC. The alkenes **4a** and **4b** are the exclusive products for reactions of **1-OBs** and **2-OBs** under these conditions. However, **3-OBs** also produces traces of alcohol **3-OH**. No base-catalyzed rearrangement of **1-OBs** or **2-OBs** to **3-OBs** was observed with tertiary amines. Brønsted plots for the elimination reactions with substituted acetate ions in aqueous solution and with tertiary amines in methanol are shown in Figs. 1 and 2, respectively.

The corresponding deuterated compounds [1,3-$^2H_2$]-1-(1-X-ethyl)indene (**d-1-X** and **d-2-X**) react slower to give alkenes. The measured kinetic deuterium isotope effects for the solvolysis and the base-promoted reactions are collected in Table 3.

The amount of *anti* elimination for reactions of **1-X** and **2-X** with different bases, measured by GC, is shown in Table 4.

Discussion

Solvent-promoted E1cB/E2 reactions

Solvolytic elimination reactions are generally thought to occur through carbocation ion pairs and free carbocation intermediates.[6] The following experimental results show that the solvolytic elimination reactions of **1-X** and **2-X** do not occur *via* such intermediates, but are E2 and/or E1cB type reactions.

(*i*) The kinetic deuterium isotope effects on the elimination reactions are large and indicate rate-limiting hydron transfer (Table 3). The isotope effects observed are too large to be attributable to elimination from reversibly formed ion-pair intermediates since isotope effects of about three, or smaller, are expected for a mechanism involving dehydronation of a highly unstable carbocationic intermediate.[6,7] Moreover, only a low concentration of strong base, such as hydroxide or hexafluoropropan-2-oxide ion, is required to give elimination exclusively. It is unreasonable that a short-lived ion pair would show such a large selectivity.

(*ii*) Large Brønsted parameters for **1-I**, **1-Br**, **2-Br** and **2-OBs** of $\beta = 0.38$, 0.37, 0.47 and 0.40, respectively, measured with substituted acetate anions (Fig. 1), indicate that the reactions have either a one-step mechanism (E2) or an irreversible carbanion mechanism ($E1cB_I$). The catalytic constants for water as the base and the halide ion as leaving group fall below the Brønsted lines, but with the brosylate leaving group the deviation is small. Very small β values are expected for a mechanism in which a reversibly formed unstable carbocationic intermediate is dehydronated in the rate-limiting step.[6,7] Accordingly, these substantial β values exclude reactions through ion pairs, either coupled with the substitution reactions or as separate reactions. However, they are consistent with E2 and $E1cB_I$ reaction mechanisms.

(*iii*) The high stereospecificity of the spontaneous reactions of **2-Br** and **2-OBs** (95–99% *anti* elimination, Table 4) supports an E2 mechanism with an antiperiplanar position of the hydron-abstracting water molecule and the leaving group. The spontaneous elimination reactions of **1-X** show 80–85% *anti* elimination (Table 4).

(*iv*) The faster elimination with **1-I** than with **1-Br** is not consistent with an ion-pair mechanism in which the leaving group acts as the hydron-abstracting base.[6,8] These results are in accord with a significant stabilization of the transition state by the partial bond breaking to the leaving group since iodine has a greater potential for such hyperconjugative stabilization.[9d]

The elimination from **1-I** is about three times faster than the elimination from the corresponding fluorene compound 9-(1-iodoethyl)fluorene,[3b] which reflects the higher acidity (~2.5 pK_a units)[5] of the indene substrate.

Table 3 Kinetic deuterium isotope effects for the reactions of **1-X** and **2-Br** in 25 vol% acetonitrile in water

Substrate[a]	Base	T/°C	k_{obs}^{H}/k_{obs}^{D}	k_{E}^{H}/k_{E}^{D}	k_{S}^{H}/k_{S}^{D}
1-I[b]	Solvent	55	1.2 ± 0.1	5.1 ± 0.5	1.02 ± 0.10
1-I	HFIP[c]	25	6.8 ± 0.3	6.8 ± 0.3	
1-Br[b]	Solvent	55	1.07 ± 0.10	5.0 ± 0.5	1.01 ± 0.10
1-Br	HFIP[c]	25	6.5 ± 0.3	6.5 ± 0.3	
1-Br	AcO^-[d]	55		5.8 ± 0.2	
2-Br[b]	Solvent	55	2.0 ± 0.2	4.6 ± 0.5	0.94 ± 0.10
2-Br	HFIP[c]	25	6.3 ± 0.3	6.3 ± 0.3	
2-Br	AcO^-[d]	55		5.9 ± 0.2	

[a] Substrate concentration 0.01–0.1 mmol dm^{-3}. [b] $[HClO_4] = 1$ mmol dm^{-3}. [c] Measured with 1–10 mmol dm^{-3} sodium hexafluoropropan-2-oxide. [d] Measured with buffer conc. 25–100 mmol dm^{-3}, $[AcO^-]:[HOAc] = 1$.

Solvolytic substitution reactions through carbocation intermediates

Solvolytic substitution competes with the elimination (Scheme 1). The relatively large rate constants of the solvolytic substitution reactions are attributable to homoallylic participation. Solvolysis is faster with the (*R*,*R*) isomer, about seven times for the bromides and five times with the brosylates (Table 1) and the homoallylic alcohol **1′-OH** is the predominant substitution product under kinetic control, $k_1'/k_1 \sim 7$. In contrast, more **2-OH** is produced than **2′-OH**, $k_2'/k_2 < 1$. This is reasonable since faster carbocation formation is expected from the (*R*,*R*) isomer owing to generation of a more stable homoallylic carbocation having the methyl group pointing away from the indene moiety.

The homoallylic alcohols **1′-OH** and **2′-OH** are isomerized under slightly acidic conditions to give the thermodynamically more stable alcohols **1-OH** and **2-OH**, respectively, as the exclusive products. Owing to the homoallylic participation, the overall substitution reactions show very high configuration retention, >95% retention with **1-X** and >98% with **2-X**. Consistently, no epimerization of the substrates is found during the reactions. Thus, if internal return occurs, it has to involve collapse of the ion pair with retention of configuration.

The solvolysis of **1-OBs** is only two times slower than that of the allylic ester **3-OBs** (Table 1). Thus, the homoallylic participation is almost as efficient as the allylic participation in stabilizing the ionization transition state.

Because of the relatively high stability of the homoallylic carbocation, no substitution product with the acetonitrile component of the solvent is formed. This is in contrast to the corresponding fluorene system which gives a significant amount of the amide product through reaction in the pool of solvent

Table 4 Stereochemistry, expressed as the fraction of *anti* elimination, of the solvent- and base-promoted elimination reactions of **1-X** and **2-X**

	Base							
Substrate[a]	Water	HO^-	AcO^-[b]	HMTA[c]	HMTA[d]	MeO^-	DABCO[e]	Q[f]
25 vol% Acetonitrile in water at 25 °C					Methanol			
1-I	80[g]	96	95	94	85			
1-Br	85[g]	94	95[g]	83	37			
2-Br	99[g]	99		99	97			
1-Cl				29	9[h]	80[i]	14[i]	19[i]
1-OBs		86	80	41	16	84	26	
2-OBs	99	97		95	85	96	90	
1-OAc						39[j]		6[j]
2-OAc						92[j]		86[j]

[a] Substrate concentration 0.01–0.1 mmol dm^{-3}. [b] Buffer ratio $[AcO^-]:[HOAc] = 100$. [c] Hexamethylenetetramine, buffer ratio $[base]:[baseH^+] = 5.5$. [d] Hexamethylenetetramine, buffer ratio $[base]:[baseH^+] = 7.6$. [e] Diazabicyclo[2,2,2]octane. [f] Quinuclidine. [g] 55 °C. [h] The same result has been reported previously at 30 °C.[16] [i] At 30 °C.[16] [j] At 30 °C.[9c]

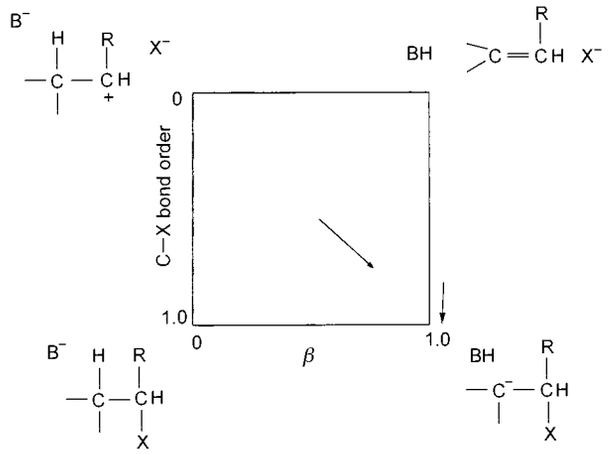


Fig. 3 Reaction coordinate–energy diagram (More O'Ferrall–Jencks diagram) for alkene-forming 1,2-elimination.[11] The horizontal and vertical axes describe the amounts of hydrogen removal and cleavage of the bond to the leaving group as measured by the Brønsted β parameter and C–X bond order, respectively. The energy contour lines are omitted. The effect of exchanging the leaving group from Br^- to BsO^- is a decrease in the energy of the carbanion, *i.e.* the lower right-hand corner of the diagram. The result for a predominantly diagonal reaction coordinate is a shift to the right giving a more carbanion-like transition state and an increase in β as indicated.

molecules which is present when the very unstable carbocation is born.[3,7,10]

Does any elimination product come from the carbocation intermediate? It is possible that traces of alkenes are formed from the ion pairs, but, as discussed above, the large elimination isotope effects reported are not consistent with a substantial fraction of alkenes formed by a carbocation route. The carbocations formed during the acidic isomerization of **1′-OH** to **1-OH** and of **2′-OH** to **2-OH** do not yield significant amounts of elimination products. Moreover, solvolysis of the 3,5-dinitrobenzoate ester of **1′-OH** in carbonate-buffered aqueous acetone at 80 °C yields predominantly **1′-OH**.[11]

Homoallylic participation has also been suggested as the course of the (unexpectedly) high stability of the fluorenylmethyl carbocation under solvolytic conditions.[3d] Thus, experimental results were recently reported indicating the intermediacy of carbocation ion pairs in solvolytic elimination and substitution reactions in aqueous solvents.[3d] Consistently, the closely related secondary substrates (*R*,*R*)- and (*R*,*S*)-9-(1-X-ethyl)fluorene (X = OBs) solvolyze to give about 90% retention of configuration with solvent water as the nucleophile.[3c] In contrast, bimolecular kinetics with mainly inversion is shown with added nucleophiles; the amount of inversion decreases with the leaving group in the following order: I > Br > OBs.[3c]

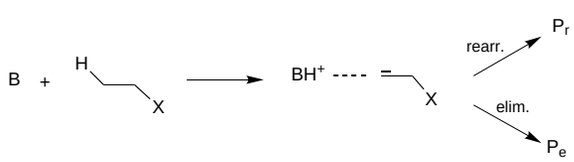
E1cB–E2 mechanistic borderline

The characteristics of the transition state of β-elimination reactions are conveniently described by More O'Ferrall–Jencks diagrams.[12] For example, let us assume that the changes in transition state caused by the exchange of leaving group in the **2-X** substrate from Br^- to BsO^- can be considered to be the effect of decreasing the energy of the carbanion intermediate in the lower right-hand corner of the diagram, since the polar sulfonyloxy group is expected to stabilize the carbanion more than the bromine group. This corresponds to a change in the transition-state position for an E2 reaction which has a diagonal transition state as shown in Fig. 3. This results in a more carbanion-like transition state with a larger β value. This is not in accord with the measured decrease in the Brønsted parameter from 0.47 to 0.40 (Fig. 1). However, an E2 transition state with a large horizontal component, corresponding to hydron transfer, is consistent with these results. Alternatively, there is a change in mechanism from E2 for **2-Br** to $E1cB_I$ for **2-OBs**, or, less likely, both reactions are of E1cB type.

Base-promoted elimination reactions of irreversible E1cB type ($E1cB_I$) are very difficult to distinguish from base-promoted E2 reactions because they are expected to show very similar characteristics.[13] However, it has been suggested that the effect of the leaving group on the rate of $E1cB_I$ reactions is only a polar one, *i.e.* an inductive effect of the leaving group on the rate-limiting ionization step. Accordingly, any positive element effect in addition to this polar effect has been suggested to be evidence for an E2 mechanism.[14] Theoretical calculations show, however, that a partial bond breaking to the putative leaving group L occurs in the transition state of hydron-transfer reactions.[15] A periplanar position between the base and L is preferred. This assistance to hydron removal by hyperconjugative interaction from the electron-withdrawing group L implies some resemblance between E2 and E1cB transition-state structures.[9]

Another approach for distinguishing the two reaction mechanisms is to estimate the lifetime of the putative intermediate. If the intermediate has no significant lifetime ($t_{\frac{1}{2}} < 10^{-13}$ s), *i.e.* there is no barrier to departure of the leaving group, a concerted reaction is enforced.

A method which has been successful in distinguishing E1cB and E2 reaction mechanisms is to study the elimination in competition with a base-catalyzed reaction. Thus, it has been possible to assign the E1cB mechanism to the base-promoted 1,2-elimination reaction of the tertiary substrate 1-(2-chloro-2-propyl)indene by demonstrating that it has an intermediate in common with the base-catalyzed 1,3-hydron transfer reaction using tertiary amines in methanol as catalysts (Scheme 3, the



Scheme 3

dashed line represents hydrogen-bonding).[9f] In the same way, a common intermediate has been demonstrated for the secondary chloride **1-Cl**.[16] The intermediate was postulated to be the carbanion hydrogen-bonded to the hydronated base. The evidence for a common intermediate was provided by the measured, unusually large kinetic deuterium isotope effects on the 1,3-hydron transfer reaction coupled with decreased isotope effects on the 1,2-elimination reaction.

Another piece of independent evidence for a common carbanion intermediate for the tertiary substrate is the fact that the total reaction rate for the amine-catalyzed reactions in methanol increases substantially when passing from a 'poor' putative leaving group to chloride, and the rearrangement rate decreases drastically when the putative leaving group is changed, *e.g.* from MeO^- to Cl^-.[9b] However, the reaction of the chloride substrate with strong base does not show any rearrangement product. The existence of a barrier for expulsion of Cl^- from the hydrogen-bonded hydronated amine-carbanion intermediate does not necessarily imply that there is a barrier for expulsion of Cl^- from the corresponding complex with methanol (which is the acid formed by the hydron-abstraction by methoxide ion). Accordingly, it is possible that the reaction has an E2 mechanism that is enforced by the disappearance of a barrier for expulsion of the chloride leaving group as shown by the dashed line in Fig. 4. Thus, we conclude that it is plausible that the reactions of the tertiary chloride and of the secondary chloride with methoxide ion, as well as with other strong bases in aqueous solution, have passed the mechanistic borderline and in fact are of enforced E2 type.

The stereochemical studies (Table 4) with **2-X** show high

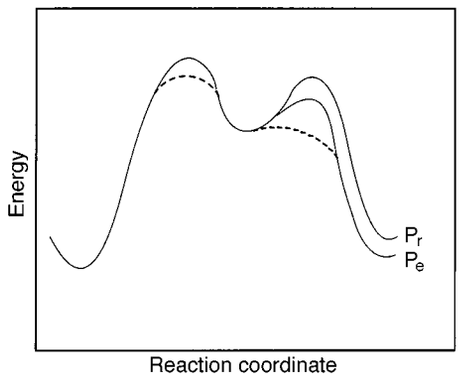


Fig. 4 Schematic diagram showing the energy barriers for the competing rearrangement and elimination reactions of **1-X** with a weak tertiary amine (——) and with methoxide ion (– – – –). The elimination reaction with MeO^- is proposed to be an enforced E2 reaction owing to the disappearance of a barrier for expulsion of the leaving group.

stereospecificity with solvent and other bases. The stereochemical results of the base-promoted reactions with the other diastereomer **1-X** are dependent on several factors. *Anti* elimination is favored by (*i*) high efficiency of the leaving group, *i.e.* a leaving group which can stabilize the E2 or E1cB transition state by hyperconjugation, (*ii*) strong base, (*iii*) a negatively charged base, *i.e.* acetate anion yields more *anti* elimination than hexamethylenetetramine (HMTA) despite similar pK_a values (4.8 and 5.1, respectively) and (*iv*) high polarity of the solvent (with HMTA as base). The base-promoted reactions of the acetates **1-OAc** and **2-OAc** have been found to be partially diastereospecific (Table 4).[9c]

The difference in thermodynamic stability of the two alkenes **4a** and **4b** is not large. The product ratio **4b**:**4a** = 3.4[9c] as measured for the methoxide-promoted elimination of **3-OAc** in methanol may be used as an estimate of the equilibrium constant. Accordingly, the difference in stability is only about 0.7 kcal mol^{-1}.

It is difficult to make a clear-cut assignment of mechanism to the elimination reactions. The mechanisms may either be of $E1cB_I$ or E2 type. However, we propose that all the observed *anti* elimination of the halides is of one-step E2 type owing to the absence of a barrier to departure of the leaving group in the putative intermediate. The antiperiplanar E2 transition state is significantly stabilized by partial bond breaking to the leaving group in the transition state. The *syn* elimination with tertiary amines in methanol is proposed to occur in a stepwise fashion *via* a hydrogen-bonded intermediate. The *syn* mode with **1-X** is favored by the absence of steric interaction of the methyl group with the adjacent phenyl hydrogen. It may also be favored by a through-space interaction between the leaving group and the hydronated base.[9c]

An OBs group is not expected to provide substantial stabilization by hyperconjugation. Despite that, the spontaneous reactions of the brosylates **1-OBs** and **2-OBs** to give elimination products are somewhat faster than those of the bromides. This should reflect the large polar effect of the 4-bromobenzenesulfonyl group and may suggest that the reactions are of E1cB type.

Brønsted β parameters for the tertiary amine promoted elimination reactions of the three brosylates are substantial as shown in Fig. 2. The brosylates react faster than the acetates **1-OAc** and **2-OAc**, *i.e.* the 1,2-elimination reactions of **1-OBs** and **2-OBs** with quinuclidine in methanol are *ca.* 18 and 23 times faster, respectively, than the corresponding reactions of the acetates, while the 1,4-elimination reaction of **3-OBs** is *ca.* 6 times faster than that of **3-OAc**. This, of course, may reflect the higher polarity of the OBs-group which more efficiently stabilizes the ionization transition states. The larger assistance of the ionization of **1-OBs** and **2-OBs** is consistent with localized charge in the transition states.[17] The charge is more efficiently stabilized by the substituent in the 1,2-elimination than in the 1,4-elimination owing to the difference in distance between the charge and the substituent.

Experimental

General procedures

NMR spectra were recorded at 25 °C with a Varian XL 300 or Unity 400 spectrometer, using frequencies of 300 and 400 MHz for ^1H and 75.4 and 100.6 MHz for ^{13}C NMR spectroscopy. Chemical shifts are indirectly referenced to TMS *via* the solvent signal ([^2H]chloroform, 7.26 and 77.0 ppm); *J* values are given in Hz. HPLC analyses were carried out with a Hewlett-Packard 1090 liquid chromatograph equipped with a diode-array detector and a thermostatted C8 (5 μm, 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 water thermostat bath. The semipreparative HPLC separations were carried out with a Hewlett-Packard 1084B HPLC apparatus using a semipreparative C8 column (7 μm, 8 × 250 mm) with methanol–water as the mobile phase. The UV spectrophotometry was performed on a Kontron Uvicon 930 spectrophotometer equipped with an automatic cell changer kept at constant temperature with water from the 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 using nitrogen as the carrier gas. A fused-silica capillary column (Rescom, SE54, 25 m, 250 μm) was used with an injection temperature of 250 °C and an oven temperature of 100 °C.

Materials

Merck silica gel 60 (240–400 mesh) was used for flash chromatography. Diethyl ether was distilled under nitrogen from sodium and benzophenone. Pyridine and dichloromethane were distilled under nitrogen from calcium hydride. Methanol and acetonitrile were of HPLC grade. Diazabicyclo[2,2,2]-octane (DABCO) was recrystallized twice from hexane. Quinuclidine was sublimed twice at reduced pressure. All other chemicals were of reagent grade and used without further purification. The synthesis of (*R*,*S*)-1-(1-hydroxyethyl)indene (**1-OH**) and (*R*,*R*)-1-(1-hydroxyethyl)indene (**2-OH**) and their deuterated analogues have been published previously.[18]

(*R*,*S*)-1-(1-Bromoethyl)indene (1-Br) and (*R*,*R*)-1-(1-bromoethyl)indene (2-Br). Phosphorus tribromide (0.77 g) was added slowly to a stirred solution of the alcohol (1 g) in benzene (10 cm^3) at 0 °C. The reaction mixture was stirred at 50 °C for 20 h and was then poured into a mixture of ice and water. The benzene layer was washed with sodium carbonate solution and dried over sodium sulfate. After removal of the solvent the residue was distilled at reduced pressure. A final purification by semipreparative HPLC gave **1-Br** accompanied by <3% alkene and **2-Br** with <1% alkene, respectively.

1-Br: $\delta_H(CDCl_3)$ 7.17–7.45 (m, 4H), 6.92 (dd, 1H), 6.64 (dd, 1H), 4.72 (m, 1H), 3.99 (m, 1H) and 1.30 (d, 3H).

2-Br: $\delta_H(CDCl_3)$ 7.20–7.70 (m, 4H), 6.91 (dd, 1H), 6.48 (dd, 1H), 4.61 (m, 1H), 3.86 (m, 1H), 1.74 (d, 3H).

(*R*,*S*)-[1,3-$^2H_2$]-1-(1-Bromoethyl)indene (d-1-Br) and (*R*,*R*)-[1,3-$^2H_2$]-1-(1-bromoethyl)indene (d-2-Br). The deuterated bromides were synthesized as described above. The deuterium contents were measured using ^1H NMR spectroscopy as >98.5 atom% ^2H in the 1- and 3-positions of the indene moiety.

(*R*,*S*)-1-(1-Iodoethyl)indene (1-I). Methyltriphenoxyphosphonium iodide (24 g), which was synthesized according to a published procedure,[19] was added to a solution of **1-OH** (6.7 g) in dry DMF (20 cm^3). The mixture was stirred at 50 °C for 2 h. Then the reaction mixture was poured into a separating funnel

containing ice, pentane (500 cm^3) and methanol (100 cm^3) and shaken thoroughly. The methanol portion was extracted with another two 100 cm^3 of pentane. The combined pentane layer was washed with two portions containing 50 cm^3 of methanol and 2 cm^3 of water. Further washing was accomplished with ice and 50 cm^3 sodium hydroxide (2 mol dm^{-3}), and finally washing with water to remove traces of base. After evaporation of the solvent, the residue oil was separated by semipreparative HPLC to give **1-I** containing <1% alkene: $\delta_H(CDCl_3)$ 7.17–7.40 (m, 4H), 6.91 (dd, 1H), 6.62 (dd, 1H), 4.80 (m, 1H), 3.90 (m, 1H), 1.48 (d, 3H).

(*R*,*S*)-[1,3-$^2H_2$]-1-(1-Iodomethyl)indene (d-1-I). d-1-I was synthesized as described above. The deuterium content was measured by ^1H NMR spectroscopy as >98.5 atom% ^2H in the 1- and 3-positions.

(*R*,*S*)-1-[1-(4-Bromophenylsulfonyloxy)ethyl]indene (1-OBs). 1-OBs was synthesized by stirring a mixture of **1-OH** (0.25 g), 4-bromophenylsulfonyl chloride (1.35 g), dry dichloromethane (5 cm^3), and dry pyridine (2.5 cm^3) at room temperature. The reaction was quenched after 1.5 h (about 50% reaction) by addition of 2 mol dm^{-3} hydrochloric acid. The water phase was extracted twice with dichloromethane. The combined organic phases were washed with water and brine and dried with sodium sulfate. Evaporation of the solvent and separation with flash chromatography on silica gel with 5% ethyl acetate in pentane, followed by recrystallization from ethanol–pentane, gave pure **1-OBs**: mp 43–44 °C; $\delta_H(CDCl_3)$ 7.24–7.86 (m, 7H), 7.15 (td, 1H, *J* 7.4, 1.2), 6.90 (dd, 1H, *J* 5.6, 1.9), 6.44 (dd, 1H, *J* 5.6, 1.9), 5.12 (m, 1H), 3.79 (m, 1H), 0.95 (d, 3H, *J* 6.4).

(*R*,*R*)-1-[1-(4-Bromophenylsulfonyloxy)ethyl]indene (2-OBs). 2-OBs was synthesized as described above: mp 82–83 °C; $\delta_H(CDCl_3)$ 7.24–7.70 (m, 7H), 7.12 (td, 1H, *J* 7.4, 1.4), 6.82 (dd, 1H, *J* 5.7, 2.0), 6.33 (dd, 1H, *J* 5.7, 2.0), 5.17 (dq, 1H, *J* 6.4, 4.2), 3.72 (m, 1H), 1.22 (d, 3H, *J* 6.4).

3-[1-(4-Bromophenylsulfonyloxy)ethyl]indene (3-OBs). 3-OBs was synthesized from 3-(1-hydroxyethyl)indene (**3-OH**) as described above for the 1-isomer. It gave a mixture of **3-OBs** and alkenes (1 : 1) which was used directly for kinetic investigations.

The syntheses of the alkenes (*Z*)- and (*E*)-1-ethylideneindene (**4a** and **4b**) have been described previously.[18]

Kinetic and product studies

The reaction solutions were prepared by mixing acetonitrile or methanol with water at room temperature (*ca.* 22 °C). For reaction at 55 °C, a few microliters of substrate solution dissolved in acetonitrile was added. Aliquots of this reaction mixture were transferred to several 2 cm^3 HPLC flasks, which were sealed with gas-tight PTFE septa and placed in an aluminium block in the water thermostat bath. The concentration of the substrate in the reaction solution was 0.01–0.1 mmol dm^{-3}. At appropriate intervals, samples were removed and analyzed using the HPLC apparatus. For reaction at 25 °C, a 2 cm^3 HPLC flask sealed with gas-tight PTFE septa was placed in the aluminum block of HPLC apparatus which was thermostatted by water from a thermostat bath. The reactions were initiated by fast addition of a few microliters of the substrate dissolved in acetonitrile.

The rate constants for the disappearance of the substrates were calculated from plots of substrate peak area *versus* time using a non-linear regression computer program. Very good pseudo-first-order behavior was seen for all the reactions studied. Separate rate constants for the elimination and substitution reactions were calculated by combining product composition data, obtained from the peak areas and the relative response factors with the observed rate constants.

The fast reactions of **1-X** and **2-X** with the strong base hexafluoropropan-2-oxide ion were followed for at least 10 half-lives by monitoring the increase in absorbance at 312 nm for **1-X**, and 308 nm for **2-X**, using thermostatted 3 cm^3 quartz cells as reaction vessels. After complete reaction, the reaction mixture was quenched with acetic acid (1 mol dm^{-3}). Analysis by HPLC showed that alkenes **4a** and **4b** were the exclusive products.

Elimination product composition studies

When the reaction was nearly complete ($t > 6\ t_{\frac{1}{2}}$), the reaction solution was quenched with 1 mol dm^{-3} aqueous acetic acid, and 1,1,1-trichloroethane or pentane was added. After shaking vigorously, the organic phase was transferred to a pear-shaped flask, and solvent was evaporated with a stream of nitrogen until *ca.* 10 μl remained. Aliquots of this solution were injected directly onto the GC column. The ratio of the two alkene stereoisomers was determined from the peak areas. Comparison with ^1H 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.

Determination of relative HPLC response factors

Five consecutive injections of a solution of pure **1-Br**, **1-I** or **2-I** in acetonitrile were analyzed by HPLC. A volume of 0.5 cm^3 of this solution was transferred to a 2 cm^3 measuring flask and 0.5 mol dm^{-3} aqueous sodium hydroxide solution (0.5 cm^3) was then added. After 20 min, when the substrate had reacted completely to form alkenes, aqueous acetic solution (1 mol. dm^{-3}, 0.5 cm^3) was added, the volume adjusted to 2 cm^3 with acetonitrile, and the sample was analyzed again. The data were used to calculate the relative response factors for the substrates and the corresponding alkene products.

The relative response factors for **1-OBs** or **2-OBs** and the corresponding alkenes were measured in the same fashion as described above, however DABCO in methanol was used instead of aqueous sodium hydroxide.

The relative response factors of **3-OBs** and alkenes were determined by a combination of NMR and HPLC analyses. The mixture of **3-OBs** and alkenes was dissolved in [^2H]chloroform and analyzed by ^1H NMR spectroscopy. The peak areas of the corresponding methyl signals were integrated and used to calculate the relative ratios of the components, assuming that the NMR signals correspond exactly to the expected number of protons. A few microliters of this solution were transferred to a 2 cm^3 HPLC flask and the solvent was removed under a stream of nitrogen. The residue was redissolved in acetonitrile and analyzed by HPLC.

The estimated errors are considered as maximum errors derived from maximum systematic errors and random errors.

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